-->

(https://www.aetna.com/)

Back Pain - Invasive Procedures

Clinical Policy Bulletins | Medical Clinical Policy Bulletins

Number: 0016

Table Of Contents

Policy History

Last Review
11/20/2023
Effective: 07/31/1995
Next Review: 01/11/2024

Review History

Definitions

Additional Information

Clinical Policy Bulletin Notes

Policy

Scope of Policy

This Clinical Policy Bulletin addresses invasive procedures for back pain.

I. **Medical Necessity**

Aetna considers *any* of the following injections or procedure medically necessary for the treatment of back pain; provided that *only one* invasive modality or procedure will be considered medically necessary at a time.

A. *Facet joint injections*

1. An initial facet injection (intra-articular and medial branch block) from C2-3 to L5-S1 is considered medically necessary for the *diagnosis* of facet pain in persons with severe chronic neck and back pain when the following criteria are met:

    a. Member has symptoms suggestive of facet joint syndrome (symptoms of facet joint syndrome include absence of radiculopathy, pain that is aggravated by extension, rotation or lateral bending of the spine and is not typically associated with any neurological deficits); *and*
    b. Facet mediated pain is confirmed by provocative testing on physical examination (to confirm that pain is exacerbated by extension and rotation); *and*
    c. Imaging studies suggest no other obvious cause of pain (such as fracture, tumor, infection, or significant extraspinal lesion)*; and*
    d. Pain limits daily activities; *and*
    e. Pain has lasted more than 3 months; *and*
    f. Pain has persisted despite six or more weeks of conservative treatment (including, systemic medications, and/or physical therapy); *and*
    g. Radiofrequency facet neurolysis is being considered.

2. Injection of no more than three (3) facet joint levels are considered medically necessary during the same session/procedure. These may be performed bilaterally during the same session for a total of up to six injections.
3. A second diagnostic facet injection (intraarticular and medial branch block) is considered medically necessary to confirm the validity of the clinical response to the initial facet injection when it is administered at the same level as the initial facet injection, and where the initial facet injection produced a positive response (i.e., resulted in an 80% relief of facet mediated pain for at least the expected minimum duration of the effect of the local anesthetic). If the initial injection did not produce a positive response, a second diagnostic injection is considered not medically necessary.

Additional sets of facet injections or medial branch blocks at the same levels and side are considered experimental and investigational because they have no proven value.

Aetna considers *diagnostic* facet joint injections *not* medically necessary where radiofrequency facet neurolysis is not being considered.

Diagnostic facet joint injections are considered experimental and investigational for neck and back pain with untreated radiculopathy.

Facet joint injections are considered experimental and investigational as *therapy f*or back and neck pain and for all other indications because their effectiveness for these indications has not been established. Note: Facet joint injections (intra-articular and medial branch blocks) containing corticosteroids are considered *therapeutic* injections.

Aetna considers ultrasound guidance of facet injections experimental and investigational because of insufficient evidence of its effectiveness.

B. *Trigger point injections*

Aetna considers trigger point injections of normal saline, corticosteroids and/or local anesthetics medically necessary for treating members with chronic neck or back pain or myofascial pain syndrome when *all* of the following selection criteria are met:

1. Conservative treatment such as bed rest, exercises, heating or cooling modalities, massage, and pharmacotherapies such as non-steroidal anti-inflammatory drugs (NSAIDS), muscle relaxants, non-narcotic analgesics, should have been tried and failed, *and*
2. Symptoms have persisted for more than 3 months, *and*
3. Trigger points have been identified by palpation; *and*
4. Trigger point injections are not administered in isolation, but are provided as part of a comprehensive pain

management program, including physical therapy, patient education, psychosocial support, and oral medication where appropriate.

A trigger point is defined as a specific point or area where, if stimulated by touch or pressure, a painful response will be induced. A set of trigger point injections means injections in several trigger points in one sitting.

Up to 4 sets of injections are considered medically necessary to diagnose the origin of a patient's pain and achieve a therapeutic effect; additional sets of trigger point injections are not considered medically necessary if no clinical response is achieved. It is not considered medically necessary to repeat injections for this indication more frequently than every 7 days.

Once a diagnosis is established and a therapeutic effect is achieved, it is rarely considered medically necessary to repeat trigger point injections more frequently than once every 2 months. Repeated injections extending beyond 12 months may be reviewed for continued medical necessity.

Trigger point injections are considered experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.

Aetna considers ultrasound or electromyography (EMG) guidance of trigger point injections experimental and investigational because of insufficient evidence of its effectiveness.

For acupuncture and dry needling, see CPB 0135 - Acupuncture and Dry Needling (../100_199/0135.html).

C. *Sacroiliac joint injections*

1. Aetna considers sacroiliac joint injections medically necessary to relieve pain associated with lower lumbosacral disturbances in members who meet *all* of the following

criteria:

a. Member has sacroiliac joint (SIJ) pain for greater than 3 months; *and*
b. Member has pain at or close to the posterior superior iliac spine (PSIS) with possible radiation into buttocks, posterior thigh, or groin and can point to the location of pain (Fortin Finger Test); *and*
c. Member has at least 3 of 5 physical examination maneuvers specific for SI joint pain:

    i. Compression
    ii. Posterior Pelvic Pain Provocation test - P4 (Thigh Thrust)
    iii. Patrick's test (Fabere)
    iv. Sacroiliac distraction test
    v. Gaenslen's test; *and*

d. Other causes of low back pain have been ruled out, including lumbar disc degeneration, lumbar disc herniation, lumbar spondylolisthesis, lumbar spinal stenosis, lumbar facet degeneration, and lumbar vertebral body fracture; *and*
e. Member has tried 6 weeks of adequate forms of conservative treatment with little or no response, including pharmacotherapy (e.g., NSAIDS), activity modification, and active therapy (including physical therapy where appropriate); *and*
f. The injections are not used in isolation, but are provided as part of a comprehensive pain management program, including physical therapy, education, psychosocial support, and oral medication where appropriate.

2. Up to 2 *therapeutic / diagnostic* sacroiliac injections are considered medically necessary to diagnose the member's pain and achieve a therapeutic effect. It is not considered medically necessary to repeat these *therapeutic / diagnostic* injections more frequently than once every 7 days.
3. Additional therapeutic sacroiliac injections are considered medically necessary if the member has improvement in

lower back pain numeric rating scale (NRS) of at least 70% of the pre-injection NRS score after fluoroscopic or CT controlled injection of local anesthetic with or without steroid into affected SI joint. If the member experiences less than a 70% reduction of pain for the expected duration of the anesthetic, additional sacroiliac joint injections are not considered medically necessary.

4. Once the diagnosis is established, up to four therapeutic sacroiliac injections, repeated no more frequently than once every 7 days, are considered medically necessary every 12 months.

Ultrasound guidance of sacroiliac joint injections is considered not medically necessary.

Sacroiliac joint injections are considered experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.

D. *Interlaminar epidural injections*

Aetna considers interlaminar epidural injections of corticosteroid preparations (e.g., Depo-Medrol), with or without added anesthetic agents, medically necessary for the following:

1. In the outpatient setting for management of members with radiculopathy or sciatica when *all* of the following are met:

    a. Pain is radicular in nature (radicular signs may include, but are not limited to, a positive straight leg raise or a dermatomal pattern of sensory loss). Note: In low back pain, radicular means pain and/or numbness that radiates below the knee; in neck pain, it is pain, numbness or weakness in the shoulder, arm, wrist, or hand; *and*
    b. Intraspinal tumor or other space-occupying lesion, or non-spinal origin for pain, has been ruled out as the cause of pain:

Where indicated for evaluating lumbar, cervical or thoracic pain, advanced diagnostic imaging should be performed within 24 months prior to initiating intralaminar epidural injections; *and*

c. Member has failed to improve after 4 or more weeks of conservative treatments (e.g., rest, systemic analgesics, physical therapy); *and*
d. Interlaminar epidural injections are provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications, where appropriate.

2. Additional interlaminar epidural injections, if the initial injection resulted in *at least two* of the following for at least two weeks:

a. A 50 % or greater relief in pain; *and*
b. Increase in the level of function/physical activity (e.g., return to work); *and*
c. Reduction in the use of pain medication and/or additional medical services such as physical therapy/chiropractic care; *and*
d. The interlaminar epidural injections are provided as part of a comprehensive pain management program, which includes physical therapy, patient education, psychosocial support, and oral medications.

Additional epidural injections are not considered medically necessary if these criteria are not met.

3. No more than one interlaminar epidural injection is considered medically necessary per session:

a. More than one interlaminar epidural injection in a single region per session is considered not medically necessary.
b. Interlaminar epidural injection of more than one region per session is considered not medically necessary.

Repeat epidural injections more frequently than every two weeks are not considered medically necessary.

4. A total of up to 3 interlaminar epidural injections per region, per episode of pain are considered medically necessary in 6 months, and up to four interlaminar epidural steroid injections per region (ie, cervical, thoracic, lumbar) per rolling 12-month period are considered medically necessary, only upon return of pain and/or deterioration in function and only when responsiveness to prior injections has occurred (ie, the individual should have at least a 50% reduction in pain and/or symptoms for two weeks).

   Additional interlaminar epidural injections per region per rolling 12-month period are considered not medically necessary and experimental and investigational because they have no proven value.

Aetna considers ultrasound guidance of epidural injections experimental and investigational because of insufficient evidence of its effectiveness.

Interlaminar epidural injections of corticosteroid preparations, with or without added anesthetic agents, are considered experimental and investigational for all other indications (e.g., non-specific low back pain [LBP] and failed back syndrome) because their effectiveness for indications other than the ones listed above has not been established.

For transforaminal epidural injections, see CPB 0722 - Transforaminal Epidural Injections (../700_799/0722.html).

E. *Non-pulsed radiofrequency facet denervation*

Aetna considers non-pulsed radiofrequency facet denervation (also known as facet neurotomy, facet rhizotomy, or articular rhizolysis) medically necessary for treatment of members with intractable cervical or back pain with or without sciatica in the outpatient setting when *all* of the following are met:

1. Member has experienced severe pain limiting activities of daily living for at least 6 months; *and*
2. Member has had no prior spinal fusion surgery at the level to be treated; *and*
3. Neuroradiologic studies are negative or fail to confirm disc herniation; *and*
4. Member has no significant narrowing of the vertebral canal or spinal instability requiring surgery; *and*
5. Member has tried and failed six or more weeks of conservative treatments such as bed rest, back supports, physiotherapy, correction of postural abnormality, as well as pharmacotherapies (e.g., anti-inflammatory agents, analgesics, and muscle relaxants); *and*
6. The member has two positive diagnostic facet joint injections (intraarticular or medial branch blocks) at the level to be treated, as evidenced by at least 80% relief of facet mediated pain for at least the expected minimum duration of the effect of the local anesthetic used.

When performing radiofrequency joint denervations/ablations, it may be necessary to perform the procedure at the same level(s) bilaterally; however, radiofrequency ablation of no more than three levels are considered medically necessary during the same session/procedure.

Provided that greater than 50% pain relief is obtained for at least twelve weeks, further facet denervation procedures should be at intervals of at least six months per level per side, at a maximum of twice per rolling calendar year. Only 1 treatment procedure per level per side is considered medically necessary in a 6-month period.

Non-pulsed radiofrequency facet denervation is considered experimental and investigational for all other indications because its effectiveness for indications other than the ones listed above has not been established.

See also CPB 0735 - Pulsed Radiofrequency (../700_799/0735.html).

F. *Spinal Fixation*

Aetna considers pedicle screws medically necessary for posterior spinal fusion (see CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html)).

Aetna considers the use of interspinous or interlaminar distraction or stabilization devices with or without lumbar laminectomy and/or fusion experimental/investigational.

Aetna considers CoFix for interlaminar/interspinous stabilization experimental and investigational.

G. *Intervertebral body fusion devices*

Aetna considers intervertebral body fusion devices (synthetic spine cages/spacers) (see Appendix) medically necessary for the following:

1. Use with allograft or autogenous bone graft in members who meet criteria for lumbar spinal fusion as outlined in CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html) and for thoracic fusion;
2. Synthetic spine cages/spacers for cervical fusion for members who meet criteria in CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html) with *any* the following indications for use of a synthetic cervical cage/spacer:

    a. Cervical corpectomy (removal of half or more of vertebral body, not mere removal of osteophytes and minor decompression) in the treatment of *one* of the following:

        i. For tumors involving one or more vertebrae, *or*
        ii. Greater than 50% compression fracture of vertebrae, *or*
        iii. Retropulsed bone fragments, *or*

iv. Symptomatic central canal stenosis caused by vertebral body pathology (such as due to fracture, tumor or congenital or acquired deformity of the vertebral body).

b. Cervical fusion for pseudarthrosis in persons with prior fusion; *or*

c. For adjacent level disease that has developed in persons with a prior cervical fusion involving a plate, in order to avoid dissection for plate removal when a stand-alone cage/spacer is being used.

Spine cages are otherwise not considered medically necessary for cervical fusion because they have not been proven more effective than bone graft for this indication.

Spine cages are considered experimental and investigational for indications other than fusion because their effectiveness for indications other than those listed above has not been established.

3. Expandable cages are considered medically necessary for members who meet criteria for fusion in CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html)and who meet *either* of the following criteria:

a. At L2-S1; *or*

b. For members with osseous defects at the fusion site (i.e., voids or gaps in bone due to trauma, surgical resection, or congenital defects).

Expandable cages are considered experimental and investigational for all other indications.

H. *Percutaneous polymethylmethacrylate vertebroplasty (PPV), kyphoplasty, or Spinejack System*

Aetna considers percutaneous polymethylmethacrylate vertebroplasty (PPV), kyphoplasty, or SpineJack System medically necessary for members with persistent, debilitating

pain in the thoracic or lumbar vertebral bodies resulting from *any* of the following:

1. Multiple myeloma; *or*
2. Painful and/or aggressive hemangiomas; *or*
3. Painful vertebral eosinophilic granuloma; *or*
4. Painful, debilitating osteoporotic acute or subacute collapse/compression fractures (proven not to be chronic on recent imaging); *or*
5. Primary malignant neoplasm of bone or bone marrow; *or*
6. Secondary osteolytic metastasis, excluding sacrum and coccyx, but including cervical; *or*
7. Steroid-induced fractures.

And only for painful, debilitating osteoporotic acute or subacute collapse/compression fractures or steroid-induced fractures, when *all* of the following criteria have been met (no conservative treatment is required for the other diagnoses):

1. The pain is localized to the level of the pathology being treated; *and*
2. Other causes of pain such as spinal stenosis or herniated intervertebral disk have been ruled out by computed tomography or magnetic resonance imaging; *and*
3. Severe debilitating pain or loss of mobility that cannot be relieved by a minimum of 6 weeks of optimal non-invasive therapy that includes physical therapy, bracing and/or oral medications; *and*
4. The affected vertebra has at least 25 % (1/4) height loss/compression, but not been extensively destroyed and is at least 1/3 of its original height with intact posterior cortex; *and*
5. Maximum of 3 vertebral fractures per procedure; *and*
6. There needs to be documentation for continuum of care for an evaluation of bone mineral density and osteoporosis education for subsequent treatment as indicated and instructed to take part in an osteoporosis prevention/treatment program.

All other indications for these procedures are considered experimental and investigational.

I. *Lateral (including extreme [XLIF], extra and direct lateral [DLIF]) interbody fusion*

Aetna considers lateral (including extreme [XLIF], extra and direct lateral [DLIF]) interbody fusion an acceptable method of performing a medically necessary anterior interbody fusion. See CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html).

J. *Coccygectomy*

Aetna considers coccygectomy medically necessary for individuals with coccygodynia who have tried and failed to respond to 6 months of conservative management.

K. *Vertebral body replacement spacers*

Aetna considers vertebral body replacement spacers (e.g., AVS AL PEEK Spacer) medically necessary for vertebral body replacement used in spine surgery for persons with a collapsed, damaged or unstable vertebral body resected or excised during total and partial vertebrectomy procedures due to tumor or trauma (vertebral body replacement should not be confused with Interspinous distraction devices (spacers) (e.g., X-Stop)).

L. *Minimally invasive transforaminal lumbar interbody fusion with direct visualization*

Aetna considers minimally invasive transforaminal lumbar interbody fusion with *direct visualization* medically necessary when criteria are met in CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html).

M. *Cementoplasty*

Aetna considers cementoplasty medically necessary for individuals with bone pain from pelvic bone metastases with reduced mobility and have failed conventional pain treatments (e.g., acetaminophen, non-steroidal anti-inflammatory drugs, and opioids). For "cementoplasty" for vertebral indications, see section on vertebroplasty.

N. *Sacroiliac joint fusion*

Aetna considers minimally invasive arthrodesis of the sacroiliac joint (e.g., iFuse) medically necessary for sacroiliac joint syndrome interfering with activities of daily living when *all* of the following criteria are met:

1. Adults 18 years of age or older with sacroiliac joint (SIJ) pain for greater than 6 months (or greater than 18 months for pregnancy induced pelvic girdle pain): *and*
2. Diagnosis of the SI joint as the primary pain generator based on *all* of the following:

    a. Member has pain at or close to the posterior superior iliac spine (PSIS) with possible radiation into buttocks, posterior thigh, or groin and can point to the location of pain (Fortin Finger Test); *and*
    b. Member has *at least 3 of 5* physical examination maneuvers specific for SI joint pain:

        i. Compression
        ii. Posterior Pelvic Pain Provocation test - P4 (Thigh Thrust)
        iii. Patrick's test (Fabere)
        iv. Sacroiliac distraction test
        v. Gaenslen's test; *and*

    c. Other causes of low back pain have been ruled out, including lumbar disc degeneration, lumbar disc herniation, lumbar spondylolisthesis, lumbar spinal stenosis, lumbar facet degeneration, and lumbar vertebral body fracture;

i. Clinician has documented that other neighboring motion segments have been evaluated and ruled out as potential pain generators, including diagnostic testing with facet/medial branch blocks and or interlaminar epidural injections, as appropriate based on the member's presentation; *and*

ii. Member has had recent (within 6 months) diagnostic imaging studies that include *all* of the following:

a. Plain X-rays and/or cross sectional imaging (CT or MRI) that excludes the presence of destructive lesions (e.g. tumor, infection), acute fracture or inflammatory arthropathy that would not be properly addressed by SIJ fusion; *and*

b. Plain X-rays of the pelvis including the ipsilateral hip to evaluate potential concomitant hip pathology; *and*

c. Cross-sectional imaging (e.g. CT or MRI) of the lumbar spine to evaluate potential concomitant neural compression or other degenerative conditions; *and*

d. Sacroiliac pathology is not caused by autoimmune disease (e.g. ankylosing spondylitis) and/or neoplasia (e.g. benign or malignant tumor) and/or crystal arthropathy; *and*

e. Member has improvement in lower back pain numeric rating scale (NRS) of at least 70% of the pre injection NRS score after two separate fluoroscopic or CT controlled injection of local anesthetic into affected SI joint within the past year. These injections must have been isolated to only the SI joint, so if they were combined with other injections at the same time (e.g., hip, trochanteric bursa, or lumbar spine) they could not be used to meet this criterion; *and*

3. Baseline lower back pain score of at least 5 on 0-10 point NRS; *and*
4. Member should have tried 6 months of adequate forms of conservative treatment with little or no response, including pharmacotherapy (e.g., NSAIDS), activity modification, and

at least three months of formal in-person physical therapy in the past year; *and*

5. Radiologic evidence of SI joint degeneration on imaging; *and*
6. Member should be nicotine-free (including smoking, use of tobacco products, and nicotine replacement therapy) for at least 6 weeks prior to surgery. For persons with recent nicotine use, documentation of nicotine cessation should include a lab report (not surgeon summary) showing blood or urinary nicotine level of less than or equal to 10 ng/ml drawn within 6 weeks prior to surgery.

Open sacroiliac joint fusion is considered medically necessary for sacroiliac joint infection, tumor involving the sacrum, and sacroiliac pain due to severe traumatic injury where a trial of an external fixator is successful in providing pain relief.

Sacroiliac joint fusions are considered experimental and investigational for all other indications because their effectiveness for indications other than the ones listed above has not been established.

O. *Intramuscular or intravenous injection of ketorolac tromethamine (Toradol)*

Aetna considers intramuscular or intravenous injection of ketorolac tromethamine (Toradol) medically necessary for the short-term (up to 5 days) treatment of adults with acute back pain and/or neck pain.

P. *The Spinal System-X (Corus)*

The Spinal System-X (corus) is a supply and not an implant, and therefore is covered as part of the global surgical fee and not separately reimbursable.

For intercostal nerve blocks, see CPB 0863 - Nerve Blocks (../800_899/0863.html).

II. Experimental and Investigational

The following are considered experimental and investigational because of insufficient evidence of their effectiveness for these indications:

- AccuraScope procedure;
- AnchorKnot Tissue Approximation Kit (Anchor Orthopedics) for lumbar discectomy;
- Annulus repair devices (Xclose Tissue Repair System, Barricaid, Disc Annular Repair Technology (DART) System);
- BacFast HD for isolated facet fusion;
- Biomet Aspen fusion system (an interlaminar fixation device) (see Appendix);
- Chemical ablation (including but not limited to alcohol, phenol, or sodium morrhuate) of facet joints;
- Chymopapain chemonucleolysis, for all indications, including the following (not an all-inclusive list):
    - Acute LBP alone
    - Cauda equina syndrome
    - For herniated discs
    - Multiple back operations (failed back surgery syndrome)
    - Neurologic disease (e.g., multiple sclerosis)
    - Pregnancy
    - Profound or rapidly progressive neurologic deficit
    - Sciatica due to a herniated disc
    - Sequestered disc fragment
    - Severe spinal stenosis
    - Severe spondylolisthesis
    - Spinal cord tumor
    - Spinal instability
    - When performed with chondroitinase ABC or agents other than chymopapain;
- Coccygeal ganglion (ganglion impar) block for coccydynia, pelvic pain, and all other indications;
- Cooled radiofrequency ablation (e.g., Coolief) for facet denervation;

- Cryoablation (cryoanesthesia, cryodenervation, cryoneurolysis, or cryosurgery) for the treatment of lumbar facet joint pain;
- Deuk Laser Disc Repair;
- Devices for annular repair (e.g., Inclose Surgical Mesh System);
- Direct visual rhizotomy (extradural transection or avulsion of other spinal nerve) for the treatment of chronic low back pain;
- DiscoGel (intradiscal alcohol injection) for the treatment of back and neck pain;
- Discseel procedure (regenerative spine procedure) for the treatment of back pain;
- Dynamic (intervertebral) stabilization (e.g., BioFlex, CD Horizon Agile Dynamic Stabilization Device, DSS Dynamic Soft Stabilization System, Dynabolt Dynamic Stabilization System, Dynesys Spinal System, Graf ligamentoplasty/Graf artificial ligament, Isobar Spinal System, NFix, Satellite Spinal System, Stabilimax NZ Dynamic Spine Stabilization System, and the Zodiak DynaMo System);
- Endoscopic disc decompression, ablation, or annular modulation using the DiscFX System;
- Endoscopic laser foraminoplasty, endoscopic foraminotomy, laminotomy, and rhizotomy (endoscopic radiofrequency ablation);
- Endoscopic transforaminal diskectomy;
- Epidural fat grafting during lumbar decompression laminectomy/discectomy;
- Epidural injections of lytic agents (e.g., hyaluronidase, hypertonic saline) or mechanical lysis in the treatment of adhesive arachnoiditis, epidural fibrosis, failed back syndrome, or other indications;
- Epidural steroid injections for the treatment of non-radicular low back pain;
- Epiduroscopy (also known as epidural myeloscopy, epidural spinal endoscopy, myeloscopy, and spinal endoscopy) for the diagnosis and treatment of intractable LBP or other indications;
- Facet chemodenervation/chemical facet neurolysis;
- Facet joint allograft implants (NuFix facet fusion, TruFuse facet fusion)
- Facet joint implantation (Total Posterior-element System (TOPS) (Premia Spine), Total Facet Arthroplasty System (TFAS) (Archus

Orthopedics), ACADIA Facet Replacement System (Facet Solutions/Globus Medical);

- Far lateral microendoscopic diskectomy (FLMED) for extra-foraminal lumbar disc herniations or other indications;
- Hardware injections/blocks;
- Injection of steroid into the ilio-lumbar ligament for the treatment of low back pain (LBP);
- Interlaminar lumbar instrumented fusion (ILIF);
- Interspinous and interlaminar distraction devices (see Appendix);
- Interspinous fixation devices (Benefix Interspinous Fixation System, CD HORIZON SPIRE Plate, PrimaLOK SP, SP-Fix Spinous Process Fixation Plate, and Stabilink interspinous fixation device) for spinal stenosis or other indications (see Appendix);
- Intracept System (intra-osseous basivertebral nerve ablation) for the treatment of low back pain, and neck pain;
- Intradiscal injections of notochordal cell-derived matrix for the treatment of intervertebral disc disease;
- Intradiscal injection of platelet-rich plasma;
- Intradiscal, paravertebral, or epidural oxygen or ozone injections;
- Intradiscal steroid injections;
- Intramuscular steroid injection for the treatment of back pain, neck pain
- Intravenous administration of corticosteroids, lidocaine, magnesium, or vitamin B12 (cyanocobalamin) as a treatment for back pain and neck pain;
- ION procedure (Ion Facet Screw System);
- Khan kinetic treatment (KKT);
- Laser facet denervation;
- Least invasive lumbar decompression interbody fusion (LINDIF);
- LinQ sacroiliac joint stabilization system for the treatment of chronic lower back pain;
- Magnetic resonance imaging-guided focused ultrasound (MRgFUS) for the treatment of lumbar facet joint pain;
- Microendoscopic discectomy (MED; same as lumbar endoscopic discectomy utilizing microscope) procedure for

decompression of lumbar spine stenosis, lumbar disc herniation, or other indications;

- Microsurgical anterior foraminotomy for cervical spondylotic myelopathy or other indications;
- Minimally invasive/endoscopic cervical laminoforaminotomy for cervical radiculopathy/lateral and foraminal cervical disc herniations or other indications;
- Minimally invasive lumbar decompression (MILD) procedure (percutaneous laminotomy/laminectomy (interlaminar approach) for decompression of neural elements under indirect image guidance) for lumbar canal stenosis or other indications;
- Minimally invasive thoracic discectomy for the treatment of back pain;
- Minimally invasive *endoscopic* transforaminal lumbar interbody fusion (endoscopic MITLIF; same as endoscopic MAST fusion) for lumbar disc degeneration and instability or other indications;
- OptiMesh grafting system;
- Percutaneous cervical and lumbar diskectomy;
- Percutaneous endoscopic diskectomy with or without laser (PELD) (also known as arthroscopic microdiskectomy or Yeung Endoscopic Spinal Surgery System [Y.E.S.S.]);
- Percutaneous lumbar discectomy (manual or automated) for treatment of degenerative disc disease;
- Piriformis muscle resection and other surgery for piriformis syndrome;
- Posterior intrafacet implants (e.g., DTRAX Cervical Cage) for posterior cervical fusion;
- Psoas compartment block for lumbar radiculopathy or myositis ossification;
- Racz procedure (epidural adhesiolysis with the Racz catheter) for the treatment of members with adhesive arachnoiditis, epidural adhesions, failed back syndrome from multiple previous surgeries for herniated lumbar disk, or other indications;
- Radiofrequency denervation for sacroiliac joint pain;
- Radiofrequency lesioning of dorsal root ganglia for back pain;

- Radiofrequency lesioning of terminal (peripheral) nerve endings for back pain;
- Radiofrequency/pulsed radiofrequency ablation of trigger point pain;
- Sacroplasty for osteoporotic sacral insufficiency fractures and other indications;
- Tendon and/or tendon sheath injections for the spine;
- Tendon sheath injections for the treatment of back pain;
- Therapeutic facet joint injections;
- Total Facet Arthroplasty System (TFAS) for the treatment of spinal stenosis;
- Ultrasound guidance of epidural injections;
- Ultrasound guidance of facet injections;
- Ultrasound or electromyography (EMG) guidance of trigger point injections;
- Vesselplasty (e.g., Vessel-X).

III. **Policy Limitations and Exclusions**

A. *Laser:*

Clinical studies have not established a clinically significant benefit of use of a laser over a scalpel in spinal surgery. No additional benefit will be provided for the use of a laser in spinal surgery.

B. *Microscope and endoscope:*

Use of a microscope or endoscope is considered an integral part of the spinal surgery and not separately reimbursable.

IV. **Related CMS Coverage Guidance**

This Clinical Policy Bulletin (CPB) supplements but does not replace, modify, or supersede existing Medicare Regulations or applicable National Coverage Determinations (NCDs) or Local Coverage Determinations (LCDs). The supplemental medical necessity criteria in this CPB further define those indications for services that are proven safe and effective where those indications

are not fully established in applicable NCDs and LCDs. These supplemental medical necessity criteria are based upon evidence-based guidelines and clinical studies in the peer-reviewed published medical literature. The background section of this CPB includes an explanation of the rationale that supports adoption of the medical necessity criteria and a summary of evidence that was considered during the development of the CPB; the reference section includes a list of the sources of such evidence. While there is a possible risk of reduced or delayed care with any coverage criteria, Aetna believes that the benefits of these criteria – ensuring patients receive services that are appropriate, safe, and effective – substantially outweigh any clinical harms.

Code of Federal Regulations (CFR): 42 CFR 417; 42 CFR 422; 42 CFR 423.

Internet-Only Manual (IOM) Citations: CMS IOM Publication 100-02, Medicare Benefit Policy Manual; CMS IOM Publication 100-03 Medicare National Coverage Determination Manual.

Medicare Coverage Determinations: Centers for Medicare & Medicaid Services (CMS), Medicare Coverage Database [Internet]. Baltimore, MD: CMS; updated periodically. Available at: Medicare Coverage Center (https://www.cms.gov/medicare/coverage/center?redirect=/center/coverage.asp). Accessed November 7, 2023.

V. Related Policies

- CPB 0135 - Acupuncture and Dry Needling (../100_199/0135.html)
- CPB 0411 - Bone and Tendon Graft Substitutes and Adjuncts (../400_499/0411.html)
- (../400_499/0411.html)CPB 0602 - Intradiscal Procedures (../600_699/0602.html)
- CPB 0722 - Transforaminal Epidural Injections (../700_799/0722.html)
- CPB 0735 - Pulsed Radiofrequency (../700_799/0735.html)

- CPB 0743 - Spinal Surgery: Laminectomy and Fusion (../700_799/0743.html)
- CPB 0863 - Nerve Blocks (../800_899/0863.html)

CPT Codes /HCPCS Codes/ICD-10 Codes

Coccygectomy:

Code	Code Description
CPT codes covered if selection criteria are met:	
27080	Coccygectomy, primary
ICD-10 codes covered if selection criteria are met:	
M53.3	Sacrococcygeal disorders, not elsewhere classified [for individuals with coccygodynia who have tried and failed to respond to 6 months of conservative management]
Facet joint injections [not covered for intradiscal and/or paravertebral oxygen/ozone injection]:	
CPT codes covered if selection criteria are met:	
64490	Injection(s), diagnostic or therapeutic agent, paravertebral facet (zygapophyseal) joint (or nerves innervating that joint) with image guidance (fluoroscopy or CT), cervical or thoracic; single level
64491	second level
64492	third and any additional level(s) level
64493	Injection(s), diagnostic or therapeutic agent, paravertebral facet (zygapophyseal) joint (or nerves innervating that joint) with image guidance (fluoroscopy or CT), lumbar or sacral; single level
64494	second level
64495	third and any additional level(s) level

Code	Code Description
CPT codes not covered for indications listed in the CPB:	
0213T	Injection(s), diagnostic or therapeutic agent, paravertebral facet (zygapophyseal) joint (or nerves innervating that joint) with ultrasound guidance, cervical or thoracic; single level
+ 0214T	second level
+ 0215T	third and any additional level(s)
0216T	Injection(s), diagnostic or therapeutic agent, paravertebral facet (zygapophyseal) joint (or nerves innervating that joint) with ultrasound guidance, lumbar or sacral; single level
+ 0217T	second level
+ 0218T	third and any additional level(s)
Other CPT codes related to the CPB:	
72275	Epidurography, radiological supervision and interpretation
76942	Ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation
77002	Fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, localization device)
77021	Magnetic resonance guidance for needle placement (eg, for biopsy, needle aspiration, injection, or placement of localization device) radiological supervision and interpretation
Other HCPCS codes related to the CPB:	
J0702	Injection, betamethasone acetate 3 mg and betamethasone sodium phosphate 3 mg
J1020	Injection, methylprednisolone acetate, 20 mg
J1030	Injection, methylprednisolone acetate, 40 mg
J1040	Injection, methylprednisolone acetate, 80 mg
J1094	Injection, dexamethasone acetate, 1 mg
J1100	Injection, dexamethasone sodium phosphate, 1mg
J1700	Injection, hydrocortisone acetate, up to 25 mg
J1710	Injection, hydrocortisone sodium phosphate, up to 50 mg
J1720	Injection, hydrocortisone sodium succinate, up to 100 mg

Code	Code Description
J2650	Injection, prednisolone acetate, up to 1 ml
J2920	Injection, methylprednisolone sodium succinate, up to 40 mg
J2930	Injection, methylprednisolone sodium succinate, up to 125 mg
J3300	Injection, triamcinolone acetonide, preservative free, 1 mg
J3301	Injection, triamcinolone acetonide, not otherwise specified, 10 mg
J3302	Injection, triamcinolone diacetate, per 5mg
J3303	Injection, triamcinolone hexacetonide, per 5mg
Q9951, Q9958 - Q9967	High and low osmolar contrast material
ICD-10 codes covered if selection criteria are met:	
M53.0 - M53.1	Cervicocranial - cervicobrachial syndrome
M53.81 - M53.83	Other specified dorsopathies [cervical region]
M54.2	Cervicalgia
M54.6	Pain in thoracic spine
M54.30 - M54.59	Sciatica and lumbago
M54.9	Dorsalgia, unspecified [backache]
ICD-10 codes not covered for indications listed in the CPB:	
C41.2	Malignant neoplasm of vertebral column
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C79.51	Secondary malignant neoplasm of bone [vertebral column]
D16.6	Benign neoplasm of vertebral column
D16.8	Benign neoplasm of pelvic bones, sacrum and coccyx
D48.0	Neoplasm of uncertain behavior of bone and articular cartilage [vertebral column]
D49.2	Neoplasm of unspecified behavior of bone, soft tissue, and skin [vertebral column]
M46.20 - M46.28	Osteomyelitis of vertebra

Code	Code Description
M46.30 - M46.39	Infection of intervertebral disc (pyogenic)
M80.08xA - M80.08xS	Age-related osteoporosis with current pathological fracture, vertebra(e)
M80.88xA - M80.88xS	Other osteoporosis with current pathological fracture, vertebra(e)
M84.38xA - M84.38xS	Stress fracture, other site [vertebrae]
M84.48xA - M84.48xS	Pathological fracture, other site [vertebrae]
M84.58xA - M84.58xS	Pathological fracture in neoplastic disease, other specified site [vertebrae]
M84.68xA - M84.68xS	Pathological fracture in other disease, other site [vertebrae]
S12.000A - S12.9xxS	Fracture of cervical vertebra and other parts of neck
S22.000A - S22.089S	Fracture of thoracic vertebra
S32.000A - S32.059S	Fracture of lumbar vertebra
S32.10xA - S32.19xS	Fracture of sacrum
Ganglion Nerve Block:	
CPT codes not covered for indications listed in the CPB:	
64450	Injection, anesthetic agent; other peripheral nerve or branch [coccygeal ganglion (ganglion impar) block]
ICD-10 codes not covered for indications listed in the CPB:	
M53.3	Sacrococcygeal disorders, not elsewhere classified [coccygodynia]

Code	Code Description
Trigger point Injections:	
CPT codes covered if selection criteria are met:	
20552	Injection(s); single or multiple trigger point(s), 1 or 2 muscles(s) [no repeats more than every 7 days, up to four sets to diagnose and achieve therapeutic effect, no additional sets if no clinical response, once diagnosed and therapeutic effect achieved, no repeats more than once every two months and beyond 12 months requires clinical review]
20553	single or multiple trigger point(s), 3 or more muscles(s) [no repeats more than every 7 days, up to four sets to diagnose and achieve therapeutic effect, no additional sets if no clinical response, once diagnosed and therapeutic effect achieved, no repeats more than once every two months and beyond 12 months requires clinical review]
CPT codes not covered for indications listed in the CPB:	
76942	Ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation
95873	Electrical stimulation for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)
95874	Needle electromyography for guidance in conjunction with chemodenervation (List separately in addition to code for primary procedure)
Other CPT codes related to the CPB:	
77002	Fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, localization device)
77021	Magnetic resonance guidance for needle placement (eg, for biopsy, needle aspiration, injection, or placement of localization device) radiological supervision and interpretation
97001 - 97139	Physical medicine and rehabilitation modalities and therapeutic procedures
Other HCPCS codes related to the CPB:	
E0200 - E0239	Heat/cold application
S9117	Back school, per visit

Code	Code Description
ICD-10 codes covered if selection criteria are met:	
M54.50 - M54.59	Low back pain
M79.10 - M79.18	Myalgia
Sacroiliac joint injections:	
CPT codes covered if selection criteria are met:	
27096	Injection procedure for sacroiliac joint, arthrography and/or anesthetic/steroid [up to two injections to diagnose and achieve therapeutic effect, no repeats more than once every 7 days, no additional injections more once every two months or beyond 12 months]
64451	Injection(s), anesthetic agent(s) and/or steroid; nerves innervating the sacroiliac joint, with image guidance (ie, fluoroscopy or computed tomography)
CPT codes not covered for indications listed in the CPB:	
76942	Ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation
Other CPT codes related to the CPB:	
77003	Fluoroscopic guidance and localization of needle or catheter tip for spine or paraspinous diagnostic or therapeutic injection procedures (epidural, subarachnoid or sacroilliac joint), including neurolytic agent destruction
HCPCS codes covered if selection criteria are met:	
G0260	Injection procedure for sacroiliac joint; provision of anesthetic, steroid and/or other therapeutic agent, with or without arthrography
Other HCPCS codes related to the CPB:	
G0259	Injection procedure for sacroiliac joint; arthrography
ICD-10 codes covered if selection criteria are met:	
M54.30 - M54.59	Sciatica and lumbago [more than 3 months duration and part of a comprehensive pain management program, including physical therapy, patient education, psychosocial support, and oral medication where appropriate]

Code	Code Description
ICD-10 codes not covered for indications listed in the CPB:	
M43.16	Spondylolisthesis, lumbar region
M47.896	Other spondylosis, lumbar region [lumbar facet degeneration]
M48.061 - M48.062	Spinal stenosis, lumbar region
M51.26	Other intervertebral disc displacement, lumbar region
M51.36	Other intervertebral disc degeneration, lumbar region
S32.000A - S32.059S	Fracture of lumbar vertebra
Epidural injections of corticosteroid preparations:	
CPT codes covered if selection criteria are met:	
62320	Injection(s), of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, including needle or catheter placement, interlaminar epidural or subarachnoid, cervical or thoracic; without imaging guidance
62321	Injection(s), of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, including needle or catheter placement, interlaminar epidural or subarachnoid, cervical or thoracic; with imaging guidance (ie, fluoroscopy or CT)
62322	Injection(s), of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, including needle or catheter placement, interlaminar epidural or subarachnoid, lumbar or sacral (caudal); without imaging guidance
62323	Injection(s), of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, including needle or catheter placement, interlaminar epidural or subarachnoid, lumbar or sacral (caudal); with imaging guidance (ie, fluoroscopy or CT)

Code	Code Description
62324	Injection(s), including indwelling catheter placement, continuous infusion or intermittent bolus, of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, interlaminarepidural or subarachnoid, cervical or thoracic; without imaging guidance
62325	Injection(s), including indwelling catheter placement, continuous infusion or intermittent bolus, of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, interlaminar epidural or subarachnoid, cervical or thoracic; with imaging guidance (ie, fluoroscopy or CT)
62326	Injection(s), including indwelling catheter placement, continuous infusion or intermittent bolus, of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, interlaminar epidural or subarachnoid, lumbar or sacral (caudal); without imaging guidance
62327	Injection(s), including indwelling catheter placement, continuous infusion or intermittent bolus, of diagnostic or therapeutic substance(s) (eg, anesthetic, antispasmodic, opioid, steroid, other solution), not including neurolytic substances, interlaminar epidural or subarachnoid, lumbar or sacral (caudal); with imaging guidance (ie, fluoroscopy or CT)
64479	Injection(s), anesthetic agent and/or steroid, transforaminal epidural, with imaging guidance (fluoroscopy or CT); cervical or thoracic, single level
+64480	each additional level (List separately in addition to code for primary procedure)
64483	Injection(s), anesthetic agent and/or steroid, transforaminal epidural, with imaging guidance (fluoroscopy or CT); lumbar or sacral, single level
+64484	each additional level (List separately in addition to code for primary procedure)

Code	Code Description
Other CPT codes related to the CPB:	
72125 - 72133	Computed tomography, spine
72141 - 72158	Magnetic resonance (eg, proton) imaging, spinal canal and contents
72275	Epidurography, radiological supervision and interpretation
97161-97168	Physical therapy evaluations
Other HCPCS codes related to the CPB:	
J1020	Injection, methylprednisone acetate, 20 mg
J1030	Injection, methylprednisone acetate, 40 mg
J1040	Injection, methylprednisone acetate, 80 mg
ICD-10 codes covered if selection criteria are met:	
M47.20 - M47.28	Other spondylosis with radiculopathy
M50.10 - M50.13	Cervical disc disorder with radiculopathy
M51.14 - M51.17	Intervertebral disc disorders with radiculopathy
M53.0 - M53.1	Cervicocranial - cervicobrachial syndrome
M53.81 - M53.83	Other specified dorsopathies [cervical region]
M54.10 - M54.18	Radiculopathy
M54.2	Cervicalgia
M54.30 - M54.59	Sciatica and lumbago
M54.6	Pain in thoracic spine
M54.9	Dorsalgia, unspecified
ICD-10 codes not covered for indications listed in the CPB:	
C41.2	Malignant neoplasm of vertebral column
C41.4	Malignant neoplasm of pelvic bones, sacrum, and coccyx
C70.1	Malignant neoplasm of spinal meninges
C72.0	Malignant neoplasm of spinal cord

Code	Code Description
C79.31	Secondary malignant neoplasm of brain
C79.49	Secondary malignant neoplasm of other parts of nervous system [includes spinal cord]
C79.51 - C79.52	Secondary malignant neoplasm of bone and bone marrow
D16.6	Benign neoplasm of vertebral column
D16.8	Benign neoplasm of pelvic bones, sacrum, and coccyx
D32.1	Benign neoplasm of spinal meninges
D33.4	Benign neoplasm of spinal cord
D42.0 - D42.9	Neoplasm of uncertain behavior of meninges
D43.0 - D43.2, D43.4	Neoplasm of uncertain behavior of brain and spinal cord
D49.7	Neoplasm of unspecified behavior of endocrine glands and other parts of nervous system
Chymopapain chemonucleolysis:	
CPT codes covered if selection criteria are met:	
62292	Injection procedure for chemonucleolysis, including discography, intervertebral disc, single or multiple levels, lumbar
Other CPT codes related to the CPB:	
62302 - 62305	Myelography via lumbar injection, including radiological supervision and interpretation
72125 - 72133	Computed tomography, spine
72141 - 72158	Magnetic resonance (eg, proton) imaging, spinal canal and contents
72240 - 72270	Myelography of spine
ICD-10 codes not covered for indications listed in the CPB:	
C41.2	Malignant neoplasm of vertebral column
C41.4	Malignant neoplasm of pelvic bones, sacrum, and coccyx
C70.1	Malignant neoplasm of spinal meninges
C72.0	Malignant neoplasm of spinal cord
C79.31	Secondary malignant neoplasm of brain

Code	Code Description
C79.49	Secondary malignant neoplasm of other parts of nervous system [includes spinal cord]
C79.51 - C79.52	Secondary malignant neoplasm of bone and bone marrow
D16.6	Benign neoplasm of vertebral column [excludes sacrum and coccyx]
D16.8	Benign neoplasm of pelvic bones, sacrum, and coccyx
D32.1	Benign neoplasm of spinal meninges
D33.4	Benign neoplasm of spinal cord
D42.0 - D42.9	Neoplasm of uncertain behavior of meninges
D43.0 - D43.2	Neoplasm of uncertain behavior of brain
D43.4	Neoplasm of uncertain behavior of spinal cord
D49.7	Neoplasm of unspecified behavior of endocrine glands and other parts of nervous system
G00.0 - G99.8	Diseases of the nervous system
G83.4	Cauda equina syndrome
M43.06 - M43.08	Spondylolysis, lumbar, lumbosacral, sacral and sacrococcygeal, region
M43.10 - M43.19	Spondylolisthesis [acquired]
M43.27 - M43.28 M53.2x7 - M53.2x8 M53.87 - M53.88	Disorders of sacrum
M43.8x9	Other specified deforming dorsopathies, site unspecified
M48.00 - M48.01 M48.03 - M48.08	Spinal stenosis, other than cervical
M48.02	Spinal stenosis, cervical region

Code	Code Description
M50.00 - M50.03	Cervical disc disorder with myelopathy
M50.20 - M50.23	Other cervical disc displacement
M51.04 - M51.05	Thoracic, thoracolumbar intervertebral disc disorder with myelopathy
M51.06 - M51.07	Intervertebral disc disorders with myelopathy, lumbar/lumbosacral region
M51.24 - M51.25	Other thoracic, thoracolumbar disc displacement
M51.26 - M51.27	Other intervertebral disc displacement, lumbar/lumbosacral regions
M53.2x7 - M53.2x8	Spinal instabilities, lumbosacral, sacral, sacrococcygeal region
M54.03 - M54.09, M62.830	Other symptoms referable to back
M54.30 - M54.32	Sciatica [due to herniated disc]
M54.50 - M54.59	Low back pain [lumbago]
M54.6	Pain in thoracic spine
M54.89 - M54.9	Other and unspecified dorsalgia
M96.1	Postlaminectomy syndrome, not elsewhere classified
O01.9 - O94	Complications of pregnancy, childbirth, and the puerperium
Q76.2	Congenital spondylolisthesis
R29.810 - R29.898	Other symptoms and signs involving the nervous and musculoskeletal systems
Z34.00 - Z34.93	Encounter for supervision of normal pregnancy

Code	Code Description
Percutaneous lumbar discectomy or laser-assisted disc decompression (LADD):	
CPT codes not covered if selection criteria are met:	
62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method, single or multiple levels, lumbar (eg, manual or automated percutaneous discectomy, percutaneous laser discectomy)
Other CPT codes related to the CPB:	
62267	Percutaneous aspiration within the nucleus pulposus, intervertebral disc, or paravertebral tissue for diagnostic purposes
62303 - 62305	Myelography via lumbar injection, including radiological supervision and interpretation
63001 - 63091	Laminectomy, discectomy and related procedures (eg, decompression of spinal cord)
63185 - 63190	Laminectomy with rhizotomy
72125 - 72133	Computed tomography, spine
72141 - 72158	Magnetic resonance (eg, proton) imaging, spinal canal and contents
72240 - 72270	Myelography of spine
77002	Fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, localization device)
HCPCS codes not covered for indications listed in the CPB:	
G0276	Blinded procedure for lumbar stenosis, percutaneous image-guided lumbar decompression (PILD) or placebo-control, performed in an approved coverage with evidence development (CED) clinical trial
Other HCPCS codes related to the CPB:	
C2614	Probe, percutaneous lumbar discectomy
ICD-10 codes not covered if selection criteria are met::	
M51.06 - M51.07	Intervertebral disc disorder with myelopathy, lumbar/lumbosacral region
M51.26- M51.27	Other intervertebral disc displacement, lumbar/lumbosacral regions
M51.35	Other intervertebral disc degeneration, thoracolumbar region

Code	Code Description
M51.36	Other intervertebral disc degeneration, lumbar region
M51.37	Other intervertebral disc degeneration, lumbosacral region
Minimally Invasive Lumbar Decompression (MILD):	
CPT codes not covered for indications listed in the CPB:	
0274T	Percutaneous laminotomy/laminectomy (intralaminar approach) for decompression of neural elements, (with or without ligamentous resection, discectomy, facetectomy and/or foraminotomy) any method under indirect image guidance (eg, fluoroscopic, CT), with or without the use of an endoscope, single or multiple levels, unilateral or bilateral; cervical or thoracic
0275T	lumbar
Radiofrequency facet denervation:	
CPT codes covered if selection criteria are met:	
64633	Destruction by neurolytic agent, paravertebral facet joint nerve(s), with imaging guidance (fluoroscopy or CT); cervical or thoracic, single facet joint [not covered for cooled radiofrequency ablation]
64634	cervical or thoracic, each additional facet joint (List separately in addition to code for primary procedure) [not covered for cooled radiofrequency ablation]
64635	lumbar or sacral, single facet joint [not covered for cooled radiofrequency ablation]
64636	lumbar or sacral, each additional facet joint (List separately in addition to code for primary procedure) [not covered for cooled radiofrequency ablation]
CPT codes not covered for indications listed in the CPB:	
64625	Radiofrequency ablation, nerves innervating the sacroiliac joint, with image guidance (ie, fluoroscopy or computed tomography)
Other CPT codes related to the CPB:	
22548 - 22812	Arthrodesis, vertebra
62302 - 62305	Myelography via lumbar injection, including radiological supervision and interpretation
64479 - 64484	Injection, anesthetic agent and/or steroid, transforaminal epidural

Code	Code Description
72125 - 72133	Computed tomography, spine
72141 - 72158	Magnetic resonance (eg, proton) imaging, spinal canal and contents
72240 - 72270	Myelography of spine
97001 - 97139	Physical medicine and rehabilitation modalities and therapeutic procedures
Other HCPCS codes related to the CPB:	
L0112 - L0999	Orthotic devices-spinal
ICD-10 codes covered if selection criteria are met:	
M53.0 - M53.1	Cervicocranial - cervicobrachial syndrome
M53.81 - M53.83	Other specified dorsopathies [cervical region]
M54.2	Cervicalgia
M54.30 - M54.59	Sciatica and lumbago
M54.6	Pain in thoracic spine
M54.9	Dorsalgia, unspecified [backache]
ICD-10 codes not covered for indications listed in the CPB:	
M43.27 - M43.29, M53.2x7 - M53.2x8, M53.87 - M53.88	Disorders of sacrum
M50.00 - M51.9	Intervertebral disc disorders
M51.A0 - M51.A5	Intervertebral annulus fibrosus defect
Z98.1	Arthrodesis status [vertebra]

Code	Code Description
Transforaminal lumbar interbody fusion:	
CPT codes covered if selection criteria are met:	
22630	Arthrodesis, posterior interbody technique, including laminectomy and/or discectomy to prepare interspace (other than for decompression), single interspace; lumbar
22632	Arthrodesis, posterior interbody technique, including laminectomy and/or discectomy to prepare interspace (other than for decompression), single interspace; each additional interspace (List separately in addition to code for primary procedure)
ICD-10 codes covered if selection criteria are met:	
C41.2	Malignant neoplasm of vertebral column, excluding sacrum and coccyx
C70.1	Malignant neoplasm of spinal meninges
C79.31 - C79.32	Secondary malignant neoplasm of brain and spinal cord
C79.49	Secondary malignant neoplasm of other parts of nervous system
C79.51 - C79.52	Secondary malignant neoplasm of bone and bone marrow
D32.1	Benign neoplasm of spinal meninges
D33.4	Benign neoplasm of spinal cord
D42.0 - D42.9	Neoplasm of uncertain behavior of meninges
D43.0 - D43.2, D43.4	Neoplasm of uncertain behavior of brain and spinal cord
D48.0	Neoplasm of uncertain behavior of bone and articular cartilage
G06.1	Intraspinal abscess and granuloma
M40.50 - M40.57	Lordosis, unspecified
M41.00 - M41.35, M41.80 - M41.9	Scoliosis

Code	Code Description
M43.00 - M43.19	Spondylolysis and spondylolisthesis
M46.20	Osteomyelitis of vertebra, site unspecified
M46.30	Infection of intervertebral disc (pyogenic), site unspecified
M48.061 - M48.07	Spinal stenosis, lumbar and lumbosacral region
M48.50x+ - M48.58x+, M80.08x+, M84.48x+, M84.58x+, M84.68x+	Pathologic fracture of vertebrae
M86.18	Other acute osteomyelitis, other site [spinal]
M86.28	Subacute osteomyelitis, other site [spinal]
M86.68	Other chronic osteomyelitis, other site [spinal]
M96.0	Pseudoarthrosis after fusion or arthrodesis
M96.5	Postradiation scoliosis
Numerous options	Nonunion of fracture [Codes not listed due to expanded specificity]
Q76.2	Congenital spondylolisthesis
S31.000+	Unspecified open wound of lower back and pelvis without penetration into retroperitoneum
S32.000+ - S32.059+	Fracture of lumbar vertebra
S33.100+ - S33.141+	Subluxation and dislocation of lumbar vertebra
S34.101+ - S34.129+	Other and unspecified injury of lumbar spinal cord
Z98.1	Arthrodesis status

Code	Code Description
Intervertebral body fusion devices:	
CPT codes covered if selection criteria are met:	
22853	Insertion of interbody biomechanical device(s) (eg, synthetic cage, mesh) with integral anterior instrumentation for device anchoring (eg, screws, flanges), when performed, to intervertebral disc space in conjunction with interbody arthrodesis, each interspace (List separately in addition to code for primary procedure)
22854	Insertion of intervertebral biomechanical device(s) (eg, synthetic cage, mesh) with integral anterior instrumentation for device anchoring (eg, screws, flanges), when performed, to vertebral corpectomy(ies) (vertebral body resection, partial or complete) defect, in conjunction with interbody arthrodesis, each contiguous defect (List separately in addition to code for primary procedure)
22859	Insertion of intervertebral biomechanical device(s) (eg, synthetic cage, mesh, methylmethacrylate) to intervertebral disc space or vertebral body defect without interbody arthrodesis, each contiguous defect (List separately in addition to code for primary procedure)
Other CPT codes related to the CPB:	
20936 - 20938	Autograft for spine surgery
63081 - 63082	Vertebral corpectomy
HCPCS codes covered if selection criteria are met:	
Synthetic cervical cages/spacers, Spine Cages, Expandable cages - no specific code (not an all-inclusive list):	
(e.g., BAK Interbody Fusion System, Ray Threaded Fusion Cage, STALIF stand-alone anterior lumbar fusion cage, carbon fiber cage)	
ICD-10 codes covered if selection criteria are met:	
C41.2	Malignant neoplasm of vertebral column
C79.51	Secondary malignant neoplasm of bone
M24.08	Loose body, other site [retropulsed bone fragments]
M25.78	Osteophyte, vertebrae [of spine causing spinal cord or nerve root compression, confirmed by imaging studies] [see criteria in CPB 743]

Code	Code Description
M48.02	Spinal stenosis, cervical region [symptomatic central canal stenosis]
M50.00 - M50.03	Cervical disc disorders with myelopathy [see criteria in CPB 743]
M50.20 - M50.23	Other cervical disc displacement [see criteria in CPB 743]
M51.34 - M51.37	Other thoracic, thoracolumbar and lumbosacral intevertebral disc degeneration [see criteria in CPB 743]
M54.11 - M54.13	Radiculopathy, cervical region [see criteria in CPB 743]
M89.78	Major osseous defect, other site
M96.0	Pseudarthrosis after fusion or arthrodesis
Q76.2	Congenital spondylolisthesis [see criteria in CPB 743]
S12.000A - S12.691S	Fracture of cervical vertebra
Percutaneous polymethylmethacrylate vertebroplasty (PPV), kyphoplasty or SpineJack System:	
CPT codes covered if selection criteria are met:	
22510 - 22511	Percutaneous vertebroplasty (bone biopsy included when performed), 1 vertebral body, unilateral or bilateral injection, inclusive of all imaging guidance; cervicothoracic or lumbosacral
22512	each additional cervicothoracic or lumbosacral vertebral body (List separately in addition to code for primary procedure)
22513 - 22514	Percutaneous vertebral augmentation, including cavity creation (fracture reduction and bone biopsy included when performed) using mechanical device (eg, kyphoplasty), 1 vertebral body, unilateral or bilateral cannulation, inclusive of all imaging guidance; thoracic or lumbar
22515	each additional thoracic or lumbar vertebral body (List separately in addition to code for primary procedure)
Other CPT codes related to the CPB::	
77080	Dual-energy X-ray absorptiometry (DXA), bone density study, 1 or more sites; axial skeleton (eg, hips, pelvis, spine)

Code	Code Description
77085	axial skeleton (eg, hips, pelvis, spine), including vertebral fracture assessment
77086	Vertebral fracture assessment via dual-energy X-ray absorptiometry (DXA)
HCPCS codes covered for indications listed in the CPB:	
C1062	Intravertebral body fracture augmentation with implant (e.g., metal, polymer) [spineJack system]
C7504	Percutaneous vertebroplasties (bone biopsies included when performed), first cervicothoracic and any additional cervicothoracic or lumbosacral vertebral bodies, unilateral or bilateral injection, inclusive of all imaging guidance
C7505	Percutaneous vertebroplasties (bone biopsies included when performed), first lumbosacral and any additional cervicothoracic or lumbosacral vertebral bodies, unilateral or bilateral injection, inclusive of all imaging guidance
C7507	Percutaneous vertebral augmentations, first thoracic and any additional thoracic or lumbar vertebral bodies, including cavity creations (fracture reductions and bone biopsies included when performed) using mechanical device (eg, kyphoplasty), unilateral or bilateral cannulations, inclusive of all imaging guidance
C7508	Percutaneous vertebral augmentations, first lumbar and any additional thoracic or lumbar vertebral bodies, including cavity creations (fracture reductions and bone biopsies included when performed) using mechanical device (eg, kyphoplasty), unilateral or bilateral cannulations, inclusive of all imaging guidance
ICD-10 codes covered if selection criteria are met:	
C41.2	Malignant neoplasm of vertebral column
C41.4	Malignant neoplasm of pelvic bones, sacrum, and coccyx
C70.1	Malignant neoplasm of spinal meninges
C72.0	Malignant neoplasm of spinal cord
C79.31	Secondary malignant neoplasm of brain

Code	Code Description
C79.49	Secondary malignant neoplasm of other parts of nervous system
C79.51 - C79.52	Secondary malignant neoplasm of bone and bone marrow
C83.30 - C95.92	Malignant neoplasm of lymphoid, hematopoietic and related tissue
D18.09	Hemangioma of other sites [painful and/or aggressive]
E88.89	Other specified metabolic disorders [painful vertebral eosinophilic granuloma]
M48.30 - M48.38	Traumatic spondylopathy
M48.50x+ - M48.58x+ M80.08+, M80.88x+ M84.58x+, M84.68x+	Pathological fracture of vertebra(e) [painful, debilitating osteoporotic acute or subacute collapse/compression fractures (proven not to be chronic on recent imaging)]
M81.0 - M81.8	Osteoporosis
S12.000+ - S12.691+ S12.9xx+, S22.000+ - S22.089+ S32.000+ - S32.2xx+	Fracture of vertebral column, without mention of spinal cord injury [steroid-induced] [with spinal cord injury, use spinal cord injury codes also]
ICD-10 codes not covered for indications listed in the CPB:	
M50.20 - M51.9	Intervertebral disc disorders
Endoscopic Spinal surgery:	
Other CPT codes related to the CPB:	
62267	Percutaneous aspiration within the nucleus pulposus, intervertebral disc, or paravertebral tissue for diagnostic purposes

Code	Code Description
62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method, single or multiple levels, lumbar (eg, manual or automated percutaneous discectomy, percutaneous laser discectomy)
77002	Fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, localization device)
Vertebral body replacement spacers (e.g., AVS AL PEEK Spacer):	
No specific code	
ICD-10 codes covered if selection criteria are met:	
M43.8X9	Other specified deforming dorsopathies, site unspecified [damaged or unstable vertebral body resected or excised during total and partial vertebrectomy procedures]
M48.50x+ - M48.58x+	Collasped vertebra, not elsewhere classified
Cementoplasty:	
CPT codes covered if selection criteria are met:	
Cementoplasty - no specific code:	
ICD-10 codes covered if selection criteria are met:	
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
Intramuscular injection of Ketorolac tromethamine (Toradol):	
Other CPT codes related to the CPB:	
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug [Toradol]); subcutaneous or intramuscular
HCPCS codes covered if selection criteria are met:	
J1885	Injection, ketorolac tromethamine per 15 mg [Toradol]
ICD-10 codes covered if selection criteria are met:	
M54.00-M54.9	Dorsalgia
Experimental and Investigational Interventions for treatment of back pain:	
Chronic Back Pain:	
CPT codes not covered for indications listed in the CPB:	
Direct visual rhizotomy, Discseel procedure, DiscoGel (intradiscal alcohol injection) - no specific code:	
0232T	Injection(s), platelet rich plasma, any site, including image guidance, harvesting and preparation when performed
20550	Injection(s); single tendon sheath, or ligament, aponeurosis

Code	Code Description
20551	single tendon origin/insertion
20560	Needle insertion(s) without injection(s); 1 or 2 muscle(s)
20561	Needle insertion(s) without injection(s); 3 or more muscles
Other CPT codes related to the CPB:	
96365 - 96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
HCPCS codes not covered for indications listed in the CPB:	
C9757	Laminotomy (hemilaminectomy), with decompression of nerve root(s), including partial facetectomy, foraminotomy and excision of herniated intervertebral disc, and repair of annular defect with implantation of bone anchored annular closure device, including annular defect measurement, alignment and sizing assessment, and image guidance; 1 interspace, lumbar [Barricaid, DART disc annular repair devices, Xclose Tissue Repair System]
J0702	Injection, betamethasone acetate 3 mg and betamethasone sodium phosphate 3 mg
J1020	Injection, methylprednisolone acetate, 20 mg
J1030	Injection, methylprednisolone acetate, 40 mg
J1040	Injection, methylprednisolone acetate, 80 mg
J1094	Injection, dexamethasone acetate, 1 mg
J1100	Injection, dexamethasone sodium phosphate, 1 mg
J1700	Injection, hydrocortisone acetate, up to 25 mg
J1710	Injection, hydrocortisone sodium phosphate, up to 50 mg
J1720	Injection, hydrocortisone sodium succinate, up to 100 mg
J1885	Injection, ketorolac tromethamine per 15 mg
J2001	Injection, lidocaine HCL for intravenous infusion 10 mg
J2650	Injection, prednisolone acetate, up to 1 ml
J2920	Injection, methylprednisolone sodium succinate, up to 40 mg
J2930	Injection, methylprednisolone sodium succinate, up to 125 mg
J3300	Injection, triamcinolone acetonide, preservative free, 1 mg

Code	Code Description
J3301	Injection, triamcinolone acetonide, not otherwise specified, 10 mg
J3302	Injection, triamcinolone diacetate, per 5 mg
J3303	Injection, triamcinolone hexacetonide, per 5 mg
J3304	Injection, triamcinolone acetonide, preservative-free, extended-release, microsphere formulation, 1 mg
J3420	Injection, vitamin B-12 cyanocobalamin, up to 1000 mg
J3475	Injection, magnesium sulfate, per 500 mg
ICD-10 codes not covered for indications listed in the CPB:	
M54.00-M54.9	Dorsalgia
Magnetic resonance imaging-guided focused ultrasound (MRgFUS):	
CPT codes not covered for indications listed in the CPB:	
Magnetic resonance imaging-guided focused ultrasound (MRgFUS) –no specific code	
ICD-10 codes not covered for indications listed in the CPB:	
M54.00 – M54.9	Dorsalgia
Experimental and investigational Interventions for treatment of neck pain:	
CPT codes not covered for indications listed in the CPB:	
DiscoGel (intradiscal alcohol injection) - no specific code:	
Other CPT codes related to the CPB:	
96365 - 96368	Intravenous infusion, for therapy, prophylaxis, or diagnosis
96372	Therapeutic, prophylactic, or diagnostic injection (specify substance or drug); subcutaneous or intramuscular
HCPCS codes not covered for indications listed in the CPB:	
J0702	Injection, betamethasone acetate 3 mg and betamethasone sodium phosphate 3 mg
J1020	Injection, methylprednisolone acetate, 20 mg
J1030	Injection, methylprednisolone acetate, 40 mg
J1040	Injection, methylprednisolone acetate, 80 mg
J1094	Injection, dexamethasone acetate, 1 mg
J1100	Injection, dexamethasone sodium phosphate, 1 mg

Code	Code Description
J1700	Injection, hydrocortisone acetate, up to 25 mg
J1710	Injection, hydrocortisone sodium phosphate, up to 50 mg
J1720	Injection, hydrocortisone sodium succinate, up to 100 mg
J1885	Injection, ketorolac tromethamine per 15 mg
J2001	Injection, lidocaine hcl for intravenous infusion, 10 mg
J2650	Injection, prednisolone acetate, up to 1 ml
J2920	Injection, methylprednisolone sodium succinate, up to 40 mg
J2930	Injection, methylprednisolone sodium succinate, up to 125 mg
J3300	Injection, triamcinolone acetonide, preservative free, 1 mg
J3301	Injection, triamcinolone acetonide, not otherwise specified, 10 mg
J3302	Injection, triamcinolone diacetate, per 5 mg
J3303	Injection, triamcinolone hexacetonide, per 5 mg
J3304	Injection, triamcinolone acetonide, preservative-free, extended-release, microsphere formulation, 1 mg
J3420	Injection, vitamin B-12 cyanocobalamin, up to 1000 mg
J3475	Injection, magnesium sulfate, per 500 mg
ICD-10 codes not covered for indications listed in the CPB:	
M54.2	Cervicalgia
Endoscopic transforaminal diskectomy:	
CPT codes not covered for indications listed in the CPB:	
62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method utilizing needle based technique to remove disc material under fluoroscopic imaging or other form of indirect visualization, with the use of an endoscope, with discography and/or epidural injection(s) at the treated level(s), when performed, single or multiple levels, lumbar [not covered for endoscopic transforaminal discectomy]
Other CPT codes related to the CPB:	
96365 - 96366	Intravenous infusion, for therapy, prophylaxis, or diagnosis (specify substance or drug [magnesium, Toradol and vitamin B12 cyanocobalamin] for the treatment of back pain)

Code	Code Description
HCPCS codes not covered for indications listed in the CPB:	
J1885	Injection, ketorolac tromethamine per 15 mg [Toradol]
J3420	Injection, vitamin B-12 cyanocobalamin, up to 1000 mg
J3475	Injection, magnesium sulfate, per 500 mg
ICD-10 codes not covered for indications listed in the CPB:	
M54.50 - M54.59	Low back pain
M54.9	Dorsalgia, unspecified
Minimally Invasive Thoracic diskectomy:	
CPT codes not covered for indications listed in the CPB:	
22532	Arthrodesis, lateral extracavitary technique, including minimal discectomy to prepare interspace (other than for decompression); thoracic
Percutaneous cervical diskectomy:	
Minimally Invasive Lumbar Decompression (MILD):	
CPT codes not covered for indications listed in the CPB:	
0274T	Percutaneous laminotomy/laminectomy (intralaminar approach) for decompression of neural elements, (with or without ligamentous resection, discectomy, facetectomy and/or foraminotomy) any method under indirect image guidance (eg, fluoroscopic, CT), with or without the use of an endoscope, single or multiple levels, unilateral or bilateral; cervical or thoracic
0275T	lumbar
HCPCS codes not covered for indications listed in the CPB:	
G0276	Blinded procedure for lumbar stenosis, percutaneous image-guided lumbar decompression (PILD) or placebo-control, performed in an approved coverage with evidence development (CED) clinical trial
ICD codes not covered for indications listed in the CPB:	
M51.26	Other intervertebral disc displacement, lumbar region

Code	Code Description
Epiduroscopy:	
Other CPT codes related to the CPB:	
62318	Injection, including catheter placement, continuous infusion or intermittent bolus, not including neurolytic substances, with or without contrast (for either localization or epidurography), of diagnostic or therapeutic substance(s) (including anesthetic, antispasmodic, opioid, steroid, other solution), epidural or subarachnoid; cervical or thoracic
62319	lumbar, sacral (caudal)
72275	Epidurography, radiological supervision and interpretation
Epidural injections of lytic agents:	
CPT codes not covered for indications listed in the CPB:	
62280	Injection/infusion of neurolytic substance (eg, alcohol, phenol, iced saline solutions), with or without other therapeutic substance; subarachnoid Ultrasonic guidance for needle placement (eg, biopsy, aspiration, injection, localization device), imaging supervision and interpretation [not covered for chemical ablation (including but not limited to alcohol, phenol or sodium morrhuate) of facet joints]
62281	epidural, cervical or thoracic [not covered for chemical ablation (including but not limited to alcohol, phenol or sodium morrhuate) of facet joints]
62282	epidural, lumbar, sacral (caudal) [not covered for chemical ablation (including but not limited to alcohol, phenol or sodium morrhuate) of facet joints]
Other CPT codes related to the CPB:	
72275	Epidurography, radiological supervision and interpretation
HCPCS codes not covered for indications listed in the CPB:	
J3470	Injection, hyaluronidase, up to 150 units
J3471	Injection, hyaluronidase, ovine, preservative free, per 1 USP unit (up to 999 USP units)
J3472	Injection, hyaluronidase, ovine, preservative free, per 1000 USP units
J3473	Injection, hyaluronidase, recombinant, 1 USP unit

Code	Code Description
ICD-10 codes not covered for indications listed in the CPB:	
G03.0 - G03.9	Meningitis due to other and unspecified causes
M43.00 - M43.9	Dorsopathies
M54.10	Radiculopathy, site unspecified
M79.2	Neuralgia and neuritis, unspecified
S12.000S - S12.691S S12.9xxS, S22.000S - S22.089S S32.000S - S32.2xxS	Fracture of vertebral column, sequela
S39.002+ - S39.003+ S39.092+ - S39.093+ S39.82x+ - S39.83x+ S39/92x+ - S39.93x+	Other injuries of other sites of trunk
Intracept System:	
CPT codes not covered for indications listed in the CPB:	
64628	Thermal destruction of intraosseous basivertebral nerve, including all imaging guidance; first 2 vertebral bodies, lumbar or sacral
64629	Thermal destruction of intraosseous basivertebral nerve, including all imaging guidance; each additional vertebral body, lumbar or sacral (List separately in addition to code for primary procedure)
ICD-10 codes not covered for indications listed in the CPB:	
M54.2	Cervicalgia
M54.50 - M54.59	Low back pain [chronic]

Code	Code Description
Intradiscal injections of notochordal cell-derived matrix:	
CPT codes not covered for indications listed in the CPB:	
Intradiscal injections of notochordal cell-derived matrix - no specific code:	
ICD-10 codes not covered for indications listed in the CPB:	
M50.00 - M50.93	Cervical disc disorders
M51.04 - M51.9	Thoracic, thoracolumbar, and lumbosacral intervertebral disc disorders
Microsurgical anterior foraminotomy:	
No specific codes	
Other CPT codes related to the CPB:	
63075 - 63078	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy
Other HCPCS codes related to the CPB:	
S2350	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy; lumbar, single interspace
S2351	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy; lumbar, each additional interspace (list separately in addition to code for primary procedure)
Sacroiliac fusion:	
CPT codes covered if selection criteria are met:	
27279	Arthrodesis, sacroiliac joint, percutaneous or minimally invasive (indirect visualization), with image guidance, includes obtaining bone graft when performed, and placement of transfixing device
27280	Arthrodesis, open, sacroiliac joint, including obtaining bone graft, including instrumentation, when performed [may be medically necessary for sacroiliac joint infection, tumor involving the sacrum, and sacroiliac pain due to severe traumatic injury where a trial of an external fixator is successful in providing pain relief]
CPT codes not covered for indications listed in the CPB:	
0775T	Arthrodesis, sacroiliac joint, percutaneous, with image guidance, includes placement of intra-articular implant(s) (eg, bone allograft(s), synthetic device(s))

Code	Code Description
0809T	Arthrodesis, sacroiliac joint, percutaneous or minimally invasive (indirect visualization), with image guidance, placement of transfixing device(s) and intraarticular implant(s), including allograft or synthetic device(s)
Other CPT codes related to the CPB:	
72200	Radiologic examination, sacroiliac joints; less than 3 views
72202	3 or more views
80323	Alkaloids, not otherwise specified [Blood or Urinary Nicotine]
97001 - 97799	Physical Medicine and Rehabilitation
99406 - 99407	Smoking and tobacco use cessation counseling visit
Other HCPCS codes related to the CPB:	
Titanium triangular implants - no specific code:	
S4995	Smoking cessation gum
S9453	Smoking cessation classes, nonphysician provider, per session
ICD-10 codes covered if selection criteria are met:	
C41.4	Malignant neoplasm of pelvic bones, sacrum and coccyx
C76.3	Malignant neoplasm of pelvis
D16.8	Benign neoplasm of pelvic bones, sacrum and coccyx
M01.x8	Direct infection of vertebrae in infectious and parasitic diseases classified elsewhere [sacroiliac joint infection]
M02.88	Other reactive arthropathies, vertebrae [sacroiliac joint infection]
M46.1	Sacroiliitis, not elsewhere classified [sacroiliac joint syndrome]
M53.3	Sacrococcygeal disorders, not elsewhere classified [sacroiliac joint syndrome]
M54.17	Radiculopathy, lumbosacral region [due to severe traumatic injury]
M54.18	Radiculopathy, sacral and sacrococcygeal region [due to severe traumatic injury]
S32.301A - S32.9xxB	Sacroiliac injuries
ICD-10 codes not covered for indications listed in the CPB:	
F17.200 - F17.299	Nicotine dependence

Code	Code Description
M11.08	Hydroxyapatite deposition disease, vertebrae [lumbar]
M11.18	Familial chondrocalcinosis, vertebrae [lumbar]
M11.28	Other chondrocalcinosis, vertebrae [lumbar]
M11.88	Other specified crystal arthropathies, vertebrae [lumbar]
M43.16	Spondylolisthesis, lumbar region
M45.6	Ankylosing spondylitis lumbar region
M47.896	Other spondylosis, lumbar region [lumbar facet degeneration]
M48.061 - M48.062	Spinal stenosis, lumbar region
M51.26	Other intervertebral disc displacement, lumbar region
M51.36	Other intervertebral disc degeneration, lumbar region
Z72.0	Tobacco use
Sacroplasty:	
CPT codes not covered for indications listed in the CPB:	
0200T	Percutaneous sacral augmentation (sacroplasty), unilateral injection(s), including the use of a balloon or mechanical device, when used, 1 or more needles, includes imaging guidance and bone biopsy, when performed
0201T	Percutaneous sacral augmentation (sacroplasty), bilateral injections, including the use of a balloon or mechanical device, when used, 2 or more needles, includes imaging guidance and bone biopsy, when performed
Racz procedure (epidural adhesiolysis with the Racz catheter):	
CPT codes not covered for indications listed in the CPB:	
62263	Percutaneous lysis of epidural adhesions using solution injection (e.g., hypertonic saline, enzyme) or mechanical means (eg, catheter) including radiologic localization (includes contrast when administered), multiple adhesiolysis sessions; 2 or more days
62264	1 day
Other CPT codes related to the CPB:	
72275	Epidurography, radiological supervision and interpretation

Code	Code Description
Microdiskectomy:	
Other CPT codes related to the CPB:	
22220 - 22226	Osteotomy of spine, including discectomy, anterior approach
62267	Percutaneous aspiration within the nucleus pulposus, intervertebral disc, or paravertebral tissue for diagnostic purposes
62287	Decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method, single or multiple levels, lumbar (eg, manual or automated percutaneous discectomy, percutaneous laser discectomy)
+ 69990	Operating microscope
77002	Fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, localization device)
Other HCPCS codes related to the CPB:	
C2614	Probe, percutaneous, lumbar discectomy
S2350	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy; lumbar, single interspace
S2351	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy; lumbar, each additional interspace (list separately in addition to code for primary procedure)
Microendoscopic discectomy (MED):	
Other CPT codes related to the CPB:	
22206	Osteotomy of spine, posterior or posterolateral approach, three columns, one vertebral segment (eg, pedicle/vertebral body subtraction); thoracic
22207	lumbar
+ 22208	each additional vertebral segment (List separately in addition to code for primary procedure)
22214	Osteotomy of spine, posterior or posterolateral approach, one vertebral segment; lumbar
+ 22216	each additional vertebral segment (List separately in addition to primary procedure)

Code	Code Description
22224	Osteotomy of spine, including discectomy, anterior approach, single vertebral segment; lumbar
+ 22226	each additional vertebral segment (List separately in addition to code for primary procedure)
62287	Aspiration or decompression procedure, percutaneous, of nucleus pulposus of intervertebral disc, any method, single or multiple levels, lumbar (eg, manual or automated percutaneous discectomy, percutaneous laser discectomy)
+ 69990	Operating microscope
77002	Fluoroscopic guidance for needle placement (eg, biopsy, aspiration, injection, localization device)
Other HCPCS codes related to the CPB:	
C2614	Probe, percutaneous, lumbar discectomy
S2350	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy; lumbar, single interspace
S2351	Discectomy, anterior, with decompression of spinal cord and/or nerve root(s), including osteophytectomy; lumbar, each additional interspace (list separately in addition to code for primary procedure)
Intercostal nerve blocks:	
CPT codes not covered for indications listed in the CPB:	
64420	Injection, anesthetic agent; intercostal nerve single
64421	intercostal nerves, multiple, regional block
ICD-10 codes not covered for indications listed in the CPB:	
G54.8	Other nerve root and plexus disorders [intercostal neuritis]
Inter-spinous distraction (X Stop Device, Coflex interspinous stablilization spinal implant, Extensure bone allograft inter-spinous spacer, Eclipse inter-spinous distraction device, and the TOPS System):	
CPT codes not covered for indications listed in the CPB:	
22867	Insertion of interlaminar/interspinous process stabilization/distraction device, without fusion, including image guidance when performed, with open decompression, lumbar; single level

Code	Code Description
22868	Insertion of interlaminar/interspinous process stabilization/distraction device, without fusion, including image guidance when performed, with open decompression, lumbar; second level (List separately in addition to code for primary procedure)
22869	Insertion of interlaminar/interspinous process stabilization/distraction device, without open decompression or fusion, including image guidance when performed, lumbar; single level
22870	Insertion of interlaminar/interspinous process stabilization/distraction device, without open decompression or fusion, including image guidance when performed, lumbar; second level (List separately in addition to code for primary procedure)
0202T	Posterior vertebral joint(s) arthroplasty (e.g., facet joint[s] replacement) including facetectomy, laminectomy, foraminotomy and vertebral column fixation, with or without injection of bone cement, including fluoroscopy, single level, lumbar spine
HCPCS codes not covered for indications listed in the CPB:	
C1821	Interspinous process distraction device (implantable)
Piriformis muscle resection:	
No specific codes	
CPT codes not covered for indications listed in the CPB:	
27006	Tenotomy, abductors and/or extensor(s) of hip, open (separate procedure)
64712	Neuroplasty, major peripheral nerve, arm or leg, open; sciatic nerve [not covered for surgery for piriformis syndrome]
ICD-10 codes not covered for indications listed in the CPB:	
G57.00 - G57.03	Lesion of sciatic nerve
M25.751 - M25.759	Osteophyte, hip
M54.30 - M54.32	Sciatica

Code	Code Description
M70.60 - M70.72	Trochanteric and other bursitis
M76.00 - M76.22	Enthesopathies, hip
Radiofrequency denervation for sacroiliac joint pain:	
CPT codes not covered for indications listed in the CPB:	
27035	Denervation, hip joint, intrapelvic or extrapelvic intrarticular branches of sciatic, femoral, or obturator nerves [not covered when specified as radiofrequency denervation for sacroiliac pain]
64625	Radiofrequency ablation, nerves innervating the sacroiliac joint, with image guidance (ie, fluoroscopy or computed tomography)
ICD-10 codes not covered for indications listed in the CPB:	
G57.00 - G57.03	Lesion of sciatic nerve
M25.751 - M25.759	Osteophyte, hip
M54.14 - M54.17	Radiculopathy, thoracic or lumbosacral region
M54.30 - M54.32	Sciatica
M70.60 - M70.72	Trochanteric and other bursitis
M72.9	Neuralgia and neuritis, unspecified
M76.00 - M76.22	Enthesopathies, hip
Facet joint implantation:	
CPT codes not covered for indications listed in the CPB:	
0219T	Placement of a posterior intrafacet implant(s), unilateral or bilateral, including imaging and placement of bone graft(s) or synthetic device(s), single level; cervical
0220T	thoracic
0221T	lumbar

Code	Code Description
0222T	each additional vertebral segment (List separately in addition to code for primary procedure)
Epidural fat grafting:	
Other CPT codes related to the CPB:	
15769	Grafting of autologous soft tissue, other, harvested by direct excision (eg, fat, dermis, fascia)
Endoscopic disc decompression:	
CPT codes not covered for indications listed in the CPB:	
62380	Endoscopic decompression of spinal cord, nerve root(s), including laminotomy, partial facetectomy, foraminotomy, discectomy and/or excision of herniated intervertebral disc, 1 interspace, lumbar

Code	Code Description
No specific codes:	
AccuraScope procedure, ACIS cage (Synthes), Anchor Knot Tissue Approximation Kit, Ancora spacer, Aspen spinous process fixation system, Benefix Interspinous Fixation System, Biomet Aspen fusion system, Brantigan, Brigade anterior plate system, Brigade (Nuvasive), Cambria anterior cervical interbody system, Cavetto cage, Centerpiece plate, Crescent cage, CD HORIZON SPIRE Plate, PrimaLOK SP, and SP-Fix Spinous Process Fixation Plate, Coccygeal ganglion (ganglion impar) blockade for pelvic pain, Degas plate, Deuk Laser Disc Repair, Diamond (Amendia), DiscFX System, Dynamic (intervertebral) stabilization devices -- BioFlex, CD Horizon Agile Dynamic Stabilization Device, Dynamic stabilization (e.g., Dynesys Spinal System and the Stabilimax NZ Dynamic Spine Stabilization System), Ebi PEEK optima spacer, Ellipse Occipito-Cervical-Thoracic spinal system, Endoscopic laser foraminoplasty, EOS spinal system (Korean Bone Bank), Epidural ozone, Extreme lateral interbody fusion (XLIF), G surgical plate system T loc, Illico pedicle screw system (Alphatec), IN:C2 spacer, Interlaminiar lumbar instrumented fusion (ILIF), Invizia plate, Kinetic-SL Dynamic Anterior Cervical Plate System, LINDIF, OptiMesh grafting system, Oxygen injection, Psoas compartment block, Radiofrequency lesioning of dorsal root ganglia, Radiofrequency lesioning of terminal (peripheral) nerve endings, Radiofrequency/pulsed radiofrequency ablation of trigger points, Stabilink interspinous fixation device, Total Facet Arthroplasty System, TSRH 3DX pedicle screws (Medtronic), Van Gogh plate, Vesselplasty (e.g., Vessel-X), Yeung Endoscopic Spinal Surgery System, Y.E.S.S., Zeus C cervical spacer, LinQ sacroiliac joint stabilization system, ION procedure (Ion Facet Screw System), Spinal System-X (Corus), CoFix (for interlaminar/interspinous stabilization)	

Background

Epidural Steroids

An epidural steroid finjection is an injection of long lasting steroid in the epidural space – that is the area which surrounds the spinal cord and the nerves coming out of it. An epidural steroid injection is used to help reduce radicular spinal pain that may be caused by pressure on a spinal nerve root as a result of a herniated disc, degenerative disc disease or spinal stenosis. This treatment is most frequently used for low back pain, though it may also be used for cervical (neck) or thoracic (midback) pain. A combination of an anesthetic and a steroid medication is injected into the epidural space near the affected spinal nerve root with the assistance of fluoroscopy which allows the physician to view the placement of the needle.

Approaches to the epidural space for the injection include:

- Caudal - the epidural needle is placed into the tailbone (coccyx) allowing the treatment of pain which radiates into the lower extremities. This approach is commonly used to treat lumbar radiculopathy after prior surgery in the low back (post-laminectomy pain syndrome).
- Cervical - the epidural needle is placed in the midline in the back of the neck to treat neck pain which is associated with radiation of pain into an upper extremity (cervical radiculopathy).
- Interlaminar - the needle is placed between the lamina of two vertebrae directly from the middle of the back. Also called translaminar, this method accesses the large epidural space overlying the spinal cord, and is the most commonly used approach for cervical, thoracic, and lumbar epidural injections. Medication is delivered to the nerve roots on both the right and left sides of the inflamed area at the same time.
- Lumbar - the epidural needle is placed in the midline in the low back to treat back pain which is associated with radiation into a lower extremity (lumbar radiculopathy).
- Thoracic - the epidural needle is placed in the midline in the upper or middle back.

- Transforaminal - the needle is placed to the side of the vertebra in the neural foramen, just above the opening for the nerve root and outside the epidural space; this method treats one side at a time.

The goal of this treatment is to reduce inflammation and block the spinal nerve roots to relieve radicular pain or sciatica. It can also provide sufficient pain relief to allow the individual to progress with their rehabilitation program.

The efficacy of epidurally administered steroids has been demonstrated without adverse consequence in a large number of patients with reproducible results. In a large number of studies, long-term relief of pain (greater than 3 months) can be achieved in at least 10 to 30% of patients, while short-term relief (less than 1 month) can be achieved in 60 to 100% of patients. Results for cervical pain are somewhat lower than those for lumbar pain. Such therapy is considered under accepted guidelines to be indicated in patients with low back and cervical pain that has not resolved after only a short period of more conservative measures since studies have shown a better response to therapy in patients whose pain is of shorter duration. Even if pain relief is temporary, it may have long-term benefit because it allows initiation of physical therapy or other rehabilitative measures at an earlier stage. Most authors indicate that a limit on number of injections is appropriate, and that most patients will respond with 3 or fewer injections.

The American Academy of Neurology's assessment on the use of epidural steroid injections in the treatment of radicular lumbosacral pain (Armond et al, 2007) concluded that:

- Epidural steroid injections may result in some improvement in radicular lumbosacral pain when determined between 2 and 6 weeks following the injection, compared to control treatment (Level C, Class I to III evidence). The average magnitude of effect is small, and the generalizability of the observation is limited by the small number of studies, limited to highly selected patient populations, the few techniques and doses studied, and variable comparison treatments.

- In general, epidural steroid injections for radicular lumbosacral pain have shown no impact on average impairment of function, on need for surgery, or on long-term pain relief beyond 3 months. Their routine use for these indications is not recommended (Level B, Class I to III evidence).
- Data on use of epidural steroid injections to treat cervical radicular pain are inadequate to make any recommendation (Level U).

Guidelines from the American Pain Society (Chou et al, 2009) questioned the clinical value of epidural injection for long-term use or for use of non-radicular back pain. A recommendation for epidural steroid injection for patients with symptomatic spinal stenosis was not offered based on insufficient or poor evidence.

Langer-Gould et al (2013) discussed the American Academy of Neurology (AAN)'s top five recommendations in the “Choosing Wisely” campaign promoting high-value neurologic medicine and physician-patient communication. They noted that 1 of the 11 finalist recommendations was “Don’t perform epidural steroid injections to treat non-radicular low back pain”.

Trigger Point Injections

Trigger point injections (TPI) are injections of saline or a local anesthetic, with or without a steroid medication, into a painful area of a muscle that contains the trigger point. The purpose of a TPI is to relax the area of intense muscle spasm, effectively inactivate the trigger point and provide prompt symptomatic pain relief. TPI is the most common interventional technique used in pain medicine.

Trigger points have also been treated with dry needling. For information on dry needling, see the Background section in CPB 0135 - Acupuncture and Dry Needling (../100_199/0135.html).

A myofascial trigger point is a discrete focal tenderness, 2-5 mm in diameter that is located in distinct tight bands or knots of skeletal muscle (AHFMR, 2002). When palpated, these hyper-irritable areas cause pain in distant areas, or referred pain zones, which are specific for each trigger point. Trigger point injection, or direct wet needling, involves injection of

fluid directly into the trigger point located in the taut muscle band. The main objective of trigger point injection is fast pain relief and elimination of muscle spasm in order to break the pain cycle. This facilitates physical therapy aimed at reducing muscle contracture and increasing range of motion. Trigger point injection is rarely used in isolation but is generally part of a multi-disciplinary approach aimed at treating both the trigger points and reducing all contributing factors (Scott and Guo, 2005; AHFMR, 2002; Sanders et al, 1999). Thus, treatment may also include patient education, psychosocial support, oral medications, and physical therapy to improve the strength and flexibility of the affected musculoskeletal systems. An assessment conducted by the Alberta Heritage Foundation for Medical Research (Scott and Guo, 2005) found that the evidence for the effectiveness of trigger point injections when used as the sole treatment for patients with chronic head, neck, and shoulder pain and whiplash syndrome was inconclusive, regardless of whether sterile water, saline, or botulinum toxin is injected. The assessment found that the combined use of dry needling and trigger point injection with procaine offers no obvious clinical benefit in the treatment of chronic craniofacial pain, while the effectiveness of trigger point injection for the treatment of cervicogenic headache is unknown. In contrast, the assessment found that trigger point injection with lidocaine may be useful in the treatment of joint pain caused by osteoarthritis (Scott and Guo, 2005). The assessment found no proof that triggers point injection is more effective than other less invasive treatments, such as physical therapy and ultrasound, in achieving pain relief, and there is some suggestion that the only advantage of injecting anesthetic into trigger points is that it reduces the pain of the needling process (Scott and Guo, 2005). Usually, approximately 3 treatments are necessary to abolish a trigger point completely (AHFMR, 2002). A number of trigger points may be injected in 1 session, but rarely more than 5. Repeated injections in a particular muscle are not recommended if 2 or 3 previous attempts have been unsuccessful (Alvarez and Rockwell, 2002; Sanders et al, 1999). The pain relief may last for the duration of the anesthetic to many months, depending on the chronicity and severity of the trigger points and the concomitant treatment of perpetuating factors. According to available guidelines, use of trigger point injections should be short-term and part of a comprehensive rehabilitation program. Available guidelines indicate that, while there are a number of uncontrolled case studies using trigger

point injections in more acute pain presentations, there is virtually no consistent evidence for its application with chronic non-malignant pain syndrome patients to date (Sanders et al, 1999; AHFMR, 2002).

Botwin and colleagues (2008) noted that myofascial pain is defined as pain that originates from myofascial trigger points in skeletal muscle. It is prevalent in regional musculoskeletal pain syndromes, either alone or in combination with other pain generators. The myofascial pain syndrome is one of the largest groups of under diagnosed and under treated medical problems encountered in clinical practice. Trigger points are commonly seen in patients with myofascial pain which is responsible for localized pain in the affected muscles as well as referred pain patterns. Correct needle placement in a myofascial trigger point is vital to prevent complications and improve efficacy of the trigger point injection to help reduce or relieve myofascial pain. In obese patients, these injections may not reach the target tissue. In the cervico-thoracic spine, a misguided or misplaced injection can result in a pneumothorax. These researchers described an ultrasound-guided trigger point injection technique to avoid this potential pitfall. Office based ultrasound-guided injection techniques for musculoskeletal disorders have been described in the literature with regard to tendon, bursa, cystic, and joint pathologies. For the interventionalist, utilizing ultrasound yields multiple advantages technically and practically, including observation of needle placement in real-time, ability to perform dynamic studies, the possibility of diagnosing musculoskeletal pathologies, avoidance of radiation exposure, reduced overall cost, and portability of equipment within the office setting. To the authors' knowledge, the use of ultrasound guidance in performing trigger point injection in the cervico-thoracic area, particularly in obese patients, has not been previously reported. A palpable trigger point in the cervico-thoracic musculature was localized and marked by indenting the skin with the tip of a plastic needle cover. The skin was then sterile prepped. Then, using an ultrasound machine with sterile coupling gel and a sterile latex free transducer cover, the musculature in the cervico-thoracic spine where the palpable trigger point was detected was visualized. Then utilizing direct live ultrasound guidance, a 25-gauge 1.5 inch needle connected to a 3-ml syringe was placed into the muscle at the exact location of the presumed trigger point. This guidance helped confirm needle placement in muscle tissue and not in an adipose tissue or any other non-musculature structure. The technique was simple to be

performed by a pain management specialist who has ultrasound system training. The authors concluded that ultrasound-guided trigger point injections may help confirm proper needle placement within the cervico-thoracic musculature. The use of ultrasound-guided trigger point injections in the cervico-thoracic musculature may also reduce the potential for a pneumothorax by an improperly placed injection.

Zhou and Wang (2014) stated that myofascial pain syndrome (MPS) is a common chronic pain condition that is characterized by distinct "trigger points". Despite current treatments with physical therapy, analgesics, anti-depressants and trigger-point injections, myofascial pain remains a challenging chronic pain condition in clinical practice. Botulinum toxin A (BTX-A) can cause prolonged muscle relaxation through inhibition of acetylcholine release. It may offer some advantages over the current treatments for MPS by providing a longer sustained period of pain relief. Despite numerous clinical trials, the efficacy of BTX-A in alleviating MPS is not well-established due to mixed results from recent clinical trials. Active trigger points are associated with referred pain and greatly impact many aspects of activities of daily living, mood, and health status. This review was designed to analyze the clinical trials regarding the efficacy of BTX-A injection of active trigger points as a treatment for MPS. The literature referenced was obtained via a computer search with Google Scholar, PubMed, Medline and Embase. Search terms included "Botulinum toxin", "myofascial pain", "trigger points", "myofascial trigger points", and "chronic pain". Additional references were retrieved from the reference list of the reports found via this search. Studies were considered eligible for inclusion if they were double-blinded, randomized, controlled trials evaluating the efficacy of BTX-A injections into trigger points for pain reduction, and if the trigger point selection in the trial included referred pain and/or local twitch response. Open-label studies, case reports, and other non-randomized studies were excluded. A total of 8 trials were found according to the above criteria. There are well-designed clinical trials to support the efficacy of trigger-point injections with BTX-A for MPS. However, further clinical trials with considerations of minimizing placebo effect, repeated dosing, adequate coverage of trigger points, and using ultrasound confirmation and guidance are required to provide conclusive evidence for BTX-A in the treatment of myofascial pain.

In a prospective, double-blinded, randomized controlled trial, Misirlioglu et al (2015) investigated the differences between local anesthetic (LA) and LA + corticosteroid (CS) injections in the treatment of piriformis syndrome (PS). A total of 57 patients having unilateral hip and/or leg pain with positive FAIR test and tenderness and/or trigger point at the piriformis muscle were evaluated. Out of 50 patients randomly assigned to 2 groups, 47 patients whose pain resolved at least 50% from the baseline after the injection were diagnosed as having PS. The 1st group (n = 22) received 5 ml of lidocaine 2% while the 2nd group (n = 25) received 4 ml of lidocaine 2% + 1 ml of betametazone under the guidance of ultrasound. Outcome measures included Numeric Rating Scale (NRS) and Likert Analogue Scale (LAS). No statistically significant difference ($p > 0.05$) was detected between the groups in NRS score values at resting ($p = 0.814$), night ($p = 0.830$), and in motion ($p = 0.145$), and LAS values with long duration of sitting ($p = 0.547$), standing ($p = 0.898$), and lying ($p = 0.326$) with evaluations at baseline, 1st week, and 1st and 3rd months after the injection. A statistically highly significant ($p < 0.005$) reduction of pain was evaluated through NRS scores at resting ($p = 0.001$), in motion ($p = 0.001$), and at night ($p = 0.001$) and LAS values with long duration of sitting ($p = 0.001$), standing ($p = 0.001$), and lying ($p = 0.001$) in both of the groups. The authors concluded that LA injections for the PS were found to be clinically effective. However, addition of CS to LA did not give an additional benefit. The main drawback of this study was its relatively small sample.

Shinomiya et al (2016) examined if differences in corticosteroid injection site influence the therapeutic effect on trigger finger and thickness of local structures such as the A1 pulley and flexor tendons. Previously untreated trigger fingers were randomly assigned to receive either (i) a true intra-sheath (group I) or (ii) an extra-sheath (group E) injection under ultrasonographic guidance. Symptom remission and recurrence rates and recurrence timing did not significantly differ between the groups. Ultrasonography revealed mean (standard deviation) pre-injection A1 pulley thicknesses of 1.1 (0.3) and 1.1 (0.2) mm in groups I and E, respectively. One month after injection, these decreased to 0.7 (0.2) and 0.8 (0.2) mm, respectively ($p < 0.05$). Furthermore, mean (standard) pre-injection flexor digitorum tendon thickness was 4.1 (0.4) and 4.0 (0.5) mm in groups I and E, respectively, and, 1 mo after injection, decreased to 3.9

(0.3) and 3.8 (0.5) mm, respectively ($p < 0.05$). However, the difference at each time-point between the 2 groups was not statistically significant. The authors concluded that true intra-sheath injection offered no apparent advantage over extra-sheath injection for treating trigger fingers because both have the same effect on local structures.

UpToDate reviews on "Subacute and chronic low back pain: Nonsurgical interventional treatment" (Chou, 2018) and "Treatment of neck pain" (Isaac, 2017) do not mention ultrasound-guidance as an adjunct for trigger point injections.

Lumbar Laminectomy With or Without Fusion

Laminectomy and laminotomy involve removal of a small part of the bony arches of the spinal canal, called the lamina, which increases the size of the spinal canal. A laminectomy or laminotomy is most commonly performed for a diagnosis of spinal stenosis. During a laminectomy the entire lamina is removed while only a portion of the lamina is removed in a laminotomy. These procedures are also often done with either a discectomy or a foraminectomy/foraminotomy.

Most individuals with acute low back problems spontaneously recover activity tolerance within 4 to 6 weeks of conservative therapy (AHCPR, 1994). Conservative therapy for acute low back pain (LBP) includes:

- Avoidance of activities that aggravate pain
- Chiropractic manipulation in the first 4 weeks if no radiculopathy
- Cognitive support and reassurance that recovery is expected
- Education regarding spine biomechanics
- Exercise program
- Heat/cold modalities for home use
- Limited bed rest with gradual return to normal activities
- Low impact exercise as tolerated (e.g., walking, swimming, stationary bike)
- Non-narcotic analgesics
- Pharmacotherapy (e.g., non-narcotic analgesics, non-steroidal anti-inflammatory drugs [NSAIDs] (as second-line choices), avoid muscle relaxants, or only use during the first week, avoid narcotics).

If conservative therapy fails to relieve symptoms of sciatica and radiculopathy and there is strong evidence of dysfunction of a specific nerve root confirmed at the corresponding level by findings demonstrated by CT/MRI, lumbar laminectomy may be proposed as a treatment option. The goal of lumbar laminectomy is to provide decompression of the affected nerve root to relieve the individual's symptoms. It involves the removal of all or part of the lamina of a lumbar vertebra. The addition of fusion with or without instrumentation is considered when there are concerns about instability.

Decompression With or Without Discectomy for Cauda Equine Syndrome

Cauda equina ("horse's tail") is the name given to the lumbar and sacral nerve roots within the dural sac caudal to the conus medullaris. Cauda equina syndrome is usually the result of a ruptured, midline intervertebral disk, most commonly occurring at the L4 to L5 level. However, tumors and other compressive masses may also cause the syndrome. Individuals generally present with progressive symptoms of fecal or urinary incontinence, impotence, distal motor weakness, and sensory loss in a saddle distribution. Muscle stretch reflexes may also be reduced. The presence of urinary retention is the single most consistent finding (Perron and Huff, 2002).

In acute cauda equine syndrome, surgical decompression as soon as possible is recommended. In a more chronic presentation with less severe symptoms, decompression could be performed when medically feasible and should be delayed to optimize the patient's medical condition; with this precaution, decompression is less likely to lead to irreversible neurological damage (Dawodu, 2005).

Cervical Laminectomy With or Without Fusion

A cervical laminectomy (may be combined with an anterior approach) is sometimes performed when acute cervical disc herniation causes central cord syndrome or in cervical disc herniations refractory to conservative measures. Studies have shown that an anterior discectomy with fusion is the recommended procedure for central or anterolateral soft disc herniation, while a posterior laminotomy-foraminotomy may be

considered when technical limitations for anterior access exist (e.g., short thick neck) or when the individual has had prior surgery at the same level (Windsor, 2006).

Discectomy alone is regarded as a technique that most frequently results in spontaneous fusion (70 to 80%). Additional fusion techniques include the use of bone grafts (autograft, allograft or artificial) with or without cages and/or the use of an anterior plate. Based on the clinical evidence, autologous or cadaveric bone grafting, with or without plating, remains the gold standard for cervical fusion. Therefore, use of an intervertebral cage for cervical fusion is considered experimental and investigational. A Cochrane systematic review (2004) reported the results of fourteen studies (n = 939) that evaluated three comparisons of different fusion techniques for cervical degenerative disc disease and concluded that discectomy alone has a shorter operation time, hospital stay, and post-operative absence from work than discectomy with fusion with no statistical difference for pain relief and rate of fusion. The authors concluded that more conservative techniques (discectomy alone, autograft) perform as well or better than allograft, artificial bone, and additional instrumentation; however, the low quality of the trials reviewed prohibited extensive conclusions and more studies with better methodology and reporting are needed.

An assessment by the BlueCross BlueShield Association Technology Evaluation Center (BCBSA, 2014) stated: "The choice of bone material for interbody fusion in [anterior cervical discectomy and fusion] ACDF has important clinical implications. Allograft bone has several drawbacks, including a minute (albeit unproven) risk of infectious disease transmission; possible immunological reaction to the allograft; and possible limited commercial availability of appropriate graft material. In contrast, the use of autograft bone in ACDF has potentially substantial morbidities at the harvest site, generally the iliac crest. These include moderate-to-severe, sometimes prolonged pain; deep infection; adjacent nerve and artery damage; and increased risk of stress fracture. Although there may be slight differences between autograft and allograft sources in the postoperative rate of union, clinical studies have demonstrated similar rates of postoperative fusion (90%–100%) and satisfactory outcomes for

single-level, anterior-plated ACDF using either bone source. Thus, the choice of graft material involves a trade-off between the risks specific to autograft harvest versus those specific to use of allograft material."

A systematic review of randomized controlled trials found no reliable evidence for use of cages over autograft for cervical spinal fusion (Jacobs et al, 2011). Noting that the number of surgical techniques for decompression and anterior cervical interbody fusion (ACIF) for cervical degenerative disc disease has increased, the investigators sought to determine which technique of ACIF gives the best outcome. From a comprehensive search, the investigators selected randomized studies that compared anterior cervical decompression and ACIF techniques, in patients with chronic single- or double-level degenerative disc disease or disc herniation. Risk of bias was assessed using the criteria of the Cochrane back review group. A total of 33 studies with 2,267 patients were included. The major treatments were discectomy alone and addition of an ACIF procedure (graft, cement, cage, and plates). The investigators stated, at best, there was very low-quality evidence of little or no difference in pain relief between the techniques. The investigators found moderate quality evidence for few secondary outcomes. The investigators found that Odom's criteria were not different between iliac crest autograft and a metal cage (risk ratio [RR]: 1.11; 95% confidence interval [CI]: 0.99-1.24). Bone graft produced more fusion than discectomy (RR: 0.22; 95% CI: 0.17-0.48). Complication rates were not different between discectomy and iliac crest autograft (RR: 1.56; 95% CI: 0.71-3.43). Low-quality evidence was found that iliac crest autograft results in better fusion than a cage (RR: 1.87; 95% CI: 1.10-3.17); but more complications (RR: 0.33; 95% CI: 0.12-0.92). The investigators concluded that, when fusion of the motion segment is considered to be the working mechanism for pain relief and functional improvement, iliac crest autograft appears to be the gold standard. The investigators stated that, when ignoring fusion rates and looking at complication rates, a cage as a gold standard has a weak evidence base over iliac crest autograft, but not over discectomy.

An evidence review by Epstein et al (2012) reached similar conclusions. These researchers (2012) noted that grafting choices available for performing anterior cervical diskectomy/fusion (ACDF) procedures have become a major concern for spinal surgeons, and their

institutions. The "gold standard", iliac crest autograft, may still be the best and least expensive grafting option; it deserves to be reassessed along with the pros, cons, and costs for alternative grafts/spacers. Although single or multilevel ACDF have utilized iliac crest autograft for decades, the implant industry now offers multiple alternative grafting and spacer devices; (allografts, cages, polyether-etherketone (PEEK) amongst others). While most studies have focused on fusion rates and clinical outcomes following ACDF, few have analyzed the "value-added" of these various constructs (e.g. safety/ efficacy, risks/complications, costs). Epstein (2012) found that the majority of studies document 95%-100% fusion rates when iliac crest autograft is utilized to perform single level ACDF (X-ray or computyed tomography [CT] confirmed at 6-12 postoperative months). Although many allograft studies similarly quote 90%-100% fusion rates (X-ray alone confirmed at 6-12 postoperative months), a recent "post hoc analysis of data from a prospective multicenter trial" (Riew KD et. al., CSRS Abstract Dec. 2011; unpublished) revealed a much higher delayed fusion rate using allografts at one year 55.7%, 2 years 87%, and four years 92%. The author found no clinically significant differences in cervical spine fusion outcomes between autograft and cages, despite an up to 10-fold difference in cost among various constructs. The author concluded that iliac crest autograft utilized for single or multilevel ACDF is associated with the highest fusion, lowest complication rates, and significantly lower costs compared with allograft, cages, PEEK, or other grafts. As spinal surgeons and institutions become more cost conscious, we will have to account for the "value added" of these increasingly expensive graft constructs.

Kersten et al (2015) stated that polyetheretherketone (PEEK) cages have been widely used during the past decade in patients with degenerative disorders of the cervical spine. Their radiolucency and low elastic modulus make them attractive attributes for spinal fusion compared with titanium and bone graft. Still, limitations are seen such as pseudoarthrosis, subsidence, and migration of the cages. The authors stated that limited evidence on the clinical outcome of PEEK cages is found in the literature other than noncomparative cohort studies with only a few randomized controlled trials. The authors conducted a systematic evidence review to assess the clinical and radiographic outcome of PEEK cages in the treatment of degenerative disc disorders and/or spondylolisthesis in the cervical spine. The systematic review included all

randomized controlled trials and prospective and retrospective nonrandomized comparative studies with a minimum follow-up of 6 months and all noncomparative cohort studies with a long-term follow-up of more than 5 years. The primary outcome variable was clinical performance. Secondary outcome variables consisted of radiographic scores. The MEDLINE, EMBASE, and Cochrane Library databases were searched according to the Preferred Reporting Items of Systematic reviews and Meta-Analyses statement and Metaanalysis Of Observational Studies in Epidemiology guidelines. A total of 223 studies were identified, of which 10 studies were included. These comprised two randomized controlled trials, five prospective comparative trials, and three retrospective comparative trials. The authors found minimal evidence for better clinical and radiographic outcome for PEEK cages compared with bone grafts in the cervical spine. No differences were found between PEEK, titanium, and carbon fiber cages. The authors stated that future studies are needed to improve methodology to minimize bias. Publication of lumbar interbody fusion studies needs to be promoted because differences in clinical and/or radiographic scores are more likely to be demonstrated in this part of the spine.

The Joint Section on Disorders of the Spine and Peripheral Nerves of the American Association of Neurological Surgeons and Congress of Neurological Surgeons (Ryken et al, 2009) conducted a systematic review to determine the efficacy of cervical interbody grafting techniques. The National Library of Medicine and Cochrane Database were queried using MeSH headings and keywords relevant to cervical interbody grafting. Abstracts were reviewed and studies that met the inclusion criteria were selected. The guidelines group assembled an evidentiary table summarizing the quality of evidence (Classes I-III). Disagreements regarding the level of evidence were resolved through an expert consensus conference. The group formulated recommendations that contained the degree of strength based on the Scottish Intercollegiate Guidelines network. Validation was done through peer review by the Joint Guidelines Committee of the American Association of Neurological Surgeons/Congress of Neurological Surgeons. The authors found that autograft bone harvested from the iliac crest, allograft bone from either cadaveric iliac crest or fibula, or titanium cages and rectangular fusion devices, with or without the use of autologous graft or substitute, have been successful in creating arthrodesis after 1- or 2-level anterior cervical

discectomy with fusion (Class II). Alternatives to autograft, allograft, or titanium cages include polyetheretherketone cages and carbon fiber cages (Class III). Polyetheretherketone cages have been used successfully with or without hydroxyapatite for anterior cervical discectomy with fusion. Importantly, recombinant human bone morphogenic protein-2 carries a complication rate of up to 23-27% (especially local edema) compared with 3% for a standard approach. The authors concluded that current evidence does not support the routine use of interbody grafting for cervical arthrodesis. Multiple strategies for interbody grafting have been successful with Class II evidence supporting the use of autograft, allograft, and titanium cages.

The Congress of Neurological Surgeons assessment (Ryken et al, 2009) stated that “class II evidence indicates that either autograft bone harvested from iliac crest, allograft bone from either cadaveric iliac crest or fibula, or titanium cages and rectangular fusion devices, with or without autologous graft or substitute are excellent interbody treatment options for obtaining cervical arthrodesis. There is an expected autograft fusion rate for non-instrumented single-level fusions better than 80% and for 2-level fusion of better than 70%. With allograft, the expected fusion rate for non-instrumented single-level fusion is > 80%, and is > 50% for 2-level fusion. The use of titanium cages carries an expectation of a fusion rate of > 70%, and often > 90% with avoidance of donor site morbidity.” The CNS assessment stated: “In choosing a graft strategy, no single type of graft has not proven consistently superior to the other. Class III evidence suggests that the surgeon consider the increased rate of subsidence with allograft but also understand that subsidence does not correlate with clinical outcome. Class III evidence also suggests that the surgeon factor in the incidence of donor pain and decrease in patient satisfaction reported with the harvest of autograft iliac crest graft.” The assessment stated: “If alternatives to auto- and allograft are preferred, therapeutic options are as follows: PEEK may be considered with or without the use of hydroxyapatite after ACDF. There is an expectation of fusion rates > 90% with fewer complications due to the absence of graft harvesting (Class III). Carbon fiber cages may be considered as well with fusion rates ranging from 55 to 62% in the larger studies (Class III). Polymethyl-methylmethacrylate may be considered to preserve intervertebral distraction after discectomy, but is a poor fusion substrate (Class II). All of the above options appear to have similar clinical outcomes equivalent to

the use of bone." The CNS assessment concluded that, "Given the generally high rates of improved clinical outcome with anterior cervical discectomy and fusion, regardless of methodology, the evaluation of medical-economic factors may play an important role in future studies."

A Senate Finance Committee Report (2012) focusing on Infuse, one substitute for bone graft, noted that company officials inserted language into studies that promoted the substitute as a better technique than the autograft technique by emphasizing the pain associated with the autograft technique.

Chemonucleolysis

Chemonucleolysis is a procedure that involves the dissolving of the gelatinous cushioning material in an intervertebral disk by the injection of chymopapain or other enzyme. The AHCPR evidence-based guideline on the management of acute back pain and the medical literature supports the use of chemonucleolysis (CNL) with chymopapain as a safe and effective alternative to surgical disc excision in the majority of patients who are candidates for surgery for intractable sciatica due to herniated nucleus pulposus (HNP). Chemonucleolysis involves the enzymatic degradation of the nucleus pulposus, and has been shown to be more effective than percutaneous discectomy since it can be successfully performed for protruded and extruded discs, just as long as the herniated disc material is still in continuity with the disc of its origin. Following CNL, in many cases, relief of sciatica is immediate; however, in up to 30% of patients, maximal relief of symptoms may take up to 6 weeks. The overall success rate for CNL in long-term follow-up (7 to 20 years) in 3,130 patients from 13 contributors averaged 77% (range of 71 to 93%), the same as that reported for surgical discectomy. In the United States, CNL is approved by the Food and Drug Administration (FDA) for use in the lumbar spine only.

On January 27, 2003, the sale and distribution of chymopapain was discontinued in the U.S. after the company producing it decided to cease its sale worldwide.

Facet Joint Blocks and Medial Branch Blocks

Facet injections, also known as facet blocks, are injections of a local anesthetic, with or without a steroid medication, into the facet joints or around the nerve supply (the medial branch nerve) to the joints. Facet injections may be given for diagnostic purposes to determine if the facet joint is the source of pain or it may be performed to treat facet pain that has previously been detected. The injections are fluoroscopically guided. If the pain is relieved, the physician will know that the facet joint appears to be the source of pain. Facet denervation may also follow a successful diagnostic facet block.

Degenerative changes in the posterior lumber facet joints have been established as a source of LBP that may radiate to the leg. Pain impulses from the medial branches of lumbar dorsal rami can be interrupted by blocking these nerves with anesthetic (facet block) or coagulating them with a radiofrequency wave (radiofrequency facet denervation). Typically, facet joint blocks are performed as a part of a work-up for back or neck pain (Wagner, 2003). Pain relief following a precise injection of local anesthetic confirms the facet joint as the source of pain. Based on the outcome of a facet joint nerve block, if the patient gets sufficient relief of pain but the pain recurs, denervation of the facet joint may be considered.

A number of uncontrolled studies have suggested positive effects of facet injections on chronic back pain (Wagner, 2003). However, randomized controlled trials (RCTs) have failed to demonstrated a benefit. A well-designed trial (n = 101) of patients who responded to a local anesthetic injection into the facet joint published in the *New England Journal of Medicine* found no difference in the likelihood of pain relief following randomization to glucocorticoid or saline facet joint injection at either 1 or 3 months post injection (Carette et al, 1991). A higher proportion of patients in the steroid injection group reported marked improvement after 6 months (46% versus 15%), but the benefit was attenuated after controlling for co-interventions used in the steroid group, and there is no biologic explanation for a delayed benefit from steroids. A second, smaller trial found no differences between steroid and/or bupivacaine injection compared to placebo (Lilius et al, 1989).

A number of systematic evidence reviews and evidence-based guidelines have evaluated the literature on facet injections for chronic back pain. Guidelines from the American Pain Society (Chou et al, 2009) stated: "We found good or fair evidence that ... facet joint injection ... are not effective." Guidelines from the American Association of Neurological Surgeons (Resnick et al, 2005) state: "Facet injections are not recommended as long-term treatment for chronic low-back pain." Guidelines from the American College of Occupational and Environmental Medicine (Hegmann, 2007) state that therapeutic facet joint injections for acute, subacute, chronic low back pain or radicular pain syndrome are "not recommended". An assessment by the Canadian Agency for Drugs and Technologies in Health (Zakaria et al, 2007) concluded: "According to the RCTs [randomized controlled trials] completed to date, FJIs [facet joint injections] with local anesthetics or steroids have not been proven to be superior to placebo for the treatment of chronic LBP [low back pain]. Steroid FJIs have not been proven to be superior to local anesthetic FJIs in the treatment of chronic neck pain secondary to a motor vehicle accident. The studies are limited. ..." An assessment for *BMJ Clinical Evidence* (McIntosh and Hall, 2007) concluded that facet injections for chronic back pain are of "unknown effectiveness". A Cochrane systematic evidence review found no clear differences between facet joint glucocorticoid and placebo injections (Staal et al, 2008). A review in UpToDate (Chou, 2009) stated: "Evidence is unavailable, unreliable, or contradictory regarding the effectiveness of glucocorticoid injections for other sites, including ... facet joint injections .... We suggest not performing these procedures for chronic low back pain".

Sacroiliac Joint Injections

Sacroiliac (SI) joint injections are performed by injecting a local anesthetic, with or without a steroid medication, into the SI joints. These injections may be given for diagnostic purposes to determine if the SI joint is the source of the low back pain or it may be performed to treat SI joint pain that has previously been detected/diagnosed. If the pain is relieved, the physician will know that the SI joint appears to be the source of pain. This may be followed up with therapeutic injections of anti-inflammatory (steroid) and/or local anesthetic medications to relieve pain for longer periods.

In a prospective, single-blinded, randomized controlled trial, Jee and colleagues (2014) compared the safety and short-term effects of ultrasound (US)-guided SIJ injections with fluoroscopy (FL)-guided SIJ injections in patients with non-inflammatory SIJ dysfunction (n = 120). All procedures were performed using an FL or US apparatus. Subjects were randomly assigned to either the FL or US group. Immediately after the SIJ injections, fluoroscopy was applied to verify the correct placement of the injected medication and intravascular injections. Treatment effects and functional improvement were compared at 2 and 12 weeks after the procedures. The verbal numeric pain scale and Oswestry Disability Index (ODI) improved at 2 and 12 weeks after the injections without statistical significances between groups. Of 55 US-guided injections, 48 (87.3%) were successful and 7 (12.7%) were missed. The FL-guided SIJ approach exhibited a greater accuracy (98.2%) than the US-guided approach. Vascularization around the SIJ was seen in 34 of 55 patients. Among the 34 patients, 7 had vascularization inside the joint, 23 had vascularization around the joint, and 4 had vascularization both inside and around the joint; 3 cases of intravascular injections occurred in the FL group. The authors concluded that the US-guided approach may facilitate the identification and avoidance of the critical vessels around or within the SIJ. Function and pain relief significantly improved in both groups without significant differences between groups. The US-guided approach was shown to be as effective as the FL-guided approach in treatment effects. However, diagnostic application in the SIJ may be limited because of the significantly lower accuracy rate (87.3%).

Radiofrequency Facet Denervation

Radiofrequency ablation (may also be referred to as RFA, percutaneous radiofrequency neuroablation, radiofrequency coagulation, radiofrequency denervation, radiofrequency lesioning, radiofrequency neuroablation, radiofrequency neurotomy or rhizotomy [articular rhizolysis]) involves the use of radiofrequency energy to denervate a nerve. One of the most commonly performed neuroablative procedures is facet denervation, which is the destruction or interruption of a facet joint nerve to relieve chronic pain in the cervical, thoracic or lumbar region of the spine.

Facet joints of the spine have joint capsules that are supplied by a branch of the posterior ramus of the spinal nerve. Percutaneous radiofrequency facet denervation, also known as radiofrequency facet joint rhizotomy or facet neurotomy, involves selective denervation using radiofrequency under fluoroscopic guidance. As a method of neurolysis, radiofrequency facet denervation has been shown to be a very safe procedure and can offer relief for many patients with mechanical LBP in whom organic pathology, most commonly a herniated lumbar disc, has been eliminated. According to the literature, it offers advantages over conventional neurolytic agents (e.g., phenol, alcohol, and hypertonic saline) because of its long lasting effects, the relative lack of discomfort, and its completely local action without any random diffusion of the neurolytic agent. Because there are no reliable clinical signs that confirm the diagnosis, successful relief of pain by injections of an anesthetic agent into the joints are necessary before proceeding with radiofrequency facet denervation. Results from many studies have shown that radiofrequency facet denervation results in significant (excellent or good) pain relief, reduced use of pain medication, increased return-to-work, and is associated with few complications. Success rate, however, depends on a careful selection of patients.

Laser Facet Denervation

Neuroablative techniques in pain management consist of several surgical and non-surgical methods to denervate a nerve. The goal of denervation is to "shut off" the pain signals that are sent to the brain from the joints and nerves. An additional objective is to reduce the likelihood of, or to delay, any recurrence by selectively destroying pain fibers without causing excessive sensory loss, motor dysfunction or other complications.

Laser ablation involves the use of laser to denervate a nerve. There is a lack of published evidence of laser facet denervation for lumbar facet pain.

Facet Chemodenervation / Chemical Facet Neurolysis

Chemical neurolysis (also referred to as chemical ablation, chemical denervation or chemodenervation) involves injection of neurolytic agents [eg, phenol, alcohol or hypertonic saline]) to denervate a nerve. The use of chemical facet injections such as alcohol, phenol and hypertonic saline has been proposed as an option for lumbar facet pain. However, there is a lack of published data to support the safety and effectiveness of this technique.

Spinal Fixation

Pedicle screw fixation systems consist of steel or titanium plates that are longitudinally inter-connected and anchored to adjacent vertebrae using bolts, hooks, or screws. Pedicle screw fixation in the spine is used to produce a rigid connection between 2 or more adjacent vertebrae in order to correct deformity and to stabilize the spine, thereby reducing pain and any neurological deficits. It is most often used in the lumbosacral spine from L1 though S1, and may also be used in the thoracic spine. Excision of tissues compressing the spinal cord (posterior decompression) is a common treatment for patients with herniated or subluxed vertebrae (spondylolisthesis), degenerative intervertebral discs, certain types of vertebral fractures, or spinal tumors. Spinal instability following decompression may be sufficiently severe to require stabilization by bony fusion (arthrodesis) of affected and adjacent vertebrae using implanted autologous bone grafts. Following placement of the graft, sufficient mechanical stability to allow its incorporation may be provided by combinations of various surgically implanted hooks, rods, or wires. However, severe instability may require surgical implantation of plates or rods anchored to vertebral pedicles using screws (pedicle screw fixation systems) in order to provide rigid 3-column fixation and minimize the risk of incomplete fusion (pseudoarthrosis or pseudarthrosis) or loss of alignment during fusion. The current medical literature suggests that rigid fixation of the lumbar spine with pedicle screws improves the chances of successful fusion as compared with patients with lumbar spine fusion not supplemented with internal fixation. Internal fusion and fixation are major operative procedures with significant risks and according to the available literature should be reserved for patients with spinal instability associated with neurological deficits, major spinal deformities, spinal fracture, spinal

dislocation or complications of tumor. Spinal fusion and pedicle screw fixation has been shown not to be effective for the treatment of isolated chronic back pain, and surgery is not advocated to treat this diagnosis in the absence of instability or neurological deficits. In July 1998, the FDA re-classified into Class II the pedicle screw spinal systems intended to provide immobilization and stabilization of spinal segments in skeletally mature patients as an adjunct to fusion in the treatment of the following acute or chronic instabilities or deformities of the thoracic, lumbar, and sacral spine: degenerative spondylolisthesis with objective evidence of neurological impairment, fracture, dislocation, scoliosis, kyphosis, spinal tumor, and failed previous fusion (pseudarthrosis). Pedicle screw systems intended for any other uses are considered post-amendment Class III devices for which pre-market approval is required.

Intervertebral Body Fusion Devices (Spine Cages)

A spine cage, also known as an interbody cage, is a small hollow cylindrical device, usually made of titanium, with perforated walls. The device is placed in the disc space between 2 vertebrae to restore lost disc height resulting from a collapsed disc and to relieve pressure on nerve roots. Currently, there are 2 intervertebral body fusion devices approved by the FDA: the BAK Interbody Fusion System (Spine-Tech, Inc.), and the Ray Threaded Fusion Cage (Surgical Dynamics, a subsidiary of United States Surgical Corporation). The BAK (Bagley and Kuslich) Interbody Fusion System and the Ray Threaded Fusion Cage (TFC) are hollow cylinders made of titanium, which may be implanted by anterior or posterior approach. Unlike pedicle screws, both of these fusion devices are permanent implants, as the literature describes bone growing into and through the implant. The safety and effectiveness of these fusion devices have not been established in 3 or more levels to be fused, previous fusion attempt at the involved level(s), spondylolisthesis or retrolisthesis of Grade II or greater. Although the BAK has received FDA approval for implantation laparoscopically, studies performed for FDA approval demonstrated significantly greater incidence of complications from anterior spinal reconstructive surgery using a laparoscopic approach than using an open approach. Furthermore, patients with laparoscopically implanted BAK fusion devices were followed for only 6 months; thus, the long-term stability of laparoscopically implanted BAK cages is unknown.

Thus, coverage of laparoscopic (endoscopic) implantation of the BAK should be denied as experimental and investigational. (See discussion of anterior endoscopic spinal reconstructive surgery above).

In a retrospective, database review, Pirkle and colleagues (2019) analyzed the rate of nonunion in patients treated with structural allograft and intervertebral cages in anterior cervical discectomy and fusion (ACDF). These investigators carried out a retrospective analysis of 6,130 patients registered in the PearlDiver national database through Humana Insurance from 2007 to 2016. All ACDF patients with anterior plating who were active in the database for at least 1 year were included in the study. Patients with a fracture history within 1 year of intervention, past arthrodesis of hand, foot, or ankle, or a planned posterior approach were excluded from the study. Patients were stratified by number of levels treated, tobacco use, and diabetic condition. Nonunion rates of structural allograft and intervertebral cage groups after 1 year were compared using Chi-squared analyses. A total of 4,063 patients were included in the allograft group, while 2,067 were included in the cage group. Overall nonunion rates were significantly higher in the cage group (5.32%) than in the allograft group (1.97%) ($p < 0.01$). When controlling for confounders, increased rates of nonunion were consistently observed in the cage group, achieving statistical significance in 25 of the 26 analyses. The authors concluded that the increased rate of nonunion associated with intervertebral cages may suggest the superiority of allograft over cages in ACDF. Level of evidence = III.

The authors noted that with any large database, there are weaknesses. The reliability of the reporting and coding was dependent upon multiple sources in an administrative data registry. These researchers were unable to obtain radiographic evidence of nonunion for individual patients and instead relied on the diagnosis codes for nonunion, an important assumption they have made in this study. As this was an observational database study, these investigators were also unable to determine the constitution of each cage placed, whether that be PEEK, titanium, mesh, or porous material. In this analysis, the authors stratified their initial population to account for the 3 most likely confounding variables for nonunion. It was entirely possible that other confounding variables exist and this may affect the analysis. Even with this large database, the nonunion patients whittled down to less than 11 patients in some sub-

analyses. One of the limitations of PearlDiver was when patient population size was less than 11, the true number was not revealed because of the potential for patient identification. The authors encountered this in some of their sub-analyses and this limited their ability to analyze the data, particularly where they attempted to control for multiple confounders. These researchers stated that future studies utilizing other data sources with sufficient sample size may be of value in further investigation. However, the PearlDiver data have been widely utilized in peer-reviewed publication. To-date, this study is the largest comparative study examining the fusion rates of ACDF using cages and structural bone graft. The authors' practice, like the majority of spine surgeons in North America, is to utilize structural bone graft in ACDF. These data suggested that allograft, when available, may be a superior option than the use of a cage in achieving arthrodesis in the cervical spine.

Key points in this study: Both structural allograft and intervertebral cage groups experienced high fusion rates. When comparing nonunion rates, these data suggested the superiority of allograft in ACDF. While the use of a cage and non-structural bone graft material remains an important surgical option, the use of allograft, when donor bone is available, may be preferable in achieving solid arthrodesis.

Vertebroplasty

Percutaneous polymethylmethacrylate vertebroplasty (PPV) is a therapeutic, interventional radiologic procedure, which consists of the injection of an acrylic bone cement (usually methyl methacrylate) into a cervical, thoracic or lumbar vertebral body lesion for the relief of pain and the strengthening of bone. The procedure is performed under fluoroscopic guidance with local anesthesia and moderate sedation. This procedure is being used for patients with lytic lesions due to bone metastases, aggressive hemangiomas, or multiple myeloma, and for patients who have medically intractable debilitating pain resulting from osteoporotic vertebral collapse.

Examples of PMMA include, but may not be limited to, Ascendx Cement, Cobalt HV, Cobalt V Radiopaque Vertebroplasty Bone Cement, Cohesion, Kyphx HV-R, Opacity+, Osteopal, Osteopal V, SPACE CpsXL, Spine-Fix

Biomimetic Bone Cement, StabiliT ER, Vertecern and Vertefix Radiopaque Bone Cement. An alternative to traditional bone cement is Cortoss Bone Augmentation Material. Cortoss is an injectable, non-resorbable synthetic material that functions as a strengthening agent for injection into vertebral bodies with compression fractures.

Results from two uncontrolled prospective studies and several case series reports, including one with 187 patients, indicated that percutaneous vertebroplasty can produce significant pain relief and increase mobility in 70% to 80% of patients with osteolytic lesions in the vertebrae. In these reports, pain relief was apparent within 1 to 2 days after injection, and appeared to persist for at least several months up to several years. While experimental studies and preliminary clinical results suggest that percutaneous vertebroplasty can also strengthen the vertebral bodies and increase mobility, it remains to be proven whether this procedure can prevent additional fractures in the injected vertebrae. In addition, the duration of effect was not known; there were no long-term follow-up data on most of these patients, and these data may be difficult to obtain and interpret in patients with an underlying malignant process because disease progression may confound evaluation of the treatment effect. Complications were relatively rare, although some studies reported a high incidence of clinically insignificant leakage of bone cement into the paravertebral tissues. In a few cases, the leakage of polymer caused compression of spinal nerve roots or neuralgia. Several instances of pulmonary embolism were also reported.

The FDA (2004) notified healthcare professionals about complications related to the use of polymethylmethacrylate bone cement to treat osteoporotic compression fractures of the spine using vertebroplasty and kyphoplasty. Reported complications, such as soft tissue damage and nerve root pain and compression, are related specifically to the leakage of bone cement. Other reported complications include pulmonary embolism, respiratory and cardiac failure, and death.

Percutaneous vertebroplasty is an in-patient procedure because it may cause compression of adjacent structures and require emergency decompressive surgery. In addition, radiation therapy or concurrent surgical interventions, such as laminectomy, may also be required in patients with compression of the spinal cord due to ingrowth of a tumor.

An assessment of percutaneous vertebroplasty by the National Institute for Clinical Excellence (NICE, 2003) concluded that "current evidence on the safety and efficacy of percutaneous vertebroplasty appears adequate".

However, 2 subsequently published RCTs published in the *New England Journal of Medicine* have found no significant benefit with vertebroplasty. In the Investigational Vertebroplasty Safety and Efficacy Trial (INVEST), Kallmes et al (2009) reported that pain and disability outcomes at 1 month in a group of patients who underwent vertebroplasty were similar to those in a control group that underwent a sham procedure. In the other trial, Buchbinder et al (2009) measured pain, quality of life, and functional status at 1 week and at 1, 3, and 6 months after sham and active vertebroplasty and found there were no significant between-group differences at any time point. As in INVEST, patients in the 2 study groups had improvement in pain.

The Society for Interventional Radiology (SIR, 2009) had identified a number of issues in interpreting these studies, including potential biases in patient selection, the use of vertebroplasty in older (greater than 3 months) fractures, and a potentially inadequate amount of polymethylmethacrylate (PMMA) that was injected into the vertebrae. The SIR concluded: "We recognize the value of randomized controlled trials and evidence-based medicine. But based on the above-discussed weakness in the studies and the degree of discordance between the outcomes of these studies, prior studies and experience, we believe it is premature and possibly incorrect – to conclude that vertebroplasty is no better than a control sham procedure (trigger point, facet injection). We suggest waiting for the results of the VERTOSS 2 trial to be published and encourage larger clinical trials to address the weaknesses of the two *New England Journal of Medicine* articles".

In a retrospective study, He and colleagues (2008) examined if a repeat percutaneous vertebroplasty (PV) is effective on pain-relief at the vertebral levels in patients who had previously undergone PV. Of the 334 procedures of PV performed in 242 patients with osteoporotic vertebral compression fractures from October 2000 to June 2006 in the authors' institute, 15 vertebrae in 15 patients with unrelieved pain in 4 to 32 days after an initial PV were treated with a repeat vertebroplasty. The clinical

outcomes were assessed by measurements of visual analog scale (VAS), and the imaging features were analyzed pre- and post-procedure. The mean volume of polymethylmethacrylate injected in each vertebra was 4.0 ml (range of 1.5 to 9 ml) in the repeat PV. During the first month of follow-up after repeat PV in this series, a mean VAS scores of the pain level was reduced from 8.6 (range of 7 to 10) pre-procedure to 1.67 points (range of 0 to 4) post-procedure, with a mean reduction of 6.93 points (range of 4 to 8). Complete and partial pain relief were reached in 11 (73%) and 4 patients (27%), respectively in a mean follow-up of 15 months. No serious complications related to the procedures occurred, however asymptomatic polymethylmethacrylate leakage around vertebrae was demonstrated on radiograph or computed tomography in 2 patients. The authors concluded that the outcomes of this series suggested that repeat PV is effective at the same vertebral levels in patients without pain-relief who underwent previous PV. Absent or inadequate filling of cement in the unstable fractured areas of the vertebral body may be responsible for the unrelieved pain after the initial PV.

An accompanying editorial by Kallmes (2008) of the afore-mentioned article stated that "[u]nfortunately, limitations in the current study likely preclude definitive answers, but still the series may help focus future studies". The editorialist also noted that while the authors found insufficient or absent filling in 100% of the failed cases, they did not provide any information regarding the frequency in which they had insufficient or absent filling in the other 227 (successful) cases. Furthermore, Kallmes is still somewhat concerned about the safety of the repeat procedure.

Absolute contraindications to percutaneous vertebroplasty or kyphoplasty (balloon-assisted vertebroplasty) include, but may not be limited to, the following:

- Allergy to bone cement or contrast media; *or*
- Asymptomatic vertebral compression fractures; *or*
- Individual is improving with medical therapy; *or*
- Nonfractured vertebral levels; *or*
- Ongoing local or systemic infection; *or*
- Osteomyelitis of the target vertebra; *or*

- Prophylactic treatment for osteoporosis to prevent future fractures; *or*
- Retropulsed bone fragment resulting in myelopathy; *or*
- Spinal canal compromise secondary to tumor resulting in myelopathy; *or*
- Uncorrected coagulation disorders.

Relative contraindications to percutaneous vertebroplasty include, but may not be limited to, the following:

- Asymptomatic retropulsion of a fracture fragment causing significant spinal compromise; or
- Asymptomatic tumor extension into the epidural space; or
- Radiculopathy in excess of vertebral pain, caused by a compressive syndrome unrelated to vertebral collapse.

Clark et al (2016) hypothesized that vertebroplasty would provide effective analgesia for patients with poorly controlled pain and osteoporotic spinal fractures of less than 6 weeks' duration. The effectiveness of vertebroplasty, using an adequate vertebral fill technique, in fractures of less than 6 weeks' duration has not been specifically assessed by previously published masked trials. This was a multi-center, randomized, double-blind, placebo-controlled trial of vertebroplasty in 4 hospitals in Sydney, Australia. These researchers recruited patients with 1 or 2 osteoporotic vertebral fractures of less than 6 weeks' duration and Numeric Rated Scale (NRS) back pain greater than or equal to 7 out of 10. They used an automated telephone randomization service provided by the National Health and Medical Research Council to assign patients (1:1; stratified according to age, degree of vertebral compression, trauma, corticosteroid use, and hospital) to either vertebroplasty or placebo, immediately before the procedure. Patients received conscious sedation. Vertebroplasty was carried out with the adequate vertebral fill technique and the placebo procedure with simulated vertebroplasty. Follow-up was for 6 months. Outcome assessors and patients were masked to treatment allocation. The primary outcome was the proportion of patients with NRS pain below 4 out of 10 at 14 days post-intervention in the intention-to-treat population. Between November 4, 2011, and December 5, 2014, a total of 120 patients were enrolled; 61 patients were randomly assigned to vertebroplasty and 59 to placebo. A total of 24 (44 %)

patients in the vertebroplasty group and 12 (21 %) in the control group had an NRS pain score below 4 out of 10 at 14 days (between-group difference 23 percentage points, 95 % CI: 6 to 39; p = 0·011); 3 patients in each group died from causes judged unrelated to the procedure. There were two serious adverse events (AEs) in each group, related to the procedure (vertebroplasty group) and the fracture (control group). The authors concluded that this trial showed effectiveness for vertebroplasty in reducing pain from osteoporotic spinal fractures of less than 6 weeks when compared with a true placebo control. Subgroup analysis suggested that most benefit from vertebroplasty was in the thoracolumbar spinal segment and further research is needed to evaluate this finding.

The authors stated that this study had several drawbacks. First, 8 patients (6 vertebroplasty and 2 placebo) did not have day-14 outcome measures because of revoking consent, delirium, or not being contactable. If all were included in the analysis and presumed to be treatment failures, there would be a minor effect on primary outcome (between-group difference 19 percentage points, 95 % CI: 3 to 35; p = 0.023). Second, 20 patients (11 vertebroplasty and 9 placebo) were unable to attend the clinic at day-14 and were interviewed by telephone. The NRS pain question did not change so this should not have affected the primary outcome. Third, 85 % of the procedures were performed in 1 center. Centers with high procedure rates could have superior outcomes possibly affecting the generalizability of these findings. This proportion was not greatly dissimilar to one masked trial where 68 % (53 of 78) of procedures were done in 1 centre and 87 % (68 of 78) in 2 centers; but was quite different to the other masked trial. in this regard, recruitment in 3 of the 4 centers proved difficult, as for previous placebo trials, and they failed to meet their enrolment targets.

In an editorial, Hijji et al (2017) stated that the clinical value of study by Clark et al (2016) may be limited. The previously performed randomized controlled trials by Kallmes et al (2009) and Buchbinder et al (2009) identified no differences in outcomes following control and vertebroplasty treatments for osteoporotic vertebral fractures; however, the study populations consisted of patients presenting early and late following the onset of their symptomology. One of the primary reasons for performing this study was to identify whether early intervention with vertebroplasty would improve patient outcomes compared to conservative management.

However, to strengthen the conclusions, especially in the setting of conflicting findings to these previous studies, the present study should have also compared early intervention to late intervention. Both previous studies were able to perform subgroup analyses with patients undergoing early intervention, maintaining the result that no benefit was achieved with vertebroplasty compared to placebo treatment. However, the patient population in the current trial only included those receiving early intervention; therefore, not allowing for this separate analysis. As such, it was difficult to conclude that it was the early intervention itself that caused the conflicting results, especially in combination with the methodological flaws mentioned previously. The authors also attempted to supplement their clinical findings with radiographic data; however, their measurements relied simply on vertebral height of the affected vertebral bodies. This also had limited utility, as the polymethylmethacrylate (PMMA) used in the vertebroplasty could substantially impact the radiographic interpretation due to its radiopaque qualities. Hijji et al (2017) noted that the study by Clark et al (2016) did improve on a few of the drawbacks exhibited in previous RCTs examining vertebroplasty; however, the flaws of this study significantly limited its ability to provide any substantial conclusions regarding the effectiveness of vertebroplasty for osteoporotic vertebral fractures. The previously performed double-blind, RCTs appeared to be of superior methodological quality, bringing into question the conflicting findings of the study by Clark et al (2016). The editorialists stated that further investigations with larger sample sizes and improved analytic and recruitment methods are needed to overcome many of the drawbacks of this study.

In a prospective, randomized , single-center study, Yang et al (2016) examined if percutaneous vertebroplasty (PVP) would offer extra benefits to aged patients with acute osteoporotic vertebral compression fractures (OVCFs) over conservative therapy (CV). Patients aged at 70 years or above with acute OVCF and severe pain from minor or mild trauma were assigned randomly to PVP and CV groups. The primary outcome was pain relief as measured by VAS score in 1-year follow-up period. The second outcome was quality of life assessed with ODI and Quality of Life Questionnaire of the European Foundation for Osteoporosis (QUALEFFO). Patient satisfaction surveys were also recorded. A total of 135 patients were enrolled, and 107 (56 in PVP group; 51 in CV group) completed 1-year follow-up. In PVP group, the vertebroplasty procedure

was performed at a mean of 8.4 ± 4.6 days (range of 2 to 21 days) after onset. Vertebroplasty resulted in much greater pain relief than did conservative treatment at postoperative day 1 ($p < 0.0001$). At every time-point of follow-up, pain relief and QOL were significantly improved in PVP group than in CV group at 1 week, 1 month, 3 months, 6 months, and 1 year (all $p < 0.0001$). The final follow-up surveys indicated that patients in PVP group were significantly more satisfied with given treatment ($p < 0.0001$). Furthermore, lower rate of complications was observed in PVP group ($p < 0.0001$). The authors concluded that in aged patients with acute OVCF and severe pain, early vertebroplasty yielded faster, better pain relief and improved functional outcomes, which were maintained for 1 year. Furthermore, it showed fewer complications than conservative treatment. Level of Evidence = II.

The authors stated that the major drawback of this trial was its single-center design with relatively small population (56 in the PVP group) and short-term follow-up (1 year). Second, the findings were not generalizable because of the small sample from a single institution. These researchers intended to continue their study with satisfactory randomization to involve multi-center researchers and determine the long-term outcomes of the procedure. Third, treatment could not be masked. Different from the blinded randomized controlled study, knowledge of the assignment may have affected patient responses to questions or researcher assessments. However, this limitation is difficult to overcome in this type of study.

In a commentary on the study by Yang et al (2016), Kaito (2016) stated that even after 2 RCTs in which patients with back pain and vertebral fracture underwent either VP or sham intervention showed no significant differences in outcomes between these procedures until 6 postoperative months in 2009, the effectiveness of VP is still controversial. These trials recently reported no significant difference between outcomes of VP and the sham intervention at 1 and 2 post-operative years. Kaito (2016) noted that although the findings of the study by Yang et al (2016) were not generalizable because of the small sample from a single institution, the authors appropriately acknowledged limitations of the design, which prohibited the drawing of a strong causal inference, and the small sample, which limited their ability to control for confounding differences. Kaito stated that Yang et al addressed an interesting and highly controversial

topic. VP is likely to be unnecessary for all patients with painful osteoporotic vertebral fractures; however, the patients who will truly benefit from surgery need to be better identified.

Kyphoplasty

Kyphoplasty (also known as balloon-assisted vertebroplasty) is a minimally-invasive orthopedic procedure, which has been developed to restore bone height lost due to painful osteoporotic compression fractures. It is a modification of the vertebroplasty procedure, and involves the insertion of 1 or 2 balloon devices into the fractured vertebral body. Once inserted, the surgeon inflates the balloon(s) to create a cavity and to compact the deteriorated bone with the intent to restore vertebral height. The balloon(s) are then removed and the newly created cavity is filled with the surgeon's choice of bone filler material, creating an internal cast for the fractured area.

The Kiva VCF Treatment System is an implantable device which has been proposed for use with a vertebroplasty or kyphoplasty procedure for reduction and treatment of spinal fractures. PMMA bone cement is used to fill the implant once it is placed.

An assessment of balloon kyphoplasty by the National Institute for Health and Clinical Excellence (NICE, 2006) concluded that "[c]urrent evidence on the safety and efficacy of balloon kyphoplasty for vertebral compression fractures appears adequate to support the use of this procedure provided that normal arrangements are in place for consent, audit and clinical governance". The NICE assessment reviewed 3 non-randomized studies, 2 of which compared balloon kyphoplasty with conventional medical care (physical and analgesic therapy) and 1 which compared the procedure with vertebroplasty. All 3 studies found that patients who had undergone balloon kyphoplasty had improved pain scores compared with the control group at a maximum follow-up of 24 months. The assessment noted that the specialist advisors to NICE expressed uncertainties about whether the improvements following balloon kyphoplasty (reduced pain and height restoration) are maintained in the long term. In clinical studies, the most common complication following balloon kyphoplasty was cement leakage, occurring in up to

11% of patients. Other potential complications of kyphoplasty include infection, allergy, and spinal cord or nerve root injury caused by incorrect needle placement.

Based on the results of an assessment, the Ontario Ministry of Health and Long Term Care (2004) reached the following conclusions about balloon kyphoplasty: "There are currently two methods of cement injection for the treatment of osteoporotic VCFs. These are vertebroplasty and balloon kyphoplasty. Although no RCT has been conducted to compare the two techniques, the existing evidence shows that balloon kyphoplasty is a reasonable alternative to vertebroplasty, given the lower reported peri-operative and long-term complications of balloon kyphoplasty".

Wardlaw et al (2009) reported positive results with kyphoplasty compared with non-surgical care in a non-blinded, multi-center RCT. The investigators randomly assigned 300 adults with 1 to 3 acute vertebral fractures to kyphoplasty (n = 149) or non-surgical care (n = 151). At 1 month, mean SF-36 Physical Component Score (PCS) improved by 7.2 points (95% confidence interval [CI]: 5.7 to 8.8) in the kyphoplasty group, and by 2.0 points (95% CI: 0.4 to 3.6) in the non-surgical group, a difference between groups that was statistically significant ($p < 0.0001$). The investigators reported that the frequency of adverse events did not differ between groups. There were 2 serious adverse events related to kyphoplasty (hematoma and urinary tract infection); other serious adverse events (such as myocardial infarction and pulmonary embolism) did not occur peri-operatively and were not related to procedure. Limitations of this study include the lack of blinding, and comparison to conservative treatment rather than a sham procedure.

The California Technology Assessment Forum (Karliner, 2009) concluded that balloon kyphoplasty meets CTAF criteria for safety, effectiveness and improvement in health outcomes for the treatment of recent (less than 3 month old) osteoporotic vertebral compression fractures confirmed by MRI.

Sacroplasty

Sacroplasty is a variation of the vertebroplasty technique, and involves the injection of polymethylmethacrylate cement into sacral insufficiency fractures for stabilization. Under fluoroscopic guidance, PMMA is injected into the sacrum at the fracture site, in an attempt to stabilize the fracture. Sacral insufficiency fractures (SIFs) can cause LBP in osteoporotic patients. Symptomatic improvement may require up to 12 months. Treatment includes limited weight-bearing and bed rest, oral analgesics, and sacral corsets. Significant mortality and morbidity are associated with pelvic insufficiency fractures. Percutaneous sacroplasty is being developed as an alternative treatment for SIF patients.

Frey et al (2007) reported on a prospective observational cohort study of the safety and efficacy of sacroplasty in consecutive osteoporotic patients with SIFs. Each procedure was performed under intravenous conscious sedation using fluoroscopy. Two bone trochars were inserted between the sacral foramen and sacroiliac joint through which 2 to 3 ml of polymethylmethacrylate was injected. A total of 37 patients, 27 females, were treated. Mean age was 76.6 years, and mean symptom duration was 34.4 days. All patients were available at each follow-up interval except 1 patient who died due to unrelated pulmonary disease before the 4-week follow-up. The investigators reported that mean VAS score at baseline was 7.7 and 3.2 within 30 mins, and 2.1 at 2, 1.7 at 4, 1.3 at 12, 1.0 at 24, and 0.7 at 52 weeks post-procedure. The investigators found that improvement at each interval and overall was statistically significant using the Wilcoxon Rank Sum Test. One case of transient S1 radiculitis was encountered. The investigators concluded that sacroplasty appears to be a safe and effective treatment for painful SIF. Limitations of this study include its small size, limited duration of follow-up, and lack of control group.

Vesselplasty

Vesselplasty (Vessel-X, A-Spine Holding Group Corp., Taipei, Taiwan) is an image-guided procedure that attempts to solve the problem of cement leakage out of the vertebral body, which can happen during both vertebroplasty and kyphoplasty. Cement leakage, a common problem with vertebroplasty particularly in lytic lesions (Mathis and Wong, 2003),

has been reported in up to 30% to 70% of cases. Most occurrences, however, are asymptomatic (Cortet et al, 1997). Vesselplasty uses a porous polyethylene terephthalate balloon to create both a cavity and contain the cement, thereby, allowing only a small amount of cement to permeate into the vertebral body.

Flors et al (2009) evaluated the use of vesselplasty to treat symptomatic vertebral compression fractures (VCFs) in 29 patients. All patients had been undergoing medical therapy for 1 or more painful VCFs. Pain, mobility, and analgesic use scores were obtained, and restoration of vertebral body height was evaluated. A 2-tailed paired Student's t test was used to compare differences in the mean scores for levels of pain, mobility, and analgesic use before and after the procedure and to evaluate changes in vertebral body height. Seven of the 29 patients had fractures in more than 1 level, for a total of 37 procedures. The cause of the vertebral collapse was osteoporosis in 27 (73%), high-impact trauma in 5 (13.5%), myeloma in 3 (8%), and metastatic fracture in 2 (5.4%). The average pain score before treatment was 8.72 +/- 1.25 (SD), whereas the average pain score after treatment was 3.38 +/- 2.35. The average mobility score before treatment was 2.31 +/- 1.94, whereas the average mobility score after treatment was 0.59 +/- 1.05 ($p < 0.001$). The average analgesic use score before treatment was 3.07 +/- 1.46, whereas it was 1.86 +/- 1.90 after treatment ($p < 0.001$). There was no evidence of clinical complications. The authors concluded that vesselplasty offers statistically significant benefits in improvements of pain, mobility, and the need for analgesia in patients with symptomatic VCFs, thus providing a safe alternative in the treatment of these fractures.

While vesselplasty appears to be a promising new technique for VCFs, there is insufficient evidence of its safety and effectiveness. Prospective, randomized, controlled studies with a larger number of patients and long-term follow-up are needed.

Epiduroscopy

Epiduroscopy involves insertion of a fiberoptic camera through the sacral hiatus into the lower epidural space, which is then guided upwards towards the lower lumbar discs and nerve roots. Epidural adhesions can be released and anesthetic and steroid injected around nerve roots. In

September 1996, the epiduroscope (myeloscope) was cleared by the FDA for visualization of the epidural space. It has been used in the outpatient setting for the diagnosis and treatment of intractable LBP. Insertion of this miniature fiberoptic scope into the epidural space allows direct visualization of scarring and placement of a catheter through which fluid is injected under pressure to break down scar tissue and lyse adhesions. Although a number of pain treatment centers advertise the availability of this technique and claim it to be successful, there is insufficient scientific evidence in the peer-reviewed medical literature to support the clinical utility of this technique for diagnosis or therapy in patients with spinal pain syndromes, including those with failed back surgery syndromes. Moreover, currently available non-invasive technologies allow adequate visualization of the epidural space to confirm pathology contained therein. An assessment of epiduroscopy for the Australian Safety and Efficacy Register of New Interventional Procedures (ASERNIP-S, 2003) concluded that "[t]here is little high-quality evidence available on the safety and efficacy of epiduroscopically guided surgery/drug delivery... More studies are needed to compare the safety and efficacy of epiduroscopy relative to other procedures". An assessment by the National Institute for Clinical Excellence (NICE, 2004) concluded that "current evidence on the safety and efficacy of endoscopic epidural procedures does not appear adequate for these procedures to be used without special arrangements for consent and for audit or research." The NICE assessment found that "The studies identified were small and uncontrolled. Some measures used in these studies to assess outcomes, such as scores of pain and function, were of unknown validity".

Epidural Lysis of Adhesions

Epidural lysis of adhesions is a pain management procedure that has been proposed as a method to relieve chronic back pain. This procedure may also be known as adhesiolysis, endoscopic adhesiolysis, epidurolysis, percutaneous adhesiolysis or percutaneous epidural neuroplasty. It differs from epidural injections as it attempts to treat the neural (nerve) adhesions that cause the pain. Epidural lysis of adhesions can be performed by use of a fiberoptic endoscope (epiduroscopy), percutaneously with the use of a catheter (flexible tube) or with the more specialized Racz catheter.

In epiduroscopy, normal saline is injected into the sacral canal to distend and decompress the epidural space; purportedly the fiberoptic endoscope can then directly disrupt the fibrosis, scar tissue or adhesions. This procedure is generally an outpatient procedure utilizing local anesthesia and light sedation.

In the percutaneous procedure utilizing the Racz catheter, the specialized epidural catheter is inserted under fluoroscopy via the sacral canal. The injection of dye (an epidurogram) may indicate the area of adhesions and provide a way to perform lesion-specific lysis utilizing the flexible wire embedded catheter. Local anesthetic, corticosteroid and hypertonic sodium chloride solution injections via the catheter are performed daily for three days. During this time the catheter is left in place and the individual is generally hospitalized.

A similar version of the procedure involves a single use catheter (instead of the Racz catheter) which is removed after the lysis is completed. The procedure may be repeated at a later date, but would require a new catheter placement.

The Racz catheter is a small caliber, flexible catheter that is introduced into the sacral hiatus and into the lumbro-sacral epidural space. The Racz catheter is used to release adhesions deliver steroids and anesthetics into the epidural space. There is no evidence from adequate well-designed RCTs in the peer-reviewed medical literature supporting the safety and effectiveness of manipulation of an indwelling epidural Racz catheter or epidural injections of hypertonic saline or hyaluronidase to relieve back pain in patients with epidural adhesions, adhesive arachnoiditis, or failed back syndrome from multiple previous surgeries for herniated lumbar disk. The Racz epidural catheter was cleared by the FDA based on a 510(k) pre-market notification (PMN) due to FDA's judgment that the device was "substantially equivalent" to devices that were marketed prior to the 1976 Medical Device Amendments to the Food, Drug and Cosmetic Act; thus, the manufacturer was not required to provide the evidence of effectiveness that is necessary to support a pre-market approval (PMA) application. Most of the reported studies of the Racz catheter are retrospective (Racz and Holubec, 1989; Manchikanti et al, 2001; Manchikanti et al, 1999) or lacking a control group (Racz et al, 1999). Manchikanti, founder and president of the American Society of

Interventional Pain Physicians (ASIPP), is a leading advocate of the use of the Racz catheter (Manchikanti et al, 1999; Manchikanti and Bakhit, 2000; Manchikanti and Singh, 2002). He is lead author of ASIPP guidelines which incorporate the Racz catheter into the management of chronic spinal pain (Manchikanti et al, 2003). Manchikanti et al (2001, 2004) has reported the results of 2 controlled clinical studies of the Racz catheter in the ASIPP's official journal Pain Physician. One of these studies involved 45 patients with chronic LBP, 30 of whom received Racz catheter treatment, and a control group of 15 patients who did not receive Racz catheter treatment. The study was unblinded and utilized a biased control group, as control group subjects were patients who refused Racz catheter treatment, either because coverage was denied by their insurer or for other reasons (Manchikanti et al, 2001). In another study, subjects with chronic LBP were randomized to a sham control group or 2 treatment groups (n = 25 in each group). Nineteen of 25 subjects in the control group were unblinded or lost to follow-up before completion of the 12-month study (Manchikanti et al, 2004). Both of these controlled clinical studies involve small groups of patients and are from the same group of investigators from a single private practice, raising questions about the generalizability of the findings (Manchikanti et al, 2001: Manchikanti et al, 2004). The small sample sizes of these studies do not allow adequate evaluation of potential adverse outcomes that may occur with the procedure (Fibuch, 1999). A Joint Health Technology Assessment of the German Medical Association and the German National Association of Statutory Health Insurance Physicians (KBV, 2003) concluded that, "due to insufficient evaluation and lack of empirical data, at present there is no convincing evidence for the efficacy or effectiveness of the Racz treatment procedure".

The National Institute for Clinical Excellence (NICE, 2004) assessed mobilization and division of epidural adhesions, and concluded that "[c]urrent evidence on the safety and efficacy of endoscopic division of epidural adhesions does not appear adequate for this procedure to be used without special arrangements for consent and for audit or research". The assessment noted that studies of epidural lysis of adhesions are "small and uncontrolled". In addition, NICE noted that "[s]ome measures used in the studies to assess outcomes, such as scores of pain and

function, were of unknown validity". NICE stated that the main safety concerns are infection, bleeding, neurological damage, epidural hematoma, and damage to the nerve roots or cauda equina.

Veihelmann et al (2006) examined if epidural neuroplasty is superior to conservative treatment with physiotherapy in treating patients with chronic sciatica with or without LBP. A total of 99 patients with chronic LBP were enrolled in this study and randomly assigned into either a group with physiotherapy (n = 52) or a second group undergoing epidural neuroplasty (n = 47). Patients were assessed before and 3, 6, and 12 months after treatment by a blinded investigator. After 3 months, the VAS score for back and leg pain was significantly reduced in the epidural neuroplasty group, and the need for pain medication was reduced in both groups. Furthermore, the VAS for back and leg pain as well as the Oswestry disability score were significantly reduced until 12 months after the procedure in contrast to the group that received conservative treatment. The authors concluded that epidural neuroplasty results in significant alleviation of pain and functional disability in patients with chronic LBP and sciatica based on disc protrusion/prolapse or failed back surgery on a short-term basis as well as at 12 months of follow-up. Moreover, these investigators stated that further prospective randomized double-blinded studies are needed to prove the effectiveness of epidural neuroplasty in comparison to placebo and in comparison to open discectomy procedures.

Microsurgical Anterior Foraminotomy

Microsurgical anterior foraminotomy has been developed to improve the treatment of intractable cervical radiculopathy. This new technique provides direct anatomical decompression of compressed nerve roots by removing the compressive spondylotic spur or disc fragments through the holes of unilateral anterior foraminotomies. Using microsurgical instruments, the surgical approach exposes the lateral aspect of the spinal column through a small incision at the front of the neck in a naturally occurring crease. The affected nerve root is exposed, and a herniated disc or bone spur is removed to decompress the nerve. By removing only the herniated portion of the disc, the procedure is intended to preserve normal disc function and avoid bone fusion. As it utilizes a microsurgical technique that minimizes laminectomy and facet trauma,

this technique does not require bone fusion or post-operative immobilization. However, there is a paucity of clinical studies to validate the effectiveness of this approach. The studies reported in the medical literature involve a small number of patients, are published by just one author, and a considerable portion of each article discusses only the technical aspects of the procedure.

Open Sacroiliac Fusion

Sacroiliac fusion involves bony fusion of the sacroiliac joint for stabilization. Sacroiliac joint (SIJ) fusion has been suggested as a possible treatment option for individuals with low back pain due to sacroiliac joint dysfunction or syndrome. This procedure may be performed by an open surgical approach or as a minimally invasive procedure in order to place plates and/or screws to develop a bony fusion across the SIJ for stabilization. There is insufficient scientific evidence to support use of sacroiliac fusion in treating LBP due to sacroiliac joint syndrome.

In the 1920's, sacroiliac dysfunction was a common diagnosis and fusion of this joint was the most common form of back surgery. However, there is little evidence that the sacroiliac joint is a common source of back pain. European guidelines on the diagnosis and treatment of pelvic girdle pain (Vleeming et al, 2004) recommend against the fusion of sacroiliac joints. The guidelines note that severe traumatic cases of pelvic girdle pain can be an exception to this recommendation, but only when other non-operative treatment modalities have failed. In that case, pre-operative assessment with an external fixator for 3 weeks to evaluate longer lasting effects of fixation, is recommended (Wahlheim, 1984; Slatis and Eskola, 1989; Sturesson et al, 1999). The authors identified no controlled trials of sacroiliac fusion. Available evidence consists of cohort studies (level D evidence) (Smith-Petersen and Rogers, 1926; Gaenslen, 1927; Hagen, 1974; Olerud and Wahlheim, 1984; Waisbrod et al, 1987; Moore, 1995; Keating, 1995; Belanger and Dall, 2001; Berthelot et al, 2001; van Zwienen et al, 2004; Giannikas et al, 2004). The guidelines note that, in all reports of fusion surgery, an operation took place only on patients in whom non-operative treatment had been unsuccessful. The cohort studies included from 2 to 77 patients and the results were assessed by

the authors as fair to excellent in 50 to 89% of the patients. However, controlled studies are necessary to reach firm conclusions about the effectiveness of this procedure in the treatment of back pain.

Guidelines on treatment of LBP from the Colorado Department of Labor and Employment (2005) state that sacroiliac joint fusion is of limited use in trauma and is considered to be under investigation for patients with typical mechanical LBP: "Until the efficacy of this procedure for mechanical low back pain is determined by an independent valid prospective outcome study, this procedure is not recommended for mechanical low back pain".

Microdiskectomy

Discectomy (diskectomy) is the most common surgical treatment for ruptured or herniated discs, particularly of the lumbar spine, though it may also be used on the cervical or thoracic spine. During a discectomy, the surgeon removes the section of the disc that is protruding from the disc wall and any other disc fragments that may be pressing on a nerve root or the spinal cord. A discectomy may be "open" or it may be performed microscopically (known as a microdiscectomy). Both procedures allow for direct visualization of the vertebra, disc and other surrounding structures. The microdiscectomy utilizes a special microscope or magnifying instrument to view the disc and nerves, which makes it possible to remove the disc material through a smaller incision. This smaller incision reduces the risk of damage to the surrounding tissues, which decreases the potential complications.

Endoscopic Diskectomy

There is insufficient evidence from clinical studies proving additional benefits from using an endoscope for performing disc decompression (such as in percutaneous endoscopic diskectomy or endoscopic laser percutaneous diskectomy (LASE)). At this time there are no reliable clinical studies of endoscopic spinal surgery that have included an adequate comparison group of patients receiving open procedures. In addition, there is limited evidence on the long-term outcomes resulting from these endoscopic procedures. Gibson et al (2002), reporting on the

results of a systematic review of studies on surgery for lumbar disc prolapse, explained that "[t]here is currently no evidence supporting endoscopic... treatment of disc prolapse".

Yeung Endoscope Spine Surgery (Arthroscopic Microdiskectomy, Percutaneous Endoscopic Diskectomy With or Without Laser (PELD))

An arthroscopic microdiscectomy, also known as a percutaneous endoscopic discectomy (PED), has been proposed as another alternative to the traditional open procedure or the microdiscectomy. A cannula is inserted, with fluoroscopic guidance, near the spine through which an endoscope and very small surgical instruments are then inserted. The herniated portion of the disc can then be removed. This procedure does not allow direct visualization of the disc or surrounding tissues and is generally performed under conscious sedation, rather than general anesthesia. Examples of devices used in an arthroscopic microdiscectomy/percutaneous endoscopic discectomy include, but may not be limited to, the AccuraScope DND, Joimax iLESSYS, Joimax TESSYS or Yeung Endoscopic Spinal System (Y.E.S.S.).

Yeung Endoscopic Spinal Surgery (YESS) (also known as arthroscopic microdiskectomy or percutaneous endoscopic diskectomy (PELD)) is an endoscopic approach to lumbar disc surgery that involves a multi-channel scope and special access cannulae that allow spinal probing in a conscious patient, diagnostic endoscopy, and "minimally invasive surgery" (Yeung and Porter, 2002). The Yeung Endoscope Spine System (Y.E.S.S.) (Richard Wolf Surgical Instrument Corp., Vernon Hills, IL) or similar specialized instruments may be used to perform these procedures. The spinal endoscope is used to direct probing and targeted fragmentectomy of disc herniations. In addition, the approach may be used for foraminoplasty, where an endoscope-assisted laser is used to widen the exit route foramina of the lumbar spine and ablate any protruding portions of the intervertebral disk. Typically, procedures are performed at several levels of the spine, either simultaneously or in close temporal succession. Other adjunctive therapeutic procedures may be performed such as applying chemonucleolytic agents, lasers, radiofrequency technology, electrothermal energy, flexible mechanical instruments or intradiscal steroids. Supporters of arthroscopic

microdiskectomy state that it provides visualization at the same time as application of therapeutic services. In addition, they argue that the ability to provoke pain while the patient is in the aware state and able to communicate during surgery allows the surgeon to better identify and treat the source of the patient's back pain. However, there is inadequate evidence to determine whether the results of arthroscopic microdiskectomy are as durable or as effective as open spinal surgery. A particular concern is whether this microendoscopic approach allows for adequate visualization of the spine during surgery. Literature to date on arthroscopic microdiskectomy has been limited to review articles and reports of retrospective case series. There are no published prospective, RCTs of arthroscopic microdiskectomy, and there are no prospective studies with long-term follow-up. In addition, the studies of Y.E.S.S. that have been published thus far have been from a single investigator group, raising questions about the generalization of the findings. Thus, arthroscopic microdiskectomy does not meet Aetna's criteria.

Minimally Invasive Lumbar Decompression Procedures

Minimally invasive approaches for laminectomy, laminotomy, foraminectomy or foraminotomy have also been proposed as a newer treatment option by some surgeons. They may utilize either an endoscopic or laparoscopic approach for the procedure, which allows direct visualization of the surgical field.

Additionally, percutaneous procedures have been proposed as an alternative surgical approach for laminectomy, laminotomy, foraminectomy or foraminotomy. The percutaneous procedures are generally performed in an outpatient setting with the individual awake but sedated. Percutaneous spinal procedures do not allow direct visualization of the surgical field. Examples of percutaneous image-guided decompression procedures for lumbar spinal stenosis are the MILD procedure and decompression with the Totalis Direct system, both of which utilize trocars to access the area of stenosis (resection of the ligamentum flavum).

The North American Spine Society defines an open procedure done through an incision of approximately one inch or more. Minimally invasive lumbar decompression is performed through small incisions of less than 1

inch. Minimally invasive lumbar decompression procedures include those performed under direct visualization using specialized tubular retractors, and procedures performed under indirect visualization.

These approaches are not supported by reliable evidence in the peer reviewed published medical literature. These centers typically advertise their "unique" methods of performing spine surgery through very small portals using specialized instruments that often have been developed by the centers themselves. These procedures are often performed while the patient is conscious under moderate sedation. Typically, several surgical procedures are performed at multiple levels simultaneously or on successive days until the patient reports pain relief or surgery is exhausted. Proponents argue that these procedures involve fewer anesthetic risks, a smaller incision, reduced blood loss, faster post-operative recovery and performance of surgery in an outpatient setting.

An important concern about this minimally invasive approach is the limited visualization of the spine, such that the surgeon cannot reliably identify and ensure complete removal all bone spurs and other structures impinging on nerves. In addition, the performance of several surgical procedures in close temporal succession does not allow adequate evaluation of the outcomes of one surgical procedure before subsequent surgical procedures are performed.

One center advertises that they manufacture special instruments and develop new techniques to perform complex microscopic laser spinal surgeries through portals of 1/4 to 1/2 of an inch under conscious sedation. They state that they have developed "unique" methods of performing endoscopic surgeries. The center states that they are the only facility that performs endoscopic spinal joint surgery, thoracic laser discectomy, endoscopic sacroiliac joint surgery, endoscopic hardware removal, or endoscopic bio-absorbable fusions or intradiscal stem cell therapy. The center also asserts that their unique minimally invasive spine surgery techniques are so advanced that patients who have failed other minimally invasive or conventional spine surgeries may benefit from their procedures. The center advertises that they have performed over 7,000 of these minimally invasive spinal surgeries. Although they state that they regularly publish their findings in peer-reviewed journals, what evidence they have published is limited to small, uncontrolled case series

focusing on short-term followup (Haufe et al, 2008; Haufe and Mork, 2007; Haufe and Mork, 2006; Haufe and Mork, 2005; Haufe and Mork, 2004).

Another center makes similar claims for the effectiveness of unique endoscopic laser spinal surgical procedures performed under conscious sedation with patented instruments. The center performs spinal procedures using videoendoscopy and specially adapted surgical probes. Procedures include specialized methods of laser diskectomy, laser lumbar facet debridement, laser foraminoplasty, and laser debridement of spinal processes. The center's website includes testimonials and a list of abstracts presented at meetings, but the center has not published the results of their procedures in peer-reviewed publications. The center recently announced initiation of an outcome study to evaluate outcomes of their procedures in persons with failed back syndrome.

Another center offers unique endoscopic laser methods of performing surgery for back and neck pain. The primary procedures include foraminotomy, laminotomy, percutaneous endoscopic discectomy, and facet thermal ablation. The center advertises the ability to complete all necessary evaluation, pre-operative preparation, surgery, and post-operative physical therapy within 1 week. The center advertises that advantages of their method of minimally invasive surgery includes no general anesthesia, no hospitalization, minimally invasive surgery, minimal scar tissue formation, and the availability of outpatient procedures. The center states that the most prominent difference between their techniques and that of other spinal centers is the endoscopic method in which they enter the body to minimize trauma, scar tissue formation, and healing times. The center states that their surgeons have performed approximately 10,000 surgeries collectively for over 10 years. Their website includes testimonials. However, they have not submitted their results for peer-review publication.

Minimally Invasive Lumbar Decompression (MILD)

MILD (Vertos Medical) is a new procedure for pain relief from symptomatic central lumbar canal stenosis. It entails limited percutaneous laminotomy and thinning of the ligamentum flavum in order to increase the critical diameter of the stenosed spinal canal.

In a retrospective study, Lingreen and Grider (2010) examined the minor adverse events and peri-procedural course associated with the MILD procedure. In addition, these researchers evaluated the effectiveness of the procedure with regard to pain relief and functional status. A total of 42 consecutive patients meeting MRI criteria for MILD underwent the procedure performed by 2 interventional pain management physicians working at the same center. The pre- and post-procedure VAS as well as markers of global function were recorded. Major and minor adverse events were tracked and patient outcomes reported. There were no major adverse events reported. Of the minor adverse events, soreness lasting 3.8 days was most frequently reported. No patients required over-night observation and only 5 required post-operative opioid analgesics. Patients self-reported improvement in function as assessed by ability to stand and ambulate for greater than 15 mins, whereas prior to the procedure 98% reported significant limitations in these markers of global functioning. Visual analog pain scores were significantly decreased by 40% from baseline; 86% of the patients reported that they would recommend the MILD procedure to others. The authors concluded that the MILD procedure appears to be a safe and likely effective option for treatment of neurogenic claudication in patients who have failed conservative therapy and have ligamentum flavum hypertrophy as the primary distinguishing component of the stenosis.

In a multi-center, non-blinded, prospective clinical study, Chopko and Caraway (2010) evaluated the clinical application and patient safety and functional outcomes of the MILD procedure in the treatment of symptomatic central canal spinal stenosis. A total of 78 patients were enrolled in the MiDAS I Study and treated with the MILD procedure for lumbar decompression. Of these patients, 6-week follow-up was available for 75 patients. Outcome measures were VAS, Oswestry Disability Index (ODI), Zurich Claudication Questionnaire (ZCQ), and SF-12v2 Health Survey. Outcomes were assessed at baseline and 6 weeks post-treatment. There were no major device or procedure-related complications reported in this patient cohort. At 6 weeks, the MiDAS I Study showed statistically and clinically significant reduction of pain as measured by VAS, ZCQ, and SF-12v2. In addition, improvement in physical function and mobility as measured by ODI, ZCQ, and SF-12v2 was statistically and clinically significant in this study. In this 75-patient series, and in keeping with a previously published 90-patient safety

cohort, the MILD procedure proved to be safe. Further, based on near-term follow-up, the MILD procedure showed efficacy in improving mobility and reducing pain associated with lumbar spinal canal stenosis. Limitations of this study were: (i) this was a preliminary report encompassing only a 6-week follow-up, and (ii) there was no control group. Deer and Kapural (2010) assessed the acute safety of the MILD procedure. Manual and electronic chart survey was conducted by 14 treating physicians located in 9 states within the United States on 90 consecutive patients who underwent the MILD procedure. Patients requiring lumbar decompression via tissue resection at the peri-laminar space, within the inter-laminar space and at the ventral aspect of the lamina were treated. Data collected included any complications and/or adverse events that occurred during or immediately following the procedure prior to discharge. Of 90 procedures reviewed, there were no major adverse events or complications related to the devices or procedure. No incidents of dural puncture or tear, blood transfusion, nerve injury, epidural bleeding, or hematoma were observed. Limitations of this study were: (i) data were not specifically collected; however, regardless of difficulty, in this series none of the procedures was aborted and none resulted in adverse events, and (ii) efficacy parameters were not collected in this safety survey. The authors concluded that this study demonstrates the acute safety of the MILD procedure with no report of significant or unusual patient complications. They noted that additional studies are currently underway to establish complication frequency and longer-term safety profile associated with this treatment.

In a prospective, case-series study, Mekhail et al (2012) reported findings of consecutive LSS patients who presented with neurogenic claudication and were treated with percutaneous lumbar decompression. Efficacy was evaluated using the Pain Disability Index (PDI) and Roland-Morris Disability Questionnaire. Pre- and post-procedure standing time, walking distance, and VAS were also monitored. Significant device- or procedure-related AEs were reported. The MILD procedure was successfully performed on 40 patients. At 12 months, both PDI and Roland-Morris showed significant improvement of 22.6 points (ANOVA, $p < 0.0001$) and 7.7 points (ANOVA, $p < 0.0001$), respectively. Walking distance, standing time, and VAS improvements were also statistically significant, increasing from 246 to 3,956 feet (ANOVA, $p < 0.0001$), 8 to 56 mins (ANOVA, $p < 0.0001$), and 7.1 to 3.6 points (ANOVA, $p < 0.0001$), respectively. Tukey

HSD test found improvement in all 5-outcome measures to be significant from baseline at each follow-up interval. No significant device- or procedure-related AEs were reported. The authors concluded that this study demonstrated significant functional improvement as well as decreased disability secondary to neurogenic claudication after the MILD procedure. Safety, cost-effectiveness, and QOL outcomes were best compared with comprehensive medical management in a randomized controlled fashion and, where ethical, to open lumbar decompression surgery.

The Centers for Medicare & Medicaid Services (CMS, 2014) concluded that percutaneous image guided lumbar decompression (PILD) for lumbar spinal stenosis (LSS) is not reasonable and necessary. The scope of the CMS national coverage analysis (NCA) included a review of the evidence on whether percutaneous image-guided lumbar decompression for LSS provides improved health outcomes in Medicare beneficiaries. The analysis also included the proprietary procedure mild®. CMS identified a number of studies related to the PILD procedure for LSS. The majority of studies were case series which have inherent limitations in providing a level of reliable evidence of benefit for a procedure, especially a procedure addressing pain. The case series for the PILD procedure suffered from additional limitations in failing to report information important for anyone to assess the clinical utility of this procedure for a particular patient. The one RCT had a small enrollment and major design flaws that called into question the results of the trial.

On January 9, 2014, CMS issued a Medicare National Coverage Determination (NCD) which allows coverage of PILD for LSS under Coverage with Evidence Development (CED) with certain conditions. The NCD required a prospective, randomized, controlled clinical trial (RCT) design. On December 7, 2016, CMS expanded this NCD to allow coverage of PILD for LSS under CED in a prospective longitudinal study using an FDA-approved/cleared device that successfully completed a CMS-approved RCT with certain conditions (CMS, 2021).

Zaina et al (2016) reported on a Cochrane review evaluating the effectiveness of different types of surgery compared with different types of non-surgical interventions in adults with symptomatic lumbar spinal stenosis..Low-quality evidence from one small study suggested no

differences at six weeks in the Oswestry Disability Index for patients treated with minimally invasive mild decompression versus those treated with epidural steroid injections (MD 5.70, 95% CI 0.57 to 10.83; 38 participants). Zurich Claudication Questionnaire (ZCQ) results were better for epidural injection at six weeks (MD -0.60, 95% CI -0.92 to -0.28), and visual analogue scale (VAS) improvements were better in the mild decompression group (MD 2.40, 95% CI 1.92 to 2.88). At 12 weeks, many cross-overs prevented further analysis. The authors concluded that "we have very little confidence to conclude whether surgical treatment or a conservative approach is better for lumbar spinal stenosis, and we can provide no new recommendations to guide clinical practice. However, it should be noted that the rate of side effects ranged from 10% to 24% in surgical cases, and no side effects were reported for any conservative treatment. No clear benefits were observed with surgery versus non-surgical treatment."

Benyamin et al (2016) concluded that 1-year results of a RCT demonstrated that MILD was statistically superior to epidural steroid injections (ESI) in the treatment of LSS patients with neurogenic claudication and verified central stenosis due to ligamentum flavum hypertrophy. Primary and secondary efficacy outcome measures achieved statistical superiority in the MILD group compared to the control group. With 95 % of patients in this study presenting with 5 or more LSS co-factors, it is important to note that patients with spinal co-morbidities also experienced statistically significant improved function that was durable through 1 year. The main drawbacks of this study included the lack of patient blinding due to significant differences in treatment protocols between study arms, including multiple ESI procedures during the study period versus one MILD procedure. Also, adjunctive pain therapy within the lumbar region was restricted, and therefore responder rates may be lower for both study groups compared to those outside of study confines. Study enrollment was not limited to patients that had never received ESI therapy.

In a prospective, multi-center, randomized controlled clinical study, Staats and colleagues (2018) evaluated the long-term durability of the minimally invasive lumbar decompression (MILD) procedure in terms of functional improvement and pain reduction for patients with lumbar spinal stenosis and neurogenic claudication due to hypertrophic ligamentum flavum. This

was a report of 2-year follow-up for MILD study patients. These investigators compared outcomes for 143 patients treated with MILD versus 131 treated with epidural steroid injections (ESI). Follow-up occurred at 6 months and at 1 year for the randomized phase and at 2 years for MILD subjects only; ODI, NPS, and ZCQ were used to evaluate function and pain. Safety was evaluated by assessing incidence of device-/procedure-related AEs. All outcome measures demonstrated clinically meaningful and statistically significant improvement from baseline through 6-month, 1-year, and 2-year follow-ups. At 2 years, ODI improved by 22.7 points, NPS improved by 3.6 points, and ZCQ symptom severity and physical function domains improved by 1.0 and 0.8 points, respectively. There were no serious device-/procedure-related AEs, and 1.3% experienced a device-/procedure-related AE. The authors concluded that MILD showed excellent long-term durability, and there was no evidence of spinal instability through 2-year follow-up. Re-operation and spinal fracture rates were lower, and safety was higher for MILD versus other lumbar spine interventions, including interspinous spacers, surgical decompression, and spinal fusion. These researchers stated that given the minimally invasive nature of this procedure, its robust success rate, and durability of outcomes, MILD is an excellent choice for 1st-line therapy for select patients with central spinal stenosis suffering from neurogenic claudication symptoms with hypertrophic ligamentum flavum.

The authors stated that the limitations of this study included the lack of a control group at 2-year follow-up. The randomized controlled portion of the study concluded at the primary end-point of 1 year, and supplementary follow-up through 2 years was conducted for the MILD patient group only. This study did not compare efficacy directly with open surgical approaches, including lumbar decompression, fusion, or spacers. Other limitations included the lack of patient blinding due to considerable differences in treatment protocols, a potentially higher non-responder rate for both groups versus standard-of-care due to study restrictions on adjunctive pain therapies, and study enrollment was not limited to patients that had never received ESI therapy.

Deer et al (2019) noted that lumbar spinal stenosis (LSS) can lead to compression of neural elements and manifest as low back pain (LBP) and leg pain. LSS has traditionally been treated with a variety of conservative (pain medications, physical therapy, epidural spinal injections) and

invasive (surgical decompression) options. Recently, several minimally invasive procedures have expanded the therapeutic options. The Lumbar Spinal Stenosis Consensus Group convened to examine the peer-reviewed literature as the basis for making minimally invasive spine treatment (MIST) recommendations. A total of 11 consensus points were defined with evidence strength, recommendation grade, and consensus level using U.S. Preventive Services Task Force (USPSTF) criteria. The Consensus Group also created a treatment algorithm. Literature searches yielded 9 studies (2 randomized controlled trials [RCTs]; 7 observational studies, 4 prospective and 3 retrospective) of MISTs, and 1 RCT for spacers. The LSS treatment choice is dependent on the degree of stenosis; spinal or anatomic level; architecture of the stenosis; severity of the symptoms; failed, past, less invasive treatments; previous fusions or other open surgical approaches; and patient co-morbidities. There is Level I evidence for percutaneous image-guided lumbar decompression as superior to lumbar epidural steroid injection, and 1 RCT supported spacer use in a non-inferiority study comparing 2 spacer products currently available. The authors concluded that MISTs should be used in a judicious and algorithmic fashion to treat LSS, based on the evidence of efficacy and safety in the peer-reviewed literature. The MIST Consensus Group recommended that these procedures be used in a multi-modal fashion as part of an evidence-based decision algorithm.

Aldahshory et al (2020) stated that the classic laminectomy for spinal decompression was the treatment of choice of the degenerative lumbar canal stenosis (LCS). Many surgeons prefer to add instrumented lumbar fusion to avoid future instability after the removal of posterior elements. Adding fusion is associated with more bleeding and longer periods of hospitalization. Minimally invasive lumbar decompression (MILD) has been advocated for successful decompression with less bleeding loss and shorter hospitalization. These researchers compared the clinical outcomes of 2 different treatment modalities for degenerative LCS: the classic laminectomy with postero-lateral transpedicular screw fixation and the MILD. A total of 50 patients with degenerative LCS were randomized from 2 institutions: Ain Shams University Hospital and Arab Contractors Medical Center, who underwent surgeries for degenerative LCS between 2016 and 2018 with 1-year follow-up. The study compared 2 cohorts: Group A -- 25 patients underwent classic lumbar laminectomy with postero-lateral transpedicular fixation, and Group B -- 25 patients

underwent MILD. There were no statistically significant differences between both treatment modalities in the VAS for leg pain and back pain, the patient satisfaction index, and the ODI after 1 year. The fusion operations were associated with higher estimates of blood loss, longer hospital stay, and more financial costs. The authors concluded that MILD had the same satisfactory results as classic laminectomy with postero-lateral fixation for the treatment of degenerative LCS with less bleeding loss and shorter hospitalization. Since the results were comparable, MILD was suggested in low-income countries as Egypt for economic reasons.

The authors stated that this study had limitations as 1-year follow-up was insufficient to evaluate the re-operation rate in case of adding fusion. Other limitations included small sample size (n = 25 in the MILD group) and lack of information regarding the BMI of each patient and the associated co-morbidities.

Ricciardi et al (2020) noted that chronic LBP can be due to many different causes, including degenerative spondylolisthesis (DS). For patients who do not respond to conservative management, surgery remains the most effective treatment. Open laminectomy alone and laminectomy and fusion (LF) for DS have been widely investigated, however, no meta-analyses have compared minimally invasive decompression with posterior elements preservation (MID) techniques and LF. Minimally invasive techniques might provide specific advantages that were not recognized in previous studies that pooled different decompression strategies together. This was a systematic review and meta-analysis, according to the PRISMA statement, of comparative studies reporting surgical, clinical and radiological outcomes of MID and LF for DS. A total of 3,202 papers were screened and 7 were finally included in the meta-analysis. MID is associated with a shorter surgical duration and hospitalization stay, and a lower intra-operative blood loss and residual LBP; however, the residual disability grade was lower in the LF group; complication rates were similar between the 2 groups . The rate of adjacent segment degeneration was lower in the MID group, whereas data on radiological outcomes were heterogeneous and not suitable for data-pooling. The authors concluded that this meta-analysis suggested that MID might be considered as an effective alternative to LF for DS. Moreover, these researchers stated that further clinical trials are needed

to confirm these findings, better investigate radiological outcomes, and identify patient subgroups that may benefit the most from specific techniques.

Fornari et al (2020) stated that degenerative LSS is a progressive disease with potentially dangerous consequences that affect QOL. Despite the detailed literature, natural history is unpredictable. This uncertainty presents a challenge making the correct management decisions, especially in patients with mild-to-moderate symptoms, regarding conservative or surgical treatment. This article focused on conservative treatment for degenerative LSS. To standardize clinical practice worldwide as much as possible, the World Federation of Neurosurgical Societies Spine Committee held a consensus conference on conservative treatment for degenerative LSS. A team of experts in spinal disorders reviewed the literature on conservative treatment for degenerative LSS from 2008 to 2018 and drafted and voted on a number of statements. During 2 consensus meetings, 14 statements were voted on. The Committee agreed on the use of physical therapy for up to 3 months in cases with no neurologic symptoms. Initial conservative treatment could be applied without major complications in these cases. In patients with moderate-to-severe symptoms or with acute radicular deficits, surgical treatment is indicated. The efficacy of epidural injections is still debated, as it showed only limited benefit in patients with degenerative LSS. The authors concluded that a conservative approach based on therapeutic exercise may be the 1st choice in patients with LSS except in the presence of significant neurologic deficits. Treatment with instrumental modalities or epidural injections is still debated. These researchers stated that further studies with standardization of outcome measures are needed to reach high-level evidence conclusions. This review noted that there is low-quality level of evidence for minimally invasive surgical decompression provides better pain reduction and improves functional mobility versus epidural steroid injections (citing the study by Zaina et al, 2016). Zaina et al (2016) concluded that they had very little confidence to conclude whether surgical treatment or a conservative approach is better for LSS, and they could provide no new recommendations to guide clinical practice. However, it should be noted that the rate of side effects ranged from 10 % to 24 % in surgical cases, and no side effects were reported for any conservative treatment. No clear benefits were observed with surgery versus non-surgical treatment. These findings suggested

that clinicians should be very careful in informing patients regarding possible therapeutic options, especially given that conservative treatments have resulted in no reported side effects. These researchers stated that high-quality research is needed to compare surgical versus conservative care for individuals with LSS. For the study by Deer et al (2019), this review noted that short- to intermediate-term benefit of epidural injections for symptomatic treatment of LSS. Benefit of caudal and interlaminar injections (local anesthetic only and local anesthetic with steroid) and transforaminal injections of local anesthetic with or without steroid. Patients exhibiting shorter-term relief of less than 3 months should not proceed with further injection therapy but rather continue down treatment algorithm to a therapeutic option directed at decompression.

Merkow et al (2020) noted that symptomatic LSS is a condition affecting a growing number of individuals resulting in significant disability and pain. Traditionally, therapeutic options have consisted of conservative measures such as physical therapy, medication management, epidural injections and percutaneous adhesiolysis, or surgery. There exists a treatment gap for patients failing conservative measures who are not candidates for surgery. Minimally invasive lumbar decompression (MILD) and interspinous process device (IPD) with Superion represent minimally invasive novel therapeutic options that may help fill this gap in management. These investigators carried out a literature review to separately evaluate these procedures and examined their safety and effectiveness. The authors concluded that the available evidence for MILD and Superion has been continuously debated. Overall, it is considered that while the procedures are safe, there is only modest evidence for effectiveness. For both procedures, these researchers have reviewed 13 studies. Based on the available evidence, MILD and Superion are safe and modestly effective minimally invasive procedures for patients with symptomatic LSS. They stated that these procedures may be incorporated as part of the continuum of therapeutic options for patients meeting clinical criteria.

Furthermore, an UpToDate review on “Lumbar spinal stenosis: Treatment and prognosis” (Levin, 2021) states that “Minimally invasive decompression -- There is long-standing interest in the development of less invasive decompression procedures, such as percutaneous lumbar decompression and/or minimally invasive lumbar decompression, which

appear in observational studies to have lower complication rates than traditional surgical techniques. It is unclear if these newer procedures offer benefit in terms of improved symptoms and function or fewer complications in routine practice compared with standard decompression with laminectomy".

Mekhail et al (2021) noted that minimally invasive lumbar decompression (the MILD Procedure; Vertos Medical, Aliso Viejo, CA) has been shown to be safe and effective for the treatment of lumbar spinal stenosis (LSS) patients with hypertrophic ligamentum flavum as a contributing factor. In a retrospective, longitudinal, observational cohort study, these researchers examined the long-term durability of the MILD Procedure through 5-year follow-up. Pain relief and opioid medications use during 12-month follow-up were also assessed. All patients diagnosed with LSS secondary to ligamentum flavum hypertrophy who underwent the MILD Procedure from 2010 through 2015 at the Cleveland Clinic Department of Pain Management were included in this trial. The primary outcome measure was the incidence of open lumbar decompression surgery at the same level(s) as the MILD Procedure during 5-year follow-up. Secondary outcome measures were the change in pain levels using the Numeric Rating Scale (NRS) and opioid medications utilization using Morphine Milligram Equivalent (MME) dose per day from baseline to 3, 6, and 12 months post-MILD Procedure; and post-procedural complications (minor or major) were also collected. A total of 75 patients received the MILD Procedure during the protocol-defined time-period and were included in the trial. Only 9 (12 %) out of 75 patients required lumbar surgical decompression during the 5-year follow-up period. Subjects experienced statistically significant pain relief and reduction of opioid medications use at 3, 6, and 12 months compared to baseline. The authors concluded that based on their analysis, the MILD Procedure was durable over 5 years and may allow elderly patients with symptomatic LSS to avoid lumbar decompression surgery while providing significant symptomatic relief. These researchers stated that these findings highlighted the potential role of the MILD procedure to significantly impact patients' quality of life (QOL) while avoiding a major health and economic burden.

The authors stated that this study bore all the drawbacks of retrospective data analysis; however, every effort was made to ensure the accuracy of data. Telephone calls were made to confirm data if needed. Possible

other confounding factors affecting the incidence of subsequent open surgery, reported pain scores, and opioid consumption may not have been measured. Missing follow-up data for a few patients may still pose a limitation for this analysis.

In a prospective, randomized controlled trial (RCT), Deer et al (2021) examined patients aged 50 to 80 years treated with the MILD procedure plus conventional medical management (CMM), compared to those treated with CMM alone, as the active control. Walking tolerance test outcomes and incidence of subsequent disallowed procedures provided objective real-world outcome data. The incidence of device or procedure-related adverse events (AEs) was analyzed. Follow-up includes 6-month, 1-year and 2-year assessments, with 1-year being primary. Patients in the MILD+CMM group were followed at 3, 4, and 5 years. This was a report of interim 6-month outcomes. Of 155 patients enrolled at 19 U.S. interventional pain management centers, 78 were allocated to CMM alone, and 77 to MILD+CMM. At 6-months, the validated walking tolerance test demonstrated statistical superiority of MILD+CMM versus CMM alone ($p < 0.001$). The incidence of patients receiving a subsequent disallowed procedure, and thereby considered treatment failures in their study group, was statistically significantly higher in CMM alone versus MILD+CMM ($p < 0.001$). There were no device or procedure-related AEs in either group. The authors concluded that at 6-months, the MILD Procedure combined with CMM provided statistically superior objective real-world outcomes versus CMM alone. There were no device or procedure-related AEs reported in either study group. With its excellent safety profile and superior efficacy, the MILD Procedure is uniquely positioned as early 1st-line therapy.

The authors stated that drawbacks of this trial included the lack of blinding, which was not possible due to the use of an active comparator that allowed for a broad range of both conservative and interventional treatments in both study groups. It was anticipated that patients in both arms may continue to receive CMM therapies throughout the study period. The real-world nature of this study, which allowed the use of CMM in both study arms at the full discretion of the investigator, was also a limitation due to use of various standard of care treatment algorithms. All CMM treatments as well as subsequent disallowed procedures were recorded. Patients who received a disallowed procedure remain in the

study and were assessed at all follow-ups. Furthermore, this was a 6-month interim report; long-term follow-up (3 to 5 years) data are needed; it's also unclear whether the statistical superiority of the MILD+CMM over CMM alone would translate into clinical superiority.

Pope et al (2021) noted that low-back pain (LBP) with accompanying neurogenic claudication is a common diagnosis in pain and spine centers around the world, with an evolving algorithm of treatment. One option for the treatment of neurogenic claudication by decompressive strategies centers on percutaneous direct decompressive techniques. Although commonly used in clinical practice, there have been no formal investigations examining the safety of percutaneous direct decompression without the use of an epidurogram and relying on osteal landmarks. In a retrospective, single-center, quantitative analysis, these investigators examined the safety of percutaneous direct decompression carried out without the use of the epidurogram. After an Investigational Review Board (IRB) exemption had been obtained from the Western IRB, data were retrospectively analyzed from July 2018 to August 2020 on patients who had undergone percutaneous direct decompression using the Mild procedure in a single center by a single physician. Data were analyzed quantitatively for reported complications within 3 months of the procedure, including nerve injury, hematoma, infection, death, or allergic reaction to contrast use. Chart review yielded 147 individual patients who had undergone percutaneous direct decompression from July 2018 to August 2020. In this data set, women out-numbered men, with an average age of 76 years, with L4 to L5 followed by L3 to L4 being the most common levels decompressed. Of the 147 patients was performed, utilizing an epidurogram versus no epidurogram for decompression, with no complications. These data were the 1st to describe the safety of percutaneous direct lumbar decompression without the use of contrast. The authors concluded that the findings of this study strongly suggested the use of an epidurogram was not necessary for the safe decompression of a patient with symptomatic spinal stenosis and neurogenic claudication utilizing percutaneous direct decompression.

The authors stated that drawbacks of this study included the retrospective nature of the study. Although the MiDAS ENCORE study of 149 patients indicated a re-operation rate of 5.6 % at 2-year follow-up and an AE rate of 1.3 %, this single-site study may not translate to a broader application

of the percutaneous direct decompressive method using a single incision and absence of an epidurogram. Furthermore, effectiveness was not examined for either group, as this study was focused on patient safety. Percutaneous decompression technique variance and effectiveness comparisons are under way. These researchers stated that prospective studies need to be performed with a direct comparison of safety and effectiveness of the new technique described in this cohort.

Deer et al (2022) provided real-world outcome data for patients with LSS suffering from neurogenic claudication secondary to hypertrophic ligamentum flavum. The MOTION Study is a prospective, multi-center RCT comparing the MILD Procedure as a 1st-line therapy in combination with non-surgical CMM versus CMM alone as the active control. Patients in the test group received the MILD Procedure at baseline. Both the MILD+CMM group and the control group were allowed unrestricted access to conventional real-world therapies. Patient-reported outcomes included the ODI, the Zurich Claudication Questionnaire, and the Numeric Pain Rating Scale. A validated Walking Tolerance Test, the incidence of subsequent lumbar spine interventions, and the occurrence of AEs were used to measure objective outcomes. A total of 69 patients in each group were analyzed at 1-year follow-up. No device- or procedure-related AEs were reported in either group. Results from all primary and secondary outcome measures showed statistical significance in favor of MILD+CMM. The authors concluded that 1-year results of this study demonstrated superiority of MILD+CMM over CMM alone for patients with LSS who were suffering from neurogenic claudication secondary to hypertrophic ligamentum flavum. Use of the validated Walking Tolerance Test to objectively measure increased ability to walk without severe symptoms provided evidence of statistically significantly better outcomes for MILD+CMM than for CMM alone. With no reported device or procedure-related AEs, the long-standing safety profile of the MILD Procedure was re-affirmed. These investigators stated that the MILD procedure is a safe, durable, minimally invasive procedure that has been shown to be effective as an early interventional therapy for patients suffering from symptomatic LSS.

These researchers stated that although the MOTION Study was designed to include a patient population commonly seen every day in the clinic, the inclusion of numerous CMM therapeutic options chosen at the

investigator's discretion provided a broad range of therapeutic options and sequencing, as is encountered in the real world. This limited control over the use of CMM, though intended in the study design, may be viewed as a study limitation. The use of CMM in both arms of this study simulates real-world practice, but it also may result in confounding, as patients were treated on the basis of routine use of the MILD Procedure in a typical clinic setting. In day-to-day practice, the MILD Procedure is not used alone but in conjunction with other conservative therapies. The non-blinded nature of the study could also be considered a limitation. The use of objective real-world outcome measures, together with independent physicians in the role of medical monitor, clinical events adjudicator, and study principal investigator, were intended to limit study bias. This was a 1-year interim report; long-term follow-up (3 to 5 years) data are needed; it's also unclear whether the statistical superiority of the MILD+CMM over CMM alone would translate into clinical superiority.

In a retrospective study, Pryzbylkowski et al (2022) examined a modified algorithm for the treatment of LSS with hypertrophic ligamentum flavum using minimally-invasive lumbar decompression (mild) with a focus on earlier intervention. Records of 145 patients treated with mild after receiving 0 to 1 epidural steroid injection (ESI) or 2+ ESIs were reviewed. Pain assessments as measured by VAS scores were recorded at baseline and 1-week and 3-month follow-ups. Improvements in VAS scores at follow-ups compared with baseline were significant in both groups. No statistically significant differences were found between the 2 groups. The authors concluded that multiple ESIs before the mild procedure showed no benefit. A modified algorithm to perform mild immediately upon diagnosis or after the failure of the 1st ESI is recommended. These researchers noted that with a safety profile similar to ESI, mild offered the potential for long-term symptom relief without first subjecting LSS patients to multiple ESI treatments.

Hagedorn et al (2022) stated that LSS affects more than 200,000 adults in the U.S., resulting in about 38,000 operations among the Medicare population and greater than $1.5 billion in hospital bills alone. Fortunately, minimally invasive lumbar decompression (MILD) and the Superion indirect decompression System have shown lasting benefit and cost savings compared to more aggressive surgical options. In a retrospective study, these investigators determined the rate of lumbar

decompression surgery following the MILD and Superion procedures. This was a pooled retrospective review of LSS patients who received MILD and/or Superion procedures between January 2011 and July 2019. Adult patients with CPT codes for MILD and Superion procedures were identified. Patients were included if they had a follow-up visit at least 2 years from the procedure date, preprocedural MRI results, and surgical notes. A total of 199 patients were included in the final analysis, of which 57 patients (28.6 %) underwent MILD procedure only, 124 patients (62.3 %) underwent Superion only, and 18 patients (9.0 %) underwent a MILD procedure initially followed by a Superion procedure. Two patients had a MILD procedure performed twice at the same level at separate encounters. A total of 4 patients in the entire cohort (2.0 %; MILD 5.3 %, Superion 0.8 %) underwent subsequent lumbar spine surgery when followed for at least 2 years. It was notable that some of these patients may not have been surgical candidates; and this may have skewed the results. The authors concluded that patients undergoing minimally invasive decompression treatment of LSS exhibited low rates of subsequent open surgery that potentially resulted in cost savings and a reduction in severe AEs. The reason for low surgical rate may reflect improvement in their symptoms, a preference to avoid surgery, or being deemed not a surgical candidate.

Laser Diskectomy

Laser discectomy is also known as laser-assisted discectomy, laser disc decompression or laser-assisted disc decompression (LADD). Though this procedure is called a discectomy, it does not actually remove the disc, but utilizes a laser to "vaporize" a small portion of the nucleus pulposus in order to purportedly decompress a herniated disc. Laser discectomy may be performed either laparoscopically or percutaneously.

Laser diskectomy involves the use of a laser to vaporize a small portion of the nucleus pulposus in order to decompress a herniated disc. In laparoscopic laser diskectomy, the procedure is done through a laparoscope, which allows visualization of the disc, disc space and other structures. The surgeon places a laser through a delivery device that has been directed under radiographic control to the disc. The annulus of the disc is opened and is then excised with a laser device which is inserted through the laparoscope. It uses many of the same techniques used in

automated percutaneous discectomy. An endoscope may be used in conjunction with this procedure to visualize the disc space and nucleus pulposus, or the procedure may be done percutaneously. By contrast, percutaneous disc decompression uses an x-ray to localize the tip of the needle/trocar to ensure that it is in the appropriate level and location. Percutaneous laser discectomy is performed under a local anesthetic. Under x-ray (fluoroscopic) guidance, a needle is inserted through the skin into the disc. A flexible quartz fiber is then threaded through the needle and into the disc, which delivers the laser energy.

The mechanism of action for pain relief in LADD is not well understood; most believe that the primary mechanism of pain reduction after LADD is its decrease in intradiscal pressure. According to the literature, laser-assisted disc decompression appears to be a safe procedure, but studies have not compared it to open surgical alternatives or other percutaneous methods. Randomized controlled trials are needed to compare current standard alternatives to both LADD and conservative treatment. A Cochrane review of surgical procedures for lumbar disc herniation concluded that "[t]here is currently no evidence supporting endoscopic (micro-suction) or laser treatment of disc prolapse" (Gibson et al, 2002). A systematic review of the literature on percutaneous endoscopic laser discectomy for the Royal Australasian College of Surgeons (Boult et al, 2000) reached similar conclusions: "Given the extremely low level of evidence available for this procedure it was recommended that the procedure be regarded as experimental until the results are available from a controlled clinical trial, ideally with random allocation to an intervention and control group".

An assessment of laser lumbar diskectomy conducted for the National Institute of Clinical Excellence (NICE, 2003) concluded that current evidence on the safety and efficacy of laser lumbar discectomy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. A systematic evidence review by Jordan et al (2003) similarly concluded that the effectiveness of laser diskectomy is "unknown".

Microdiscectomy

Microdiscectomy refers to removal of protruding disc material, using an operating microscope to guide surgery. Dent (2001) recently assessed the evidence supporting the use of microdiscectomy for prolapsed intervertebral disc, and found no evidence of differences in clinical outcomes between microdiscectomy and standard open discectomy. A Cochrane review found evidence that microdiscectomy takes longer to perform than standard open discectomy (Gibson et al, 2002). The review found no evidence of difference in short- or long-term symptom relief or complications, or length of inpatient stay. Similarly, a systematic assessment of the literature by Jordan et al (2003) concluded that microdiskectomy has not been shown to be more effective than standard diskectomy.

Microendoscopic Discectomy

Microendoscopic discectomy (MED) procedure combines conventional lumbar microsurgical techniques with endoscopy and is performed at an outpatient setting. It is employed for the treatment of lumbar spine stenosis and lumbar disc herniation. It has been suggested that MED is less invasive (no damage to muscle, bone or soft tissue) compared with traditional open microdiscectomy. Moreover, MED allegedly allows an early return to work. However, this endoscopic procedure is difficult because of the limited exposure and 2-dimensional video display. The potential injury of the nerve root and prolonged surgical time remain as matters of serious concern. Currently, there is insufficient evidence to support the clinical value of this procedure especially its long-term effectiveness.

Muramatsu et al (2001) examined if MED was minimally invasive with respect to the nerve roots, cauda equina, and paravertebral muscles by comparing the post-operative magnetic resonance imaging findings in patients treated by MED and the conventional Love's method. The authors concluded that MED had an effect on the nerve roots and cauda equina that was comparable with that of Love's method. The magnetic resonance images of the route of entry failed to show that MED is appreciably less invasive with respect to the paravertebral muscles. Furthermore, in a review on the various minimally invasive procedures

available for the treatment of lumbar disc disease, Maroon (2002) stated that although all percutaneous techniques (including MED) have been reported to yield high success rates, to date no studies have demonstrated any of these to be superior to microsurgical discectomy, which continues to be regarded as the standard with which all other techniques must be compared.

Far Lateral Microendoscopic Diskectomy (FLMED)

Extra-foraminal lumbar disc herniations (ELDHs) at the lumbo-sacral junction are an uncommon cause of L5 radiculopathy. The surgical anatomy of the extra-foraminal space at L5 to S1 is challenging for the various open surgical approaches that have been described for ELDHs in general. Reports specifically describing minimally invasive surgical approaches to lumbo-sacral ELDHs are lacking.

There is currently insufficient evidence to support the use of far lateral microendoscopic discectomy (FLMED). O'Toole and colleagues (2007) reported the novel use of far lateral microendoscopic discectomy (FLMED) to lumbo-sacral ELDH. To better define the unique anatomical features of extra-foraminal approaches to the lumbo-sacral junction as they apply to minimal access techniques. A cadaveric investigation a well as a clinical case were performed, and a thorough review of the literature was conducted. A single patient with an extra-foraminal disc herniation at the lumbo-sacral junction underwent evaluation and surgery. The patient's self-reported pain levels were documented. Physiologic outcome was judged on pre- and post-operative motor and sensory examinations. Functional capacity was assessed by work status and ability to perform activities of daily living. Far lateral microendoscopic discectomy was performed in 2 fresh human cadavers at the lumbo-sacral junction. Qualitative assessments of the surgical anatomy were made, and intra-operative fluoroscopy and endoscopic photographs were obtained to document the findings. A patient with refractory pain and sensori-motor deficits from compression of the L5 nerve root by an ELDH underwent FLMED. The literature was carefully reviewed for the epidemiology of ELDHs at the lumbo-sacral junction and the surgical techniques used to treat them. The postero-lateral surgical corridor to the lumbo-sacral disc was consistently constrained by the sacral ala and to a lesser extent the lateral facet and L5 transverse process. Resection of the superior ala

exposed the exiting nerve root and provided ample access to the disc. In the clinical case, the patient enjoyed immediate pain relief, was discharged in 3 hours, and returned to full work and social activities. Follow-up neurological examination revealed no sensory or motor deficit. The authors concluded that FLMED offers a safe and effective approach to ELDHs at the lumbo-sacral junction by combining satisfactory visualization for adequate resection of the sacral ala with the benefits of reduced tissue injury and faster recovery times that accompany minimally invasive techniques.

Pirris and colleagues (2008) noted that surgical access to ELDHs is complicated due to the unique anatomical constraints of the region. Minimizing complications during microdiscectomies at the level of L5 to S1 in particular remains a challenge. The authors reported on a small series of patients and provided a video presentation of a minimally invasive approach to L5 to S1 ELDHs utilizing a tubular retractor with microscopic visualization.

Dynamic Stabilization

Failed back surgery syndrome (FBSS) is reported to occur in 5 to 50% of cases of lumbar spine operation. A marked rise in the number of performed spinal procedures has also led to an increase in the number of FBSS cases, which is the consequence of biological, psychological, social, and/or economical causes. Patient selection and correct indications are of key importance for successful surgical intervention of this syndrome. Surgical interventions that have been used for FBSS treatment include decompression, stabilization and fusion, as well as dynamic stabilization/neutralization procedures (Chrobok et al, 2005).

Dynamic spinal stabilization devices are proposed as a way to provide immobilization and stabilization of spinal segments in skeletally mature individuals as an adjunct to fusion in the treatment of chronic instabilities or deformities of the thoracic, lumbar and sacral spine including, but not limited to, degenerative spondylolisthesis (with objective evidence of neurologic impairment) or previous failed spinal fusion. They are also cleared by the US Food and Drug Administration (FDA) for individuals who are receiving fusions with autogenous graft only, those

who are having the device fixed or attached to the lumbar or sacral spine and those who are having the device removed after the development of a solid fusion mass.

These devices attach to the spine by way of titanium alloy screws that have been implanted into the spinal bone. Two screws are implanted per vertebra in two or three adjacent vertebrae. The protruding ends of the screws are attached to polyethylene-terephthalate cords. These cords are surrounded by a set of solid polycarbonate-urethane spacers. The system is designed to stabilize the spine by the polyethylene cords pulling against the spinal motions that separate the vertebrae. At the same time, the polycarbonate spacers push against the spinal motions that compress the vertebrae. These devices differ from traditional instrumentation used during spinal fusion, as they are non-rigid and allow some movement of the spine segments. Examples of dynamic spinal stabilization devices include, but may not be limited to, the Dynesys Stabilization System, the BAR Posterior Pedicle Screw System and the N Fix II Pedicle Screw System.

The use of rigid instrumentation in the treatment of degenerative spinal disorders seems to increase the fusion rate of the lumbar spine. However, rigid devices are associated with adverse effects such as pseudoarthrosis and adjacent segment degeneration. The use of semi-rigid and dynamic devices has been advocated to decrease such adverse effects of rigid fixation and thereby to attain a more physiological bony fusion (Korovessis et al, 2004). Dynamic stabilization systems (e.g., the Dynesys Spinal System) are intended to restrict segmental motion and thus prevent further degeneration of the lumbar spine. The Dynesys, a non-fusion pedicle screw stabilization system (a flexible posterior stabilization system), was developed in an attempt to overcome the inherent disadvantages of rigid instrumentation and fusion. It uses flexible materials threaded through pedicle screws rather than rigid rods or bone grafts alone as an adjunct to fusion. The Dynesys is installed posteriorly, and does not require bone to be taken from the hip, as is required in other fusion procedures. It is designed to prevent over-loading the disc, but it restricts extension and loses lordosis (Sengupta and Mulholland, 2005; Putzier et al, 2005).

The Dynesys Spinal System (Centerpulse Spine-Tech, Inc., Minneapolis, MN) was cleared by the FDA via a 510(k) pre-market notification in March 2004. According to the product labeling, it is indicated to provide stabilization of spinal segments in skeletally mature patients as an adjunct to fusion in the treatment of the chronic instabilities or deformities of the thoracic, lumbar and sacral spine: degenerative spondylolisthesis with objective evidence or neurological impairment, kyphosis; and failed previous fusion (pseudoarthrosis). In addition, the product labeling states that the Dynesys system is intended for use in persons who meet all of the following criteria:

- Patients who are receiving fusions with autologous graft only; and
- Patients who are having the device attached to the lumbar or sacral spine; and
- Patients who are having the device removed after the development of a solid fusion mass.

The Dynesys Stabilization System has also been proposed for immobilization and stabilization of spinal segments without a spinal fusion procedure; at this time the FDA has not approved this application. Although the Dynesys has been in clinical use for several years, there is insufficient evidence demonstrating that implantation of this device results in improved health outcomes compared to standard treatments.

A more recent development has been a hybrid device, the Zimmer DTO Implant, which combines the Dynesys Dynamic Stabilization System with the rigid stabilization of the OPTIMA ZS Spinal System. This device is an attempt to offer a new segmental solution for treating degenerative lumbar spine pathologies with different stages of degeneration at contiguous levels.

Dynamic spinal stabilization devices may also be semi-rigid in design. These devices purportedly allow less spinal movement than the non-rigid, but more than traditional spinal fusion instrumentation. Examples of semi-rigid devices include the CD HorizoN Agile Dynamic Spinal Stabilization Device and the Isobar Spinal System.

In a RCT, Korovessis et al (2004) examined the short-term effects of rigid versus semi-rigid and dynamic instrumentation on the global and segmental lumbar spine profile, subjective evaluation of the result, and the associated complications. The study did not examine objective functional outcomes. They compared 3 equal groups of 45 adult patients, who underwent primary decompression and stabilization for symptomatic degenerative lumbar spinal stenosis. Patients were randomly selected and received either the rigid (Group A), or semi-rigid (Group B), or dynamic (Group C) spinal instrumentation with formal decompression and fusion. The mean ages for the 3 groups were 65 +/- 9, 59 +/- 16, and 62 +/- 10 years, respectively. All patients had detailed roentgenographical study including computed tomography (CT) scan and magnetic resonance imaging (MRI) before surgery to the latest follow-up observation. The following roentgenographical parameters were measured and compared in all spines: lumbar lordosis (L1 to S1), total lumbar lordosis (T12 to S1), sacral tilt, distal lordosis (L4 to S1), segmental lordosis, vertebral inclination, and disc index. The SF-36 health survey and visual analog scale (VAS) was used before surgery to the latest evaluation. All patients were evaluated after a mean follow-up of 47 +/- 14 months. Both lumbar and total lordosis correction did not correlate with the number of the levels instrumented in any group. Total lordosis was slightly decreased after surgery (3%, $p < 0.05$) in Group C. The segmental lordosis L2 to L3 was increased after surgery by 8.5% ($p < 0.05$) in Group C, whereas the segmental lordosis L4 to L5 was significantly decreased in Groups A and C by 9.8% ($p = 0.01$) and 16.2% ($p < 0.01$), respectively. The disc index L2 to L3 was decreased after surgery in Groups A and C by 17% ($p < 0.05$) and 23.5% ($p < 0.05$), respectively. The disc index L3 to L4 was increased in Group C by 18.74% ($p < 0.01$). After surgery, the disc index L4 to L5 was decreased in all 3 groups: Group A by 21% ($p = 0.01$), Group B by 13% ($p < 0.05$), and Group C by 13.23% ($p < 0.05$). The disc index L5 to S1 was significantly decreased in Group B by 13% ($p < 0.05$). The mean pre-operative scores of the SF-36 before surgery were 11, 14, and 13 for Groups C, B, and A, respectively. In the first year after surgery, there was a significant increase of the pre-operative SF-36 scores to 65, 61, and 61 for Groups C, B, and A, respectively, that represents an improvement of 83%, 77%, and 79%, respectively. In the second year after surgery and thereafter, there was a further increase of SF-36 scores of 19%, 23%, and 21% for Groups C, B, and A, respectively. The mean pre-operative scores

of VAS for LBP for Groups C, B, and A were 5, 4.5, and 4.3, respectively, and decreased after surgery to 1.9, 1.5, and 1.6, respectively. The mean pre-operative scores of the VAS for leg pain for Groups C, B, and A were 7.6, 7.1, and 6.9, respectively, and decreased after surgery to 2.5, 2.5, and 2.7, respectively. All fusions healed radiologically within the expected time in all 3 groups without pseudoarthrosis or malunion. Delayed hardware failure (1 screw and 2 rod breakages) without radiological pseudoarthrosis was observed in 2 patients in Group C 1 year and 18 months following surgery. There was no adjacent segment degeneration in any spine until the last evaluation. These investigators concluded that all 3 instrumentations applied over a short area for symptomatic degenerative spinal stenosis almost equally maintained the pre-operative global and segmental sagittal profile of the lumbosacral spine and was followed by similarly significant improvement of both self-assessment and pain scores. Hardware failure occurred at a low rate following dynamic instrumentation solely without radiologically visible pseudoarthrosis or loss of correction. These researchers further noted that because of the similar clinical and radiological data in all 3 groups and the relative small number of patients that were included in each group, it is difficult to make any recommendation in favor of any instrumentation.

Putzier et al (2005) examined the effect of dynamic stabilization on the progression of segmental degeneration after nucleotomy. A total of 84 patients underwent nucleotomy of the lumbar spine for the treatment of symptomatic disc prolapse. Additional dynamic stabilization (the Dynesys system) was performed in 35 subjects. All patients showed signs of initial disc degeneration (Modic Type I - changes in the vertebral end plate are frequently associated with degenerative disc disease. Type 1 changes include decreased signal intensity on T1-weighted and increased signal intensity on T2-weighted MRI). Evaluation was carried out before surgery, 3 months after surgery, and at follow-up. The mean duration of follow-up was 34 months. Examinations included radiographs, MRI, physical examination, and subjective patient evaluation using Oswestry score and VAS. Clinical symptoms, Oswestry score, and VAS improved significantly in both groups after 3 months. At follow-up, a significant increase in the Oswestry score and in the VAS was seen only in the non-stabilized group. In the dynamically stabilized group, no progression of disc degeneration was noted at follow-up, while radiological signs of accelerated segmental degeneration existed in the solely nucleotomized group. There were no

implant-associated complications. These investigators concluded that the Dynesys system is useful to prevent progression of initial degenerative disc disease of lumbar spinal segments following nucleotomy. Moreover, the same group of researchers noted that the Dynesys system seems not to be indicated for treating marked deformities or if osseous decompression needs to be performed (Putzier et al, 2004).

In contrast to the observation of Korovessis et al (2004) and Putzier et al (2005), a number of investigators have questioned whether the Dynesys Spinal System offers any clinical advantages over rigid instrumentation (Hopf et al, 2004; Grob et al, 2005; Schwarzenbach et al, 2005).

In a clinical trial, Hopf et al (2004) compared the use of artificial disc replacement with dynamic stabilization procedure (Dynesys' method) in the treatment of patients with LBP. Indications for the operation were unsuccessful conservative treatment for over 6 months, segmental pain, age of less than 45 years, evidence of mono- or bi-segmental disc degeneration, with or without disc prolapse, demonstrated by MRI, exclusion of psychogenic disease and positive pre-operative, diagnostic measures such as facet joint infiltration and discography. These investigators stated that in younger patients with mono- or bi-segmental disc degeneration there is an indication for the implantation of an artificial disc. Contraindications for the operation are facet joint arthrosis and age of over 45 years. The investigators commented that the indication in subjects with a classic FBSS is still unclear, the improvement of the instrumentation and a further adaptation of the systems to the known biomechanics of the lumbar spine are mandatory as is an intensive discussion of the operative procedure in the case of revision operations. These authors further noted that the Dynesys' method, with the inherent danger of segmental kyphozitation, a published, significant revision quota combined with a reduction of motility, does not fulfill this criterion.

In a retrospective study, Grob and colleagues (2005) assessed patient-oriented outcome after implantation of the Dynesys Spinal System. A total of 50 consecutive patients instrumented with the Dynesys over the preceding 40 months were invited to complete a postal, patient-oriented follow-up questionnaire. The data from 31 of these subjects (11 men and 20 women; mean age of 50 years), with at least 2 years' follow-up, were analyzed. The primary indication for surgery was degenerative disease

(disc/stenosis) with associated "instability"; 11 of 31 (35%) patients had had prior spinal surgery. One-level instrumentation was performed in 32% cases, 2-level instrumentation in 52% cases, 3-level in 13% cases, and 4-level in 3% cases. Thirteen of 31 (42%) patients underwent additional decompression. Within the 2-year follow-up period, 6 of 31 (19%) patients had needed or were scheduled for another surgical intervention. At follow-up, mean back and leg pain (0 to 10 VAS) were 4.7 and 3.8, respectively. The following global outcomes were reported: (i) back symptoms – 67% improved, 30% same, 3% worse; (ii) leg symptoms - 64% improved, 21% same, 14% worse; (iii) ability to do physical activities/sports - 40% improved, 33% same, 27% worse; (iv) quality of life - 50% improved, 37% same, 13% worse; (v) how much the operation helped - 29% helped a lot, 23% helped, 10% only helped a little, 35% didn't help, 3% made things worse. These investigators concluded that their findings indicated that both back and leg pain are, on average, still moderately high 2 years following instrumentation with the Dynesys Spinal System. Only 50% of the patients declared that the operation had helped and had improved their overall quality of life; less than 50% reported improvements in functional capacity. The re-operation rate following implantation of the Dynesys was relatively high. The investigators concluded that these results provide no support for the notion that semi-rigid fixation of the lumbar spine resulted in better patient-oriented outcomes than those typical of fusion.

In a recent review on posterior dynamic stabilization systems, Schwarzenbach et al (2005) stated that their experience with the Dynesys has shown that this method has limitations in "elderly patients with osteoporotic bone or in patients with a severe segmental macro-instability combined with degenerative spondylolisthesis and advanced disc degeneration. Such cases have an increased risk of failure. Only future randomized evaluations will be able to address the potential reduction of accelerated adjacent segment degeneration. The few posterior dynamic stabilization systems that have had clinical applications so far have produced clinical outcomes comparable with fusion. No severe adverse events caused by these implants have been reported. Long-term follow-up data and controlled prospective randomized studies are not available for most of the cited implants but are essential to prove the safety, efficacy, appropriateness, and economic viability of these methods".

In a review on dynamic stabilization in the surgical management of painful lumbar spinal disorders, Nockels (2005) concluded that posterior dynamic stabilization systems may provide benefit comparable to fusion techniques, but without the elimination of movement. Moreover, the author also noted that further study (well-designed prospective, randomized, controlled trial) is needed to ascertain optimal design and clinical indications.

In a systematic evidence review on non-rigid stabilization procedures for the treatment of LBP, the National Institute for Health and Clinical Excellence (NICE, 2005) stated that "current evidence on the safety of these procedures is unclear and involves a variety of different devices and outcome measures. Therefore, these procedures should not be used without special arrangements for consent and for audit or research". Additionally, the specialist advisors to the Institute's Interventional Procedures Advisory Committee noted that these procedures may be undertaken concurrently with disc decompression or discectomy. Thus, it is difficult to ascertain what clinical benefit is derived from the implants themselves. The specialist advisors noted that the reported adverse events include infection, malpositioned or broken screws leading to nerve root damage, cerebrospinal fluid leak, failure of the bone/implant interface, and failure to control pain. The theoretical risks with the techniques include: device failure (particularly long-term), increased lordosis, and root damage caused by loose or misaligned screws.

Welch and colleagues (2007) presented the preliminary clinical outcomes of dynamic stabilization with the Dynesys spinal system as part of a multi-center randomized prospective FDA investigational device exemption (IDE) clinical trial. This study included 101 patients from 6 IDE sites (no participants were omitted from the analysis) who underwent dynamic stabilization of the lumbar spine with the Dynesys construct. Patient participation was based on the presence of degenerative spondylolisthesis or retrolisthesis (Grade I), lateral or central spinal stenosis, and their physician's determination that the patient required decompression and instrumented fusion for 1 or 2 contiguous spinal levels between L1 and S1. Subjects were evaluated pre-operatively, post-operatively at 3 weeks, and then at 3-, 6-, and 12-month intervals. The 100-mm VAS was used to score both lower-limb and back pain. Patient functioning was evaluated using the Oswestry Disability Index (ODI), and

the participants' general health was assessed using the Short Form-12 questionnaire. Overall, patient satisfaction was also reported. One hundred one patients (53 women and 48 men) with a mean age of 56.3 years (range of 27 to 79 years) were included. The mean pain and function scores improved significantly from the baseline to 12-month follow-up evaluation, as follows: leg pain improved from 80.3 to 25.5, back pain from 54 to 29.4, and ODI score from 55.6 to 26.3%. The authors concluded that the early clinical outcomes of treatment with Dynesys are promising, with lessening of pain and disability found at follow-up review. Dynesys may be preferable to fusion for surgical treatment of degenerative spondylolisthesis and stenosis because it decreases back and leg pain while avoiding the relatively greater tissue destruction and the morbidity of donor site problems encountered in fusion. However, long-term follow-up care is still recommended.

In a prospective case series, Kumar et al (2008) examined the radiological changes in the intervertebral disc after Dynesys dynamic stabilization. A total of 32 patients who underwent Dynesys procedure and have completed 2-year follow-up MRI scans were included in this study. Pre-operative and 2-year post-operative lumbar MRI scans were evaluated by 2 independent observers. T2-weighted mid-sagittal images were used and disc degeneration were classified according to the Woodend classification of disc degeneration. Anterior and posterior intervertebral disc heights were also measured. Of the 32 patients, 20 patients underwent Dynesys procedure alone and 12 underwent additional fusion at 1 or more levels. A total of 70 levels were operated on, of which 13 levels were fused. There was a statistically significant increase in the mean Woodend score at the operated levels in the Dynesys alone group, a change from 1.95 before surgery to 2.52 after surgery ($p < 0.001$). The mean Woodend scores changed from 1.27 pre-operative to 1.55 post-operative ($p = 0.066$) at the proximal adjacent levels, and from 1.37 to 1.62 at the distal levels ($p = 0.157$). There was good inter-observer agreement (weighted k score of 0.819). The anterior intervertebral disc height reduced by 2 mm from 9.25 to 7.17 ($p < 0.001$). The posterior disc height increased by 0.14 mm but this change insignificant. The authors concluded that disc degeneration at the bridged and adjacent segment seems to continue despite Dynesys dynamic stabilization.

The Stabilimax NZ Dynamic Spinal Stabilization System is an investigational device that is being evaluated for the treatment of patients with symptomatic spinal stenosis. The Stabilimax NZ is inserted and fixed to the vertebra by means of pedicle screws in exactly the same manner a fusion device is inserted and attached. The only difference is that for the Stabilimax NZ no bone graft will be placed around or between the vertebra to promote bone growth for fusion. It should be noted that a clinical trial sponsored by Applied Spine Technologies to evaluate if the Stabilimax NZ is at least as safe and effective as the control therapy of fusion in patients receiving decompression surgery for the treatment of clinically symptomatic spinal stenosis at 1 or 2 contiguous vertebral levels from L1 to S1 has been suspended (Applied Spine Technologies, 2008); the reason for this suspension is unclear.

Graf artificial ligament stabilization (Graf) is primarily used to stabilize the unstable vertebral segment without rigid fusion (Noorani and Topfer, 2006). The Graf technique involves insertion of pedicle screws into each vertebra to be stabilized which are then attached to one another with Dacron loops. This method has the theoretical advantages of simplicity (to surgeons familiar with the insertion of pedicle screws), avoidance of bone graft donor site problems, and allowing a spinal fusion to be attempted at a later date if considered necessary (Noorani and Topfer, 2006). The concept of ligament stabilization was introduced by H. Graf in the early 1990s and performed in patients with chronic back pain as a less invasive technique than spinal or posterio-lateral fusion.

In a retrospective, long-term, follow-up study, Kanayama et al (2007) reported minimum 10-year follow-up results of posterior dynamic stabilization using Graf artificial ligament (Graf ligamentoplasty) and evaluated the role and limitations of this procedure in the treatment of degenerative lumbar disorders. A total of 56 consecutive patients who underwent Graf ligamentoplasty were reviewed at a minimum 10-year follow-up. Forty-three patients in the original cohort had sufficient clinical and radiographical follow-up for analysis. The pathologies included degenerative spondylolisthesis in 23 patients, disc herniation with flexion instability in 13 patients, spinal stenosis with flexion instability in 4 patients, and degenerative scoliosis in 3 patients. Single-level procedures were performed in 36 patients; multi-level procedures were performed in 7 patients. Radiographical and clinical assessments were performed

before surgery and at the final follow-up. Disability due to LBP and/or sciatic symptoms was significantly improved in the patients with degenerative spondylolisthesis or flexion instability. However, degenerative scoliosis and/or laterolisthesis were associated with poor clinical improvement. In radiographical assessment, segmental lordosis was maintained in 10.9 degrees, and flexion-extension motion was averaged 3.6 degrees at the final follow-up. Facet arthrodesis eventually occurred in 14 patients (32.6%) at an average of 82 months after surgery. Additional surgeries were required in 3 patients (7.0%) for adjacent segment pathologies. The authors concluded that long-term results showed that Graf ligamentoplasty is an effective treatment option for low-grade degenerative spondylolisthesis and flexion instability. However, this procedure has limitations to correct spinal deformity, and is not advocated for the treatment of degenerative scoliosis and laterolisthesis.

In a discussion of the afore-mentioned study, Fraser (2007) stated that "[p]erhaps the main value of this retrospective study is the finding that Graf ligamentoplasty is not effective in the treatment of patients with degenerative scoliosis, but the long-term efficacy of the Graf procedure for other lumbar conditions is yet to be proven".

Putzier et al (2010) compared dynamic fixation of a clinically asymptomatic initially degenerated segment adjacent to fusion (iASD), with circumferential lumbar fusion alone. A total of 60 patients with symptomatic degeneration of L5/S1 or L4/L5 (Modic greater than or equal to 2 degrees) and asymptomatic iASD (Modic = 1 degrees, confirmed by discography) were divided into 2 groups; 30 patients were treated with circumferential single-level fusion (SLF). In dynamic fixation transition (DFT) patients, additional posterior dynamic fixation of iASD was performed. Pre-operatively, at 12 months, and at a mean follow-up of 76.4 (60 to 91) months, radiological (MRI, X-ray) and clinical (ODI, VAS, satisfaction) evaluations assessed fusion, progression of adjacent segment degeneration (PASD), radiologically adverse events, functional outcome, and pain. At final follow-up, 2 non-fusions were observed in both groups. A total of 6 SLF patients and 1 DFT patient presented a PASD. In 2 DFT patients, a PASD occurred in the segment superior to the dynamic fixation, and in 1 DFT patient, a fusion of the dynamically fixated segment was observed. A total of 4 DFT patients presented radiological implant failure. While no differences in clinical scores were observed

between groups, improvement from pre-operative conditions was significant (all $p < 0.001$). Clinical scores were equal in patients with PASD and/or radiologically adverse events. The authors do not recommend dynamically fixating the adjacent segment in patients with clinically asymptomatic iASD. The lower number of PASD with dynamic fixation was accompanied by a high number of implant failures and a shift of PASD to the superior segment.

In summary, despite some preliminary evidence that dynamic stabilization systems (e.g., the Dynesys) have produced clinical outcomes comparable to that of fusion, the clinical value of dynamic stabilization awaits the findings of prospective, RCTs, which are an essential requirement for practice of evidence-based medicine.

Inter-Spinous Distraction and Interlaminar Stabilization Procedures

Lumbar spinal stenosis (LSS) refers to narrowing of the lumbar spinal canal, lateral recess, or foramen resulting in neurovascular compression that may lead to pain. Spinal stenosis may be classified by etiology (e.g., congenital or acquired) or symptomatology (e.g., radiculopathy, neurogenic claudication, or mechanical back pain). It can also be classified radiographically, by the location of the stenosis (e.g., central canal, lateral recess, or intervertebral foramen) or by the presence of deformity such as spondylolisthesis or scoliosis. Overlapping in the classification of LSS can occur in that central stenosis with thecal sac compression usually leads to neurogenic claudication, while lateral recess compression is associated with compression of an individual nerve root, thus resulting in radiculopathy. Although symptoms may arise from narrowing of the spinal canal, not all patients with narrowing develop symptoms. The reason why some patients develop symptomatic stenosis and others do not is still unknown. Therefore, LSS does not refer to the pathoanatomical finding of spinal canal narrowing. It is a clinical syndrome of lower extremity pain caused by mechanical compression on neural elements or their vascular supply (Truumees, 2005).

Non-surgical treatments (e.g., activity modification, medications such as NSAIDs, physical therapy that focuses on flexion-based exercises, as well as epidural steroid injections) are usually the first treatment choice for patients suffering from neurogenic intermittent claudication (NIC)

secondary to LSS. If symptoms failed to improve with non-surgical treatments, decompressive surgery (e.g., laminectomy, facetectomy, multi-level laminotomies, fenestration, distraction laminoplasty, and microscopic decompression), with or without fusion, may be necessary. Moreover, several studies reported that surgical treatment produces better outcomes than non-surgical treatment in the short-term; however, the results tend to deteriorate with time (Yuan et al, 2005).

While fusion operations have traditionally been used to manage many disorders of the lumbar spine related to instability, pain, or deformity, concern over the long-term effects of fusion on adjacent spinal segments has led to the development of new approaches such as inter-spinous distraction procedures.

Examples of US Food and Drug Administration (FDA) approved interspinous process spacers include, but may not be limited to, the Superion Interspinous Spacer, the X-Stop Interspinous Process Decompression (IPD) System and the X-Stop PEEK IPD System.

Interspinous process decompression is a minimally invasive surgical procedure that is proposed to relieve the symptoms of lumbar spinal stenosis in those patients who do not respond to conservative, nonsurgical treatment. The procedure involves implanting interspinous process decompression spacers between the spinous processes of the vertebrae which appear to be the source of the symptoms. The spacers can be implanted at one or two lumbar levels and are designed to remain in place without being permanently affixed to the bone or ligamentous structures of the spine.

The X-Stop Inter-Spinous Process Distraction/Decompression System (St. Francis Medical Technologies, Inc., Alameda, CA) was developed to provide an alternative therapeutic. The principal behind the X-Stop (eXtension-Stop) is that by decompressing the affected spinal segment and maintaining it in a slightly flexed position (and also preventing extension) the symptoms of LSS can be relieved. Additionally, it allows the patient to resume their normal posture rather than flex the entire spine. The X-Stop is made of titanium alloy and is available in 5 sizes – 6, 8, 10, 12, and 14 mm in diameter. It consists of 2 major parts: (i) the

universal wing, and (ii) the main body (with oval spacer and tissue expander). The wings prevent anterior and lateral movement while the supraspinous ligament prevents posterior displacement. The oval spacer swivels, making it self-aligning relative to the uneven surface of the spinous process. This ensures that no sharp edges come into contact with the spinous process and that compressive loads are distributed equally on the surface of the bone.

The X-Stop Inter-Spinous Process Distraction/Decompression System gained FDA's PMA in November 2005 for use in alleviating the symptoms of patients with LSS. The X-Stop is intended to be used in patients with symptomatic LSS at 1 or 2 levels who have failed at least 6 months of conservative treatment. Under local anesthesia, the implant is inserted between the spinous processes of the affected level(s), and prevents extension at those levels. Talwar et al (2005) stated that patients with lower bone mineral density must be approached with more caution during insertion of the inter-spinous process implant.

According to SFMT Europe B.V., a subsidiary of St. Francis Medical Technologies, the X-Stop is indicated for any of the following conditions:

- Axial-load induced back pain; or
- Baastrup's syndrome (also known as kissing spines); or
- Contained herniated nucleus pulposus; or
- Degenerative and/or iatrogenic (post-discectomy) disc syndrome; or
- Facet syndrome; or
- Neurogenic intermittent claudication due to central and/or lateral-recess LSS; or
- Spondylolisthesis up to grade 1.5 (of 4) (about 35%), with NIC; or
- Unloading of disc adjacent to a lumbar fusion procedure, primary or secondary.

There is a scarcity of randomized controlled studies on the clinical value of the X-Stop for the indications listed above, especially its long-term (over 2 years) benefits. Currently, available evidence on this device is mainly from J.F. Zucherman and K.Y. Hsu (developers of this technology), and their associates.

Verhoof and colleagues (2008) stated that the X-Stop inter-spinous distraction device has been reported to be an alternative to conventional surgical procedures in the treatment of symptomatic degenerative lumbar spinal stenosis. However, the effectiveness of the X-Stop in symptomatic degenerative lumbar spinal stenosis caused by degenerative spondylolisthesis is not known. A cohort of 12 consecutive patients with symptomatic lumbar spinal stenosis caused by degenerative spondylolisthesis were treated with the X-Stop inter-spinous distraction device. All patients had LBP, neurogenic claudication and radiculopathy. Pre-operative radiographs revealed an average slip of 19.6%. Magnetic resonance imaging of the lumbo-sacral spine showed a severe stenosis. In 10 patients, the X-Stop was placed at the L4 to L5 level, whereas 2 patients were treated at both, L3 to L4 and L4 to L5 level. The mean follow-up was 30.3 months. In 8 patients, a complete relief of symptoms was observed post-operatively, whereas the remaining 4 patients experienced no relief of symptoms. Recurrence of pain, neurogenic claudication, and worsening of neurological symptoms was observed in 3 patients within 24 months. Post-operative radiographs and MRI did not show any changes in the percentage of slip or spinal dimensions. Finally, secondary surgical treatment by decompression with postero-lateral fusion was performed in 7 patients (58%) within 24 months. The authors concluded that the X-Stop inter-spinous distraction device showed an extremely high failure rate, defined as surgical re-intervention, after short term follow-up in patients with spinal stenosis caused by degenerative spondylolisthesis. They do not recommend the X-Stop for the treatment of spinal stenosis complicating degenerative spondylolisthesis.

Lindsey et al (2003) examined the kinematics of the instrumented lumbar spine and adjacent levels due to the insertion of the X-Stop. Seven lumbar spines (L2 to L5) were tested in flexion-extension, lateral bending, and axial rotation. Images were taken during each test to determine the kinematics of each motion segment. The X-Stop was inserted at the L3 to L4 level, and the test protocol was repeated. These researchers found that the X-Stop does not significantly alter the kinematics of the motion segments adjacent to the instrumented level.

In a study using 7 cadaveric spines (L2 to L5), Fuchs et al (2005) noted that the X-Stop may be used in conjunction with a unilateral medial facetectomy or unilateral total facetectomy. However, it should not be

used in conjunction with bilateral total facetectomy. In another cadaveric L2 to L5 spine study (n = 7), Wiseman et al (2005) reported that inter-spinous process decompression by placing the X-Stop between the L3 to L4 spinous processes will unlikely cause adjacent level facet pain or accelerated facet joint degeneration. Furthermore, pain induced from pressure originating in the facets and/or posterior anulus of the lumbar spine may be relieved by inter-spinous process decompression. Richards et al (2005) quantified the effect of the X-Stop on the dimensions of the spinal canal and neural foramina during flexion and extension. By means of a positioning frame, 8 specimens (L2 to L5) were positioned to 15 degrees of flexion and 15 degrees of extension. Each specimen was assessed using magnetic resonance imaging (MRI), with and without the X-Stop, placed between the L3 to L4 spinous processes. Canal and foramina dimensions were compared between the intact and implanted specimens. These investigators concluded that the X-Stop prevents narrowing of the spinal canal and foramina in extension.

Lee and colleagues (2004) reported their preliminary findings on the use of the X-Stop for LSS in elderly patients (n = 10). Subjects were evaluated post-operatively by MRI and the Swiss Spinal Stenosis Questionnaire. Cross-sectional areas of the dural sac and intervertebral foramina at the stenotic level were measured post-operatively and compared with the pre-operative values. After implantation of the X-Stop, the cross-sectional area of the dural sac increased 16.6 mm2 (22.3%) and intervertebral foramina increased 22 mm2 (36.5%). The intervertebral angle as well as the posterior disc height changed significantly. A total of 70% of the patients stated that they were satisfied with the surgical outcome.

In a multi-center, prospective, randomized, controlled trial, Zucherman and colleagues (2005) compared the outcomes of X-Stop treated NIC patients (n = 100) with their non-operatively treated counterparts (n = 91). The primary outcomes measure was the Zurich Claudication Questionnaire (ZCQ) – a patient-completed, validated instrument for NIC. At every follow-up visit, X-Stop treated patients had significantly better outcomes in each domain of the ZCQ. At 2 years, the X-Stop treated patients improved by 45.4% over the mean baseline Symptom Severity score compared with 7.4% in the control group; the mean improvement in

the Physical Function domain was 44.3% in the X-Stop group and -0.4% in the control group. In the X-Stop group, 73.1% patients were satisfied with their treatment compared with 35.9% of control patients.

Siddiqui et al (2007) reported on the one year results of a prospective observational study of the X Stop interspinous implant for the treatment of lumbar spinal stenosis. Forty consecutive patients were enrolled and surgically treated with X Stop implantation. The X Stop device was implanted at the stenotic segment, which was either at 1 or 2 levels in each patient. Sixteen of 40 patients failed to complete all clinical questionnaires at each of the specified time intervals and were excluded from the study. The investigators reported that, by 12 months after surgery, 54% of the 24 remaining patients reported clinically significant improvement in their symptoms, 33 reported clinically significant improvement in their physical function, and 71% expressed satisfaction with the procedure. Twenty-nine percent of patients required caudal epidural after 12 months for recurrence of their symptoms of neurogenic claudication. The investigators noted that, although this study indicates that the X Stop offers significant short-term improvement, these results were less favorable than the previous randomized clinical study. Limitations of this study include the lack of a control group, short duration of follow-up, and high proportion of dropouts.

In a literature review, Christie et al (2005) evaluated the mechanisms of action and effectiveness of inter-spinous distraction devices in managing symptomatic lumbar spinal pathology. They stated that these devices continue to be evaluated in clinical trials; and that although the use of inter-spinous implants is still experimental, the early results are promising, and it is likely that future studies will establish a niche for them in the management of lumbar spinal pathology.

Bono and Vaccaro (2007) reviewed interspinous process devices for the lumbar spine, and stated that, although some clinical data exist for some of these devices, defining the indications for these minimally invasive procedures will be crucial. "Indications should emerge from thoughtful consideration of data from randomized controlled studies".

Based upon a systematic evidence review on inter-spinous distraction procedures for spinal stenosis causing neurogenic claudication in the lumbar spine, the National Institute for Health and Clinical Excellence (NICE, 2006) concluded that "evidence of efficacy is limited and is confined to the medium and short term. These procedures should only be used in the context of special arrangements for consent, audit and research". Additionally, the specialist advisors to the Institute's Interventional Procedures Advisory Committee noted that given the fluctuating symptoms associated with this condition, the assessment of outcomes in clinical studies may be unreliable. Furthermore, some advisors questioned the long-term effectiveness of the procedure.

The questions regarding the long-term effectiveness of the X-Stop raised by Christie et al (2005) as well as some specialist advisors of the National Institute for Health and Clinical Excellence's Interventional Procedures Advisory Committee (2006) are congruous with those raised by documents released by the FDA in 2004 prior to a public hearing on the product. The FDA's PMA review stated that "although the device can be inserted with a minimally invasive operative technique as an outpatient procedure with generally a local anesthetic a decision as to the safety and effectiveness of this device is based solely on 24 month data because information on the patient outcomes after 24 months is not available. This information becomes important when looking at pain relief and return to function. Even though the goal of the study was accomplished showing a significant, statistical difference between the investigational and control groups, more patients report improvement at 12 months than at 24 months. Contrary to what has been observed in spinal fusion studies, in this study, a percentage of patients whose symptoms improved at 6 and 12 months show a trend of regression of pain and function symptoms toward baseline levels. There appears to be a trend with early pain relief but the data suggests that in about 15% of patients initially successfully treated by the X-stop had only temporary relief".

On August 31, 2004, the FDA's Orthopaedic and Rehabilitation Devices Panel voted 5 to 3 to recommend a "not approvable" decision on the PMA for the X-Stop. The Panel cited concern with the need to identify the patient population that is most likely to benefit from the device, noting that overall effectiveness was not demonstrated in a majority of the clinical study population. The Panel also cited concerns with the longer term

effectiveness of the device (longer than 2 years), with potential bias in the clinical study, and with the need for radiographic or other objective evidence of the device's mechanism of effect on the spine in patients.

As a condition of approval, the FDA has required the manufacturer to conduct a post-marketing study of the long-term safety and effectiveness of the X-Stop in patients who received the X-Stop under the Investigational Device Exemption (IDE). The FDA has required the manufacturer to conduct an additional post-approval study involving 240 patients at up to 8 clinical sites.

Guidelines from the North American Spine Society (NASS, 2007) concluded that there was insufficient evidence to support the use of the XSTOP in persons with lumbar spinal stenosis. The NASS guidelines noted: "Although the study cited in support of this recommendation is a level I study, it is a single study. Therefore, until further evidence is published there remains insufficient evidence to make a recommendation [about the use of the XSTOP in lumbar spinal stenosis]". More recently, guidelines from the North American Spine Society (NASS, 2011) concluded: "there is insufficient evidence at this time to make a recommendation for or against the placement of an interspinous process spacing device in patients with lumbar spinal stenosis."

In summary, the clinical value of X-Stop for patients with LSS is still uncertain. In particular, whether its reported benefit will decline over time will require more research with longer-term evaluation. Additionally, further randomized controlled studies are needed to compare these inter-spinous process implants with traditional surgical interventions such as laminectomy and/or fusion.

In December 2004, the FDA granted 510(k) approval for ExtenSure bone allograft inter-spinous spacer device, which is a cylindrically fashioned piece of allograft bone intended to effect distraction, restore and maintain the space between 2 adjacent spinous processes and indirectly decompress a stenotic spinal canal at 1 or 2 levels. The procedure promotes fusion of the allograft to the spinous process above, while allowing motion between the allograft and the spinous process below. It is thought that this would provide a long-term solution to implant stability while retaining segmental motion. It may also be used to facilitate fusion

between 2 or more adjacent spinous processes. This is similar to the action of the X-Stop device. However, there is a lack of clinical studies demonstrating effectiveness of the ExtenSure device.

The TOPS System, a total posterior arthroplasty implant, is an alternative to spinal fusion that is designed to stabilize but not fuse the affected vertebral level following decompression surgery to alleviate pain stemming from lumbar spinal stenosis while maintaining range of motion. It is indicated for patients with lower back and leg pain resulting from moderate-to-severe lumbar spinal stenosis at a single level between L3 and L5 that may be accompanied by facet arthrosis or degenerative spondylolisthesis. The TOPS System is not available for commercial use in the United States. Enrollment for an FDA investigational device exemption study commenced in May 2008.

In a review of the evidence on surgery for LBP for the American Pain Society's clinical practice guideline, Chou et al (2009) concluded that surgery for radiculopathy with herniated lumbar disc and symptomatic spinal stenosis is associated with short-term benefits compared to non-surgical therapy, though benefits diminish with long-term follow-up in some trials. For non-radicular back pain with common degenerative changes, fusion is no more effective than intensive rehabilitation, but associated with small -to-moderate benefits compared to standard non-surgical therapy. Moreover, they stated that although there is fair evidence that an inter-spinous spacer device is moderately more effective than non-surgical therapy for 1- or 2-level spinous stenosis, there are insufficient data to evaluate long-term benefits and harms.

The Coflex (Paradigm Spine) is an interlaminar spinal stabilization device for persons with lumbar stenosis that is implanted following laminectomy and decompression. The device is intended to provide benefits over fusion, including durable pain relief, maintenance of spinal motion, reduced hypermobility of adjancent segments resulting in reduced degeneration at adjacent levels. A pivotal randomized controlled clinical trial evaluated the noninferiority of the Coflex interlaminar stabilization with instrumented posterolateral spinal fusion (pedicle screw fixation) in subjects with back pain and spinal stenosis and no or mild instability (up to grade 1 spondylolisthesis) who had failed conservative management. The primary outcome of the study is improvements in Oswestry Disability

Index (ODI) score, and secondary outcomes include the Visual Analog Scale (VAS) back and leg pain, and the Zurich Claudication Questionnaire (ZCQ) score. Other endpoints measured include range of motion at the level adjacent to the procedure, as range of motion has been found to be related to the development of adjacent level degeneration and disease. Subjects were followed over a two-year period. Limitations of the study include the lack of blinding and the intermediate duration of the study. In addition, the study compared the effectiveness of the Coflex device with spinal fusion in spinal stenosis subjects with no instability; however, the benefits of spinal fusion this group of patients is uncertain.

In a prospective, randomized, multi-center, FDA IDE trial, Davis et al (2013a) evaluated the safety and effectiveness of Coflex interlaminar stabilization compared with posterior spinal fusion (PSF) in the treatment of 1- and 2-level spinal stenosis and degenerative spondylolisthesis. A total of 322 patients (215 Coflex and 107 fusions) from 21 sites in the U.S. were enrolled between 2006 and 2010. Subjects were randomized to receive laminectomy and Coflex interlaminar stabilization or laminectomy and postero-lateral spinal fusion with spinal instrumentation in a 2:1 ratio. Overall device success required a 15-point reduction in ODI, no re-operations, no major device-related complications, and no post-operative epidural injections. Patient follow-up at minimum 2 years was 95.3% and 97.2% in the Coflex and fusion control groups, respectively. Patients taking Coflex experienced significantly shorter operative times ($p < 0.0001$), blood loss ($p < 0.0001$), and length of stay ($p < 0.0001$). There was a trend toward greater improvement in mean ODI scores in the Coflex cohort ($p = 0.075$). Both groups demonstrated significant improvement from baseline in all VAS back and leg parameters. Patients taking Coflex experienced greater improvement in Short-Form 12 physical health outcomes ($p = 0.050$) and equivalent mental health outcomes. Coflex subjects experienced significant improvement in all ZCQ outcomes measures compared with fusion (symptom severity [$p = 0.023$]; physical function [$p = 0.008$]; satisfaction [$p = 0.006$]). Based on the FDA composite for overall success, 66.2% of Coflex and 57.7% of fusions succeeded ($p = 0.999$), thus demonstrating non-inferiority. The overall adverse event rate was similar between the groups, but Coflex had a higher re-operation rate (10.7% versus 7.5%, $p = 0.426$). At 2 years, fusions exhibited increased angulation ($p = 0.002$) and a trend toward

increased translation (p = 0.083) at the superior adjacent level, whereas Coflex maintained normal operative and adjacent level motion. The authors concluded that Coflex interlaminar stabilization is a safe and effective alternative, with certain advantages compared with lumbar spinal fusion in the treatment of spinal stenosis and low-grade spondylolisthesis.

In a prospective, randomized, multi-center FDA IDE trial, Davis et al (2013b) evaluated the safety and effectiveness of Coflex Interlaminar Stabilization compared with PSF to treat low-grade spondylolisthesis with spinal stenosis. A total of 322 patients from 21 sites in the U.S. were enrolled between 2006 and 2008 for the IDE trial. The current study evaluated only the subset of patients from this overall cohort with Grade 1 spondylolisthesis (99 in the Coflex group and 51 in the fusion group). Subjects were randomized 2:1 to receive decompression and Coflex interlaminar stabilization or decompression and PSF with spinal instrumentation. Data collected included peri-operative outcomes, ODI, back and worse leg VAS scores, 12-Item Short Form Health Survey, ZCQ, and radiographic outcomes at a minimum of 2 years. The FDA criteria for overall device success required the following to be met: 15-point reduction in ODI, no re-operations, no major device-related complications, and no post-operative epidural injections. At a minimum of 2 years, patient follow-up was 94.9% and 94.1% in the Coflex and fusion control groups, respectively. There were no group differences at baseline for any demographic, clinical, or radiographic parameter. The average age was 63 years in the Coflex cohort and 65 years in the fusion cohort. Coflex subjects experienced significantly shorter operative times (p < 0.0001), less estimated blood loss (p < 0.0001), and shorter length of stay (p < 0.0001) than fusion controls. Both groups experienced significant improvements from baseline at 2 years in ODI, VAS back, VAS leg, and ZCQ, with no significant group differences, with the exception of significantly greater ZCQ satisfaction with Coflex at 2 years. The FDA overall success was achieved in 62.8% of Coflex subjects (59 of 94) and 62.5% of fusion controls (30 of 48) (p = 1.000). The re-operation rate was higher in the Coflex cohort (14 [14.1%] of 99) compared with fusion (3 [5.9%] of 51, p = 0.18), although this difference was not statistically significant. Fusion was associated with significantly greater angulation and translation at the superior and inferior adjacent levels compared with baseline, while Coflex showed no significant radiographic changes at the operative or index levels. The authors concluded that low-grade

spondylolisthesis was effectively stabilized by Coflex and led to similar clinical outcomes, with improved per-operative outcomes, compared with PSF at 2 years. Re-operation rates, however, were higher in the Coflex cohort. Patients in the fusion cohort experienced significantly increased superior and inferior level angulation and translation, while those in the Coflex cohort experienced no significant adjacent or index level radiographic changes from baseline. Coflex Interlaminar Stabilization is a less invasive, safe, and equally effective clinical solution to PSF to treat low-grade spondylolisthesis, and it appears to reduce stresses at the adjacent levels.

The major drawback associated with these 2 studies were: (i) lack of patient blinding, (ii) these studies did not assess the effectiveness of a fusion group consisting of lumbar intervertebral cages or BMP, and (iii) it is possible a subset of patients with a stable slip and with minimal back pain may benefit from decompression only, without the need for stabilization. Furthermore, long-term data are needed to ascertain if motion preservation with the Coflex device will lead to lower re-operation rates for adjacent level disease compared with fusion.

Also, an UpToDate review on " Subacute and chronic low back pain: Surgical treatment" (Chou, 2013) does not mention Coflex/interlaminar stabilization as a therapeutic option.

The pivotal investigational device exemption (IDE) trial for Coflex® Interlaminar Technology was a non-blinded, randomized, multi-center, non-inferiority trial of Coflex® compared to postero-lateral fusion with pedicle screw fixation. A total of 344 patients were randomized in a 2:1 ratio (215 Coflex® and 107 fusion controls, with 22 protocol violators). This study was conducted in a restricted population with numerous exclusion criteria. Compared to fusion, implantation of the Coflex® device required less operative time (98.0 versus 153.2 mins) and resulted in less blood loss (109.7 versus 348.6 cc) and a shorter hospital stay (1.9 versus 3.2 days). Composite clinical success (a combination of a minimum 15-point improvement in Oswestry Disability Index (ODI), no re-operations, no device-related complications, and no epidural steroid injections in the lumbar spine) at 24 months achieved non-inferiority compared to postero-lateral fusion (66.2% Coflex® and 57.7% fusion). Secondary

effectiveness criteria, which included the ZCQ, visual analog score (VAS) for leg and back pain, Short Form-12 (SF-12), time to recovery, patient satisfaction, and several radiographic endpoints, tended to favor the Coflex® group by Bayesian analysis. In this analysis, non-overlapping confidence intervals imply statistically reliable group differences. For example, ZCQ composite success was achieved in 78.3% of Coflex® patients (95% confidence interval [CI]: 71.9% to 84.7%) compared to 67.4% of controls (95% CI: 57.5% to 77.3%). The percentage of device-related adverse events was the same for the 2 groups (5.6% Coflex® and 5.6% control), and a similar percentage of asymptomatic spinous process fractures were observed. The FDA considered the data in this non-blinded study to support reasonable assurance of safety and effectiveness for device approval, but approval is conditional on 2 additional studies that will provide longer-term follow-up (in the IDE cohort) and evaluate device performance under actual conditions of use (decompression alone versus decompression with Coflex®).

Wouter et al (2014) commented that the FDA does not demand that the experimental treatment for a device is compared with the "gold standard." The author noted that interspinous process device (IPD) treatment with bony decompression was approved in the United States,after the publication of an FDA study on IPD treatment (citing Davis, et al., 2013). However, this study did not compare the experimental treatment (IPD) with the "gold standard" (bony decompression) but with another experimental treatment (bony decompression with fixation techniques). Wouter, et al. (2014) noted that most studies of interspinous process devices (IPD) did not compare the results with other interventions and most did not have prospective study designs. The authors stated that it took 30 years (from the introduction of the Wallis IPD in 1984 until 2013) until 2 prospective studies of IPDs were published that compared IPD treatment with conventional (surgical) care (citing Moojen, et al., 2013; Davis, et al., 2013; Moojen, et al., 2010; Stromqvist, et al., 2013). These studies showed that treatment with IPD was not superior to bony decompression without implants and that IPD treatment resulted in a higher reoperation rate (citing Moojen, et al., 2013: Stromqvist, et al., 2013). A third study of an IPD (X-Stop) was terminated because of the high number of reoperations (complications) in the experimental (IPD) group (Lønne, 2013).

Richter et al (2010) reported a prospective case control study of the Coflex® device in 60 patients who underwent decompressive surgery. The 2-year follow-up from this study was published in 2014 (Richter et al). These investigators prospectively evaluated the outcome of symptomatic lumbar spinal stenosis (LSS) treated with decompressive surgery alone in comparison with additional implantation of the Coflex® interspinous device. A total of 62 patients with symptomatic LSS were treated with decompressive surgery; 31 of these patients received an additional Coflex® device. Pre-operatively and post-operatively, disability and pain scores were measured using the ODI, the Roland-Morris Disability Questionnaire, the VAS, and the pain-free walking distance. Patients underwent post-operative assessments at 3, 6, 12, and 24 months including the above-mentioned scores and patient satisfaction. There was a significant improvement ($p < 0.001$) in the clinical outcome assessed in the ODI, the Roland-Morris Disability Questionnaire, the VAS, and the pain-free walking distance at all times of re-investigation compared with the base line in both groups. Up to 2 years after surgery, there were no significant differences between both groups in all ascertained parameters, including the patient satisfaction and subjective operation decision. The authors concluded that the results of this first prospective controlled study indicated that the additional placement of a Coflex® interspinous device does not improve the already good clinical outcome after decompressive surgery for LSS in the 24-month follow-up interval.

In a randomized controlled trial, Moojen et al (2013) examined if interspinous process device implantation is more effective in the short-term than conventional surgical decompression for patients with intermittent neurogenic claudication due to lumbar spinal stenosis. A total of 203 participants were referred to the Leiden-The Hague Spine Prognostic Study Group between October 2008 and September 2011; 159 participants with intermittent neurogenic claudication due to lumbar spinal stenosis at 1 or 2 levels with an indication for surgery were randomized. A total of 80 participants received an interspinous process device and 79 participants underwent spinal bony decompression. The primary outcome at short-term (8 weeks) and long-term (1 year) follow-up was the Zurich Claudication Questionnaire score. Repeated measurements were made to compare outcomes over time. At 8 weeks, the success rate according to the Zurich Claudication Questionnaire for the interspinous process device group (63%, 95% confidence interval

[CI]: 51% to 73%) was not superior to that for standard bony decompression (72%, CI: 60% to 81%). No differences in disability (Zurich Claudication Questionnaire; p = 0.44) or other outcomes were observed between groups during the 1st year. The repeat surgery rate in the interspinous implant group was substantially higher (n = 21; 29%) than that in the conventional group (n = 6; 8%) in the early post-surgical period (p < 0.001). The authors concluded that this double blinded study could not confirm the hypothesized short-term advantage of interspinous process device over conventional "simple" decompression and even showed a fairly high re-operation rate after interspinous process device implantation. Furthermore, for orthopedic studies with implanted device, 1 year follow-up would not be considered long-term.

Mohi Eldin (2014) evaluated the safety and effectiveness of the Coflex Dynamic Distraction Stabilization (DDS) device in treating patients with degenerative diseases of the lumbar spine (DDLS), especially lumbar canal stenosis (LCS), to confirm its indications for implantation and to evaluate the clinical outcomes of patients. This study was part of a multi-center prospective, case-controlled study in Egypt to determine the safety and efficacy of minimally invasive spinal procedures; of these, the Coflex implant, a functionally dynamic U-shaped titanium interspinous implant, was included in the present study. From June 2008 until July 2013, these researchers treated 42 patients with this Coflex procedure. Median follow-up was 22.5 months. At the time of follow-up, all patients completed questionnaires and underwent clinical examination and spinal radiography. A significant number of patients showed pain relief. Pre-operatively, 30/42 (71%) patients complained of moderate or severe low back pain (LBP). Post-operatively, the LBP in 6 (14%) patients did improve, 24 (57%) even showed no low back pain anymore. Mean pre-operative walking distance was less than 1,000m in 36 (86%) patients. Post-operatively, all 42 (100%) patients could walk greater than 1,000m. Significant pain relief (greater than 50%) in months was calculated. Radiological results showed that endplate angles when were acute pre-operatively, always became less acute post-operatively, and the foraminal height always increased. Segmental range of motion (ROM) showed maintenance of the dynamic movements at the operated level. Disc height showed significant changes after the procedure in both anterior and posterior disc heights. The authors noted that merging the clinical and radiological results of the current study suggested that these effects

produce a clinical benefit for LCS patients treated with the Coflex spacer. Though this series has limitations of a smaller sample size, it nevertheless confirmed the satisfactory results. These researchers stated that they will continue to follow the patients enrolled in this study, together with new cases and will report on the longer follow-up. This was a small study (n = 42) with mid-term follow-up (median of 22.5 months). There is a lack of data on durability; well-designed studies with more subjects and longer follow-up are needed.

Yuan et al (2017) retrospectively compared the at least 5-year clinical and radiological outcomes of Coflex stabilization and PLIF for lumbar degenerative disease. Eighty-seven consecutive patients with lumbar degenerative disease were retrospectively reviewed. Forty-two patients underwent decompression and Coflex interspinous stabilization (Coflex group), 45 patients underwent decompression and PLIF (PLIF group). Clinical and radiological outcomes were evaluated. Coflex subjects experienced less blood loss, shorter hospital stays and shorter operative time than PLIF (all $p < 0.001$). Both groups demonstrated significant improvement in Oswestry Disability Index and visual analogue scale back and leg pain at each follow-up time point. The Coflex group had significantly better clinical outcomes during early follow-up. At final follow-up, the superior and inferior adjacent segments motion had no significant change in the Coflex group, while the superior adjacent segment motion increased significantly in the PLIF group. At final follow-up, the operative level motion was significantly decreased in both groups, but was greater in the Coflex group. The reoperation rate for adjacent segment disease was higher in the PLIF group, but this did not achieve statistical significance (11.1% vs. 4.8%, $p = 0.277$). Both groups provided sustainable improved clinical outcomes for lumbar degenerative disease through at least 5-year follow-up.

In an extension of the study repoted by Davis, et al. in 2013, Musacchio, et al. (2016) reported on five-year outcomes of a prospective, randomized, controlled trial conducted at 21 centers. Patients with moderate to severe lumbar stenosis at one or two contiguous levels and up to Grade I spondylolisthesis were randomized (2:1 ratio) to decompression and interlaminar stabilization (D+ILS; n=215) using the Coflex Interlaminar Stabilization device or decompression and fusion with pedicle screws (D+PS; n=107). Clinical evaluations were made

preoperatively and at 6 weeks and 3, 6, 12, 18, 24, 36, 48, and 60 months postoperatively. Overall FDA success criteria required that a patient meet 4 criteria: 1) >15 point improvement in Oswestry Disability Index (ODI) score; 2) no reoperation, revision, removal, or supplemental fixation; 3) no major device-related complication; and 4) no epidural steroid injection after surgery. At 5 years, 50.3% of D+ILS vs. 44% of D+PS patients (p>0.35) met the composite success criteria. Reoperation/revision rates were similar in the two groups (16.3% vs. 17.8%; p >0.90). Both groups had statistically significant improvement through 60 months in ODI scores with 80.6% of D+ILS patients and 73.2% of D+PS patients demonstrating >15 point improvement (p>0.30). VAS, SF-12, and ZCQ scores followed a similar pattern of maintained significant improvement throughout follow-up. On the SF-12 and ZCQ, D+ILS group scores were statistically significantly better during early follow-up compared to D+PS. In the D+ILS group, foraminal height, disc space height, and range of motion at the index level were maintained through 5 years. This study compared the effectiveness of the Coflex device with spinal fusion in spinal stenosis subjects, some with low-grade spondylolisthesis; however, the benefits of spinal fusion in persons with spinal stenosis with low-grade spondylolisthesis are uncertain (see, e.g., Försth, et al., 2016; Puel & Moojen, 2016; Ghogawala, et al., 2016).

The Work Loss Data Institute's guideline on "Low back – lumbar & thoracic (acute & chronic)" (2013) listed interspinous decompression device (X-Stop) as one of the interventions/procedures that were considered, but was not recommended.

The North American Spine Society (NASS)'s clinical guideline on "Diagnosis and treatment of degenerative lumbar spondylolisthesis" (2014) stated that "There is insufficient and conflicting evidence to make a recommendation for or against the efficacy of interspinous spacers versus medical/interventional treatment in the management of degenerative lumbar spondylolisthesis patients. Grade of Recommendation: I (Insufficient Evidence)".

Puzzilli et al (2014) evaluated patients who were treated for symptomatic lumbar spinal stenosis with interspinous process decompression (IPD) implants compared with a population of patients managed with conservative treatment. A total of 542 patients affected by symptomatic

lumbar spine degenerative disease were enrolled in a controlled trial; 422 patients underwent surgical treatment consisting of X-STOP device implantation, whereas 120 control cases were managed conservatively. Both patient groups underwent follow-up evaluations at 6, 12, 24, and 36 months using the Zurich Claudication Questionnaire, the visual analog scale (VAS) score and spinal lumbar X-rays, CT scans and MR imaging. One-year follow-up evaluation revealed positive good results in the 83.5% of patients treated with IPD with respect to 50% of the non-operative group cases. During the first 3 years, in 38 out of the 120 control cases, a posterior decompression and/or spinal fixation was performed because of unsatisfactory results of the conservative therapy. In 24 (5.7%) of 422 patients, the IPD device had to be removed, and a decompression and/or pedicle screw fixation was performed because of the worsening of neurological symptoms. The authors concluded that these findings supported the effectiveness of surgery in patients with stenosis; IPD may offer an effective and less invasive alternative to classical microsurgical posterior decompression in selected patients with spinal stenosis and lumbar degenerative disk diseases.

Doulgeris et al (2015) compared an interspinous fusion device with posterior pedicle screw system in a lateral lumbar interbody lumbar fusion. These researchers biomechanically tested 6 cadaveric lumbar segments (L1 to L2) under an axial preload of 50N and torque of 5Nm in flexion-extension, lateral bending and axial rotation directions. They quantified range of motion, neutral zone/elastic zone stiffness in the following conditions: intact, lateral discectomy, lateral cage, cage with interspinous fusion, and cage with pedicle screws. A complete lateral discectomy and annulectomy increased motion in all directions compared to all other conditions. The lateral cage reduced motion in lateral bending and flexion/extension with respect to the intact and discectomy conditions, but had minimal effect on extension stiffness. Posterior instrumentation reduced motion, excluding interspinous augmentation in axial rotation with respect to the cage condition. Interspinous fusion significantly increased flexion and extension stiffness, while pedicle screws increased flexion/extension and lateral bending stiffness, with respect to the cage condition. Both posterior augmentations performed equivalently throughout the tests except in lateral bending stiffness where pedicle screws were stiffer in the neutral zone. The authors concluded that a lateral discectomy and annulectomy generated immediate

instability. Stand-alone lateral cages restored a limited amount of immediate stability, but posterior supplemental fixation increased stability. Both augmentations were similar in a single level lateral fusion in-vitro model, but pedicle screws are more equipped for coronal stability. They stated that an interspinous fusion is a less invasive alternative than pedicle screws and is potentially a conservative option for various interbody cage scenarios.

Hirsch et al (2015) stated that lumbar spinal stenosis is a major public health issue. Interspinous devices implanted using minimally invasive techniques may constitute an alternative to the reference standard of bony decompression with or without intervertebral fusion. However, their indications remain unclear, due to a paucity of clinical and biomechanical data. These investigators evaluated the effects of four interspinous process devices implanted at L4 to L5 on the intervertebral foramen surface areas at the treated and adjacent levels, in flexion and in extension. Six fresh frozen human cadaver lumbar spines (L2 to sacrum) were tested on a dedicated spinal loading frame, in flexion and extension, from 0 to 10 N·m, after preparation and marking of the L3 to L4, L4 to L5, and L5 to S1 foramina. Stereoscopic 3D images were acquired at baseline then after implantation at L4 to L5 of each of the 4 devices (Inspace®, Synthes; X-Stop®, Medtronic; Wallis®, Zimmer; and Diam®, Medtronic). The surface areas of the 3 foramina of interest were computed. All 4 devices significantly opened the L4 to L5 foramen in extension. The effects in flexion separated the devices into 2 categories. With the 2 devices characterized by fixation in the spinous processes (Wallis® and Diam®), the L4 to L5 foramen opened only in extension; whereas with the other 2 devices (X-Stop® and Inspace®), the L4 to L5 foramen opened not only in extension, but also in flexion and in the neutral position. None of the devices implanted at L4 to L5 modified the size of the L3 to L4 foramen. X-Stop® and Diam® closed the L5 to S1 foramen in extension, whereas the other 2 devices had no effect at this level. The authors concluded that these findings demonstrated that interspinous process devices modified the surface area of the interspinous foramina in-vitro. They stated that clinical studies are needed to clarify patient selection criteria for interspinous process device implantation.

Lee et al (2015) conducted a systematic literature review of interspinous dynamic stabilization, including Diam®, Wallis®, Coflex, and X-STOP®, to assess its safety and efficacy. A literature search was done in Korean and English, by using eight domestic databases which included KoreaMed and international databases, such as Ovid Medline, Embase, and the Cochrane Library. A total of 306 articles were identified, but the animal studies, preclinical studies, and studies that reported the same results were excluded. As a result, a total of 286 articles were excluded and the remaining 20 were included in the final assessment. Two assessors independently extracted data from these articles using predetermined selection criteria. Qualities of the articles included were assessed using Scottish Intercollegiate Guidelines Network (SIGN). The complication rate of interspinous dynamic stabilization has been reported to be 0% to 32.3% in 3- to 41-month follow-up studies. The complication rate of combined interspinous dynamic stabilization and decompression treatment (32.3%) was greater than that of decompression alone (6.5%), but no complication that significantly affected treatment results was found. Interspinous dynamic stabilization produced slightly better clinical outcomes than conservative treatments for spinal stenosis. Good outcomes were also obtained in single-group studies. No significant difference in treatment outcomes was found, and the studies compared interspinous dynamic stabilization with decompression or fusion alone. The authors of the systematic review concluded that no particular problem was found regarding the safety of the technique. Its clinical outcomes were similar to those of conventional techniques, and no additional clinical advantage could be attributed to interspinous dynamic stabilization. However, few studies have been conducted on the long-term efficacy of interspinous dynamic stabilization. Thus, the authors suggest further clinical studies be conducted to validate the theoretical advantages and clinical efficacy of this technique.

The Australian Medical Services Advisory Committee (MSAC, 2017) found insufficient evidence to support the Coflex Interlaminar Stabilization device. MSAC considered that the evidence comparing use of the device with decompression and fusion, and with decompression alone, for LSS was too limited to support the listing and no evidence was presented comparing use of the device to other alternatives for mild degenerative instability alone. MSAC noted that any resubmission would require high quality trial evidence that compared the benefits, harms and cost-

effectiveness of using the device with decompression alone, and with decompression and fusion. Such a resubmission should also clarify the appropriate patient population who need 'stabilization'.

Patel et al (2015a) noted that interspinous spacers are a less-invasive treatment alternative compared with surgical decompression for patients with LSS unresponsive to conservative care. High-quality comparative data with these devices are lacking. In a prospective, multi-center, randomized, controlled, IDE non-inferiority trial, these researchers determined the 2-year outcomes in patients with intermittent neurogenic claudication secondary to moderate LSS who were treated with the Superion interspinous process spacer. Patients presenting with intermittent neurogenic claudication secondary to moderate LSS who failed at least 6 months of non-surgical management were randomly allocated to treatment with the Superion spacer or a control spacer (X-Stop) and followed for 2 years. A total of 391 randomized patients were implanted with Superion (n = 190) or control (n = 201) spacers at 29 sites in the U.S. between August 2008 and December 2011. Implants were successfully implanted in 99.5 % of patients with Superion and 99.0 % of control patients. The primary composite end-point of this study was met, which demonstrated that the Superion spacer was non-inferior to the X-Stop spacer. Leg pain, the predominant patient complaint, decreased in severity by 70 % during 2 years in each group. Most (77 %) patients achieved leg pain clinical success (improvement greater than or equal to 20 mm) at 2 years. Back pain clinical success (improvement greater than or equal to 20 mm) was 68 %, with no differences between groups; ODI clinical success (greater than or equal to 15 % point improvement) was achieved in 65 % of patients. The rates of complications and re-operations were similar between groups. The authors concluded that the Superion interspinous process spacer relieved symptoms of intermittent neurogenic claudication secondary to moderate LSS in the majority of patients through 2 years. These researchers stated that the Superion device may represent a reasonable therapeutic option for this patient population.

The authors stated that this study had several drawbacks. The long-term durability of interspinous process spacers is currently unknown and requires further investigation. In addition, the generalizability of these findings may only be applicable to patients with radiographically

confirmed moderate LSS with no more than low-grade spondylolisthesis deformities. The finding that patients with a spinous process fracture yielded similar long-term clinical results to patients without a spinous process fracture brought into question the mechanisms of mechanical action of these devices. Finally, a comparison of interspinous process spacers with non-surgical treatment or surgical decompression was not performed; thus this randomized study provided no information on these interesting questions.

Patel et al (2015b) provided the 3-year clinical outcomes from the randomized, controlled FDA IDE trial of the Superion for the treatment of moderate degenerative LSS. The Superion was evaluated in the treatment of subjects aged 45 years or older suffering from symptoms of intermittent neurogenic claudication, secondary to a confirmed diagnosis of moderate degenerative LSS at 1 or 2 contiguous levels from L1 to L5. Patients were treated between June 2008 and December 2011 at 31 investigational sites. A total of 391 subjects were included in the randomized study group consisting of 190 Superion and 201 X-STOP control subjects. The primary composite end-point was individual patient success based on 4 components: improvement in 2 of 3 domains of the Zurich Claudication Questionnaire, no re-operations at the index level, no major implant/procedure-related complications, and no clinically significant confounding treatments. At 3 years, the proportion of subjects achieving the primary composite end-point was greater for Superion (63/120, 52.5 %) than for X-STOP (49/129, 38.0 %) ($p = 0.023$) and the corresponding success rates exceeded 80 % for each of the individual components of the primary end-point in the Superion group (range of 81 % to 91%). Improvements in back and leg pain severity as well as back- and disease-specific functional outcomes were also maintained through 36 months. The authors concluded that the 3-year outcomes from this RCT demonstrated durable clinical improvement consistently across all clinical outcomes for the Superion in the treatment of patients with moderate degenerative LSS.

These researchers stated that the durable clinical results achieved with the Superion in the current study were further reflected in a low conversion rate to surgical decompression of only 14 % (26/190) at 3 years. This finding may have a profound effect on the health economics and societal costs of treating the increasing number of patients suffering

from spinal stenosis. Indeed, approximately 40 % of patients treated conservatively to alleviate early signs of spinal stenosis ultimately require decompression surgery within 10 years due to persistently worsening symptoms. They stated that the use of an InterSpinous Spacer at the appropriate juncture in the continuum of care may obviate the need for decompression surgery in the majority of patients carefully selected in accordance with the approved indications for use. This study provided short-term follow-up data.

Parker et al (2015) noted that LSS is a painful and debilitating condition resulting in healthcare costs totaling tens of billions of dollars annually. Initial treatment consists of conservative care modalities such as physical therapy, NSAIDs, opioids, and steroid injections. Patients refractory to these therapies can undergo decompressive surgery, which has good long-term efficacy but is more traumatic and can be associated with high post-operative AE rates. Interspinous spacers have been developed to offer a less-invasive alternative. These researchers compared the costs and quality adjusted life years (QALYs) gained of conservative care (CC) and decompressive surgery (DS) to a new minimally-invasive interspinous spacer. A Markov model was developed evaluating 3 strategies of care for LSS. If initial therapies failed, the model moved patients to more invasive therapies. Data from the Superion FDA clinical trial, a prospective spinal registry, and the literature were used to populate the model. Direct medical care costs were modeled from 2014 Medicare reimbursements for healthcare services; QALYs came from the SF-12 PCS and MCS components. The analysis used a 2-year time horizon with a 3 % discount rate. CC had the lowest cost at $10,540, while Spacers and DS were nearly identical at about $13,950. CC also had the lowest QALY increase (0.06), while Spacers and DS were again nearly identical (0.28). The incremental cost-effectiveness ratios (ICER) for Spacers compared to CC was $16,300 and for DS was $15,200. The authors concluded that both the Spacer and DS strategies were far below the commonly cited $50,000/QALY threshold and produced several times the QALY increase versus CC, suggesting that surgical care provided superior value (cost/effectiveness) versus sustained conservative care in the treatment of LSS.

The authors stated that the limitations inherent in this study had significant implications for its interpretation. As in many studies using economic models, the treatments were not all randomized against one another. If outcomes were related to patient characteristics, this could cause bias in the comparisons. To address differences in patients at baseline, these investigators modeled failure rates and QALYs gained as a function of baseline ODI, and adjusted when indicated. While small sample sizes, such as those used in this model, did not in themselves cause bias, they did lead to more variable estimates of each treatment's effectiveness, and thus more uncertainty in the comparisons. This may be especially true during the 2nd year after the procedure, when the original sample size was somewhat reduced. However, this base case failure rates were within the range of other studies. For DS, the failure rate was 9.2 % over 2 years, somewhat higher than 6.8 % from Burnett, but similar to 8.9 % (35/394) reported from the SPORT study. In addition, results from the probabilistic sensitivity analysis (PSA) were similar to the base case analysis, showing higher cost and greater QALYs gained for the surgical strategies compared to the CC strategy. Utility was estimated as a function of age, sex, SF-12 MCS and PCS scores. These researchers did not recognize a utility decrement when a patient suffered an AE or incurred an inpatient rehabilitation facility (IRF) stay; but because these were short-term events, they would have had minor impact on 2-year utility. The QALYS gained by 2 years were also similar to previous studies. For Spacer, the QALY gained was 0.144 which compared to 0.14 from Skidmore and 0.15 from Burnett. Similarly, the DS QALY gained was 0.15, which compared to 0.08 from Skidmore and 0.16 from Burnett and 0.17 from Tosteson. Finally, the analysis was limited to a 2-year time horizon due to the available data. LSS is a lifetime condition, so longer time horizons may be of interest even in the commercial insurance market. It will be important to extend the time horizon of this and other studies as longer-term data become available on interspinous spacers.

Lonne et al (2015) noted that LSS is the most common indication for operative treatment in elderly. Laminectomy has been the "gold standard", but minimally invasive decompression (MID) is now widely used. Another minimally invasive surgery option is X-Stop showing good result compared with non-operative treatment, but showing higher re-operation rate than laminectomy. In a prospective, multi-center RCT,

these researchers compared the effect of X-Stop with MID in patients with neurogenic intermittent claudication due to LSS. These researchers enrolled 96 patients aged 50 to 85 years, with symptoms of neurogenic intermittent claudication within 250-m walking distance and 1- or 2-level LSS, randomized to either MID or X-Stop. Primary outcome was ZCQ in this intention-to-treat (ITT) analysis. Secondary outcome was ODI, EuroQol 5-dimensional questionnaire, NRS 11 for LBP and leg pain, and risk for secondary surgery and complications. No significant differences were found in ZCQ between the groups at any follow-ups. Both groups had a statistical and clinical significant improvement at 6 weeks and throughout the 2-year observation period. The number of patients having secondary surgery due to persistent or recurrent symptoms was significantly higher in the X-Stop group (95 % CI: 6.5 (1.3 to 31.9). Complication rate was similar and low, but more severe for MID. The authors concluded that both MID and X-Stop led to significant symptom improvements. There were no significant clinical differences in effect between the methods at any of the follow-up time points. X-Stop had significant higher risk of secondary surgery. Complication was more severe for MID.

Lauryssen et al (2015) compared the 2-year clinical outcomes of a prospective, RCT of an FDA-approved interspinous spacer with the compilation of published findings from 19 studies of decompressive laminectomy for the treatment of LSS. Back and leg pain, ODI, and ZCQ values were compared between spacer- and laminectomy-treated patients pre-operatively and at 12 and 24 months. Percentage improvements between baseline and 24 months uniformly favored patients treated with the spacer for back pain (65 % versus 52 %), leg pain (70 % versus 62 %), ODI (51 % versus 47 %) and ZCQ symptom severity (37 % versus 29 %) and physical function (36 % versus 32 %). The authors concluded that both treatments provided effective and durable symptom relief of claudicant symptoms. This stand-alone interspinous spacer offered the patient a minimally invasive option with less surgical risk. This study provided short-term follow-up data (24 months).

Nunley et al (2017a) determined the 4-year clinical outcomes in patients with moderate LSS treated with minimally invasive stand-alone interspinous process decompression using the Superion device. The 4-

year Superion data were extracted from a randomized, controlled FDA IDE. Patients with intermittent neurogenic claudication relieved with back flexion who failed at least 6 months of non-surgical management were enrolled. Outcomes included ZCQ symptom severity (ss), physical function (pf) and patient satisfaction (ps) subdomains, leg and back pain VAS, and ODI. At 4-year follow-up, 89 of the 122 patients (73 %) provided complete clinical outcome evaluations. At 4 years after index procedure, 75 of 89 patients with Superion (84.3 %) demonstrated clinical success on at least 2 of 3 ZCQ domains. Individual component responder rates were 83 % (74/89), 79 % (70/89), and 87 % (77/89) for ZCQss, ZCQpf, and ZCQps; 78 % (67/86) and 66 % (57/86) for leg and back pain VAS; and 62 % (55/89) for ODI. Patients with Superion also demonstrated percentage improvements over baseline of 41 %, 40 %, 73 %, 69 %, and 61 % for ZCQss, ZCQpf, leg pain VAS, back pain VAS, and ODI. Within-group effect sizes all were classified as very large (greater than 1.0): 1.49, 1.65, 1.42, 1.12, and 1.46 for ZCQss, ZCQpf, leg pain VAS, back pain VAS, and ODI. The authors concluded that minimally invasive implantation of the Superion device provided long-term, durable relief of symptoms of intermittent neurogenic claudication for patients with moderate lumbar spinal stenosis

Nunley et al (2017b) stated that lumbar spinal stenosis is the most common indication for spine surgery in older adults. Interspinous process decompression (IPD) using a stand-alone spacer that functions as an extension blocker offers a minimally invasive therapeutic option for intermittent neurogenic claudication associated with spinal stenosis. This study evaluated the 5-year clinical outcomes for IPD (Superion®) from a randomized controlled FDA non-inferiority trial. Outcome measures included Zurich Claudication Questionnaire (ZCQ) symptom severity (ss), physical function (pf), and patient satisfaction (ps) subdomains, leg and back pain visual analog scale (VAS), and Oswestry Disability Index (ODI). At 5 years, 84% of patients (74 of 88) demonstrated clinical success on at least 2 of 3 ZCQ domains. Individual ZCQ domain success rates were 75% (66 of 88), 81% (71 of 88), and 90% (79 of 88) for ZCQss, ZCQpf, and ZCQps, respectively. Leg and back pain success rates were 80% (68 of 85) and 65% (55 of 85), respectively, and the success rate for ODI was 65% (57 of 88). Percentage improvements over baseline were 42%, 39%, 75%, 66%, and 58% for ZCQss, ZCQpf, leg and back pain VAS, and ODI, respectively (all $p < 0.001$). Within-group effect sizes were classified as

very large for 4 of 5 clinical outcomes (i.e., greater than 1.0; all p < 0.0001); 75% of IPD patients were free from re-operation, revision, or supplemental fixation at their index level at 5 years. The authors concluded that after 5 years of follow-up, IPD with a stand-alone spacer provided sustained clinical benefit. Financial support for this work was provided by VertiFlex, Inc. (Carlsbad, CA).

Zhao et al (2017) stated that IPD were widely used for the treatment of lumbar spinal stenosis (LSS). However, whether IPD was superior to bony decompression (DP) was still debated. These investigators compared the clinical outcomes of IPD to DP for LSS. PubMed, Cochrane library, Cochrane Central Register of Controlled Trials (CCTR), Ovid Medline, China national knowledge internet database, Wan Fang database were searched on August 8,2016. Studies were identified using selection criteria and analysis was performed with Review Manager Version 5.3. A total of 4 RCTs (7 articles) were included, with 200 patients in the IPD group and 200 patients in DP group. There was no significant difference in hospital stay time (p = 0.36), VAS leg pain scores (p = 0.83), and complication rates (p = 0.20) for IPD alone versus DP. However, IPD alone showed higher VAS low back pain scores (p = 0.03) and re-operation rates (p < 0.0001) between the 2 therapy groups. Two studies' results showed the IPD group had lower cost-effectiveness. The authors concluded that although patients who received IPD may obtain several benefits in the short-term, it was associated with higher costs, re-operation rates. These researchers stated that larger sample size studies and longer follow-up are needed to evaluate the IPD.

Poetscher et al (2018) noted that degenerative LSS is a condition related to aging in which structural changes cause narrowing of the central canal and intervertebral foramen. It is currently the leading cause for spinal surgery in patients over 65 years; IPDs were introduced as a less invasive surgical alternative, but questions regarding safety, efficacy, and cost-effectiveness are still unanswered. These researchers provided complete and reliable information regarding benefits and harms of IPDs when compared to conservative treatment or decompression surgery and suggested directions for forthcoming RCTs. They searched Medline, Embase, Cochrane Library, Scopus, and LILACS for randomized and quasi-randomized trials, without language or period restrictions, comparing IPDs to conservative treatment or decompressive surgery in

adults with symptomatic degenerative LSS. Data extraction and analysis were conducted following the Cochrane Handbook. Primary outcomes were pain assessment, functional impairment, ZCQ, and re-operation rates. Secondary outcomes were quality of life (QOL), complications, and cost-effectiveness. The search strategy resulted in 17 potentially eligible reports. At the end, 9 reports were included and 8 were excluded. Overall quality of evidence was low; 1 trial compared IPDs to conservative treatment: IPDs presented better pain, functional status, QOL outcomes, and higher complication risk; 5 trials compared IPDs to decompressive surgery: pain, functional status, and QOL had similar outcomes; IPD implant presented a significantly higher risk of re-operation. These investigators found low-quality evidence that IPDs resulted in similar outcomes when compared to standard decompression surgery. Primary and secondary outcomes were not measured in all studies and were often published in incomplete form. Sub-group analysis was not feasible. Difficulty in contacting authors may have prevented us of including data in quantitative analysis. The authors concluded that patients submitted to IPD implants had significantly higher rates of re-operation, with lower cost-effectiveness. These researchers stated that future trials should improve in design quality and data reporting, with longer follow-up periods. They stated that until conclusive evidence becomes available, therapeutic options must be chosen very carefully on an individual patient basis, with full disclosure of unproven clinical benefits and presumably higher risk of re-operation.

Nunley et al (2018a) noted that LSS causes significant pain and functional impairment, and medical management has increasingly included the prescription of opioid-based analgesics; IPD provides a minimally-invasive therapeutic option for LSS. This study estimated the type, dosage, and duration of opioid medications through 5 years of follow-up after IPD with the Superion Indirect Decompression System. Data were obtained from the Superion-treatment arm of a randomized controlled non-inferiority trial. The prevalence of subjects using opiates was determined at baseline through 60 months. Primary analysis included all 190 patients randomized to receive the Superion device. In a subgroup of 98 subjects, these investigators determined opioid-medication prevalence among subjects with a history of opioid use. At baseline, almost 50 % (94 of 190) of subjects were using opioid medication. Thereafter, there was a sharp decrease in opioid-medication

prevalence from 25.2 % (41 of 163) at 12 months to 13.3 % (20 of 150) at 24 months to 7.5 % (8 of 107) at 60 months. Between baseline and 5 years, there was an 85 % decrease in the proportion of subjects using opioids. A similar pattern was also observed among subjects with a history of opiates prior to entering the trial. The authors concluded that stand-alone IPD was associated with a marked decrease in the need for opioid medications to manage symptoms related to LSS. In light of the current opiate epidemic, such alternatives as IPD may provide effective pain relief in patients with LSS without the need for opioid therapy.

The authors stated that this study had several limitations. In the absence of a non-surgical control, these researchers were unable to estimate the comparative natural history of opioid usage among LSS patients treated conservatively. Although medication prescribing was captured on a compulsory basis for all study subjects, the trial was not designed to evaluate opioid usage as a primary or secondary outcome. As an ancillary variable, data collection methods lacked a standardized methodology to quantify opioid usage. Consequently, this post-hoc analysis was constrained to prevalence estimates within specified post-operative follow-up intervals and limited only to those patients who remained implanted with the study device and who were free of a re-operation at the index surgical level.

Deer et al (2019a) stated that LSS can lead to compression of neural elements and manifest as LBP and leg pain. LSS has traditionally been treated with a variety of conservative (pain medications, physical therapy, epidural spinal injections) and invasive (surgical decompression) options. Recently, several minimally invasive procedures have expanded the therapeutic options. The Lumbar Spinal Stenosis Consensus Group convened to evaluate the peer-reviewed literature as the basis for making minimally invasive spine treatment (MIST) recommendations. A total of 11 consensus points were clearly defined with evidence strength, recommendation grade, and consensus level using U.S. Preventive Services Task Force criteria. The Consensus Group also created a treatment algorithm. Literature searches yielded 9 studies (2 RCTs; 7 observational studies, 4 prospective and 3 retrospective) of minimally invasive spine treatments, and 1 RCT for spacers. The LSS therapeutic choice is dependent on the degree of stenosis; spinal or anatomic level; architecture of the stenosis; severity of the symptoms; failed, past, less

invasive treatments; previous fusions or other open surgical approaches; and patient co-morbidities. There is Level I evidence for percutaneous image-guided lumbar decompression as superior to lumbar epidural steroid injection, and 1 RCT supported spacer use in a non-inferiority study comparing 2 spacer products currently available. The authors concluded that MISTs should be used in a judicious and algorithmic fashion to treat LSS, based on the evidence of safety and efficacy in the peer-reviewed literature. The MIST Consensus Group recommended that these procedures be used in a multi-modal fashion as part of an evidence-based decision algorithm.

In a review on “The emerging evidence for utilization of a percutaneous interspinous process decompression device to treat symptomatic lumbar adjacent-segment degeneration”, Deer et al (2019b) concluded that “Indirect lumbar decompression via interspinous spacer is an emerging minimally invasive technique for patients with a history of implanted spinal cord stimulators or spinal instrumentation who continue to experience symptoms due to progressive neurogenic claudication”.

Zini et al (2019) examined the literature regarding IPD that mainly focused on comparison with conservative treatment and surgical decompression for the treatment of degenerative LSS (DLSS). The authors noted that IPD are diverse mini-invasive devices placed with fluoroscopic guidance under local anesthesia between the spinal processes at the DLSS level in order to obtain nerve decompression. It has been demonstrated to be more effective than a conservative treatment for DLSS; treatment failure appeared to be significantly lower in the IPD group, while complications appeared to be more frequent for the implant group compared to the conservative treatment. These researchers stated that low quality evidence indicated that outcomes regarding pain, functional status and QOL were similar comparing IPD with surgical procedures; however, treatment failure was significantly higher in IPD group compared to decompressive surgery because of complication as dislocation of the device and erosion/fracture of the spinous process that could be avoided with spinoplasty or “lack of success” almost related to patient selection; cost-effectiveness of IPD is still being debated. The authors concluded that a prospective,

randomized study to evaluate the efficacy of pure percutaneous IPD plus preventive spinoplasty versus spinal laminectomy with long (greater than 24 months) term follow-up is highly desirable.

Merkow et al (2020) noted that symptomatic LSS is a condition affecting a growing number of individuals resulting in significant disability and pain. Traditionally, therapeutic options have consisted of conservative measures such as physical therapy, medication management, epidural injections and percutaneous adhesiolysis, or surgery. There exists a treatment gap for patients failing conservative measures who are not candidates for surgery. Minimally invasive lumbar decompression (MILD) and IPD with Superion represent minimally invasive novel therapeutic options that may help fill this gap in management. These researchers carried out a literature review to examine these procedures and evaluate their safety and effectiveness. The available evidence for MILD and Superion has been continuously debated. Overall, it is considered that while the procedures are safe, there is only modest evidence for effectiveness. For both procedures, these investigators have reviewed 13 studies. Based on the available evidence, MILD and Superion are safe and modestly effective minimally invasive procedures for patients with symptomatic LSS. It is the authors' recommendation that these procedures may be incorporated as part of the continuum of therapeutic options for patients meeting clinical criteria.

In a retrospective review, Tram et al (2020) examined the literature on the efficacy and complications associated with decompression and interspinous devices (ISDs) used in surgeries for LSS. LSS is a debilitating condition that affects the lumbar spinal cord and spinal nerve roots; however, a comprehensive report on the relative efficacy and complication rate of ISDs as they are compared to traditional decompression procedures is currently lacking. The PubMed data-base was queried to identify clinical studies that exclusively investigated decompression, those that exclusively investigated ISDs, and those that compared decompression with ISDs. Only prospective cohort studies, case series, and RCTs that evaluated outcomes using the VAS, ODI, or JOA scores were included. A random-effects model was established to assess the difference between pre-operative and the 1- to 2-year post-operative VAS scores between ISD surgery and lumbar decompression. This study included 40 papers that matched the selection criteria. A total

of 25 decompression-exclusive clinical trials with 3,386 patients and a mean age of 68.7 years (range of 31 to 88 years) reported a 2.2 % incidence rate of dural tears and a 2.6 % incidence rate of post-operative infections. A total of 8 ISD-exclusive clinical trials with 1,496 patients and a mean age of 65.1 (range of 19 to 89 years) reported a 5.3 % incidence rate of post-operative leg pain and a 3.7 % incidence rate of spinous process fractures; 7 studies that compared ISDs and decompression in 624 patients found a re-operation rate of 8.3 % in ISD patients versus 3.9 % in decompression patients; they also reported dural tears in 0.32 % of ISD patients versus 5.2 % in decompression patients. A meta-analysis of the RCTs found that the differences in pre-operative and post-operative VAS scores between the 2 groups were not significant. Both decompression and ISD interventions were unique surgical interventions with different therapeutic efficacies and complications. The authors concluded that the collected studies did not consistently demonstrate superiority of either procedure over the other but understanding the differences between the 2 techniques could help tailor treatment regimens for patients with LSS. These researchers stated that careful patient selection remains crucial for either surgical procedure to ensure optimal surgical outcomes tailored to each patient. They stated that more diverse studies are needed to determine the superiority of one technique over the other for different patient populations.

The authors stated that limitations of this study included inconsistent reporting of measurements among studies. Inconsistencies were also found in the extent of complications reported, with more exhaustive studies reporting unique complications, while some studies simply stated that no major complications were encountered. Another limitation of this paper was the variation in post-operative care, which was important for long-term complications such as re-operation rates.

Furthermore, an UpToDate review on “Lumbar spinal stenosis: Treatment and prognosis” (Levin, 2020) states that “Intraspinous spacer implantation -- A potentially less invasive treatment option involves implanting a device between the spinous processes at one or two vertebral levels, relieving compression. This procedure is said to be appropriate for those patients with spinal stenosis without spondylolisthesis who have intermittent claudication symptoms that are exacerbated in extension and relieved in flexion. A randomized, multicenter study in 191 patients compared the

implantation of the X STOP implant, a titanium alloy device, with nonoperative treatment. At 6 months, symptoms were relieved in 52 % of treated patients, compared with 9 % of controls. Benefit was maintained at 2 and 4 years of follow-up and was associated with reduced disability and improved quality of life. Subsequent uncontrolled observations have found that implantation of the X STOP device has been efficacious in many patients, if not in as large a proportion as was found in the clinical trial. While radiologic improvement in spinal canal and neuroforaminal narrowing can be measured after surgery, these changes are not correlated with clinical benefit and are not maintained over time in most patients. These procedures appear to be associated with higher rates of subsequent surgery than patients initially treated with laminectomy. Adverse effects also appear to be more commonly reported in general clinical experience; these include discitis/osteomyelitis, device dislocations, spinous process fractures, recurrent disc herniation, hematoma, cerebrospinal fluid fistula, and foot drop. It is unclear how this newer procedure compares with the standard surgical procedure, decompressive laminectomy, in terms of effectiveness, side effects, recovery time, and long-term outcomes. This treatment does not appear to be helpful in patients who have spondylolisthesis". Furthermore, intraspinous spacer implantation is not listed in the "Summary and Recommendations" section of this review.

Interspinous Fixation Devices

Spinous process fixation is promoted as a minimally invasive spine surgery technique that stabilizes the lumbar spine with less dissection and trauma to the vertebra than the current gold standard, pedicle screw (PS) fixation (Lopez, et al., 2016). Interspinous fixation devices (IFD) aim to provide rigidity comparable with PS fixation by bilaterally securing plates to the lateral aspects of 2 adjacent spinous processes, effectively clamping the motion segment together. IFD implantation has been applied to posterolateral and interbody fusion procedures. Certain IFD products are designed to achieve additional stability through interspinous bony fusion. Proponents have noted that IFD placement is a more expedient procedure that requires a single, less obtrusive midline incision. Multiple IFDs have been designed and are indexed in the literature using various terminology, including spinous process clamps, plates, and anchors. These are not to be confused with interspinous spacers" (X-Stop®,

Wallis®, or Diam® devices), which reduce extension through dynamic stabilization with the aim of decreasing symptoms of lumbar spinal stenosis.

Lopez et al (2016) systematically reviewed the available literature on interspinous rigid fixation/fusion devices (IFD) to explore the devices' efficacy and complication profile. A systematic review of the past 10 years of English literature was conducted according to PRISMA guidelines. The timeframe was chosen based on publication of the first study containing a modern IFD, the SPIRE, in 2006. All PubMed publications containing MeSH headings or with title or abstract containing any combination of the words "interspinous," "spinous process," "fusion," "fixation," "plate," or "plating" were included. Exclusion criteria consisted of dynamic stabilization devices (X-Stop®, Diam®, etc.), cervical spine, pediatrics, and animal models. The articles were blinded to author and journal, assigned a level of evidence by Oxford Centre of Evidence-Based Medicine (OCEBM) criteria, and summarized in an evidentiary table. A total of 293 articles were found in the initial search, of which 15 remained after examination for exclusion criteria. No class I or class II evidence regarding IFDs was found. IFDs have been shown by methodologically flawed and highly biased class III evidence to reduce instability at 1 year, without statistical comparison of complication rates against other treatment modalities.

Hartman et al (2019) noted that the use of the Vertiflex interspinous spacer is a recent minimal invasive procedure useful in the treatment of lumbar spinal stenosis (LSS). It is used mostly by interventional pain physicians who can also perform the minimally invasive lumbar decompression (MILD procedure). Previously when a patient had clinical symptomatic neurogenic claudication (NC) and radiologic findings of lumbar stenosis and had failed conservative treatment, the options were decompressive laminectomy, laminectomy with pedicle fixation at 1 or more levels or laminotomy combined with interlaminar stabilization (Coflex implant). These procedures were performed by neurosurgeons and orthopedic spine surgeons. However, the majority of patients with LSS are elderly and have multiple co-morbidities that could make open spinal surgery, even when limited to 1 level, an anesthesia risk as well as vulnerable to the risk associated with hospitalization and recovery after spine surgery. The minimally invasive approaches to interspinous

stabilization make it possible to treat localized symptomatic stenosis in a broader group of patients that do not want or could not, have general anesthesia or extensive lumbar surgery, especially in the prone position. The authors examined the use of the Vertiflex implant in an elderly population with significant co-morbidities who underwent successful outpatient implantation at 1 or 2 levels. This article looked at the role of medical co-morbidities that may make larger open surgery and general anesthesia higher risk or even contraindicated. The treating physician's specialty and experience with different procedures must also be considered as well as the age, anesthesia risk and co-morbidities such as obesity, diabetes and cardio-pulmonary restrictions that may make the option of procedures such as MILD or Vertiflex reasonable. This study did not provide any clinical data regarding the effectiveness of the Vertiflex device for the treatment of LSS.

Tekmyster et al (2019) stated that interspinous process decompression (IPD) used the Superion Indirect Decompression System (Vertiflex, Carlsbad, CA). Peri-operative and clinical data were captured via a registry for patients treated with IPD for LSS with intermittent NC. A total of 316 physicians at 86 clinical sites in the U.S. participated in this medical device registry. Patient data were captured from in-person interviews and a phone survey. Outcomes included intra-operative blood loss, procedural time, leg and back pain severity (100-mm VAS), patient satisfaction and treatment approval at 3 weeks, 6 and 12 months. The mean age of registry patients was 73.0 ± 9.1 years of which 54 % were women. Mean leg pain severity decreased from 76.6 ± 22.4 mm pre-operatively to 30.4 ± 34.6 mm at 12 months, reflecting an overall 60 % improvement. Corresponding responder rates were 64 % (484 of 751), 72 % (1,097 of 1,523) and 75 % (317 of 423) at 3 weeks, 6 and 12 months, respectively. Back pain severity improved from 76.8 ± 22.2 mm pre-operatively to 39.9 ± 32.3 mm at 12 months (48 % improvement); 12-month responder rate of 67 % (297 of 441). For patient satisfaction at 3 weeks, 6 and 12 months, 89 %, 80 %, and 80 % were satisfied or somewhat satisfied with their treatment and 90 %, 75 %, and 75 % would definitely or probably undergo the same treatment again. In the phone survey, the rate of revision was 3.6 % (51 of 1,426). The authors concluded that these registry findings supported the clinical adoption of minimally invasive IPD in patients with NC associated with LSS. It should be noted that financial support for this work was provided by Vertiflex,

Inc. Furthermore, GT reported grants from Vertiflex, during the conduct of the study. DS reported personal fees from Vertiflex, outside the submitted work. KC was paid for time to enroll patients and track data in PRESS registry from Vertiflex, during the conduct of the study. He also received personal fees from Boston Scientific and Vertiflex, outside the submitted work. LJR serves as consultant/instructor for Vertiflex and Boston Scientific. JEB is an independent advisor to Vertiflex and was remunerated for assistance in manuscript development.

In a retrospective analysis, Falowski et al (2021) examined the use of an interspinous fixation (ISF) device as performed by interventional pain physicians. These investigators identifying 32 patients with the diagnosis of lumbar degenerative disc disease (DDD) with secondary diagnosis of LSS being treated with ISF with Aurora Spine Zip Interspinous Spacer. Serious adverse events (AEs), specifically nerve injury, hematoma, infection, and death, were analyzed quantitatively for reported complications within 90 days from the procedure. Furthermore, visual analog scale (VAS) was analyzed for patient reported outcomes; AE rate was 0 % with no incidences of re-operation, or device removal. Estimated blood loss (EBL) was recorded as less than 50 cc for all patients. The pre-operative pain assessment demonstrated an average pain score of 8.1 and a post-operative pain score of 2.65 equating to a percentage pain reduction of 67 %. The authors concluded that this promising case series added another potential tool to the armamentarium of the interventional pain physician in the treatment of moderate-to-severe LSS and DDD. This broadens the application to degenerative changes, spondylolisthesis, and multiple pain generators such as disc degeneration and facet joint hypertrophy, which is not treated by indirect decompression alone such as with an interspinous spacer. It is an option to patients who have decreased morbidity and significant efficacy. Moreover, these researchers stated that a prospective, multi-center study is planned to further evaluate the effectiveness of this implant in terms of a composite patient success endpoint, including function, pain relief, disability, and AEs.

The authors stated that drawbacks of the study included its retrospective nature, lack of functional outcome measures, region-specific pain scores, and detailed analysis of patient demographics including quantitative radiographic analysis, and physical examination.

Welton et al (2021) noted that current evidence suggests placement of the Superion interspinous spacer (SISS) device compared with laminectomy or laminotomy surgery offers an effective, less invasive therapeutic option for patients with symptomatic lumbar spinal stenosis (LSS). Both SISS placement and laminectomy or laminotomy have risks of complications and a direct comparison of complications between the 2 procedures has not been previously studied. In a retrospective review, these researchers compared the short-term complications of the SISS with laminectomy or laminotomy and highlighted device-specific long-term outcomes with SISS. A total of 189 patients who received lumbar level SISSs were compared with 378 matched controls who underwent primary lumbar spine laminectomy or laminotomy; data were collected from the American College of Surgeons National Surgical Quality Improvement Program (ACS-NSQIP) database. Complications analyzed included rates of wound infection, pulmonary embolism (PE), deep venous thrombosis (DVT), urinary tract infection (UTI), sepsis, septic shock, cardiac arrest, death, as well as re-operation within 30 days of index surgery. Differences between groups were analyzed using the $\chi 2$ test. Device-specific complication (DSC) rates included device malfunction or misplacement (DM), device explantation (DE), spinous process fracture (SPF), and subsequent spinal surgery (SSS). No differences in demographics or co-morbidities existed between groups. There was no significant difference in rates of complications between groups. A total of 44.4 % of patients in the SISS group experienced DSCs with 11.1 % of patients experiencing DM, 21.1 % experiencing an SPF, 20.1 % requiring DE, and 24.3 % requiring SSS. Having at least 1 DSC significantly increased odds of SSS, odds ratio (OR) > 120, $p < 0.0001$. The authors concluded that rates of 30-day complications in the SISS group were not significantly different from patients undergoing laminectomy or laminotomy. Rates of 2-year DSC within SISS and cumulative risk associated with these complications should be studied further as they likely represent a substantial additional cost to the healthcare system that may not be justified by improved patient outcomes. Level of Evidence = IV.

These researchers stated that this study was limited by its retrospective design and the comparison of 2 separate data sets that were both gathered before their investigation. Comparing 2 separate databases limited the ability to match patients. Each data set contained unique and

limited variables that dictated what characteristics these investigators were able to match the patients on, inherently introducing confounding variables in this process. The ACS-NSQIP dataset was more extensive in documenting patient co-morbidities and complication rates in comparison to the SISS device data, which were provided by the instrumentation company, except for ACS-NSQIP data only tracking post-operative complications and re-operations for 30 days. Variables and patient characteristics that were not clearly defined in the SISS data set were subsequently not used for matching purposes. This included important factors such as operating room time, length of stay (LOS), and cost of index surgery. Through this process these researchers thoroughly analyzed, de-emphasized, and appropriately weighted variables from the SISS dataset that showed any signs of inconsistency in data gathering or recording in the attempt to limit inherent bias in the data collected by the manufacturer of the device. The cost of index surgery as well as subsequent revisions was not documented in either dataset and should be tracked and examined in future studies. Furthermore, this study was limited by a small sample size (n = 189 patients who received lumbar level SISSs). The authors stated that future studies should look to match a larger cohort of patients with controls based on more extensive demographic, co-morbidity factors, and spinal levels treated to achieve more reliable outcomes. Furthermore, the absence of patient-reported outcome scores limited the ability for evaluation of patient function and satisfaction with each procedure.

Aggarwal and Chow (2021) stated that LSS is a condition of progressive neurogenic claudication that can be managed with lumbar decompression surgery or less invasive interspinous process devices after failed conservative therapy. Popular interspinous process spacers include X-Stop, Vertiflex and Coflex, with X-Stop being taken off market due to its AEs profile. These researchers carried out a disproportionality analysis to examine if a statistically significant signal exists in the t3 interspinous spacers and the reported AEs using the Manufacturer and User Facility Device Experience (MAUDE) database maintained by the U.S. Food and Drug Administration (FDA). Statistically significant signals were found with each of the 3 interspinous spacer devices (Coflex, Vertiflex, and X-Stop) and each of the following AEs: fracture, migration, and

pain/worsening symptoms. The authors concluded that further studies such as randomized controlled trials (RCTs) are needed to validate these findings.

These researchers stated that the medical device reports that were submitted to the FDA and posted on the MAUDE database were submitted by healthcare professionals and patients. Each and every AE may not be reported. Selection bias exists in that only the AEs reported were included in the analysis. The incidence or prevalence of an event could not be determined from this database. This analysis was carried out on the passive surveillance system of the MAUDE database. As such, direct comparisons could not be made between devices and AEs signals. Furthermore, analyses from the database could find statistically significant signals between a device and an AE but could not prove causality between them; RCTs would be needed to do that. However, X-Stop has been taken off the market so RCTs for it may not be available. Analysis of the medical device reports has advantages in identifying signals in real-world situations and in diverse populations, which is near impossible with the limited number of subjects used in the randomized clinical trials.

Piriformis Muscle Resection

Piriformis syndrome is believed to be a condition in which the piriformis muscle, a narrow muscle located in the buttocks, compresses or irritates the sciatic nerve. There is debate within the medical community whether this is a discrete condition, since it lacks objective evidence, and thus can not be reliably evaluated. Pain associated with piriformis syndrome is exacerbated in prolonged sitting. Specific physical findings are tenderness in the sciatic notch and buttock pain in flexion, adduction, and internal rotation of the hip. Imaging modalities are rarely helpful. Physical therapy is a mainstay of conservative treatment; and is usually enhanced by local injections (Papadopoulos and Khan, 2004). There is insufficient evidence regarding the effectiveness of resection of the piriformis muscle as a treatment for piriformis syndrome.

Endoscopic Laser Foraminoplasty

Endoscopic laser foraminoplasty (decompression) is primarily employed to treat patients with back pain caused by a prolapsed intervertebral disc. This endoscope-assisted laser technique is used to widen the lumbar exit route foramina in the spine. A laser is inserted to ablate portions of the intervertebral disc that have protruded. Hafez and associates (2001) noted that laser ablation of bone and ligament for nerve root decompression using the Ho: YAG laser may offer substantial advantages, but the risk of serious complication may only be avoided if the technique is combined with saline irrigation.

Knight and colleagues (2001) reported that the complication rate of endoscopic laser foraminoplasty is significantly lower than that reported following conventional spinal surgery. From these results, these investigators concluded that endoscopic laser foraminoplasty as a treatment for chronic LBP and sciatica presents less risk to a patient than conventional methods of spinal surgery. On the other hand, the National Institute for Clinical Excellence's (2003) guidance on this procedure stated that current evidence on the safety and effectiveness of endoscopic laser foraminoplasty does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research. Moreover, the Specialist Advisors believed the effectiveness of this procedure to be unproven; and they also noted a number of potential complications including nerve injury and infection. Takeno et al (2006) stated that percutaneous lumbar disc decompression is associated with significant risk of disc, end-plate, and nerve root injuries, contrary to the general belief that the procedure is minimally invasive. Their findings highlight the need for careful diagnosis and sufficient technical skill when selecting percutaneous lumbar disc decompression as a treatment option.

Percutaneous Discectomy

Percutaneous disc decompression is a procedure specifically for a herniated disc in which the core of the disc has not broken through the disc wall. Performed through a needle in the skin, it is a form of surgery in which small bits of disc are removed to relieve pressure on the nerves surrounding the disc. The procedure may be performed with a cutting

instrument or laser. Although the literature indicates that open laminectomy is an acceptable and, at times, necessary method of treatment for herniated intervertebral discs, percutaneous discectomy has emerged as a method of treatment for contained and non-migrated sequestered herniated discs. It has taken on 2 different forms: the selective removal of nucleus pulposus from the herniation site with various manual and automated instruments under endoscopic control (percutaneous nucleotomy with discoscopy, arthroscopic microdiscectomy, percutaneous endoscopic discectomy); the other is the removal of nucleus pulposus from the center of the disc space with one single automated instrument (automated percutaneous lumbar discectomy) to achieve an intradiscal decompression.

Automated percutaneous lumbar discectomy (APLD), or automated percutaneous mechanical lumbar discectomy, is another newer approach for surgical treatment of herniated discs. In this procedure, under local anesthesia and fluoroscopic guidance, a cannula is inserted into the disc; an automated cutting and aspiration device is then inserted through the cannula and the disc material is removed. As with the arthroscopic microdiscectomy/PED, APLD does not allow direct visualization of the disc or surrounding tissues. An example of a device used for this type of procedure includes, but may not be limited to, the Stryker Dekompressor Lumbar Discectomy Probe.

Automated percutaneous discectomy refers to techniques using minimal skin incisions (generally several, all less than 3 to 5 mm) to allow small instruments to be inserted, using radiography to visualize these instruments, and using extensions for the surgeon to reach the operative site without having to dissect tissues. Lasers to vaporize the nucleus pulposus have become an additional percutaneous option. Proponents of percutaneous lumbar discectomy cite several potential advantages over open discectomy procedures, including reduced morbidity, less potential for perineural scarring, less intra-operative blood loss, fewer complications of epidural fibrosis, transverse myelitis or disc space infection, reduced patient recovery times, and a faster return to normal activity. Initial case series focusing on lumbar disc disease reported encouraging results and the technique was widely adopted (Onik, 1990; Fiume et al, 1994; Ohnmeiss et al, 1994; Kotilainen and Valtonen, 1998). However, controlled trials reported less impressive results.

An interventional guidance on laser lumbar discectomy issued by the National Institute for Health and Clinical Excellence (NICE, 2003) stated that "Current evidence on the safety and efficacy of laser lumbar discectomy does not appear adequate to support the use of this procedure without special arrangements for consent and for audit or research". The guidance noted that in an uncontrolled study of 348 patients with chronic back pain, 210 (60%) patients reported good or excellent results at 1 year, however, the validity of the studies on this procedure were compromised by high rates of loss to follow-up and the lack of long-term data on efficacy outcomes.

A review of minimally invasive procedures for disorders of the lumbar spine (Deen et al, 2003) stated that "Percutaneous lumbar diskectomy techniques hold considerable promise; however, lumbar microdiskectomy is the gold standard for surgical treatment of lumbar disk protrusion with radiculopathy".

A National Institute for Health and Clinical Excellence (NICE, 2005) guidance on automated percutaneous mechanical lumbar discectomy stated that "Current evidence suggests that there are no major safety concerns associated with automated percutaneous mechanical lumbar discectomy. There is limited evidence of efficacy based on uncontrolled case series of heterogeneous groups of patients, but evidence from small randomised controlled trials shows conflicting results. In view of the uncertainties about the efficacy of the procedure, it should not be used without special arrangements for consent and for audit or research".

A Cochrane review on surgical interventions for lumbar disc prolapse (Gibson and Waddell, 2007) examined the evidence on automated percutaneous discectomy and laser discectomy. The reviewers found four trials on automated percutaneous discectomy that met their inclusion criteria: 2 trials that compared automated percutaneous discectomy with chymopapain (Revel, 1993; Krugluger, 2000) and 2 that compared automated percutaneous discectomy with microdiscectomy (Chatterjee, 1995; Haines, 2002). The reviewers reported that the results from these 4 trials suggested that automated percutaneous discectomy produced inferior results to either more established procedure. The reviewers found 2 trials that met their inclusion criteria on laser discectomy: 1 trial compared the effects of a Nd-YAG-laser with that of a diode laser (Paul

and Hellinger, 2000) and reported slight vaporization with both lasers and excellent shrinkage of disc tissue, however, no comparative outcome results were published; the other trial compared chemonucleolysis with laser discectomy (Steffen and Wittenberg, 1997) and reported that the study results favored chemonucleolysis. The reviewers concluded that while microdiscectomy gives broadly comparable results to open discectomy, the evidence on other minimally invasive techniques remains unclear (with the exception of chemonucleolysis using chymopapain, which is no longer widely available).

Nezer and Hermoni (2007) reviewed the evidence for percutaneous discectomy and percutaneous intradiscal radiofrequency thermocoagulation from 4 leading evidence-based databases: the National Institute for Clinical Excellence (NICE), which is an independent organization responsible for providing national guidance on treatments, the Cochrane Library, which is the largest library world-wide for systematic reviews and randomized controlled trials, the Center for Review and Dissemination at the University of York, which undertakes reviews of research about the effects of interventions in health and social care and finally, a search via Medline. The authors concluded that "The results from those systematic reviews and randomized trials show that, at present, unless or until better scientific evidence is available, automated percutaneous discectomy and laser discectomy should be regarded as research techniques".

Goupille et al (2007) reviewed the literature on percutaneous laser disc decompression for treating lumbar disc herniation and stated that "[e]xperimental and clinical studies have investigated the modality of percutaneous laser disc decompression, but no consensus exists on the type of laser to use, the wavelength, duration of application, or appropriate energy applied. Studies have evaluated the impact of different techniques on the amount of disc removed, intradisc[al] pressure, and damage to neighboring tissue. Several open studies have been published, but their methodology and conclusions are questionable, and no controlled study has been performed". The authors concluded that "Although the concept of laser disc nucleotomy is appealing, this treatment cannot be considered validated for disc herniation-associated radiculopathy resistant to medical treatment".

A California Technology Assessment (2008) reviewed the scientific evidence for percutaneous laser disc decompression in the treatment of symptomatic lumbar disc herniation and found no published randomized, concurrently controlled, blinded trials comparing outcomes of percutaneous laser disc decompression with conventional conservative measures or open discectomy or laminectomy. The authors reported that the published articles concerning percutaneous laser disc decompression are almost all uncontrolled case series: 2 non-randomized comparative trials (Ohnmeiss et al, 1994, Tassi, 2006) and 1 systematic review (Boult et al, 2000) of percutaneous laser disc decompression have been published. The assessment stated that "The published data are not sufficient to conclude that the efficacy and safety of the percutaneous laser disc decompression procedure have been established in the investigational setting, let alone under conditions of usual medical practice. Percutaneous laser disc decompression requires further evaluation in a randomized controlled trial to assess its efficacy as an alternative treatment for symptomatic lumbar disc herniation".

An assessment by the National Institute for Health and Clinical Excellence (NICE, 2008) of percutaneous endoscopic laser lumbar diskectomy concluded that "[c]urrent evidence on the safety and efficacy of percutaneous endoscopic laser lumbar discectomy is inadequate in quantity and quality. Therefore this procedure should only be used with special arrangements for clinical governance, consent, and audit or research". The specialist advisors to NICE considered theoretical adverse events to include a higher risk of nerve or dural injury because of the poor visual field and disorientation, and a higher probability of missed fragments. One specialist advisor stated that there had been cases of heat damage to the cauda equine when laser was used for lumbar discectomy with concomitant foraminoplasty.

An assessment by NICE (2008) reached similar conclusions about the unproven status of percutaneous endoscopic laser cervical diskectomy. The NICE assessment concluded that "[c]urrent evidence on the safety and efficacy of percutaneous endoscopic laser cervical diskectomy is inadequate in quantity and quality. Available evidence reviewed by NICE was limited to uncontrolled case series". The specialist advisors to NICE considered the most important theoretical risk of the procedure to be heat damage to nerve roots or to the spinal cord, potentially leading to

quadriplegia. One specialist advisor stated that neurological damage had occurred in a patient as a result of using laser in the spine. The NICE review committee noted that the extent to which laser ablation was used instead of, or in addition to, mechanical methods of removing prolapsed disc material was unclear in much of the published evidence.

All of the trials reviewed above focused on lumbar disc herniation. There were no clinical trials of percutaneous discectomy of cervical or thoracic disc herniation.

Xclose™ Tissue Repair System

An annular (annulus) repair/closure may be performed following a spinal decompression (discectomy) surgery. It has been proposed that annular closure may reduce the risk of disc reherniation and the need for a fusion. Examples of devices used in an annular repair include the Inclose Surgical Mesh System and Xclose™ Tissue Repair System.

The Xclose™ Tissue Repair System (Anulex Technologies, Inc., Minnetonka, MN) has received 510(k) clearance for use in soft tissue approximation for procedures such as general and orthopedic surgery. It is being investigated as a method of soft tissue re-approximation of the anulus fibrosus after a lumbar discectomy procedure. However, there is insufficient evidence of the clinical effectiveness of the Xclose™ Tissue Repair System following a lumbar discectomy procedure. Randomized controlled studies are needed to determine whether closing the anulus following a lumbar discectomy procedure will result in improved clinical outcomes (i.e., decrease in re-herniation rates). To evaluate the benefits of anulus fibrosis repair utilizing the Xclose™ Tissue Repair system, Anulex is sponsoring a prospective, controlled, randomized study that will compare discectomy patients who receive anular repair using the Xclose™ Tissue Repair System to those who receive a standard discectomy without using the Xclose™. However, results from this study have not yet been published in the peer-reviewed medical literature.

Barricaid Annular Closure Device

An assessment of annulus fibrosus repair after lumbar discectomy by the Ludwig Boltzmann Institute for Heatlh Technology Assessment (Semlitsch & Geiger-Gritsch, 2019) found that the closure of anular defects after discectomy using the Barricaid device could be a meaningful intervention for a selected group of patients with a large anular defect to prevent reherniations and reoperations. However, a significant number of patients experienced problems with device integrity over a period of two years. In addition, these results are based on a few studies with a high risk of bias and published long-term results beyond a period of two years are missing. Similar results in terms of clinical effectiveness and safety were obtained for the Xclose™ system. However, only results from a single randomized controlled trial with a high risk of bias are available.

In a randomized, multi-center trial, Nanda et al (2019) examined if implanting an annular closure device (ACD) following lumbar discectomy in patients with large defects in the annulus fibrosus lowers the risk of re-operation after 4 years. Patients with large annular defects following single-level lumbar discectomy were intra-operatively randomized to additionally receive an ACD or no treatment (controls). Clinical and imaging follow-up were performed at routine intervals over 4 years of follow-up. Main outcomes included re-operations at the treated lumbar level, leg pain scores on a visual analog scale (VAS), Oswestry Disability Index (ODI), and Physical Component Summary (PCS) and Mental Component Summary (MCS) scores from the SF-36 questionnaire. Among 550 patients (ACD 272, control 278), the risk of re-operation over 4 years was 14.4% with ACD and 21.1% with controls ($p = 0.03$). The reduction in re-operation risk with ACD was not significantly influenced by patient age ($p = 0.51$), sex ($p = 0.34$), body mass index (BMI; $p = 0.21$), smoking status ($p = 0.85$), level of herniation ($p = 0.26$), leg pain severity at baseline ($p = 0.90$), or ODI at baseline ($p = 0.54$). All patient-reported outcomes improved in each group from baseline to 4 years (all $p < 0.001$). The percentage of patients who achieved the minimal clinically important difference without a re-operation was proportionally higher in the ACD group compared to controls for leg pain ($p = 0.07$), ODI ($p = 0.10$), PCS ($p = 0.02$), and MCS ($p = 0.06$). The authors concluded that the addition of a bone-anchored ACD following lumbar discectomy in

patients with large post-surgical annular defects reduced the risk of re-operation and provided better long-term pain and disability relief over 4 years compared to lumbar discectomy only.

The authors stated that this study had several drawbacks. First, the results presented were applicable only to patients with large post-discectomy annular defects, who accounted for approximately 30% of all lumbar discectomy cases. Implantation of an ACD in patients with small annular defects cannot be justified clinically given the inherently low risk of symptom recurrence in these individuals. Additional patient characteristics that were crucial to achieving positive results included adequate disc height and non-osteoporotic bone mineral density (BMD) of the lumbar spine. Second, the decision to re-operate involved shared decision-making between the patient and surgeon and, thus, there was potential for bias in the reported re-operation rates. Finally, 5-year follow-up in this study is ongoing and these long-term outcomes are anxiously awaited to provide final comparative efficacy, safety, and cost-utility results of bone-anchored ACD implantation.

Kienzler et al (2019) noted that a larger defect in the annulus fibrosus following lumbar discectomy is a well-known risk factor for re-herniation. Procedures intended to prevent re-herniation by sealing or occluding the annular defect warrant study in high-risk patients. In a randomized, multi-center study, these researchers examined the 3-year results of lumbar discectomy with a bone-anchored annular closure device (ACD) or lumbar discectomy only (controls) in patients at high-risk for re-herniation. Trial included patients with sciatica due to lumbar intervertebral disc herniation who failed conservative treatment. Patients with large annular defects after lumbar limited microdiscectomy were intra-operatively randomly assigned to receive ACD or control. Clinical and imaging follow-up was performed at routine intervals over 3 years. Main outcomes included rate of re-herniations, re-operations, and endplate changes; leg and back pain scores on a visual analog scale (VAS); Oswestry Disability Index (ODI); Physical Component Summary (PCS) and Mental Component Summary (MCS) scores from the SF-36; and adverse events (AEs) adjudicated by a data safety monitoring board. Among 554 randomized patients, the modified intent-to-treat (ITT) population consisted of 272 patients in which ACD implantation was attempted and 278 receiving control; device implantation was not

attempted in 4 patients assigned to ACD. Outcomes at 3 years favored ACD for symptomatic re-herniation (14.8 % versus 29.5 %; p < 0.001), re-operation (11.0 % versus 19.3 %; p = 0.007), leg pain (21 versus 30; p < 0.01), back pain (23 versus 30; p = 0.01), ODI (18 versus 23; p = 0.02), PCS (47 versus 44; p < 0.01), and MCS (52 versus 49; p < 0.01). The frequency of all-cause serious AEs was comparable between groups (42.3 % versus 44.5 %; p = 0.61). The authors concluded that the addition of a bone-anchored ACD in patients with large annular defects following lumbar discectomy reduced the risk of re-herniation and re-operation; and had a similar safety profile over 3-year follow-up compared with lumbar limited discectomy only.

The authors stated that this study had several drawbacks. First, these findings were not applicable to all patients undergoing lumbar discectomy, but only the approximately 30 % of cases at high-risk of re-herniation due to a large post-surgical annular defect. The ACD is not intended to be used in patients with smaller defects since treatment with a permanent implant is difficult to justify in this population due to the relatively low risk of re-herniation. Second, lack of patient and outcome-assessor blinding to treatment allocation may have biased patient-reported outcomes or the decision to re-operate. Third, while CT imaging with core laboratory reading is a strength of this trial, it may also be perceived as a limitation since the application of CT findings to routine clinical practice is unclear. Finally, longer follow-up is needed in this younger patient population to determine the durability of effect with ACD and to ensure there are no concerning late-onset safety or device-related complications. While there was no association of vertebral endplate changes (VEPC) with clinical complications over 3 years among patients who received ACD, this should be confirmed in long-term follow-up. It should also be noted that some of the investigators (P. Klassen, L. Miller, R. Assaker, and C. Thome) reported consultancy with Intrinsic Therapeutics.

In a randomized, multi-center trial, Nanda et al (2019) examined if implanting an ACD following lumbar discectomy in patients with large defects in the annulus fibrosus lowers the risk of re-operation after 4 years. Patients with large annular defects following single-level lumbar discectomy were intra-operatively randomized to additionally receive an ACD or no treatment (controls). Clinical and imaging follow-up were performed at routine intervals over 4 years of follow-up. Main outcomes

included re-operations at the treated lumbar level, leg pain scores on a VAS, ODI, PCS and MCS scores from the SF-36 questionnaire. Among 550 patients (ACD 272, control 278), the risk of re-operation over 4 years was 14.4 % with ACD and 21.1 % with controls (p = 0.03). The reduction in re-operation risk with ACD was not significantly influenced by patient age (p = 0.51), sex (p = 0.34), body mass index (BMI; p = 0.21), smoking status (p = 0.85), level of herniation (p = 0.26), leg pain severity at baseline (p = 0.90), or ODI at baseline (p = 0.54). All patient-reported outcomes improved in each group from baseline to 4 years (all p < 0.001). The percentage of patients who achieved the minimal clinically important difference without a re-operation was proportionally higher in the ACD group compared to controls for leg pain (p = 0.07), ODI (p = 0.10), PCS (p = 0.02), and MCS (p = 0.06) . The authors concluded that the addition of a bone-anchored ACD following lumbar discectomy in patients with large post-surgical annular defects reduced the risk of re-operation and provided better long-term pain and disability relief over 4 years compared to lumbar discectomy only.

The authors stated that this study had several drawbacks. First, the results presented were applicable only to patients with large post-discectomy annular defects, who accounted for approximately 30 % of all lumbar discectomy cases. Implantation of an ACD in patients with small annular defects could not be justified clinically given the inherently low risk of symptom recurrence in these individuals. Additional patient characteristics that were crucial to achieving positive results included adequate disc height and non-osteoporotic bone mineral density (BMD) of the lumbar spine. Second, the decision to re-operate involved shared decision-making between the patient and surgeon and; thus, there was potential for bias in the reported re-operation rates. Finally, 5-year follow-up in this study is ongoing and these long-term outcomes are anxiously awaited to provide final comparative efficacy, safety, and cost-utility results of bone-anchored ACD implantation. It should be noted that Mark P Arts reported consultancy with Intrinsic Therapeutics; personal fees from Zimmer-Biomet, EIT, and Silony, outside the submitted work; and receipt of royalties from EIT. Larry Miller reported consultancy with Intrinsic Therapeutics.

In a prospective RCT, Cho et al (2019) examined the effectiveness of a novel annular closure device (ACD) for preventing lumbar disc herniation (LDH) recurrence and re-operation compared with that of conventional lumbar discectomy (CLD). These researchers compared CLD with discectomy utilizing the Barricaid ACD. Primary radiologic outcomes included disc height, percentage of pre-operative disc height maintained, and re-herniation rates. Additional clinical outcomes included visual analog scale (VAS) scores for back and leg pain, Oswestry Disability Index (ODI) scores, and 12-item short-form health survey (SF-12) quality of life (QOL) scores. Outcomes were measured at pre-operation and at 1 week, 1, 3, 6, 12, and 24 months post-operation. A total of 60 patients (30 CLD, 30 ACD) were enrolled in this study. At 24-month follow-up, the disc height in the ACD group was significantly greater than that in the CLD group (11.4 ± 1.5 versus 10.2 ± 1.2 mm, p = 0.006). Re-herniation occurred in 1 patient in the ACD group versus 6 patients in the CLD group ($\chi 2 = 4.04$, p = 0.044). Back and leg VAS scores, ODI scores, and SF-12 scores improved significantly in both groups compared with pre-operative scores in the first 7 days following surgery and remained at significantly improved levels at a 24-month follow-up. However, no statistical difference was found between the 2 groups. The authors concluded that lumbar discectomy with the Barricaid ACD was more effective at maintaining disc height and preventing re-herniation compared with conventional discectomy. These researchers stated that these findings suggested that adoption of ACD in lumbar discectomy could help improve the treatment outcome.

The authors stated that this study had 2 main drawbacks. First, the 2-year follow-up, in which 70 % or fewer patients were actually followed-up, was short and limited the veracity with which conclusions could be applied in the long-term. However, it provided important early information regarding the stability and survivability of the device. These findings mirrored those of other investigators who examined this ACD and found that the device ensured maintenance of favorable clinical scores and lower rates of re-herniation. Second, the low sample size of this cohort (n = 30 in the ACD group) limited the ability to extrapolate results to larger populations.

Miller et al (2020) stated that patients with lumbar disc herniation and associated sciatica are often referred for lumbar discectomy. The surgical defect in the annulus fibrosus is typically left unrepaired after lumbar discectomy. Patients with large post-surgical annular defects (greater than or equal to 6 mm width) have a higher risk of symptom recurrence and re-operation compared to those with small defects. In these high-risk patients, a treatment gap exists due to the lack of effective treatments for durable annulus fibrosus repair. These investigators highlighted the therapeutic need and summarized the clinical results of a bone-anchored ACD (Barricaid) that was designed to fill the treatment gap in patients with large post-surgical annular defects. Clinical results were summarized by means of a systematic review with meta-analysis of 2 randomized and 2 non-randomized controlled studies. The authors stated that professional societal recommendations and clinical study results support the adoption of bone-anchored annular closure for use in properly selected patients undergoing lumbar discectomy who are at high-risk for re-herniation due to a large post-surgical defect in the annulus fibrosus. The risks of symptomatic re-herniation and re-operation were approximately 50 % lower in patients treated with lumbar discectomy and the Barricaid device compared to lumbar discectomy only, representing a clinically effective treatment strategy. Furthermore ,these researchers stated that stated that as more clinical study data continue to accrue demonstrating the positive long-term results of the Barricaid device, treatment of large defects in the annulus fibrosus during the index surgery may become the standard of care to prevent future symptomatic re-herniations and associated re-operations. It should be noted that this paper was funded by Intrinsic Therapeutics. L Miller has received personal fees from Intrinsic Therapeutics. One peer reviewer was a co-investigator in a randomized-controlled trial of the Barricaid device.

Kienzler et al (2021) noted that an ACD could potentially prevent recurrent herniation by blocking larger annular defects after limited microdiscectomy (LMD). In a non-comparative, single-center study, these researchers analyzed the incidence of endplate changes (EPC) and outcome after LMD with additional implantation of an ACD to prevent re-herniation. This analysis included data from a RCT study-arm of patients undergoing LMD with ACD implantation as well as additional patients undergoing ACD implantation at the authors' institution. Clinical findings (VAS, ODI), radiological outcome (re-herniation, implant integrity, volume

of EPC) and risk factors for EPC were assessed. A total of 72 patients (37 men, age of 47 ± 11.63 years) underwent LMD and ACD implantation between 2013 and 2016. A total of 71 (99 %) patients presented with some degree of EPC during the follow-up period (14.67 ± 4.77 months). In the multi-variate regression analysis, localization of the anchor was the only significant predictor of EPC (p = 0.038). The largest EPC measured 4.2 cm3. Re-herniation was documented in 17 (24 %) patients (symptomatic: n = 10; asymptomatic: n = 7); 6 (8.3 %) patients with symptomatic re-herniation underwent re-discectomy. Implant failure was documented in 19 (26.4 %) patients including anchor head breakage (n = 1, 1.3 %), dislocation of the whole device (n = 5, 6.9 %), and mesh dislocation into the spinal canal (n = 13, 18 %). Mesh subsidence within the EPC was documented in 15 (20.8 %) patients; 7 (9.7 %) patients underwent explantation of the entire, or parts of the device. The authors concluded that clinical improvement after LMD and ACD implantation was proven in this trial. High incidence and volume of EPC did not correlate with clinical outcome. The ACD might prevent disc re-herniation despite implant failure rates. Mechanical friction of the polymer mesh with the endplate was most likely the cause of EPC after ACD. Moreover, these researchers stated that long-term clinical and radiological assessments is needed to examine the consequences of these findings. These investigators stated that limitations of this study were the fact that this was a non-comparative, single-center study with a small patient cohort.

Peredo et al (2021) stated that recently, a number of implantable devices and techniques have been developed to prevent re-herniation, yet these systems do not biologically repair the annulus fibrosus (AF). Examples of such systems include the AnchorKnot Tissue Approximation Kit (Anchor Orthopedics, Mississauga, ON, Canada) and Barricaid (Intrinsic Therapeutics, Inc., Woburn, MA). The AnchorKnot system enables minimally invasive visualization of the surgical field and is intended to minimize the removal of disc tissue and to close the AF defect with sutures. Although reports indicated the device has been used in multiple clinics, systematic evaluation of its safety and efficacy for disc repair is not yet available, apart from an in-vivo porcine study. The device is currently only indicated for visualization of the surgical field. In contrast, Barricaid obtained FDA approval in 2019 for the prevention of disc re-herniation following a limited discectomy (4 to 6 mm tall and 6 to 12 mm wide lesion) in the lumbar spine. The device has a titanium body that is

inserted into the adjacent vertebra and a polyester fabric mesh that is placed adjacent to the disc lesion following discectomy to prevent recurrent herniation. Several risks were identified following the long-term implantation of the Barricaid device in a worst-case baboon animal model study used to assess device safety. The study, reported in the summary of safety and effectiveness data FDA report, included implantation of the device at the L4 to L5 and L5 to L6 lumbar spine levels in 9 mature male baboons. Evidence of vertebral endplate disruption, device subsidence beyond the endplates, inflammation, fibrosis, osteolysis, and osteophyte formation was found after 12-months of device implantation, suggesting there were multiple risks associated with the Barricaid device implantation. Since its FDA approval, early follow-up clinical studies have reported beneficial outcomes 2 years post-implantation, such as the reduction in symptomatic disc re-herniations and low complication rates; however, these reports also highlighted that device implantation led to higher prevalence of endplate changes. The long-term safety and effectiveness of the device, especially concerning the damage of the vertebral bone and endplate during device fixation, remains to be determined.

In a secondary analysis of a multi-center randomized clinical study, Thome et al (2021) examined if a bone-anchored annular closure device in addition to lumbar microdiscectomy would result in lower re-herniation and re-operation rates versus lumbar microdiscectomy alone. This trial reported the 5-year follow-up for enrolled patients between December 2010 and October 2014 at 21 clinical sites. Patients in this study had a large annular defect (6 to 10 mm width) following lumbar microdiscectomy for treatment of lumbar disc herniation. Statistical analysis was performed from November to December 2020. Subjects were treated with lumbar microdiscectomy with additional bone-anchored annular closure device (device group) or lumbar microdiscectomy only (control group). Main outcomes and measures included the incidence of symptomatic re-herniation, re-operation, and AEs as well as changes in leg pain, ODI, and health-related QOL (HR-QOL) when comparing the device and control groups over 5 years of follow-up. Among 554 randomized subjects (mean [SD] age: 43 [11] years; 327 [59 %] were men), 550 were included in the modified ITT efficacy population (device group: n = 272; 270 [99 %] were White); control group: n = 278; 273 [98 %] were White) and 550 were included in the as-treated safety population

(device group: n = 267; control group: n = 283). The risk of symptomatic re-herniation (18.8 % [SE, 2.5 %] versus 31.6 % [SE, 2.9 %]; p < 0.001) and re-operation (16.0 % [SE, 2.3 %] versus 22.6 % [SE, 2.6 %]; p = 0.03) was lower in the device group. There were 53 re-operations in 40 patients in the device group and 82 re-operations in 58 patients in the control group. Scores for leg pain severity, ODI, and HR-QOL significantly improved over 5 years of follow-up with no clinically relevant differences between groups. The frequency of serious AEs was comparable between the treatment groups. Serious AEs associated with the device or procedure were less frequent in the device group (12.0 % versus 20.5 %; difference, -8.5 %; 95 % CI: -14.6 % to -2.3 %; p = 0.008). The authors concluded that in patients who were at high risk of recurrent herniation following lumbar microdiscectomy owing to a large defect in the annulus fibrosus, this study's findings suggested that annular closure with a bone-anchored implant lowered the risk of symptomatic recurrence and re-operation over a 5-year of follow-up period. These researchers stated that the findings of this study suggested that implantation with an annular closure device represented a safe and durable preventative strategy in patients at high risk for lumbar disc re-herniation following microdiscectomy.

The authors stated that this study had several drawbacks. First, the results were generalizable only to patients with large defects in the annulus fibrosus following lumbar discectomy. Second, most patients and all investigators were aware of treatment assignment; thus, it was possible that re-operation rates may have been influenced by performance bias. Third, patients in the trial were treated with limited lumbar discectomy with little to no removal of disc material within the intervertebral space. It was possible that lower re-herniation rates could be achieved with aggressive disc resection, although intervertebral instability and spondylosis progression were potential risks with this surgical technique. Fourth, although end-plate changes in the device group were associated with a benign clinical course through 5 years of follow-up, their natural history over longer term follow-up is currently unclear. Finally, although the 5-year follow-up visit rate of 73 % was typical of long-term clinical trials of spinal devices, the potential for bias owing to missing data must be acknowledged.

In a meta-analysis, Wang et al (2023) examined the safety and effectiveness of the various annular defect repair methods that have emerged in recent years. These investigators carried out a meta-analysis of randomized controlled trials (RCTs) and non-RCTs. Studies from PubMed, Embase, and the Cochrane Library (CENTRAL) on lumbar disc herniation (LDH) treatment with annular repair published from inception to April 2, 2022 were included. They summarized the safety and effectiveness of annular repair techniques based on a random-effects model meta-analysis. A total of 7 RCTs and 8 observational studies with a total of 2,161 subjects met the inclusion criteria. The pooled data analysis showed that adding the annular repair technique reduced post-operative recurrence rate, re-operation rate, and loss of inter-vertebral height compared with lumbar discectomy alone. Subgroup analysis based on different annular repair techniques showed that the Barricaid Annular Closure Device (ACD) was effective in preventing re-protrusion and reducing re-operation rates, while there was no significant difference between the other subgroups. The annulus fibrosus suture (AFS) did not improve the post-operative Oswestry Disability Index (ODI). No statistically significant difference was observed in the incidence of adverse events (AEs) between the annular repair and control groups. The authors concluded that lumbar discectomy combined with ACD can effectively reduce the post-operative recurrence and re-operation rates in patients with LDH. AFS alone was less effective in reducing recurrence and re-operation rates and did not improve post-operative pain and function. Annular repair may help maintain post-operative disc height; moreover, these researchers stated that further studies are needed to confirm this finding. Currently, biomaterials lack application value but can improve post-operative pain and function. Combining them with AFS may be an adequate alternative at this stage; further studies are needed to confirm these findings. The authors noted that all current annular repair technologies are safe, and biomaterials with better performance will be the main direction of future development.

The authors stated that this meta-analysis had several drawbacks. First, due to the current level of technical development and research, there is a lack of high-quality RCTs. These researchers included randomized controlled and observational studies, which may reduce the level of evidence of this study. Second, some confounding factors, including BMI and the male-to-female ratio, were not sufficiently reported in some

studies. Similarly, there was a high degree of heterogeneity in some of the pooled results, and these investigators were unable to identify the source of heterogeneity. Moreover, due to a lack of adequate literature and large heterogeneity, the authors were unable to further examine some comprehensive results for the subgroup analysis based on annular repair. Finally, as for the possible differences between studies, these researchers did not perform a net meta-analysis to further compare the advantages and disadvantages of different interventions.

Radiofrequency Denervation for Sacroiliac Joint Pain

Cohen et al (2008) carried out a randomized placebo-controlled study in 28 patients with injection-diagnosed sacroiliac joint pain. Fourteen patients received L4 to L5 primary dorsal rami and S1 to S3 lateral branch radiofrequency (RF) denervation using cooling-probe technology after a local anesthetic block, and 14 patients received the local anesthetic block followed by placebo denervation. Patients who did not respond to placebo injections crossed-over and were treated with RF denervation using conventional technology. One, 3, and 6 months after the procedure, 11 (79%), 9 (64%), and 8 (57%) RF-treated patients experienced pain relief of 50% or greater and significant functional improvement. In contrast, only 2 patients (14%) in the placebo group experienced significant improvement at their 1-month follow-up, and none experienced benefit 3 months after the procedure. In the cross-over group (n = 11), 7 (64%), 6 (55%), and 4 (36%) experienced improvement 1, 3, and 6 months after the procedure. One year after treatment, only 2 patients (14%) in the treatment group continued to demonstrate persistent pain relief. The authors concluded that these results provide preliminary evidence that L4 and L5 primary dorsal rami and S1-S3 lateral branch RF denervation may provide intermediate-term pain relief and functional benefit in selected patients with suspected sacroiliac joint pain. They stated that larger, multi-centered studies with long-term follow-up and comprehensive outcome measures are needed to confirm these results, further establish safety and determine the optimal candidates and treatment parameters.

Drawbacks of this study, albeit a randomized controlled one, include small number of patients as well as "poor" long-term results (only 14% in the treatment group showed continued pain relief after 1 year). In addition, a

systematic review on sacroiliac joint interventions (Hansen et al, 2007) concluded that the evidence for RF neurotomy in managing chronic sacroiliac joint pain is limited.

In an observational study, Karaman et al (2011) examined the safety and effectiveness of novel cooled RF application for sacral lateral-branch denervation. Patients experiencing chronic sacroiliac pain were selected for this study. Fluoroscopy guidance cooled RF denervation was applied on the L5 dorsal ramus and the S1 to S3 lateral branches on patients who had twice undergone consecutive joint blockages to confirm the diagnosis and obtained at least 75% pain relief. At the 1st, 3rd and 6th month post-operatively, the patients' pain was evaluated using a VAS, and their physical function was evaluated with the ODI. Cooled RF was applied on a total of 15 patients. Prior to the procedures, the median VAS score (interquartile range) was 8 (7 to 9), but at the 1st, 3rd and 6th month, this had fallen to 3 (1 to 4), 2 (1 to 3) and 3 (2 to 4). The baseline median ODI score (interquartile range) was 36 (32 to 38), while at the 1st, 3rd and 6th month, it was 16 (8 to 20), 12 (9 to 18) and 14 (10 to 20), respectively. At the final control, while 80% of the patients reported at least a 50% decline in pain scores, 86.7% of those reported at least a 10-point reduction in ODI scores. The authors concluded that the cooled RF used for sacroiliac denervation was an effective and safe method in the short-to-intermediate term. The major drawbacks of this study were its small sample size (n = 15) and short follow-up period (6 months). The authors stated that RCTs with longer follow=up period are needed.

Stelzer et al (2013) retrospectively evaluated the use of cooled RF lateral branch neurotomy (LBN) to treat chronic SIJ-mediated LBP in a large European study population. The electronic records of 126 patients with chronic LBP who underwent treatment with cooled RF LBN were identified. Subjects were selected for treatment based on physical examination and positive response (greater than or equal to 50% pain relief) to an intra-articular SIJ block. Cooled RF LBN involved lesioning the L5 dorsal ramus and lateral to the S1, S2, and S3 posterior sacral foraminal apertures. Visual analog scale pain scores, quality of life, medication usage, and satisfaction were collected before the procedure, at 3 to 4 weeks post-procedure (n = 97), and once again between 4 and 20 months post-procedure (n = 105). When stratified by time to final follow-up (4 to 6, 6 to 12, and greater than 12 months, respectively): 86%,

71%, and 48% of subjects experienced greater than or equal to 50% reduction in VAS pain scores, 96%, 93%, and 85% reported their quality of life as much improved or improved, and 100%, 62%, and 67% of opioid users stopped or decreased use of opioids. The authors concluded that the current results showed promising, durable improvements in pain, quality of life, and medication usage in a large European study population, with benefits persisting in some subjects at 20 months after treatment. The main drawbacks of this study were its retrospective nature, lack of a control group, difficulty in contacting certain subjects, missing data for some subjects, as well as variable length of time to final follow-up.

Ho and colleagues (2013) noted that SIJ pain is a common cause of chronic LBP. Different techniques for RF denervation of the SIJ have been used to treat this condition. However, results have been inconsistent because the variable sensory supply to the SIJ is difficult to disrupt completely using conventional RF. Cooled RF is a novel technique that uses internally cooled RF probes to enlarge lesion size, thereby increasing the chance of completely denervating the SIJ.
These researchers evaluated the effectiveness of cooled RF denervation using the SInergy™ cooled RF system for SIJ pain. The charts of 20 patients with chronic SIJ pain who had undergone denervation using the SInergy™ cooled RF system were reviewed at 2 years following the procedure. Outcome measures included the Numeric Rating Scale for pain intensity, Patient Global Impression of Change, and Global Perceived Effect for patient satisfaction. Fifteen of 20 patients showed a significant reduction in pain (a decrease of at least 3 points on the Numeric Rating Scale). Mean Numeric Rating Scale for pain decreased from 7.4 ± 1.4 to 3.1 ± 2.5, mean Patient Global Impression of Change was "improved" (1.4 ± 1.5), and Global Perceived Effect was reported to be positive in 16 patients at 2 years following the procedure. The authors concluded that cooled RF denervation showed long-term effectiveness for up to 2 years in the treatment of SIJ pain. Limitations of this study included: (i) small sample size (n = 20), (ii) it was a retrospective review with no placebo-control or sham-control group, and (iii) no comparison with conventional RF treatment for SIJ pain.

Facet Joint Implantation

Facet joint replacement/implant is a new device/procedure for facet joint degeneration, which may be used in conjunction with a spinal fusion. It is purported as a system for facet joint reconstruction, matching the joint shape and size in order to provide pain relief, normal motion and stability. An example of this device includes, but may not be limited to, the Acadia Facet Replacement System. Please note: the Acadia is not US Food and Drug Administration (FDA) approved; it is currently in an ongoing clinical trial.

Spinal facet (zygapophyseal) joints are diarthroidal joints that provide both sliding articulation and load transmission features. In addition to the intervertebral disc, facet joints help to support axial, torsional and shear loads that act on the spinal column. Thus, facet joints play an important role in maintaining segmental stability of the spinal cord. Pathology of the facet joints may result in back/neck pain as well as segmental instability within the spine. One of the most common treatment for spinal trauma or degenerative diseases/disorders is arthrodesis (spinal fusion) of one or more vertebral segments. However, spinal fusion decreases function by limiting the range of motion (ROM) for patients in flexion, extension, rotation, and lateral bending. It also creates increased stresses that may lead to accelerated degeneration of adjacent non-fused vertebral segments. Furthermore, pseudoarthrosis, as a result of an incomplete or ineffective fusion, may reduce or even eliminate the desired pain relief. Finally, migration of the fusion device may occur.

Researchers have tried to recreate the natural biomechanics of the spine by the use of artificial discs, which provide for articulation between vertebral bodies to recreate the full ROM allowed by the elastic properties of the natural intervertebral disc that directly connects two opposed vertebral bodies. However, artificial discs available to date do not fully address the mechanics of motion of the spinal column.

Facet joint implantation is a new approach to overcome the shortcomings of currently available devices/implants. These implants are employed to replace a bony portion of the facets so as to remove the source of arthritic-, traumatic-, or other disease-mediated pain. In conjunction with artificial disc replacements, facet joint implantation may represent a way

to recreating a fully functional motion segment that is compromised due to disease or trauma. This combination can supposedly eliminate all sources of pain, return full function and ROM, and completely restore the natural biomechanics of the spinal column. Moreover, degenerative or traumatized facet joints may be replaced in the absence of disc replacement when the natural intervertebral disc is unaffected by the disease or trauma. Facet implants include a superior implant for placement on a superior articulating surface and an inferior implant for placement on an inferior articulating surface. These facet implants are positioned within the affected facet joint(s) for distraction, thus increasing the area of the canals and openings through which the spinal cord and nerves must pass, and decreasing pressure on the spinal cord and/or nerve roots. These implants can be inserted via a lateral or posterior approach.

While facet joint implants are designed to provide patients with degenerative or traumatized facet a motion-preserving alternative to spinal fusion, and to restore the natural motion, stability, and balance to the spine, there is currently a lack of evidence regarding their clinical benefits. The North American Spine Society's guideline on the diagnosis and treatment of degenerative lumbar spinal stenosis (2007), the American College of Occupational and Environmental Medicine's guideline on low back disorders (2007), and the Work Loss Data Institute's guideline on low back - lumbar and thoracic (2008) did not mention the use of facet implant/arthroplasty. Furthermore, in a review on the treatment of neck pain by the Bone and Joint Decade 2000-2010 Task Force on neck pain and its associated disorders facet implant/arthroplasty is not mentioned as an option (Carragee et al, 2009).

Lateral Interbody Fusion

A proposed minimally invasive approach to spinal fusion uses a laparoscope (endoscope), and purports to decrease injury to surrounding tissues and promote a quicker recovery time. There are several types of these procedures/techniques including, but not limited to, direct lateral interbody fusion (DLIF), extreme lateral interbody fusion (XLIF), and laparoscopic anterior lumbar interbody fusion (LALIF).

The aim of lateral interbody fusion in the lumbar spine is to achieve a spinal fusion procedure via a lateral approach in order to avoid the major muscle groups in the back (posterior approach) or the organs and blood vessels in the abdomen (anterior approach) (NICE, 2009). A probe is inserted under fluoroscopic guidance through the psoas muscle, to lie alongside the affected disc, via a lateral approach.

Nerve monitoring is recommended to avoid damage to motor nerves. However, lower limb dysthesia may occur from damage of sensory nerves (NICE, 2009). In one study, 30% of patients developed post-operative numbness, and in 2/3 of these patients the numbness lasted longer than 1 month (Bergey et al, 2004).

Extreme lateral interbody fusion (XLIF) is a novel surgical technique for anterior lumbar interbody fusion. In XLIF (NuVasive, Inc., San Diego, CA) access to the disc space is achieved through 2 small incisions from the side of the body instead of through the muscles of the back. The proposed benefits of XLIF include reduced operative time, reduced blood loss, minimal scarring and reduced hospital stay. However, the procedure is technically difficult to perform and vertebral access is limited to those vertebrae of the spine that are available from the side of the body.

Because the extreme lateral lumbar approach is relatively new, long-term data about XLIF is not currently available and the published data "is sparse at best" (Bahtia et al, 2008). In a feasibility study of XLIF for anterior lumbar interbody fusion (n = 13), Ozgur, et al (2006) reported that the technique allowed anterior access to the disc space without an approach surgeon or the complications of an anterior intra-abdominal procedure; however, the authors concluded that longer-term follow-up and data analysis are needed. A paucity of significant long-term data exists in the literature regarding outcomes of XLIF (Bahtia et al, 2009).

Direct lateral interbody fusion (DLIF) uses a similar approach as XLIF. Knight et al (2009) reported on the results of a prospective chart review (n = 98) of complications from DLIF or XLIF compared to a historical cohort of patients who underwent an open posterior approach. The investigators reported that there was no statistically significant difference in the total complication rate between patients treated with lateral interbody fusion techniques (22.4%) and patients treated with an open postero-lateral

approach (22.5%). In the lateral interbody fusion group, nerve root damage occurred in 3% (2/58) of patients; both showed residual motor effects at 1-year follow-up.

Eck et al (2007) stated in a review of anterior minimally invasive back procedures that minimally invasive techniques for lumbar spine fusion are often associated with significantly greater incidence of complications and technical difficulty than their associated open approaches. An assessment of lateral interbody fusion techniques, including extreme, extra and direct lateral interbody fusion, by the National Institute for Health and Clinical Excellence (NICE, 2009) concluded that current evidence on the safety and efficacy of lateral interbody fusion in the lumbar spine is inadequate in quantity and quality. The assessment noted that a very limited number of clinical efficacy outcomes were reported.

The North American Spine Society (NASS) Operative Coding Committee (Mitchell, 2006) stated that XLIF should be reported using the same Current Procedural Terminology (CPT) codes as an anterior interbody fusion. In addition, NASS has concluded that lateral interbody fusion (XLIF or DLIF) should not be considered experimental or investigational (Baker, 2010). NASS has stated that, while additional clinical outcomes data would be helpful for any surgical procedure including lateral interbody fusion, these data are not needed to endorse continued use of these forms of interbody fusion. NASS explained that "if one were to consider [lateral interbody fusion] as experimental or investigational, than one would need to conclude that there is only one correct method of performing an anterior lumbar interbody fusion, that all surgeons access the spine through the exact same tissue planes, and that the disc and vertebral bodies are all accessed in the exact same orientation. Not only is this technically impossible, it is not verifiable" (Baker, 2010).

Minimally Invasive / Endoscopic Cervical Laminoforaminotomy

Choi et al (2007) performed a prospective analysis of the first 20 patients operated for cervical radiculopathy by a new modification of trans-corporeal anterior cervical foraminotomy technique. To evaluate early results of a functional disc surgery in which decompression for the cervical radiculopathy is done by drilling a hole in the upper vertebral body and most of the disc tissue is preserved. A total of 20 patients

suffering from cervical radiculopathy not responding to conservative treatment were chosen for the new technique. Upper vertebral trans-corporeal foraminotomy was performed with the modified technique in all the patients. All the patients experienced immediate/early relief of symptoms. No complications of vertebral artery injury, Horner's syndrome or recurrent laryngeal nerve palsy were noted. Modified trans-corporeal anterior cervical microforaminotomy is an effective treatment for cervical radiculopathy. It avoids unnecessary violation of the disc space and much of the bony stabilizers of the cervical spine. The authors stated that short-term results of this technique are quite encouraging; longer-term analysis can help in outlining the true benefits of this technique.

Holly et al (2007) described the surgical indications, technique, and preliminary clinical outcomes in a series of patients who underwent the 2-level minimally invasive posterior cervical foraminotomy procedure. This report was composed of 21 consecutive patients with cervical radiculopathy who underwent a minimally invasive 2-level posterior cervical foraminotomy at the authors' institution between 2003 and 2005. Magnetic resonance imaging demonstrated foraminal or postero-lateral pathology at 2 ipsilateral adjacent spinal levels in each patient. Radicular arm pain was the most common presenting symptom, and was encountered in all 21 patients. The mean follow-up for the patients was 23 months (range of 12 to 36). Complete resolution of pre-operative symptoms was achieved in 19 out of 21 patients (90%). Sixteen patients were discharged home the same day of surgery, and the mean estimated blood loss was 35 ml (range of 10 to 100 ml). There were no peri-operative complications. The authors concluded that minimally invasive 2-level posterior cervical foraminotomy can be safely performed on an outpatient basis with results comparable to that of conventional foraminotomy. This procedure should be considered as a potential alternative to 2-level anterior cervical discectomy and fusion or open foraminotomy in selected patients.

In an editorial on minimally invasive/endoscopic versus "open" posterior cervical laminoforaminotomy, Epstein (2009) stated that there is a need to address the complications of minimally invasive surgery in general, and minimally invasive/endoscopic laminoforaminotomy in particular to make it clear when minimally invasive is not only minimally effective, but also potentially "maximally" harmful.

Minimally Invasive Transforaminal Lumbar Interbody Fusion (MITLIF)

Minimally invasive transforaminal lumbar interbody fusion is performed through small incisions using specialized retractors that gradually open an operative corridor through the muscles rather than pulling the muscles aside as with conventional open surgery. Endoscopes are used to visualize the spine and TLIF is performed with specialized instruments through the retractors with less trauma to soft tissues, which may result in reduced operative time and hospitalization. The operation is carried out by means of fluoroscopic guidance.

Although operative time, blood loss and hospitalization were lower for MITLIF compared with more traditional procedures, there was little difference between MITLIF and open TLIF in the single study that compared them, except for lower blood loss and a higher number of complications in the MITLIF group. Overall, due to deficiencies in study design and the relatively small numbers of patients studied, the evidence is insufficient to demonstrate long-term safety and effectiveness of MITLIF, or to determine whether this technique is equivalent to open TLIF or more established surgeries such as anterior-posterior lumbar interbody fusion (APLIF) and posterior lumbar interbody fusion (PLIF). It is also unknown how the various techniques for MITLIF compare with one another.

Isaacs and associates (2005) retrospectively compared 20 patients receiving MITLIF with 24 patients receiving traditional PLIF. All patients had grade I or II spondylolisthesis or mechanical LBP and radiculopathy and had failed conservative therapy. Two interbody grafts were placed with bilateral pedicle screws using Medtronic instrumentation in the MITLIF group. One senior surgeon supervised all MITLIF operations, while 5 surgeons performed the PLIF operations. Mean operative time was 300 mins in MITLIF recipients versus 276 mins in PLIF recipients. For the MITLIF and PLIF groups, respectively, the mean estimated blood loss (EBL) was 226 and 1147 ml ($p < 0.001$); mean hospital length of stay (HLOS) was 3.4 versus 5.1 days ($p < 0.02$) and complications occurred in 1 versus 6 patients in these groups, respectively. The retrospective nature of this design limits the ability to draw firm conclusions regarding efficacy.

In a case-series study, Deutsch and Musacchio (2006) prospectively evaluated 20 patients with degenerative disc disease (DDD); all of whom had failed conservative therapy and who received MITLIF with unilateral pedicle screw placement. Mean operative time was 246 mins, mean EBL was 100 ml and mean HLOS was 2.5 days. At follow-up from 6 to 12 months, a good result (greater than 20% decrease in ODI) was observed in 17/20 (85%) patients with no improvement in 3 (15%). Mean ODI decreased from 57% to 25%, VAS score decreased from 8.3 to 1.4 ($p < 0.005$) and 13/20 (65%) patients displayed some degree of fusion at 6 months. Cerebrospinal fluid (CSF) leaks occurred in 2 patients, and 1 new post-operative radiculopathy was observed, which resulted in further surgery to re-adjust a pedicle screw.

Villavicencio et al (2006) retrospectively compared outcomes in 167 consecutive patients with DDD treated with MITLIF (n = 73), open TLIF (n = 51), or APLIF (n = 43). Patients who underwent MITLIF had fewer previous surgeries (18%) compared with TLIF (39%) or APLIF (49%) recipients. The mean operative time for APLIF was 455 mins, for MITLIF 255 mins, and open TLIF 222 mins. The mean blood loss for APLIF was 550 ml, for minimally invasive TLIF 231 ml, and open TLIF 424 ml. The mean hospitalization time for APLIF was 7.2 days, for MITLIF 3.1 days, and open TLIF 4.1 days. The total rate of complications was 76.7% for APLIF, including 62.8% major and 13.9% minor complications. The MITLIF patients group had the total 30.1% rate of complications, 21.9% of which were minor and 8.2% major complications. There were no major complications in the open TLIF patients group, with 35.3% minor complications. The authors concluded that APLIF is associated with a more than 2 times higher complication rate, significantly increased blood loss, and longer operative and hospitalization times than both percutaneous and open TLIF for lumbar disc degeneration and instability. This study was limited by its retrospective design.

In a retrospective study, Scheufler and co-workers (2007) reported technique, clinical outcomes, and fusion rates of percutaneous transforaminal lumbar interbody fixation (pTLIF). Results were compared with those of mini-open transforaminal lumbar interbody fixation (oTLIF) using a muscle splitting (Wiltse) approach. Percutaneous transforaminal lumbar interbody fixation was performed in 43 patients with single-level and 10 patients with bi- or multi-level lumbar discopathy or degenerative

pseudolisthesis resulting in axial back pain and claudication, pseudo-radicular, or radicular symptoms. Post-operative pain was significantly lower after pTLIF after the second post-operative day ($p < 0.01$). The overall clinical outcome was not different from oTLIF at 8 and 16 months. The authors concluded that pTLIF allows for safe and efficient minimally invasive treatment of single and multi-level degenerative lumbar instability with good clinical results. They stated that further prospective studies investigating long-term functional results are needed to evaluate the definitive merits of percutaneous instrumentation of the lumbar spine.

Park and Foley (2008) discussed their retrospective review study results in 40 patients who underwent MITLIF for symptomatic spondylolisthesis utilizing this approach. Thirty cases involved a degenerative spondylolisthesis while the remaining 10 were isthmic. The minimum follow-up was 24 months with a mean of 35 months. The authors concluded that MITLIF for symptomatic spondylolisthesis appears to be an effective surgical option with results that compare favorably to open procedures. However, the findings of this study are limited by study design, small patient numbers and the lack of a control group.

TruFuse Facet Fusion

TruFuse facet fusion (miniSURG Corp., Clearwater, FL) is a minimally invasive back procedure that uses specially designed bone dowels made from allograft material (donated cortical bone) that are inserted into the facet joints. The procedure is designed to stop facet joints from moving and is intended to eliminate or reduce back pain caused by facet joint dysfunction. There are no published studies of the effectiveness of the TruFuse product in the peer reviewed published literature. A systematic evidence review of TruFuse by the American Association of Neurological Surgeons (AANS) concluded, "[t]here is insufficient objective information to evaluate the safety and utility of this device or to make recommendations regarding clinical usage".

Nu-Fix

Nu-Fix (Nutech Medical, Birmingham, AL) is a cortical screw that is used for facet arthrosis with spine pain, Nu-Fix was cleared by the FDA based upon a 510(k) premarket notification. This allograft interference screw is

percutaneuosly or through stab incision, inserted into the facet joint (cervical, thoracic, or lumbar) to stiffen the joint and promote fusion.

A technical assessment of Nufix prepared by the American Association of Neurological Surgeons (2009) reached the following conclusions about the Nufix: "Nu-Fix is FDA approved as a threaded bone dowel for minimally invasive facet fusion. Marketing has been primarily aimed at non-surgeons in out patient pain clinic settings. There is no published data to assess safety, efficacy, or outcomes. There is no relevant biomechanical data available to use as a comparison to currently performed spinal fusion procedures. Manufacturer sponsored literature is very limited in number, scope and follow-up. In conclusion there is insufficient objective information to evaluate the safety and utility of this device or to make recommendations regarding clinical usage".

Epidural Fat Graft During Lumbar Decompression Laminectomy/Discectomy

Epidural fat grafts have been used to prevent epidural and perineural fibroses. In a case series study, Martin-Ferrer (1989) reported failure of autologous fat grafts to prevent post-operative epidural fibrosis in surgery of the lumbar spine in 3 patients. Hypertrophic epidural scarring occurred in these 3 cases despite the presence of autologous fat grafts. Histopathological examination of the fat removed from 2 patients who were operated on a second time showed a fibrotic infiltration into the fat graft. One randomized study (Mackay et al, 1995) found no reduction in fibrosis with use of epidural fat graft in lumbar laminectomy and discectomy. A non-randomized comparative study (Gorgulu et al, 2004) found no improvement in long-term outcomes with use of epidural fat grafts in lumbar disc surgery. Moreover, there were reports of cauda equina syndrome following hemi-ilaminectomy and discectomy for lumbar disc herniation. Computed tomography-scan revealed the migration of the free fat graft used for preventing peridural scar formation; and removal of the graft resulted in patients' recovery (Urvoy et al, 1990; Imran and Halim, 2005).

Interlaminar Lumbar Instrumented Fusion (ILIF)

Interlaminar lumbar instrumented fusion (ILIF) combines direct neural decompression with an allograft inter-spinous spacer to maintain the segmental distraction and a spinous process fixation plate to maintain stability for eventual segmental fusion. Nuvasive, Inc. (San Diego, CA) is conducting a clinical trial to evaluate ILIF in patients with single-level degenerative disc disease (DDD) of the lumbar spine. The estimated completion date is July 2012.

Sharma et al (2011) evaluated the radiographical change in the coronal and sagittal plane alignment of the lumbar spine after the lateral lumbar interbody fusion (LLIF) approach using XLIF cages (Nuvasive, Inc.). Radiographical and clinical outcomes, and complications associated with the approach were also described. A retrospective review of 43 consecutive patients' pre-operative, immediate post-operative, and 1-year follow-up radiographs was done. All patients had LLIF procedure performed for lumbar DDD, spondylolisthesis, or de novo scoliosis. The radiographical measurements were taken to assess change in the sagittal and coronal plane alignment of the individual instrumented disc level, overall lumbar spine, and lumbar scoliotic curves. The radiographs were also analyzed for fusion at 1 year, end-plate fracture, and other complications. Patients' hospital and clinic charts were reviewed to identify the complications and patient outcomes. There was a mean correction of 3.7 degrees ($p \leq 0.001$) at each instrumented disc level in coronal plane in 87 instrumented levels. Similarly, there was a mean gain of 2.8 degrees ($p \leq 0.001$) of lordosis at each level. In 25 patients with lumbar scoliosis (greater than 10 degrees), mean scoliosis angle correction was 10.4 degrees ($p = 0.001$, 43%). There was no significant change in the overall coronal or sagittal plane alignment of the lumbar spine. The most common post-operative complication (25%) was anterior thigh pain, which was transitory in the majority of cases. End-plate breach was common at the instrumented disc levels; however, it was non-progressive in most of the cases, and did not affect the fusion or alignment at the instrumented levels. The outcome scores were improved significantly at the final follow-up. The authors concluded that the LLIF approach is effective in correcting the coronal plane deformity and in gaining lordosis at individual instrumented levels. They parallelized adjacent end plates to correct the lumbar scoliotic curves. The

complications are mostly approach-related and transitory. The authors stated that a larger cohort with long-term follow-up is needed to establish the advantages and shortcomings of the procedure.

Khan Kinetic Treatment (KKT)

The Khan Kinetic Treatment, manufactured by Datrend Systems Inc (Richmond, British Columbia, Canada), is a medical device for the treatment of spine-related abnormalities causing pain. According to the manufacturer, the KKT uses high-frequency small-amplitude sinusoidal waves to vibrate the vertebrae and repeatedly activate associated neuromuscular structures, which evoke multiple mechanisms of pain relief. In a small, unblinded, randomized trial without placebo control, Desmoulin et al (2007) presented their initial findings on the use of KKT as a chronic neck pain treatment. They reported that, compared with a control group, the treatment group lowered both their self-recorded neck pain scores ($p = 0.012$) as well as pain medication dose ($p = 0.048$), although current functional assessment questionnaires (range of motion, overall activity, and recreation/work activities) did not detect changes ($p = 0.233$, 0.311, and 0.472, respectively). Limitations of this study included a lack of blinding and lack of placebo control. The authors concluded that although they await randomized, placebo-controlled trials and additional results from ongoing mechanistic studies, initial results show that KKT is potentially an effective treatment for chronic neck pain and may contribute to the reduction of pain relieving. Other published literature on KKT spine treatment consists of a study of the effect of KKT in an animal model (Desmoulin et al, 2010).

The OptiMesh Grafting System

OptiMesh is a conformable, porous, polymeric containment device that is inserted into the evacuated disc space and filled with a mixture of cortico-cancellous allograft with demineralized bone matrix, autograft, and bone marrow aspirate to aid traumatic fracture repair and interbody fusion. Evidence is limited to a single case study that utilized OptiMesh for a compression fracture. Long-term safety and effectiveness have not been established. OptiMesh received 510(k) approval in November, 2003 as a class II device. The device is intended to maintain bone graft material within a vertebral defect. This device is contraindicated for patients with

instability and does not provide structural support. The safety and effectiveness of OptiMesh used for fusion of the interbody space has not been established. Further studies are needed to evaluate its safety and effectiveness.

Inamasu et al (2008) reported a patient with a flexion-distraction injury of the L1 vertebra treated with a combination of short-segment posterior fixation and Optimesh (Spineology Inc., St. Paul, MN), a flexible balloon-shaped mesh that is deployed into the fractured vertebra together with allograft. The patient, a 47-year-old man, was admitted after sustaining a motor vehicle accident. Imaging studies showed an L1 compression fracture. The patient had no neurological deficits and was treated conservatively. However, intense back pain persisted and significant kyphosis was noted when he mobilized. Review of the imaging studies strongly suggested disruption of the posterior spinal ligaments. Surgical intervention was performed to address both restoration of the posterior tension band and anterior column height simultaneously. The combined procedure consisted of short-segment posterior fixation from T12 to L2, and placement of OptiMesh filled with allograft into the L1 vertebral body. The anterior column height was restored and spinal alignment was corrected by the procedure, and the patient's back pain subsided soon after the procedure. The role of minimally invasive procedures for reconstruction of the vertebral column height, including the OptiMesh system, in patients with thoracolumbar compression fracture seems promising. However, the long-term effectiveness of these new techniques is unknown. It also remains to be seen how the delivery of allograft into the fractured vertebra via OptiMesh affects remodeling, and whether the restored vertebral height is maintained.

Zheng et al (2010) noted that the OptiMesh bone graft containment system has been used for vertebral compression fractures and percutaneous lumbar interbody fusion. The filled mesh bag serves as the interbody device providing structural support to the motion segment being fused. No biomechanical data of this new device are available in the literature. These researchers examined the biomechanics of lumbar motion segments instrumented with stand-alone OptiMesh system augmented with posterior fixation using facet or pedicle screws and the effectiveness of discectomy and disc distraction. A total of 24 fresh human cadaveric lumbar motion segments were divided into 2 groups. In

the control group, multi-directional flexibility testing was carried out after an intact condition and standard transforaminal lumbar interbody fusion (TLIF) procedure. In the OptiMesh group, testing was carried out following intact, stand-alone OptiMesh procedure, OptiMesh with facet screws (placed using the trans-facet approach), and OptiMesh with pedicle screws and rods. Range of motion (ROM) was calculated for each surgical treatment. The lordosis and disc height change of intact and instrumented specimens were measured in the lateral radiographs to examine the disc space distraction. In the OptiMesh group, cyclic loading in flexion extension (FE) was employed to measure cage subsidence or collapse (10,000 cycles at 6 Nm). After biomechanical testing, all the specimens were dissected to inspect the discectomy and end-plate preparation. The area of discectomy was measured. The mean ROM of the intact specimens was 2.7°, 7.4°, and 7.2° in axial torsion (AT), lateral bending (LB), and FE, respectively. There was no difference between the control group and OptiMesh group. The mean ROM of the stand-alone OptiMesh system decreased to 2.4°, 5.1°, and 4.3° in AT, LB, and FE. The ROM decreased to 0.9° in AT, 2.2° in LB, and 0.9° in FE with OptiMesh system and facet screws. On average, OptiMesh system with pedicle screws and rods reduced the ROM to 1.3° in AT, 1.6° in LB, and 1.1° in FE. Compared with the intact condition and stand-alone OptiMesh system, both posterior fixation options had significant statistical difference ($p < 0.001$). In AT, ROM of facet screws was lower than that of pedicle screws ($p < 0.05$). There was no statistical difference between the facet and pedicle screws in LB and FE ($p > 0.05$). The mean volume of bone graft packed into each bag was 8.3 ± 1.5 cc. The average increase of lordosis was 0.6° ± 1.0° after meshed bag was deployed. The average distraction achieved by the OptiMesh system was 1.0 ± 0.6 mm. The average prepared area of discectomy was 42 % of the total disc. The disc height change after cyclic loading was 0.2 mm. No subsidence or collapse was reported. The authors concluded that the OptiMesh system offered large volume of bone graft in the disc space with small access portals. The OptiMesh system had similar construct stability to that of standard TLIF procedure when posterior fixation was applied. However, the amount of distraction was limited without additional distraction tools. With the anterior support provided by the expandable meshed bag, facet screws had comparable construct stability to that of pedicle screws.

Slightly higher stability was observed in facet screws in AT. This was a cadaveric study. Moreover, these researchers stated that further clinical studies are needed to examine the clinical success of this technique.

Driver et al (2021) noted that transforaminal lumbar interbody fusion remains a critical procedure for patients with lumbar degenerative disc disease (DDD). Increasingly minimally invasive techniques have been proposed to minimize muscle dissection and tissue damage with the goal of minimizing pain and length of stay (LOS). These researchers stated that a prospective, multi-center investigational device exempt (IDE) trial is underway evaluating a novel conformable mesh interbody fusion device in subjects undergoing single-level fusion for DDD. Patients meeting inclusion and exclusion criteria were offered enrollment. There is no comparative group in this study. The objective of this trial was to establish the short- and long-term safety and effectiveness of a novel conformable mesh interbody fusion device in subjects undergoing single-level fusion for DDD unresponsive to conservative care. A total of 102 subjects were enrolled across 10 sites; 99 subjects remained available for follow-up at 12-months. Physical evaluations/imaging were carried out serially through 12-months. Validated assessment tools included 100-mm visual analog scale (VAS) for pain, ODI for function, and computerized tomography (CT) scan for fusion. Independent committees were used to identify adverse events (AEs) and for assessment of radiographic fusion. Reductions in low back pain (LBP)/leg pain and improvements in functional status occurred early and were maintained through 12-month follow-up. Mean VAS-LBP change from baseline to 6-weeks post-op (-46 mm) continued to improve through 12 months (-51 mm). Similar trends were observed for leg pain. Mean ODI change from baseline to 6 weeks post-op (-17) was almost doubled by 12 months (-32). Fusion rates at 12-months were high (98 %). No device-related serious AEs occurred. The authors concluded that the 12-month outcomes showed excellent patient compliance and positive outcomes for pain, function, fusion, and device safety. Clinical improvements were observed by 6-weeks post-op and appeared durable up to 1 year later. These investigators stated that a novel mesh interbody device may provide an alternative means of interbody fusion that reduced connective tissue disruption. Level of Evidence = III.

Chi et al (2021) stated that interbody fusion is a widely used and accepted procedure for the treatment of advanced debilitating lumbar DDD. Increasingly, surgeons are seeking interbody devices that are large for stability and grafting purposes but can be inserted with less invasive techniques. To achieve these contrary objectives a novel, conformable mesh interbody fusion device was designed to be placed in the disc space through a small portal and filled with bone graft in-situ to a large size. This design could reduce the risk of trauma to surrounding structures while creating a large graft footprint that intimately contours to the patient's own anatomy. The purpose of this IDE trial was to examine the peri-operative and long-term results of this novel conformable mesh interbody fusion device. This investigation is a prospective, multi-center, single-arm, Food and Drug Administration (FDA) and institutional review board (IRB)-approved IDE, performance goal trial. A total of 102 adults presenting with DDD at a single level between L2 and S1 and unresponsive to 6 months conservative care had instrumented lumbar interbody fusion. Validated assessment tools include 100-mm VAS for pain, ODI for function, single question survey for patient satisfaction, and CT scan for fusion. Patients were enrolled across 10 geographically distributed sites. Pain/ODI surveys, physical evaluations, and imaging were carried out serially through 24 months. Specifically, CT was carried out at 12 and, if not fused, 24 months. Independent radiologists assessed CTs for fusion. An independent committee adjudicated AEs. Patients with complete data at 24 months were included in the analysis. A total of 96 (96, 94 % follow-up rate) patients (57.0 ± 12.0 years, 50.0 % female, body mass index [BMI] of 30.6 ± 4.9) reported average decreased LBP from baseline of 45.0 ± 26.6 at 6 weeks and 51.4 ± 26.2 at 24 months. Right/left leg pain reduced by 28.9 ± 36.7/37.8±32.4 at 6 weeks and 30.5 ± 33.0/40.3 ± 34.6 at 24 months. Mean ODI improved 17.1 ± 18.7 from baseline to 6 weeks and 32.0 ± 18.5 by 24 months. At 24 months, 91.7 % of patients rated their procedure as excellent/good. Fusion rates were 97.9 % (94/96) at 12 months, and 99 % (95/96) at 24 months. Mean operative time, estimated blood loss (EBL), and LOS were 2.6 ± 0.9 hours, 137 ± 217 ml, and 2.3 ± 1.2 days, respectively. No device-related serious AEs occurred. The authors concluded that clinically significant outcomes for pain, function, fusion, and device safety were demonstrated in this population. Substantial clinical improvements occurred by 6 weeks post-operative and continued to improve to 24

months. These investigators stated that the successful outcomes observed in this trial supported use of this novel device in an instrumented lumbar interbody fusion. Level of Evidence = III.

The authors stated that the limitations of this study included the relatively small number of subjects and that it was a single-arm trial that did not compare directly to other established methods for achieving interbody fusion. Moreover, they stated that as with many advances in medicine, adoption of this technique must occur in the context of the abundant literature pertaining to interbody fusion.

Radiofrequency / Pulsed Radiofrequency Ablation of Trigger Point Pain

Tamimi et al (2009) noted that clinical reports using pulsed radiofrequency (PRF) have shown promise in the treatment of a variety of focal, neuropathic conditions. To date, scant data exist on the use of PRF to treat myofascial and neuromatous pain. All cases in which PRF was used to treat myofascial (trigger point) and neuromatous pain within the authors' practice were evaluated retrospectively for technique, efficacy, and complications. Trigger points were defined as localized, extremely tender areas in skeletal muscle that contained palpable, taut bands of muscle. A total of 9 patients were treated over an 18-month period. All patients had longstanding myofascial or neuromatous pain that was refractory to previous medical management, physical therapy, and trigger point injections. Eight out of 9 patients experienced 75 to 100% reduction in their pain following PRF treatment at initial evaluation 4 weeks following treatment. Six out of 9 (67%) patients experienced 6 months to greater than 1 year of pain relief. One patient experienced no better relief in terms of degree of pain reduction or duration of benefit when compared with previous trigger point injections. No complications were noted. The authors concluded that this review suggested that PRF could be a minimally invasive, less neurodestructive treatment modality for these painful conditions and that further systematic evaluation of this treatment approach is warranted.

Lee et al (2011) noted that recently, clinical reports using PRF have shown favorable effects in the treatment of a variety of focal pain areas, even in non-nervous tissues; however, the mechanism of effect

underlying this treatment to non-nervous tissue remains unclear. These researchers reported the case of a 67-year old male who presented with pain reliving point in the posterior neck. The patient had pain in the posterior neck for 3 years. The pain subsided with pressure applied to a point in the posterior neck. There were no specific abnormal findings on laboratory testing and radiological examinations. After PRF treatment to the pain-relieving point, he had pain relief that lasted more than 5 months.

Coflex

Bae et al (2015) stated that approved treatment modalities for the surgical management of lumbar spinal stenosis encompass a variety of direct and indirect methods of decompression, though all have varying degrees of limitations and morbidity which potentially limit the efficacy and durability of the treatment. The Coflex inter-laminar stabilization (ILS) implant examined under a Food and Drug Administration (FDA) Investigational Device Exemption (IDE) clinical trial, is shown to have durable outcomes when compared to posterolateral fusion in the setting of post-decompression stabilization for stenotic patients. Other clinical and radiographic parameters, more indicative of durability, were also evaluated. The data collected from these parameters were used to expand the FDA composite clinical success (CCS) endpoint; thus, creating a more stringent Therapeutic Sustainability Endpoint (TSE). The TSE allows more precise calculation of the durability of ILS when compared to the fusion control group. These investigators performed a retrospective analysis of data generated from a prospective, randomized, level-1 trial that was conducted at 21 US sites. A total of 344 per-protocol subjects were enrolled and randomized to ILS or fusion after decompression for lumbar stenosis with up to grade 1 degenerative spondylolisthesis. Clinical, safety, and radiographic data were collected and analyzed in both groups; 4-year outcomes were assessed, and the TSE was calculated for both cohorts. The clinical and radiographic factors thought to be associated with therapeutic sustainability were added to the CCS endpoints which were used for pre-market approval (PMA). Success rate, comprised of no second intervention and an ODI improvement of greater than or equal to 15 points, was 57.6% of ILS and 46.7% of fusion patients ($p = 0.095$). Adding lack of fusion in the ILS cohort and successful fusion in the fusion cohort showed a CCS of 42.7% and 33.3%, respectively. Finally, adding adjacent level success to both

cohorts and maintenance of foraminal height in the Coflex cohort showed a CCS of 36.6% and 25.6%, respectively. With additional follow-up to 5 years in the U.S. PMA study, these trends are expected to continue to show the superior therapeutic sustainability of ILS compared to posterolateral fusion after decompression for spinal stenosis. The authors concluded that there are clear differences in both therapeutic sustainability and intended clinical effect of ILS compared to posterolateral fusion with pedicle screw fixation after decompression for spinal stenosis. There are CCS differences between Coflex and fusion cohorts noted at 4 years post-op similar to the trends revealed in the 2 year data used for PMA approval. They stated that when therapeutic sustainability outcomes are added to the CCS, ILS is proven to be a sustainable treatment for stabilization of the vertebral motion segment after decompression for lumbar spinal stenosis. This study provided mid-term (4 years) follow-up; long-term follow-up is needed to determine the durability of the Coflex inter-spinous device. The author also noted that the radiographic indicators of long-term therapeutic sustainability utilized in this study were supported by the literature and further validation through extended follow-up will be of benefit.

Musacchio and colleagues (2016) stated that if non-operative treatment for lumbar stenosis fails, surgery may be considered. This traditionally includes decompression often combined with fusion. Desire for less extensive surgery led to developing new techniques and implants, including an interlaminar device designed with the goal of providing segmental stability without fusion, following decompression. These researchers examined 5-year outcomes associated with an interlaminar device. This prospective, randomized, controlled trial was conducted at 21 centers. Patients with moderate-to-severe lumbar stenosis at 1 or 2 contiguous levels and up to Grade I spondylolisthesis were randomized (2:1 ratio) to decompression and interlaminar stabilization (D+ILS; n = 215) using the Coflex Interlaminar Stabilization device or decompression and fusion with pedicle screws (D+PS; n = 107). Clinical evaluations were made pre-operatively and at 6 weeks and 3, 6, 12, 18, 24, 36, 48, and 60 months post-operatively. Overall, Food and Drug Administration success criteria required that a patient meet 4 criteria: (i) greater than 15 point improvement ODI score; (ii) no re-operation, revision, removal, or supplemental fixation; (iii) no major device-related complication; and

(iv) no epidural steroid injection after surgery. At 5 years, 50.3% of D+ILS versus 44% of D+PS patients (p > 0.35) met the composite success criteria. Re-operation/revision rates were similar in the 2 groups (16.3% versus 17.8%; p > 0.90). Both groups had statistically significant improvement through 60 months in ODI scores with 80.6% of D+ILS patients and 73.2% of D+PS patients demonstrating greater than 15 point improvement (p > 0.30). VAS, SF-12, and ZCQ scores followed a similar pattern of maintained significant improvement throughout follow-up. On the SF-12 and ZCQ, D+ILS group scores were statistically significantly better during early follow-up compared to D+PS. In the D+ILS group, foraminal height, disc space height, and range of motion at the index level were maintained through 5 years. The authors concluded that both treatment groups achieved and maintained statistically significant improvements on multiple outcome assessments throughout 5-year follow-up. On some clinical measures, there were statistically significant differences during early follow-up favoring D+ILS. At no point were there significant differences favoring D+PS. They stated that results of this 5-year follow-up study demonstrated that decompression and interlaminar stabilization with coffle is a viable alternative to traditional decompression and fusion in the treatment of patients with moderate-to-severe stenosis at 1 or 2 lumbar levels. (This appeared to be 1 of the 2 post-approval studies that are required for the continued FDA approval of the Coflex)

This study provided mid-term (5 years) results; long-term safety and effectiveness of the coffle has yet to be established. Another drawback of this study was that it was not blinded during follow-up, which may have introduced a bias. Furthermore, as the authors noted that “There is always difficulty in determining how to address patients who undergo additional surgery or injections after the study surgery, as their outcome measures may then be reflecting the effect of the additional intervention rather that the index procedure. In the current protocol, these patients were classified outcome failures in the composite assessment of success, and excluded from the analyses of individual outcome assessments such as VAS and ZCO”.

Nomura (2016) stated that Auerbach’s group (Davis et al, 2013) proposed a new spinal fusion option using the novel spinal implant Coflex Interlaminar Stabilization (ILS) (Paradigm Spine), which was approved by

the Food and Drug Administration, with 2-year results from prospective and randomized study published in Spine in 2013. The Coflex ILS is a U-shaped titanium device implanted in the interlaminar space with the “U” placed within millimeters of the dura after laminectomy. This has superior and inferior wings that are crimped against the spinous process to provide stability. Implantation is done by simply placing the device into the interlaminar space between the superior and inferior spinous processes after bilateral segmental laminectomy. Functionally, the device acts as a third joint and offloads the facet joints, providing neutral stabilization while maintaining normal spinal kinematics. Furthermore, it allows for compression in extension while permitting normal flexion, allowing maintenance of sagittal balance and lordosis as well as rotational and translational motion as opposed to fusion. Additionally, the mechanical offloading of the facets aids in the relief of back pain and maintenance of foraminal height over time. Hence, this implant appears ideal in overcoming time-dependent degenerative changes after laminectomy; however, further long-term safeguard examination is needed …. If the long-term outcome of decompression plus ILS is almost the same as that of decompression alone, the latter would be more favorable because it has no graft-related complication, as described above. Further comparative studies of ILS stabilization to decompression alone, especially performed using a minimally invasive technique, are interesting …. the ILS has applications for various types of degenerative lumbar disorders as it may be sufficient beneficial for long-term outcomes. A further report on the ILS is appreciated.

Pan et al (2016) retrospectively evaluated the radiography change of LSS treated with the implantation of Coflex inter-spinous device. A total of 60 patients (34 men and 26 women) with LSS who underwent the decompression and Coflex device implanted surgery from January 2010 to December 2013 were followed-up. The mean age of the patients was 59.4 years. There were 33 cases underwent Coflex surgery and 27 cases underwent Topping-off surgery. The Coflex segment ranged from L1/2 to L4/5 (L1-2: 1, L2-3: 5, L3-4: 19, L4-5: 35). The foraminal height (FH), foraminal width (FW) and intervertebral space height (ISH) change of the Coflex segment as well as its adjacent segment were recorded pre-/post-operatively and at last follow-up. Meanwhile, the ODI and VAS were measured in all patient pre-/post-operatively and at last follow-up. The measurement data were recorded as x ± s. And the independent and

paired samples t-test was used to conduct the statistical analysis. The FH increased from (19.82 ± 2.38) mm to (22.28 ± 2.95) mm ($p < 0.05$) post-operatively, and the FH decreased to (19.31 ± 3.32) mm at the last follow up($p > 0.05$, compared to the post-operation). The average FW was 11.2 mm, 11.58 mm and 11.12 mm at pre-/post-operation and follow up, which had no significant different change($p > 0.05$). The post-operative ISH increased from (7.84 ± 1.56) mm to (10.05 ± 2.39) mm ($p < 0.05$), and the ISH decreased to (7.91 ± 1.77) mm at the last follow up($p > 0.05$, compared to the post-operation). The amount of the decreased FH and ISH had no significant difference when comparing the Coflex segment with its adjacent (Coflex ± 1) segments ($p > 0.05$). The lumbar lordosis (LL) was 43.13° ± 15.93°, 38.41° ± 10.82° and 43.10° ± 13.21° at pre-/post-operation and follow up, there was no significant difference between pre- and post-operation ($p > 0.05$). All patients showed statistically significant improvement($p < 0.05$) in the clinical outcome assessed in the VAS and ODI at the time of follow up compared to the pre-operation. The ODI score decreased from 65.12 ± 13.56 to 9.89 ± 1.77; the VAS score decreased from 8.02 ± 1.81 to 1.66 ± 0.51. The authors concluded that Coflex device could temporarily improve the FH and ISH after operation. However, it could not maintain the improvement as the follow-up time extended. The surgical decompression is the responsible factor for the good clinical outcome but not the improvement of FH.

Zhang and colleagues (2018) examined the curative effect of dynamic fixation Coflex treatment for patients with degenerative lumbar spinal stenosis. In the present study, a total of 78 patients with degenerative lumbar spinal stenosis were recruited and divided equally into the control group (n = 39)and observation group (n = 39). The control group was treated with traditional decompression fusion and the observation group received dynamic fixation Coflex system. Surgery and hospitalization were shorter in the observation group than in the control group. Intra-operative blood loss and drainage volume after surgery were significantly lower in the observation group compared to the control group. The treatment effective rate for the observation group was significantly higher; VAS, ODI and Japanese Orthopedic Association pain and functional scores as well as post-operative vertebral canal area and adjacent segment quantitative scores improved after surgery in the 2 groups, but the observation group showed greater improvement. The authors

concluded that the curative effect of dynamic fixation Coflex treatment for degenerative lumbar spinal stenosis demonstrated advantages over traditional surgery, including less trauma and bleeding, pain reduction, improved post-operative rehabilitation, and lower incidence of adjacent segment degeneration. Moreover, they stated that dynamic fixation Coflex treatment for patients with degenerative lumbar spinal stenosis featured remarkable effects. It can reduce the influence on adjacent segments and delay degeneration, which improves spine stability. However, the sample size of this study was small (n = 39 for the Coflex group) and the follow-up time was short (12 months), which requires a further study of large sample size and long-term follow-up.

Kleck and Burger (2018) reported the development of bilateral symptomatic facet joint cysts in a 78-year old man who had been treated with decompression and placement of a Coflex device (Paradigm Spine) at L3 to L4 and L4 to L5. Pre-operative imaging clearly demonstrated fluid in the facet joints without cysts. He underwent standard surgical treatment, but developed symptomatic facet joint cysts at 4 months post-operatively. The patient was treated with a revision decompression and replacement of the devices; there were no issues at the 32-month follow-up. The authors concluded that while the Coflex device has possible long-term biomechanical advantages, vigilance with adherence to appropriate decompression surgical technique is necessary.

Dong et al (2018) examined if Coflex implantation following spinal decompression provided better clinical outcomes compared with traditional decompression and fusion for symptomatic lumbar spinal stenosis through mid-term follow-up. A total of 100 patients who were confirmed L4/L5 lumbar spinal stenosis was surveyed from June 2007 to June 2010. They were randomly and equally divided into 2 groups: 50 cases underwent spinal decompression with Coflex implantation, and 50 cases were treated with spinal decompression with fixation and fusion. The operation time, intra-operative blood loss, ambulation time, and hospitalization days, Japanese Orthopedic Association scores, VAS scores, ODI and SF-36 scores were compared between the 2 groups. The ROM and the height loss at adjacent segments (L3/L4 and L5/S1) were measured pre-operative and post-operative, respectively. Adjacent segment degeneration at L3/L4 and L5/S1 was assessed by Pfirrmann classification. Complications were also recorded. The average age was

57.6 ± 5.9 years old in Coflex implantation group and 59.0 ± 6.7 years old in fusion group, respectively. The average follow-up period was 7.12 ± 1.1 year in Coflex implantation group and 7.31 ± 1.6 year in fusion group, respectively. JOA, ODI, VAS and SF-36 scores were improved at the last follow-up in all the 2 groups with significant differences ($p < 0.01$) compared with those pre-operative, but no statistical differences between the 2 groups ($p > 0.05$). The intervertebral heights of adjacent segments were decreased at the last follow-up and the ranges of intervertebral motions were increased in both groups. The height loss and the ROM increase of adjacent segments were greater in fusion group than those in Coflex group with statistical significant difference ($p < 0.01$). At the last follow-up, adjacent segment disc Pfirrmann grade progressed more obviously in fusion group compared with that in Coflex group, and there was significant difference ($p < 0.05$) between the 2 groups. The authors concluded that based on the present study, it showed that Coflex implantation and fusion after spinal decompression had the same clinical outcomes and satisfaction in treatment of symptomatic lumbar spinal stenosis after 7 years follow-up. However, Coflex implantation had the advantages of less bleeding loss, less trauma and quick recovery. Compared with fusion surgery, Coflex implantation had also advantages in maintaining intervertebral height and delaying intervertebral disc degeneration of adjacent segments.

Moreover, the authors stated that the main drawbacks of this study were: the number of cases was small (n = 50 in the Coflex-treated group), and the follow-up period was not long enough (mid-term follow-up; approximately 7 years). These researchers stated that further research is needed prior to wide application.

Schmidt and colleagues (2018) noted that surgical decompression is extremely effective in relieving pain and symptoms due to lumbar spinal stenosis (LSS). Decompression with interlaminar stabilization (D+ILS) is as effective as decompression with postero-lateral fusion for stenosis, as shown in a major US FDA pivotal trial. These researchers reported a multi-center, randomized controlled trial (RCT) in which D+ILS was compared with decompression alone (DA) for treatment of moderate-to-severe LSS. Under approved institutional ethics review, a total of 230 patients (1:1 ratio) randomized to either DA or D+ILS (Coflex, Paradigm Spine) were treated at 7 sites in Germany. Patients had moderate-to-

severe LSS at 1 or 2 adjacent segments from L3 to L5. Outcomes were evaluated up to 2 years post-operatively, including ODI scores, the presence of secondary surgery or lumbar injections, neurological status, and the presence of device- or procedure-related severe adverse events (SAEs). The composite clinical success (CCS) was defined as combining all 4 of these outcomes, a success definition validated in a US FDA pivotal trial. Additional secondary end-points included visual analog scale (VAS) scores, Zürich Claudication Questionnaire (ZCQ) scores, narcotic usage, walking tolerance, and radiographs. The overall follow-up rate was 91% at 2 years. There were no significant differences in patient-reported outcomes at 24 months ($p > 0.05$). The CCS was superior for the D+ILS arm ($p = 0.017$). The risk of secondary intervention was 1.75 times higher among patients in the DA group than among those in the D+ILS group ($p = 0.055$). The DA-arm had 228% more lumbar injections (4.5% for D+ILS versus 14.8% for DA; $p = 0.0065$) than the D+ILS one. Patients who underwent DA had a numerically higher rate of narcotic use at every time-point post-surgically (16.7% for D+ILS versus 23% for DA at 24 months). Walking Distance Test results were statistically significantly different from baseline; the D+ILS group had greater than 2 times the improvement of the DA. The patients who underwent D+ILS had greater than 5 times the improvement from baseline compared with only 2 times the improvement from baseline for the DA group. Foraminal height and disc height were largely maintained in patients who underwent D+ILS, whereas patients treated with DA showed a significant decrease at 24 months post-operatively ($p < 0.001$). The authors concluded that this study showed no significant difference in the individual patient-reported outcomes (e.g., ODI, VAS, ZCQ) between the treatments when viewed in isolation. The CCS (survivorship, ODI success, absence of neurological deterioration or device- or procedure-related SAEs) was statistically superior for ILS. Microsurgical D+ILS increased walking distance, decreased compensatory pain management, and maintained radiographic foraminal height, extending the durability and sustainability of a decompression procedure. While the CCS was statistically superior for ILS, it is unclear whether these findings are also clinically significant. Furthermore, this study provided only short-term follow-up (up to 2 years); long-term follow-up data are needed.

The authors also stated that this study had drawbacks. Despite being a RCT, imperfections in its conduct meant that some patients were lost to follow-up, and there were some missing data. Also, any randomized trial that is industry-sponsored raises the question of bias, even if the bias was unintentional.

Furthermore, UpToDate reviews on “Lumbar spinal stenosis: Treatment and prognosis” (Levin, 2018) and “Subacute and chronic low back pain: Surgical treatment" (Chou, 2018) do not mention “Coflex / dynamic distraction stabilization / interlaminar stabilization” as a therapeutic option.

The CoFlex-F Implant

The Coflex-F implant is a posterior, non-pedicle supplemental fixation device intended for use with an interbody cage as an adjunct to fusion at a single level in the lumbar spine (L1 to S1) that can be delivered through a minimally invasive approach. The implant is a type of posterior fixation instrumentation intended to rigidly hold vertebrae together while spinal fusion occurs. It is intended for attachment to the spinous processes for the purpose of achieving stabilization to promote fusion in patients suffering from DDD, with or without attendant grade I spondylolisthesis. On October 6, 2010, the Coflex-F implant was cleared by the FDA via the 501(k) process for the purpose of achieving stabilization to facilitate fusion in patients treated for DDD (defined as back pain of discogenic origin with degeneration of the disc confirmed by history and radiographic studies); with up to grade 1 spondylolisthesis. However, the Belgian Health Care Knowledge Center (2011) stated that that it is unclear what data for the Coflex-F was submitted for FDA clearance.

An UpToDate review on "Lumbar spinal stenosis: Treatment and prognosis" (Levin, 2012) states that "Intraspinous spacer implantation – A potentially less invasive treatment option involves implanting a device between the spinous processes at one or two vertebral levels, relieving compression. This procedure is said to be appropriate for those patients with spinal stenosis without spondylolisthesis who have intermittent claudication symptoms that are exacerbated in extension and relieved in flexion .... It is unclear how this newer procedure compares with the standard surgical procedure, decompressive laminectomy, in terms of

effectiveness, side effects, recovery time and long-term outcomes. This treatment does not appear to be helpful in patients who have spondylolisthesis".

Coccygectomy

Patel et al (2008) stated that coccydynia is a term that refers to pain in the region of the coccyx. Most cases are associated with abnormal mobility of the coccyx which may trigger a chronic inflammatory process leading to degeneration of this structure. In some patients this instability may be detected on dynamic radiographs. Non-surgical management remains the gold standard treatment for coccydynia, consisting of decreased sitting, seat cushioning, coccygeal massage, stretching, manipulation, local injection of steroids or anesthetics, and postural adjustments. Those patients who fail these conservative modalities may potentially benefit from coccygectomy. However, surgical intervention is typically reserved for patients with evidence of advanced coccygeal instability (e.g., subluxation or hypermobility) or spicule formation, as this population appears to exhibit the greatest improvement post-operatively.

Trollegaard et al (2010) reported that between 1993 and 2008, a total of 41 patients underwent total coccygectomy for coccydynia which had failed to respond to 6 months of conservative management. Of these, 40 patients were available for clinical review and 39 completed a questionnaire giving their evaluation of the effect of the operation. Excellent or good results were obtained in 33 of the 41 patients, comprising 18 of the 21 patients with coccydynia due to trauma, 5 of the 8 patients with symptoms following childbirth and 10 of 12 with idiopathic onset. In 8 patients the results were moderate or poor, although none described worse pain after the operation. The only post-operative complication was superficial wound infection, which occurred in 5 patients and which settled fully with antibiotic treatment. One patient required re-operation for excision of the distal cornua of the sacrum. The authors concluded that total coccygectomy offered satisfactory relief of pain in the majority of patients regardless of the cause of their symptoms.

The Work Loss Data Institute’s clinical practice guideline on “Low back - lumbar & thoracic (acute & chronic)” (2011) recommended the use of coccygectomy. Furthermore, an UpToDate review on “Coccydynia

(coccygodynia)" (Fletcher, 2012) suggests that coccygectomy be performed only as a last resort for intractable cases.

BacFast HD

According to the manufacturer, BacFast HD (Hyper-Demineralized) is a demineralization technology used to expose the collagen surface. With the use of HD technology and increased collagen surface area, BacFast HD also provides the graft with osteo-inductive properties without compromising the structural integrity of the graft. These characteristics, coupled with an osteo-conductive design through increased surface contact and locking edges to prevent migration, BacFast HD is engineered with a focus on fusion as well as facet stabilization. Benefits of the facet stabilization procedure using BacFast HD are thought to include (i) osteo-inductive surface for enhanced fusion, (ii) stabilization of the spine, and (iii) reduction of pain, blood loss, and tissue/bone destruction.

Oxygen-Ozone Therapy (Injection)

Kallewaard and colleagues (2010) stated that an estimated 40% of chronic lumbosacral spinal pain is attributed to the discus intervertebralis. Degenerative changes following loss of hydration of the nucleus pulposus lead to circumferential or radial tears within the annulus fibrosus. Annular tears within the outer annulus stimulate the ingrowth of blood vessels and accompanying nociceptors into the outer and occasionally inner annulus. Sensitization of these nociceptors by various inflammatory repair mechanisms may lead to chronic discogenic pain. The current criterion standard for diagnosing discogenic pain is pressure-controlled provocative discography using strict criteria and at least 1 negative control level. The strictness of criteria and the adherence to technical detail will allow an acceptable low false-positive response rate. The most important determinants are the standardization of pressure stimulus by using a validated pressure monitoring device and avoiding overly high dynamic pressures by the slow injection rate of 0.05 mL/s. A positive discogram requires the reproduction of the patient's typical pain at an intensity of greater than 6/10 at a pressure of less than 15 psi above opening pressure and at a volume less than 3.0 ml. Perhaps the most important and defendable response is the failure to confirm the discus is

symptomatic by not meeting this strict criteria. Various interventional treatment strategies for chronic discogenic LBP unresponsive to conservative care include reduction of inflammation, ablation of intradiscal nociceptors, lowering intra-nuclear pressure, removal of herniated nucleus, and radiofrequency ablation of the nociceptors. Unfortunately, most of these strategies do not meet the minimal criteria for a positive treatment advice. In particular, single-needle radiofrequency thermo-coagulation of the discus is not recommended for patients with discogenic pain (2 B-). Interestingly, a little used procedure, radiofrequency ablation of the ramus communicans, does meet the (2 B+) level for endorsement. The authors concluded that there is currently insufficient proof to recommend intradiscal electrothermal therapy (2 B±) and intradiscal biacuplasty (0). It is advised that ozone discolysis, nucleoplasty, and targeted disc decompression should only be performed as part of a study protocol; future studies should include more strict inclusion criteria.

In a systematic review and meta-analysis of RCTs, Magalhaes et al (2012) evaluated the therapeutic results of percutaneous injection of ozone for LBP secondary to disc herniation. A comprehensive literature search was conducted using all electronic databases from 1966 through September 2011. The quality of individual articles was assessed based on the modified Cochrane review criteria for randomized trials and criteria from the Agency for Healthcare Research and Quality. The outcome measure was short-term pain relief of at least 6 months or long-term pain relief of more than 6 months. A total of 8 observational studies were included in the systematic review and 4 randomized trials in the meta-analysis. The indicated level of evidence for long-term pain relief was II-3 for ozone therapy applied intradiscally and II-1 for ozone therapy applied paravertebrally. The grading of recommendation was 1C for intradiscal ozone therapy and 1B for paravertebral ozone therapy. The authors concluded that ozone therapy appears to yield positive results and low morbidity rates when applied percutaneously for the treatment of chronic LBP. The main drawbacks of this review were the lack of precise diagnosis and the frequent use of mixed therapeutic agents. The meta-analysis included mainly active-control trials. No placebo-controlled trial was found.

The Work Loss Data Institute's clinical guideline on "Low back - lumbar & thoracic (acute & chronic)" (2011) listed oxygen-ozone therapy (injection) as interventions/procedures that are under study and are not specifically recommended.

In a prospectively randomized, single-blind study, Elawamy and co-workers (2018) evaluated the quality of pain alleviation using 2 different doses of intradiscal injections of O_3-O_2 mixture. A total of 60 patients with symptomatizing single lumbar disc herniation (DH) were subjected to O_3-O_2 intradiscal injection and randomly allocated into 1 of 2 groups; group A: received 10 ml, 40 µg/ml of O_3-O_2; and group B: received 10 ml, 30 µg/ml of O_3-O_2. Pain score and functional ability of the patients using the VAS and ODI were evaluated after 1, 6, and 12 months and compared to the basal values. Patient satisfaction and reduction of DH were evaluated after the 6th month. There were no significant differences between the 2 groups regarding the clinical outcome; however both the ODI and VAS evaluations showed highly significant improvement (decreased) ($p < 0.01$) after injection and during the entire follow-up period. There were highly significant negative correlations between the DH reduction percentage and both the VAS and ODI scores after 6 months in both of the groups. The authors concluded that intradiscal injection of O_3-O_2 mixture was a very valuable maneuver in the reduction of DH size and improvement of pain quality, with either ozone concentrations of 40 µg/ml or 30 µg/ml.

The authors stated that this study was limited by a small sample size (n = 60); it was also an active control trial, which may explain the insignificant difference in between the groups, in addition to being a single-blind trial. Moreover, these researchers noted that they did find that an O3-O2 mixture can offer rapid onset and sustained improvement of LBP.

Rahimzadeh and associates (2018) noted that intervertebral disc herniation with the pressure on the surrounding neural structures is one of the most important causes of chronic LBP, which sometimes leads to open surgery. Intradiscal intervention such as laser irradiation or ozone injection have been used to reduce the pressure inside the disc. In this clinical trial, these 2 methods were compared with each other. A total of 40 patients with back pain radiating to lower limb due to lumbar intervertebral disc herniation were selected. These patients were randomly divided into 2 equal groups for percutaneous intradiscal

intervention. The Laser Disc Decompression Group (LDG) (n = 20) was exposed to 1,500 J of laser irradiation into the disc center. In the Ozone Injection Group (OZG) patients (n = 20), 6 mL of ozone 30 µg/ml was injected into the center of the disc. Considering the level of neural root involvement, both groups received 20 mg of triamcinolone injection via transforaminal epidural. Patients were followed-up for 12 months regarding score on VAS and life performance improvement based on ODI and satisfaction level. No difference was found between the 2 groups for ODI variable before intervention, whereas OZG showed better ODI scores in the measured time intervals. In LDG, only a significant difference in terms of ODI score was found between the times of before surgery and the first month. The authors concluded that intradiscal ozone injection could be an effective and cost-effective method for treatment of patients with discogenic back pain.

The authors stated that this study had some drawbacks such as lack of a control group receiving placebo; lack of morphological assessment of disc and surrounding structures; lack of MRI control; small sample size (n = 20 in both groups); and limited time-frame (12 months) for patients' assessment.

In a systematic review, Costa and colleagues (2018) examined the safety and effectiveness of ozone therapy for LBP in patients with lumbar disc herniation. These researchers carried out a systematic search in PubMed and Scopus, followed by a 3-step selection process. Data was processed by 2 independent reviewers and information was gathered based in pre-defined variables. Only articles performed in humans; original and English written; on treatment with ozone; comparing the result of ozone therapy (experimental group) with another non-ozone intervention (control group); and on patients with lumbar pain and disc hernia, were included. From 439 references retrieved after duplicates removal, inclusion and exclusion criteria were applied, and 7 studies were included in the final revision; 1 article compared treatment with ozone versus placebo, 1 ozone and global postural re-education versus global postural re-education alone, 2 the combination of ozone with steroid versus steroid alone, 2 ozone versus steroid, and 1 ozone versus micro-discectomy. All but the study comparing ozone application with micro-discectomy, showed similar or better results in the experimental group. Only 3 studies evaluated the presence of side effects. In 2 papers no complication was reported, and in

the other, a low percentage of adverse effects was observed, not significantly different between the 2 study groups. The authors concluded that only a small number of poor quality studies on ozone effect in LBP and disc herniation were available for inclusion in this review. Nevertheless, these reported an improvement in pain and functional scores with its application. Complications, mostly minor, but potentially serious were under-reported. These researchers stated that additional studies with adequate and consistent methodologies are needed before the role of ozone can be established in the management of LBP.

Minimally Invasive Sacroiliac Joint Fusion

Sacroiliac joint (SIJ) fusion has been suggested as a possible treatment option for individuals with low back pain due to sacroiliac joint dysfunction or syndrome. This procedure may be performed by an open surgical approach or as a minimally invasive procedure in order to place plates and/or screws to develop a bony fusion across the SIJ for stabilization. The iFUSE Implant System consists of small titanium implants placed across the sacroiliac joint to stabilize and fuse it via a minimally invasive (percutaneous) approach with use of fluoroscopy to visualize proper placement of the implants. Other minimally invasive systems for SIJ fusion include the SIJFuse Sacroiliac Joint Fusion Device System, Silex Sacroiliac Joint System and SImmetry Sacroiliac Joint Fusion System.

In a consecutive case-series study, Buchowski et al (2005) described the outcome of sacro-iliac joint (SIJ) arthrodesis for SIJ disorders, with the hypothesis that SI arthrodesis leads to improved post-operative function. The patient population consisted of 20 patients undergoing SIJ arthrodesis between December 1994 and December 2001. Patients undergoing concomitant procedures at the time of SIJ arthrodesis were excluded. The 3 men and 17 women in the study group had an average age of 45.1 years (range of 21.8 to 66.4 years), a mean duration of symptoms of 2.6 years (range of 0.5 to 8.0 years), and a mean follow-up period of 5.8 years (range of 2.0 to 9.0 years). Outcome measures included general health and function, clinical evaluation, and radiographic assessment. For all 20 patients, non-operative treatment had failed, and for all, the diagnosis was confirmed by pain relief with intra-articular SIJ injections under fluoroscopic guidance. Sacroiliac joint arthrodesis (via a modified Smith-Petersen technique) was recommended only when a

positive response to the injection was noted, and patients had recurrence of symptoms after the initial positive response. Pre-operative and post-operative general health and function were assessed via the 36-item Short-Form (SF-36) Health Survey and American Academy of Orthopaedic Surgeons (AAOS) Modems Instrument, which were collected prospectively. Medical records and plain radiographs were reviewed retrospectively to determine the clinical and radiographic outcome. Multiple etiologies of sacroiliac symptoms were observed: SIJ dysfunction (13 patients), osteoarthritis (5 patients), and spondyloarthropathy and SIJ instability (1 each). Seventeen patients (85%) had solid fusion. Fifteen patients (75%) completed pre-operative and post-operative SF-36 forms. Significant ($p < \text{or} = 0.05$) improvement occurred in the following categories: physical functioning, role physical, bodily pain, vitality, social functioning, role emotional, as well as neurogenic and pain indices. Improvement (not statistically significant) was also noted in general and mental health. The authors concluded that for carefully selected patients, SI arthrodesis appears to be a safe, well-tolerated, and successful procedure, leading to significant improvement in functional outcome and a high fusion rate. Limitations of this study were: (i) the 85% fusion rate may be an over-estimation because more precise methods (such as a CT scan) were not used to confirm successful arthrodesis, (ii) small number of patients (n = 20), and (iii) only 75% of patients were available for follow-up.

Wise and Dall (2008) compared efficacy and outcomes of a new technique for SI arthrodesis. This study described the radiographic and clinical outcomes of this procedure. A total of 13 consecutive patients underwent minimally invasive SI arthrodesis between February and December 2004 at a single teaching hospital and were prospectively followed. Six patients had bilateral fusions for a total of 19 joints. The average age was 53.1 (range of 45 to 62). Average body mass index was 31.2 (range of 21.9 to 46.9). Mean follow-up was 29.5 months (range of 24 to 35). Diagnosis was confirmed using fluoroscopically guided intra-articular injections of local anesthetic and corticosteroid when their pain was relieved 2 or more hours. Arthrodesis was only performed on patients with positive injections who subsequently had their symptoms recur. Outcome measurements included radiographic assessment for fusion and improvement in VAS for LBP, leg pain, and dyspareunia. Computed

tomography scan to evaluate implant placement was performed post-operatively and again at 6 months to assess fusion. The overall fusion rate was 89% (17/19 joints). Significant improvements were seen in final LBP score on a VAS (0 to 10) (average improvement 4.9, p < or = 0.001). Leg pain improved an average of 2.4 (p = 0.013). Dyspareunia improved an average of 2.6 (p = 0.0028). One patient was revised to an open arthrodesis secondary to nonunion and persistent pain. There were no infections or neurovascular complications. The authors concluded that minimally invasive SI arthrodesis via a percutaneous posterior approach is a safe and efficacious procedure, leading to a high fusion rate and significant improvement in LBP, leg pain, and dyspareunia. Limitations of this study were its small sample size and the lack of a control group.

In a consecutive case-series study, Al-Khayer (2008) reported a new percutaneous SIJ arthrodesis technique utilizing a Hollow Modular Anchorage screw. Pre-operative and post-operative Oswestry Disability Index (ODI), VAS for pain, and post-operative subjective patients' satisfaction were assessed for all patients. Minimum 2 years follow-up was documented. A total of 9 patients underwent SIJ arthrodesis with the new technique. The mean ODI value dropped from 59 (range of 34 to 70) pre-operatively to 45 (range of 28 to 60) post-operatively (p < or = 0.005). The mean VAS value dropped from 8.1 (range of 7 to 9) pre-operatively to 4.6 (range of 3 to 7) post-operatively (p < or = 0.002). The mean patients' satisfaction was 6.8 (range of 5 to 8). The authors concluded that the new technique may offer a safe and effective treatment for intractable SIJ pain. Limitations of this study were its small sample size, lack of a control group, and despite the encouraging radiographic findings, the exact fusion status of SIJ arthrodesis cannot be determined by plain radiographs.

Khurana et al (2009) examined the effects of percutaneous fusion of the SIJ with hollow modular anchorage screws. These investigators reviewed 15 consecutive patients, 11 women and 4 men, with a mean age of 48.7 years (37.3 to 62.6), who between July 2004 and August 2007 had undergone percutaneous SI fusion using hollow modular anchorage screws filled with demineralized bone matrix. Each patient was carefully assessed to exclude other conditions and underwent pre-operative CT and MR scans. The diagnosis of symptomatic SI disease was confirmed by an injection of local anesthetic and steroid under image intensifier

control. The short form-36 questionnaire and Majeed's scoring system were used for pre- and post-operative functional evaluation. Post-operative radiological evaluation was performed using plain radiographs. Intra-operative blood loss was minimal and there were no post-operative clinical or radiological complications. The mean follow-up was for 17 months (9 to 39). The mean short form-36 scores improved from 37 (23 to 51) to 80 (67 to 92) for physical function and from 53 (34 to 73) to 86 (70 to 98) for general health ($p = 0.037$). The mean Majeed's score improved from 37 (18 to 54) pre-operatively to 79 (63 to 96) post-operatively ($p = 0.014$). There were 13 good to excellent results. The remaining 2 patients improved in short form-36 from a mean of 29 (26 to 35) to 48 (44 to 52). Their persistent pain was probably due to concurrent lumbar pathology. The authors concluded that percutaneous hollow modular anchorage screws are a satisfactory method of achieving SI fusion.

In a retrospective study, Rudolf (2012) evaluated the safety and effectiveness of minimally invasive SIJ fusion using a series of triangular, porous plasma spray coated titanium implants. A total of 50 consecutive patients were treated by a single orthopedic spine surgeon in private practice. Medical charts were reviewed for peri-operative metrics, complications, pain, quality of life and satisfaction with surgery. All patients were contacted at a 24 months post-op to assess SIJ pain, satisfaction with surgery and work status. An early and sustained statistically significant improvement in pain function was identified at all post-operative time points (ANOVA, $p < 0.000$). A clinically significant improvement (greater than 2 point change from baseline) was observed in 7 out of 9 domains of daily living. The complication rate was low and more than 80% of patients would have the same surgery again. The authors concluded that minimally invasive SIJ fusion appears to be a safe and effective procedure for the treatment of SIJ disruption or degenerative sacroiliitis. The drawbacks of this study included its retrospective design, small sample size, a single surgeon’s experience, a non-standard outcomes measure, and the lack of a comparator group. Moreover, the author noted that prospective studies are currently underway to further evaluate this technology.

In a retrospective study, Sachs and Capobianco (2012) evaluated the safety and effectiveness of minimally invasive SIJ arthrodesis via an ileo-sacral approach in patients who were refractory to conservative care.

These investigators reported on the first 11 consecutive patients treated with a novel minimally invasive SIJ fusion system by a single surgeon. Medical charts were reviewed for peri-operative metrics and baseline pain scores recorded using a 0 to 10 numerical rating scale. Ninety one percent (91%) of patients were female and the average patient age was 65 years (range of 45 to 82). Mean baseline pain score (SD) was 7.9 (+/- 2.2). Mean pain score at the 12 month follow-up interval was 2.3 (+/- 3.1), resulting in an average improvement of 6.2 points from baseline, representing a clinically and statistically significant (p = 0.000) improvement. Patient satisfaction was very high with 100% indicating that they would have the same surgery again for the same result. The authors concluded that the findings of this small case series illustrated the safety and effectiveness of minimally invasive SIJ fusion using a series of triangular porous plasma coated titanium implants in carefully selected patients. Moreover, they stated that larger multi-centered studies are needed.

The Work Loss Data Institute's clinical guideline on "Low back - lumbar & thoracic (acute & chronic)" (2011) does not mention sacroiliac joint fusion as a therapeutic option. In fact, the Work Loss Data Institute's clinical guideline on "Hip & pelvis (acute & chronic)" (2011) listed sacroiliac joint fusion as one of the interventions/procedures were considered, but are not recommended. In a systemic review on "The therapeutic effectiveness of sacroiliac joint interventions" (Hansen et al, 2012), sacroiliac joint fusion is not mentioned as a therapeutic option. Furthermore, American College of Occupational and Environmental Medicine's clinical guideline on "Low back disorders" (ACOEM, 2011) did not recommend sacroiliac joint fusion for any low back pain conditions because of insufficient evidence.

In a retrospective study, Sachs and Capobianco (2013) reported on the safety and effectiveness of MIS SIJ arthrodesis using a series of triangular, porous plasma coated implants in patients who were refractory to conservative care. These investigators reported on the first 40 consecutive patients with 1-year follow-up data that underwent MIS SIJ fusion with the iFUSE Implant System (SI-BONE, Inc., San Jose, CA) by a single surgeon. Medical charts were reviewed for demographics, peri-operative metrics, complications, pain scores, and satisfaction. Mean age was 58 years (range of 30 to 81) and 75% of patients were female. Post-

operative complications were minimal and included transient trochanteric bursitis (5%), facet joint pain (20%), and new LBP (2.5%). There were no re-operations at 1 year. Mean pain score improved from 8.7 (1.5 SD) at baseline to 0.9 (1.6) at 12 months, a 7.8-point improvement ($p < 0.001$). Patient satisfaction was very high. The authors concluded that the results of this case series reveal that MIS SIJ fusion using the iFUSE Implant System is a safe and effective treatment option in carefully selected patients. This was an extension of the 2012 study by these investigators. The findings of this small study are promising. Moreover, the authors stated that “additional prospective controlled trials are underway”.

Miller et al (2013) stated that MIS SIJ arthrodesis was developed to minimize the risk of iatrogenic injury and to improve patient outcomes compared with open surgery. Between April 2009 and January 2013, a total of 5,319 patients were treated with the iFUSE SI Joint Fusion System® for conditions including SIJ disruption and degenerative sacroiliitis. A database was prospectively developed to record all complaints reported to the manufacturer in patients treated with the iFUSE device. Complaints were collected through spontaneous reporting mechanisms in support of ongoing mandatory post-market surveillance efforts. Complaints were reported in 204 (3.8%) patients treated with the iFUSE system. Pain was the most commonly reported clinical complaint (n = 119, 2.2%), with nerve impingement (n = 48, 0.9%) and recurrent SIJ pain (n = 43, 0.8%) most frequently cited. All other clinical complaints were rare (less than or equal to 0.2%). Ninety-six revision surgeries were performed in 94 (1.8%) patients at a median follow-up of 4 (range of 0 to 30) months. Revisions were typically performed in the early post-operative period for treatment of a symptomatic mal-positioned implant (n = 46, 0.9%) or to correct an improperly sized implant in an asymptomatic patient (n = 10, 0.2%). Revisions in the late post-operative period were performed to treat symptom recurrence (n = 34, 0.6%) or for continued pain of undetermined etiology (n = 6, 0.1%). The authors concluded that analysis of a post-market product complaints database demonstrated an overall low-risk of complaints with the iFUSE SIJ Fusion System in patients with degenerative sacroiliitis or SIJ disruption. The authors noted that the initial results are promising; however, clinical effectiveness outcomes were not assessed in this study.

Noting that there is minimal literature published on percutaneous fixation of the sacroiliac joint, Kim, et al. (2014) reported on a retrospective review of 31 patients operated on by a single surgeon. The investigators reported that 27 patients expressed satisfaction, 4 patients did not. Pain relief was noted to be Complete (16 patients), Excellent (5 patients), Good (9 patients), and Fair (1 patients). Four patients had postoperative complications. These were infected hematoma (2), L5 nerve root irritation (1), and L5-S1 discitis (1). One patient required revision. On 6 month postop CT scan, 18/19 patients had radiographic evidence of bone ingrowth and bone into or across the SI joint was evident in 8/19 patients. Lucency was noted around at least one implant in 5/19 patients.

In an editorial regarding “Stabilization of the sacroiliac joint”, Shaffrey and Smith (2013) stated that “There are numerous unanswered questions regarding patient selection for SIJ fusion or stabilization. There are an increasing number of surgical techniques for treating SIJ pathology and it is not clear which method may provide the best outcomes. Without prospective trials with non-conflicted surgeons and standardized selection criteria, the true role for SIJ fusion procedures in the management of chronic lower back pain will remain murky. The consequences of the unsupported enthusiasm for the surgical management of discogenic back pain still negatively impacts the public perception of spinal surgeons. Much more high quality information is needed regarding the surgical management of SIJ pathology before widespread use of this technique should be adopted”.

Whang and colleagues (2015) noted that sacroiliac (SI) joint pain is a prevalent, under-diagnosed cause of lower back pain. SI joint fusion can relieve pain and improve quality of life in patients who have failed non-operative care. To-date, no study has concurrently compared surgical and non-surgical treatments for chronic SI joint dysfunction. These researchers conducted a prospective randomized controlled trial of 148 subjects with SI joint dysfunction due to degenerative sacroiliitis or sacroiliac joint disruptions who were assigned to either minimally invasive SI joint fusion with triangular titanium implants (n = 102) or non-surgical management (NSM, n = 46). SI joint pain scores, Oswestry Disability Index (ODI), Short-Form 36 (SF-36) and EuroQol-5D (EQ-5D) were collected at baseline and at 1, 3 and 6 months after treatment commencement. Six-month success rates, defined as the proportion of

treated subjects with a 20-mm improvement in SI joint pain in the absence of severe device-related or neurologic SI joint-related adverse events or surgical revision, were compared using Bayesian methods. Subjects (mean age of 51, 70% women) were highly debilitated at baseline (mean SI joint VAS pain score 82, mean ODI score 62). Six-month follow-up was obtained in 97.3%. By 6 months, success rates were 81.4% in the surgical group versus 23.9% in the NSM group (difference of 56.6%, 95% posterior credible interval 41.4 to 70.0%, posterior probability of superiority > 0.999). Clinically important (greater than or equal to 15 point) ODI improvement at 6 months occurred in 75% of surgery subjects versus 27.3% of NSM subjects. At 6 months, quality of life improved more in the surgery group and satisfaction rates were high. The mean number of adverse events in the first 6 months was slightly higher in the surgical group compared to the non-surgical group (1.3 versus 1.0 events per subject, p = 0.1857). The authors concluded that the 6-month follow-up from this level 1 study showed that minimally invasive SI joint fusion using triangular titanium implants was more effective than non-surgical management in relieving pain, improving function and improving quality of life in patients with SI joint dysfunction due to degenerative sacroiliitis or SI joint disruptions. This was a study with short-term follow-up (6 months); well-designed studies with long-term follow-up are needed to ascertain the clinical effectiveness of SI fusion.

Soriano-Baron et al (2015) stated that minimally invasive placement of SIJ fusion implants is a potential treatment for SIJ disruptions and degenerative sacroiliitis. Biomechanical studies of screw fixation within the sacrum have shown that placement and trajectory are important in the overall stability of the implant. Although clinical results have been promising, there is the possibility that a more optimal arrangement of implants may exist.

Zaidi et al (2015) stated that the SI joint (SIJ) and surgical intervention for treating SIJ pain or dysfunction has been a topic of much debate in recent years. There has been a resurgence in the implication of this joint as the pain generator for many patients experiencing low-back pain, and new surgical methods are gaining popularity within both the orthopedic and neurosurgical fields. There is no universally accepted gold standard for diagnosing or surgically treating SIJ pain. The authors systematically reviewed studies on SIJ fusion in the neurosurgical and orthopedic

literature to investigate whether sufficient evidence exists to support its use. A literature search was performed using MEDLINE, Google Scholar, and OvidSP-Wolters Kluwer Health for all articles regarding SIJ fusion published from 2000 to 2014. Original, peer-reviewed, prospective or retrospective scientific papers with at least 2 patients were included in the study. Exclusion criteria included follow-up shorter than 1-year, non-surgical treatment, inadequate clinical data as determined by 2 independent reviewers, non-English manuscripts, and nonhuman subjects. A total of 16 peer-reviewed journal articles met the inclusion criteria: 5 consecutive case series, 8 retrospective studies, and 3 prospective cohort studies. A total of 430 patients were included, of whom 131 underwent open surgery and 299 underwent minimally invasive surgery (MIS) for SIJ fusion. The mean duration of follow-up was 60 months for open surgery and 21 months for MIS. SIJ degeneration/arthrosis was the most common pathology among patients undergoing surgical intervention (present in 257 patients [59.8%]), followed by SIJ dysfunction (79 [18.4%]), postpartum instability (31 [7.2%]), post-traumatic (28 [6.5%]), idiopathic (25 [5.8%]), pathological fractures (6 [1.4%]), and HLA-B27+/rheumatoid arthritis (4 [0.9%]). Radiographically confirmed fusion rates were 20% to 90% for open surgery and 13% to 100% for MIS. Rates of excellent satisfaction, determined by pain reduction, function, and quality of life, ranged from 18% to 100% with a mean of 54% in open surgical cases. For MIS patients, excellent outcome, judged by patients' stated satisfaction with the surgery, ranged from 56% to 100% (mean of 84%). The re-operation rate after open surgery ranged from 0% to 65% (mean of 15%). Re-operation rate after MIS ranged from 0% to 17% (mean of 6%). Major complication rates ranged from 5% to 20%, with 1 study that addressed safety reporting a 56% adverse event rate. The authors concluded that surgical intervention for SIJ pain is beneficial in a subset of patients. However, with the difficulty in accurate diagnosis and evidence for the efficacy of SIJ fusion itself lacking, serious consideration of the cause of pain and alternative treatments should be given before performing the operation.

Duhon et al (2016) reported on a prospective uncontrolled industry sponsored study of subjects with SI joint dysfunction who underwent minimally invasive SI joint fusion with triangular titanium implants. One hundred ninety-four patients were enrolled between August 2012 and

December 2013 at 26 sites. Of these, 10 withdrew prior to SI joint fusion and data from 12 subjects at a single site were eliminated due to the site's persistent non-compliance with the study protocol, leaving 172 subjects enrolled and treated. Two additional sites were terminated more than 1 year into the study for protocol non-compliance, resulting in 3 additional subjects not having 24-month study follow-up. Subjects underwent structured assessments preoperatively and at 1, 3, 6, 12, 18 and 24 months postoperatively, including SIJ pain ratings (0-100 visual analog scale), Oswestry Disability Index (ODI), Short Form-36 (SF-36), EuroQOL-5D (EQ-5D), and patient satisfaction. Adverse events were collected throughout follow-up. All participating patients underwent a high-resolution pelvic CT scan at 1 year. The primary study endpoint, evaluated at six months after the most recent SI joint fusion, was a binary success/failure composite endpoint. A subject was considered a success if all of the following were met: reduction from baseline VAS SI joint pain by at least 20 points, absence of device-related serious adverse events, absence of neurological worsening related to the sacral spine, and absence of surgical re-intervention (removal, revision, reoperation, or supplemental fixation) for SI joint pain. Of the 172 participants, 167 (97.1%) had 6-month follow-up, 157 (91.3%) had 12-month follow-up and 149 (86.6%) had 24-month follow-up. At month 6, 138 of 172 subjects met the study's success endpoint definition, for an intent-to-treat success rate of 80.2% (95% posterior credible interval 73.8-85.7%). Using available data only, the 12-month success rate was 127/159 (79.9%) and the 24-month success rate was 119/149 (79.9%). SIJ pain decreased from 79.8 at baseline to 30.4 at 12 months and 26.0 at 24 months ($p<.0001$ for change from baseline). ODI decreased from 55.2 at baseline to 31.5 at 12 months and 30.9 at 24 months ($p<.0001$ for change from baseline). The proportion of subjects taking opioids for SIJ or low back pain decreased from 76.2% at baseline to 55.0% at 24 months ($p <.0001$). At the time of the report, 8 subjects (4.7%) had undergone one or more revision SIJ surgeries. 7 device-related adverse events occurred. CT scan at one year showed a high rate (97%) of bone adherence to at least 2 implants on both the iliac and sacral sides with modest rates of bone growth across the SIJ.

The authors stated that this study had 2 main drawbacks. First, the lack of a concurrent control group undergoing non-surgical treatment. Secondly, a 24-month follow-up rate that was not as high as desired. Furthermore,

13.4% of subjects were lost to follow-up during the study or did not have 24-month visits. Pain and ODI scores in exiting subjects were higher than subjects who continued to participate; however, the impact of missing values on pain and ODI scores were analyzed and found to be minor, and did not affect overall study conclusions.

Polly et al (2016) described short and mid-term results of a randomized controlled trial of minimally invasive SIJ fusion. Subjects with SIJ dysfunction were randomly assigned to minimally invasive SIJ fusion with triangular titanium implants (SIJF, n = 102) or non-surgical management (NSM, n = 46). SIJ pain (measured with a 100-point visual analog scale, VAS), disability (measured with Oswestry Disability Index, ODI) and quality of life scores were collected at baseline and at scheduled visits to 24 months. Diagnosis of SIJ dysfunction was based on a history of pain at or near the SI joint, positive provocative testing on at least 3 of 5 physical examination tests, and at least a 50% decrease in pain after image-guided injection/arthrogram into the SI joint with local anesthetic.Crossover from non-surgical to surgical care was allowed after the 6-month study visit was complete. After the 6-month visit, 39 of 44 (89%) NSM subjects who were still participating crossed over to surgical treatment, and all crossover procedures were SIJF using the study device. The authors stated that subjects who had crossed over were not included in the report because they are continuing to be evaluated. In the SIJF group, 13 subjects withdrew prior to month 24. One site was terminated after 12-month subject visits were complete due to "persistent non-compliance with the study protocol." The primary study endpoint, evaluated at 6 months after the most recent SIJF, was a binary success/failure composite measure. A subject was considered to be a success if all of the following criteria were met: reduction in VAS SIJ pain score by at least 20 points from baseline, absence of device-related serious adverse events, absence of neurological worsening related to the lumbosacral nerve roots, and absence of surgical re-intervention (i.e. removal, revision, reoperation, or supplemental fixation) for SIJ pain. By month 6, 84 of 102 SIJF subjects (82%, 95% posterior credible interval [CI] 74-89%) and 12 of 46 NSM subjects (26%, 14-41%) met the study's primary success endpoint. In the SIJF group, the mean SIJ pain score improved from 82.3 at baseline to 30.1 at 6 month follow-up, 28.6 at 12 months and 26.7 at 24 months. In the NSM group, mean SIJ pain improved from 82.2 to 70.3 at 6 months (12.2-point improvement).

Limitations include lack of blinding and large crossovers after 6 months. In addition, the nonsurgical option described usual care “consistent with existing US practices and directed by each site investigator for each subject” and not an intensive multidisciplinary back pain intervention (Chou, et al., 2009). This was an industry sponsored study; the study sponsor also performed the statistical analysis and participated in the writing.

Also note that there is no gold standard for the diagnosis of sacroiliac joint dysfunction. In the study by Polly, diagnosis of SIJ pain was defined as pain elicited on at least 3 of 5 physical examination provocative tests. Note that the study authors cited a systematic evidence review by Szadek, et al. (2009) to support the diagnostic validity of provocative test criteria for sacroiliac joint pain; however, this systematic evidence review had a number of important flaws, including a lack of consideration of the quality of the studies in synthesizing results (CRD, 2014). The main drawbacks of this study were: (i) the lack of a sham control (i.e., incision and dissection to the ilium, possible drilling, but no implant placement), (ii) the study was industry-sponsored, (iii) in the SIJ fusion group, these researchers were unable to determine the separate contributions of the surgical procedure itself as opposed to post-operative rehabilitation to pain and disability relief and improvement in quality of life, (iv) short-term follow-up – these investigators reported relatively early (1 year) outcomes, trial follow-up continued to 2 years, and (v) moderate sample size – SIJ fusion (n = 102).

Sturesson et al (2017) reported on the short-term (6 month) results of a randomized study of minimally invasive SIJ fusion (SIJF) versus conservative management (CM) in subjects (n=103) with chronic sacroiliac joint pain. At 6 months, mean LBP improved by 43.3 points in the SIJF group and 5.7 points in the CM group (difference of 38.1 points, $p < 0.0001$). This study suffers from similar limitations as the study by Polly, et al.

The North American Spine Society (2015) has posted online insurance coverage policy recommendation for sacroiliac joint fusion. The coverage recommendation notes: "Due to the relatively moderate evidence, it is particularly critical that inclusion criteria are scrutinized and patient

selection is executed with vigilance. The procedure itself has proven to be relatively safe. There is a valid concern for bias in that the overwhelming majority of the data produced so far has been industry-sponsored and generally composed of case series. However there are some data on five-year outcomes that demonstrate sustained benefit that does not appear to degrade from 1 year to 5 year time-points. The committee will revisit the quality of forthcoming evidence as it is produced in re-evaluations of the indications and coverage of this procedure."

In a retrospective study with long-term (up to 6 years) follow-up, Vanaclocha and colleagues (2018) determined responses to conservative management (CM), SIJ denervation, and SIJF in patients with SIJ pain unresponsive to CM. A total of 137 patients with SIJ pain seen in an out-patient neurosurgery clinic who received either CM (n = 63), sacroiliac denervation (n = 47), or minimally invasive SIJF (n = 27) were included in this analysis. At each routine clinic visit, patients completed pain scores and ODI. Additional data were extracted from medical charts. Patients treated with continued CM had no long-term improvement in pain (mean worsening of 1 point) or disability (mean ODI worsened by 4 to 6 points), increased their use of opioids, and had poor long-term work status; SIJF patients had large improvements in SIJ pain (mean of 6 points), large improvements in disability (mean of 25 points), a decrease in opioid use, and good final work status. Sacroiliac denervation patients had intermediate responses (0 to 1 and 1 to 2 points, respectively). The authors concluded that in patients with SIJ pain unresponsive to CM, SIJF resulted in excellent long-term clinical responses, with low opioid use and better work status compared to other treatments. This study had several drawbacks: (i) It is not a randomized trial, (ii) patients in the CM group had some demographic and clinical factors that were different from those treated with SI denervation and SIJF groups, and (iii) although some patients have 6-year follow-up, mean follow-up in this study was just under 4 years, and further follow-up is of interest.

Dengler, et al. (2017) stated that devices to fuse the SIJ are now commercially available, but high-quality evidence supporting their effectiveness is limited. The investigators reported on the 12-month outcomes of a trial (6-months outcomes reported by Sturesson, et al., described above) to evaluate the safety and effectiveness of conservative

management (CM) to minimally invasive sacroiliac joint fusion (SIJF) in 103 patients with chronic LBP originating from the SIJ. Patients were randomly assigned to CM (n = 51) or SIJF using triangular titanium implants (n = 52). CM consisted of "optimization of medical therapy" (not further defined), individualized physiotherapy, and information and reassurance. Physical therapy was short term (twice a week for "up to" 8 weeks), and a full quarter of subjects had 15 or fewer physical therapy sessions. The primary outcome was the difference in change in self-rated LBP at 6 months using a 0 - 100 visual analog scale (VAS). Other effectiveness and safety endpoints, including leg pain, disability using Oswestry Disability Index (ODI), quality of life using EQ-5D, and SIJ function using active straight leg raise test (ASLR), were assessed up to 12 months. At 12 months, mean LBP improved by 41.6 VAS points in the SIJF group vs. 14.0 points in the CM group (treatment difference of 27.6 points, $P < 0.0001$). Mean ODI improved by 25.0 points in the SIJF group vs. 8.7 points in the CM group ($P < 0.0001$). Mean improvements in leg pain and EQ-5D scores were large after SIJF and superior to those after CM. CM patients were allowed to crossover to SIJF after 6 months. Patients who crossed to surgical treatment had no pre-crossover improvement in pain and ODI scores; after crossover, improvements were as large as those originally assigned to SIJF. One case of postoperative nerve impingement occurred in the surgical group. Two SIJF patients had recurrent pain attributed to possible device loosening and one had postoperative hematoma. In the CM group, one crossover surgery patient had recurrent pain requiring a revision surgery. Primary limitations of the study was short term nature, with crossovers allowed after 6 months, lack of blinding, and subjective nature of self-assessed outcomes. Almost half (43 percent) of subjects assigned to CM crossed over to surgery by the first followup at 6 months, confounding interpretation of the results. In addition, similar to the study by Polly, et al. described above, the study did not employ best standard of care intensive multidisciplinary back pain intervention to the conservative management group (Chou, et al., 2009). This was an industry sponsored study; the study sponsor also participated in the statistical analysis and writing.

Spain, et al. (2017) retrospectively identified all patients in a surgical practice who underwent SIJ fixation or fusion between 2003 and 2015. Using both chart review and focused contact with individual patients, the authors determined the likelihood of surgical revision.

Revision rates were compared using Kaplan-Meier survival analysis. Thirty-eight patients underwent SIJ fixation with screws and 274 patients underwent SIJ fusion using triangular titanium implants. Four-year cumulative revision rates were 30.8% for fixation and 5.7% for fusion. The authors found that SIJ fixation with screws had a much higher revision rate compared to SIJ fusion with triangular titanium implants designed for bone adherence. The study described herein was sponsored by the product manufacturer, who also helped with statistical analysis.

Bornemann et al (2016) noted that SIJ syndrome can cause various symptoms and may also be one reason for persistent low back pain, especially in patients with prior spinal fusions. If conservative treatments fail to improve symptoms, arthrodesis surgery can be considered. Minimally invasive approaches have emerged recently providing a good alternative to conventional methods. A novel triangular implant system (iFuse) can achieve an arthrodesis of the SIJ without the use of additional screws or bone material. These investigators evaluated the short-term safety and effectiveness of the implant system. A total of 24 patients were included in the study and treated with the iFuse system. In addition to demographic data, pain intensity (visual analog scale [VAS]) and functional impairment (Oswestry-disability index [ODI]) were assessed prior to surgery and 1 month, 3 months, 6 months, 12 months and 24 months thereafter. During surgery and the follow-up period all adverse events (AEs) were documented and the correct implant position was controlled via plain radiographs. VAS scores and ODI improved significantly directly after surgery from 84.3 ± 9.2 mm to 40.7 ± 9.2 mm and from 76.8 ± 9.2% to 40.7 ± 9.2% ($p < 0.001$). The ODI improved further to 31 ± 5.4% after 24 months whereas the VAS improved until the 3 months examination and 10 stayed constant between 27.7 mm and 26.5 mm to 27 ± 6.6 mm at 24 months. No AEs, intra-operative complications, implant mal-positioning or loosening could be recorded at any time. The author concluded that the iFuse system is an effective and safe treatment for minimally invasive surgical arthrodesis of the SIJ. Pain and functional impairment can be significantly improved. However, they stated that in addition to this case series, further controlled studies are needed, particularly in terms of a previous spinal fusion history.

National Institute for Health and Clinical Excellence's guideline on "Minimally invasive sacroiliac joint fusion surgery for chronic sacroiliac pain" (NICE, 2017) provides the following recommendations:

- Current evidence on the safety and efficacy of minimally invasive sacroiliac (SI) joint fusion surgery for chronic SI pain is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.
- Patients having this procedure should have a confirmed diagnosis of unilateral or bilateral SI joint dysfunction due to degenerative sacroiliitis or SI joint disruption.
- Conservative treatments for SI joint pain include analgesics, non-steroidal anti-inflammatory drugs, physiotherapy, manipulative therapy, intra-articular SI joint corticosteroid injections, periarticular injections, botulinum toxin injections and radiofrequency denervation. Surgical treatment is considered for persistent chronic symptoms that are unresponsive to conservative treatment. Surgical techniques include open SI joint fusion surgery or minimally invasive SI joint fusion using percutaneous implants to stabilize the joint and treat joint pain.

Kancherla and co-workers (2017) determined morbidity, complications, and patient reported outcomes from minimally invasive SIJF. Patients diagnosed by more than 2 physical examination maneuvers and subjective relief from a CT-guided lidocaine-bupivacaine-steroid injection underwent SIJF after failing conservative management (CM) with a combination of oral anti-inflammatory medications, physical therapy, and pelvic belt stabilization. Peri-operative data collected include EBL and operative time, ODI, SF-12, VAS, and functional status were analyzed. All complications were noted. The study cohort of 45 cases (69% women) achieved post-operative survey follow-up at 9.9 and 32.3 months; SF-12 physical component summary statistically improved while all other scores were equivalent. Mean EBL and operative time were 22 ml and 36 minutes, respectively. Initial survey showed that 64% of patients discontinued narcotics (29/45), 71% did not use an assistive device (32/45), and 15.6% did not work due to pain (7/45); 73% of patients stated they would have the surgery again (33/45). For the second survey, 65% of patients discontinued narcotics (26/40), 70% did not use an

assistive device (28/40), and 17.5% did not work due to pain (7/40). A history of thoracolumbar instrumentation (16/45) did not significantly affect outcomes; 3 complications described by screw malposition with neurologic deficit (6.7%) were treated with screw re-positioning (1 case) and removal of a single superior implant (2 cases) with time to revision of 2.2 months. All 3 ultimately had resolution of radicular pain. The authors concluded that percutaneous SIJF offered minimal morbidity and acceptable functional outcomes. While women and those with a prior history of lumbar instrumentation may be at increased risk of having SIJ dysfunction requiring surgical intervention, it was not found to affect post-operative functional outcomes when compared to the non-instrumented group. They stated that the findings of this series suggested that a thorough work-up with strict indications was paramount in achieving good functional outcomes with this technique. Ultimately, a significant number of patients may have suboptimal outcomes and this must be taken into consideration when counseling patients regarding operative intervention. The drawbacks of this study included a small sample size and all those associated with a retrospective review. While these researchers did obtain pre-operative VAS scores, they did not have any other pre-operative data for post-operative comparison. Also, 16 patients were excluded from the original 57 patients due to lack of data points, which could suggest selection bias. Lastly, the objective of this study was to demonstrate clinical outcomes based on a less invasive fusion procedure. Unfortunately, these investigators were unable to document any evidence of radiographic fusion bed given the technique of surgery utilized. The on-growth of bone onto the implants did not project nicely in any radiographic platform. The authors assumed on post-operative follow-up imaging that a fusion had taken place if there were no radiographic signs of loosening/loss of fixation (halos around the implants).

Rappoport and colleagues (2017) stated that proper diagnosis and treatment of SIJ pain remains a clinical challenge. Dysfunction of the SIJ can produce pain in the lower back, buttocks, and extremities. Triangular titanium implants for minimally invasive surgical arthrodesis have been available for several years, with reputed high levels of success and patient satisfaction. These investigators reported on a novel hydroxyapatite-coated screw for surgical treatment of SIJ pain. Data were prospectively collected on 32 consecutive patients who underwent minimally invasive SIJ fusion with a novel hydroxyapatite-coated screw.

Clinical assessments and radiographs were collected and evaluated at 3, 6, and 12 months post-operatively. Mean (SD) patient age was 55.2 ± 10.7 years, and 62.5% were women. More patients (53.1%) underwent left versus right SIJ treatment, mean operative time was 42.6 ± 20.4 minutes, and estimated blood loss did not exceed 50 ml. Over-night hospital stay was required for 84% of patients, and the remaining patients needed a 2-day stay (16%). Mean pre-operative VAS back and leg pain scores decreased significantly by 12 months post-operatively ($p < 0.01$). Mechanical stability was achieved in 93.3% (28/30) of patients, and all patients who were employed pre-operatively returned to work within 3 months; 2 patients who needed revision surgery reported symptom improvement within 3 weeks and did not require subsequent surgery. The authors concluded that positive clinical outcomes were reported 1 year post-operatively after implantation of a novel implant to treat SIJ pain. Moreover, they stated that future clinical studies with larger samples are needed to evaluate long-term patient outcomes.

In a prospective, multi-center RCT, Dengler and associates (2017) compared the safety and effectiveness of CM to minimally invasive SIJF in patients with chronic LBP originating from the SIJ. Subjects were 103 adults in spine clinics with chronic LBP originating from the SIJ. Patients were randomly assigned to CM (n = 51) or SIJF using triangular titanium implants (n = 52); CM consisted of optimization of medical therapy, individualized physiotherapy, and adequate information and reassurance as part of a multi-factorial treatment. The primary outcome was the difference in change in self-rated LBP at 6 months using a 0 to 100 VAS. Other effectiveness and safety end-points, including leg pain, disability using ODI, quality of life (QOL) using EQ-5D, and SIJ function using active straight leg raise test (ASLR), were assessed up to 12 months. At 12 months, mean LBP improved by 41.6 VAS points in the SIJF group versus 14.0 points in the CM group (treatment difference of 27.6 points, $p < 0.0001$). Mean ODI improved by 25.0 points in the SIJF group versus 8.7 points in the CM group ($p < 0.0001$). Mean improvements in leg pain and EQ-5D scores were large after SIJF and superior to those after CM; CM patients were allowed to crossover to SIJF after 6 months. Patients who crossed to surgical treatment had no pre-crossover improvement in pain and ODI scores; after crossover, improvements were as large as those originally assigned to SIJF. One case of post-operative nerve impingement occurred in the surgical group; 2 SIJF patients had recurrent

pain attributed to possible device loosening and 1 had post-operative hematoma. In the CM group, 1 crossover surgery patient had recurrent pain requiring a revision surgery. The authors concluded that for patients with chronic LBP originating from the SIJ, minimally invasive SIJF with triangular titanium implants was safe and more effective than CM in relieving pain, reducing disability, and improving patient function and QOL. They stated that their findings suggested that minimally invasive SIJF may be a reasonable option for patients with SIJ pain not responsive to non-surgical care. The main drawbacks of this study were (i) the lack of blinding, (ii) the subjective nature of self-assessed outcomes, and (iii) short-term follow-up (12 months).

In a retrospective study with long-term (up to 6 years) follow-up, Vanaclocha and colleagues (2018) determined responses to conservative management (CM), SIJ denervation, and SIJF in patients with SIJ pain unresponsive to CM. A total of 137 patients with SIJ pain seen in an out-patient neurosurgery clinic who received either CM (n = 63), sacroiliac denervation (n = 47), or minimally invasive SIJF (n = 27) were included in this analysis. At each routine clinic visit, patients completed pain scores and ODI. Additional data were extracted from medical charts. Patients treated with continued CM had no long-term improvement in pain (mean worsening of 1 point) or disability (mean ODI worsened by 4 to 6 points), increased their use of opioids, and had poor long-term work status; SIJF patients had large improvements in SIJ pain (mean of 6 points), large improvements in disability (mean of 25 points), a decrease in opioid use, and good final work status. Sacroiliac denervation patients had intermediate responses (0 to 1 and 1 to 2 points, respectively). The authors concluded that in patients with SIJ pain unresponsive to CM, SIJF resulted in excellent long-term clinical responses, with low opioid use and better work status compared to other treatments. This study had several drawbacks: (i) It is not a randomized trial, (ii) patients in the CM group had some demographic and clinical factors that were different from those treated with SI denervation and SIJF groups, and (iii) although some patients have 6-year follow-up, mean follow-up in this study was just under 4 years, and further follow-up is of interest.

Cummings and Capobianco (2013) reported outcomes from 18 patients with 12 months of postoperative follow-up following minimally invasive sacroiliac joint fusion. Demographics, complications, and clinical

outcomes using VAS for pain, ODI for back function and SF-36 for quality of life (QOL) were collected pre-operatively and at 3, 6 and 12 months post-operatively. Mean age was 64 years and 67% of patients were women. There were no intra-operative complications and 1 explant at 3 months for malposition. All patient-reported outcomes showed both clinically and statistically significant improvement at 12 months ($p < 0.001$ for each of the following): VAS improved by 6.6 points, ODI scores improved by -37.5 points. One year SF-12 physical and mental component (PCS, MCS) scores approximated population normal scores for both physical and mental functioning. Patient satisfaction with outcomes was high at 95%; 89% said would have the same surgery again. The authors concluded that MIS SI joint fusion using a series of triangular porous TPS coated titanium implants is a safe and effective procedure for patients with SI joint disorders who have failed conservative care.

The authors noted that although the current study sample size was small (n = 18), the results were very encouraging. Favorable outcomes in this cohort underscore the necessity to suspect the SI joint as a pain generator in patients with low back pain especially after lumbar spine surgery. Results for this reported procedure in patients with instrumented fusion are as favorable as in patients with no prior lumbar surgical history. They state that this procedure has the potential to significantly benefit the elderly population, who are not candidates for other conventional techniques due to poor bone quality, delayed healing and reduced mobility.

Duhon et al (2013) reported early results of a multi-center prospective single-arm cohort of patients with SI joint degeneration or disruption who underwent minimally invasive fusion using the iFuse Implant System. The safety cohort included 94 subjects at 23 sites with chronic SI joint pain who met study eligibility criteria and underwent minimally invasive SI joint fusion with the iFuse Implant System between August 2012 and September 2013. Subjects underwent structured assessments preoperatively, immediately post-operatively, and at 1, 3, and 6 months post-operatively, including SI joint and back pain VAS, ODI, SF-36, and EuroQoL-5D (EQ-5D). Patient satisfaction with surgery was assessed at 6 months. The effectiveness cohort included the 32 subjects who have had 6-month follow-up to-date. Mean subject age was 51 years (n = 94,

safety cohort) and 66% of patients were women. Subjects were highly debilitated at baseline (mean VAS pain score 78, mean ODI score 54); 3 implants were used in 80% of patients; 2 patients underwent staged bilateral implants; 23 adverse events (AEs) occurred within 1 month of surgery and 29 additional events occurred between 30 days and latest follow-up; 6 AEs were severe but none were device-related. Complete 6-month post-operative follow-up was available in 26 subjects. In the effectiveness cohort, mean (± standard deviation) SI joint pain improved from a baseline score of 76 (± 16.2) to a 6-month score of 29.3 (± 23.3, an improvement of 49 points, $p < 0.0001$), mean ODI improved from 55.3 (± 10.7) to 38.9 (± 18.5, an improvement of 15.8 points, $p < 0.0001$) and SF-36 PCS improved from 30.7 (± 4.3) to 37.0 (± 10.7, an improvement of 6.7 points, $p = 0.003$); 90% of subjects who were ambulatory at baseline regained full ambulation by month 6; median time to full ambulation was 30 days. Satisfaction with the procedure was high at 85%. The authors concluded that minimally invasive SI joint fusion using the iFuse Implant System was safe; mid-term follow-up indicated a high rate of improvement in pain and function with high rates of patient satisfaction. These researchers stated that study enrollment and follow-up are ongoing.

The authors stated that this study had several drawbacks. First, the study lacked an active control group. However, given that all participating patients had chronic pain (a mean of 5 years of pain and at least 6 months of SI joint pain under the care of a physician) and had failed conservative care, the likelihood of high response rates with continued conservative management was likely to be low. Second, the study used ODI to assess baseline disability due to back pain and post-operative improvement related to pain. While ODI was designed for lower back pain and not SI joint pain, in the absence of validated SI joint instruments, ODI was a reasonable proxy, and improvements observed to date appear clinically significant. The improvements in ODI in this study were similar to those reported after percutaneous SI joint fusion. Similarly, the improvements in SF-36 quality of life scores were similar to those observed in a retrospective case series of patients undergoing percutaneous SI joint fusion using hollow modular anchorage screws plus demineralized bone matrix. Finally, while the procedure was termed arthrodesis and the goal of the procedure was to fuse the SI joint, the rate of SI joint fusion was not known. Radiographic analysis in the current

study (based primarily on 1-year CT scan) is in progress and results will be reported elsewhere. These were of interest as the procedure used did not directly decorticate the joint and did not involve placement of bone graft.

Cher and Poly (2016) stated that the SIJ is an important cause of LBP. The degree to which minimally invasive surgical fusion of the SIJ improves health state utility has not been previously documented. Health state utility values were calculated using the EQ-5D and SF-36 at baseline and 6 and 12 months after SIJ fusion surgery in subjects participating in a prospective, multi-center clinical trial (n = 172). Values were compared with individuals who participated in a nationally representative cross-sectional survey (National Health Measurement Study [NHMS], n = 3,844). Health utility values in the SIJ cohort were compared with those of the NMHS participants using both weighted linear regression and calculation of “health quantile” (i.e., percentile of health normalized to the NHMS cohort adjusted for age and gender). Baseline health state utility was significantly depressed in SIJ patients compared with normal subjects (SF-6D 0.509 versus 0.789, SF-36 physical component summary 31.7 versus 49.2, SF-36 mental component summary 8.5 versus 53.8, EQ-5D 0.433 versus 0.868; all $p < 0.0001$ after adjustment for age and gender). In the SIJ cohort, all the measures improved by 6 months post-operatively, and improvements were sustained at 12 months. Baseline health quantile was low (5th percentile) in the SIJ cohort and improved significantly at follow-up. The authors concluded that QOL was markedly impaired in patients with SIJ pain compared with age- and gender-matched cohorts. SIJ fusion in this cohort resulted in a substantial improvement in health state utility, bringing the population back toward the expected levels of overall health. The quantile approach helped to explain the degree to which health was improved compared with age- and gender-matched cohorts. The study from which data analyzed in this report was derived was sponsored by SI-BONE; and DJ Cher is an employee of SI-BONE.

Araghi et al (2017) documented 6-month results of the first 50 patients treated in a prospective, multi-center study of a minimally invasive (MI) sacroiliac joint (SIJ) fusion system. This cohort included 50 patients who had MI SI joint fusion surgery and completed 6 month follow-up. Average age at baseline was 61.5 years, 58% were women, and SIJ-related pain

duration was greater than or equal to 2 years in 54.0% of patients; VAS SIJ pain, ODI, QOL and opioid use were assessed pre-operatively and at 6 months. At 6 months, mean VAS pain demonstrated a significant reduction from 76.2 at baseline to 35.1 (54% reduction, $p < 0.0001$), with 72% of patients attaining the minimal clinically important difference (MCID, greater than or equal to 20 point improvement). Mean ODI improved from 55.5 to 35.3 at 6 months ($p < 0.001$), with 56% of patients achieving the MCID (greater than or equal to 15 point improvement). Prior to surgery 33/50 (66%) of patients were taking opioids, but by 6 months the number of patients taking opioids had decreased by 55% to 15/50 (30%). Few procedural complications were reported. Two procedure-related events required hospitalization: a revision procedure (2%) for nerve impingement and 1 case of ongoing low back pain (LBP). The authors concluded that analysis of patients treated with MI SIJ fusion using the SImmetry System demonstrated that the procedure can be performed safely and resulted in significant improvements in pain, disability, and opioid use at 6 months. Moreover, they stated that longer term follow-up in this study will determine whether these improvements are durable, as well as the associated radiographic fusion rates.

The authors noted that the greatest limitations with this trial were the sample size (n = 50) and limited follow-up (6 months). The current data represented the first interim analysis of what will be the largest cohort of patients prospectively enrolled in a trial to evaluate both fusion and pain following MI SIJ fusion surgery. An additional 200 patients are planned to be enrolled to provide enough statistical power to determine contributing factors to fusion and pain relief. At present, this interim analysis of 50 patients provided sufficient positive outcome data to validate continuing with the trial protocol through 2 years of follow-up. Another limitation of this trial was a lack of a control group. The comparison of minimally invasive SIJ fixation to non-surgical therapy was previously established in a randomized trial reported by Polly et al. Results from the trial demonstrated that the surgery group had a substantially significant improvement in pain compared to non-surgical therapy group. Greater improvement in disability and QOL was also shown in the surgical group with results lasting through 2 years. In light of the superior results shown with SIJ surgery, the authors felt that there was no clinical equipoise to suggest that additional randomized controlled trials (RCTs) would be acceptable. Instead, the purpose of this trial was to evaluate patient

outcomes using the technology of decortication, bone grafting and threaded implants described herein. In this discussion the results were compared to a similar study of another MI SIJ fusion system. While this comparison provided relevant context, it must be acknowledged that differences in methodology, investigational site standards of care, and even changes in public attitudes toward opioid painkillers could impact differences seen in the results of the 2 studies.

Darr et al (2018) reported clinical and functional outcomes of SIJ fusion (SIJF) using triangular titanium implants (TTI) in the treatment of chronic SI joint dysfunction due to degenerative sacroiliitis or SIJ disruption at 3 years post-operatively. A total of 103 subjects with SIJ dysfunction at 12 centers were treated with TTI in 2 prospective clinical trials and enrolled in this long-term follow-up study. Subjects were evaluated in study clinics at study start and again at 3, 4, and 5 years. Mean (SD) pre-operative SIJ pain score was 81.5, and mean pre-operative ODI was 56.3. At 3 years, mean pain SIJ pain score decreased to 26.2 (a 55-point improvement from baseline, $p < 0.0001$). At 3 years, mean ODI was 28.2 (a 28-point improvement from baseline, $p < 0.0001$). In all, 82% of subjects were very satisfied with the procedure at 3 years. EuroQol-5D (EQ-5D) time trade-off index improved by 0.30 points ($p < 0.0001$). No adverse events (AEs) definitely related to the study device or procedure were reported; 1 subject underwent revision surgery at year 3.7. SIJ pain contralateral to the originally treated side occurred in 15 subjects of whom 4 underwent contralateral SIJF. The proportion of subjects who were employed outside the home full- or part-time at 3 years decreased somewhat from baseline ($p = 0.1814$), and the proportion of subjects who would have the procedure again was lower at 3 years compared to earlier time-points. The authors concluded that in long-term (3-year) follow-up, minimally invasive trans-iliac SIJF with TTI was associated with improved pain, disability, and QOL with relatively high satisfaction rates.

The authors stated that the primary disadvantage of this study was the lack of long-term data from a concurrent control group receiving only non-surgical treatment. In the INSITE study, most subjects in the non-surgical control group who experienced inadequate pain relief at month 6 crossed-over to surgical care. However, long-term non-surgical follow-up appeared to be associated with very poor outcomes. Another limitation was that several sites in INSITE and SIFI could not participate in the

current study due to either low numbers of subjects or lack of clinical trial resources; subjects at participating sites had slightly larger 24-month improvements in SIJ pain and ODI compared to those at non-participating sites. The calculated impact on 3-year scores reported herein was small – approximately 4 points for VAS SIJ pain and 2.4 points for ODI. Another limitation was that the data from this study of triangular implants were not applicable to clinical outcomes from devices with other designs and fusion strategies for SIJF.

Cross et al (2018) noted that SIJ degeneration is a common source of LBP. A recently developed MI SIJ fusion system incorporates decortication, placement of bone graft and fixation with threaded implants (DC/BG/TF). A total of 19 patients who had MI SIJ fusion with DC/BG/TF were enrolled at 3 centers. Fusion was assessed in CT images obtained 12 and 24 months post-operatively by an independent radiographic core laboratory. LBP was assessed using a 0 to 10 numerical pain scale (NPS) pre-operatively and at 12 and 24 months post-operatively. At 12 months, 15/19 patients (79%) had bridging bone across the SIJ, and at 24 months 17/18 patients (94%) available for follow-up had SIJ fusion. Of the patients with bridging bone 88% had fusion within the decorticated area, with solid fusion in 83%. A significant reduction in NPS scores was demonstrated, representing a 73% reduction in average LBP. The authors concluded that the patients in this series demonstrated significant improvement in LBP. Fusion rates at 24 months demonstrated promise for this system, which utilized the established orthopedic principles of DC/BG/TF to achieve arthrodesis. These researchers stated that further study is needed to demonstrate comparative fusion rates for different implant systems and predictive correlation to clinical outcomes.

The authors stated that weaknesses in this study included the small patient sample size (n = 19). Importantly, it was not powered to detect associations between radiographic fusion status and clinical outcomes and instead, the primary outcome assessment was radiographic fusion. The paucity of reported fusion rates versus clinical outcomes demanded further investigation; larger prospective, comparative studies should enable predictive association of pre-operative variables, fusion status and implant system characteristics to clinical outcomes.

An assessment of sacroiliac joint fusion by the RTI International–University of North Carolina Evidence-based Practice Center for the Washington State Healthcare Authority Health Technology Assessment Program (Kahwati, et al., 2018) reached the following conclusions: "Among patients meeting diagnostic criteria for SI joint pain or dysfunction and who have not responded adequately to conservative care, minimally invasive SI joint fusion surgery with the iFuse Implant System is more effective than conservative management for reducing pain and improving function, and is likely cost-effective. Minimally invasive SI joint fusion surgery with iFuse is also more effective than open fusion for reducing pain and is associated with a shorter hospital length of stay. Serious adverse events from surgery with iFuse are infrequently reported in controlled studies but may be higher in usual practice based on evidence from uncontrolled studies. The incidence of revision surgery is likely no higher than 3.4% at 2 years. Limited evidence is available that compares open fusion to minimally invasive fusion or that evaluates procedures other than iFuse."

The Washington State Health Technology Assessment Committee reviewed the data on sacroiliac joint fusion for sacroiliac syndrome (2019). The agency medical directors (2019) found that available studies of sacroiliac joint fusion for sacroiliac pain suffer from a number of significant limitations leading to a serious risk of bias.

- Most studies are uncontrolled
- Controlled studies suffer from a number of limitations, including:
    - a lack of sham studies or studies with an independent masked assessment of outcome;
    - a lack of an adequate evidence-based multidisciplinary conservative management comparator; and
    - a lack of a diagnostic gold standard for sacroiliac joint syndrome
- In addition, all available studies are funded by the device manufacturer
- Available studies reported a wide range of adverse events, and failed to employ standardized definitions or a common protocol for safety data assessment

They explained that, inclusion criteria in studies of sacroiliac fusion varied, and were typically a combination of physical exam tests (3 out of 5 tests positive) and reduction of pain (variable degree, often 50% or 80%) with sacroiliac anesthetic injection, with variable requirements for imaging guidance of the injection. They also noted that the physical exam parameters had poor reliability. Citing van Tilburg, et al. (2017), the Kappa values for pooled parameters of inter-rater reliability for physical exam for sacroiliac joint pain was less than 0.20. They also noted that an analysis using combined data from two trials (1 randomized controlled trial [INSITE] and 1 uncontrolled trial [SIFI], total N = 320) (citing Dengler, et al., 2017; Polly, et al., 2016; Duhon, et al., 2016) found no relationship between the level of immediate response to sacroiliac joint block (average percent decrease in pain after injection from 40% to 100%) and 6- and 12-month pain and disability scores among patients undergoing sacroiliac joint fusion. They explained that, in clinical studies, the "conservative management" comparator was defined at providers' discretion, not an evidence-based multidisciplinary management program. Regarding safety, they found no common protocols for data assessment or standardized definitions, with a range of reported adverse events for iFuse of 0 to 30%. They concluded that the evidence for efficacy of sacroiliac joint fusion for sacroiliac joint syndrome is based on unblinded, manufacturer-funded trials with a high risk of bias and lack of objective data. The noted that serious adverse events may be under-reported in trials.

In a prospective, multi-center, RCT, Dengler and colleagues (2019) compared the safety and effectiveness of minimally invasive SIJ arthrodesis using triangular titanium implants and conservative management in patients with chronic SIJ pain. This study enrolled adults with chronic SIJ pain assigned to either conservative management or SIJ arthrodesis with triangular titanium implants. The study end-points included self-rated LBP (VAS), back dysfunction (ODI), and QOL; 90% of subjects in both groups completed the study. Between June 6, 2013, and May 15, 2015, a total of 103 subjects were randomly assigned to conservative management (n = 51) or SIJ arthrodesis (n = 52). At 2 years, the mean LBP improved by 45 points (95% CI: 37 to 54 points) after SIJ arthrodesis and 11 points (95% CI: 2 to 20 points) after conservative management, with a mean difference between groups of 34 points ($p < 0.0001$). The mean ODI improved by 26 points (95% CI: 21 to 32 points)

after SIJ arthrodesis and 8 points (95% CI: 2 to 14 points) after conservative management, with a mean difference between groups of 18 points ($p < 0.0001$). Parallel improvements were observed in QOL. In the SIJ arthrodesis group, the prevalence of opioid use decreased from 56% at baseline to 33% at 2 years ($p = 0.009$), and no significant change was observed in the conservative management group (47.1% at baseline and 45.7% at 2 years). Subjects in the conservative management group, after cross-over to the surgical procedure, showed improvements in all measures similar to those originally assigned to SIJ arthrodesis. In the first 6 months, the frequency of AEs did not differ between groups ($p = 0.664$). By 24 months, these researchers observed 39 SAEs after SIJ arthrodesis, including 2 cases of SIJ pain, 1 case of a post-operative gluteal hematoma, and 1 case of post-operative nerve impingement. The analysis of CT imaging at 12 months following SIJ arthrodesis showed radiolucencies adjacent to 8 implants (4.0% of all implants). The authors concluded that minimally invasive SIJ arthrodesis with triangular titanium implants was safe and effective at 2 years for the treatment of chronic SIJ pain and provided lasting improvements compared with conservative management. They stated that these findings suggested that minimally invasive SIJ arthrodesis may be a reasonable option for patients with SIJ pain not responsive to 6 months of conservative management. This study provided only short-term (2 years) follow-up data.

The authors noted that the main drawback of this study was a lack of subject and outcome assessor blinding, which would have been challenging because implants were radiopaque and preventing subjects from seeing their radiographic studies would have been impossible. The large effect sizes seen strongly argued against a marked contribution from placebo effects. Although this trial followed non-surgical European guidelines for the treatment of SIJ pain with intensive physical therapy provided, it was possible that more intensive conservative management might have provided somewhat better results. An additional drawback was the high cross-over rate after 6 months. Finally, these investigators stated that this trial used SIJ arthrodesis with a single system (triangular titanium implants); whether these findings apply to other SIJ arthrodesis surgical approaches, systems, and devices is not known. Except for smoking status, baseline parameters were distributed evenly across treatment groups. Subjects assigned to SIJ arthrodesis were more likely to be smokers; if smoking reduces the rate of bone-healing, as is

commonly accepted, the increased proportion of smokers in the SIJ arthrodesis group would have biased study results against SIJ arthrodesis. Post-randomization interventions or subject behaviors that could have impacted the study's results were not readily apparent; some subjects in the conservative management group received prolonged physical therapy, which theoretically could have increased its effect. The collection of information to support the calculation of health indices (e.g., Charlson Comorbidity Index31) and further opioid history during a 6-month period prior to the study start could also have been helpful. An analysis of predictors of response in the conservative management group is also of interest; however, the sample size was too small to accomplish this goal.

An independent randomized controlled trial of sacroiliac joint fusion for sacroiliac pain is currently ongoing (NCT03507049). This prospective randomized double blinded controlled mulitcenter trial will examine whether there is a difference in SI joint pain in patients operated with minimally invasive arthrodesis of the SI joint compared to a sham operated control group.

Cryoablation for the Treatment of Lumbar facet Joint Pain

Barlocher and colleagues (2003) carried out a prospective study to examine the efficacy of kryorhizotomy, an alternative procedure for lumbar medial branch neurotomy, in the treatment of lumbar facet syndrome (LFS). A total of 50 patients with chronic LBP, in whom pain was relieved by controlled diagnostic medial branch blocks of the lumbar zygapophyseal (facet) joints, underwent lumbar medial branch kryorhizotomy. Outcome was evaluated using the VAS score and assessment of work capacity. All outcome measures were repeated at 6 weeks, 6 months, and 1 year after surgery. At 1-year follow-up examination, 31 (62 %) of 50 patients experienced a good response to lumbar facet kryorhizotomy. Good results with pain relief of 50 % or more were obtained in 85 % of patients without previous spinal surgery but only in 46 % who had undergone previous spinal surgery. This difference was statistically significant. In 5 patients (16 %) in whom a good initial benefit was observed but who experienced increased pain within 6 weeks after kryorhizotomy, the beneficial result was regained after an early repeated procedure. There were no side effects. Overall, 19 (38 %) of 50

procedures were not considered successful. In 6of these 19 cases a rigid stabilization of the involved segment provided permanent pain relief. The authors concluded that based on this study, patients with LFS who have not undergone previous spinal surgery benefited significantly from percutaneous lumbar kryorhizotomy. Kryorhizotomy, which has virtually no risk, appeared to be a valuable alternative technique to lumbar medial branch neurotomy.

Staender and associates (2005) prospectively evaluated the therapeutic effect of computerized tomography (CT)-guided kryorhizotomy in the treatment of patients with lumbar facet joint syndrome (LFJS) and examined prognostic factors that predict this effect. Between February 2001 and March 2004, CT-guided kryorhizotomy of facet joints was carried out in 76 patients with LFJS. A diagnosis was established after 3 positive CT-guided medial nerve branch blocks. Outcome was determined by evaluating the results of a standardized questionnaire, including VAS score, use of medication, ability to work, and physical conditions. Measurement was carried out before treatment and repeated post-operatively at 3 days, 3 months, and every 6 months thereafter. On September 2004, all patients underwent clinical re-evaluation. The median follow-up period was 22.5 months (range of 6 to 43 months); the median interval to pain reduction was 6 months (range of 0.1 to 31 months) after the 1st kryorhizotomy. The mean VAS pain score was 6.7 pre-operatively and 2.9, 3.2, and 3.4 at 3 days, 3 months, and 6 months post-operatively, respectively. In 40 % of patients pain was reduced for 12 months or longer. In patients in whom there was no prior surgical treatment of the relevant spinal segment, the duration of pain relief was significantly longer than in patients who had previously undergone surgery ($p < 0.03$); 18 patients underwent a 2nd, 7 a 3rd, and 1 a 4rth kryorhizotomy. No patient reported any side effect. The use of CT guidance guaranteed an exact needle-tip position control and documentation for repeated procedures. The authors concluded that CT-guided kryorhizotomy was a minimally invasive and repeatable treatment that yielded good long-term results in patients with LFJS.

Birkenmaier et al (2007) stated that facet joint pain is an important aspect of degenerative lumbar spine disease, and radiofrequency medial branch neurotomy remains an established therapy, while cryodenervation has still been poorly examined. This study was undertaken to examine the effects

of medial branch cryodenervation in the treatment of lumbar facet joint pain. This was a prospective clinical case series. Patient selection was based on the history, physical examination and positive medial branch blocks. Percutaneous medial branch cryodenervation was performed using a Lloyd Neurostat 2000. Target parameters were LBP (VAS), limitation of activity (McNab) and overall satisfaction. A total of 50 patients were recruited, and 46 completed the study. The follow-up time was 1 year. At 6 weeks, 33 patients (72 %) were pain-free or had major improvement of LBP; 13 (28 %) had no or little improvement. Including failures, mean LBP decreased significantly from 7.7 pre-operatively to 3.2 at 6 weeks, 3.3 at 3 months, 3.0 at 6 months and 4.2 at 12 months ($p < 0.0001$). Limitation of the activities of daily living improved parallel to reduced pain. The authors concluded that these findings suggested that medial branch cryodenervation is a safe and effective treatment for lumbar facet joint pain. Moreover, they stated that at the 12 month follow-up period, the failure rate rose to 43 %.

Wolter and co-workers (2011) noted that LFJS is the cause of pain in 15 to 54 % of the patients with LBP. There are few studies of cryotherapy for LFJS, focusing mainly on pain scores rather than further outcome measures. In a retrospective, observational study, these researchers determined the long-term outcome after cryoneurolysis of lumbar facet joints, looking at pain scores, pain-related impairment patient satisfaction, and pain-related anxiety/depression. In a 4-year period, a total of 117 cryoneurolyses were carried out in 91 patients under CT guidance in the prone position. Data from patient charts and questionnaires pre- and post-treatment were evaluated. The mean pain rating decreased from 7.70 pre-treatment to 3.72 post-treatment. In the post-interventional 3 months follow-up, this value rose to 4.22. At follow-up (mean of 1.7 years, range of 6 to 52 months), the mean VAS was 4.99. The pain disability index revealed statistically significant improvements in the following items: familiar and domestic duties, recreation, social activities, profession and vitally indispensable activities ($p < 0.05$). Hospital anxiety and depression scale (HADS) scores for depression showed a statistically significant decline after therapy, whereas scores for anxiety did not. A subgroup of patients who did not benefit from cryoneurolysis had elevated depression scores. The authors concluded that cryoneurolysis for LFJS could lead to favorable results with sustained pain relief, amelioration of pain-related disability and reduction of depression scores.

An UpToDate review on “Subacute and chronic low back pain: Nonsurgical interventional treatment” (Chou, 2013) discusses the use of facet joint injection and medial branch block; but does not mention the use of cryoablation as a therapeutic option.

Minimally Invasive Thoracic Discectomy

Kasliwal and Deutsch (2011) stated that the management of symptomatic thoracic disc herniation (TDH) has evolved tremendously ever since the first laminectomy was performed. The last decade has witnessed the evolution of minimally invasive approaches for TDH most of which have been posterior/postero-lateral. Traditional anterior approaches involve a thoracotomy or more recently, thoracoscopic techniques. The authors described a less invasive anterior retropleural surgical approach to address central thoracic disk herniations that is less extensive than a thoracotomy and allows better anterior access than posterior or postero-lateral approaches. The retropleural approach allows the use of the operative microscope with a tubular retractor in the anterior thoracic spine. A total of 7 patients with central disc herniation who were managed with the minimally invasive lateral retropleural approach from 2007 to 2010 at their institution were included in the study. Surgical technique consisted of a lateral position followed by retro-pleural exposure through tubular retractor system without the need of intra-operative lung collapse. Clinical details including age, sex, clinical presentation, surgical details, complications and outcome at last follow-up were analyzed. Patients age ranged in age from 30 to 70 years (mean of 52 years). The duration of symptoms ranged from 4 days to 3 years. All patients presented with thoracic myleopathy on physical examination. The average length of stay in the hospital was 2.6 days (range of 1 to 4 days). Follow-up was available for all the patients. Myelopathy was assessed by the Nurick scale. On examination, 3 of 7 patients improved by 1 point on the Nurick scale. No patient deteriorated after surgery. There were no complications related to the approach. The authors concluded that a minimally invasive retropleural approach using tubular retractor system for central thoracic disc herniation is feasible and may be a less invasive anterior alternative to a thoracotomy. This was a small feasibility study.

Regev et al (2012) noted that surgical decompression of thoracic disc herniations is technically challenging because retraction of the thecal sac in this area must be avoided. Standard open thoracic discectomy procedures require fairly extensive soft tissue dissection and vertebral resection to provide safe decompression of the spinal cord. These researchers described their experience using a minimally invasive, transforaminal thoracic discectomy (MITTD) technique for the treatment of thoracic disc herniation. A total of 12 patients undergoing MITTD were evaluated pre-operatively and post-operatively at 1-, 3-, and 6-month intervals with neurologic examination, and were graded using the American Spinal Injury Association (ASIA) impairment scale and a pain visual analog scale (VAS). Thoracic instability and bony fusion were assessed clinically and radiographically with plain radiographs and computed tomography (CT) scans. Surgical time, blood loss, complications, and hospital length of stay were recorded. Twelve patients (7 men and 5 women) underwent MITTD. The median surgical time was 128 (80 to 185) minutes, the median estimated blood loss was 100 (30 to 250) mL, and the median hospital stay was 2 (1 to 4) nights. All discs were successfully removed, and a CT or magnetic resonance imaging confirmed adequate cord decompression in all cases. All patients reported easing of neurologic symptoms and improved walking ability. The median VAS scores improved from 4.5 to 2 for back pain. The ASIA score improved from D to E in the 2 patients who suffered from motor weakness. Pre-operative sensory deficit was reduced in 3 of the 5 patients. Patients who suffered from sexual and urinary disturbances did not report improvement. Serious systemic or local complications and neurologic deterioration were not reported. The authors concluded that the transforaminal approach enabled sufficient access to the midline of the spinal canal without extensive resection of the facet joint or the adjacent pedicle. Because most of the osseous and ligamentous structures were preserved, additional instrumentation was not required to prevent postoperative instability. They stated that these early results suggested that minimally invasive thoracic discectomy by transforaminal microscopic technique is a valuable choice in the management of thoracic disc herniation. These preliminary results need to be validated by well-designed studies.

In a case-series study, Smith et al (2013) presented operative details and clinical follow-up of a series of patients with thoracic disk herniation treated with the minimally invasive technique of thoracic microendoscopic diskectomy (TMED). TMED was performed in 16 consecutive patients (age range of 18 to 79 years old) with 18 thoracic disk herniations. One patient with a calcified herniation in a direct ventral location was not included in this series. Patients were positioned prone, and a tubular retractor system was placed through a muscle dilating approach. The procedure was performed with endoscopic visualization. Outcomes were assessed using modified McNab criteria. There were no complications, and no case required conversion to an open procedure. The mean operative time was 153 minutes per level, and mean blood loss was 69 mL per level. Mean hospital stay was 21 hours. At a mean follow-up of 24 months (median of 22 months), 13 patients (81%) had excellent or good outcomes, 1 patient (6%) had a fair outcome, and 2 patients (13%) had poor outcomes. The 2 patients with poor outcomes had neurologic diagnoses (multiple sclerosis and multiple systems atrophy) that were ultimately proven to be responsible for their symptoms and deficits. The authors concluded that TMED is a safe and effective minimally invasive postero-lateral approach for the treatment of thoracic disk herniations that lacks the morbidity associated with traditional approaches. The findings of this case-series study need to be validated by well-designed studies.

Furthermore, the Work Loss Data Institute's clinical practice guideline on "Low back - lumbar & thoracic (acute & chronic)" (2011) did not mention the use of minimally invasive thoracic discectomy as a therapeutic option.

Dynamic (Intervertebral) Stabilization

Li and colleagues (2011) explored the value of application of Bioflex dynamic stabilization system in treating multi-segment lumbar degenerative disease. Clinical data of 13 patients with multi-segment lumbar degenerative disease (8 males and 5 females; average age of 65.0 years, range of 51 to 72) were retrospectively analyzed between April 2008 and May 2009. The involved area included L3 to S1 in 7 cases, L2 to S1 in 3 cases, L3 to L5 in 1 cases, L4 to S1 in 2 cases. All patients underwent decompression, dynamic stabilization with Bioflex system, according to the severity of degenerative disc with/without interbody fusion. The clinical effects were evaluated by VAS, ODI. Range of motion

and fusion segments were also observed. The mean follow-up period was 19.5 months (range of 12 to 26). The mean operative time was 183.4 mins (range of 90 to 240) and the mean volume of blood loss was 610.2 ml (range of 400 to 1,220 ml). The mean VAS score was 7.8 +/- 1.3 pre-operatively, 2.3 +/- 0.9 post-operatively and 2.1 +/- 0.8 at the last follow-up. The average ODI was (60.50 +/- 4.40)% pre-operatively, (17.80 +/- 2.10)% post-operatively and (16.20 + 2.40)% at the last follow-up. The VAS and ODI significant improved in post-operatively ($p < 0.05$), and there was no statistical difference between post-operative and last follow-up ($p > 0.05$). ROM of whole lumbar and non-fused segment showed obviously decreased and adjacent segment showed insignificant increased. The fusion rate of interbody fusion level was 95.0% (19/20). The authors concluded that the preliminary clinical results showed the Bioflex system combined with intebody fusion is a safe and effective technique in treating multi-segment lumbar degenerative disease. These preliminary findings need to be validated by well-designed studies.

Zhang and associates (2012) examined the short-term effectiveness of ISOBAR TTL semi-rigid dynamic stabilization system (ISOBAR TTL system) in treatment of lumbar degenerative disease. Between June 2007 and May 2011, a total of 38 cases of lumbar degenerative disease were treated, including 24 males and 14 females with an average age of 51.2 years (range of 21 to 67). The disease duration was 8 months to 10 years (mean of 4.7 years). In 38 cases, there were 4 cases of grade I spondylolisthesis, 11 cases of lumbar instability and lumbar disc protrusion, 21 cases of lumbar spinal stenosis and lumbar disc protrusion, and 2 cases of post-operative recurrence of lumbar disc protrusion. There were 22 cases of adjacent segment disc degeneration. All cases underwent posterior decompression and implantation of ISOBAR TTL system. The double-segment-fixed patients underwent interbody fusion. Visual analog scale and Japanese Orthopedic Association scores for LBP were used to evaluate clinical outcomes. The ROM at the semi-rigid dynamic stabilization segment was also measured. The other cases achieved healing of incision by first intention, except 1 case of delayed healing. All the patients were followed-up for 8 to 53 months (mean of 27.8). After operation, ISOBAR TTL system showed reliable fixation, and no loosening, breakage, or kyphosis deformity occurred. No adjacent segment degeneration was observed. The ROM of the fixed segments was 0 to 1 degrees in 3 cases, 1 to 2 degrees in 4 cases, 2 to 3 degrees

in 14 cases, 3 to 4 degrees in 15 cases, and greater than 4 degrees in 2 cases. At last follow-up, the VAS score was 1.93 +/- 2.43, and was significantly lower than pre-operative score (8.20 +/- 1.78) (t = 7.761, p = 0.000). Japanese Orthopedic Association score was 23.06 +/- 7.75, and was significantly higher than pre-operative score (4.87 +/- 3.44) (t = 10.045, p = 0.000). According to Stauffer-Coventry evaluation standard, the results were excellent in 32 cases, good in 3 cases, fair in 2 cases, and poor in 1 case, with an excellent and good rate of 92.1%. The authors concluded that good short-term effectiveness can be achieved by surgical intervention with ISOBAR TTL system in treatment of lumbar degenerative disease. The results of this small study need to be validated by well-designed studies.

Li and co-workers (2013) retrospectively evaluated the indications, safety and efficacy of a new dynamic stabilization system (the Isobar TTL Semi-Rigid Rod System, Scient'x, Bretonneux, France) for the treatment of lumbar degenerative disease in 37 consecutive patients (M:F = 16:21, mean age of 40.2 years) with lumbar degenerative disease who underwent surgery between June 2006 and May 2009. One patient was lost to follow-up. Clinical outcomes were evaluated using the ODI and the VAS; ROM and disc height index (DHI) were assessed with radiography. Patients were followed for a mean of 24 months (range of 12 to 36 months). At the 3-month follow-up, there was significant improvement in VAS and ODI ($p < 0.05$); at long-term follow-up VAS showed additional significant improvement ($p < 0.05$) and ODI remained stable. At short-term follow-up, DHI was significantly restored ($p < 0.05$) and ROM declined slightly (but not significantly); however, at long-term follow-up DHI was significantly reduced ($p < 0.05$) compared to short-term follow-up and ROM was significantly decreased compared to the pre-operative values ($p < 0.05$). There were new signs of degeneration at adjacent levels in 14 patients (39%) on long-term follow-up MRI. Revision was required in 3 patients (8%) 24 months after the first operation due to adjacent segment disease. Screw loosening was observed in 4 patients (11%). The authors concluded that the Isobar System after microsurgical decompression for lumbar degenerative disease provided excellent improvement in leg and back pain and patient satisfaction at late follow-up; however, evidence to suggest that Isobar outperforms traditional fusion is lacking. Moreover, they stated that larger studies of longer duration are warranted.

Total Facet Arthroplasty System

The Total Facet Arthroplasty System (TFAS; Facet Solutions, Inc., Hopkinton, MA) is a non-fusion spinal implant indicated for treatment of moderate-to-severe spinal stenosis. The TFAS replaces the diseased facets (and lamina, if necessary, to attain adequate decompression) following surgical removal.

Phillips et al (2009) stated that lumbar fusion is traditionally used to restore stability after wide surgical decompression for spinal stenosis. The TFAS is a motion-restoring implant suggested as an alternative to rigid fixation after complete facetectomy. In a biomechanical in-vitro study, these researchers investigated the effect of TFAS on the kinematics of the implanted and adjacent lumbar segments. A total of 9 human lumbar spines (L1 to sacrum) were tested in flexion-extension (+8 to -6Nm), lateral bending (+/-6Nm), and axial rotation (+/-5Nm). Flexion-extension was tested under 400 N follower preload. Specimens were tested intact, after complete L3 laminectomy with L3 to L4 facetectomy, after L3 to L4 pedicle screw fixation, and after L3 to L4 TFAS implantation. Range of motion was assessed in all tested directions. Neutral zone and stiffness in flexion and extension were calculated to assess quality of motion. Complete laminectomy-facetectomy increased L3 to L4 ROM compared with intact in flexion-extension (8.7 +/- 2.0 degrees to 12.2 +/- 3.2 degrees, $p < 0.05$) lateral bending (9.0 +/- 2.5 degrees to 12.6 +/- 3.2 degrees, $p = 0.09$), and axial rotation (3.8 +/- 2.7 degrees to 7.8 +/- 4.5 degrees $p < 0.05$). Pedicle screw fixation decreased ROM compared with intact, resulting in 1.7 +/- 0.5 degrees flexion-extension ($p < 0.05$), 3.3 +/- 1.4 degrees lateral bending ($p < 0.05$), and 1.8 +/- 0.6 degrees axial rotation ($p = 0.09$). The Total Facet Arthroplasty System restored intact ROM ($p > 0.05$) resulting in 7.9 +/- 2.1 degrees flexion-extension, 10.1 +/- 3.0 degrees lateral bending, and 4.7 +/- 1.6 degrees axial rotation. Fusion significantly increased the normalized ROM at all remaining lumbar segments, whereas TFAS implantation resulted in near-normal distribution of normalized ROM at the implanted and remaining lumbar segments. Flexion and extension stiffness in the high-flexibility zone decreased after facetectomy ($p < 0.05$) and increased after simulated fusion ($p < 0.05$). The Total Facet Arthroplasty System restored quality of motion parameters (load-displacement curves) to intact ($p > 0.05$). The quality of motion parameters for the whole lumbar spine mimicked L3 to

L4 segmental results. The authors concluded that TFAS restored ROM and quality of motion at the operated segment to intact values and restored near-normal motion at the adjacent segments.

Sjovold et al (2012) noted that to gain insight into a new technology, a novel TFAS was compared to a rigid posterior fixation system (UCR). The axial and bending loads through the implants and at the bone-implant interfaces were evaluated using an ex- vivo biomechanical study and matched finite element analysis. Kinematic behavior has been reported for TFAS, but implant loads have not. Implant loads are important indicators of an implant's performance and safety. The rigid posterior fixation system is used for comparison due to the extensive information available about these systems. Unconstrained pure moments were applied to 13 L3 to S1 cadaveric spine segments. Specimens were tested intact, following decompression, UCR fixation and TFAS implantation at L4 to L5. UCR fixation was via standard pedicle screws and TFAS implantation was via PMMA-cemented trans-pedicular stems. Three-dimensional 10 Nm moments and a 600 N follower load were applied; L4 to L5 disc pressures and implant loads were measured using a pressure sensor and strain gauges, respectively. A finite element model was used to calculate TFAS bone-implant interface loads. UCR experienced greater implant loads in extension ($p < 0.004$) and lateral bending ($p < 0.02$). Under flexion, TFAS was subject to greater implant moments ($p < 0.04$). At the bone-implant interface, flexion resulted in the smallest TFAS (average = 0.20 Nm) but greatest UCR (1.18 Nm) moment and axial rotation resulted in the greatest TFAS (3.10 Nm) and smallest UCR (0.40 Nm) moments. Disc pressures were similar to intact for TFAS but not for UCR ($p < 0.04$). The authors concluded that these findings were most applicable to the immediate post-operative period prior to re-modeling of the bone-implant interface since the UCR and TFAS implants are intended for different service lives (UCR – until fusion, TFAS – indefinitely). The Total Facet Arthroplasty System reproduced intact-like anterior column load-sharing – as measured by disc pressure. The highest bone-implant moment of 3.1 Nm was measured in TFAS and for the same loading condition the UCR interface moment was considerably lower (0.4 Nm). For other loading conditions, the differences between TFAS and UCR were smaller, with the UCR sometimes having larger values and for others the TFAS was larger. The long-term physiological meaning of these findings was unknown and demonstrated the need for a

better understanding of the relationship between spinal arthroplasty devices and the host tissue as development of next generation motion-preserving posterior devices that hope to more accurately replicate the natural functions of the native tissue continues.

The TFAS clinical trial is a multi-center, prospective, randomized controlled clinical trial comparing the safety and effectiveness of the TFAS to spinal fusion surgery in the treatment of moderate-to-severe degenerative lumbar spinal stenosis. However, the status of this clinical trial is unknown (last verified February 2009).

The AccuraScope Procedure

The AccuraScope procedure is employed to treat LBP. It entails the use of a thin, flexible catheter that is inserted into the center of the spinal canal. Once inside the spinal canal, the catheter can be maneuvered to multiple levels of the lumbar spine, both sides. Using a high-definition camera and other diagnostic tools, the procedure's goals are

(i) to pin-point all sources of chronic lower spine symptoms and (ii) treat them with advanced tools including a laser. This out-patient procedure usually takes less than 45 minutes. However, there is a lack of evidence regarding the effectiveness of the AccuraScope procedure.

Chemical Ablation of Facet Joints

The American Society of Anesthesiologists Task Force on Chronic Pain Management/American Society of Regional Anesthesia and Pain Medicine's practice guidelines on "Chronic pain management" (2010) stated that "Conventional or other thermal radiofrequency ablation of the dorsal root ganglion should not be routinely used for the treatment of lumbar radicular pain". Furthermore, an UpToDate review on "Subacute and chronic low back pain: Nonsurgical interventional treatment" (Chou, 2014) states that "Glucocorticoid injections into the facet joint have not been shown to be effective in the treatment of low back pain. A 2009 American Pain Society guideline recommends against their use. There are limited data regarding the efficacy of facet joint injection with glucocorticoids. Two evidence-based reviews concluded that there is not sufficient evidence to support their use. Similarly, a more recent trial

comparing facet joint glucocorticoid injection and systemic glucocorticoids found no difference in either pain or functional capacity over six months between the groups, although patients receiving facet injections had a decrease in nonsteroidal antiinflammatory drug use. Blocks to the medial branch of the primary dorsal ramus, innervating the facet joints have been used both diagnostically and therapeutically for presumed facet joint pain. However, there are no trials comparing efficacy of medial branch blocks to placebo injections".

The Deuk Laser Disc Repair®

Deuk Laser Disc Repair® is a surgical technique that incorporates 3 distinct procedures including a selective partial discectomy, foraminoplasty, and annular debridement. All of the results of full-length articles in peer-reviewed journals of the Deuk Laser Disc Repair® are from a single investigator group. These studies did not include internal comparison groups of patients undergoing ACDF.

Deukmedjian et al (2012) stated that cervical Deuk Laser Disc Repair® is a novel full-endoscopic, anterior cervical, trans-discal, motion preserving, laser assisted, non-fusion, out-patient surgical procedure to safely treat symptomatic cervical disc diseases including herniation, spondylosis, stenosis, and annular tears. These researchers described a new endoscopic approach to cervical disc disease that allows direct visualization of the posterior longitudinal ligament, posterior vertebral endplates, annulus, neuroforamina, and herniated disc fragments. All patients treated with Deuk Laser Disc Repair® were also candidates for ACDF. A total of 142 consecutive adult patients with symptomatic cervical disc disease underwent Deuk Laser Disc Repair® during a 4-year period. This novel procedure incorporates a full-endoscopic selective partial decompressive discectomy, foraminoplasty, and posterior annular debridement. Post-operative complications and average volume of herniated disc fragments removed were reported. All patients were successfully treated with cervical Deuk Laser Disc Repair®. There were no post-operative complications. Average volume of herniated disc material removed was 0.09 ml. The authors concluded that potential benefits of Deuk Laser Disc Repair® for symptomatic cervical disc disease include lower cost, smaller incision, non-fusion, preservation of segmental motion, out-patient, faster recovery, less post-operative

analgesic use, fewer complications, no hardware failure, no pseudoarthrosis, no post-operative dysphagia, and no increased risk of adjacent segment disease as seen with fusion.

Deukmedjian et al (2013) stated that the Deuk Laser Disc Repair® is a new full-endoscopic surgical procedure to repair symptomatic cervical disc disease. In this study, a prospective cohort of 66 consecutive patients underwent cervical Deuk Laser Disc Repair® for 1 (n = 21) or 2 adjacent (n = 45) symptomatic levels of cervical disc disease and were evaluated post-operatively for resolution of headache, neck pain, arm pain, and radicular symptoms. All patients were candidates for ACDF or arthroplasty. The Mann-Whitney Wilcoxon test was used to calculate p values. All patients (n = 66) had significant improvement in pre-operative symptoms with an average symptom resolution of 94.6%. Fifty percent (n = 33) had 100% resolution of all pre-operative cervicogenic symptoms. Only 4.5% (n = 3) had less than 80% resolution of pre-operative symptoms. Visual analog scale significantly improved from 8.7 pre-operatively to 0.5 post-operatively ($p < 0.001$) for the cohort. Average operative and recovery times were 57 and 52 minutes, respectively. There were no peri-operative complications. Recurrent disc herniation occurred in 1 patient (1.5%). Average post-operative follow-up was 94 days and no significant intergroup difference in outcomes was observed ($p = 0.111$) in patients with less than 90 days (n = 52) or greater than 90 days (n = 14, mean 319 days) follow-up. No significant difference in outcomes was observed ($p = 0.774$) for patients undergoing 1- or 2-level Deuk Laser Disc Repair®. Patients diagnosed with post-operative cervical facet syndrome did significantly worse ($p < 0.001$). The authors concluded that Deuk Laser Disc Repair® is a safe and effective alternative to ACDF or arthroplasty for the treatment of 1 or 2 adjacent symptomatic cervical disc herniations with an overall success rate of 94.6%.

Least Invasive Lumbar Decompression Interbody Fusion (LINDIF)

In a case-series study, Osman (2012) the feasibility of the least invasive lumbar decompression, interbody fusion (LINDIF) and percutaneous pedicle screw implantation, for disorders which are usually treated by open decompression, fusion and pedicle screw implantation. Patients completed VAS forms and Roland-Morris questionnaires pre- and post-

operatively. Surgical procedures included arthroscopic decompression of the foramina and the discs; end-plate preparation and implantation of allograft bone chips and BMP-2 on collagen carrier; and percutaneous implantation of pedicle screws. Patients' charts were reviewed for operative notes, hospital stay, medications, and imaging studies. The latest x-ray and CT scan films were reviewed and analyzed. Patients were followed up for the minimum of 6 months. Outcome measures included operating time; intra-operative blood loss; hospital stay; VAS scores for back and leg pain; Roland-Morris Disability Questionnaire; and post-operative imaging studies. A total of 60 patients met the inclusion criteria. The average age is 52.8 years. The duration of illness ranged 2 months to 32 years. All patients had back and leg pain. Follow-up averaged 12 months; OR time was 2:90 hours. Estimated blood loss averaged 57.6 cc. Hospital stay averaged 2.6 days. Pre- and post-operative back pain averaged 7.5 and 2, respectively ($p < 0.005$). Pre- and post-operative leg pain averaged 7.0 and 1.7, respectively ($p < 0.005$). A total of 47 imaging studies available at the last visits including x-ray and CT scan, showed solid fusion in 28 (59.6%) patients, stable fixation in 17 (36.2%), and osteolysis around the pedicle screws in 2 patients (4.2%). All patients had improved motor function and 2 patients complained of residual numbness; 8 (13%) patients complained of residual discomfort on the extension of the lumbar spine; 1 patient (1.6%) had medial penetration of 1 S1 screw with S1 nerve root irritation which required revision; 1 patient with painful loose pedicle screws required hardware removal. Both patients had satisfactory outcome after their 2nd operations. The authors concluded that the LINDIF produced satisfactory results in all demographics. Anesthesia time was consistently short, blood loss was negligible. Hospital stay was brief for most healthy patients irrespective of age. The results of this study demonstrated how drastically the surgery related morbidity, and the economics thereof, can be reduced. They stated that the outcomes relating to patients in the age group of 71 to 90 years are particularly encouraging, given their increasing proportion in the population. The findings of this study need to be validated by well-designed studies.

Microsurgical Lumbar Sequestrectomy for the Treatment of Lumbar Disc Herniation

Ran and colleagues (2015) stated that lumbar disc removal is currently the standard treatment for lumbar disc herniation. No consensus has been achieved whether aggressive disc resection with curettage (discectomy) versus conservative removal of the offending disc fragment alone (sequestrectomy) provides better outcomes. These researchers compared the re-herniation rate and clinical outcomes between discectomy and sequestrectomy by literature review and a meta-analysis. They performed a systematic search of PubMed, Medline, Embase and the Cochrane Library up to June 1, 2014. Outcomes of interest assessing the 2 techniques included demographic and clinical baseline characteristics, peri-operative variables, complications, recurrent herniation rate and post-operative functional outcomes. A total of 12 eligible trials evaluating discectomy versus sequestrectomy were identified including 1 RCT, 5 prospective and 6 retrospective comparative studies. In contrast to discectomy, sequestrectomy was associated with significantly less operative time ($p < 0.001$), lower VAS for LBP ($p < 0.05$), less post-operative analgesic usage ($p < 0.05$) and better patients' satisfaction ($p < 0.05$). Recurrent herniation rate, re-operation rate, intra-operative blood loss, hospitalization duration and VAS for sciatica were without significant difference. The authors concluded that according to their pooled data, sequestrectomy entailed equivalent re-herniation rate and complications compared with discectomy, but maintained a lower incidence of recurrent LBP and higher satisfactory rate. They stated that high-quality prospective RCTs are needed to evaluate these 2 procedures.

In a meta-analysis, Huang et al (2015) compared the effects of sequestrectomy and microdiscectomy in the treatment of patients with lumbar herniated discs (LHD). Clinical trials published in PubMed, Embase, and Web of Science were systematically reviewed to compare the effects of sequestrectomy and microdiscectomy for LHD. Outcomes included re-herniation rate, duration of surgery, length of hospital stay, and post-operative VAS scales for leg and back pains. A fixed-effects or random-effects were used to pool the estimates, depending on the heterogeneity among the studies. A total of 5 cohorts and 2 RCTs with a total of 929 patients met the inclusion criteria and were included in this

meta-analysis. All patients underwent sequestrectomy or microdiscectomy. Pooled estimates showed that patients treated with sequestrectomy had comparable effects in re-herniation rate (RR = 1.36, 95% CI: 0.81 to 2.27; p = 0.240), length of hospital stay (WMD = -0.22 days, 95% CI: -0.45 to 0.01; p = 0.060), and post-operative VAS scales for leg pain (WMD = 0.53, 95% CI: -1.54 to 2.60; p = 0.617) or back pain (WMD = 0.18, 95% CI: -1.64 to 2.00; p = 0.846), but had a shorter duration of surgery (WMD = -6.97 minutes, 95% CI: -12.15 to -1.78; p = 0.008), when compared with those treated with microdiscectomy. The authors concluded that based on the current evidence, sequestrectomy significantly reduced the operational time, but had similar effects on re-herniation rate, length of hospital stay, and post-operative VAS scales for leg and back pains, when compared with microdiscectomy. They stated that further well-designed RCTs are needed to validate these findings.

In a systematic review, Azarhomayoun et al (2015) compared the effects of sequestrectomy versus conventional microdiscectomy for LDH. These investigators searched Medline and Embase from 1980 to November 2014. They selected RCTs and non-randomized prospective studies of conventional discectomy versus sequestrectomy for adult patients with LDH that evaluated the following primary outcomes: radicular pain or LBP as measured by a VAS, or neurological deficits of the lower extremity. These researchers also evaluated the following secondary outcomes: complications of surgery, re-herniation rate, duration of hospital stay, post-operative analgesic use, and health-related quality-of-life measures. Two authors independently reviewed citations and articles for inclusion. They assessed the risk of bias, synthesized data, and the level evidence using standard methodological procedures as recommended by the Cochrane Back Review Group. These investigators identified 5 studies (746 participants) of sequestrectomy versus microdiscectomy; 1 study was RCT and the other 4 were non-randomized prospective comparisons; all studies were assessed as being at a high-risk of bias. There were no significant differences for leg pain, LBP, functional outcomes, complications, and hospital stay or recurrence rate for 2 years (level of evidence: Low). Sequestrectomy was associated with less analgesic consumption versus discectomy (level of evidence: Very low). The authors concluded that sequestrectomy and standard microdiscectomy were associated with similar effects on pain after surgery, recurrence rate,

functional outcome, and complications; more evidence is needed to determine whether sequestrectomy is associated with less post-operative analgesic consumption (Level of Evidence: 2).

Intradiscal Steroid Injections

Nguyen and colleagues (2017) noted that refer for invasive procedure is usually at the bottom of the LBP treatment algorithm. In this study, one invasive procedure – injection of prednisolone acetate 25-mg following discography – produced a short-term reduction in, but not elimination of, pain as compared with no treatment. However, the benefit was gone within 1 year. The process of discography, though, seemed to improve both pain and function in patients whether or not they received an injection. That benefit could be simply due to participation in a research study.

Cooled Radiofrequency Ablation for Facet Denervation

McCormick et al (2014) stated that while cooled radiofrequency ablation (C-RFA) appeared to be a promising technology for joint denervation, outcomes of this technique for the treatment of lumbar facet syndrome have not been described. These researchers reported clinical outcomes in a case series of patients treated with C-RFA for lumbar facet syndrome. Consecutive patients aged 18 to 60 years diagnosed with lumbar facet syndrome, confirmed by greater than or equal to 75% symptom relief with at least 1 set of diagnostic medial branch nerve blocks, who underwent C-RFA between January 2007 and December 2013 in an urban academic pain center were included. The respective proportions of participants who reported greater than or equal to 50% improvement in pain and in function were calculated. Change in median NRS score, daily morphine equivalent consumption (DME), and medication quantification scale III (MQS III) score were measured. A total of 12 patients underwent C-RFA; 3 were lost to follow-up. The median and 25% to 75% interquartile range (IQR) for age was 44 years (35, 54). The median duration of follow-up was 34 months, IQR (21, 55). The percentage and 95% confidence interval (CI) of patients who reported greater than or equal to 50% improvement in pain was 33% CI (12%, 64%) and in function was 78%, CI (41%, 96%). There was no significant change in DME or MSQ III score. Approximately 50% of patients sought additional healthcare by

long-term follow-up. No complications were reported. The authors concluded that the findings of this is case-series study suggested that C-RFA may improve function and to a lesser degree pain at long-term follow-up. Moreover, they stated that a randomized, controlled trial is needed.

Walega and Roussis (2014) noted that RFA of medial branch nerves is considered a safe and effective treatment for chronic facet joint pain in the cervical, thoracic, and lumbosacral spine. Cooled radiofrequency ablation is gaining popularity over conventional thermal RFA in pain management. However, complications of C-RFA have not been reported in the literature. These investigators presented a first report of 3rd-degree skin burn resulting from C-RFA electrode use for the treatment of facet syndrome. A 61-year old woman (BMI of 21.8 kg/m(2)) with thoracic facet syndrome underwent C-RFA of the T1 to T4 medial branch nerves. Lesioning at the superior-lateral aspect of the thoracic transverse processes at each level was performed. During lesioning of the T2 MBN on the T3 transverse process, skin blanching 15 mm in diameter was noted around the introducer needle with patient complaints of severe, localized pain. Post-procedurally the skin injury at this level worsened in appearance, with a 20 mm × 4 mm skin defect, which took nearly 5 months to heal. With C-RFA, internally cooled electrodes are capable of creating large volume spherical lesions, a size advantage over conventional RFA. The authors concluded that although C-RFA lesion size may overcome the anatomic variability of target nerve location and potentially improve pain outcomes, added vigilance is needed in thin patients and in anatomic regions of minimal subcutaneous tissue between the lesion target and the dermis. Skin burns at the site of the RF electrode are a potential risk under such conditions.

Furthermore, an UpToDate review on “Subacute and chronic low back pain: Nonsurgical interventional treatment” (Chou, 2017) suggested not performing radiofrequency denervation for chronic LBP due to available data that are inconsistent and the authors suggested that, compared with placebo, radiofrequency denervation may modestly reduce pain in the short-term; however, there does not appear to be clear long-term benefit. Also, there is no mention of “cooled” RFA for treatment of back pain.

Cheng and colleagues (2013) noted that SI joint pain is a common cause of LBP. Cooled radiofrequency ablation (c-RFA) of the lateral branches was recently introduced with the hypothesis that it creates larger lesions to overcome the anatomic variability of the lateral branches and achieve better outcomes as compared with the traditional RFA (t-RFA). In a comparative study, these researchers examined if c-RFA is superior over t-RFA in providing longer pain relief. Data on 88 patients were retrospectively collected between January 2006 and June 2009. Patients' pain relief was registered as less than 50%, 50% to 80%, or greater than 80% at 1, 3, 6, and 12 months after procedure. The duration of pain relief, defined as the time until the patient reported less than 50% pain relief, served as the primary outcome. Demographic, morphometric, and procedural characteristics were analyzed using standard descriptive statistics and univariable tests. The relationship between RFA technique and duration of pain relief was evaluated using multi-variable Cox regression. Among the 88 patients, 30 received t-RFA and 58 received c-RFA. These investigators did not find a significant univariable relationship between RFA technique and duration of pain relief either before ($p = 0.76$, Sun test) or after ($p = 0.95$, Wald test) adjusting for the potentially confounding variables. Both cooled and traditional RFAs provided greater than 50% pain reduction for 3 to 6 months in majority of the patients. The authors concluded that the findings of this study did not reveal evidence that c-RFA of the lateral branches provided longer relief of SI joint pain as compared with t-RFA.

Patel (2016) reported the long-term outcomes of cooled RF ablation (CRF) lateral branch neurotomy (LBN) as a treatment for SI region pain. Whereas the 1-, 3-, 6-, and 9-month outcomes of this procedure compared to sham treatment were previously reported, this current report shows the 12-month outcomes of CRF/LBN treatment for SI region pain. This study originally included 51 subjects who were randomized 2:1 to receive CRF/LBN treatment or a sham intervention, respectively, for SI region pain. Subjects and assessors were blinded for 3 months. At that time, sham participants were permitted to receive CRF/LBN, designated as "cross-over" study subjects, and followed for 6 additional months. For the purpose of this evaluation, the original CRF/LBN-treated study subjects were followed for a total of 12 months. Study participants were 18 to 88 years of age and had chronic (symptomatic for greater than 6 months) axial back pain. All subjects were qualified for study inclusion

following positive responses to dual lateral branch blocks. Lateral branch neurotomy was performed by CRF to ablate the S1 to S3 lateral branches and the L5 dorsal ramus. Pain was measured by a NRS and Short Form 36-bodily pain (SF36-BP) scores. The ODI and Short Form 36-physical functioning (SF36-PF) assessment each served to evaluate subject disability. Treatment successes ("responders") in the originally treated CRF/LBN group at 12 months, and in the cross-over group at 6 months, were also determined. In the original CRF/LBN treatment group, 12-month outcomes compared to baseline were favorable, with a mean 2.7 point drop in the NRS score, a 13.9 decrease in the ODI, and a 15.8 increase in SF-36BP. In the cross-over study group, 6-month outcomes were also favorable, with a mean NRS score decrease of 2.5 points, a reduction in ODI of 8.8, and an increase in SF36-BP of 11.9. The authors concluded that these favorable 12-month results illustrated the durability of effective CRF/LBN-mediated treatment of SI region pain for selected patients. Furthermore, successful CRF/LBN treatments in unblinded cross-over study subjects demonstrated the unlikelihood that such positive outcomes were attributable to a "placebo" effect, and suggested that CRF/LBN is an effective therapeutic option for alleviating pain, and improving physical function and QOL, with few complications.

McCormick et al (2019) stated that no previous study has assessed the outcomes of cooled radiofrequency ablation (C-RFA) of the medial branch nerves (MBN) for the treatment of lumbar facet joint pain nor compared its effectiveness with traditional RFA (T-RFA). In a blinded, prospective study, these researchers examined 6-month outcomes for pain, function, psychometrics, and medication usage in patients who underwent MBN C-RFA versus T-RFA for lumbar Z-joint pain. Patients with positive diagnostic MBN blocks (greater than 75 % relief) were randomized to MBN C-RFA or T-RFA. The primary outcome was the proportion of “responders” (greater than or equal to 50 % numeric rating scale (NRS) reduction) at 6 months. Secondary outcomes included NRS, Oswestry Disability Index (ODI), and Patient Global Impression of Change. A total of 43 patients were randomized to MBN C-RFA (n = 21) or T-RFA (n = 22). There were no significant differences in demographic variables ($p > 0.05$). A greater than or equal to 50 % NRS reduction was observed in 52 % (95 % confidence interval [CI]: 31 % to 74 %) and 44 % (95 % CI: 22 % to 69 %) of subjects in the C-RFA and T-RFA groups, respectively ($p = 0.75$). A greater than or equal to 15-point or greater than or equal to 30 %

reduction in ODI score was observed in 62 % (95 % CI: 38 % to 82 %) and 44 % (95 % CI: 22 % to 69 %) of subjects in the C-RFA and T-RFA groups, respectively (p = 0.21). The authors concluded that when using a single diagnostic block paradigm with a threshold of greater than 75 % pain reduction, treatment with both C-RFA and T-RFA resulted in a success rate of approximately 50 % when defined by both improvement in pain and physical function at 6-month follow-up. While the success rate was higher in the C-RFA group, this difference was not statistically significant. Moreover ,these researchers stated that future study should use the effect size or success rate demonstrated in this prospective study for power calculation.

The authors stated that this study had several drawbacks. The primary drawback was the relatively small sample size; 5 patients dropped-out after being enrolled by prior to randomization; selection bias was possible but not dissimilar to other studies of procedural interventions in which individuals may elect for additional non-invasive care prior to undergoing intervention. Further, subjects were lost to follow-up; of 43 subjects who underwent treatment intervention, 3 (7 %) did not report outcomes for the full 6-month duration of the study. A drop-out effect could have altered the overall outcome of the study. Analysis by conservative worst-case scenario definitions (treating all subjects lost to follow-up as treatment failures) would adjust the treatment success rate to 50 % (95 % CI: 29 % to 71 %) and 59 % (95 % CI: 9 % to 80 %) for pain reduction and functional improvement, respectively, in the C-RFA group. 20-gauge rather than 16-gauge or 18-gauge RFA electrodes were used for conventional ablations; as such, the success rate in the T-RFA group may be lower than would be expected when using larger gauge electrodes. Furthermore, some providers use bi-polar lead placement, longer lesion duration times, higher lesioning temperatures or longer active tips when employing C-RFA, all of which expanded the size of the lesion and may increase the chance of successful MBN capture. A heterogeneous group of 5 faculty members, assisted by Pain Medicine fellows, performed these procedures; difference in experience level with the procedural technique may have influenced patient outcomes, although this heterogeneity did improve generalizability of the reported findings. Finally, RFA represents a treatment that is implemented with the goal of long-term treatment; these investigators measured a primary outcome at 6 months, and did not follow subjects beyond this time period, but future study would ideally

capture outcomes at a post-RFA time point of at least 1 year. Indeed, it is conceivable that an inter-group difference may have been observed if outcomes had been examined beyond 6 months.

Davis et al (2019) stated that as a follow-up to the 6-month report, these investigators examined the analgesic effect of C-RFA in patients with knee osteoarthritis (OA) 12 months post-intervention and its ability to provide pain relief in patients who experienced unsatisfactory effects of intra-articular steroid injection (IAS); 78 % (52/67) of patients originally treated with C-RFA were examined at 12 months, while at 6 months post-IAS, 82 % (58/71) of those patients crossed-over to C-RFA and examined 6 months later. At 12 months, 65 % of the original C-RFA group had pain reduction greater than or equal to 50 %, and the mean overall drop was 4.3 points ($p < 0.0001$) on the NRS; 75 % reported “improved” effects. The cross-over group demonstrated improvements in pain and functional capacity ($p < 0.0001$). No unanticipated adverse events (AEs) occurred. The authors concluded that the findings of this study demonstrated that analgesia following C-RFA for OA knee pain could last for at least 12 months and could rescue patients who continue to experience intolerable discomfort following IAS.

The authors stated that a limitation of this study was the 1-way cross-over option, from IAS to C-RFA, but not vice versa. This paradigm was consistent with the intention of the study to test C-RFA as a rescue intervention for knee OA, rather than long-standing, conservative IAS. The limitations of this portion of the study were that the remaining IAS group sample size was not large enough to carry out statistical test-based comparisons between the originally treated C-RFA patients and the IAS group members at 12 months, outcomes of the originally treated C-RFA group and those of the crossed-over cohort could not be directly compared at 6 months, because the groups were derived from 2 different study populations, and an effect of C-RFA on opioid use could not be detected, perhaps due to alternate patient conditions that also utilized opioids as therapy. Furthermore, the late addition of the amendment to collect X-rays at the final visit limited the ability to capture data on a large portion of the patients enrolled.

Intradiscal Injection of Platelet-Rich Plasma

In a preliminary clinical trial, Akeda and colleagues (2017) determined the safety and initial effectiveness of intradiscal injection of autologous platelet-rich plasma (PRP) releasate in patients with discogenic LBP. Inclusion criteria for this study included chronic LBP without leg pain for more than 3 months; 1 or more lumbar discs (L3/L4 to L5/S1) with evidence of degeneration, as indicated via MRI; and at least 1 symptomatic disc, confirmed using standardized provocative discography. Platelet-rich plasma releasate, isolated from clotted PRP, was injected into the center of the nucleus pulposus. Outcome measures included the use of a VAS and the Roland-Morris Disability Questionnaire (RDQ), as well as X-ray and MRI (T2-quantification). Data were analyzed from 14 patients (8 men and 6 women; mean age of 33.8 years). The average follow-up period was 10 months. Following treatment, no patient experienced AEs or significant narrowing of disc height. The mean pain scores before treatment (VAS, 7.5 ± 1.3; RDQ, 12.6 ± 4.1) were significantly decreased at 1 month, and this was generally sustained throughout the observation period (6 months after treatment: VAS, 3.2 ± 2.4, RDQ; 3.6 ± 4.5 and 12 months: VAS, 2.9 ± 2.8; RDQ, 2.8 ± 3.9; $p < 0.01$, respectively). The mean T2 values did not significantly change after treatment. The authors demonstrated that intradiscal injection of autologous PRP releasate in patients with LBP was safe, with no AEs observed during follow-up. Moreover, they stated that future prospective, randomized, double-blinded, and placebo-controlled studies are needed to determine the effectiveness of this treatment.

Ultrasound Guidance for Sacroiliac Joint Injections

In a prospective, randomized, controlled trial, Soneji et al (2016) compared the accuracy and effectiveness of ultrasound (US) and fluoroscopy (FL) guidance for sacro-iliac joint (SIJ) injections. A total of 40 patients with chronic moderate-to-severe low back pain (LBP) secondary to SIJ arthritis were randomized to receive US- or FL-guided unilateral SIJ injections. Primary outcomes included pain at 1 month measured by numerical rating scale (NRS) scores. Secondary outcomes included NRS scores at 24 hours, 72 hours, 1 week, and 3 months after injection, physical functioning at 1 month after the procedure, procedure time, incidence of intra-articular and peri-articular needle placement, patient

discomfort, overall patient satisfaction, and daily opioid consumption. There was no significant difference in NRS pain scores between the 2 groups at 1 month or at any other follow-up points. A significant reduction from baseline mean NRS scores was observed in both groups at 1 month after injection (US 22.7%, p = 0.025; FL 37.3%, p < 0.001). There was no significant difference in procedure-related variables, physical functioning, discomfort, opioid utilization, and patient satisfaction between the 2 groups. The authors concluded that US-guided SIJ injection with fluoroscopic confirmation has similar accuracy and efficacy to fluoroscopy alone for SIJ injections in patients with chronic LBP secondary to SIJ arthritis. This was a small study (n = 40); its main drawback was the lack of a control group (i.e., SIJ injection without imaging guidance).

Perry et al (2016) stated that US-guidance has been proposed as an alternative imaging modality for SIJ injections. Few studies have studied the accuracy of this modality for the procedure. In a controlled laboratory study, these investigators determined the accuracy of US-guided SIJ injections using a cadaveric model. The study was performed in the Skills Laboratory of the American Sports Medicine Institute in St. Vincent's Hospital, Birmingham, AL. A total of 17 cadaveric SIJs were injected under US-guidance and dissected to determine the accuracy of intra-articular injections. Main outcome measure was the presence of intra-articular spread of a white paint marker in the SIJ after US-guided injection. Of 17 SIJs, 15 (88.2%) were accurately injected intra-articularly. One of the joints with no intra-articular spread was found to be partially frozen at the time of dissection, and the 2nd joint was considered an unsuccessful injection before dissection due to difficulty entering the joint under US-guidance because of marginal osteophytes at the joint line. Of the 15 joints with intra-articular placement, 5 joints (33.3%) showed partial extra-articular spread at the time of initial injection and required re-direction of the needle under US-guidance, and 3 joints (20%) had extra-articular spread that was not seen during US. The authors concluded that US allowed intra-articular injection in 88.2% of joints in this cadaveric study; it did not expose the patient to radiation, as seen with FL-guidance, which is currently the gold standard for this injection. In addition, US may allow visualization of extra-articular spread when caused by extra-articular needle placement, which can allow for re-direction of the needle to achieve intra-articular injection. Level of Evidence = IV.

Furthermore, an UpToDate review on “Subacute and chronic low back pain: Nonsurgical interventional treatment” (Chou, 2017) states that "The sacroiliac joints are thought to be the source of low back pain in some patients. Effective methods for diagnosing and treating sacroiliac joint pain in patients without spondyloarthropathy remain controversial. Periarticular steroid injection does not require radiographic guidance. One small (n = 24), randomized trial found periarticular sacroiliac joint glucocorticoid injection more effective than local anesthetic injection for pain relief (change in pain of -40 versus -13 mm on a 100 mm visual analogue scale 1 month after injection) in patients with chronic pain in the sacroiliac joint area and at least 1 physical exam finding for sacroiliac pain. These results should be considered preliminary, due to the small sample size and relatively short-term follow-up. There are no randomized trials of intraarticular sacroiliac joint steroid injection in patients without spondyloarthropathy".

Posterior Cervical Cages

Supplemental posterior instrumentation has been widely used to enhance stability and improve fusion rates in higher risk patients undergoing anterior cervical discectomy and fusion (ACDF) (Voronov, et al., 2016). These typically involve posterior lateral mass or pedicle screw fixation with significant inherent risks and morbidities. More recently, cervical cages placed bilaterally between the facet joints (posterior cervical cages) have been used as a less disruptive alternative for posterior fixation.

Voronov, et al. (2016) compared the stability achieved by both posterior cages and ACDF at a single motion segment and determine the stability achieved with posterior cervical cages used as an adjunct to single- and multilevel ACDF. Seven cadaveric cervical spine (C2-T1) specimens were tested in the following sequence: intact, C5-C6 bilateral posterior cages, C6-C7 plated ACDF with and without posterior cages, and C3-C5 plated ACDF with and without posterior cages. Range of motion in flexion-extension, lateral bending, and axial rotation was measured for each condition under moment loading up to ±1.5 Nm. All fusion constructs significantly reduced the range of motion compared to intact in flexion-extension, lateral bending, and axial rotation ($P<0.05$). Similar stability was achieved with bilateral posterior cages and plated ACDF at a single level. Posterior cages, when placed as an adjunct to ACDF, further

reduced range of motion in both single- and multilevel constructs ($P<0.05$). The investigators concluded that the biomechanical effectiveness of bilateral posterior cages in limiting cervical segmental motion is comparable to single-level plated ACDF. Furthermore, supplementation of single- and multilevel ACDF with posterior cervical cages provided a significant increase in stability and therefore may be a potential, minimally disruptive option for supplemental fixation for improving ACDF fusion rates.

McCormick, et al. (2016) reported on one-year clinical and radiographic outcomes of 10 patients with single level cervical radiculopathy due to spondylosis and stenosis treated with a minimally disruptive instrumented fusion procedure employing bilateral posterior cervical cages. A retrospective study of 10 patients with one-year follow-up who underwent cervical fusion using bilateral posterior cervical cages placed between the facet joints was conducted at a single center. Neck Disability Index (NDI), Visual Analog Scale (VAS) for neck and arm pain, neurological status, adverse events, x-rays and computed tomography (CT) were collected at baseline and 6-weeks, 3-, 6- and 12-months postoperatively. X-ray and CT were assessed for segmental and overall cervical lordosis, fusion, and device retention. Subject age range was 51 to 78 years with a mean of 68 (6 male, 4 female). Five patients were treated at C5-6, four at C6-7, and one at C4-5. NDI and VAS scores significantly improved immediately after surgery; outcomes were sustained at one year. NDI scores improved from a mean of 35 at baseline to 15 at one year. Mean scores on VAS for neck pain improved from a baseline of 8 to 2.5 at one year. Results were similar for arm pain on VAS; scores improved from 7.5 to 1.5 pre- and post-op, respectively. Evidence of fusion was observed for all subjects on lateral flexion/extension plain film radiographs. Bridging bone on CT was present in 9 subjects; findings were indeterminate for one subject. No significant change in segmental or overall lordosis was observed. There were no device breakages, device back out, or surgical re-interventions at one year. The authors concluded that one-year results show favorable improvements in pain and function in subjects with single level cervical radiculopathy due to spondylosis and foraminal stenosis treated with minimally disruptive posterior cervical fusion using bilateral cervical cages.

Transforaminal Endoscopic Discectomy

Hoogland and colleagues (2008) performed a prospective, cohort evaluation of consecutive patients who underwent endoscopic transforaminal discectomy (ETD) for recurrent lumbar disc herniation, after previous discectomy. These investigators reviewed complications and results of the ETD for recurrent herniated disc with a 2-year follow-up. Between January 1994 and November 2002, 262 patients with primarily radicular problems underwent an ETD for a recurrent herniated disc; 238 of these patients (90.84%) completed 2-year follow-up questionnaire. Initial surgery of 82 patients was performed in-house, 180 external. Average age was 46.4 years. The female/male ratio was 29/71%. At 2-year follow-up, 85.71% of patients rated the result of the surgery as excellent or good; 9.66% reported a fair and 4.62% patients an unsatisfactory result. Average improvement of back pain of 5.71 points and 5.85 points of leg pain on the VAS scale (1 to 10). According to Mac Nab, 30.67% of the patients felt fully regenerated, 50% felt their functional capacity to be slightly restricted, 16.81% felt their functional capacity noticeably restricted, and 2.52% felt unimproved or worse. All patients participated in a 3-month follow-up to establish the peri-operative complications. The overall complication rate was 10/262 (3.8%), including 3 nerve root irritations and 7 early recurrent herniation (less than 3 month). There was no case of infection or discitis. After 3 months and within 2 years, 4 patients have been treated for a recurrent herniated disc in the authors' own center and 7 patients have been treated elsewhere, resulting in a recurrence rate 11/238 (4.62%). The authors concluded that ETD for recurrent disc herniation appeared to be an effective method with few complications and a high patient satisfaction. The main drawback of this study was its relative short-term follow-up (2 years).

Gibson and associates (2012) described transforaminal endoscopic spinal surgery (TESS) using HD-video technology, that is generally performed as a day case procedure under sedation or light general anesthesia, and collated the evidence comparing the technique to micro-discectomy. The method of TESS was described and an electronic literature search performed to identify papers reporting clinical outcomes. International data were translated where necessary and proceedings' abstracts included. In addition, papers held by the authors and colleagues in personal libraries were carefully cross-referenced to the obtained

database. Analysis of the data supported the use of a transforaminal endoscopic approach to the lumbar intervertebral disc and suggested that outcomes following surgery were at least equivalent to those following micro-discectomy. Significant cost-savings in terms of in-patient stay may be generated. In addition, there was also some evidence supporting endoscopic surgery for relief of foraminal stenosis. The authors concluded that based on current evidence there are good arguments supporting a more wide-spread adoption of transforaminal endoscopic surgery for the treatment of lumbar disc prolapse with or without foraminal stenosis. Moreover, these researchers noted that although still relatively scarce, RCT evidence including their own, suggested that outcomes at least equate and were probably better than those from micro-discectomy in selected patients.

In a retrospective study, Jasper et al (2013a) evaluated the benefit of transforaminal endoscopic discectomy and foraminotomy in geriatric patients with single level and multi-level lumbar disc herniation and lumbar radiculopathy. After Institutional Review Board (IRB) approval, charts from 50 consecutive patients aged 75 and older with complaints of lower back and radicular pain who underwent 1 or more endoscopic procedures between 2007 and 2011 were reviewed. The average pain relief 6 months post-operatively was reported to be 71.8%, good results as defined by MacNab. The average pre-operative VAS score was 9.04, indicated in the questionnaire as severe and constant pain. The average 6 month post-operative VAS score was 2.63, indicated in the questionnaire as mild and intermittent pain. The authors concluded that endoscopic discectomy was a safe and effective alternative to open back surgery. The 6-month follow-up data appeared to indicate that an ultra-minimally invasive approach to the geriatric spine that has a low complication rate, avoided general anesthesia, and was out-patient might be worth studying in a prospective, longer term way. The main drawback of this study was that it was a retrospective study and only offered 6 month follow-up data for geriatric patients undergoing endoscopic spine surgery.

Jasper et al (2013b) noted that transforaminal endoscopic surgery has evolved from an intra-discal procedure to a true foraminal epidural procedure where both a targeted discectomy and foraminal decompression can be performed. These investigators described the

success of transforaminal decompression for radiculopathy using pre-operative selective nerve root block as part of a treatment algorithm for single level and multi-level lumbar disc herniation. After IRB approval, charts from 195 patients with complaints of lower back and radicular pain who received 1 or more endoscopic discectomy procedures were reviewed; VAS was applied to each patient pre-operatively and 6 months after the procedure. Patients with multi-level pathologies receiving 1 procedure had an average relief of 69.7% attributed to correct diagnosis of the inflicting level as opposed to 83.9% improvement in patients with a single level herniation. The authors concluded that patients with single level lumbar herniation receiving 1 endoscopic discectomy had excellent outcomes, but with a good response to a selective nerve root block as a pre-operative adjunct, patients with multi-level disc herniation also had significant benefit from single level endoscopic discectomy. This study had the same limitations and may have had overlapping subjects with their earlier trial (Jasper et al, 2013a).

Jasper et al (2014) stated that transforaminal endoscopic discectomy and foraminotomy is an ultra-minimally invasive outpatient surgical option available to obese patients that does not require general anesthesia and does not necessitate additional retraction due to additional thicker soft tissue. These researchers assessed the benefit of transforaminal endoscopic discectomy and foraminotomy in obese patients with single-level lumbar disc herniation and lumbar radiculopathy. After IRB approval, charts from 82 consecutive patients with BMIs of at least 30 kg/m2 who had undergone single-level endoscopic lumbar discectomies and foraminotomies were retrospectively identified and categorized according to BMI: Class I obesity, BMI 30.0 to 34.9 kg/m2; Class II obesity, BMI 35.0 to 39.9 kg/m2; or Class III obesity, BMI greater than or equal to 40.0 kg/m2. Patients aged 40 and older (average age of 61.8, 40% women) with complaints of lower back and radicular pain who underwent endoscopic procedures between 2007 and 2012 were reviewed. The average pain relief 1 year post-operatively was reported to be 68.4% for Class I, 66.1% for Class II, and 43.5% for Class III. The average pre-operative VAS scores were 8.8 for Class I, 9.2 for Class II, and 9.0 for Class III, all as indicated in the questionnaire as describing severe and constant pain. The average 1 year post-operative VAS scores were 2.6 for Class I, 3.0 for Class II, and 3.2 for Class III, indicated in the questionnaire as mild and intermittent pain. There were no infections or

other complications reported and the re-herniation rate for the 1 year was 7.5% in Class I, 12.5% in Class II, and 0% in Class III. The authors concluded that endoscopic discectomy was a safe and effective alternative to open back surgery. The 1-year follow-up data appeared to indicate that an ultra-minimally invasive approach to the obese spine patient that has a low complication rate, avoided general anesthesia, was performed in the lateral position, and was out-patient might be worth studying in a prospective, longer term way. This study had the same limitations and may have had overlapping subjects with their earlier trials (Jasper et al, 2013a; and Jasper et al, 2013b).

Sclafani and co-workers (2015) stated that minimally invasive transforaminal endoscopic procedures can achieve spinal decompression through either direct or indirect techniques. Subtle variations in trajectory of the surgical corridor can dictate access to the pathologic tissue. Two general strategies exist: the intra-discal "inside-out" technique and the extra-discal, intra-canal (IC) technique. The IC technique utilizes a more lateral transforaminal approach than the intra-discal technique, which allows for a more direct decompression of the spinal canal. These researchers carried out an assessment of IC patient outcome data obtained through analysis of a previously validated MIS Prospective Registry. Post-hoc analysis was performed on the MIS Prospective Registry database containing 1,032 patients. A sub-group of patients treated with the endoscopic IC technique was identified. Patient outcome measures after treatment of symptomatic disk herniation and neuro-foraminal stenosis were evaluated. A total of 86 IC patients were analyzed. Overall, there was significant improvement in employment and walking tolerance as soon as 6 weeks post-op as well as significant 1 year VAS and ODI score improvement. Sub-analysis of IC patients with 2 distinct primary diagnoses was performed. Group IC-1 (disc herniation) showed improvement in Oswestry disability index (ODI) and VAS back and leg outcomes at 1 year post-op. Group IC-2 (foraminal stenosis) showed VAS back and leg score improvement at 1 year post-op but did not demonstrate significant improvement in overall ODI outcome at any time-point. The 1-year re-operation rate was 2% (1/40) for group IC-1 and 28% (5/18) for group IC-2. The authors concluded that the initial results of the MIS Registry IC subgroup showed a significant clinical improvement when the technique was employed to treat patients with lumbar disc

herniation. The treatment of foraminal stenosis could lead to improved short-term clinical outcome but was associated with a high re-operation rate at 1 year post-op.

The authors stated that the main limitation of this study was the inconsistent rate of data collection at scheduled follow-up intervals, including the 1-year follow-up period. Although data collection through a prospective registry allowed post-hoc extraction of a large sample size, there was inherently less stringent monitoring of patient data collection than with a RCT. Additionally, this study did not record the duration of symptoms prior to surgical intervention and did not include a non-surgical control group. Nevertheless, this study of endoscopic transforaminal discectomy demonstrated promising results in patients with symptomatic disc herniation.

Gadjradj et al 92016) stated that throughout the last decades, full-endoscopic techniques to treat lumbar disc herniation (LDH) have gained popularity in clinical practice. To-date, however, no Class I evidence on the efficacy of percutaneous transforaminal endoscopic discectomy (PTED) has been published, and studies describing its safety and short- and long-term efficacy are scarce. These investigators evaluated the safety and clinical outcomes in patients undergoing PTED for LDH. Patients who underwent PTED for LDH between January 2009 and December 2012 were prospectively followed. The primary outcomes were the VAS score for leg pain and the score on the Quebec Back Pain Disability Scale (QBPDS). Secondary outcomes were the perceived experience with the local anesthesia used and satisfaction with the results after 1 year using Likert-type scales. The pre-treatment means were compared with the means obtained 6 and 52 weeks after surgery using paired t-tests. A total of 166 patients underwent surgery for a total of 167 LDHs. The mean duration of surgery (± SD) was 51.0 ± 9.0 mins. The 1-year follow-up rate was 95.2%. The mean reported scores on the VAS and QBPDS were 82.5 ± 17.3 mm and 60.0 ± 18.4 at baseline, respectively. Six weeks after surgery, the scores on the VAS and QBPDS were significantly reduced to 28.8 ± 24.5 mm and 26.7 ± 20.6, respectively ($p < 0.001$). After 52 weeks of follow-up, the scores were further reduced compared with baseline scores ($p < 0.001$) to 19.6 ± 23.5 mm on the VAS and 20.2 ± 18.1 on the QBPDS. A total of 4 complications were observed, namely 1 dural tear, 1 deficit of ankle dorsiflexion, and 2

cases of transient paresis in the foot due to the use of local anesthetics. The authors concluded that PTED appeared to be a safe and effective intervention for LDH and had similar clinical outcomes compared to conventional open micro-discectomy. Moreover, they stated that high-quality RCTs are needed to study the efficacy and cost-effectiveness of PTED.

The authors stated that the present study had several limitations. Due to the design, a proper control group is lacking; however, as previously mentioned, the objective of this study was not to emphasize the merits of PTED over other procedures, but to share the short- and long-term results that showed its potential. Moreover, PTED also has a long learning curve due to the concept of a 2D view. Surgeons are exposed to different landmarks, another direction of approach, and a laborious identification of anatomical structures during surgery. Considering the long learning curve of PTED and potential bias, all surgeries were performed by a single neurosurgeon who already had extensive experience in performing the PTED technique.

Pan et al (2016) compared the safety and efficacy of percutaneous transforaminal endoscopic spine system (TESSYS) and traditional fenestration discectomy (FD) in treatment of lumbar disc herniation (LDH). A total of 106 LDH patients were divided into TESSYS group (n = 48) and FD group (n = 58); VAS, ODI, Japanese Orthopedic Association (JOA), and modified MacNab criteria were used for efficacy evaluation. Post-operative responses were compared by enzyme-linked immunosorbent assay (ELISA) based on detection of serum IL-6, CRP, and CPK levels. In the TESSYS group, compared with the FD group, these researchers observed, shorter incision length, less blood loss, shorter hospital stay, lower hospitalization cost, shorter recovery time, lower complication rate (all $p < 0.001$), and lower VAS scores of lumbago and skelalgia at 3 days and 1, 3, and 6 months post-operatively (all $p < 0.05$). At 24 and 48 hours post-operatively, CRP level was remarkably higher in the FD group compared to the TESSYS group ($p < 0.001$). Further, comparison of IL-6 levels at 6, 12, 24, and 48 hours post-operatively revealed significantly higher levels in the FD group than in the FESSYS group (all $p < 0.001$). The authors concluded that TESSYS had clinical advantages over FD and entailed less trauma and quicker post-operative recovery, suggesting that TESSYS was well-tolerated by

patients and was a better approach than FD in surgical treatment of LDH. This was a relatively small (n = 48 in the TESSY group) study with short-term follow-up (6 months).

The authors stated that this study had several drawbacks. TESSYS was not suitable for patients with lumbar spinal stenosis, lumbar instability, or intervertebral space stenosis. TESSYS was highly effective in a narrow set of patients and, therefore, traditional surgical procedures are still very valuable in the clinic. As lifestyles and physical activities change in society, researchers would need to periodically re-assess their options to effectively treat LDH.

Ren et al (2017) described a percutaneous endoscopic herniotomy technique by using a unilateral approach for lumbar disc herniation with bilateral obvious symptoms. From June 2014 to October 2015, a total of 26 patients who had back as well as bilateral leg pain and/or weakness due to lumbar disc herniation were treated by transforaminal endoscopic lumbar discectomy (TELD), with a unilateral approach. Clinical outcomes were evaluated via a VAS (0 to 10), and functional status was assessed with the ODI (0 to 100%) post-operatively and 3 and 12 months post-operatively. Surgical satisfaction rate was assessed during the final follow-up. The mean VAS for leg pain on the operative side improved from pre-operative 8.39 ± 1.84 to 2.18 ± 1.26 post-operatively, 1.96 ± 0.83 at 3 months post-operatively, and 2.05 ± 1.42 at 1 year post-operatively ($p < 0.01$). The mean VAS for leg pain on the contralateral was 7.12 ± 1.74 and improved to 1.57 ± 1.66 post-operatively, 1.22 ± 1.58 at 3 months post-operatively, and 1.15 ± 1.35 at 1 year post-operatively ($p < 0.01$). The mean pre-operative ODI was 83.63 ± 8.49, with 23.58 ± 7.24 at 1 week post-operatively, 19.81 ± 11.26 at 3 months post-operatively, and 17.54 ± 13.40 at 12 months post-operatively ($p < 0.01$). Good or excellent global results were obtained in 96.2% of patients. The authors concluded that TELD could be effective for lumbar disc herniation causing bilateral symptoms, through 1 working channel.

The authors stated that the limitations of this study included that relatively short follow-up period (12 months) and the size of patient cohort (n = 26).

Gibson et al (2017) stated that transforaminal endoscopic discectomy (TED) minimizes para-spinal muscle damage. These researchers compared clinical outcomes of TED to micro-discectomy (Micro). A total of 143 patients, age 25 to 70 years and less than 115 kg of weight, with single-level lumbar prolapse and radiculopathy, were recruited and randomized – 70 received TED under conscious sedation and 70 Micro under general anesthesia; ODI, VAS of back and leg pain, and Short Form Health Survey indices (SF-36) were measured pre-operatively and at 3, 12 and 24 months. All outcome measures improved significantly in both groups ($p < 0.001$). Affected side leg pain was lower in the TED group at 2 years (1.9 ± 2.6 versus 3.5 ± 3.1, $p = 0.002$). Hospital stay was shorter following TED (0.7 ± 0.7 versus 1.4 ± 1.3 days, $p < 0.001$); 2 Micro patients and 5 TED patients required revision giving a relative risk of revision for TED of 2.62 (95% CI: 0.49 to 14.0). The authors concluded that functional improvements were maintained at 2 years in both groups with less ongoing sciatica after TED. A greater revision rate after TED was offset by a more rapid recovery.

The authors stated that the drawbacks of this study included the non-blinded nature of the trial. Both surgeon and patient were aware of their treatment and the senior surgeon acknowledged a specific interest in endoscopy that may introduce bias. However, all outcomes were collected independently and were patient-reported. The data were scrutinized by all authors. Different anesthetic techniques were used which may favor shorter length of stay in the TED group. This was pragmatic as it was considered safer to perform TED under conscious sedation. Though length of stay was significantly shorter in the TED group, this was a secondary outcome measure and the study was not powered to detect differences therein. No record was made of any litigation pertaining to any presenting injury. Finally, data were analyzed ‘‘as treated’’ not as ‘‘intention-to-treat’’. This was considered acceptable as only 1 case crossed-over between treatment arms and this was due to equipment failure not clinical choice; 13 patients (9.3%) were lost to follow-up by 2 years. This was within the 10% allowed by the power calculation and was significantly less than the 20% required by a level 1 trial.

Kim et al (2017) reported the surgical procedure and preliminary clinical results of percutaneous endoscopic stenosis lumbar decompression (PESLD) technique using a uniportal-contralateral approach for bilateral decompression of degenerative spinal stenosis. Electronic medical records of 48 consecutive patients who were treated between January 2016 and August 2016 were reviewed retrospectively. All patient received PESLD through the uniportal-contralateral approach. These investigators analyzed the outcomes using the VAS, Macnab criteria, ODI, and complication rate. There were 48 cases (15 men, and 33 women). Mean age of patients was 62.44 ± 8.68 years. Mean symptom duration was 20.13 ± 16.87 months. Neurogenic intermittent claudication was 550 m on average. Follow-up period was 7.75 ± 2.28 months (range of 5 to 13 months); VAS and ODI decreased significantly ($p < 0.001$) and decreased by 1.073 and 5.795 odds ratio (OR), respectively, in contralateral foraminotomy cases. Macnab outcome grade was good-to-excellent in 96% of patients. Dural tear occurred in 3 cases (6.25%), and 2 cases (4.17%) required transforaminal lumbar interbody fusion operation after this procedure. The authors concluded that these preliminary findings of this uniportal-contralateral PESLD technique was encouraging (96% demonstrated a good-to-excellent outcome), and the procedure was safe. Moreover, these researchers stated that long-term follow-up and a more detailed study for more accurate results of this technique is needed.

Cementoplasty

Iannessi et al (2011) noted that the current gold standard treatment of localized painful bone lesion is radiotherapy but this technique has limitations. In a prospective study, these researchers demonstrated that cementoplasty is an efficient alternative for these palliatives indications when lesions involve extra-spinal bones. They prospectively followed 20 patients who received a percutaneous cementoplasty on painful lytic bone lesions between May 2008 and May 2010; 17 patients also had difficulty walking in relation to the pain experienced. The clinical indication for treatment was severe pain (greater than or equal to 4 on the numeric scale) due to bone lesion on CT or MRI. All procedures (except 1) were performed under local anesthesia. Feasibility was 100% without immediate complications. The patients experienced a significant and rapid decrease of their pain (4.1 points, $p < 000.1$) and this effect was sustained over the long-term (7.75 months of follow-up on average); 64%

of patients treated on the lower limbs and pelvis improved mobility. The authors concluded that percutaneous cementoplasty may be a safe and effective palliative treatment for localized painful lytic lesion. Combining CT and fluoroscopic guidance appeared to be the safer option because of extra-vertebral localization. Smart fill of the bone and careful selection of patient determined the effectiveness of the procedure. Diffuse painful lesions and long bone diaphysis should not be good indications.

Rollinghoff et al (2013) noted that percutaneous cement augmentation systems have been proven to be an effective treatment for vertebral compression fractures in the last 10 years. A special form available since 2009 is the radiofrequency (RF) kyphoplasty in which the applied energy raises the viscosity of the cement. These investigators examined if a smaller cement amount in radiofrequency kyphoplasty can also restore vertebral body height in osteoporotic vertebral compression fractures. The treatment was minimally invasive using the StabiliT vertebral augmentation system by DFine. In a retrospective study from 2011 to January 2012, 35 patients underwent RF kyphoplasty for 49 fresh osteoporotic vertebral compression fractures. From the clinical side the parameters, demographics and pain relief using a visual analog scale (VAS: 0 to 100 mm) were collected. For the radiological outcome the vertebral body height (anterior, mean and posterior vertebral body height with kyphosis angle) after surgery and after 3 months was measured and compared to the cement volume. All patients still had permanent pain on the fractured level after conservative treatment. The time from initial painful fracture to treatment was 3.0 weeks ± 1.3. Average VAS results decreased significantly from 71 ± 9.2 pre-operatively to 35 ± 6.2 post-operatively ($p < 0.001$) and to 30 ± 5.7 ($p < 0.001$) after 3 months. With a mean cement volume in the thoracic spine of 2.9 ± 0.7 ml (1.8 to 4.1) and lumbar spine of 3.0 ± 0.7 ml (2.0 to 5.0), there was a significant vertebral body height restoration. Anterior and mean vertebral body heights significantly increased by an average of 2.3 and 3.1 mm, kyphosis angle significantly decreased with an average of 2.1° at 3-month follow-up ($p < 0.05$). In 2 vertebrae (4.1%) a minimal asymptomatic cement leakage occurred into the upper disc. In 2 patients (5.7%) there were new fractures in the directly adjacent segment that were also successfully treated with radiofrequency kyphoplasty. The authors concluded that with a mean cement volume of 3.0 ml radiofrequency kyphoplasty achieved rapid and short-term improvements of clinical symptoms with a significant

restoration of vertebral body height. There was no correlation between restoration of vertebral body height and pain relief. With a cement leakage of 4.1% RF kyphoplasty was a safe and effective minimally invasive percutaneous cement augmentation procedure.

In a retrospective study, Sun et al (2014) examined the effect of treatment with cementoplasty in patients with painful bone metastases in the extra-spinal region. This study was conducted to review 51 consecutive patients who underwent cementoplasty under CT or fluoroscopic guidance, a total of 65 lesions involving the ilium, ischium, pubis, acetabulum, humeral, femur and tibia. In 5 patients with a high risk of impending fracture in long bones based on Mirels' scoring system, an innovative technique using a cement-filled catheter was applied. The clinical effects were evaluated using the VAS pre-operatively and post-operatively. All patients were treated successfully with a satisfying resolution of painful symptoms at 3 months' follow-up. Cement leakage was found in 8 lesions without any symptoms; VAS scores decreased from 8.19 ± 1.1 pre-operatively to 4.94 ± 1.6 at 3 days, 3.41 ± 2.1 at 1 month and 3.02 ± 1.9 at 3 months post-operatively. There was a significant difference between the mean pre-operative baseline score and the mean score at all of the post-operative follow-up points ($p < 0.01$). The authors concluded that cementoplasty is an effective technique for treating painful bone metastases in extra-spinal regions, which is a valuable, minimally invasive, method that allows reduction of pain and improvement of patients' quality of life.

Kim et al (2014) stated that percutaneous stabilization (PS; percutaneous flexible nailing and intramedullary bone cement injection) was performed at lower extremity long bones in patients with multiple bone metastases with short life expectancy to get mechanical stability and local tumor control. These researchers evaluated the usefulness of PS by clinical status, F-18-FDG PET-CT and bone scintigraphy (BS). Patients comprised 15 patients (total 20 sites) who had undergone PS for the metastatic bone tumors of lower extremity long bones (femur and tibia). After percutaneous flexible nailing, bone cement was injected (mean amount = 15.5 ± 6.4 ml). Patients' clinical status was evaluated by VAS. Qualitative assessment of PET-CT and BS was categorized by improved, stable and aggravated states of PS lesion. Quantitative assessment of PET-CT was performed by maximum and mean standardized uptake

value (SUVmax and SUVmean). Percutaneous stabilization was performed in all of the patients without complication, and showed significant pain improvement of VAS (7.2 ± 0.2 versus 2.8 ± 0.3, $p < 0.001$); PS lesion showed improved state in 65% (13/20) and stable state in 35% (7/20). However, naive bony metastatic lesion showed mostly aggravated state in 90% (19/20) in the same patients, which was significantly different compared with PS lesion ($p < 0.001$). In PS lesion, SUVmax (10.1 ± 6.9 versus 7.1 ± 5.2, $p = 0.008$) and SUVmean (6.2 ± 4.8 versus 4.6 ± 3.7, $p = 0.008$) showed significantly decreased uptake after PS. The authors concluded that by PS in lower extremity long bones, patients can reduce regional pain, and has the possibility of local tumor control. They stated that PS can be performed for lower extremity bone metastasis in poor general condition to perform conventional intramedullary nailing.

Cazzato et al (2015) noted that percutaneous cementoplasty (PC) is rarely applied to long bone tumors, since cement is not considered to be sufficiently resistant to torsional forces. These investigators reviewed the literature to understand the effects of percutaneous long bone cementoplasty (PLBC) in terms of analgesia, limb function and complications. This study followed the Cochrane's guidelines for systematic reviews of interventions. Inclusion criteria were (i) prospective/retrospective studies concerning PC; (ii) cohort including at least 10 patients; (iii) at least 1 patient in the cohort undergoing PLBC; (iv) published in English; and (v) results not published by the same author more than once. A total of 1,598 articles were screened and 13 matched the inclusion criteria covering 196 PLBC patients. Pain improvement was high in 68.2% patients ($\sigma = 0.2$) and mild in 27.4% ($\sigma = 0.2$). Functional improvement was high in 71.9% patients ($\sigma = 0.1$) and mild in 6% ($\sigma = 0.1$). Use of PLBC correlated with pain reduction ($p < 0.001$). Secondary fractures occurred in 16 cases (8%, $\sigma = 2.5$); other complications in 2% cases. Percutaneous stabilization (PS) was coupled with PLBC in 17% of cases without any subsequent fracture; PS was not associated with absence of secondary fracture ($p = 0.08$). The authors concluded that PLBC is safe, offering good pain relief and recovery of impaired limb function. Secondary fractures are uncommon and PS may reduce their occurrence. However, no evidence is currently available to support PS plus PLBC as compared to PLBC alone.

Guarnieri e al (2015) stated that vertebroplasty (VP) is a percutaneous mini-invasive technique developed in the late 1980s as antalgic and stabilizing treatment in patients affected by symptomatic vertebral fracture due to porotic disease, traumatic injury and primary or secondary vertebral spine tumors. The technique consists of a simple metameric injection of an inert cement (poly-methyl-methacrylate, PMMA), through a needle by trans-peduncular, para-peduncular or trans-somatic approach obtaining a vertebral augmentation and stabilization effect associated with pain relief. The technique is simple and fast, and should be performed under fluoroscopy or CT guidance in order to obtain a good result with low complication rate. The authors illustrated the utility of VP, the indications-contraindications criteria, how to technically perform the technique using imaging guidance, and the results and complications of this treatment in patients affected by symptomatic vertebral compression fracture.

Muto et al (2016) stated that vertebral cementoplasty is a well-known mini-invasive treatment to obtain pain relief in patients affected by vertebral porotic fractures, primary or secondary spine lesions and spine trauma through intra-metameric cement injection. Two major categories of treatment are included within the term vertebral cementoplasty: the first is vertebroplasty in which a simple cement injection in the vertebral body is performed; the second is assisted technique in which a device is positioned inside the metamer before the cement injection to restore vertebral height and allow a better cement distribution, reducing the kyphotic deformity of the spine, trying to obtain an almost normal spine biomechanics. The authors described the most advanced techniques and indications of vertebral cementoplasty, having recently expanded the field of applications to not only patients with porotic fractures, but also spine tumors and trauma.

The National Institute for Health and Care Excellence’s clinical practice guideline on “Percutaneous cementoplasty for palliative treatment of bony malignancies” (2006) stated that “Current evidence on the safety and efficacy of percutaneous cementoplasty for the palliative treatment of bony malignancies is limited, but appears adequate to support the use of this procedure in patients for whom other treatments have failed, provided that the normal arrangements are in place for consent, audit and clinical governance”.

Furthermore, the Scottish Intercollegiate Guidelines Network's clinical guideline on "Control of pain in adults with cancer" (2008) stated that "Patients with bone pain from pelvic bone metastases proving difficult to control by pharmacological means and reduced mobility should be considered for percutaneous cementoplasty".

Intracept System (Intra-Osseous Basivertebral Nerve Ablation) for the Treatment of Low Back Pain

Becker and colleagues (2017) noted that lumbar axial back pain arising from degenerative disc disease continues to be a challenging clinical problem whether treated with non-surgical management, local injection, or motion segment stabilization and fusion. These researches determined the efficacy of intra-osseous basi-vertebral nerve (BVN) ablation (Intracept System, Relievant Medsystems, Inc, Redwood City, CA) for the treatment of chronic lumbar back pain. Patients meeting pre-defined inclusion or exclusion criteria were enrolled in a study using RF energy to ablate the BVN within the vertebral bodies adjacent to the diagnosed level. Patients were evaluated at 6 weeks, and 3, 6, and 12 months post-operatively. A total of 17 patients with chronic, greater than 6 months, LBP unresponsive to at least 3 months of conservative care were enrolled; 16 patients were treated successfully following screening using MRI finding of Modic type I or II changes and positive confirmatory discography to determine the affected levels. The treated population consisted of 8 men and 8women; the mean age was 48 years (34 to 66 years). Self-reported outcome measures were collected prospectively at each follow-up interval. Measures included the ODI, VAS score, and SF-36. Mean baseline ODI of the treated cohort was 52 ± 13, decreasing to a mean of 23 ± 21 at 3 months follow-up ($p < 0.001$). The statistically significant improvement in ODI observed at 3 months was maintained through the 12-month follow-up. The mean baseline VAS score decreased from 61 ± 22 to 45 ± 35 at 3 months follow-up ($p < 0.05$), and the mean baseline physical component summary increased from 34.5 ± 6.5 to 41.7 ± 12.4 at 3 months follow-up ($p = 0.03$). The authors concluded that ablation of the BVN for the treatment of chronic LBP significantly improved patients' self-reported outcome early in the follow-up period; the improvement persisted throughout the 1-year study period. It should be noted that this was an industry-sponsored study; it was a small (n = 17) with a relatively short-term follow-up (12 months).

In a prospective, randomized, double-blind, sham-controlled, multi-center study, Fischgrund and associates (2018) evaluated the safety and efficacy of RFA of the BVN for the treatment of CLBP in a FDA-approved IDE trial. The BVN has been shown to innervate endplate nociceptors which are thought to be a source of CLBP. A total of 225 patients diagnosed with CLBP were randomized to either a sham (78 patients) or treatment (147 patients) intervention. The mean age within the study was 47 years (range of 25 to 69) and the mean baseline ODI was 42. All patients had type I or type II Modic changes of the treated vertebral bodies. Patients were evaluated pre-operatively, and at 2 weeks, 6 weeks and 3, 6 and 12 months post-operatively. The primary end-point was the comparative change in ODI from baseline to 3 months. At 3 months, the average ODI in the treatment-arm decreased 20.5 points, as compared to a 15.2 point decrease in the sham-arm. In the intention-to-treat population, the difference in change in ODI (the prespecified primary endpoint) between subjects assigned to intraosseous basivertebral nerve ablation and subjects assigned to sham treatment was not statically significantly different ($p = 0.109$) ($p = 0.019$, per-protocol population). A responder analysis based on ODI decrease of greater than or equal to 10 points showed that 75.6% of patients in the treatment-arm as compared to 55.3% in the sham-arm exhibited a clinically meaningful improvement at 3 months. The authors concluded that patients treated with RFA of the BVN for CLBP exhibited significantly greater improvement in ODI at 3 months and a higher responder rate than sham-treated controls. They stated that BVN ablation represents a potential minimally invasive treatment for the relief of CLBP. These researchers stated that the ability in the SMART trial to distinguish the active treatment from the sham treatment suggested that ablation of the BVN has therapeutic value, although the overall pain response in a given patient is a complex function of the combined effects of placebo and treatment. However, it is unclear why the 3-month follow-up was chosen as the primary end-point. Could it be that ODI questionnaire between the treatment and sham groups were non-significant at 6- and 12-month post-operatively. The least squares mean (LSM) improvement in VAS in the treatment-arm was 2.97, 3.04, and 2.84 cm at 3, 6, and 12 months, respectively. The LSM improvement in VAS in the sham-arm was 2.36, 2.08, and 2.08 cm at 3, 6, and 12 months, respectively. There were no difference between the 2

groups at 3 months; however, the differences between the 2 groups attained statistical significance at 6 and 12 months (clinical significant of these differences was unclear).

Fischgrund et al (2019) reported the 2-year clinical outcomes for chronic low back pain (CLBP) patients treated with radiofrequency (RF) ablation of the basi-vertebral nerve (BVN) in a randomized controlled trial that previously reported 1-year follow-up. A total of 147 patients were treated with RF ablation of the BVN in a randomized controlled trial designed to demonstrate safety and efficacy as part of a Food and Drug Administration (FDA)-Investigational Device Exemption (IDE) trial. Evaluations, including patient self-assessments, physical and neurological examinations, and safety assessments, were performed at 2 and 6 weeks, and 3, 6, 12, 18, and 24 months post-operatively. Participants randomized to the sham control arm were allowed to cross-over to RF ablation at 12 months. Due to a high rate of cross-over, RF ablation treated participants acted as their own control in a comparison to baseline for the 24-month outcomes. Clinical improvements in the Oswestry Disability Index (ODI), visual analog scale (VAS), and the Medical Outcomes Trust Short-Form Health Survey Physical Component Summary were statistically significant compared to baseline at all follow-up time points through 2 years. The mean percent improvements in ODI and VAS compared to baseline at 2 years were 53.7 and 52.9%, respectively. Responder rates for ODI and VAS were also maintained through 2 years with patients showing clinically meaningful improvements in both: ODI greater than or equal to 10-point improvement in 76.4% of patients and ODI greater than or equal to 20-point improvement in 57.5%; VAS greater than or equal to 1.5 cm improvement in 70.2% of patients. The authors concluded that patients treated with RF ablation of the BVN for CLBP exhibited sustained clinical benefits in ODI and VAS and maintained high responder rates at 2 years following treatment. They stated that basi-vertebral nerve ablation appeared to be a durable, minimally invasive treatment for the relief of CLBP. This was an extension study (2-year follow-up) of their earlier study that provided 1-year follow-up (Fischgrund et al, 2018).

In a prospective, single-arm, open-label study, Truumees et al (2019) examined the effectiveness of intraosseous RF ablation of the BVN for the treatment of vertebrogenic-related CLBP in typical spine practice

settings using permissive criteria for study inclusion (n = 28). Consecutive patients with CLBP of at least 6 months duration and with Modic Type 1 or 2 vertebral endplate changes between L3 and S1 were treated with RF ablation of the BVN in up to 4 vertebral bodies. The primary end-point was patient-reported change in ODI from baseline to 3 months post-procedure. Secondary outcome measures included change in VAS, SF-36, EQ-5D-5L, and responder rates. Median age was 45 years; baseline ODI was 48.5; VAS was 6.36; 75% of the study patients reported LBP symptoms for greater than or equal to 5 years; 25% were actively using opioids; and 61% were previously treated with injections. Mean change in ODI at 3 months post-treatment was - 30.07 + 14.52 points ($p < 0.0001$); mean change in VAS was - 3.50 + 2.33 ($p < 0.0001$); 93% of patients achieved a greater than or equal to 10-point improvement in ODI, and 75% reported greater than or equal to 20-point improvement. The authors concluded that minimally invasive RF ablation of the BVN demonstrated a significant improvement in pain and function in this population of real-world patients with chronic vertebrogenic-related LBP.

The authors stated that potential limitations to generalizability include the use of research coordinators, a medical monitor, and a defined pre-screening process. However, pure effectiveness trials are nearly impossible to perform without some research infra-structure to promote population homogeneity and ensure data quality. Additional potential criticisms may include the relatively small sample (n = 28) and short follow-up (3 months) for the primary end-point. However, durability of the 3-month results up to 24 months has been established previously, and these researchers will continue to collect longer term outcomes as a part of this study.

Khalil et al (2019) noted that current literature suggests that degenerated or damaged vertebral end-plates are a significant cause of CLBP that is not adequately addressed by standard care. Prior 2-year data from the treatment arm of a sham-controlled randomized controlled trial (RCT) showed maintenance of clinical improvements at 2 years following RF ablation of BVN. In a prospective, parallel, open-label RCT conducted at 20 U.S. sites, these researchers compared the effectiveness of intraosseous RF ablation of the BVN to standard care for the treatment of CLBP in a specific subgroup of patients suspected to have vertebrogenic related symptomatology. A total of 140 patients with CLBP of at least 6

months duration, with Modic Type 1 or 2 vertebral end-plate changes between L3 to S1, were randomized 1:1 to undergo either RF ablation of the BVN or continue standard care; ODI was collected at baseline, 3, 6, 9, and 12-months post-procedure. Secondary outcome measures included a 10-point VAS for LBP, ODI and VAS responder rates, SF-36, and EQ-5D-5L. The primary end-point was a between-arm comparison of the mean change in ODI from baseline to 3 months post-treatment. Patients were randomized 1:1 to receive RF ablation or to continue standard care. Self-reported patient outcomes were collected using validated questionnaires at each study visit. An interim analysis to evaluate for superiority was pre-specified and overseen by an independent data management committee (DMC) when a minimum of 60% of patients had completed their 3-month primary end-point visit. The interim analysis showed clear statistical superiority ($p < 0.001$) for all primary and secondary patient-reported outcome measures in the RF ablation arm compared to the standard care arm. This resulted in a DMC recommendation to halt enrollment in the study and offered early cross-over to the control arm. These results were comprised of the outcomes of the 104 patients included in the intent-to-treat (ITT) analysis of the 3-month primary end-point, which included 51 patients in the RF ablation arm and 53 patients in the standard care arm. Baseline ODI was 46.1, VAS was 6.67, and mean age was 50 years. The percentage of patients with LBP symptoms greater than or equal to 5 years was 67.3%. Comparing the RF ablation arm to the standard care arm, the mean changes in ODI at 3 months were -25.3 points versus -4.4 points, respectively, resulting in an adjusted difference of 20.9 points ($p < 0.001$). Mean changes in VAS were -3.46 versus -1.02, respectively, an adjusted difference of 2.44 cm ($p < 0.001$). In the RF ablation arm, 74.5% of patients achieved a greater than 10-point improvement in ODI, compared with 32.7% in the standard care arm ($p < 0.001$). The authors concluded that minimally invasive RF ablation of the BVN led to significant improvement of pain and function at 3-months in patients with chronic vertebrogenic related LBP.

The authors stated that limitations of this study included the use of a non-structured standard care control and open label design. In addition, industry funding is a potential source of study bias. This report only provided short-term 3-month outcomes from the planned interim analysis and long-term results from the complete study cohort are underway. Although this study was designed to collect longer-term data from both

randomized groups, a review of the study results from the planned interim analysis led to the independent DMC's recommendation to halt enrollment and offered early cross-over to patients in the standard care group. It was noted that the Informed Consent regulations and the Declaration of Helsinki require that study participants be advised of any new information from the study that may impact their willingness to continue, and the results of the interim analysis would have such an impact, especially on the control group. Ultimately, the DMC determined that is was not ethical to continue the control arm, and that further enrollment into the treatment arm was not needed. As a result, follow-up will be limited in the standard care patients in the final analysis to results collected up to the point of cross-over or study exit. Further follow-up of the treatment arm patients for 5 years is underway as a single arm study, and control subjects that elected to cross-over to treatment are being followed at 3 and 6 months post-procedure. Finally, another important limitation of this study was a lack of generalizability to the broader CLBP population who did not meet the strict clinical and radiographic criteria of this study.

Fischgrund et al (2020) reported on the 5-year outcomes of the U.S. treated patients in the active treatment arm of the aformentioned study. Of the 117 US treated patients 100 (85%) were available for review with a mean follow-up of 6.4 years (5.4-7.8 years). Mean ODI score improved from 42.81 to 16.86 at 5-year follow-up, a reduction of 25.95 points ($p < 0.001$). Mean reduction in VAS pain score was 4.38 points (baseline of 6.74, $p < 0.001$). In total, 66% of patients reported a > 50% reduction in pain, 47% reported a > 75% reduction in pain, and 34% of patients reported complete pain resolution. Composite responder rate using thresholds of ≥ 15-point ODI and ≥ 2-point VAS for function and pain at 5 years was 75%. The current study is the 5-year follow-up of subjects assigned to intraosseous basivertebral nerve ablation (Fischgrund, et al., 2020). This study, however, does not include a comparison group. Because the study was not able to demonstrate statistically significant differences between the active treatment and control groups during the randomized portion of the study for the prespecified primary endpoint, change in ODI at 3 months, in subjects as randomized, conclusions about the effectiveness of this procedure cannot be reached.

Markman et al (2020) hypothesized that CLBP patients reporting reduced opioid use have superior functional outcomes following RF ablation (RFA) of the BVN. This post-hoc analysis from a sham-controlled trial examined short-acting opioid use from baseline through 1 year. Opioid use was stratified into 3 groups by 2 blinded external reviewers. Two-sample t-tests were used to compare ODI and VAS measurements between those patients who increased or decreased their opioid usage compared to baseline. Actively treated patients with decreased opioid use at 12 months had a mean ODI improvement of 24.9 ± 16.0 (n = 27) compared to 7.3 ± 9.8 (n = 18) for patients reporting increased opioid use ($p < 0.001$). In the sham-arm, the improvements in ODI were 17.4 ± 16.1 (n = 19) and 1.2 ± 14.3 (n = 5; $p = 0.053$) for the patients reporting decreased versus increased opioid usage, respectively. Actively treated patients reporting decreased opioid use had a mean improvement in VAS of 3.3 ± 2.5 (n = 27) compared to 0.6 ± 1.8 (n = 18) for patients reporting increased opioid use ($p < 0.001$). In the sham-arm, the improvements in VAS were 2.5 ± 2.6 (n = 19) and 1.4 ± 1.9 (n = 5; $p = 0.374$) for patients reporting decreased versus increased opioid use, respectively. The authors concluded that subjects undergoing BVN ablation who decreased opioid use had greater improvement in ODI and VAS scores compared with those reporting increased opioid usage. There was an association between functional benefit from BVN ablation and reduced opioid use. Moreover, these researchers stated that the findings of this study suggested that the ability to lower or eliminate opioid usage through a minimally invasive surgical procedure may represent an important improvement to the treatment armamentarium for CLBP and warrants further investigation. It should also be noted that this study was funded by Relievant Medsystems; and 3 of the co-authors (Drs. Fischgrund, Rhyne, and Vajkoczy) had a consulting relationship with the study's device manufacturer.

The authors stated that this post-hoc analysis had several drawbacks. Opioid use was monitored using self-reported patient questionnaires, asking about the past week's dosage, which relied on patient recall. Patients receiving long-acting opioid therapy for CLBP were excluded from the protocol, which may account for the relatively low baseline opioid usage in the study population; however, most patients taking opioids for CLBP are treated with short-acting opioids. This sub-analysis sample size was relatively small, with 77 total patients in the active and sham

treatment groups taking opioids at the time of enrollment, which may have limited the ability to detect differences using inferential analyses for some end-point measures. Furthermore, whereas analyses of opioid sparing effects and outcomes followed the pre-specified outcomes and analyses of the trial protocol statistical analysis plan, this sub-analysis was not pre-planned and was executed after database lock and unblinding, potentially introducing bias.

The International Society for the Advancement of Spine Surgery's guideline on "Intraosseous ablation of the basivertebral nerve for the relief of chronic low back pain" (Lorio et al, 2020) stated that intraosseous ablation of the BVN is a new procedure; its limitations included industry funding is a potential source of study bias for the available data reviewed, limited number of studies, short-term follow-up for the majority of studied patients, and unknown effect on the primary degenerative process.

The International Society for the Advancement of Spine Surgery's guideline on "Intraosseous ablation of the basivertebral nerve for the relief of chronic low back pain" (Lorio et al, 2020) provided the following information:

Intraosseous ablation of the BVN from the L3 through S1 vertebrae may be considered medically indicated for individuals with CLBP when all the following criteria are met:

- CLBP of at least 6 months duration,
- Failure to respond to at least 6 months of non-surgical management, and
- MRI-demonstrated Modic change 1 (MC1) or Modic change 2 (MC20 in at least 1 vertebral endplate at 1 or more levels from L3 to S1

Intraosseous ablation of the BVN is a new procedure not previously performed. As such, this procedure currently should be reported with Current Procedural Terminology 22899 (unlisted procedure, spine).

Limitations:

- Industry funding is a potential source of study bias for the available data reviewed.
- Limited number of studies.
- Short-term follow-up for the majority of studied patients.
- Unknown effect on the primary degenerative process.

Tieppo Francio et al (2020) noted that intervertebral disc degeneration has historically been the etiological target of chronic LBP; however, disc degeneration is not necessarily directly associated with pain, and many other anatomical structures are potential etiologies. The vertebral endplates have been postulated to be a source of vertebral pain, where these endplates become particularly susceptible to increased expression of nociceptors and inflammatory proliferation carried by the BVN, expressed on diagnostic imaging as Modic changes. This is useful diagnostic information that could aid physicians to phenotype a subset of LBP, which is known as vertebral pain, in order to directly target interventions, such as BVN ablation, to this significant pain generator. In this review, these investigators examined the safety, efficacy, and the rationale behind the use of BVN ablation for the treatment of vertebral pain. Their current literature review of available up-to-date publications using BVN ablation in the treatment of vertebral pain suggested that there is limited, but moderate-quality evidence that this is an effective intervention for reduction of disability and improvement in function, at short- and long-term follow-up, in addition to limited moderate-quality evidence that BVN RFA is superior to conservative care for pain reduction, at least at 3-month follow-up. The authors concluded that there is a highly clinical and statistically significant treatment effect of BVN ablation for vertebral pain with clinically meaningful benefits in pain reduction, functional improvements, opioid dose reduction, and improved quality of life (QOL). There were no reported device-related patient deaths or serious AEs based on the available literature. They stated that BVN ablation is a safe, well-tolerated and clinically beneficial intervention for vertebral pain, when proper patient selection and surgical/procedural techniques are applied. Moreover, these researchers stated that additional non-industry funded, high-quality research and perhaps a more generalizable patient population is needed to confirm these findings.

The authors stated that according to the constraints of their review, there were only 15 studies published to-date on the subject matter. Among these, 2 were directly supported by industry funding, which increased the risk of publication bias. This study was a review of the literature following the PRISMA guidelines and summarizing a quality appraisal table of published literature, including RCTs, systematic reviews, observational studies and narrative reviews. From a statistical standpoint, this study reviewed each finding from each study published to-date and described these statistics in detail, including primary outcomes, estimates, sample size, authors, publication year/journal, follow-up, etc. Although the methodology followed the PRISMA guidelines, this study had limitations and was not a systematic review. Again, there were only 15 studies to review, which satisfied the inclusion and exclusion criteria. It is always prudent to comment on the limitations of generalizability in such a setting. Furthermore, this review examined 3 different technical approaches, by many different physicians, from different backgrounds, with presumably differing amounts of experience with the procedure itself. Therefore, a high level of heterogeneity was introduced. Most importantly, the only commentary that could truly be pulled from this review was subject to the selection criteria from which the patients were selected in each study. While BVN RFA may prove to be a successful treatment, these researchers could only comment on its success as it related to the rigid selection criteria upon which the foundational studies were completed. Any extrapolation of these findings to a differing patient population should be considered experimental and not supported by the data discussed in this review. Again, these investigators urged readers to be cognizant that while there has yet to be a study published to-date on the amount of patients who may qualify for BVN RFA via the selection criteria described in the Fischgrund or Khalil studies in general practice, but there is an inherent understanding among spine providers that the percent of patients who meet such a rigid criteria for treatment is likely low in clinical practice.

Markman et al (2020) tested the hypothesis that chronic LBP patients reporting reduced opioid use have superior functional outcomes following BVN RFA. This post-hoc analysis from a sham-controlled trial examined short-acting opioid use from baseline through 1 year. Opioid use was stratified into 3 groups by 2 blinded external reviewers. Two-sample t-tests were used to compare ODI and VAS measurements between those

patients who increased or decreased their opioid usage compared to baseline. Actively treated patients with decreased opioid use at 12 months had a mean ODI improvement of 24.9 ± 16.0 (n = 27) compared to 7.3 ± 9.8 (n = 18) for patients reporting increased opioid use ($p < .001$). In the sham-arm, the improvements in ODI were 17.4 ± 16.1 (n = 19) and 1.2 ± 14.3 (n = 5; $p = 0.053$) for the patients reporting decreased versus increased opioid usage, respectively. Actively treated patients reporting decreased opioid use had a mean improvement in VAS of 3.3 ± 2.5 (n = 27) compared to 0.6 ± 1.8 (n = 18) for patients reporting increased opioid use ($p < 0.001$). In the sham-arm, the improvements in VAS were 2.5 ± 2.6 (n = 19) and 1.4 ± 1.9 (n = 5; $p = 0.374$) for patients reporting decreased vs increased opioid use, respectively. The authors concluded that subjects undergoing BVN ablation who decreased opioid use had greater improvement in ODI and VAS scores compared with those reporting increased opioid usage. There was an association between functional benefit from BVN ablation and reduced opioid use. Moreover, these researchers stated that the findings of this study suggested that the ability to lower or eliminate opioid usage via a minimally invasive surgical procedure may represent an important improvement to the treatment armamentarium for chronic LBP and warrants further investigation.

The authors stated that this post-hoc analysis had several limitations. Opioid use was monitored using self-reported patient questionnaires, asking about the past week's dosage, which relied on patient recall. Patients receiving long-acting opioid therapy for chronic LBP were excluded from the protocol, which may account for the relatively low baseline opioid usage in the study population; however, most patients taking opioids for chronic LBP were treated with short-acting opioids. This sub-analysis sample size was relatively small, with 77 total patients in the active and sham treatment groups taking opioids at the time of enrollment, which may have limited the ability to detect differences using inferential analyses for some endpoint measures. Furthermore, whereas analyses of opioid sparing effects and outcomes followed the pre-specified outcomes and analyses of the trial protocol statistical analysis plan, this sub-analysis was not pre-planned and was executed after database lock and unblinding, potentially introducing bias.

Urits et al (2021) stated that chronic LBP affects a significant portion of patients worldwide and is a major contributor to patient disability; however, it is a difficult problem to diagnose and treat. The prevailing model of chronic LBP has presumed to follow a discogenic model, but recent studies have shown a vertebrogenic model that involves the basivertebral nerve (BVN). Radiofrequency (RF) ablation of the BVN has emerged as a possible non-surgical therapy for vertebrogenic LBP. These investigators provided a comprehensive review of vertebrogenic pain diagnosis and the current understanding of BVN ablation as treatment. The authors concluded that reproducible large randomized controlled trials (RCTs) are still needed for clinicians to gain full confidence in using this treatment in practice. Additionally, further research is needed on the anatomy of the vertebrae to optimize the method of treatment. These studies can help to elucidate the role of RF ablation in the management of CLBP and improve the quality of life of CLBP patients in the near future.

In a systematic review, Conger et al (2021) examined the effectiveness of intraosseous basivertebral nerve radiofrequency (RF) neurotomy for the treatment of chronic LBP with type 1 or 2 Modic changes. Subjects were individuals aged greater than 18 years with chronic LBP with type 1 or 2 Modic changes; and they underwent intraosseous basivertebral nerve radiofrequency neurotomy. The primary outcome of interest was the proportion of individuals with greater than or equal to 50 % pain reduction. Secondary outcomes included greater than or equal to 10-point improvement in function as measured by Oswestry Disability Index (ODI) as well as greater than or equal to 2-point reduction in pain score on the visual analog scale (VAS) or numeric rating scale (NRS), and decreased use of pain medication. Three reviewers independently assessed publications before May 15, 2020 in Medline and Embase and the quality of evidence was examined using the Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) framework. Of the 725 publications screened, 7 studies with 321 subjects were included in the final analysis. The reported 3-month success rate for greater than or equal to 50 % pain reduction ranged from 45 % to 63 %. Rates of functional improvement (greater than or equal to 10-point ODI improvement threshold) ranged from 75 % to 93 %. For comparison to sham treatment, the relative risk (RR) of treatment success defined by greater than or equal to 50 % pain reduction and greater than or equal to

10-point ODI improvement was 1.25 (95 % confidence interval [CI]: 0.88 to 1.77) and 1.38 (95 % CI: 1.10 to 1.73), respectively. For comparison to continued standard care treatment the RR of treatment success defined by greater than or equal to 50 % pain reduction and greater than or equal to 10-point ODI improvement was 4.16 (95 % CI: 2.12 to 8.14) and 2.32 (95 % CI: 1.52 to 3.55), respectively. The authors concluded that there is moderate-quality evidence that suggested this procedure is effective in reducing pain and disability in patients with chronic LBP who are selected based on type 1 or 2 Modic changes, among other inclusion and exclusion criteria used in the published literature to date. These researchers stated that success of the procedure appeared to be dependent on effective targeting of the BVN. Moreover, they stated that non-industry funded high-quality, large prospective studies are needed to confirm these findings.

Smuck et al (2021) noted that vertebral endplates, innervated by the BVN, are a source of chronic LBP correlated with Modic changes. A randomized trial comparing BVN ablation to standard care (SC) recently reported results of an interim analysis. In a prospective, open-label RCT, these investigators reported the results of the full randomized trial, including the 3-month and 6-month between-arm comparisons, 12-month treatment arm results, and 6-month outcomes of BVN ablation in the former SC arm. This trial of BVN ablation versus SC was carried out in 23 U.S. sites with follow-up at 6 weeks, 3, 6, 9, and 12 months; SC patients were re-baselined and followed-up for 6 months following BVN ablation. The primary endpoint was the between-arm comparison of mean Oswestry Disability Index (ODI) change from baseline; secondary endpoints were visual analog scale (VAS), Short Form (SF-36), EuroQual Group 5 Dimension 5-Level Quality of Life (EQ-5D-5L), responder rates, and rates of continued opioid use. A total of 140 were randomized. Results from BVN ablation (n = 66) were superior to SC (n = 74) at 3 months for the primary endpoint (mean ODI reduction, difference between arms of -20.3 (confidence interval [CI]: -25.9 to -14.7 points; $p < 0.001$)), VAS pain improvement (difference of -2.5 cm between arms (CI: -3.37 to -1.64, $p < 0.001$)) and quality of life (QOL) outcomes. At 12 months, BVN ablation demonstrated a 25.7 ± 18.5 points reduction in mean ODI ($p < 0.001$), and a 3.8 ± 2.7 cm VAS reduction ($p < 0.001$) from baseline, with 64 % demonstrating greater than or equal to 50 % reduction and 29 % pain-free. Similarly, the former SC patients who elected BVN ablation (92

%) demonstrated a 25.9 ± 15.5 point mean ODI reduction ($p < 0.001$) from baseline. The proportion of opioid use did not change in either group ($p = 0.56$). The authors concluded that BVN ablation demonstrated significant improvements in pain and function over SC, with treatment results sustained through 12 months in patients with chronic LBP of vertebrogenic origin. Moreover, these researchers stated that this is not a treatment for all chronic LBP patients as these findings were limited to a subset of patients with vertebrogenic chronic LBP who met the study's strict clinical and radiographic criteria.

The authors stated that this study had several drawbacks. Despite robust improvements in pain, no significant differences in opioid use were observed at 6-month follow-up. While surprising on the surface, this was common in studies of populations with chronic pain. Many effective chronic pain interventions, such as spinal cord stimulation, fail to demonstrate reduction in opioid use. This disconnect between pain reduction and opioid use highlighted the known complexity of factors driving opioid use, beyond changes in pain. Accordingly, longer-term follow-up may be needed to observe changes in opioid behaviors as demonstrated by a secondary analysis of data from the previous sham-controlled RCT of BVN ablation that showed opioid reduction in the subgroup reporting improvements in pain during long-term follow-up. Additional drawbacks included the potential sources of bias, such as the non-structured SC control, the open-label design, and industry funding. Another important drawback of this study was a lack of generalizability to the broader chronic LBP population given the strict clinical and radiographic criteria.

Koreckija et al (2021) noted that vertebral endplates, innervated by the basivertebral nerve, can be a source of vertebrogenic LBP when damaged with inflammation, visible as types 1 or 2 Modic changes. A RCT compared basivertebral nerve ablation (BVNA) to standard care (SC) showed significant differences between arms at 3- and 6-month follow-up. At 12 months, significant improvements were sustained for BVNA. These investigators reported results of the BVNA arm at 24-months. This was a continual report of a prospective, open-label, single-arm, follow-up of the BVNA treatment arm of a RCT in 20 U.S. sites with visits at 6 weeks, 3, 6, 9, 12 and 24 months. Paired comparisons to baseline were made for the BVNA arm at each time-point for ODI, VAS,

SF-36, EQ-5D-5L, and responder rates. A total of 140 patients were randomized, 66 to BVNA. In the 58 BVNA patients completing a 24-month visit, 67 % had back pain for greater than 5 years, 36 % were actively taking opioids at baseline, 50 % had prior epidural steroid injections, and 12 % had prior low back surgery. Improvements in ODI, VAS, SF-36 PCS, and EQ-5D-5L were statistically significant at all time-points through 2 years. At 24 months, ODI and VAS improved 28.5 ± 16.2 points (from baseline 44.5; $p < 0.001$) and 4.1 ± 2.7 cm (from baseline 6.6; $p < 0.001$), respectively. A combined responder rate of ODI greater than or equal to 15 and VAS greater than or equal to 2 was 73.7 %. A greater than or equal to 50 % reduction in pain was reported in 72.4 % of patients and 31.0 % were pain-free at 2 years. At 24 months, only 3 (5 %) of patients had BVNA-level steroid injections, and 62 % fewer patients were actively taking opioids. There were no serious device or device-procedure related AEs reported through 24 months. The authors concluded that intraosseous BVNA demonstrated an excellent safety profile and significant improvements in pain, function, and QOL that are sustained through 24 months in patients with chronic vertebrogenic LBP.

The authors stated that drawbacks of this study included potential sources of bias, such as an open-label design, industry-funding, and a non-structured standard care control. Multiple processes were implemented in this RCT to limit any potential selection or results bias in this industry-funded study including an independent medical monitor confirming inclusion of a primary vertebrogenic population, 3rd-party monitoring of source data, the independent adjudication of events and interventions by the clinical event committee, and data analysis by a 3rd-party statistical firm and reporting overseen the independent data management committee. Results of this study were consistent with 12-month results for a non-industry funded single-arm study of intraosseous BVNA compared to SC. Furthermore, although this study population was derived from a RCT, there may have been a nocebo effect in this study where it was impossible to blind patients to their treatment, and closer observation and management of patients when participating in a research study may have led to an enhanced treatment effect. However, these investigators noted that an open-label study design is acceptable in a post-market environment where the treatment effect has previously been demonstrated in comparison to a sham procedure, and treatment

outcomes have remained consistent across studies and through long-term follow-up; further suggesting that improvements are largely due to the intervention.

Kim et al (2021) noted that paraspinal muscle spasm caused by pain from a lumbar degenerative disc is frequently examined in patients with LBP; RFA surgery could alleviate paraspinal muscle spasms. In a prospective, single-center study, these researchers carried out RFA surgery on the high-intensity zone (HIZ) and hypersensitive sinuvertebral nerve (SVN) and BVN to examine its outcome. The paravertebral muscle cross-sectional area (CSA) was measured on magnetic resonance imaging (MRI) before and after surgery to evaluate the effect of RFA surgery on the paravertebral muscle. This comparative study was carried out on 2 different uni-portal spinal endoscopic surgery groups; 23 patients who underwent RFA surgery for chronic discogenic LBP and 45 patients who underwent posterior decompression surgery for lumbar spinal stenosis with 12 months of follow-up. Paravertebral muscle CSA, Schiza grade, Modic type, and HIZ size were measured on pre- and post-operative MRI. An endoscopic video review was performed to evaluate the presence of intra-operative twitching and grade the degree of epidural neovascularization and adhesion; VAS, modified ODI, ODI and MacNab's criteria were evaluated for outcome measures. Intra-operative endoscopic video evaluation showed neovascularization and adhesion adjacent to the disc and pedicle. In the RFA surgery group, there were 7 patients (30.43 %) with grade-2 and 16 (69.57 %) with grade-3 neovascularization; intra-operative twitching was observed in 19 out of 23 patients (82.61 %). After performing an RFA on the SVN and BVN for the treatment of discogenic LBP, the results showed significant improvement in pain and disability scores . The mean CSA of the paraspinal muscle in the RFA surgery group was significantly increased after surgery at the L4 to L5 and L5 to S1 levels (L4 to L5: 3,901 ± 1,096.7 mm^2 to 4,167 ± 1,052.1 mm^2, p = 0.000; L5 to S1: 3,059 ± 968.5 mm^2 to 3,323 ± 1,046.2 mm^2, p = 0.000) compared to pre-operative CSA. The authors concluded that hypersensitive SVN and BVN were strongly associated with epidural neovascularization with adhesion and the pathological pain pathway in degenerative disc disease. Epidural neovascularization with adhesion reflected aberrant neurological connections, which were associated with reflex inhibitory mechanisms of the multifidus muscle, which induced spasm. RFA treatment of the region of epidural neovascularization with

adhesion effectively treated chronic discogenic LBP and could induce paraspinal muscle spasm release. This study was limited by its small sample size (n = 23 I the RFA surgery group) and relatively short-term follow-up (12 months).

The authors stated that this study has several drawbacks. First, the study populations were not homogeneous in age, gender, pathology, or number of patients; thus, the results may not have represented the actual difference between these 2 patient groups. Second, to reduce modification to the minimum, the CSA was assessed by carefully outlining the muscle mass, excluding fat and fibrous tissue external to the muscle fascia, and measuring the average value from 2 consecutive slices. Although value modification was minimized in this way, it could not be excluded entirely. Third, the study did not show changes in the entire lumbar paravertebral muscle, because only the L4 to L5 and L5 to S1 levels were included. These researchers stated that a larger prospective trial with 3D muscle reconstruction using specific software (Muscl' X or custom software) should be carried out to measure the entire muscle volume. Fourth, the changed muscle observed after surgery may not have been permanent. These investigators noted that despite these drawbacks, this trial was meaningful as a 1st step to find an aberrant pathway between the hypersensitive SVN, BVN, and paraspinal muscles, especially the multifidus.

Koreckija et al (2021) noted that vertebral endplates, innervated by the BVN, can be a source of vertebrogenic LBP when damaged with inflammation, visible as types 1 or 2 Modic changes. A RCT compared BVN ablation (BVNA) to standard care (SC) showed significant differences between arms at 3- and 6-month follow-up. At 12 months, significant improvements were sustained for BVNA. These investigators reported results of the BVNA arm at 24-months. This was a continual report of a prospective, open-label, single-arm, follow-up of the BVNA treatment arm of a RCT in 20 U.S. sites with visits at 6 weeks, 3, 6, 9, 12 and 24 months. Paired comparisons to baseline were made for the BVNA arm at each time-point for ODI, VAS, SF-36, EQ-5D-5L, and responder rates. A total of 140 patients were randomized, 66 to BVNA. In the 58 BVNA patients completing a 24-month visit, 67 % had back pain for greater than 5 years, 36 % were actively taking opioids at baseline, 50 % had prior epidural steroid injections, and 12 % had prior low back

surgery. Improvements in ODI, VAS, SF-36 PCS, and EQ-5D-5L were statistically significant at all time-points through 2 years. At 24 months, ODI and VAS improved 28.5 ± 16.2 points (from baseline 44.5; $p < 0.001$) and 4.1 ± 2.7 cm (from baseline 6.6; $p < 0.001$), respectively. A combined responder rate of ODI greater than or equal to 15 and VAS greater than or equal to 2 was 73.7 %. A greater than or equal to 50 % reduction in pain was reported in 72.4 % of patients and 31.0 % were pain-free at 2 years. At 24 months, only 3 (5 %) of patients had BVNA-level steroid injections, and 62 % fewer patients were actively taking opioids. There were no serious device or device-procedure related AEs reported through 24 months. The authors concluded that intraosseous BVNA demonstrated an excellent safety profile and significant improvements in pain, function, and QOL that are sustained through 24 months in patients with chronic vertebrogenic LBP.

The authors stated that drawbacks of this study included potential sources of bias, such as an open-label design, industry-funding, and a non-structured standard care control. Multiple processes were implemented in this RCT to limit any potential selection or results bias in this industry-funded study including an independent medical monitor confirming inclusion of a primary vertebrogenic population, 3rd-party monitoring of source data, the independent adjudication of events and interventions by the clinical event committee, and data analysis by a 3rd-party statistical firm and reporting overseen the independent data management committee. Results of this study were consistent with 12-month results for a non-industry funded single-arm study of intraosseous BVNA compared to SC. Furthermore, although this study population was derived from a RCT, there may have been a nocebo effect in this study where it was impossible to blind patients to their treatment, and closer observation and management of patients when participating in a research study may have led to an enhanced treatment effect. However, these investigators noted that an open-label study design is acceptable in a post-market environment where the treatment effect has previously been demonstrated in comparison to a sham procedure, and treatment outcomes have remained consistent across studies and through long-term follow-up; further suggesting that improvements are largely due to the intervention.

In a review on the current evidence and future directions of “Intraosseous basivertebral nerve radiofrequency ablation for the treatment of vertebral body endplate low back pain”, Michalik et al (2021) stated that BVN-RFA appeared to be an effective treatment for a subset of patients with CLBP and evidence of Modic change types 1 and 2 in the L3 to S1 VEPs who have failed to respond to conservative treatment. However, all studies performed to-date have been industry sponsored, and future non-industry-funded trials are needed to confirm these findings.

In a systematic review with single-arm meta-analysis, Conger et al (2022a) provided an estimate of the effectiveness of BVN RFA for the treatment of vertebrogenic LBP. Subjects were persons aged 18 years or older with chronic LBP associated with type 1 or 2 Modic changes. Interventions included sham, placebo procedure, active standard care treatment, or none. Outcome measures included the proportion of patients treated with BVN RFA who reported 50 % or greater pain score improvement on a VAS or numeric rating scale (NRS). The main secondary outcome was 15-point or higher improvement in ODI score. A total of 3 reviewers independently examined articles published before December 6, 2021, in Medline and Embase. The Grades of Recommendation, Assessment, Development, and Evaluation (GRADE) framework was used to assess the overall quality of evidence. Of the 856 unique records screened, 12 publications met the inclusion criteria, representing 6 unique study populations, with 414 subjects allocated to receive BVN RFA. Single-arm meta-analysis showed a success rate of 65 % (95 % confidence interval [CI] 51 % to 78 %) and 64 % (95 % CI: 43 % to 82 %) for 50 % or greater pain relief at 6 and 12 months, respectively. Rates of 15-point or higher ODI score improvement were 75 % (95 % CI: 63 % to 86 %) and 75 % (95 % CI: 63 % to 85 %) at 6 and 12 months, respectively. The authors concluded that according to GRADE, there was moderate-quality evidence that BVN RFA effectively reduced pain and disability in most patients with vertebrogenic LBP. Moreover, these researchers stated that further high-quality studies are needed to improve the understanding of the effectiveness of this procedure.

The authors stated that there were important limitations to this review and for the existing literature related to BVN RFA. First, randomized controlled trial (RCTs), although not without their own limitations, continue to represent the gold-standard study design in medical research. Despite

the growing interest in the treatment of vertebrogenic LBP, the present updated review found no new RCTs examining BVN RFA compared with sham or any other treatment. Second, the majority of studies that met the inclusion criteria were supported by industry funding. When the evidence for treatment came entirely from industry-funded studies, there is an increased risk for bias given the inherent conflict of interest, limiting the publication of negative results. However, it is notable that results from 2 independently performed studies showed similarly high proportions of patients reporting clinically significant pain relief and functional improvement up to 12 months after BVN RFA. This review was supported by an investigator-initiated research grant from Relievant Medsystems, which produced a device frequently used for BVN RFA. However, the sponsor had no role in the design or conduct of the review or approval of the final manuscript. The protocol, search, data extraction, and statistical analysis were all developed and performed independently without input or oversight from the sponsor.

Conger et al (2022b) provided the following information:

- Accumulated damage to the discovertebral complex may result in chemical and mechanical sensitization of endplate nocioceptors resulting in chronic vertebrogenic LBP;
- Midline LBP, pain exacerbation by physical activity, sitting, and forward flexion are factors associated with treatment success after BVN RFA;
- In appropriately selected patients, BVN RFA results in substantial reduction in pain and disability in the majority of those treated at 12 months, with similar long-term outcomes at 5 years;
- The presence of MC1 or MC2 is currently the best radiographic indicator of vertebrogenic pain. Outcomes after BVN RFA are not impacted by the volume of MC, location of MC, degree of disc degeneration, or presence/size of endplate defects. Patients with MC1 versus MC2 experience similar rates of success after BVN RFA;
- Clinicians are encouraged to select patients for BVN RFA based upon the clinical and radiographic criteria used in published studies to date.

Moreover, these investigators stated that exploration of clinical, imaging, or other characteristics associated with vertebrogenic LBP may enable further progress in patient selection for BVN RFA. Enhanced diagnostics to isolate the source(s) of pain and further differentiate annular pain from vertebrogenic pain, such as MR spectroscopy and novel MRI sequences such as IDEAL and UTE may also be of value. Evidence suggested a correlation between MC and increased endplate metabolic activity as detected by Single Positron Emission Computed Tomography (SPECT/CT) or bone scintigraphy, but further study is needed to examine whether or not such findings are suggestive of vertebrogenic pain. Early research in serum biomarkers linked to vertebrogenic pain appeared promising. Finally, objective monitoring of real-life physical performance using wearables recently demonstrated the ability to identify kinematic and behavioral markers of spine disease. Ongoing investigation in these areas may lead to more accurate phenotypes of Vertebrogenic LBP and influence treatment paradigms.

Schnapp et al (2022) stated that chronic LBP is a leading cause of disability worldwide and its pathophysiology remains poorly understood, a problem exacerbated by the heterogeneity of the patient population with chronic LBP. Although the intervertebral discs are often implicated in chronic LBP, studies have demonstrated strong innervation of the vertebral endplates by the BVN; thus, making it a possible target for ablation in the treatment of vertebra-genic chronic LBP. These investigators examined the available evidence on the safety and effectiveness of BVN ablation as a therapeutic modality for chronic LBP; and discussed the possible study biases and gaps in the current knowledge to provide insight on future research. This study was carried out in accordance with the following 5-stage methodological framework for scoping reviews: (i) identifying the research question; (ii) identifying relevant studies; (iii) selecting studies; (iv) charting the data; and (v) collating, summarizing and reporting the results. A total of 3 databases (PubMed, Web of Science, Embase) were searched using the keywords "basivertebral", "nerve", and "ablation". From March 2002 to March 2022, a total of 47 articles were identified, of which 12 were included in this scoping review. The authors concluded that current research has shown that BVN ablation might be a promising treatment for chronic LBP in patients exhibiting Modic type 1 or 2 endplate changes, while additional research on the association between Modic changes and LBP is still

needed to gain widespread use and acceptance of this new treatment modality. The introduction of new devices and a larger number of independent studies would greatly enhance the confidence in the outcomes reported with this treatment modality in order to ultimately benefit patients, clinicians, and society.

The authors stated that this study had several drawbacks. First, a very specific chronic pain population is typically utilized for this intervention. The inclusion criteria leave many who experience chronic LBP ineligible for the procedure. Second, study demographics need to be more diversified to truly represent the chronic LBP population. Third, there was a lack of true control groups due to high cross-over rates in published studies. Fourth, very few high-level or long-term studies have been published. Fifth, funding for many of the studies published on the subject was industry-led. With an already limited amount of published research, a need for out-of-industry funding is required to avoid any possibility of bias.

Boody et al (2022) stated that multiple studies have shown the safety and effectiveness of basivertebral nerve radiofrequency ablation (BVN RFA) for improving low back pain (LBP) related to the vertebral endplate; however, the influence of patient demographic and clinical characteristics on treatment outcome is unknown. In a retrospective study, these investigators carried out a pooled cohort study of 3 clinical trials of patients with vertebral endplate pain identified by Type 1 and/or Type 2 Modic changes and a correlating presentation of anterior spinal element pain. This study entailed 33 global study centers with patients (n = 296) successfully treated with BVN RFA. Participant demographic and clinical characteristics were analyzed with stepwise logistic regression to identify predictors of treatment success. Three definitions of treatment success were defined: (i) 50 % or greater visual analog scale (VAS) pain improvement, (ii) 15-point or more Oswestry Disability Index (ODI) improvement, and (iii) 50 % or more VAS or 15-point or more ODI improvement from baseline. Low back pain of 5 years or more duration and higher ODI scores at baseline increased the odds of treatment success, whereas baseline opioid use and higher Beck Depression Inventory (BDI) scores reduced these odds. However, the 3regression models demonstrated receiver-operating characteristics (ROC) of 62 % to70 % areas under the curve (AUC); therefore, limiting predictive

capacity. The authors concluded that this analysis identified no demographic or clinical characteristic that meaningfully increased or reduced the odds of treatment success from BVN RFA. On the basis of these findings and the high response rates from the 3 analyzed trials, these investigators recommended the use of objective imaging biomarkers (Type 1 and/or 2 Modic changes) and a correlating presentation of anterior spinal element pain to determine optimal candidacy for BVN RFA.

The authors stated that this study had several drawbacks. First, despite a robust retrospective analysis of available demographic and clinical characteristics derived from the prior clinical trials, the potential effect of unknown confounding variables affecting the results cannot be determined. Second, 5 subjects were missing ODI or VAS outcomes data and thus could not be included in the analysis. However, the proportion of missing baseline or outcomes variables was small, and these investigators did not believe that this influenced the present findings. Third, the creation of a more lenient model (lower p value thresholds for inclusion of variables into the predictive model) might have identified more predictive factors. Nevertheless, model thresholds and responder definitions were designed for clinical relevance to support treatment decisions.

McCormick et al (2022a) developed pain location "maps" and examined the relationship between LBP-exacerbating activities and treatment response to BVN RFA in patients with clinically suspected vertebral endplate pain (VEP). These researchers carried out an aggregated cohort study of 296 patients treated with BVN RFA at 33 centers in 3 prospective trials. Participant demographics, pain diagrams, and LBP-exacerbating activities were analyzed for predictors using stepwise logistic regression. Treatment success definitions were: (i) 50 % or greater VAS, (ii) 15-point or higher ODI, and (iii) 50 % or greater VAS or 15-point or higher ODI improvements at 3 months post-BVN RFA. Midline LBP correlated with BVN RFA treatment success in individuals with clinically-suspected VEP. Duration of pain 5 years or more (odds ratio [OR] 2.366), lack of epidural steroid injection within 6 months before BVN RFA (OR 1.800), lack of baseline opioid use (OR 1.965), LBP exacerbation with activity (OR 2.099), and a lack of LBP with spinal extension (OR 1.845) were factors associated with increased odds of

treatment success. Regressions AUCs were under 70 %, indicative of low predictive value. The authors concluded that this study showed that midline LBP correlated with BVN RFA treatment success in individuals with VEP. While none of the regression models demonstrated strong predictive value, the pain location and exacerbating factors identified in this analysis may aid clinicians in identifying patients where VEP should be more strongly suspected. The use of objective imaging biomarkers (Type 1 and/or 2 Modic changes) and a correlating presentation of anterior spinal element pain remain the most useful patient selection factors for BVN RFA.

The authors stated that a strength of this analysis was that all patients were part of a prior clinical trial with similar inclusion/exclusion criteria for a more homogenous population of primary VEP for discerning predictive pain characteristics of BVN RFA. However, this was also a limitation because the cohort did not entirely reflect an LBP population with mixed etiologies. Furthermore, the predictive model was limited to the variables collected in the trials; thus, unknown predictive variables may exist. Finally, these findings represented associations but not causation.

McCormick et al (2022b) examined associations between endplate and motion segment magnetic resonance imaging (MRI) characteristics and treatment outcomes following BVN RFA in patients with clinically suspected VEP. These researchers carried out an aggregated cohort study of 296 participants treated with BVN RFA from 3 prospective clinical trials. Baseline MRI characteristics were analyzed using stepwise logistic regression to identify factors associated with treatment success. Predictive models used 3 definitions of treatment success: (i) 50 % or greater LBP VAS, (ii) 15-point or higher ODI, and (iii) 50 % or greater VAS or 15-point or higher ODI improvements at 3-months post-BVN RFA. The presence of lumbar facet joint fluid (OR 0.586) reduced the odds of BVN RFA treatment success in individuals with clinically suspected VEP. In patients with a less advanced degenerative disc disease (DDD) profile, a greater than 50 % area of the endplate with bone marrow intensity changes (BMIC) was predictive of treatment success (OR 4.689). Both regressions AUCs were under 70 %, indicating low predictive value. All other vertebral endplate, intervertebral disc, nerve roots facet joint, spinal segmental alignment, neuroforamina, lateral recesses, and central canal MRI characteristics were not associated with BVN RFA success. The

authors concluded that in patients with vertebrogenic LBP with Modic changes, the presence of degenerative findings of the anterior and posterior column was not associated with a clinically important impact on BVN RFA treatment success. None of the models demonstrated strong predictive value, indicating that the use of objective imaging biomarkers (Type 1 and/or 2 Modic changes) and a correlating presentation of pain remain the most useful patient selection factors for BVN RFA.

The authors stated that this study had 2 main drawbacks. First, the potential impact of blinding differences between the 3 studies (1 study being double- blinded and 2 studies being open-label) needs to be considered. To evaluate this, individual study regressions were conducted and compared to the aggregate results. While there were differences in variables that met the final stepwise regression model inclusion, there were no notable differences in overall regression findings for predictors of BVN RFA treatment success or failure for VEP. Second, the exploratory nature of this study without pre-specified hypotheses that were powered due to the set sample of the prior clinical studies that was available. These researchers retrospectively examined the statistical power and found ORs of 1.5 and 2.0 to have a fairly low power (about 22 % to 53 %), but those of 2.5 and higher had power of at least 85 %, and as high at 88 % when the OR was 3.0. Therefore, if the effect of the candidate variables was fairly large, there was good power to detect it. Variables that had only a small effect on the probability of response were unlikely to be detected, but usually would be of less clinical interest. Given that the overall prediction was modest, it was likely that some important predictors such as the psychological components of pain, were not included as candidates with this retrospective study and a restricted data set.

It should be noted that the studies by Boody et al (2022) and McCormick et al (2022a and 2022b) reported the same patient populations.

Huang et al (2022) noted that LBP is one of the most prevalent musculoskeletal ailments in the U.S. Intraosseous RFA of the BVN is an effective and durable therapy for LBP and can be offered to patients who have chronic LBP of greater than 6 months of duration, failure to respond

to non-invasive therapies for 6 months, with either Modic Type I or Type II changes at L3 to S1. The authors reviewed the anatomy and physiology, patient selection, technique, and evidence regarding BVN ablation.

The International Society for the Advancement of Spine Surgery's policy statement on "intraosseous basivertebral nerve ablatio" (Lorio et al, 2022) states that "Intraosseous ablation of the BVN is supported by a basic and clinical evidence foundation, including a systematic review; a level-I, sham-controlled RCT, a second level-I RCT against standard conservative management, 3 single group prospective studies and a post hoc secondary analysis. Outcome data > 5 years (mean 6.4 years) following a single BVNA procedure suggest the durability of the treatment effect".

The ISASS policy statement notes that intraosseous ablation of the BVN from the L3 through S1 vertebrae may be considered medically indicated for individuals with CLBP when All of the following criteria are met:

- CLBP of at least 6-month duration;
- Failure to respond to at least 6 months of non-surgical management;
- Magnetic resonance imaging-demonstrated* MC1 or MC2 in at least 1 vertebral endplate at 1 or more levels from L3 to S1 (*Endplate changes, inflammation, edema, disruption, and/or fissuring);
- Fibrovascular bone marrow changes (hypointense signal for Modic type 1);
- Fatty bone marrow changes (hyperintense signal for Modic type 2).

BVNA is NOT indicated in the following:

- Patients with severe cardiac or pulmonary compromise;
- Presence of implanted pulse generator(s) (e.g., pacemaker and defibrillator)/electronic implants except for circumstances where a specific patient safety precaution may be implemented;
- Co-existence of other obvious radiographic etiology for patient's axial CLBP requiring a medically necessary surgical intervention;
- Active or chronic infection -- systemic or local;
- Patients who are pregnant;

- Skeletally immature patients (generally age less than 18 years);
- Current or post-trauma, tumor, infection, or poor bone quality compromising vertebral pedicle/body;
- Cauda equina syndrome defined as neural compression causing neurogenic bowel or bladder dysfunction;
- Radiographic confirmation of gross spinal instability including angular or translatory instability (grade 2 or greater spondylolisthesis) at index level(s);
- Morbid obesity precluding satisfactory procedural imaging;
- Targeted ablation zone is less than 10 mm away from a sensitive structure not intended for ablation;
- Situation where unintended tissue damage may result based on the clinical assessment by the physician;
- Application with electrosurgical instruments NOT tested and specified for use with the current FDA clearance for the relevant Requests for Designation.

The American Society of Pain and Neuroscience's best practice guidelines on "The diagnosis and treatment of vertebrogenic pain with basivertebral nerve ablation" (Sayed et al, 2022) states that chronic LBP (CLBP) is a worldwide leading cause of pain and disability. Degenerative disc disease has been the presumptive etiology in the majority of cases of CLBP. More recent study and treatments have discovered that the vertebral endplates play a large role in CLBP in a term defined as vertebrogenic back pain. As the vertebral endplates are highly innervated via the BVN, this has resulted in a reliable target in treating patients suffering from vertebrogenic LBP (VLBP). The application of BVN ablation for patients suffering from VLBP is still in its early stages of adoption and integration into spine care pathways. BVN ablation is grounded in a solid foundation of both pre-clinical and clinical evidence. With the emergence of this therapeutic option, the American Society of Pain and Neuroscience (ASPN) identified the need for formal evidence-based guidelines for the proper identification and selection of patients for BVN ablation in patients with VLBP. ASPN formed a multi-disciplinary work group tasked to examine the available literature and form best practice guidelines on this subject. Based on the United States Preventative Task Force (USPSTF) criteria for grading evidence, gave BVN ablation Level A grade evidence with high certainty that the net benefit is substantial in appropriately selected individuals. The authors

concluded that BVNA represents a promising treatment for patients suffering from chronic LBP of a vertebrogenic nature. As LBP is known to arise from numerous etiologies, careful diagnosis and patient selection for those with vertebrogenic pain as the primary source of symptomatology is vital for optimal outcomes. Current evidence supports long-term improvement in pain and function in properly selected patients for BVNA. The ASPN best practice guidelines for BVNA provides guidance to clinicians for appropriate, effective, and safe implementation of BVNA into clinical practice. The ASPN BVN guidelines are intended to be a living document with updated guidelines published at appropriate intervals in the future.

Furthermore, an UpToDate review on “Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment” (Chou, 2022) does not mention Intracept / intra-osseous basivertebral nerve ablation as a management / therapeutic option.

Intradiscal Injections of Notochordal Cell-Derived Matrix for the Treatment of Intervertebral Disc Disease

Bach and colleagues (2018) noted that the socioeconomic burden of chronic back pain related to intervertebral disc (IVD) disease is high and current treatments are only symptomatic. Minimally invasive strategies that promote biological IVD repair should address this unmet need. Notochordal cells (NCs) are replaced by chondrocyte-like cells (CLCs) during IVD maturation and degeneration. The regenerative potential of NC-secreted substances on CLCs and mesenchymal stromal cells (MSCs) has already been demonstrated. However, identification of these substances remains elusive. These researchers examined the regenerative NC potential by using healthy porcine NC-derived matrix (NCM) and used the dog as a clinically relevant translational model. NCM increased the glycosaminoglycan and DNA content of human and canine CLC aggregates and facilitated chondrogenic differentiation of canine MSCs in-vitro. Based on these results, NCM, MSCs and NCM+MSCs were injected in mildly (spontaneously) and moderately (induced) degenerated canine IVDs in-vivo and, after 6 months of treatment, were analyzed. NCM injected in moderately (induced) degenerated canine IVDs exerted beneficial effects at the macroscopic and MRI level, induced collagen type II-rich extracellular matrix production, improved the disc

height, and ameliorated local inflammation. MSCs exerted no (additive) effects. The authors concluded that NCM induced in-vivo regenerative effects on degenerated canine IVDs. They stated that NCM may, comparable to demineralized bone matrix in bone regeneration, serve as “instructive matrix”, by locally releasing growth factors and facilitating tissue repair. Thus, intradiscal NCM injection could be a promising regenerative treatment for IVD disease, circumventing the cumbersome identification of bioactive NC-secreted substances. These investigators noted that this was the 1st study that showed that intradiscally injected NCM could potentially be a promising treatment for human and canine IVD disease, by harnessing the NC regenerative and anti-inflammatory potential, and circumventing the challenging identification of bioactive NC-secreted factors. This approach should be feasible in light of the wide clinical application of demineralized bone matrix within the bone regeneration field. They stated that future studies should focus on removal of nucleic acid from NCM, and the mechanism of NCM-mediated regeneration.

Spinal Fusion for Bertolotti’s Syndrome

The cause of LBP with Bertolotti's syndrome (chronic, persistent LBP and radiographically diagnosed transitional lumbar vertebra) remains controversial, and various treatments such as local injection of anesthetic and/or steroid, RF coagulation, surgical resection, and spinal fusion have been reported. Santavirta and colleagues (1993) surgically treated 16 patients with Bertolotti's syndrome; 8 had posterolateral fusion and another 8 resection of the transitional articulation; 13 patients had in addition to the chronic LBP, suffered from repeated episodes or chronic sciatica. In 6 cases with resection treatment, local injections were administered at the transitional articulation before deciding for resection of the transitional joint; each patient reported transient relief of pain, while this pre-operative test did not correlate with successful outcome of treatment; 6 patients had to be treated with 2nd operations; 10 of the 16 operatively treated patients showed improvement of the LBP, and this result was similar in the group treated with fusion and in that treated with resection; 7 had no LBP at follow-up, and the improvement according to the Oswestry pain scale was similar in the 2 groups, and statistically significant; 11 patients still had persisting episodes of sciatica (versus 13 pre-operatively). The average disability according to the Oswestry total

disability scale was 30%, corresponding with moderate outcome, and both operatively treated groups did equally well. At follow-up the 1st disc above the fused segments was found to be degenerated in 7 out of 8 cases, and in the group treated with resection the 1st disc above the transitional vertebra was degenerated in 5 cases.

Li and co-workers (2014) noted that Bertolotti's syndrome consists of LBP caused by lumbosacral transitional vertebrae (LSTVs) and LSTV-associated biomechanical spinal changes. There is a lack of consensus regarding the cause, clinical significance, and treatment of this condition. These investigators characterized the clinical presentation of patients with Bertolotti's syndrome and described a minimally invasive surgical treatment for this condition. A total of 7 patients who underwent minimally invasive para-median tubular-based resection of the LSTV for Bertolotti's syndrome were identified over the course of 5 years. Diagnosis was based on patient history of chronic LBP, radiographic findings of LSTV, and pain relief on trigger-site injection with steroid and/or anesthetics. Electronic medical records were reviewed to identify demographics, operative data, and outcomes. All patients presented with severe, chronic LBP lasting an average of 8 years that was resistant to non-operative care. At presentation, 6 (86%) of 7 patients experienced radicular pain that was ipsilateral to the LSTV. Radiographic evidence showed a presence of LSTV in all patients on the left (43%), right (29%), or bilaterally (29%). Degenerative disc changes at the L4 to L5 level immediately above the anomalous LSTV were observed in 6 of 7 (86%) patients; these changes were not observed at the level below the LSTV. Following pseudo-joint injection, all patients experienced temporary relief of their symptoms. All patients underwent a minimally invasive, para-median tubular-based approach for resection of the LSTV; 3 (43%) of 7 patients reported complete resolution of LBP, 2 (29%) of 7 patients had reduced LBP, and 2 patients (29%) experienced initial relief but return of LBP at 1 and 4 years post-operatively; 3 (50%) of the 6 patients with radicular pain had complete relief of this symptom. The median follow-up time was 12 months. No intra-operative complication was reported; 2 (29%) of 7 patients developed post-operative complications including 1 with a wound hematoma and another with new L5 radiculopathy that resolved 2 years after surgery. The authors concluded that diagnosis of Bertolotti's syndrome should be considered with adequate patient history, imaging studies, and diagnostic injections. A minimally invasive surgical

approach for resection of the LSTV was presented here for symptomatic treatment of select patients with Bertolotti's syndrome whose conditions were refractory to conventional therapy and who had pain that could be attributed to the LSTV. Several short-term complications were noted with this procedure, but overall this procedure is effective for treating symptoms related to Bertolotti's syndrome.

Jancuska and colleagues (2015) stated that LSTV are increasingly recognized as a common anatomical variant associated with altered patterns of degenerative spine changes. These researchers focused on the clinical significance of LSTV, disruptions in normal spine biomechanics, imaging techniques, diagnosis, and treatment. A PubMed search using the specific key words "LSTV", "lumbosacral transitional vertebrae" and "Bertolotti's Syndrome" was performed. The resulting group of manuscripts from this search was evaluated. LSTV were associated with alterations in biomechanics and anatomy of spinal and para-spinal structures, which have important implications on surgical approaches and techniques. LSTV were often inaccurately detected and classified on standard antero-posterior (AP) radiographs and MRI. The use of whole-spine images as well as geometric relationships between the sacrum and lumbar vertebra increase accuracy. Uncertainty regarding the cause, clinical significance, and treatment of LSTV persists. Some authors suggested an association between LSTV types II and IV and LBP. Pseudo-articulation between the transverse process and the sacrum creates a "false joint" susceptible to arthritic changes and osteophyte formation potentially leading to nerve root entrapment. The diagnosis of symptomatic LSTV was considered with appropriate patient history, imaging studies, and diagnostic injections. A positive radionuclide study along with a positive effect from a local injection helped distinguish the transitional vertebra as a significant pain source. Surgical resection is reserved for a subgroup of LSTV patients who fail conservative treatment and whose pain is definitively attributed to the anomalous pseudo-articulation. The authors noted that the literature contains a total of 43 cases of surgical intervention for symptomatic LSTV; 27 patients were treated with resection, 8 underwent fusion, 6 patients were treated for far-out syndrome, and the remaining 2 cases involved surgical intervention for extraforaminal nerve root impingement or pain contralateral to the LSTV. Only Santavirta et al (1993) compared the surgically treated patients to a conservative treatment control group. The results of surgical

treatment were only slightly better. The authors of these cases advocated for operative treatment of Bertolotti's syndrome in very select patients whose refractory pain is definitively attributed to the transitional vertebrae. The authors concluded that given the paucity of evidence, further investigations with larger patient cohorts and longer follow-up are needed to better understand the association between the anomalous transverse process and LBP that occurred with LSTV and to better demonstrate the effectiveness of surgical intervention.

Holm and co-workers (2017) noted that Bertolotti's syndrome refers to the possible association between the congenital malformation LSTV and LBP. Several treatments have been proposed including steroid injections, resections of the LSTV, laminectomy, and lumbar spinal fusion. These researchers compared the clinical outcomes in previous trials and case reports for these treatments in patients with LBP and LSTV. A PubMed search was conducted. These investigators included English studies of patients diagnosed with LSTV treated with steroid injection, laminectomy, spinal fusion or resection of the transitional articulation. Of 272 articles reviewed, 20 met the inclusion criteria. Their level of evidence were graded I to V and the clinical outcomes were evaluated. Only 1 study had high evidence level (II). The remainders were case series (level IV). Only 5 studies used validated clinical outcome measures. A total of 79 patients were reported: 31 received treatment with steroid injections, 33 were treated with surgical resection of the LSTV, 8 received lumbar spinal fusion, and 7 cases were treated with laminectomy. Surgical management appeared to improve the patient's symptoms, especially patients diagnosed with "far out syndrome" treated with laminectomy. Clinical outcomes were more heterogenetic for patient's treated with steroid injections. The literature regarding Bertolotti's syndrome is sparse and generally with low evidence. Non-surgical management (e.g., steroid injections) and surgical intervention could not directly be compared due to lack of standardization in clinical outcome. Generally, surgical management appeared to improve patient's clinical outcome over time, whereas steroid injection only improved the patient's symptoms temporarily. The authors concluded that further studies with larger sample size and higher evidence are needed for the clinical guidance in the treatment of Bertolotti's syndrome.

Discseel Procedure (Regenerative Spine Procedure) for the Treatment of Back Pain

According to Discseel, the Discseel procedure supposedly can repair one's damaged spinal disc, using an FDA-approved biologic fibrin, allowing patients to avoid risky spinal fusions and discectomies. This is possible because the fibrin is able to repair and seal damaged spinal disc, where spine surgery, including spinal fusions, can't. During the Disceel procedure, the physician will inject fibrin into the damaged disc, which will seal the disc. The entire procedure is observed through live x-rays.

In a retrospective, observational, pilot study, Kirchner and Anitua (2016) examined the clinical outcome of plasma rich in growth factors (PRGF-Endoret) infiltrations (1 intradiscal, 1 intra-articular facet, and 1 transforaminal epidural injection) under fluoroscopic guidance-control in patients with chronic LBP. A total of 86 patients with a history of chronic LBP and DDD of the lumbar spine who met inclusion and exclusion criteria were recruited between December 2010 and January 2012; 1 intradiscal, 1 intra-articular facet, and 1 transforaminal epidural injection of PRGF-Endoret (fibrin was embedded with a pool of growth factors) under fluoroscopic guidance-control were carried out in 86 patients with chronic LBP in the operating theater setting. Descriptive statistics were performed using absolute and relative frequency distributions for qualitative variables and mean values and standard deviations for quantitative variables. The non-parametric Friedman statistical test was used to determine the possible differences between baseline and different follow-up time-points on pain reduction after treatment. Pain assessment was determined using a VAS at the 1st visit before (baseline) and after the procedure at 1, 3, and 6 months. The pain reduction after the PRGF-Endoret injections showed a statistically significant drop from 8.4 ± 1.1 before the treatment to 4 ± 2.6, 1.7 ± 2.3, and 0.8 ± 1.7 at 1, 3, and 6 months after the treatment, respectively, with respect to all the time evaluations ($p < 0.0001$) except for the pain reduction between the 3rd and 6th month whose signification was lower ($p < 0.05$). The analysis of the VAS over time showed that at the end-point of the study (6 months), 91% of patients showed an excellent score, 8.1% showed a moderate improvement, and 1.2% were in the inefficient score. The authors concluded that fluoroscopy-guided infiltrations of intervertebral discs and

facet joints with PRGF in patients with chronic LBP resulted in significant pain reduction assessed by VAS. One of the keywords in this study was fibrin matrix.

The authors stated that this study had several drawbacks. The absence of a control (placebo) group in this study was certainly a limitation. There were other weaknesses in this study as to these researchers did not perform a previous diagnostic block for patients' selection, and thus, their diagnosis and selection of patients relied on a careful clinical examination. Another drawback to this study was the lack of measurement of physical activity levels before and after the treatment. Last but not the least, to limit the bias of a single assessment, the self-reported VAS pain scale should have been associated with other health survey questionnaires, which encompassed pain and functional evaluation. These researchers stated that in the light of several limitations of this trial, a RCT is considered imperative.

Furthermore, UpToDate reviews on "Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment" (Chou, 2019a), "Subacute and chronic low back pain: Nonsurgical interventional treatment" (Chou, 2019b), and "Subacute and chronic low back pain: Surgical treatment" (Chou, 2019c) do not mention fibrin injection as a therapeutic option.

Intramuscular Steroid Injection for the Treatment of Neck Pain

In a meta-analysis, Nouged and colleagues (2019) examined the effectiveness of local anesthetic trigger-point injections in adults with myofascial pain syndrome (MPS) in the head, neck, and shoulder regions compared to dry needling, placebo, and other interventions; RCTs using local anesthetic injections in adults diagnosed with MPS were included, and searches were conducted in the Cochrane Library, Medline via PubMed, Web of Science and Embase. The initial search strategy yielded 324 unduplicated references up to April 1, 2018. A total of 15 RCTs were included, with 884 adult patients diagnosed with MPS. Meta-analysis showed a significant improvement in VAS pain scale of 1.585 units at 1 to 4 weeks in the local anesthetic group compared to the dry needling group ($p = 0.020$). However, when only including double-blinded studies, the effect was not statistically significant ($p = 0.331$). There was also a

significant improvement in pain of 0.767 units with local anesthetic at 2 to 8 weeks compared to placebo (p = 0.007). No statistically significant differences were found in other secondary outcomes between local anesthetic and all other interventions. The authors concluded that although local anesthetics provided a significant improvement in pain compared to dry needling, evidence was of low quality, and sensitivity analyses including only double-blinded studies provided no statistically significant difference, and that additional studies are needed to confirm these findings.

An UpToDate reviews on “Treatment and prognosis of cervical radiculopathy” (Robinson and Kothari, 2019) does not mention intramuscular steroid injection as a therapeutic option.

Furthermore, an UpToDate review on “Treatment of neck pain” (Isaac, 2019) states that “Routine use of corticosteroid should be discouraged due to its propensity to cause local muscle necrosis”.

Anterior Lumbar Interbody Fusion (ALIF) for Degenerative Disk Disease / Back Pain

Rao et al (2015) stated that there is limited information on clinical outcomes after anterior lumbar interbody fusion (ALIF) based on the indications for surgery. In a prospective, clinical study, these researchers compared the clinical and radiological outcomes of ALIF for each surgical indication. This trail included 125 patients who underwent ALIF over a 2-year period. Patients were examined pre-operatively and post-operatively. Outcome measures included the Short Form-12 (SF-12), Oswestry disability index (ODI), visual analog scale (VAS) and patient satisfaction index (PSI). After a mean follow-up of 20 months, the clinical condition of the subjects was significantly better than their pre-operative status across all indications. A total of 108 patients had a PSI score of 1 or 2, indicating a successful clinical outcome in 86 %. Patients with degenerative disk disease (DDD) with and without radiculopathy, spondylolisthesis, and scoliosis had the best clinical response to ALIF, with statistically significant improvement in the SF-12, ODI, and VAS. Failed posterior fusion and adjacent segment disease showed statistically significant improvement in all of these clinical outcome scores, although the mean changes in the SF-12 Mental Component Summary, ODI, and

VAS (back pain) were lower. The overall radiological fusion rate was 94.4 %. Superior radiological outcomes (fusion of greater than 90 %) were observed in patients with DDD with and without radiculopathy, spondylolisthesis, and failed posterior fusion, whereas in adjacent segment disease, it was 80 %. The authors concluded that ALIF was an effective treatment for DDD with and without radiculopathy and spondylolisthesis. Moreover, these researchers stated that although results were promising for scoliosis, failed posterior fusion, and adjacent segment disease, further studies are needed to establish the effectiveness of ALIF in these conditions.

Mobbs et al (2015) noted that degenerative disc and facet joint disease of the lumbar spine is common in the aging population, and is one of the most frequent causes of disability. Lumbar spondylosis may result in mechanical back pain, radicular and claudicating symptoms, reduced mobility and poor quality of life (QOL). Surgical interbody fusion of degenerative levels is a therapeutic option to stabilize the painful motion segment, and may provide indirect decompression of the neural elements, restore lordosis and correct deformity. The surgical options for interbody fusion of the lumbar spine include: posterior lumbar interbody fusion (PLIF), transforaminal lumbar interbody fusion (TLIF), minimally invasive transforaminal lumbar interbody fusion (MI-TLIF), oblique lumbar interbody fusion/anterior to psoas (OLIF/ATP), lateral lumbar interbody fusion (LLIF) and ALIF. The indications may include: discogenic/facetogenic low back pain (LBP), neurogenic claudication, radiculopathy due to foraminal stenosis, lumbar degenerative spinal deformity including symptomatic spondylolisthesis and degenerative scoliosis. In general, traditional posterior approaches are frequently used with acceptable fusion rates and low complication rates, however they are limited by thecal sac and nerve root retraction, along with iatrogenic injury to the para-spinal musculature and disruption of the posterior tension band. Minimally invasive (MIS) posterior approaches have evolved in an attempt to reduce approach related complications. Anterior approaches avoid the spinal canal, cauda equina and nerve roots, however have issues with approach-related abdominal and vascular complications. Furthermore, lateral and OLIF techniques have potential risks to the lumbar plexus and psoas muscle. These investigators comprehensively reviewed the available literature and evidence for different LIF techniques. They proposed a set of recommendations and guidelines for

the indications for interbody fusion options. In addition, these researchers provided a description of each approach, and showed the potential benefits and disadvantages of each technique with reference to indication and spine level performed.

The authors stated that disadvantages of the ALIF technique include approach-related complications such as retrograde ejaculation, visceral and vascular injury. They also noted that there were multiple limitations in this systematic review. Some studies reported ALIF and TLIF combined with posterolateral fusion, thus skewing the potential fusion results and outcomes. Furthermore, studies revealed a heterogeneous patient population, with different levels and pathologies reported that impacted radiological fusion rates and clinical outcomes; thus, the conclusions could not be made regarding the effects of different levels and pathologies on clinical outcomes. These researchers stated that ALIF, TLIF and PLIF remain the more commonly performed techniques for LIF; LLIF has established its place as a robust technique for deformity correction and interbody fusion, with OLIF requiring further studies and data to establish its place. Moreover, these researchers also stated that available data suggested that anterior techniques are superior to posterior in terms of disc height restoration, lumbar lordosis and deformity correction, and that clinical outcomes and fusion rates were similar to those in posterior techniques; however, these data were based on heterogeneous studies with multiple indications and therefore comparison was difficult to make.

Vieli et al (2019) noted that as a possible therapeutic option for chronic lower back pain (CLBP) due to single-level DDD, the efficacy of ALIF has been reviewed various times in the existing literature. However, a scarcity of data exists pertaining to ALIF procedures performed in a short-stay setting using an Enhanced Recovery after Surgery (ERAS) protocol, especially concerning the safety. These investigators examined prospectively collected data to study the safety and efficacy of short-stay ERAS ALIF in treatment of single-level DDD; VAS in both back and leg pain along with the ODI were used to collect measure outcomes. The primary end-point was a minimum clinically important difference (MCID) of greater than or equal to 30 % for the ODI at 12 months. A total of 44 patients underwent surgery after failed long-term conservative treatment; MCID was achieved in 78 %. Age was the only significant factor in

association with MCID (p = 0.03), while gender, Modic changes, results of prognostic tests, prior surgery and smoking status had no significant influence on either MCID or change scores for any outcome measure. One complication in the form of transient new radiculopathy occurred in 1 patient (2.3 %). The authors concluded that with overall positive outcomes in terms of both safety and efficacy, an ALIF procedure with subsequent implementation of an ERAS protocol in a short-stay setting could be an option for strictly selected patients with CLBP. Moreover, these researchers stated that further study, possibly with a larger sample size, is needed to validate these findings.

The authors stated that this study was largely limited by the small sample size (n = 44) and partly incomplete data, which resulted in low statistical power. Furthermore, although this was not the focus of this study, the finding pertaining to prognostic factors may be less powerful due to the low sample size, and the one statistically significant finding may have been arrived at by multiple testing. However, all data were derived from a prospective registry. All procedures were conducted in a single-center, which may have led to further bias. The results may not be applicable to all treatment groups since the subjects were already highly selected on the grounds of a positive Pantaloon Cast Test, and hence the analysis regarding patient-reported outcomes only concerned subsets of the general surgical population. In a similar manner, these findings might not be applicable to older adults, since the data-set did not include patients over the age of 62 years.

Shah et al (2019) stated that lumbar spinal stenosis is defined as narrowing of the lumbar spinal canal, which causes compression of the spinal cord and nerves. Spinal stenosis could cause leg pain and potentially back pain that can affect the QOL. Ultimately, surgical decompression is needed to alleviate the symptoms. In this review, these investigators used several important studies to compare lumbar laminectomy alone versus lumbar laminectomy and fusion. They also compared the effectiveness of more novel surgical approaches, stand-alone ALIF, and stand-alone LLIF. These techniques have their own advantages and disadvantages in which many factors must be taken into account before choosing a surgical approach. Furthermore, the patient's anatomy and pathology, lifestyle, and desires should be analyzed to help determine the ideal surgical strategy. These researchers stated that there

have not been many studies regarding stand-alone ALIF surgery for lumbar stenosis; however, since the advances in interbody cages, it has shown very promising results.

AnchorKnot Tissue Approximation Kit for Lumbar Discectomy

The AnchorKnot Tissue Approximation Kit (Anchor Orthopedics XT Inc., Burlington, MA) was developed to augment the existing standard of care for herniated disc repair procedures. The AnchorKnot Tissue Approximation Kit may be considered for patients undergoing herniated disc repair procedures if the surgeon identifies that the tissue is amenable to repair. This procedure may not be appropriate for all patients, and not all patients may benefit. However, there is a lack of evidence regarding the clinical effectiveness of the AnchorKnot Tissue Approximation Kit for any indication.

DiscoGel (Intradiscal Alcohol Injection) for the Treatment of Back and Neck Pain

de Seze et al (2013) noted that sciatica is a common disease; between 13 % and 40 % of the general population will experience at least 1 episode of sciatica due to spinal disc herniation and nerve root irritation. In some specialist centers, percutaneous intradiscal techniques can be applied as an intermediate measure between conservative treatment and surgery, with a view to avoiding the AEs associated with surgical discectomy. DiscoGel is a percutaneously implanted medical device for the treatment of lumbar sciatica due to a herniated disc. These researchers performed an open, prospective, observational study to examine if the prior use of air disc manometry could limit the risk of nerve root irritation reportedly associated with nucleolysis and administration of DiscoGel, and examine the technique's safety and efficacy. A total of 79 DiscoGel-treated patients were systematically reviewed. A nurse anesthetist examined each patient's pain levels during the procedure itself. The therapist evaluated the patient on inclusion and 8 weeks after the DiscoGel procedure. A 3rd assessment was based on a telephone interview (by an independent assessor) at least 4 months after the procedure. Pain levels immediately after the DiscoGel procedure (1.7 ± 2.0) were markedly lower than before the procedure (5.5 ± 2.3); there were no complications. Two months after DiscoGel administration, the

initial pain level had fallen by an average of 74 ± 34 %. The outcome was quite stable over time (mean follow-up of 8 months). At the end of the follow-up period, 60.7 % of the patients were pain-free, 76 % considered the treatment outcome to be good or very good, 74 % had returned to work and 76 % would recommend the treatment to a friend. The authors concluded that the favorable outcomes associated with the procedure should now be confirmed in a controlled trial.

Sayhan et al (2018) stated that radiopaque gelified ethanol (RGE; DiscoGel, Gelscom SAS, France) is used as a chemo-nucleolysis substance in treating intradiscal herniation, showing good results without complications. It has also been used in cervical disc herniations (CDHs), demonstrating the potential efficacy of this substance. In a cross-sectional, single-center study, these investigators examined the safety and long-term effectiveness of DiscoGel in patients with CDH and chronic neck pain. The trial was carried out from November 2013 to May 2016 on patients visiting Sakarya University Training and Research Hospital's pain clinic. Each patient was evaluated before the procedure (baseline) and at 1, 3, 6, and 12 months after the procedure, using the VAS score for pain, the ODI score to measure degree of disability, and estimate QOL for those with pain; this coincided with scores on the Neuropathic Pain Questionnaire (DN4) for differential diagnoses. A total of 33 patients with CDH underwent the same treatment with DiscoGel between November 2013 and May 2016. Significant pain relief was noted, as opposed to pre-operative pain, at 1, 3, 6, and 12 months after the procedure according to each patient's self-evaluation ($p = 0.01$). Differences in VAS, ODI, and DN4 scores between 1, 3, 6, and 12 months with the same variables were not statistically significant. There were no complications with the procedure. The authors concluded that RGE was a potential alternative to surgery for patients with pain at the cervical level. However, these researchers stated that that more studies with longer follow-up intervals with RGE are needed for assessment of the technique's efficiency. The drawbacks of this study were that this trial was conducted retrospectively, which led to problems with long-term follow-up data. Furthermore, this study was performed with a small group of patients ($n = 33$).

Kuhelj e al (2019) stated that percutaneous image-guided intradiscal injection of gelified ethanol was introduced to treat herniated disc disease lately. These researchers examined the clinical efficacy and durability

over a 36-months period. A total of 83 patients (47 men, 36 women, mean age of 48.9 years (18 to 79 years) were treated between May 2014 and December 2015 for 16 cervical and 67 lumbar contained CDHs. For pain assessment evaluation, the VAS was used. Physical activity, the use of analgesics, patients' satisfaction with the treatment results and patient's willingness to repeat the treatment were also evaluated. A total of 59 patients responded to questionnaire; 89.8 % had significant reduction in VAS after 1 month ($p < 0.001$); 76.9 % of patients with cervical symptoms and 93.5 % of patients with lumbar symptoms. In the cervical group, it remained stable, while in the lumbar group, VAS decreased even more during 36 months ($p = 0.012$), and 1 ingle patient had spinal surgery. Moderate and severe physical disability prior to treatment (96.6 %) was reduced to less than 30 % after 12 months. The majority of active patients returned to their regular job (71.1 %); 78 % needed less analgesics. Only 5.1 % patients were not satisfied with the treatment and 10.2 % would not repeat the treatment if needed. The authors concluded that percutaneous image-guided intradiscal injection of gelified ethanol was safe, effective and durable therapy for chronic contained cervical and lumbar herniations. Due to minimal invasiveness and long-lasting benefits, this kind of treatment should be proposed to designated group of patients as 1st-line therapy.

The author stated that the major drawback of this study was that the number of patients included, especially in cervical group was relatively low. Larger cohort might show different results. More than 1/4 of patients did not respond to questioner, so these researchers were able to follow-up only 59 patients for the designated period. Observational character of the study could also not exclude additional external parameters (such as different techniques for pain reduction including physical activity, exercises, additional or alternative analgesics, acupuncture, etc.) possibly influencing results, especially long-term VAS reduction. These investigators stated that a large, double-blinded, randomized study would be helpful in confirming these findings.

Hashemi et al (2020) noted that LBP secondary to discopathy is a common pain disorder. Multiple minimally invasive therapeutic modalities have been proposed; however, to-date no study has compared percutaneous laser disc decompression (PLDD) with intradiscal injection of DiscoGel. These investigators introduced the 1st study on patient-

reported outcomes of DiscoGel versus PLDD for radiculopathy. A total of 72 patients were randomly selected from either a previous strategy of PLDD or DiscoGel, which had been performed in the authors' center during 2016 to 2017. Subjects were asked about their NRS scores, ODI scores, and progression to secondary treatment. The mean NRS scores in the total cohort before intervention was 8.0, and was reduced to 4.3 in the DiscoGel group and 4.2 in the PLDD group after 12 months, which was statistically significant. The mean ODI score before intervention was 81.25 %, which was reduced to 41.14 % in the DiscoGel group and 52.86 % in the PLDD group after 12 months, which was statistically significant. Between-group comparison of NRS scores after 2 follow-ups were not statistically different (p = 0.62); but the ODI score in DiscoGel was statistically lower (p = 0.001); 6 cases (16.67 %) from each group reported undergoing surgery after the follow-up period, which was not statistically different. The authors concluded that both techniques were equivalent in pain reduction but DiscoGel had a greater effect on decreasing disability after 12 months, although the rate of progression to secondary treatments and/or surgery was almost equal in the 2 groups.

This study had several drawbacks. The present analysis was performed in a Persian context, which limited the generalizability of findings since it may not be representative for other settings. Also, the lack of a comparison population for conservative therapies in the course of symptoms was another limitation for which future multi-central extensive studies with comparison groups are recommended to further document the safety, efficacy, and effectiveness of PLDD and intradiscal injection of DiscoGel in discopathies. These researchers stated that although several cohort studies have been published, to-date no study had been performed comparing PLDD with intradiscal injection of DiscoGel.

In a randomized, double-blind, clinical study, Papadopoulos et al (2020) compared 2 new techniques: intradiscal injection of DiscoGel (group D), and the combination of intradiscal PRF and DsicoGel injection (PRF+D), regarding their efficacy in discogenic LBP treatment. The final sample was randomized into group A (n = 18, D) and group B (n = 18, PRF+D). During the procedure, 4 patients from group B were excluded from the study. Groups A and B were assessed regarding the pain score (VAS; 0 to 10), before the interventional procedures, and 1, 3, 6, and 12 months after. Secondary objectives of the study were to compare the 2 groups

regarding the results of the Roland Morris Disability Questionnaire, Lanss score, and QOL score (EQ-5D). There was no significant evidence for an overall difference in pain score between the 2 groups (analysis of variance, F = 3.24, df = 1, p = 0.084), except for the 6th and 12th months, when group B presented a statistically important difference compared with group A (Wilcoxon test). Group B appeared to be more effective, with a statistically significant difference, compared with group A regarding the secondary objectives of the study. The authors concluded that after rigorous and comprehensive assessment by an independent observer, both Discogel alone and Discogel in combination with PRF produced tangible improvements in pain, function, QOL, and consumption of analgesics, which were sustained at 12 months. The drawbacks of this study were its small sample size (n = 18 in group A and n = 14 in group B), and it relatively short-erm follow-up (12 months).

SpineJack System for the Treatment of Osteoporotic Vertebral Compression Fractures (VCFs)

In a prospective, randomized study, Vanni et al (2012) examined the outcomes of vertebral augmentation with SpineJack system compared to balloon kyphoplasty (BKP) for the treatment of patients with osteoporotic vertebral compression fractures (OVCFs) (type A1 fractures). A total of 300 patients were included in this study. A total of 150 patients were treated with the SpineJack system and 150 were treated with BKP. Clinical and radiological assessments included pain relief, functional capacity and vertebral body (VB) height restoration, which were measured at baseline and at 1, 6 and 12 months post-procedure. The authors concluded that the findings of this study showed significantly greater VB height restoration in the SpineJack group compared to the BKP group. This was demonstrated by the fact that 85 % of patients in the SpineJack group achieved more than 50 % VB height restoration whereas only 58 % of patients in the BKP group achieved similar VB height restoration.

Noriega et al (2016) stated that in patients with OVCFs, both SpineJack (SJ) and BKP led to a rapid and marked improvement in clinical signs. In a prospective, mono-centric, investigator-initiated, pilot study, these investigators compared 2 percutaneous vertebral augmentation procedures (SpineJack and Kyphx Xpander balloon) in the treatment of

OVCF. A total of 30 patients were randomized to receive SJ (n = 15) or BKP (n = 15). Analgesic consumption, back pain intensity (VAS and ODI) scores were recorded pre-operatively, at 5 days and 1, 3, 6, and 12 months post-surgery; QOL (EQ-VAS score) was evaluated at 1, 3, 6, and 12 months. Spine X-rays were performed 48 hours prior to procedure and 5 days, 6, and 12 months post-treatment. SpineJack resulted in a significantly shorter intervention period (23 mins versus 32 mins; $p < 0.001$), a strong, rapid, and long-lasting decline in pain (94 % versus 82 % at 12 months) and in functional disability (94 % versus 90 % at 12 months), a greater and sustainable mean correction of anterior (12 ± 13 % versus 0 ± 7 % for BKP, $p = 0.003$) and central height (12 ± 10 % versus 2 ± 6 % for BKP, $p = 0.001$) at 12 months, and a larger restoration of the vertebral body angle still evident 12 months after implantation (-4.4° ± 5.8° versus 0.2° ± 3.0° for BKP; $p = 0.012$). The authors concluded that the findings of this pilot study showed that both techniques were safe and efficient for the treatment of OVCF. Radiological results indicated that the SpineJack procedure had a higher potential for vertebral body height restoration and maintenance over time.

In a retrospective, observational study, Lin et al (2016) reviewed the medical records of 75 patients with severe OVCFs to compare the outcomes following treatment with either the SpineJack system (36 patients) or VP (39 patients). These researchers treated 36 patients with kyphoplasty with intravertebral reduction device (IRD group) and 39 through VP (VP group). The patient characteristics were comparable in both groups. The kyphotic angle (KA) and its restoration were more favorable after IRD than after VP. Although anterior body heights (ABHs) were not different in either group, their restoration was more efficient after IRD than after VP. Middle body heights (MBHs), their restoration, and their refracture rates were better after IRD than after VP; VAS pain scores and complication rates were not different between the groups. The incidences of adjacent or non-adjacent fractures were not different between the 2 groups. The authors concluded that the findings of this study showed that more efficient VB height restoration and KA correction could be obtained after treatment with the SpineJack system than with VP. This was most clearly reflected by the significant and more efficient restoration of mid-VB height and the reduction in refracture incidence observed in the SpineJack-treated group as compared to the VP-treated group.

In a 3-year extension to the prospective, pilot study, Noriega et al (2019) examined the long-term safety and clinical performance of the SpineJack system compared to BKP for the treatment of painful OVCFs. Of the 30 patients randomized for the pilot study, a total of 28 patients completed the extension study. The mean follow-up duration was 37.1 ± 10.4 months in the SpineJack group, and 38.0 ± 7.8 months in the BKP group. Over the 3-year follow-up, it was found that VB height restoration, vertebral body angle correction and kyphosis correction was significantly better in the SpineJack group compared to the BKP group. The final mean European Quality of Life Group 5 Dimensions Questionnaire score (EQ-5Dindex) was also significantly in favor of the SpineJack group, which reflected an improved QOL.

In a prospective, case-series, Hasanein and Shater (2019) examined the safety and effectiveness of the SpineJack system in 17 patients for the treatment of recent OVCFs (type A1.2, A1.3 and A3.1 fractures) over a mean follow-up of 7.4 ± 1.2 months (range of 6 to 12 months). The mean duration of the fractures was 6.4 ± 0.72 weeks (range of 5 to 8 weeks). These investigators reported significant improvements in both the mean VAS pain score and mean ODI score at the final follow-up visit. Post-operative imaging further showed significant improvements in the mean Beck index and mean local KA in this patient group.

In a prospective, case-series study, Arabmotlagh et al (2019) examined the clinical and radiological outcomes of pain relief and VB height restoration in 31 patients with OVCFs (type A1 fractures) who were treated with the SpineJack system. Patients were followed for up to 12 months after the procedure. Statistically significant improvements were observed in mean VAS scores after surgery and at the 3- and 12-month follow-up visits. Mean ABH was also significantly increased from 1.5 cm to 1.9 cm following treatment with the SpineJack system; but was reduced to 1.8 cm at 12 months post-procedure. The authors concluded that although a reduction in ABH was observed at 12 months following the SpineJack procedure, it was noteworthy that the reported gain in ABH was still significantly higher than the pre-operative value.

In a retrospective, observational study, Huang et al (2020) examined the results of vertebral augmentation with the SpineJack (SJ) system compared to VP for the treatment of patients with single-level OVCFs. A

total of 74 patients were included in this trial. A total of 42 were treated with the SpineJack system, and 32 were treated with VP. Clinical and radiological assessments included pain relief, degree of kyphosis and VB height restoration, which were measured at baseline, 24 hours, 3 months and 12 months post-procedure. Subjects in the SpineJack group achieved significantly better kyphosis correction and VB height restoration with a lower rate of cement leakage (SJ 21.4 % versus VP 37.5 %) and adjacent level fractures (ALFs) (SJ 2.3 % versus VP 15.6 %) than the VP group. The authors concluded that subjects in the SpineJack system group achieved better kyphosis correction and VB height restoration than percutaneous VP; SpineJack implantation wass safe and may not increase the risk of subsequent VCFs.

In a retrospective, observational study, Chi et al (2020) analyzed the medical records of 57 patients with OVCFs associated with spinal canal encroachment who were treated with either the SpineJack system or VP. A total of 16 were treated with the SpineJack system, and 41 were treated with VP. Clinical assessments included measures of pain relief (VAS scores), functional capacity (ODI scores) and QOL (European Quality of Life – VAS scores) while radiological assessments included KA correction and VB height restoration. Measurements were collected and assessed at baseline, 1 week and 3, 6 and 12 months post-procedure. The authors concluded that the findings of this study suggested that treatment with the SpineJack system could provide significantly better VB height restoration and KA correction than VP for at least 1 year following the procedure.

Jacobson (2020) presented a case of short-term symptomatic failure with continued vertebral collapse after a T12 kyphoplasty for an acute fracture in a severely osteoporotic elderly patient. The original trajectory of the unilateral balloon and subsequently injected bone cement failed to fill the fracture, allowing further vertebral collapse that resulted in a rapid return of pain. Within 30 days, a titanium intravertebral body implant, SpineJack (Stryker Corp, Kalamazoo, MI), combined with injection of polymethylmethacrylate (PMMA) bone cement, was placed in the collapsed area. This provided both sagittal and coronal partial correction of the collapse, fuller distribution of bone cement throughout the fractured vertebrae, and rapid reduction of pain. which was found to have been maintained at the long-term follow-up. The author reviewed the technical issues causing failure of vertebral augmentation (VA) as well as the

advantage of providing a permanent internal scaffolding to ensure stabilization of any fracture, especially where there is a high risk for progressive instability, such as the thoracic-lumbar junction. This was a single-case study; its findings need to be validated by well-designed studies.

Long et al (2020) noted that OVCF is a common cause of pain and disability and is steadily increasing due to the growth of the elderly population. To-date, percutaneous vertebroplasty (PVP) and percutaneous kyphoplasty (PKP) are almost universally accepted as appropriate vertebral augmentation procedures for OVCFs. There are many advantages of vertebral augmentation, such as short surgical time, performance under local anesthesia, and rapid pain relief; however, there are certain issues regarding the utilization of these vertebral augmentations, such as loss of vertebral height, cement leakage, and adjacent vertebral refracture. Hence, the treatment for OVCF has changed in recent years. Satisfactory clinical results have been obtained worldwide after application of the OsseoFix System, the SJ System, radiofrequency kyphoplasty (RFK) of the vertebral body, and the Kiva VCF treatment system. The authors stated that considering the short-term follow-up, the results and function of the SJ system need to be studied in a larger series, and future studies should focus on long-term clinical and radiological outcomes.

Chang et al (2021) stated that VP, KP, SJ, RFK, Kiva system (Kiva), Sky kyphoplasty system (SK), and conservative treatment are widely used in the treatment of OVCFs; however, it is still unclear which approach is the best intervention. These researchers examined the safety and effectiveness of VP, KP, SJ, RFK, Kiva, SK, and CT in the treatment of OVCFs; RCTs and cohort studies comparing VP, KP, SJ, RFK, Kiva, SK, or CT for the treatment of OVCFs were identified on the basis of data-bases including PubMed, the Cochrane Library, Web of Science, and Springer Link. A network meta-analysis was carried out using STATA 15.1. A total of 56 studies with 6,974 patients and 7 interventions were included in this study. The results of the surface under the cumulative probability demonstrated that SK was the best intervention in decreasing VAS scores and recovering middle vertebral height; RFK was the best intervention in improving ODI scores and decreasing incidence of new fractures; SJ was the best intervention to restore kyphosis angle; and

Kiva was the best intervention to reduce incidence of bone cement leakage. Cluster analysis showed that SK was the preferable intervention based on the outcomes of VAS, ODI, middle vertebral height, and kyphotic angle, and RFK was the preferable treatment in decreasing the incidence of AEs. In this network meta-analysis, node-splitting analysis and loop inconsistency analysis showed no significant inconsistencies. The authors concluded that SK may be the most effective treatment in relieving pain, improving the QOL, and recovering vertebral body height and kyphotic angle, while RFK may be the safest intervention for OVCFs. However, considering the limitations of this study, more high-quality trials are needed in the future to confirm the current conclusion.

In a retrospective, cohort study of 62 patients with 69 OVCFs, Chiang et al (2021) compared the outcomes following treatment with the SpineJack system (34 patients with 38 OVCFs) and BKP (28 patients with 31 OVCFs). The mean follow-up duration was 11.68 ± 0.99 months in the SpineJack group, and 12.19 ± 0.76 months in the BKP group. Pain relief (VAS scores) and functional capacity (ODI scores) were obtained via telephonic interviews with the patients or their families, were significantly improved within each group but not between the treatment groups. Radiological measurements for ABH, MBH, posterior VB height (PBH) and KA were collected at 1-week post-procedure and at the final follow-up visit. The SpineJack group had significantly improved ABH, MBH, and KA corrections compared to the BKP group. In particular, superior MBH restoration and maintenance of the restoration was noted in the SpineJack group, which was consistent with the findings of the SAKOS trial.

In a retrospective, observational study, Yeh et al (2021) analyzed the medical records of 354 patients with acute, subacute or non-union OVCFs to compare the safety and effectiveness of treatment across 5 different vertebral augmentation procedures. The randomized treatment groups included those treated with VP (88 patients), BKP (124 patients), the SpineJack system (60 patients), an intravertebral expandable pillar (IVEP) (46 patients) and vesselplasty (36 patients). Pain relief, KA reduction, average VB height restoration, occurrence of ALFs and cement leakage were assessed during the 1-year follow-up after vertebral augmentation. The SpineJack group experienced significantly greater VB height restoration and KA correction than the VP group along with better

outcomes in these categories than all other groups; and also had the lowest rate of cement leakage (1.7 %). Although significant improvements were found in VAS pain scores for all treatments groups, no significant differences were noted between the groups.

In a retrospective, cohort study, England et al (2021) examined the safety and clinical outcomes following vertebral augmentation using the SpineJack implant for treatment of VCF in a U.S. patient population. An IRB-approved, retrospective study of SpineJack implants used in vertebral augmentation was performed from November 2018 to February 2020. Outcome objectives included pain improvement, vertebral body height (VH) restoration, improvement in local KA (LKA), and incidence of ALF. Complications were reviewed to examine safety of the procedure. A total of 30 patients with VCF (60 % women; mean [SD] age of 62.7 [± 12.8] years) underwent a total of 53 vertebral augmentations with 106 SpineJack implants. Worst pain scores decreased significantly from 8.7 to 4.3 (95 % CI of the change [Δ]: 4.3 to 4.4; $p < 0.001$). MBH and ABH significantly increased from 13.1 ± 0.2 to 15.9 ± 0.2 mm (95 % CI Δ: 2.6 to 2.9 mm; $p < 0.001$) and 15.6 ± 0.2 to 16.8 ± 0.2 mm (95 % CI Δ: 1.1 to 1.4 mm; $p < 0.001$), respectively. LKA was significantly decreased from 10.0 ± 2.1 to 7.4 ± 2.1 degrees (95 % CI Δ: 2.4 to 2.8 degrees; $p < 0.001$); 4 patients (13 %) sustained 10 ALF over a median (IQR) follow-up period of 94 (17.5 to 203) days. There were no major AEs during the follow-up period. The authors concluded that vertebral augmentation with SpineJack implants of patients with VCF resulted in significantly decreased pain, restored VH, and improved LKA, without major AEs; however, 13 % of patients sustained ALF during a median follow-up period of 3 months.

SpineJack System for the Treatment of Traumatic VCFs

In a prospective, observational study, Noriega et al (2015a) examined the safety and effectiveness of the SpineJack system in 32 patients for the treatment of OVCFs or traumatic VCFs (TVCFs). Clinical assessments included pain, functional capacity, QOL and analgesic intake. Statistically significant improvements were found in all clinical outcomes while no device or surgery-related complications were reported. Immediate and

sustained pain relief, as well as durable clinical improvement in functional capacity and QOL, were observed after the procedure and throughout the 12-month follow-up period.

In another prospective, observational registry study, Noriega et al (2015b) further examined the safety and clinical performance of the SpineJack system in 103 patients for the treatment of TVCFs or traumatic VCFs associated with osteoporosis (type A1 to A3 fractures). The median time from trauma to surgery was 6 days for traumatic fractures and 12 days for osteoporosis-related fractures. Clinical and radiological assessments included pain, analgesic intake, functional capacity, QOL and LKA, which were measured at baseline, 48 hours, 3 months and 12 months post-procedure. According to the 1-year study results, significant immediate pain relief was observed at 48 hours and maintained over the follow-up period. A marked decrease in analgesic intake for patients requiring strong or moderate analgesics was also found at 48 hours and similarly maintained over time. Significant improvements in disability and QOL were obtained at both 3 and 12 months while a significant and immediate decrease of KA was observed at 48 hours after surgery. The authors concluded that despite a smaller reduction observed at 3 and 12 months, the global improvement in kyphosis remained statistically significant compared to baseline.

In a retrospective, case series study, Renaud (2015) examined pain relief in 77 patients with A1 to A3 fractures due to medium- or high-energy trauma or osteoporosis following treatment with the SpineJack system over a mean follow-up of 35 months (range of 6 to 67 months). The time to surgery was less than 15 days in 74.4 % of cases. Study results showed a significant decline in mean VAS pain scores from baseline through the follow-up period. Pain scores improved by 77 % at hospital discharge and gradually increased to 86 % after 12 months. A total of 3 complications were observed, but none was related to the SpineJack device.

In a prospective, case-series study, Baeesa et al (2015) examined the clinical and radiological outcomes of pain relief and VB height restoration in 27 patients with TVCFs or OVCFs (type A1 and A3 fractures) who were treated with the SpineJack system. All patients underwent surgery within 6 weeks from the time of injury. Statistically significant improvements

were found in mean VAS scores at 24 hours and at the 3-, 6- and 12-month follow-up visits. Furthermore, significant mean VB height restoration was also achieved in the anterior (3.56 mm), middle (2.49 mm) and posterior (1.28 mm) portions of the vertebra, which were maintained at the 12-month follow-up.

In a retrospective, observational study, Crespo-Sanjuan et al (2017) examined the minimum amount of bone cement needed to maintain a long-term reduction of traumatic, osteoporotic and malignant vertebral fractures following treatment with the SpineJack system over a mean follow-up of 77 months. A total of 178 patients with type A1 to A3 fractures and no neurological deficits were included in this case-series study. Bone cement equivalent to 25 % of the VB filling volume, when combined with the SpineJack implant, was deemed sufficient to prevent re-collapse in osteoporotic and traumatic type A3 fractures. Clinical assessments included measures of pain relief (VAS scores), functional capacity (ODI scores) and QOL (European Quality of Life Group 5 Dimensions Questionnaire - VAS and European Quality of Life – VAS scores). Marked improvements in all clinical outcomes were observed throughout the follow-up period.

In a consecutive, case-series study, Munoz Montoya et al (2018) evaluated pain relief and functional status in 20 patients with TVCFs or OVCFs (type A1 to A4 fractures) who were treated with the SpineJack system. Statistically significant improvements were reported in the mean VAS scores and mean ODI scores at 6 months post-procedure.

In a retrospective, case-series study, Descamps et al (2019) reviewed medical records of 104 patients with stable TVCFs or OVCFs (type A1 to A3 fractures) who were treated with the SpineJack system. The mean time between trauma and surgery for this patient group was 3.5 days and 1.8 days between hospitalization and surgery. Clinical and radiological assessments included pain, functional status, VB height, LKA and traumatic regional angulation, which were measured at baseline, 24 hours, 6 weeks and at the final follow-up visit post-procedure. Study results demonstrated significant immediate pain relief at 24 hours that lasted through the final follow-up while significant corrective gains were also found in the KA and regional traumatic angle. The authors noted that

although some extent of adjacent disc degeneration was noted in this study, this did not impact the results for pain control or sagittal balance restoration.

In a prospective, observational study, Kerschbaumer et al (2019) compared the clinical and radiological findings of the SpineJack system treatment with and without posterior fixation in TVCF patients over a mean follow-up of 2.3 years. The treatment groups were comprised of 60 patients for the SpineJack standalone treatment and 14 patients for the SpineJack treatment combined with additional posterior fixation. Mean time from trauma to surgery was 3 ± 6 days in the former group and 17 ± 55 days in the latter group. Pain relief and functional capacity, as measured by VAS scores and ODI scores, were not significantly different between the treatment groups. Significant corrective gains in vertebral wedge angle were found within each group but there was no difference in wedge angle between the groups. The corrective gains observed in regional KA were highly significant within the same groups.

In a retrospective, observational study, Venier et al (2019) examined the results of vertebral augmentation with the SpineJack system or VB stents with or without posterior instrumentation in traumatic, osteoporotic and neoplastic burst fractures. A total of 51 patients with posterior wall retropulsion and no neurological deficits were included in this trial. Of the 53 fractured VBs treated, 7 were treated with the SpineJack system and 46 were treated with VB stents. Significant improvements were found in VAS pain scores at 1- and 6-month post-procedure compared to baseline. A significant difference was also detected in the degree of posterior wall retropulsion before and after the procedure, as well as in the VB height restoration achieved (mean gain of 5.8 mm). The authors concluded that these findings showed that the SpineJack system could be used as a standalone treatment or in combination with posterior stabilization to correct posterior wall retropulsion or restore VB height in burst fractures.

In a retrospective, case-series study, Meyblum et al (2020) reviewed the medical records of 51 patients with A3 or A4 fractures due to low- or high-energy trauma that had posterior wall involvement. Pain, vertebral KA and posterior wall protrusion were assessed at baseline and at 4 to 6 weeks after vertebral augmentation with the SpineJack system.

Significant pain relief was observed among 42 of 51 patients (82.4 %) while a significant decrease in mean KA and posterior wall protrusion was also found across all patients following treatment. Overall, study results suggested that SpineJack system could aid in the treatment and prevention of further posterior wall protrusion in VCF patients without neurological deficits.

In a consecutive, case-series study of 44 patients with acute (less than 2 weeks) traumatic thoracolumbar burst fractures (type A3), Noriega et al (2021) examined the long-term outcomes following treatment with the SpineJack system over a mean follow-up of 5.6 years. The clinical outcomes of pain relief, functional capacity, and analgesic consumption were analyzed for this patient sample while the radiological outcomes of VB height, LKA and traumatic regional angulation were also evaluated at baseline, at 1 month after treatment and at the end of the follow-up period. Statistically significant improvements were found in both pain and disability at 1-month post-procedure, which was also reflected in the finding that 75 % of patients did not take any analgesics for back pain at 1 month after surgery. Patients further showed significant VB height restoration and correction of local and traumatic regional KAs. It was noteworthy that all of the improvements observed were maintained throughout the follow-up period of 5.6 years.

In a retrospective study, Lofrese et al (2022) examined the medical records of 57 patients with type A2, A3 and A4 fractures due to medium- or high-energy trauma who were treated with the SpineJack system. Patients were carefully selected based on pedicle integrity and a spread calculation to quantify VB fragment displacement. The functional outcomes of pain, disability, QOL and analgesic consumption, in addition to the radiological outcomes of VB height restoration and kyphosis correction, were evaluated at 1-, 6- and 12-month post-procedure. A total of 57 patients were included in the study. Patients aged greater than 60 years reported worse kyphosis correction (less than 4°) with more post-operative complications, while vertebral plasticity in younger patients, fragmentation-related greater re-modeling in A3/A4 fractures, and treatments within 7 days of trauma determined superior wedging corrections, with better EQ-5D-post and mRS-fup. Cement leakages did not affect functional outcome, while female gender and American Society of Anesthesiologists (ASA) score of 3 to 4 were associated with worse

ODI-fup and VAS-fup. Although fracture characteristics and radiological outcome did not negatively influence the clinical outcome, A2 fracture was a risk factor for complications; thus, indirectly compromising both the functional and radiological outcome. The authors concluded that the SpineJack system was a safe and effective treatment for restoring VB height in the vast majority of thoracolumbar burst fractures (A3 and A4) with a spread of less than 30 %. Since the SpineJack procedures performed greater than or equal to 7 days after trauma were more often associated with post-operative complications, the authors recommended that surgery take place within 1 week of injury.

Tendon Sheath injections for the Treatment of Back Pain

Cho et al (2019) noted that calcific tendinitis is commonly found in the rotator cuff; however, it is very rare in the long biceps tendon (LBT). Furthermore, calcific tendinitis involving the LBT in the hemiplegic shoulder after a stroke has not been previously reported. These researchers presented the case of a 63-year old man who suffered from a stroke and atypical calcific tendinitis involving the LBT as a rare cause of hemiplegic shoulder pain. The patient had experienced intractable pain in the right hemiplegic shoulder for more than 6 months with a waxing and waning course. Marked tenderness to palpation was present at the biceps tendon adjacent to the bicipital groove. Ultrasound (US) and computed tomography (CT) revealed a long, blade-shaped, circumscribed, cloudy and irregular dense calcific deposit in the LBT site, distal to the bicipital groove. The patient underwent US-guided corticosteroid injection at the posterior intra-articular joint. Symptoms failed to resolve; these investigators injected an additional corticosteroid into the biceps tendon sheath adjacent to the calcific deposit. This procedure provided satisfactory relief, and follow-up US revealed mild diminution of the calcification through absorption. The authors concluded that this was the 1st report on atypical calcific tendinitis involving the LBT causing hemiplegic shoulder pain following a stroke.

Furthermore, an UpToDate review on “Subacute and chronic low back pain: Nonsurgical interventional treatment” (Chou, 2020) does not mention tendon sheath injection as a therapeutic option.

Cervical Spine Cages

Teton and colleagues (2020) noted that common interbody graft options for anterior cervical discectomy and fusion (ACDF) include allograft and polyetheretherketone (PEEK). PEEK has gained popularity due to its radiolucent properties and a modulus of elasticity similar to that of bone. PEEK devices also result in higher billing costs than allograft, which may drive selection. A previous study found a 5-fold higher rate of pseudarthrosis with the use of PEEK devices compared with structural allograft in single-level ACDF. In a retrospective study, these investigators reported on the occurrence of pseudarthrosis with PEEK devices versus structural allograft in patients who underwent multi-level ACDF. These researchers evaluated 81 consecutive patients who underwent a multi-level ACDF and had radiographic follow-up for at least 1 year. Data were collected on age, sex, BMI, tobacco use, pseudarthrosis, and rate of re-operation for pseudarthrosis. Logistic regression was used for data analysis. Of 81 patients, 35 had PEEK implants and 46 had structural allograft. There were no significant differences between age, sex, smoking status, or BMI in the 2 groups. There were 26/35 (74 %) patients with PEEK implants who demonstrated radiographic evidence of pseudarthrosis, compared with 5/46 (11 %) patients with structural allograft ($p < 0.001$, OR 22.2); 5 patients (14 %) with PEEK implants required re-operation for pseudarthrosis, compared with 0 patients with allograft ($p = 0.013$). The authors concluded that the findings of this study reinforced previous findings on 1-level ACDF outcomes and suggested that the use of PEEK in multi-level ACDF resulted in statistically significantly higher rates of radiographic pseudarthrosis and need for revision surgery than allograft. Surgeons should consider these findings when determining graft options, and reimbursement policies should reflect these discrepancies.

The main drawback of this study was its retrospective nature and the inadvertent biases that this study design may have introduced. Bone quality studies were not routinely carried out; thus, it was possible that a difference in bone health could have existed between the groups. In terms of the surgical procedure, standardized use of plate and screw fixation would improve the comparison between the 2 groups. These investigators included the longest possible follow-up time for each patient, though this resulted in a difference between average follow-up times for

the 2 groups. This difference was deemed not to be an issue, however, as rates of pseudarthrosis were higher in the PEEK group despite having longer average follow-up time for fusion to occur. Future studies could set a minimum follow-up time of 2 years (instead of 1 year) to most accurately capture fusion rates; however, in this study the average radiographic follow-up was more than 2 years in the allograft group and nearly 3 years in the PEEK group. While CT is considered by many to be the gold standard for radiographic assessment of pseudarthrosis, not every patient had a cervical spine CT performed at least 1 year after surgery. Flexion and extension radiographs were included in this review, as these were more useful than static radiographs for evaluating fusion status. Furthermore, there were 13 different surgeons involved in these procedures, which made standardization of technique and practice patterns difficult; however, this increased the external validity of these findings. These researchers stated that future prospective studies may provide further evidence on this topic.

In a systematic review, Jain et al (2020) compared reported fusion rates after anterior cervical discectomy and fusion (ACDF) using structural allograft versus polyetheretherketone (PEEK) interbody devices in patients with cervical spine degeneration. Secondary objectives were to compare differences in rates of subsidence and re-operation and in patient-reported outcomes between the 2 groups. These researchers carried out a review of the English-language literature using various databases; they identified 4,702 articles. After these investigators employed inclusion and exclusion criteria, 14 articles (7 randomized controlled trials [RCTs], 4 prospective studies, and 3 retrospective studies) reporting fusion rates of structural allograft or PEEK interbody devices were eligible for this analysis. No RCTs compared outcomes of structural allograft versus PEEK interbody devices. Extracted data included authors, study years, study designs, sample sizes, patient ages, duration of follow-up, types of interbody devices used, fusion rates, definition of fusion, re-operation rates, subsidence rates, and patient-reported outcomes. Fusion rates were 82 % to 100 % for allograft and 88 % to 98 % for PEEK interbody devices. The reported data were insufficient to perform meta-analysis. Structural allograft had the highest reported rate of re-operation (14 %), and PEEK interbody devices had the highest reported subsidence rate (18 %). Patient-reported outcomes improved in both groups. There was insufficient high-quality evidence to

compare the associations of various PEEK modifications with fusion rates. The authors concluded that fusion rates were similar between structural allograft and PEEK interbody devices when used for ACDF for cervical spine degeneration. Currently, there is insufficient high-quality evidence to assess associations of PEEK modifications with fusion rates. Moreover, these researchers stated that future high-quality research is needed to examine the outcomes of various modified PEEK devices and bone graft substitutes and extenders. Level of Evidence: II.

The authors stated that drawbacks are inherent in systematic reviews. In this study, heterogeneity of fusion assessment, stringent inclusion and exclusion criteria, and possible missed cases contribute to the limitations. The discrepancy in fusion assessment prevented these researchers from performing a meta-analysis. Furthermore, the lack of Level I evidence with a direct comparison of structural allograft versus PEEK made it difficult to form robust conclusions.

Buyuk et al (2020) noted that PEEK and machined allograft interbody spacers are among devices used as fusion adjuncts in ACDF. Most results were good-to-excellent; however, some patients developed pseudarthrosis. In a retrospective cohort study, these researchers compared the re-operation rates for pseudarthrosis following 1- or 2-level ACDF with PEEK or allograft cages. These investigators reviewed patients who underwent 1- or 2-level ACDF. The rate of subsequent surgery for pseudarthrosis was calculated for cases confirmed by computerized tomography (CT). Patient-reported outcomes were collected at post-index surgery follow-up and post-revision ACDF follow-up. Radiographic parameters were assessed at a minimum of 1-year post-op on all patients. A total of 209 patients were included: 167 received allograft and 42 received PEEK. Subsidence was demonstrated in 31 % of allograft and 29 % of PEEK patients. There were no significant differences in clinical outcomes between allograft and PEEK groups. Clinical outcomes were not adversely affected by subsidence. Re-operation for pseudarthrosis was performed in 8 % of allograft patients and 14 % of PEEK patients (not statistically different). Improvement in patient-reported outcome was significantly better for patients without symptomatic post-operative pseudarthrosis. The authors concluded that both allograft and PEEK spacers were acceptable options for ACDF surgery. Similar clinical outcomes and rates of radiographic subsidence

were found. Subsidence was not a factor in clinical outcomes. Re-operation for pseudarthrosis was associated with poor outcomes. A higher incidence of revision for symptomatic pseudarthrosis occurred in the PEEK group; however, this was not statistically significant.

The authors stated that limitations to this study included those inherent of any retrospective review; however, given the paucity of data regarding this topic this represented the 1st step towards a higher-level study (randomized prospective trial) to answer the research question of which spacer option has a higher association with symptomatic pseudarthrosis following 1- or 2-level ACDF. Second, the disproportion sample sizes (allograft, 167 patients, and PEEK, 42 patients) may have an effect on the results. However, these researchers noted that this disparity mirrors North American surgeon preferences for allograft over PEEK. Third, these investigators studied only symptomatic pseudarthrosis. Other important diagnoses that may require revision surgery (e.g., adjacent segment level disease and kyphosis) were not included. Fourth, all of the subjects were plated; thus, these researchers were unable to study this as a factor. Fourth, differences in surgical techniques have the potential to affect outcomes. The projected effects of these technical differences on fusion and symptomatic pseudarthrosis are difficult to evaluate given the nature of the study. These researchers stated that a future prospective study by a single surgeon, comparing both PEEK and allograft with equal number of patients in each group could yield more definitive conclusions to the research question.

Moo et al (2020) noted that allografts and PEEK cages are the 2 most commonly used materials in ACDF; however, their effectiveness in 2-level ACDF remains controversial. In a retrospective study, these researchers compared the clinical and radiological outcomes of 2-level ACDF with plate fixation using either a structural allograft (SA) or a PEEK cage. From 2010 to 2015, a total of 88 consecutive patients underwent 2-level ACDF, of whom 53 received an allograft and 35 patients received a PEEK cage. All PEEK cages were filled with local autografts. All clinical outcomes were prospectively collected before and 6 months and 2 years after surgery. Clinical effectiveness was evaluated using a visual analog scale (VAS) for neck pain and limb pain, the Neck Pain and Disability Score (NPDS), the Neck Disability Index (NDI), the Neurogenic Symptom Score (NSS), and the Japanese Orthopedic Association score (JOAS).

Radiological outcomes were assessed pre-operatively, immediately after surgery, and at the final follow-up. A pre-operative comparison revealed no difference between the 2 patient groups in terms of age, sex, body mass index (BMI), smoking status, pre-operative symptoms, operation level, or follow-up (mean of 42.8 months). No differences in the improvements in clinical outcomes were observed between the 2 groups. Both groups showed significant improvement in mean disc height, segmental height, and segmental lordosis post-operatively. The fusion rate for the PEEK cage was 100 % at both levels, while the fusion rate for the allograft group was 98.1 % at the cephalad level and 94.2 % at the caudad level ($p > 0.05$). Subsidence at the cephalad level occurred in 22.9 % (8/35) of segments in the PEEK group and 7.7 % (4/52) of segments in the allograft group ($p = 0.057$). At the caudal level, a higher incidence of cage subsidence was noted in the PEEK group than in the allograft group [37.1 % (13/35) versus 15.4 % (8/52)] ($p = 0.02$). Overall, subsidence was noted in 30 % (21/70) of the PEEK group and in 11 % (12/104) of the allograft group ($p < 0.05$). The authors concluded that the use of PEEK cages resulted in a higher rate of subsidence in 2-level ACDF than the use of allografts. Two-level ACDF using either allografts or PEEK cages resulted in similar clinical outcomes, radiological improvements in alignment and fusion rates.

The authors stated that this study had several drawbacks, such as its retrospective nature, small sample size, and operations performed by multiple surgeons. Furthermore, the relationship between bone density and cage subsidence was not analyzed. The dimensional aspects of the allograft and the PEEK cage in relation to subsidence and fusion rate were also not examined in this trial. The endplate margin of the vertebrae might not be well defined, and the potential measurement error must also be taken into account. It was difficult to accurately examine bone bridge formation and evaluate dynamic motion on lateral radiographs, and CT scans may not be possible in all cases.

In an observational, cohort study, Menon et al (2021) compared 1-year peri-operative complications between SA and synthetic cage (SC) for ACDF using a national database. The TriNetX Research Network was retrospectively queried. Patients undergoing initial 1- or multi-level ACDF surgery between October 1, 2015 and April 30, 2019 were propensity score matched based on age and co-morbidities. The rates of 1-year

revision ACDF surgery and reported diagnoses of pseudoarthrosis, surgical site infection (SSI), and dysphagia were compared between SA and SC techniques. These investigators carried out a comparison of 1-year outcomes between propensity score matched cohorts on 3,056 patients undergoing 1-level ACDF and 3,510 patients undergoing multi-level ACDF. In 1-level ACDF patients, there was no difference in 1-year revision ACDF surgery ($p = 0.573$), reported diagnoses of pseudoarthrosis ($p = 0.413$), SSI ($p = 0.620$), or dysphagia ($p = 0.529$) between SA and SC groups. In multi-level ACDF patients, there was a higher rate of revision surgery (SA 3.8 % versus SC 7.3 %, odds ratio [OR] = 1.982, $p < 0.001$) in the SC group, and a higher rate of dysphagia in the SA group (SA 15.9 % versus SC 12.9 %). The authors concluded that while the overall revision and complication rate for 1-level ACDF remained low despite interbody graft selection, SC implant selection may result in higher rates of revision surgery in multi-level procedures despite yielding lower rates of dysphagia. These researchers stated that large-scale, prospective comparison of SA and SC for ACDF is needed before the superiority of either implant can be concluded.

Goldberg et al (2022) stated that anterior cervical discectomy and fusion (ACDF) is a common procedure to address cervical spine pathology. The most common grafts used are titanium, polyetheretherketone (PEEK), or structural allograft. Comparison of fusion rate is difficult due to non-standardized methods of assessment. These investigators stratified studies by method of fusion assessment and carried out a systematic review of fusion rates for titanium, PEEK, and allograft. They wanted to determine which of the common implants used in ACDF has the highest reported rate of fusion? An experienced librarian conducted a 5-database systematic search for published articles between January 1, 1990, and august 7, 2021. Studies carried out in adults with at least 1 year of radiographic follow-up were included. The primary outcome was the rate of fusion; fusion criteria were stratified into 6 classes based upon best practices. A total of 34 studies met inclusion criteria; 10 studies involving 924 patients with 1,094 cervical levels, used tier 1 fusion criteria and 6 studies (309 patients and 367 levels) used tier 2 fusion criteria. A total of 47 % of the studies used class 3 to 6 fusion criteria and were not included in the analysis. Fusion rates did differ between titanium (average of. 87.3 %, range of 84 % to 100 %), PEEK (average of 92.8 %, range of 62 % to 100 %), and structural allograft (average of 94.67 %, range of 82 % to

100 %). The authors concluded that after stratifying studies by fusion criteria, significant heterogeneity in study design and fusion assessment prohibited the performance of a meta-analysis. Fusion rate did not differ by graft type. Important surgical goals aside from fusion rate, such as degree of deformity correction, could not be assessed. These researchers stated that future studies with standardized high-quality methods of assessing fusion, are needed.

The authors stated that several limitations are inherent in the study design. As with all systematic reviews, the present study was subject to publication bias. The number of studies, the heterogeneity of the study procedures, fusion criteria, and lack of studies directly comparing interbody materials, limited the ability to conduct a risk-of-bias analysis or meta-analysis. The generalizability of these findings was limited by the inclusion and exclusion criteria that were employed. In many countries, ACDF is carried out without anterior plating or with cages without integrated instrumentation. In this study, these investigators did not include such studies to remove the confounding effects of anterior plating and/or integrated instrumentation. In doing so, these researchers may have missed differences between graft materials that may be apparent when studied in the setting of entirely stand-alone grafts. Lack of level 1 evidence comparing allograft versus PEEK versus titanium grafts limited the strength of the study conclusions. Additional high-quality evidence, in the form of prospective clinical trials with standardized fusion criteria, is needed. A significant strength of this systematic review was the reduction of heterogeneity in radiographic fusion assessment via the use of a prospectively determined fusion criteria ranking system. An additional strength was the comprehensive literature search and adherence to the PRISMA-guidelines. This study focused on rate of fusion as the primary endpoint; however, fusion rate is not the only goal of surgery. Depending on the indication, other important surgical objectives include deformity correction and relief of neural element compression. As a result, it was possible that while fusion rate was similar across cage/graft types, certain cages may offer profound advantages in distinct situations. For example, synthetic cages may offer a superior result in the correction of severe deformity. Endpoints such as these could not be assessed in the present study; but will be the subject of future studies.

In addition to available articles, more recently published studies have also found equivalent or worse outcomes with the use of PEEK or other synthetic cervical cages compared to allograft (Buyuk et al, 2020; D'Antonio et al, 2023; Epstein et al, 2022; Goldberg et al, 2022; Goz et al, 2019; Jain et al, 2020; Krause et al, 2018; Marrache et al, 2020; Menon et al, 2021; Moo et al, 2020; Pirkle et al, 2019; Powers et al, 2023; Raad et al, 2023; Rodrigues et al, 2023; Ryu et al, 2021; Shukla et al, 2023; Teton et al, 2020; Villavicencio et al, 2022; Wang et al, 2019; Yang et al, 2019)".

In a prospective, randomized, blinded clinical trial, Villavicencio et al (2022) examined clinical and radiological outcomes in patients undergoing ACDF surgeries randomized to receive either PEEK or SA. Patients undergoing 1- to 3-level ACDF with single anterior plate fixation were randomized (1:1 ratio) to receive either cortical allograft or PEEK interbody spacers. Radiographic and clinical outcomes were assessed at 3, 6, 12, and 24 months with an additional post-operative radiographic assessment. A total of 120 patients were enrolled and randomized. Comparing clinical outcomes, no differences in arm or neck pain scores were noted; however, there was a statistically significant ($p \leq 0.041$) improvement in SF-36 PCS scores for the SA group at all follow-up time-points and a tendency toward lower disability scores. Overall, evidence of radiographic fusion was achieved in 87 (91.6 %) patients: 5 (10.2 %) and 3 (6.5 %) patients had pseudoarthrosis ($p = 0.72$) in the PEEK and SA groups, respectively. At 24 months' follow-up time, any cervical or segmental alignment restoration achieved with surgery was lost and no statistically significant changes were detected when all levels of surgery were included. Likewise, there were no statistically significant differences between the groups for anterior or posterior body height measurements at the 24 months' follow-up. Approximately 20 % of patients had anterior and posterior subsidence, all grade 0 regardless of the group assignment. The authors concluded that comparable radiographic outcomes were observed for patients undergoing 1- to 3-level PEEK versus SA-assisted ACDF surgeries. Although MCID comparisons suggested that SA and PEEK-treated patients exhibited similar clinical outcomes, testing that incorporated the magnitude of the change suggested that there may be a statistically significant greater magnitude of improvement for the SA group patients; however, further studies with a larger sample size are needed to determine if a true effect exists.

In a retrospective, cohort study, D'Antonio et al (2023) examined if PEEK or titanium alloy cages would increase the rate of pseudarthrosis development or revision surgery rate compared with SA following ACDF and identified if the cage type would result in differences in patient-reported outcome measures (PROMs) versus SA. All patients aged 18 years or older who underwent primary 1- to 4-level ACDF at a single center were identified. Propensity matching was carried out to compare patients' PEEK or titanium alloy cages with SA. Multi-variate logistic regression analysis was conducted to examine the effect of interbody spacer composition on the likelihood of pseudarthrosis development. Of the 502 patients who received SA and had 1-year post-operative dynamic radiographs, 96 patients were propensity matched to 32 patients who received a PEEK cage, and 162 patients were propensity matched to 54 patients who received a titanium alloy cage. Multi-variate logistic regression analysis identified that PEEK cage implants (OR, 3.34; $p = 0.007$) predicted pseudarthrosis development compared with SA implantation. Titanium alloy cage (OR, 1.64; $p = 0.156$) implantation was not predictive of pseudarthrosis; 1-year post-operative PROMs were not significantly different between patients who received PEEK or titanium alloy cages and those who received SA (all $p > 0.05$). The authors concluded that compared with SA, receiving a PEEK cage increased the risk of pseudarthrosis development following ACDF, whereas receiving a titanium alloy cage had no significant effect on pseudarthrosis development. One-year post-operative PROs were similar between patients who received SA, PEEK, and titanium alloy interbody spacers.

Powers et al (2023) noted that implants represent a large component of surgical cost, with several available options for ACDF. Rising ACDF volume highlights the need for accurate cost characterization among implant configurations to inform efficient utilization. A cohort study of patients who underwent 1-level or 2-level ACDF in 2017 was carried out using the MarketScan national insurance databases, which contain de-identified clinical and financial data. Implant configurations included plate with cage, stand-alone cage, and plate with SA. Patients who switched insurance providers within 2 years after surgery or underwent concurrent posterior cervical surgery, cervical disk arthroplasty, or cervical corpectomy were excluded. A combined plate/cage and stand-alone cage group was compared with the SA group followed by the comparison of the plate/cage and stand-alone cage groups. In total, 30-day, 90-day, and 2-

year aggregate costs; component costs of physical therapy, injections, medications, psychological treatment, and subsequent spine surgery; and re-operation rates were evaluated. Of 1,723 patients identified, 360 (20.9 %) underwent surgery with plate/cage, 184 (10.7 %) with stand-alone cage, and 1,179 (68.4 %) with SA. Aggregate costs were lower in the SA group compared with the combined cage group at 90 days ($36,428 versus $39,875, p = 0.04) and 2 years ($64,951 versus $74,965, p = 0.005) post-operatively. There were no significant differences in aggregate costs between the plate/cage and stand-alone cage groups. The 2-year re-operation rate was higher in the combined cage compared with the SA group (23.9 % versus 10.9 %, p < 0.001) and was also higher in the stand-alone cage compared with the plate/cage group (32.0 % versus 19.7 %, p = 0.002). The authors concluded that compared with alternative ACDF constructs, Sa was associated with lower post-operative costs and re-operation rates. These researchers stated that although costs were similar, re-operation rates were lower with plate/cage constructs compared with those of stand-alone cages.

In a retrospective study, Raad et al (2023) caried out a cost-analysis comparing synthetic cage (SC) versus allograft (Allo) over a 5-year time horizon. These investigators developed a decision-analysis model comparing the use of Allo versus SC for a hypothetical 60-year-old patient with cervical spondylotic myelopathy undergoing 1-level ACDF surgery. A comprehensive literature review was conducted to estimate probabilities, costs (2020 US dollars [USD]) and QALYs gained over a 5-year period. A probabilistic sensitivity analysis using a Monte Carlo simulation of 1,000 patients was performed to calculate incremental cost-effectiveness ratio and net monetary benefits. 1-way deterministic sensitivity analysis was performed to estimate the contribution of individual parameters to uncertainty in the model. The use of Allo was favored in 81.6 % of the iterations at a societal willing-to-pay threshold of 50,000 USD/QALY. Allo dominated (higher net QALYs and lower net costs) in 67.8 % of the iterations. The incremental net monetary benefit in the Allo group was 2,650 USD at a willing-to-pay threshold of 50,000 USD/QALY. 1-way deterministic sensitivity analysis revealed that the cost of the index surgery was the only factor which significantly contributed to uncertainty. The authors concluded that cost-utility analysis suggested that Allo maybe a more cost-effective option compared with SCs in adult patients undergoing ACDF for cervical spondylotic myelopathy.

In a retrospective, cohort study, Rodriquez et al (2023) examined the post-operative outcomes and economic costs of ACDF procedures using synthetic biomechanical intervertebral cage (BC) SA implants. Adult patients who underwent an ACDF procedure between 2007 and 2016 were included. Patient records were extracted from MarketScan, a national registry that captures person-specific clinical utilization, expenditures, and enrollments across millions of inpatient, outpatient, and prescription drug services. Propensity-score matching (PSM) was employed to match the patient cohorts across demographic characteristics, co-morbidities, and treatments. Of 110,911 patients, 65,151 (58.7 %) received BC implants while 45,760 (41.3 %) received SA implants. Patients who underwent BC surgeries had slightly higher re-operation rates within 1 year after the index ACDF procedure (3.3 % versus 3.0 %, p = 0.004), higher post-operative complication rates (4.9 % versus 4.6 %, p = 0.022), and higher 90-day re-admission rates (4.9 % versus 4.4 %, p = 0.001). After PSM, the post-operative complication rates did not vary between the 2 cohorts (4.8 % versus 4. 6%, p = 0.369), although dysphagia (2.2 % versus 1.8 %, p < 0.001) and infection (0.3 % versus 0.2 %, p = 0.007) rates remained higher for the BC group. Other outcome differences, including re-admission and re-operation, decreased. Physician's fees remained high for BC implantation procedures. The authors found marginal differences in clinical outcomes between BC and SA ACDF interventions in the largest published database cohort of adult ACDF surgeries. After adjusting for group-level differences in co-morbidity burden and demographic characteristics, BC and SA ACDF surgeries showed similar clinical outcomes; however, physician's fees, however, were higher for BC implantation procedures.

Wang et al (2023) stated that both SA and PEEK have been used for ACDF. There were reports that PEEK exhibits a higher pseudarthrosis rate than SA. These investigators compared pseudarthrosis, revision, subsidence, and loss of lordosis rates in patients with PEEK and SA. These researchers carried out a retrospective review of patients who were treated with ACDF at their hospital between 2005 and 2017. Inclusion criteria were adult patients with either PEEK or SA, anterior plate fixation, and a minimum 2-year follow-up. Exclusion criteria were hybrid PEEK and allograft cases, additional posterior surgery, adjacent corpectomies, infection, tumor, stand-alone or integrated screw and cage devices, bone morphogenetic protein (BMP) use, or lack of a minimum 2-

year follow-up. Demographic variables, number of treated levels, interbody type (PEEK cage versus SA), graft packing material, pseudarthrosis rates, revision surgery rates, subsidence, and cervical lordosis changes were collected. These data were analyzed by Pearson's Chi-square test (or Fisher's exact test, according to the sample size and expected value) and Student t-test. A total of 168 patients (264 levels total, mean follow-up time 39.5 ± 24.0 months) were analyzed; 61 patients had PEEK, and 107 patients had SA. Pseudarthrosis rates for 1-level fusions were 5.4 % (PEEK) and 3.4 % (SA) ($p > 0.05$); 2-level fusions were 7.1 % (PEEK) and 8.1 % (SA) ($p > 0.05$); and 3-level or more fusions were 10 % (PEEK) and 11.1 % (SA) ($p > 0.05$). There was no statistical difference in the subsidence magnitude between PEEK and SA in 1-, 2-, and 3 or more-level ACDF ($p > 0.05$). Post-operative lordosis loss was not different between cohorts for 1- and 2-level surgeries. The authors concluded that in 1- and 2-level ACDF with plating involving the same number of fusion levels, there was no statistically significant difference in the pseudarthrosis rate, revision surgery rate, subsidence, and lordosis loss between PEEK cages and SA.

Intra-Muscular Corticosteroid Injection for the Treatment of Back Pain

Currently, there is insufficient evidence to support the use of intra-muscular (IM) corticosteroid injection for the treatment of back pain.

Friedman and colleagues (2008) stated that parenteral corticosteroids are not recommended for acute, radicular LBP, though their role in this disease process is ill-defined. To-date, this medication class has only been studied in a highly selected group of patients requiring hospitalization. In a randomized, double-blind, placebo-controlled, clinical trial of patients with radicular LBP who presented to an emergency department (ED) within 1 week of pain onset, these researchers hypothesized that a single IM 160-mg dose of methylprednisolone acetate would improve pain and functional outcomes 1 month after ED discharge if the corticosteroid were administered early in disease symptomatology. Adults between the ages of 21 and 50 who presented to an ED with LBP and a positive straight leg raise test were enrolled. The primary outcome was change in pain intensity on an 11-point NRS 1 month after ED visit. Secondary outcomes 1 month after ED discharge included analgesic use,

functional disability and adverse medication effects. A total of 637 patients were approached for participation, 133 were eligible, and 82 were randomized. Baseline characteristics were comparable between the groups. The primary outcome, a comparison of the mean improvement in pain intensity, favored methylprednisolone by 1.3 (p = 0.10). Some secondary outcomes favored methylprednisolone, such as use of analgesic medication within the previous 24 hours (22 % versus 43 %, 95 % CI for difference of 20 %: 0 % to 40 %) and functional disability (19 % versus 49 %, 95 % CI for difference of 29 %: 9 % to 49 %). Adverse medication effects 1 week after ED discharge were reported by 32 % of methylprednisolone and 24 % of placebo patients (95 % CI for difference of 9 %: -12 % to 30 %). The authors concluded that this trial was a negative study. They stated that although there was a suggestion of benefit of methylprednisolone acetate in a population of young adults with acute radicular LBP, further investigation with a larger sample of patients is needed.

The authors stated that drawbacks of this work included the sample size. This study was under-powered for the difference between groups that were observed. These investigators based the sample size calculation on an estimate of the difference between pain scores of 2.0 NRS units, a value that has been suggested as a clinically robust difference. However, a more commonly used estimate in ED-based pain studies was a value of 1.3 NRS units. In order to detect this difference at the conventional significance level of 0.05, it would require slightly more than 200 subjects. A 2nd drawback was the dose of methylprednisolone acetate used. A dose was chosen that these researchers believed would minimize type II error without exposing participants to undue harm. Because this dose was well-tolerated, these investigators would use the same dosage in future investigations. Third, 51 patients were eligible to participate in this study but were not randomized because they refused to participate or because there was a logistical impediment, such as unavailability of investigational medication. These researchers did not collect data on these patients; therefore, they were uncertain that this study cohort mirrored a true population of young adults who present to an urban ED with radicular LBP. Finally, as the study required 4 years to complete, it was possible that there were changes in the data collection and secular trends that could affect findings such as changes in care for the control group; however, the investigational protocol was strictly

adhered to via on-going training of the research associates. Further, the research environment and clinical practices for treating radicular LBP were stable during this time period.

An UpToDate review on “Treatment of acute low back pain” (Knight et al, 2021) states that “Systemic glucocorticoids -- There is no evidence to support the use of systemic glucocorticoids in acute nonspecific back pain. Small, randomized trials in patients with nontraumatic back pain presenting to the emergency department comparing systemic steroids with placebo have found no benefits”.

Also, an UpToDate review on “Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment” (Chou, 2021) states that “Systemic corticosteroids -- No trial has evaluated systemic corticosteroids for the treatment of subacute or chronic nonradicular low back pain. However, extrapolating from trials of acute low back pain in which these agents did not improve pain or function, we do not treat patients with subacute or chronic low back pain with corticosteroids”.

Furthermore, an UpToDate review on “Acute lumbosacral radiculopathy: Treatment and prognosis” (Levin et al, 2021) states that “Systemic glucocorticoids -- In the clinical experience of some experts, systemic glucocorticoid treatment may provide partial pain relief for select patients with acute lumbosacral radiculopathy. Acknowledging that any benefit is likely modest, one author of this topic employs a course of oral prednisone (60 to 80 mg daily) for 5 to 7 days for patients with acute lumbosacral radiculopathy who do not respond well to analgesics and activity modification. This is followed by a rapid taper to discontinuation over the following 7 to 14 days. However, the other authors generally do not use systemic glucocorticoids in this setting. The available evidence suggests that systemic glucocorticoid therapy has either limited benefit or no benefit”.

Magnetic Resonance Imaging-Guided Focused Ultrasound (MRgFUS) for the Treatment of Lumbar Facet Joint Pain

Tiegs-Heiden and colleagues (2019) noted that magnetic resonance imaging-guided focused ultrasound (MRgFUS) is a non-invasive modality that allows for precise tissue ablation with sparing of surrounding

structures. Early reports of the use of MRgFUS for the treatment of facet joint OA are promising. These researchers presented the findings of a case of facet joint pain treated successfully by MRgFUS at their institution. The authors concluded that MRgFUS ablation of the lumbar facet joints is a promising therapy for facet joint-mediated LBP. It may be of particular benefit in patients with limited or refractory response to conventional treatments. Moreover, these researchers stated that because there is currently very little peer-reviewed evidence, continued research is needed to confirm the safety and effectiveness of the procedure. Depending on future results, it has the potential to make a substantial impact on the treatment model for this extremely common and burdensome problem.

The authors stated that challenges for this technique include the complex nature of LBP, with numerous potential contributing etiologies; thus, it is important to ensure appropriate patient selection. Patients must not have any contraindications to MRI, such as non-approved implants, claustrophobia, or inability to lie still. Furthermore, because of size limitations based on the MRI bore and ExAblate system, not all patients are physically able to undergo this treatment. Finally, there is a risk of skin burn if there are air bubbles between the transducer and the patient's skin. Care must be taken to ensure continuous monitoring of the treatment field for air bubbles. Because the technique induces coagulative necrosis of the targeted tissues, care must be taken by the proceduralist to identify the desired target on MRI and to examine the safety of the beam path in order to avoid damage to tissue outside the treatment area.

LinQ Sacroiliac Joint Stabilization System

Kaye et al (2021) noted that acute and chronic pain are public health issues that clinicians have been battling for years. Opioid drugs have been a therapeutic option for both acute and chronic pain; however, they can result in unwanted complications and are a major contributor to the current opioid epidemic. The SI joint is a common cause of both acute and chronic LBP, affecting approximately 15 % to 25 % of patients with axial LBP, and up to 40 % of patients with ongoing pain following lumbar fusion. Recent advances in the treatment of SI joint pain have led to the development of a wide variety of SI joint fusion devices. These fusion

devices were designed to stabilize the joints themselves in order that they become immobile and, in theory, can no longer be a source for pain. This is a minimally invasive procedure aimed to address chronic pain without subjecting patients to lengthy surgery or medications, including opioids with the potential for addiction and abuse. Minimally invasive SI fusion can be performed by a lateral approach (i.e., iFuse, Tricor) or posterior approach (i.e., CornerLoc, LinQ, Rialto). The posterior approach requires the patient to be in the prone position but allows for less disruption of muscles with entry. LinQ is a sacroiliac joint fusion system pioneered by PainTEQ (Tampa, FL) that employs a minimally invasive posterior percutaneous approach. The procedure entails initial decortication of the joint followed by insertion of the LinQ allograft spacer complete with demineralized bone matrix. (DBM) In a retrospective case series of 16 patients with chronic SI joint dysfunction who received the LinQ SI joint fusion system, improved pain and decreased opioid consumption were reported (Kim et al, 2020). A multi-center prospective study of the LinQ system, SECURE (Single-arm, Multicenter, Prospective, Clinical Study on a Novel Minimally Invasive Posterior SI Fusion Device), is currently enrolling patients, 100 patients across 9 centers, with the objective to examine pain, AEs, neurological progression, and the need for re-intervention. The authors concluded that more data are needed to determine which fusion system may be best for a particular patient. They stated that SI fusion devices are a promising approach of treating chronic LBP related to the SI joint.

Deer et al (2021) stated that recent advancements in technology have paved the way for SIJ fusion via a posterior approach, which aims to minimize complications and enhance recovery. In a retrospective, observational, multi-center study, these researchers introduced the concept of the posterior approach to SIJ fusion as a feasible adjunct and salvage technique for patients with inadequate pain relief from other minimally invasive surgical procedures, and to validate its effectiveness via a multi-center data analysis. Patients with refractory SIJ pain were treated by interventional pain physicians at 1 of the 8 different pain management centers. All patients underwent posterior SIJ fusion via the LinQ sacroiliac fusion procedure. Demographical data were collected, in addition to patient-reported pain relief. A total of 111 patients were included in the study and underwent posterior SIJ fusion for refractory SIJ-related pain following the use of SCS, interspinous spacer (ISS),

intrathecal drug delivery (IDDS), and/or MILD. Overall, the mean patient reported pain relief following posterior SIJ fusion was 67.6 %. In patients with a history of FBSS, the mean patient reported pain relief was 76.5 %. The authors concluded that in this retrospective case series of patients with continued intolerable pain following SCS, ISS, IDDS, or MILD, a novel posterior SIJ fusion device provided significant pain relief in a salvage manner. These early results suggested that this intervention may be a therapeutic option to consider in these patients.

The authors stated that this trial had several drawbacks. First, the study was a retrospective review and was limited by the inherent weaknesses of this study design, including the lack of a control group. Second, while some patients were followed-up for more than 1 year, the mean follow-up time period was less than 12 months. However, these data were encouraging, and demonstrated the need for controlled studies across multiple centers with larger patient groups to assess which post-salvage device candidate is best suited for this procedure. Third, these investigators did not include health-related QOL outcome measures, and this would be an important area of study in future publications.

Sayed et al (2021) noted that SIJ pathology is a cause of LBP that may be difficult to diagnose and challenging to treat. Open and minimally invasive (MI) lateral approach fusions have been used for the treatment of sacroiliitis over the last 20 years. A novel MI posterior approach SIJ fusion technique employs a posteriorly placed transfixing device with single-point S1/S2 level or mid-segment SIJ fixation (LinQ procedure). Current safety and effectiveness data for this novel procedure are lacking. These investigators reviewed multi-center retrospective 12 months or greater outcomes data in patients receiving the LinQ procedure, with sub-analysis of patients with prior lumbar fusions. Patients with sacroiliitis refractory to conservative care with short-term benefit from diagnostic local anesthetic SIJ injections receiving MI posterior approach SIJ fusion with allograft were included from different centers including both academic and private practice. NRS scores at baseline (pre-procedural) and most recent follow-up were reviewed across three institutions. Of 110 patients who received MI SIJ fusion, 50 patients had sufficient data for evaluation of outcomes at least 12 months post-implant. The average time out from implant at follow-up was 612.2 days for all unique patients. The average NRS was 6.98 pre-fusion and

3.06 at last follow-up; 24 patients had prior lumbar surgery of which 17 had prior lumbar fusions. Average NRS for this subset was 6.85 at baseline and 2.86 at last follow-up with an average follow-up of 613.2 days out from implant. No major AEs or complications were associated with any of the 50 implants. The authors concluded that real-world evidence suggested that MI posterior SIJ fusion with the LinQ procedure is a viable approach for medically refractory sacroiliitis management with long-term efficacy and safety. Moreover, these researchers stated that further prospective studies are needed to fully evaluate this technique.

The authors stated that this study had several drawbacks. It was a retrospective, observational study to examine the rate of complications associated with device utilization and patient-reported outcomes. Due to the timing of initial chart review, many of the patients excluded were not 12 months out from their initial implant or have not presented for their 12 month follow up. To avoid further bias and confounding factors, patients with insufficient data at the authors' desired endpoint of 12 months were excluded. This resulted in a smaller sample size. Being a relatively new procedure and the need for sufficient follow-up to truly examine therapy effectiveness, time mark of at least 12 months post-implant was employed as the primary endpoint. Because of this, many patients were subsequently ineligible to be included in this review. However, it is the authors objective to provide observational long-term results for this new therapy and to provide guidance until prospective studies are complete to further delineate the effectiveness of this therapy. As a result, this was not a comparative study to delineate if this is superior to other means of management. A standard protocol is needed to evaluate device fixation and arthrodesis to fully ascertain the fidelity of the device remaining fixed in the joint. A prospective, multi-center study on this surgical technique is currently in progress. Furthermore, the data reviewed were insufficient to discuss risk factors for device failure or success. This was not a hypothesis-driven study, so findings were observational only and no ITT analysis was carried out. Although significant, the results observed in this study may have multiple confounding factors including recall bias, response bias, and interviewer bias as patients have failed traditional therapies before participating in the SIJ fusion. These investigators stated that further structured multi-center prospective studies are needed to fully examine this technique for management of sacroiliitis.

Smoking Cessation and Spinal/SI Joint Fusion Outcomes

In a systematic review and meta-analysis of published observational cohort studies, Pearson et al (2016) examined the increased risk smokers have of experiencing a delayed and/or non-union in fractures, spinal fusion, osteotomy, arthrodesis or established non-unions. These investigators employed Medline, Embase, Allied and Complementary Medicine Database (AMED) as well as Web of Science Core Collection from 1966 to 2015 to gather data. Observational cohort studies that reported adult smokers and non-smokers with delayed and/or non-union or time to union of the fracture, spinal fusion, osteotomy, arthrodesis or established non-union were eligible. Total of 2 authors screened titles, abstracts and full papers. Data were extracted by 1 author and checked independently by a second. The relative risk ratios (RRs) of smoking versus non-smoking and the mean difference (MD) in time to union patients developing a delayed and/or non-union were calculated. The search identified 3,013 articles; of which, 40 studies were included. The meta-analysis of 7,516 procedures revealed that smoking was linked to an increased risk of delayed and/or non-union. When considered collectively, smokers have 2.2 (1.9 to 2.6) times the risk of experiencing delayed and/or non-union. In all the subgroups, the increased risk was always 1.6 times or higher that of non-smokers. In the patients where union did occur, it was a longer process in the smokers. The data from 923 procedures were included and revealed an increase in time to union of 27.7 days (14.2 to 41.3). The authors concluded that the findings of this study showed that smokers took 27.7 days (14.2 to 41.3) longer for union to occur for fractures, osteotomy, arthrodesis and established non-union. Smokers had double the risk of non-union 2.2 (1.9 to 2.6) for fractures, osteotomy, arthrodesis and established non-union. Smokers should be encouraged to abstain from smoking to improve the outcome of these orthopedic treatments.

Dengler et al (2017) noted that 3 recently published prospective studies have shown that minimally invasive sacroiliac joint fusion (SIJF) using triangular titanium implants produced better outcomes than conservative management for patients with pain originating from the SIJ. Due to limitations in individual trial sample size, analyses of predictors of treatment outcome were not performed. In a pooled patient-level analysis of 2 multi-center randomized controlled trials (RCTs) and 1 prospective,

single-arm, multi-center trial, these researchers identified predictors of outcome of conservative and minimally invasive surgical management of pain originating from the SIJ. They pooled individual patient data from the 3 studies and used random effects models with multi-variate regression analysis to identify predictors for treatment outcome separately for conservative and minimally invasive surgical treatment. Outcome measures included VAS, ODI, and EuroQOL-5D (EQ-5D). These investigators included 423 patients assigned to either non-surgical management (NSM, n = 97) or SIJF (n = 326) between 2013 and 2015. The reduction in SIJ pain was 37.9 points larger [95 % confidence interval (95 % CI): 32.5 to 43.4, p < 0.0001] in the SIJF group than in the NSM group. Similarly, the improvement in ODI was 18.3 points larger (9 5% CI: 14.3 to 22.4), p < 0.0001). In NSM, these investigators found no predictors of outcome. In SIJF, a reduced improvement in outcome was predicted by smoking (p = 0.030), opioid use (p = 0.017), lower patient age (p = 0.008), and lower duration of SIJ pain (p = 0.028). The authors concluded that these findings supported the view that SIJF resulted in better treatment outcome than conservative management of SIJ pain and that a higher margin of improvement could be predicted in non-smokers, non-opioid users, and patients of increased age and with longer pain duration. Level of Evidence = 1.

Phan et al (2018) stated that anterior lumbar interbody fusion (ALIF) is a surgical technique indicated for the treatment of several lumbar pathologies. Smoking has been suggested as a possible cause of reduced fusion rates after ALIF, although the literature regarding the impact of smoking status on lumbar spine surgery is not well established. In a retrospective study, these researchers examined the impact of peri-operative smoking status on the rates of peri-operative complications, fusion, and adverse clinical outcomes in patients undergoing ALIF surgery. They carried out an analysis on a prospectively maintained database of 137 patients, all of whom underwent ALIF surgery by the same primary spine surgeon. Smoking status was defined by the presence of active smoking in the 2 weeks before the procedure. Outcome measures included fusion rates, surgical complications, SF-12, and ODI. Patients were separated into non-smokers (n = 114) and smokers (n = 23). Univariate analysis demonstrated that the percentage of patients with successful fusion differed significantly between the groups (69.6 % versus 85.1 %, p = 0.006). Pseudarthrosis rates were shown to

be significantly associated with peri-operative smoking. Results for other post-operative complications and clinical outcomes were similar for both groups. On multi-variate analysis, the rate of failed fusion was significantly greater for smokers than non-smokers (odds ratio [OR] 37.10, p = 0.002). The authors concluded that the rate of successful fusion after ALIF surgery was found to be significantly lower for smokers compared with non-smokers. No significant association was found between smoking status and other peri-operative complications or adverse clinical outcomes.

Zhuang et al (2020) noted that smoking cessation represents an opportunity to reduce both short- and long-term effects of smoking on complications after lumbar fusion and smoking-related morbidity and mortality. However, the cost-effectiveness of smoking-cessation interventions before lumbar fusion is not fully known. These investigators created a decision-analytic Markov model to examine the cost-effectiveness of 5 smoking-cessation strategies (behavioral counseling, nicotine replacement therapy [NRT], bupropion or varenicline monotherapy, and a combined intervention) before single-level, instrumented lumbar postero-lateral fusion (PLF) from the health payer perspective. Probabilities, costs, and utilities were obtained from published sources. These researchers calculated the costs and quality-adjusted life years (QALYs) associated with each strategy over multiple time horizons and accounted for uncertainty with probabilistic sensitivity analyses (PSAs) consisting of 10,000 second-order Monte Carlo simulations. Every smoking-cessation intervention was more effective and less costly than usual care at the lifetime horizon. In the short-term, behavioral counseling, NRT, varenicline monotherapy, and the combined intervention were also cost-saving, while bupropion monotherapy was more effective but more costly than usual care. The mean lifetime cost savings for behavioral counseling, NRT, bupropion monotherapy, varenicline monotherapy, and the combined intervention were $3,291 (standard deviation [SD], $868), $2,571 (SD, $479), $2,851 (SD, $830), $6,767 (SD, $1,604), and $34,923 (SD, $4,248), respectively. The minimum efficacy threshold (relative risk [RR] for smoking cessation) for lifetime cost savings varied from 1.01 (behavioral counseling) to 1.15 (varenicline monotherapy). A PSA revealed that the combined smoking-cessation intervention was always more effective and less costly than usual care. The authors concluded that even brief smoking-cessation

interventions yielded large short-term and long-term cost savings. Smoking-cessation interventions before PLF could both reduce costs and improve patient outcomes as health payers/systems shift toward value-based reimbursement (e.g., bundled payments) or population health models. Level of Evidence = II.

Debono et al (2021) stated that enhanced recovery after surgery (ERAS) evidence-based protocols for peri-operative care have led to improvements in outcomes in numerous surgical areas, through multi-modal optimization of patient pathway, reduction of complications, improved patient experience and reduction in the length of stay. ERAS represent a relatively new paradigm in spine surgery. In a multi-disciplinary consensus review, these investigators summarized the literature and proposed recommendations for the peri-operative care of patients undergoing lumbar fusion surgery with an ERAS program. Under the impetus of the ERAS Society, a multi-disciplinary guideline development group was constituted by bringing together international experts involved in the practice of ERAS and spine surgery. This group identified 22 ERAS items for lumbar fusion. They performed a systematic search in the English language in Medline, Embase, and Cochrane Central Register of Controlled Trials. Systematic reviews, RCTs, and cohort studies were included, and the evidence was graded according to the GRADE system. Consensus recommendation was reached by the group after a critical appraisal of the literature. A total of 256 articles were included to develop the consensus statements for 22 ERAS items; 1 ERAS item (pre-habilitation) was excluded from the final summary due to very poor quality and conflicting evidence in lumbar spinal fusion. From these remaining 21 ERAS items, 28 recommendations were included. All recommendations on ERAS protocol items were based on the best available evidence. These included 9 pre-operative, 11 intra-operative, and 6 post-operative recommendations. They spanned topics from pre-operative patient education and nutritional evaluation, intra-operative anesthetic and surgical techniques, and post-operative multi-modal analgesic strategies. The level of evidence for the use of each recommendation was presented. The ERAS Society recommend a combined smoking cessation therapy at a minimum of 4 weeks before surgery. Quality of Evidence = Moderate; recommendation grade = Strong.

In a retrospective review of prospectively collected registry data, Gatot et al (2022) examined the effect of smoking on 2 years post-operative functional outcomes, satisfaction, and radiologic fusion in non-diabetic patients undergoing minimally invasive transforaminal lumbar interbody fusion (TLIF) for degenerative spine conditions. Prospectively collected registry data of non-diabetic patients who underwent primary single-level minimally invasive TLIF in a single institution was reviewed. Patients were stratified based on smoking history. All patients were examined pre-operatively and post-operatively using the Numerical Pain Rating Scale for back pain and leg pain, ODI, SF-36 Physical and Mental Component Scores. Satisfaction was evaluated using the North American Spine Society (NASS) questionnaire . Radiographic fusion rates were compared. A total of 187 patients were included, of which 162 were non-smokers, and 25 had a positive smoking history. In this multi-variate analysis, smoking history was insignificant in predicting for minimal clinically important difference attainment rates in Physical Component Score and fusion grading outcomes. However, in terms of satisfaction score, positive smoking history remained a significant predictor (OR = 4.7, 95 % confidence interval [CI]: 1.10 to 20.09, p = 0.036). The authors concluded that non-diabetic patients with a positive smoking history had lower satisfaction scores but comparable functional outcomes and radiologic fusion 2 years after single-level TLIF. These investigators stated that thorough pre-operative counseling and smoking cessation advice may help to improve patient satisfaction following minimally invasive spine surgery. Level of Evidence = III.

Khalid et al (2022) stated that while there are several reports on the impact of smoking tobacco on spinal fusion outcomes, there is minimal literature on the influence of modern smoking cessation therapies on such outcomes. These researchers examined the outcomes of single-level lumbar fusion surgery in active smokers and in smokers undergoing recent cessation therapy. MARINER30, an all-payer claims database, was used to identify patients undergoing single-level lumbar fusions between 2010 and 2019. The primary outcomes were the rates of any complication, symptomatic pseudarthrosis, need for revision surgery, and all-cause re-admission within 30 and 90 days. The exact matched population analyzed in this study contained 31,935 patients undergoing single-level lumbar fusion with 10,645 (33 %) in each of the following groups:

- active smokers;
- patients on smoking cessation therapy; and
- those without any smoking history.

Patients undergoing smoking cessation therapy have reduced odds of developing any complication following surgery (OR 0.86, 95 % CI: 0.80 to 0.93) when compared with actively smoking patients. Non-smokers and patients on cessation therapy had a significantly lower rate of any complication compared with the smoking group (9.5 % versus 17 % versus 19 %, respectively). The authors concluded that when compared with active smoking, pre-operative smoking cessation therapy within 90 days of surgery decreased the likelihood of all-cause post-operative complications. However, there were no between-group differences in the likelihood of pseudarthrosis, revision surgery, or re-admission within 90 days.

In a systemic review and meta-analysis, Nunna et al (2022) examined the effect of tobacco smoking on risk of nonunion following spinal fusion. These investigators carried out a systematic search of Medline, Embase, Cochrane Central Register of Controlled Trials, and the Cochrane Database of Systematic Reviews from inception to December 31, 2020. Cohort studies directly comparing smokers with non-smokers that provided the number of non-unions and fused segments were included. Following data extraction, the risk of bias was assessed using the Quality in Prognosis Studies Tool, and the strength of evidence for non-union was examined using the Grading of Recommendations Assessment, Development and Evaluation (GRADE) working group criteria. All data analysis was carried out in Review Manager 5, and a random effects model was used. A total of 20 studies assessing 3,009 participants, which included 1,117 (37 %) smokers, met inclusion criteria. Pooled analysis found that smoking was associated with increased risk of non-union compared to not smoking 1 year or less following spine surgery (RR 1.91, 95 % CI: 1.56 to 2.35). Smoking was significantly associated with increased non-union in those receiving either allograft (RR 1.39, 95 % CI: 1.12 to 1.73) or autograft (RR 2.04, 95 % CI: 1.54 to 2.72). Both multi-level and single-level fusions carried increased risk of non-union in smokers (RR 2.30, 95 % CI: 1.64 to 3.23; RR 1.79, 95 % CI 1.12 to 2.86, respectively). The authors concluded that smoking status carried a global risk of non-union for spinal fusion procedures regardless of follow-up

time, location, number of segments fused, or grafting material. Moreover, these investigators stated that further comparative studies with robust methodology are needed to establish treatment guidelines tailored to smokers.

Connor et al (2022) noted that tobacco use is associated with complications after surgical procedures, including poor wound healing, surgical site infections, and cardiovascular events. In a retrospective, database study, these researchers used the Nationwide Readmissions Database (NRD) to determine if tobacco use is associated with increased 30- and 90-day re-admission among patients undergoing surgery for degenerative spine disorders. Patients who underwent elective spine surgery were identified in the NRD from 2010 to 2014. The study population included patients with degenerative spine disorders treated with discectomy, fusion, or decompression. Descriptive and multi-variate logistic regression analyses were carried out to identify patient and hospital factors associated with 30- and 90-day re-admission, with significance set at p value of < 0.001. Within 30 days, 4.8 % of patients were re-admitted at a median time of 9 days. The most common reasons for 30-day re-admission were post-operative infection (12.5 %), septicemia (3.5 %), and post-operative pain (3.0 %). Within 90 days, 7.3 % were re-admitted at a median time of 18 days. The most common reasons for 90-day re-admission were post-operative infection (9.6 %), septicemia (3.5 %), and pneumonia (2.3 %). After adjustment for patient and hospital characteristics, tobacco use was independently associated with re-admission at 90 days (OR 1.05, 95 % CI: 1.03 to 1.07, p < 0.0001; but not 30 days (OR 1.02, 95 % CI: 1.00 to 1.05, p = 0.045). The authors concluded that tobacco use was associated with re-admission within 90 days after cervical and thoracolumbar spine surgery for degenerative disease. Tobacco use is a known risk factor for adverse health events and therefore should be considered when selecting patients for spine surgery.

Cooled Radiofrequency Denervation for Sacroiliac Joint Pain

McCormick and associates (2019) stated that no previous study has examined the outcomes of cooled RF ablation (C-RFA) of the medial branch nerves (MBNs) for the treatment of lumbar facet joint (LFJ) pain nor compared its effectiveness to traditional RFA (T-RFA). In a blinded,

prospective trial, these researchers examined 6-month outcomes for pain, function, psychometrics, and medication usage in patients who underwent MBN C-RFA versus T-RFA for lumbar Z-joint pain. Patients with positive diagnostic MBN blocks (greater than 75 % relief) were randomized to MBN C-RFA or T-RFA. The primary outcome was the proportion of "responders" (greater than or equal to 50 % NRS reduction) at 6-months. Secondary outcomes included NRS, ODI, and Patient Global Impression of Change (PGIC). A total of 43 subjects were randomized to MBN C-RFA (n = 22) or C-RFA (n = 21). There were no significant differences in demographic variables (p's > 0.05). A greater than or equal to 50 % NRS reduction was observed in 52 % (95 % CI: 31 % to 74 %) and 47 % (95 % CI: 26 % to 71 %) of subjects in the C-RFA and T-RFA groups, respectively (p = 0.75). A greater than or equal to 15-point or greater than or equal to 30 % reduction in ODI score was observed in 62 % (95 % CI: 39 % to 80 %) and 42 % (95 % CI: 22 % to 66 %) of subjects in the C-RFA and T-RFA groups, respectively (p = 0.21). The authors concluded that when using a single diagnostic block paradigm with a threshold of greater than 75 % pain reduction, C-RFA resulted in a treatment success rate greater than 50 % when defined by pain reduction, and greater that 60 % when defined by improvement in physical function, at 6-month follow-up. No significant differences were observed between the 2 RFA modalities. Moreover, these researchers stated that future study should use the effect size or success rate demonstrated in this prospective study for power calculation.

The authors stated that the main drawback of this study was the relatively small sample size (n = 21 in the C-RFS group). Also, 5 patients dropped out after being enrolled by prior to randomization; selection bias was possible but not dissimilar to other studies of procedural interventions in which individuals may elect for additional non-invasive care before undergoing intervention. Furthermore, subjects were lost to follow-up; of 43 participants who underwent treatment intervention, 3 (7 %) did not report outcomes for the full 6-month duration of the study. A drop-out effect could have altered the overall outcome of the study. Analysis by conservative worst-case scenario definitions (treating all subjects lost to follow-up as treatment failures) would adjust the treatment success rate to 50 % (95 % CI: 29 % to 71 %) and 59 % (95 % CI: 39 % to 80 %) for pain reduction and functional improvement, respectively, in the C-RFA group. 20-G rather than 16-G or 18-G RFA electrodes were used for

conventional ablations; as such, the success rate in the T-RFA group may be lower than would be expected when using larger gauge electrodes. In additional, some providers used bipolar lead placement, longer lesion duration times, higher lesioning temperatures or longer active tips when employing C-RFA, all of which expanded the size of the lesion and may increase the chance of successful MBN capture. A heterogeneous group of 5 faculty members, assisted by Pain Medicine fellows, carried out these procedures; difference in experience level with the procedural technique may have influenced patient outcomes, although this heterogeneity did improve generalizability of the reported findings. Finally, RFA represents a treatment that is implemented with the goal of long-term treatment; these researchers measured a primary outcome at 6 months; and did not follow subjects beyond this time period; thus, future study would ideally capture outcomes at a post-RFA time-point of at least 1 year. Indeed, it is conceivable that an inter-group difference may have been observed if outcomes had been evaluated beyond 6 months.

In a systematic review and meta-analysis, Shih and colleagues (2020) compared the effectiveness of different RF techniques (thermal, pulsed, and cooled RF) for the treatment of patients with LFJ or SIJ pain. The selection criteria included age of greater than 18 years; patients suffering from LFJ or SIJ pain; and patients receiving RF treatments. A total of 4 electronic databases, including PubMed, Embase, Cochrane Library, and ISI Web of Knowledge were systematically searched from inception until December 2019 for relevant articles. The search was performed on January 2, 2020. When the outcomes among articles showed heterogeneity, then a random-effects model was adopted to calculate the effect size; otherwise, a fixed-effects model was adopted. All 3 techniques showed significant improvements in LFJ or SIJ pain for up to 12 months compared with the baseline level; however, no significant differences among the 3 techniques were observed at any follow-up visits except for possibly a trend for variance in effectiveness. For the treatment of LFJ pain, cooled RF was the most effective, followed by thermal RF and then pulsed RF as the least, respectively, for the follow-up visit at 6 months. No serious complications were reported after receiving treatment using the 3 techniques. The authors concluded that sequentially, cooled RF followed by thermal RF and then pulsed RF for the treatment of patients with LFJ pain were identified as most to least effective at the 6-month follow-up.

Candan and Gungor (2021) noted that C-RFA is a newer technique and may have some theoretical advantages over T-RFA. In a retrospective, single-center study, these investigators examined the safety and effectiveness of C-RFA for the treatment of LFJ-mediated pain. They evaluated 185 C-RFA performed on 105 patients. All patients with axial lower back pain who received the preliminary diagnosis of LFJ-mediated pain and refractory to conservative therapy underwent diagnostic medial branch blocks. C-RFA was recommended to those patients who responded favorably to 2 sets of diagnostic medial branch blocks. Pain scores in NRS were recorded pre-treatment and post-treatment at different time-points. The primary outcome measures were NRS score and average % improvement from baseline at each time-point. A significant pain relief was determined by a decrease of greater than or equal to 50 % of mean NRS. Secondary outcome measure was the time to repeat treatment with subsequent C-RFA; AEs were also recorded. Primary outcome measure determined as the improvement in NRS, for at least 50 % or more, was achieved in both 1st (4 to 8 weeks) and 2nd (greater than 2 months to 6 months) follow-up (FU) with 60.5 % and 53.6 % reduction in NRS, respectively. Subgroup analysis comparing the younger (less than 50 years of age) and older (greater than or equal to 50 years of age) age groups showed superior pain relief with C-RFA in the older (greater than or equal to 50) age group, both in the 1st (4 to 8 weeks) and 2nd (greater than 2 months to 6 months) FU time-points (63.4 % and 58.4 % reduction in NRS, respectively). The authors concluded that these findings suggested that C-RFA was a safe and effective treatment modality to achieve targeted pain relief in all age groups lasting at least 6 months for the treatment of LFJ-mediated pain. The duration of pain relief with C-RFA was comparable to, but not significantly longer than, the duration of pain relief achieved with T-RFA as reported in the literature for the treatment of chronic LFJ-related pain.

The authors stated that drawbacks of this study were: This was a single-center study, which was designed as a retrospective and data-based research with the aim of examining the safety and effectiveness of C-RFA of medial branches. Data were affected by patients lost to follow-up.

In a retrospective study, Kawamoto and co-workers (2021) examined pain relief following RF denervation of the SIJ. The secondary objective was to evaluate pain intensity and relief duration. Data were collected from the

medical records of patients undergoing RF denervation for SIJ-mediated LBP from January 2015 to December 2017. A total of 78 patients were studied (age of 18 and 65 years, of both genders, ASA I - II). The patients were submitted to denervation of SIJ by 3 types of RF (conventional, pulsed, and cooled). The following parameters were evaluated, number of patients who obtained greater than 50 % pain relief; pain intensity, measured using the VAS (before the procedure and 15, 30, 90 and 180 days after, performed by the same evaluator); and the use of complementary analgesic for 2 weeks. Of the 78 included patients, 56 (71.8 %) underwent conventional RF, 9 (11.5 %) underwent pulsed RF, and 13 (16.7 %) underwent C-RFA. There were losses to follow-up including 40 patients who underwent conventional RF, 5 who underwent pulsed RF, and 12 who underwent C-RFA, who were retained for 6 months. There was significant pain relief with the 3 types of RF for up to 6 months of follow-up, with no difference among the types. After 6 months, 90.2 % of patients who underwent conventional RF, 100 % who underwent pulsed RF, and 91.7 % who underwent C-RFA maintained greater than or equal to 50 % pain relief. Complementary analgesics were used by 95 % of the patients who underwent conventional RF, 80 % who underwent pulsed RF, and 91 % who underwent C-RFA 2 weeks after the procedure. There were mild AEs, such as edema, hematoma, and local pain, without complications. The authors concluded that RF denervation of the SIJ was effective and promoted a long-lasting analgesic effect. Moreover ,these researchers stated that the limitations of this trial were the number of pulsed and C-RFA was low and in a retrospective study some data may be missing, especially from follow-up (12 of the 13 patients I the C-RFA group were lost in follow-up).

Furthermore, an UpToDate review on “Subacute and chronic low back pain: Nonsurgical interventional treatment” (Chou, 2022) provides the following recommendations:

We also suggest not performing the following treatments for chronic low back pain (Grade 2B):

- Intradiscal electrothermal therapy (IDET) and percutaneous intradiscal radiofrequency thermocoagulation (PIRFT)
- Radiofrequency denervation.

Trigger Point Injections with Normal Saline

Kongsagul et al (2019) noted that based on the histological confirmation of the presence of nerve structure in the fascia, hence, myofascial pain was treated by the mechanism referred to as interfascial block. To-date, the studies of physiological saline for treating patients with myofascial pain has been limited. Ultrasound (US) guided with physiological saline injection (PSI) technique has been routinely practiced among patients with myofascial pain in outpatient service at the Department of Rehabilitation Medicine, King Chulalongkorn Memorial Hospital. These investigators reviewed data including the percentage of patients responding, acceptable pain period, and adverse events (AEs). Electronic medical reports among 142 patients receiving US-guided PSI from August 1, 2016, to November 20, 2017, at the Department of Rehabilitation Medicine, King Chulalongkorn Memorial Hospital, were retrospectively reviewed by the 1st author. Procedures were performed by the last author. The analysis was independently performed by the 1st author. A total of 142 patients with complete medical records were compatible with analysis . The average age of patients was 55 years. Most of the patients were women (68.3 %). Most of the patients (76.8 %) had chronic suffering from myofascial pain. Approximately half of the patients (56.4 %) received pain-relieving medications. Upper trapezius muscle (19.5 %) was the most common muscle receiving the procedure, followed by multifidus (10.0 %) and quadratus lumborum (9.5 %). Most of the patients (86.8%) received the procedure for 1 muscle. Approximately 30 % of the patients were able to stop pain-relieving medications after the procedure. The median of acceptable pain period was 63 days. The percentage of patients having an acceptable pain period of greater than 3 months was 43.9 %. No major AEs were demonstrated. The authors concluded that US-guided PSI technique demonstrated pain reduction in 72.8 % of the analyzed patients, with an acceptable pain period of 63 days. No major AEs were demonstrated among all the patients. This technique should be considered as another invasive procedure for eradication myofascial trigger point.

Roldan et al (2020) stated that myofascial pain syndrome (MPS) originates in the muscle and fascia. MPS presents with referred pain specific for each muscle and a trigger point that reproduces the symptoms. Trigger-point-injection (TPI) is an effective approach to

treating MPS. Some TPI agents, however, are associated with systemic and local side effects. These researchers examined the effectiveness of TPI with a conventional active drug mixture (CADM) versus that with normal saline solution (NS) alone in patients with MPS presenting to the emergency department (ED). Subjects were randomly assigned to receive TPI with NS or with CADM. Pain intensity was scored using a 0 to 10 numeric rating scale (NRS) prior to and after TPI, before discharge and 2 weeks after TPI. Among 48 patients analyzed, 23 received TPI with NS. The mean pain scores were as follows: immediately before TPI, 7.59 (NS) and 7.44 (CADM); immediately after TPI, 2.22 (NS) and 1.76 (CADM); prior to discharge, 1.52 (NS) and 1.76 (CADM). At 2-week follow-up, the mean pain scores were 4.29 (NS) and 4.14 (CADM). Pain was significantly reduced after TPI in both groups. At 2 weeks, the mean pain scores were similar between the groups. No adverse events (AEs) were reported. The authors concluded that in cases of MPS in the ED, pain can be controlled with TPI independent of the injectate; TPI with NS may be preferred over CADM because of its lower cost and more favorable side effect profile.

In a pilot study, Cho et al (2022) examined the effectiveness of new targeted TPIs using isotonic saline in patients with chronic tension-type headache (CTTH). Of 121 patients with headache who were retrospectively reviewed, 19 were included in this study and were categorized into 2 groups: those who received TPIs more than 4 times (group 1); and those who received TPIs less than, or equal to, 4 times (group 2). Subjects received US-guided isotonic saline injections into the active trigger points once-weekly. The primary outcome was an effect on headache intensity, determined using the VAS, whereas the secondary outcome was an effect on quality of life (QOL), evaluated using the Henry Ford Hospital Headache Disability Inventory (HDI). The mean symptom duration of the 19 patients (11 men and 8 women; mean age of 52.5 years; and range of 23 to 81 years) was 16 months. The most frequently injected muscle was the splenius capitis. Patient demographics were similar between the 2 groups ($p > 0.05$). Simple linear regression revealed that symptom duration ($p = 0.001$) and baseline VAS score ($p = 0.009$) were significantly associated with the number of injections. At 1 month after the 1st injection, the mean VAS and HDI scores in group 2 were significantly lower than those in group 1 ($p < 0.05$), whereas the scores significantly decreased immediately after the last injection in both

groups ($p < 0.05$). No adverse effects were reported in any patient. The authors concluded that these findings indicated that the administration of new targeted TPIs using isotonic saline into the head and neck muscles of patients with CTTH could effectively relieve headache intensity and safely improve their QOL.

Furthermore, an UpToDate review on "Subacute and chronic low back pain: Nonsurgical interventional treatment" (Chou, 2022) states that "Local or trigger point injection -- A systematic review found no clear differences between local or trigger point injections with a local anesthetic, with or without a corticosteroid, and control interventions (saline or dry needle injections, or ethyl chloride plus acupressure) for short-term (7 days to 2 months) pain relief in 3 trials of patients with subacute or chronic low back pain. All trials had methodological shortcomings and evaluated heterogeneous injection methods. One trial evaluated an injection over the iliac crest, one evaluated injections over the iliolumbar ligament, and one evaluated trigger point injections. The limited benefit observed in heterogeneous, low-quality studies does not support their widespread use".

Glossary of Terms

Term	Definition
Trigger point	A specific point or area where, if stimulated by touch or pressure, a painful response will be induced. A set of trigger point injections means injections in several trigger points in one sitting.

Appendix

Oswestry Low Back Disability Questionnaire (https://www.rehab.msu.edu/_files/_docs/oswestry_low_back_disability.pdf)

Numeric Rating Scale (NRS) (https://www.physio-pedia.com/Numeric_Pain_Rating_Scale)

Provocative Tests of the Sacroiliac Region

Provocative tests of the sacroiliac region are thought to indicate sacroiliac joint dysfunction when at least 3 different tests reproduce the patient's typical pain in the SI region, including:

- Compression test, also called the approximation test, stresses the SI joint structures, in particular the posterior SI joint ligament, to attempt to replicate the patient's symptoms.
- Thigh thrust test involves the examiner applying downward pressure along the femur with the patient supine. Pain at the ilium or SI joint suggests SI joint dysfunction.
- Patrick's sign is also referred to as the Fabere test. The examiner flexes, abducts, externally rotates, and extends the affected leg so that the ankle of that leg is on top of the opposite knee (a figure of 4 configuration). The affected leg is then slowly lowered toward the examining table. A negative result occurs when the test leg falls at least parallel to the opposite leg. A positive test result occurs when the affected leg remains above the opposite leg and pain arises unilaterally in the active hip.
- Distraction test, also known as the gaping test, is positive for pain sacroiliac joint dysfunction or other pelvic abnormalities when downward pressure is applied simultaneously to the iliac crest when the patient is in supine position.
- Gaenslen's test is accomplished with the patient supine. One hip is flexed by pushing the patient's knee to their chest, while simultaneously extending the opposite hip joint. This maneuver stresses both sacroiliac joints. Posterior pelvic pain indicates a positive test.

Non-Covered Interspinous Fixation Devices

Considered experimental and investigational; not an all-inclusive list:

- Affix II and Affix II Mini Spinous Process Plating System (NuVasive)
- Aileron Interspinous Fixation System (Life Spine)

- Aspen MIS Fusion System (Biomet)
- Aspen Spinous Process Fixation System (Lanx)
- Axle (X-Spine)
- BacFuse (Pioneer Surgical)
- Benefix Interspinous Fixation System
- Biomet Aspen fusion system
- BridgePoint (Alphatec)
- CD Horizon Spire Fixation System (Medtronic Sofamor Danek)
- Coflex-F (Paradigm Spine)
- Inspan (Spine Frontier)
- Minuteman Interspinous Interlaminar Fusion Device (Spinal Simplicity)
- PrimaLOK SP (OsteoMed)
- Octave (Life Spine)
- StabiLink MIS Interspinous Fixation Device (Southern Spine)
- SP-Fix Spinous Process Fixation System (Globus Medical).

Non-Covered Interspinous and Interlaminar Distraction Devices

Considered experimental and investigational; not an all-inclusive list:

- Aperius PercLID System (Kyphon/ Medtronic Spine)
- Coflex Interlaminar Technology Implant (Paradigm Spine)
- CoRoent Extensure (Nuvasive)
- DIAM Spinal Stabilization System (Medtronic Sofamor Danek)
- ExtenSure (Nuvasive)
- FLEXUS (Globus Medical)
- Falena Interspinous Decompression Device (Mikai Spine)
- Helifix Interspinous Spacer System (Alphatec Spine)
- In-Space (Synthes)
- NL-Prow Interspinous Spacer (Non-Linear Technologies)
- Stenofix (Synthes)
- Superion ISS Interspinous Spacer System (VertiFlex)
- Wallis System (Abbott Spine/ Zimmer Spine)
- X-STOP Interspinous Process Decompression (IPD) System (Kyphon/ Medtronic Spine)
- X-STOP PEEK Interspinous Process Decompression (IPD) System (Kyphon/ Medtronic Spine).

Spine Cages

Not an all-inclusive list, considered medically necessary when criteria are met:

- A-CIFT SoloFuse (SpineFrontier)
- ACIS cage (Synthes)
- Acromed Lumbar I/F Cage (Depuy)
- Aero AL (Stryker)
- Aero C (Stryker)
- Aesculap PEEK
- Alamo Spine Cage (Alliance Spine)
- Aleutian Spacer System (K2M)
- ALIF Spine Truss System (4web)
- Alphatec Novel TL Spacer System
- Anatomic PEEK PTC cervical fusion system (Medtronic)
- Ancora spacer (Zimmer)
- AnyPlus PEEK TLIF (GS Medical)
- Apache spacer (Genesys)
- Arch ODL spacer (Synthes)
- Arena-C (SpineFrontier)
- Ascential (Stryker)
- Athlet (Signus)
- Avenue-L (Zimmer Biomet)
- AVS Anchor-L Lumbar Cage System (Stryker)
- AVS AS PEEK (Stryker)
- AVS Navigator (Stryker)
- AVS PL PEEK (Stryker)
- BAK Interbody Fusion System (Zimmer)
- Bengal Corpectomy Cage (Depuy)
- BoneBac Interbody System (Thompson MIS)
- Brantigan (DePuy)
- Brigade (Nuvasive)
- Bullet-Tip PEEK VBR/IBF (RTI Surgical)
- CALIX cage (X-Spine)
- Cambria anterior cervical interbody system (Integra\Theken Spine)
- Capstone PEEK Cage (Medtronic)
- Cascadia TL implant system (K2M)
- Cavetto cage (Neurostructures)
- Cezanne II (Accel Spine)
- Chesapeake Spinal System (K2M)
- Cimplicity (SpineSmith)
- Clariance TLIF cage
- Clydesdale (Medtronic)
- Co Roent XL (Nuvasive)
- Coalition Spacer (Globus)
- Concorde Bullet Spine System (DePuy Synthes)
- Construx Mini PTC Spacer System (Orthofix)
- Continental (Globus)
- Corelink Anterior Cervical Interbody Cage System (Foundation)

- Cornerstone PSR Spinal System (Medtronic)
- CoRoent Interbody Cage (Nuvasive)
- Cougar Cage System (Depuy)
- Coveris (Camber)
- C-Plus IBF (Pioneer Sugical\RTI Surgical)
- Crescent cage (Medtronic)
- Devex TLIF Cage (DePuy)
- Dorado (Spine Frontier)
- Ebi PEEK optima spacer (Biomet)
- Emerald cervical PEEK system (Glasir)
- Eminent Sidewinder DLIF PEEK Cage
- Endoskeleton TCS (Titan Spine)
- Express IBFD (Advanced Vertebral Solutions)
- Foundation Cervical Interbody Device (CoreLink)
- Fuse (Medtronic)
- FuseLox Lumbar Cage (Captiva Spine)
- Harpoon, Hawkeye, Hornet, Shark (ChoiceSpine)
- Honour cage (Nexxt Spine)
- Honour Orb (Nexxt Spine)
- IN:C2 spacer (SpineSmith)
- InFill Lateral Interbody Device (Pinnacle Spine)
- Innovasis Box PEEK IBF System
- Innovasis C-Box PEEK cage
- Interfuse - T (Vertebral Technologies)
- Irix-C (X Spine)
- Juliet TL Lumbar Interbody Fusion Device (Spineart)
- LANX Lateral Cage
- LDR ROI-A Implant System
- Leopard (DuPuy)
- Levo fixed cage (non-expandable) (Alphatec Spine)
- LLC Reveal VBR System (Theken)
- Lucent Magnum (Spinal Elements)
- Lucent TiBond Interbody System (Spinal Elements)
- Luna Interbody Fusion System (Benvenue)
- Magnum + Stand-alone Lumbar Interbody Fusion system (Spinal Elements)
- Maxim Surgical X-Treme interbody fusion system
- MectaLIF transforaminal lumbar interbody fusion device (Genesys)
- Medyssey BN
- NanoLOC (Titan)
- Nanovis cage
- Novel Spinal System (Alphatec Spine)
- OLIF PEEK (Medtronic)
- OLIF 51 (Medtronic)
- Orio-AL, Orio-C, Orio-PL, Orio-TL (SpineCraft)
- Osteofix Pillar (AL, SA, PL, TL)
- OsteoStim (Biomet)
- Pathway AVID (Custom Spine)
- Pillar SA PEEK Spacer (Orthofix)
- Pioneer Interbody Fusion (IBF)/Vertebral Body

Replacement System (C-Plus)
- Precision Vault ALIF System (Precision Spine)
- Prevail Interbody Device (Medtronic)
- PRO-LINK Stand-Alone Cervical Spacer System (Life Spine)
- Pulse cervical cage system (DePuy)
- Ravine (K2M)
- Ray Threaded Fusion Cage (Synthes)
- Renovis PEEK ALIF Cage
- ROI-C (LDR)
- Scarlet AC-T Secured Anterior Cervical Cage (SpineArt)
- Silverstone IBF System (Altus Spine)
- Solitaire C Cervical Spacer System (Biomet)
- Spine 360 plate & cage for cervical fusion
- Spine 360 Cervical Interbody Fusion System
- Spine Vu c-POD Intervertebral Body Fusion Device (Integra\Theken)
- Stalif-C (Cervical Cage) (Centinel Spine)
- Stalif Midline and Stalif Midline ABO Screws (Centinel Spine)
- Stingray (Spine 360)
- Surgical Titanium Mesh (Depuy)
- Sustain-O (Globus)
- Syncage (Synthes)
- SYNFIX LR system (Synthes)
- T-Pal (Synthes)
- Timberline Cage (Lanx)
- TiNano (Aurora Spine)
- TiLink-T (Acuity Surgical)
- Titanium PL cage (Stryker)
- Tomcat (Choice Spine)
- Transcontinental (Globus)
- Tryptik CA (Spineart)
- Valeo C (Amedica)
- Valeo II LL (Amedica)
- Vault ALIF system (Precision Spine)
- Velofix (U & I Corporation)
- Vertigraft (Lifenet)
- Vertu TiBond PEEK cage
- Vu POD (Integra\Theken)
- XP L Spinal System (Arcadius)
- Zavation PEEK cage
- Zero-P Zero-Profile Anterior Cervical Interbody Fusion Device (Synthes)
- Zeus A (Amendia)
- Zeus C cervical spacer (Amendia)
- Zeus L (Amendia)
- Zeus T (Amendia)
- Zimmer TM-S cervical fusion device
- Zyston Curved Spacer System (Biomet)
- Zyston Straight Spacer System (Biomet).

Expandable Spine Cages

Considered medically necessary when criteria for expandable cages are met; not an all-inclusive list:

- Acculif Expandable Cage (Stryker)
- Bengal Stackable (DePuy Synthes)
- Elevate Expandable Cage (Medtronic)
- Globus Altera Expandable Cage
- Globus Caliber Expandable Cage
- Globus Fortify Corpectomy Spacer
- Globus Latis Expandable Cage
- Globus Magnify
- Globus Magnify S
- Globus Rise
- Leva Expandable Cage (Spine Wave, Inc)
- Nuvasive X-Core Expandable Cage
- Omni VBR Expandable cage (Ulrich)
- Per 360 expandable cage (Interventional Spine)
- Staxx XD Expandable Cage (Spine Wave, Inc)
- Ulrich ADDPlus
- Wenzel Spine Varilift Expandable Cage

Pedicle Screw Systems

Considered medically necessary when criteria are met; not an all-inclusive list:

- ABC Cervical Plating System (Aesculap)
- Accufit ALIF plate (Precison Spine)
- AcuFx Thinline (Zimmer)
- Aesculap S4
- Alphatec ASPIDA anterior lumbar plating system
- Altus Cervical Spine Plate System
- Anax (U & I Corporation)
- Antegra plate (Synthes)
- Anterior cervical stabilization system (Southern Spine)
- Anterior tension band (ATB) (Synthes)
- Apelo (Atlas Spine)
- Apex Deformity Spine System (SpineCraft)
- Arch ODL Fixation System (Synthes)
- Arsenal (Alphatec Spine)

- Archon Anterior Cervical Plate System (NuVasive)
- Armada Spinal System (NuVasive)
- Aspect Plate and Screws (Pioneer Surgical)
- Assure (Globus)
- Astra Spine System (SpineCraft)
- Athena (Royal Oak Medical)
- Atlantis Translational Plate for Cervical Fusion (Medtronic)
- Aviator Anterior Cervical plating system (Stryker)
- Balboa plate (SeaSpine)
- Binary plates and screws (Genesys spine)
- Biomet MaxAn Cervical Plate System
- Blackbird spinal system (Choice Spine)
- Blueridge Cervical Plate and Screws (K2M)
- Brigade anterior plate system (NuVasive)
- Cabo (SeaSpine)
- Caplox II Spinal System (non-cervical) (Captiva Spine)
- CapSure PS3 Spine System (Spine Wave, Inc)
- Cayman KZ plate (Signus)
- CD Horizon Legacy Spinal System (Medtronic)
- CD Horizon Spine Fixation System (Medtronic)
- Centerpiece plate (Medtronic)
- Cequence anterior cervical plate (Pioneer Surgical)
- CerviFix Cervical Spine Locking Plate (CSLP) (Synthes)
- Click'X pedicle screw system (Synthes)
- Coral Spinal System (Integra\Theken)
- Corelink Tiger pedicle screws
- CREO system (Globus)
- Decade plate (NuVasive)
- Degas plate (Accel Spine)
- Denali Degenerative Spine System (K2M)
- Diamond (Amendia)
- Dio Medical Rex Anterior Cervical Plate System
- DynaTran anterior cervical plate (Stryker)
- Eagle plate (DePuy)
- Ellipse Occipito-Cervical-Thoracic spinal system (Globus)
- EOS spinal system (Korean Bone Bank)
- Erisma - LP (Clariance)
- Everest Pedicle Screw Spinal System (K2M)
- Excella (Innovasis)
- Expedium Verse System (DePuy Synthes)
- Express pedicle screw and rod system (X-Spine)
- Firebird (Orthofix)
- Flamenco (Ulrich)
- Fortress Pedicle Screw System (Spineology)
- Fortex pedicle screw (X-spine)
- Fortibridge plate (Nanovis)
- G surgical plate system T LOC
- Genesis TiLock

- Globus XTEND plate
- Gruve (Life Spine)
- Hallmark plate for cervical fusion (Orthofix)
- Hyper-C (DenGen)
- Iliad spinal thoracolumbar system (Medyssey)
- Illico pedicle screw system (Alphatec)
- Invizia plate (Zimmer)
- Invue plate (SpineFrontier)
- Iris anterior cervical plate (Life Spine)
- Kinetic-SL Dynamic Anterior Cervical Plate System (Life Spine)
- King Cobra Anterior Cervical Plate (Eminent Spine)
- Lanx Pedicle Screw Spinal System
- Leucadia (Phygen LLC)
- Lineum OCT spine system (Biomet)
- Lnk thoraco-lumbar pedicle screw system (Aegis)
- Lotus System (Spinal Elements)
- Malibu (SeaSpine)
- Mambo plate (Ulrich)
- Manta Ray Anterior Cervical Plate System (Theken Spine)
- Mantis (Stryker)
- Medical Mesa System (K2M)
- Medical N Cervical Plate System (Sharp Medical Spine)
- Medyssey Zenius spinal system
- Mercury Spine Element screw and rod system (Spinal Elements)
- MonoPoly Pedicle Screw System (Signus)
- Mosaic System (Spinal Elements)
- Mountaineer OCT Spinal System (DePuy)
- MUST pedicle screw system (Medacta)
- Nautilus Thoracolumbar Spinal System (Life Spine)
- NEO SL (Life Spine)
- Newport MIS system (Integra\Thesen)
- Nex-Link rods and screws (Zimmer)
- Ni-lock (Spine Wave, Inc)
- Osteonics Techtonix System (Stryker)
- Optio-C Anterior Cervical Plate (Zimmer)
- Pagoda (Odev)
- Palisade (Spineology)
- Pathfinder NXT Sequoia Pedicle Screw (Zimmer)
- Pedfuse pedicle screw system (SpineFrontier)
- Perpos pedicle screws (i-Spine)
- Phoenix Minimally Invasive Spinal Fixation System (Orthofix)
- Pioneer Posterior Occipito-Cervico-Thoracic (OCT) System
- Polaris 5.5 (Biomet)
- Polyaxial spinal system (Zimmer)
- Precept Spinal System (NuVasive)

- Preference Pedicle Screw System (Amedica)
- Proliant Polyaxial Pedicle Screw System (Exactech)
- Quantum (RTI Surgical)
- Quintex anterior plating system (Aesculap)
- Reflex Hybrid Anterior Cervical Plate System (Stryker)
- Reform (Precision Spine)
- Reliance Screw System (Reliance Medical Systems)
- ReSet (SpineFrontier)
- ReSpond (SpineFrontier)
- ReTurn (SpineFrontier)
- Revere stabilization system (Globus)
- Revolve Pedicle Screw (Globus)
- Rhausler anterior cervical plate system
- Romeo MIS (Spineart)
- Santis Hybrid Pedicle Screw System (Lanterna Medical Technologies)
- Sapphire Anterior Cervical Plate System (Spinal Elements)
- Savannah High Top (Amendia)
- Sintea Plustek's Posterior Lumbar System Pedicle Screws
- Skyline (DePuy)
- Sniper screws (Spine Wave, Inc)
- Snowcap anterior cervical plate (Biomet)
- Solera screws (Medtronic)
- SpheRx DBR H (NuVasive)
- Spider Cervical Plating System
- Spinal USA Simplicity Solo (X-Spine)
- Spine 360 Talon Pedicle screw system
- Spine ST360 (Zimmer)
- Spire Z (Medtronic)
- Starfire (ChoiceSpine)
- Streamline TL (RTI Surgical)
- Struxxure plate (Nexxt Spine)
- SureLOK PC Posterior Cervical System (Precision Spine)
- Swift Anterior Cervical Plate System (DePuy)
- Synapse (Synthes)
- Tempus Cervical Plate system (Neurostructures)
- Timberline Plate (Biomet)
- Trestle Anterior Cervical Plating System (Alphatec)
- Trinica Anterior Cervical Plate (Zimmer)
- TSRH 3DX pedicle screws (Medtronic)
- Typhoon (ChoiceSpine)
- Uniplate 2 (DePuy)
- Valencia Pedicle Screws (Altus)
- Valiant ALIF plate system (Biomet)
- Van Gogh plate (CTL Medical)
- Vectra (Synthes)
- Venus Facet Screw System (Apollo Spine)
- Vertex Reconstruction System (Medtronic)
- Viper Screws (DePuy)
- Virage system (Zimmer)
- Vitality (Zimmer)
- VuePoint OCT System (NuVasive)

- XIA 3 (Stryker)
- XIA 4.5 (Stryker)
- Zavation Pedicle Screw System
- Zavation cervical plate
- Zevo anterior cervical plate system (Medtronic)
- Zodiac Posterior screws (Alphatec)
- Zou plate (Corelink).

References

The above policy is based on the following references:

Facet Joint Injections

1. American College of Occupational and Environmental Medicine (ACOEM). Neck and upper back complaints. Elk Grove Village, IL: American College of Occupational and Environmental Medicine (ACOEM); 2004.
2. American Society of Anesthesiologists Task Force on Chronic Pain Management, American Society of Regional Anesthesia and Pain Medicine. Practice guidelines for chronic pain management: An updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. Anesthesiology. 2010;112(4):810-833.
3. Bigos S, Bowyer O, Braen G, et al. Acute low back problems in adults. Clinical Practice Guideline No. 14. AHCPR Publication No. 95-0642. Rockville, MD: Agency for health Care Policy and Research (AHCPR); December 1994.
4. Canadian Agency for Drugs and Technologies in Health (CADTH). Facet joint injection as diagnostic and therapeutic tools for pain of the cervical and lumbar spine: A review of clinical and cost-effectiveness. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2011.
5. Carette S, Marcoux S, Truchon R, et al. A controlled trial of corticosteroid injections into facet joints for chronic low back pain. N Engl J Med. 1991;325(14):1002-1007.

6. Chou R, Loeser JD, Owens DK, et al.; American Pain Society Low Back Pain Guideline Panel. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: An evidence-based clinical practice guideline from the American Pain Society. Spine (Phila Pa 1976). 2009;34(10):1066-1077.
7. Chou R. Subacute and chronic back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; 2009.
8. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed November 2014.
9. Dreyfuss PH, Dreyer SJ, Herring SA. Lumbar zygapophysial (facet) joint injections. Spine. 1995;20(18):2040-2047.
10. el-Khoury GY, Renfrew DL. Percutaneous procedures for the diagnosis and treatment of lower back pain: Diskography, facet-joint injection, and epidural injection. AJR Am J Roentgenol. 1991;157(4):685-691.
11. Falco FJ. Lumbar spine injection procedures in the management of low back pain. Occup Med. 1998;13(1):121-149.
12. Gunzburg R, Szpalski M. Facet joint injections. Bull Hosp Jt Dis. 1996;55(4):173-175.
13. Hashimoto R, Raich A, Ecker E, et al. Spinal injections. Health Technology Assessment. Olympia, WA: Washington State Health Care Authority; November 10, 2010.
14. Jackson RP. The facet syndrome. Myth or reality? Clin Orthop. 1992;(279):110-121.
15. Lilius G, Harilainen A, Laasonen EM, et al. Chronic unilateral low-back pain. Predictors of outcome of facet joint injections. Spine. 1990;15(8):780-782.
16. Lilius G, Laasonen EM, Myllynen P, et al. Lumbar facet joint syndrome. A randomised clinical trial. J Bone Joint Surg [Br]. 1989;71(4):681-684.
17. Manchikanti L. Facet joint pain and the role of neural blockade in its management. Curr Rev Pain. 1999;3(5):348-358.
18. Marks RC, Houston T, Thulbourne T. Facet joint injection and facet nerve block: A randomised comparison in 86 patients with chronic low back pain. Pain. 1992;49(3):325-328.
19. McIntosh G, Hall H. Low back pain (chronic). In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; May 2007.

20. Moran R, O'Connell D, Walsh MG. The diagnostic value of facet joint injections. Spine. 1988;13(12):1407-1410.
21. Resnick DK, Choudhri TF, Dailey AT, et al; American Association of Neurological Surgeons/Congress of Neurological Surgeons. Guidelines for the performance of fusion procedures for degenerative disease of the lumbar spine. Part 13: Injection therapies, low-back pain, and lumbar fusion. J Neurosurg Spine. 2005;2(6):707-715.
22. Revel M, Poiraudeau S, Auleley GR, et al. Capacity of the clinical picture to characterize low back pain relieved by facet joint anesthesia. Proposed criteria to identify patients with painful facet joints. Spine. 1998;23(18):1972-1976; discussion 1977.
23. Schleifer J, Kiefer M, Hagen T. Lumbar facet syndrome. Recommendation for staging before and after intra-articular injection treatment. Radiologe. 1995;35(11):844-847.
24. Staal JB, de Bie RA, de Vet HCW, et al. Injection therapy for subacute and chronic benign low-back pain. Cochrane Database Syst Rev. 2008;(2):CD001824.
25. Wagner AL. Paraspinal injections: Facet joint and nerve root blocks. eMedicine Radiology Topic 884. Omaha, NE: eMedicine.com; updated June 17, 2003.
26. Zakaria D, Skidmore B. Facet joint injection as a diagnostic and therapeutic tool for spinal pain: A review of clinical and cost effectiveness. Technology Report No. 77. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2007.

Trigger Point Injections

1. Alberta Heritage Foundation for Medical Research (AHFMR). Trigger point injections for non-malignant chronic pain. TechNote. TN 39. Edmonton, AB: AHFMR; December 2002.
2. Alvarez DJ, Rockwell PG. Trigger point injections: Diagnosis and management. Am Fam Physician. 2002;65:653-660.
3. American Medical Association (AMA). Assessing & treating persistent nonmalignant pain: An overview. Pain Management: Online Series. Continuing Medical Education Library. Chicago, IL: AMA; December 2003.
4. Bigos S, Bowyer O, Braen G, et al. Acute low back problems in adults. Clinical Practice Guideline No. 14. AHCPR Publication No.

95-0642. Rockville, MD: Agency for Health Care Policy and Research (AHCPR); December 1994.

5. Borg-Stein J, Stein J. Trigger points and tender points: One and the same? Does injection treatment help? Rheum Dis Clin North Am. 1996;22(2):305-322.
6. Botwin KP, Sharma K, Saliba R, Patel BC. Ultrasound-guided trigger point injections in the cervicothoracic musculature: A new and unreported technique. Pain Physician. 2008;11(6):885-889.
7. Cummings TM, White AR. Needling therapies in the management of myofascial trigger point pain: A systematic review. Archiv Phys Med Rehab, 2001;82(7):986-992.
8. Han SC, Harrison P. Myofascial pain syndrome and trigger-point management. Reg Anesth. 1997;22(1):89-101.
9. Hong CZ, Hsueh TC. Difference in pain relief after trigger point injections in myofascial pain patients with and without fibromyalgia. Arch Phys Med Rehabil. 1996;77(11):1161-1166.
10. Hopwood MB, Abram SE. Factors associated with failure of trigger point injections Clin J Pain. 1994;10(3):227-234.
11. Isaac Z. Treatment of neck pain. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2017.
12. Janssens LA. Trigger point therapy. Probl Vet Med. 1992;4(1):117-124.
13. Jayson MI. Fibromyalgia and trigger point injections. Bull Hosp Jt Dis. 1996;55(4):176-177.
14. Misirlioglu TO, Akgun K, Palamar D, et al. Piriformis syndrome: Comparison of the effectiveness of local anesthetic and corticosteroid injections: A double-blinded, randomized controlled study. Pain Physician. 2015;18(2):163-171.
15. Peloso P, Gross A, Haines T, et al. Medicinal and injection therapies for mechanical neck disorders. Cochrane Database Syst Rev. 2007;(3):CD000319.
16. Sanders SH, Harden RN, Benson SE, Vicente, PJ. Clinical practice guidelines for chronic non-malignant pain syndrome patients II: An evidence-based approach. J Back Musculoskeletal Rehabil. 1999;13:47-58.
17. Sanders SH, Rucker KS, Anderson KO, et al. Clinical practice guidelines for chronic non-malignant pain syndrome patients. J Back Musculoskeletal Rehab. 1995;5:115-120.

18. Sanders SH. Integrating practice guidelines for chronic pain: From the Tower of Babel to the Rosetta Stone. APS Bulletin. 2000;10(6).
19. Scott A, Guo B. Trigger point injections for chronic non-malignant musculoskeletal pain. Health Technology Assessment 35. Edmonton, AB: Alberta Heritage Foundation for Medical Research; January 2005.
20. Scott NA, Guo B, Barton PM, Gerwin RD. Trigger point injections for chronic non-malignant musculoskeletal pain: A systematic review. Pain Med. 2009;10(1):54-69.
21. Shinomiya R, Sunagawa T, Nakashima Y, et al. Impact of corticosteroid injection site on the treatment success rate of trigger finger: A prospective study comparing ultrasound-guided true intra-sheath and true extra-sheath injections. Ultrasound Med Biol. 2016;42(9):2203-8.
22. Staal JB, de Bie RA, de Vet HCW, et al. Injection therapy for subacute and chronic benign low back pain. Cochrane Database Syst Rev. 2008;(2):CD001824.
23. Van Tulder M, Koes B. Low back pain and sciatica (chronic). In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; April 2006.
24. Zhou JY, Wang D. An update on botulinum toxin A injections of trigger points for myofascial pain. Curr Pain Headache Rep. 2014;18(1):386.

Sacroiliac Joint Injections

1. Bigos S, Bowyer O, Braen G, et al. Acute low back problems in adults, Clinical Practice Guideline No. 14. AHCPR Publication No. 95-0642. Rockville, MD: Agency for Health Care Policy and Research (AHCPR); December 1994.
2. Bollow M, Braun J, Taupitz M, et al. CT-guided intraarticular corticosteroid injection into the sacroiliac joints in patients with spondyloarthropathy: Indication and follow-up with contrast-enhanced MRI. J Comput Assist Tomogr. 1996;20(4):512-521.
3. Braun J, Bollow M, Seyrekbasan F, et al. Computed tomography guided corticosteroid injection of the sacroiliac joint in patients with spondyloarthropathy with sacroiliitis: Clinical outcome and

followup by dynamic magnetic resonance imaging. J Rheumatol. 1996;23(4):659-664.
4. Falco FJ. Lumbar spine injection procedures in the management of low back pain. Occup Med. 1998;13(1):121-149.
5. Jee H, Lee JH, Park KD, et al. Ultrasound-guided versus fluoroscopy-guided sacroiliac joint intra-articular injections in the noninflammatory sacroiliac joint dysfunction: A prospective, randomized, single-blinded study. Arch Phys Med Rehabil. 2014;95(2):330-337.
6. Maugars Y, Mathis C, Berthelot JM, et al. Assessment of the efficacy of sacroiliac corticosteroid injections in spondylarthropathies: A double-blind study. Br J Rheumatol. 1996;35(8):767-770.
7. Maugars Y, Mathis C, Vilon P, et al. Corticosteroid injection of the sacroiliac joint in patients with seronegative spondylarthropathy. Arthritis Rheum. 1992;35(5):564-568.
8. Schwarzer AC, Aprill CN, Bogduk N. The sacroiliacj oint in chronic low back pain. Spine. 1995;20(1):31-37.
9. Swezey RL. The sacroiliac joint. Nothing is sacred. Phys Med Rehabil Clin N Am. 1998;9(2):515-519, x.
10. Wittenberg RH, Steffen R, Ludwig J. [Injection treatment of non-radicular lumbalgia] Orthopade. 1997;26(6):544-552.

Epidural Steroid Injections for Relief of Back Pain

1. Armon C, Argoff CE, Samuels J, Backonja MM; Therapeutics and Technology Assessment Subcommittee of the American. Assessment: Use of epidural steroid injections to treat radicular lumbosacral pain: Report of the Therapeutics and Technology Assessment Subcommittee of the American Academy of Neurology. Neurology. 2007;68(10):723-729.
2. Arnasson O, Carlsson CA, Pellettieri L. Surgical and conservative treatment of cervical spondylotic radiculopathy and myelopathy, Acta Neurochir (Wein). 1987;84:48-53.
3. Benzon HT. Epidural steroid injections for low back pain and lumbosacral radiculopathy. (Review article) Pain. 1986;24:277-295.
4. Bigos S, Bowyer O, Braen G, et al. Acute low back problems in adults, Clinical Practice Guideline No. 14. AHCPR Publication No.

95-0642. Rockville, MD: Agency for Health Care Policy and Research (AHCPR); December 1994.

5. Binder A. Neck pain. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; May 2006.
6. Bush K, Hillier S. Outcome of cervical radiculopathy treated with periradicular/epidural corticosteroid injections: A prospective study with independent clinical review. Eur Spine J. 1996;5(5):319-325.
7. Henschke N, Kuijpers T, Rubinstein SM, et al. Injection therapy and denervation procedures for chronic low-back pain: A systematic review. Eur Spine J. 2010;19(9):1425-1449.
8. Institute for Clinical Systems Improvement (ICSI). Fluoroscopically guided transforaminal epidural steroid injections for lumbar radicular pain. Technology Assessment Report. Bloomington, MN: ICSI; 2004.
9. Jordan J, Konstantino K, Morgan TS, Weinstein J. Herniated lumbar disc. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; November 2006.
10. Koes B, van Tulder M. Low back pain and sciatica (acute). In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; November 2004.
11. Koes BW, Scholten RJ, Mens JM, et al. Efficacy of epidural steroid injections for low-back pain and sciatica: A systematic review of randomized clinical trials. Pain. 1995;63(3):279-288.
12. Langer-Gould AM, Anderson WE, Armstrong MJ, et al. The American Academy of Neurology's top five choosing wisely recommendations. Neurology. 2013;81(11):1004-1011.
13. Nelson L, Aspegren D, Bova C. The use of epidural steroid injection and manipulation on patients with chronic low back pain. J Manipulative Physiol Ther. 1997;20(4):263-266.
14. Peloso P, Gross A, Haines T, et al. Medicinal and injection therapies for mechanical neck disorders. Cochrane Database Syst Rev. 2007;(3):CD000319.
15. Price C, Arden N, Coglan L, Rogers P. Cost-effectiveness and safety of epidural steroids in the management of sciatica. Health Technol Assess. 2005;9(33):1-74.
16. Rosen CD, Kahanovitz N, Bernstein R, et al. A retrospective analysis of the efficacy of epidural steroid injections. Clin Orthop. 1988;228:270-272.

17. Rowlingson J. Epidural steroids in treating failed back surgery syndrome. Anesth Analg. 1999;88(2):240-242.
18. Rowlingson JC, Kirschenbaum LP. Epidural analgesic techniques in the management of cervical pain. Anesth Analg. 1986;65:938-942.
19. Rozenberg S, Dubourg G, Khalifa P, et al. Efficacy of epidural steroids in low back pain and sciatica. A critical appraisal by a French Task Force of randomized trials. Critical Analysis Group of the French Society for Rheumatology. Rev Rhum Engl Ed. 1999;66(2):79-85.
20. Sager JVSV, Sharma R, Sharma S. Epidural steroid injection in non-specific low backache. J Indian Med Assoc. 1989;87(9):208-209.
21. Staal JB, de Bie RA, de Vet HC, et al. Injection therapy for subacute and chronic low back pain: An updated Cochrane review. Spine. 2009;34(1):49-59.
22. Staal JB, de Bie RA, de Vet HCW, Sturmans F. Injection therapy for subacute and chronic benign low back pain. Cochrane Database Syst Rev. 2008;(2):CD001824.
23. van Tulder M, Koes B. Low back pain and sciatica (chronic). In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; April 2006.

Chymopapain Chemonucleolysis

1. Bigos S, Bowyer O, Braen G, et al. Acute low back pain in adults. Clinical Practice Guideline No. 14. AHCPR Publication No. 95-0642. Rockville, MD: Agency for Health Care Policy and Research (AHCPR); December 1994.
2. Bradbury N, Wilson LF, Mulholland RC. Adolescent disc protrusions. A long-term follow-up of surgery compared to chymopapain. Spine. 1996;21(3):372-377.
3. Brown MD. Update on chemonucleolysis. Spine. 1996;15(24 Suppl):62S-68S.
4. Couto JM, Castilho EA, Menezes PR. Chemonucleolysis in lumbar disc herniation: A meta-analysis. Clinics. 2007;62(2):175-180.
5. Garreau C, Dessarts I, Lassale B, et al. Chemonucleolysis: Correlation of results with the size of the herniation and the dimensions of the spinal canal. Eur Spine J. 1995;4(2):77-83.

6. Gibson JNA, Waddell G. Surgical interventions for lumbar disc prolapse. Cochrane Database Syst Rev. 2007;(2):CD001350.
7. Henschke N, Kuijpers T, Rubinstein SM, et al. Injection therapy and denervation procedures for chronic low-back pain: a systematic review. Eur Spine J. 2010;19(9):1425-1449.
8. Javid MJ, Nordby EJ. Lumbar chymopapain chemonucleolysis. Neurosurg Clin N Am. 1996;7(1):17-27.
9. Javid MJ. Chemonucleolysis versus laminectomy. A cohort comparison of effectiveness and charges. Spine. 1995;20(18):2016-2022.
10. Javid MJ. Postchemonucleolysis discectomy versus repeat discectomy: A prospective 1- to 13-year comparison. J Neurosurg. 1996;85(2):231-238.
11. Louwaege A, Goubau J, Deldycke H, et al. Efficiency of discography followed by chemonucleolysis in the treatment of sciatica. J Belge Radiol. 1996;79(2):68-71.
12. Nordby EJ, Fraser RD, Javid MJ. Chemonucleolysis. Spine. 1996;21(9):1102-1105.
13. Poynton AR, O'Farrell DA, Mulcahy D, et al. Chymopapain chemonucleolysis: A review of 105 cases. J R Coll Surg Edinb. 1998;43(6):407-409.

Percutaneous Lumbar Discectomy

1. Agency for Healthcare Research and Quality (AHRQ). Treatment of degenerative lumbar spinal stenosis. Volume 1. Evidence report; Volume 2. Evidence tables and bibliography. Evidence Report/Technology Assessment 32. Rockville, MD: AHRQ; 2001.
2. Bosacco SJ, Bosacco DN, Berman AT, et al. Functional results of percutaneous laser discectomy. Am J Orthop. 1996;25(12):825-828.
3. Boult M, Fraser RD, Jones N, et al. Percutaneous endoscopic laser discectomy. Aust N Z J Surg. 2000;70(7):475-479.
4. Boult M, Jones N. A systematic review of percutaneous endoscopic laser discectomy (update and reappraisal). ASERNIP-S Report No. 5. Stepney, SA: Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S); 2000.

5. California Technology Assessment Forum (CTAF). Percutaneous laser disc decompression for treatment of lumbar disc prolapse. A Technology Assessment. San Francisco, CA: CTAF; June 2008.
6. Castro WH, Jerosch J, Hepp R, Schulitz KP. Restriction of indication for automated percutaneous lumbar discectomy based on computed tomographic discography. Spine. 1992;17(10):1239-1243.
7. Chatterjee S, Foy PM, Findlay GF. Report of a controlled clinical trial comparing automated percutaneous lumbar discectomy and microdiscectomy in the treatment of contained lumbar disc herniation. Spine. 1995;20(6):734-738.
8. Choy DS, Ascher PW, Ranu HS, et al. Percutaneous laser disc decompression: A new therapeutic modality. Spine. 1992;17(8):949-956.
9. Conway DP. Reassessment of automated percutaneous lumbar diskectomy for herniated disks. DATTA Evaluation. Chicago, IL: American Medical Association; April 24, 1991.
10. Davis JK. Early experience with laser disc compression. J Fla Med Assoc. 1992;79(1):37-39.
11. Deen HG, Fenton DS, Lamer TJ. Minimally invasive procedures for disorders of the lumbar spine. Mayo Clin Proc. 2003;78(10):1249-1256.
12. Fiume D, Parziale G, Rinaldi A, et al. Automated percutaneous discectomy in herniated lumbar discs treatment: Experience after the first 200 cases. J Neurosurg Sci. 1994;38(4):235-237.
13. Gibson JNA, Waddell G. Surgical interventions for lumbar disc prolapse. Cochrane Database Syst Rev. 2007;(2):CD001350.
14. Goupille P, Mulleman D, Mammou S, et al. Percutaneous laser disc decompression for the treatment of lumbar disc herniation: A review. Semin Arthritis Rheum. 2007;37(1):20-30.
15. Jordan J, Konstantinou K, Morgan TS, Weinstein J. Herniated lumbar disc. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; November 2006.
16. Kahanovitz N, Viola K, Goldstein T, Dawson E. A multicenter analysis of percutaneous diskectomy. Spine. 1990;15(7):713-715.
17. Kotilainen E, Valtonen S. Long-term outcome of patients who underwent percutaneous nucleotomy for lumbar disc herniation: Results after a mean follow-up of 5 years. Acta Neurochir (Wien). 1998;140(2):108-113.

18. Krugluger J, Knahr K. Chemonucleolysis and automated percutaneous discectomy - a prospective randomized comparison. International Orthopaedics (SICOT). 2000;24:167-169.
19. Mochida J, Toh E, Nishimura K, et al. Percutaneous nucleotomy in lumbar disc herniation. Spine. 1993;18(15):2212-2217.
20. National Institute for Clinical Excellence (NICE). Automated percutaneous mechanical lumbar discectomy. Interventional Procedure Guidance 141. London, UK: NICE; 2005.
21. National Institute for Clinical Excellence (NICE). Endoscopic laser foraminoplasty. Interventional Procedure Guidance 31. London, UK: NICE; December 2003.
22. National Institute for Clinical Excellence (NICE). Laser lumbar discectomy. Interventional Procedure Guidance 27. London, UK: NICE; 2003.
23. Nezer D, Hermoni D. [Percutaneous discectomy and intradiscal radiofrequency thermocoagulation for low back pain: Evaluation according to the best available evidence]. Harefuah. 2007;146(10):747-750, 815.
24. Norwegian Centre for Health Technology Assessment (SMM). Treatment of lumbar disc herniation. SMM-Report 1/2001. Oslo, Norway: SMM; 2001.
25. Ohnmeiss DD, Guyer RD, Hochschuler SH. Laser disc decompression. The importance of proper patient selection. Spine. 1994;19(18):2054-2058.
26. Onik G, Helms CA. Automated percutaneous lumbar diskectomy. Am J Roentgenol. 1991;156(3):531-538.
27. Onik G, Mooney V, Maroon JC, et al. Automated percutaneous lumbar diskectomy: A prospective multi-institutional study. Neurosurgery. 1990;26(2):228-232.
28. Paul M, Hellinger J. Nd-YAG (1064nm) versus diode (940nm) PLDN: A prospective randomised blinded study. Proceedings of the First Interdisciplinary World Congress on Spinal Surgery and related disciplines. 2000:555-8.
29. Quigley MR. Percutaneous laser discectomy. Neurosurg Clin N Am. 1996;7(1):37-42.
30. Rasmussen FO, Amundsen T, Vandvik B. Lumbar disk prolapses and radiological spinal intervention. What do the randomized

controlled trials say? Tidsskr Nor Laegeforen. 1998;118(16):2478-2480.

31. Revel M, Payan C, Vallee C, et al. Automated percutaneous lumbar discectomy versus chemonucleolysis in the treatment of sciatica: A randomized multicenter trial. Spine. 1993;18(1):1-7.
32. Sakou T, Masuda A. Percutaneous diskectomy for lumbar disk herniation. A preliminary report. Clin Orthop. 1993;286:174-179.
33. Schatz SW, Talalla A. Preliminary experience with percutaneous laser disc decompression in the treatment of sciatica. Can J Surg. 1995;38(5):432-436.
34. Sherk HH, Black J, Rhodes A, et al. Laser discectomy. Clin Sports Med. 1993;12(3):569-577.
35. Sherk HH, Black J, Rhodes A, et al. Lasers in orthopedic surgery: Laser diskectomy. Orthopedics. 1993;16:573-576.
36. Sortland O, Kleppe H, Aandahl M, Blikra G. Percutaneous lumbar discectomy. Technique and clinical result. Acta Radiol. 1996;37(1):85-90.
37. Steffen R, Wittenberg RH, Kraemer J. Chemonucleolysis versus laser disc decompression - a prospective randomised trial. J Bone Joint Surg. 1997; Vol. 79-B:247.
38. Stevens CD, Dubois RW, Larequi-Lauber T, et al. Efficacy of lumbar discectomy and percutaneous treatments for lumbar disc herniation. Soz Praventivmed. 1997;42(6):367-379.
39. Tassi GP. Comparison of results of 500 microdiscectomies and 500 percutaneous laser disc decompression procedures for lumbar disc herniation. Photomed Laser Surg. 2006;24(6):694-697.
40. Teng GJ, Jeffery RF, Guo JH, et al. Automated percutaneous lumbar discectomy: A prospective multi-institutional study. J Vasc Interv Radiol. 1997;8(3):457-463.
41. Washington State Department of Labor and Industries (WSDLI), Office of the Medical Director. Percutaneous discectomy for disc herniation. Technology Assessment. Olympia, WA: WSLDI; February 2004.

Non-Pulsed Radiofrequency Facet Denervation

1. American Society of Anesthesiologists. Practice guidelines for chronic pain management. A Report by the American Society of

Anesthesiologists Task Force on Pain Management, Chronic Pain Section. Anesthesiology. 1997;86:995-1004.

2. Bigos S, Bowyer O, Braen G, et al. Acute low back problems in adults. Clinical Practice Guideline No. 14. AHCPR Publication No 95-0642. Rockville, MD. Agency for Health Care Policy & Research (AHCPR); December 1994.
3. Binder A. Neck pain. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; May 2006.
4. Bogduk N, Long DM. Percutaneous lumbar medical branch neurotomy: A modification of facet denervation. Spine. 1980;5(2):193-200.
5. Bogduk N, Macintosh J, Marsland A. Technical limitations to the efficacy of radiofrequency neurotomy for spinal pain. Neurosurgery. 1987;20(4):529-535.
6. California Technology Assessment Forum (CTAF). Percutaneous radiofrequency neurotomy for treatment of chronic pain from the upper cervical (C2-3) spine. A Technology Assessment. San Francisco, CA: CTAF; June 20, 2007.
7. Cho J, Park YG, Chung SS. Percutaneous radiofrequency lumbar facet rhizotomy in mechanical low back pain syndrome. Stereotact Funct Neurosurg. 1997;68(1-4 Pt 1):212-217.
8. Goupille P, Cotty P, Fouquet B, et al. Denervation of the posterior lumbar vertebral apophyses by thermocoagulation in chronic low back pain. Results of the treatment of 103 patients. Rev Rhum Ed Fr. 1993;60(11):791-796.
9. Henschke N, Kuijpers T, Rubinstein SM, et al. Injection therapy and denervation procedures for chronic low-back pain: A systematic review. Eur Spine J. 2010;19(9):1425-1449.
10. Institute for Clinical Systems Improvement (ICSI). Percutaneous radiofrequency ablation for facet-mediated neck and back pain. Technology Assessment Report. Bloomington, MN: ICSI; 2005.
11. Jerosch J, Castro WH, Halm H, et al. Long-term results following percutaneous facet coagulation. Z Orthop Ihre Grenzgeb. 1993;131(3):241-247.
12. Lord SM, Barnsley L, Wallis BJ, et al. Percutaneous radio-frequency neurotomy for chronic cervical zygapophyseal-joint pain. N Engl J Med. 1996;335:1721-1726.
13. Mehta M, Wynn Parry CB. Mechanical back pain and the facet joint syndrome. Disabil Rehabil. 1994;16(1):2-12.

14. Murtagh J, Foerster V. Radiofrequency neurotomy for lumber pain. Issues in Emerging Health Technologies Issue 83. Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); 2006.
15. Niemisto L, Kalso E, Malmivaara A, et al. Radiofrequency denervation for neck and back pain. Cochrane Database Syst Rev. 2003;(1):CD004058.
16. Niemisto L, Kalso E, Malmivaara A, et al. Radiofrequency denervation for neck and back pain: A systematic review within the framework of the Cochrane Collaboration Back Review Group. Spine. 2003;18(16):1877-1888.
17. North RB, Han M, Zahurak M, Kidd DH. Radiofrequency lumbar facet denervation: Analysis of prognostic factors. Pain. 1994;57(1):77-83.
18. Oudenhoven RC. The role of laminectomy, facet rhizotomy, and epidural steroids. Spine. 1979;4(2):145-147.
19. Rashbaum RF. Radiofrequency facet denervation. Orthop Clin N Am. 1983;14(3):569-575.
20. Savitz MH. Percutaneous radiofrequency rhizotomy of the lumbar facets: Ten years' experience. Mt Sinai J Med. 1991;8(2):177-178.
21. Shealy CN. Facet denervation in the management of back and sciatica pain. Clin Orthop. 1976;15:157-164.
22. Shealy CN. Percutaneous radiofrequency denervation of spinal facets: Treatment for chronic back pain and sciatica. J Neurosurg. 1975;43:448-451.
23. Stolker RJ, Vervest AC, Groen GJ. Percutaneous facet denervation in chronic thoracic spinal pain. Acta Neurochir (Wien). 1993;122(1-2):82-90.

Spinal Fixation

1. Boos N, Webb JK. Pedicle screw fixation in spinal disorders: A European view. European Spine J. 1997;6:2-18.
2. Brantigan JW, Steffee AD, Keppler L, et al. Posterior lumbar interbody fusion technique using the variable screw placement spinal fixation system. State of the art review. Spine. 1992;6:175-200.

3. Cope R, Henstorf JE, Gaines RW. A new interpeduncular screw fixation system: Biomechanics, radiologic appearances and complications of the Steffee spine plate implant. Ann Chir. 1990;44:67-72.
4. Dickman CA, Fessler RG, MacMillan M, et al. Transpedicular screw-rod fixation of the lumbar spine: Operative technique and outcome in 104 cases. J Neurosurg. 1992;77:860-870.
5. Hamill CL, Lenke LG, Bridwell KH, et al. The use of pedicle screw fixation to improve correction in the lumbar spine of patients with idiopathic scoliosis. Spine. 1996;21(10):1241-1249.
6. Rechtine GR, Sutterlin CE, Wood GW, et al. The efficacy of pedicle screw/plate fixation on lumbar/lumbosacral autogenous bone graft fusion in adult patients with spondylolisthesis. J Spinal Disorders. 1996;9(5):382-391.
7. Rhee JM, Bridwell KH, Won DS, et al. Sagittal plane analysis of adolescent idiopathic scoliosis: The effect of anterior versus posterior instrumentation. Spine. 2002;27(21):2350-2356.
8. Ricciardi JE, Pfleuger PC, Isaza JE. Transpedicular fixation for the treatment of isthmic spondylolisthesis in adults. Spine. 1995;20(17):1917-1922.
9. Schnee CL, Freese A, Ansell LV. Outcome analysis of adults with spondylolisthesis treated with posterolateral fusion and transpedicular screw fixation. J Neurosurg. 1997;86:56-63.
10. Schwab FJ, Nazarian DG, Mahmud F. Effects of spinal instrumentation on fusion of the lumbosacral spine. Spine. 1995;20(18):2023-2028.
11. Smith SJ, Glade MJ. Pedicle screw fixation systems for spinal instability. Diagnostic and Therapeutic Technology Assessmen (DATTA). Chicago, IL: American Medical Association; December 1996.
12. U.S. Department of Health and Human Services, Public Health Service, Food and Drug Administration. Orthopedic devices: Classification and reclassification of pedicle screw spinal systems. Fed Regist. 1998;63(143):40025-40041.
13. Vaccaro AR, Garfin SR. Internal fixation (pedicle screw fixation) for fusions of the lumbar spine. Spine. 1995;20(Suppl 24):157S-165S.
14. Van Brussel K, Vander Sloten J, Van Audekercke. Internal fixation of the spine in traumatic and scoliotic cases. The potential of

pedicle screws. Tech Health Care. 1996;4:365-384.
15. Washington State Department of Labor and Industries. Guidelines for lumbar fusion (arthrodesis). Olympia, WA: Washington State Department of Labor and Industries; June 2001.
16. West JL, Bradford DS, Ogilvie JW. Results of spinal arthrodesis with pedicle screw-plate fixation. J Bone Joint Surg. 1991;8(73-A):1179-1183.
17. Yuan HA, Garfin SR, Dickman CA. A historical cohort study of pedicle screw fixation in thoracic, lumbar and sacral spinal fusions. Spine. 1994;19(20S):2279S-2299S.
18. Zdeblick T. A prospective, randomized study of lumbar fusion – preliminary results. Spine. 1993;18(8):983-991.
19. Zindrick MR. The role of transpedicular fixation systems for stabilization of the lumbar spine. Orthop Clin North Am. 1991;22(2):333-344.

Intervertebral Body Fusion Devices (Spine Cages)

1. Barnett AA. News: Science and Medicine. Two spinal fusion devices recommended for U.S. approval. Lancet. 1996;347(9014):1543.
2. Burkus JK. Intervertebral fixation: Clinical results with anterior cages. Orthop Clin North Am. 2002;33(2):349-357.
3. Hacker RJ, Follett KA. Comparison of interbody fusion approaches for disabling low back pain. Spine. 1997;22(6):660-666.
4. O'Brien JP. Education & debate: Controversies in management. Should backache be treated with spinal fusion? Spinal fusion is the only treatment for discogenic pain. Br Med J. 1996;312(7022):38-39.
5. Pirkle S, Kaskovich S, Cook D, et al. Cages in ACDF are associated with a higher nonunion rate than allograft. A stratified comparative analysis of 6130 patients. Spine. 2019;44(6):384-388.
6. Ray CD. Threaded fusion cages for lumbar interbody fusions: An economic comparison with 360 degree fusions. Spine. 1997;22(6):681-685.
7. Ray DC, Lehmann TR. Threaded titanium cages for lumbar interbody fusions. Spine. 1997;22(6):667-680.

8. Sandhu HS, Turner S, Kabo JM, et al. Distractive properties of a threaded interbody fusion device. An in vivo model. Spine. 1996;21(10):1201-1210.
9. Tencer AF, Hampton D, Eddy S. Biomechanical properties of threaded inserts for lumbar interbody spinal fusion. Spine. 1995;20(22):2408-2414.
10. U.S. Food and Drug Administration (FDA). BAK interbody fusion with instrumentation. Summary of Safety and Effectiveness Data. PMA 950002. Rockville, MD: FDA; May 23, 1996.
11. Wilson-MacDonald J. Education & debate: Controversies in management. Should backache be treated with spinal fusion? The case for spinal fusions is unproved. Br Med J. 1996;312(7022):39-40.

Cervical Spine Cages

1. Acosta FL Jr, Aryan HE, Chou D, Ames CP. Long-term biomechanical stability and clinical improvement after multilevel corpectomy and circumferential reconstruction of the cervical spine using titanium mesh cages. J Spinal Disord Tech. 2008;21(3):165-174.
2. Anderson DG, Albert TJ. Bone grafting, implants, and plating options for anterior cervical fusions. Orthop Clin North Am. 2002;33(2).
3. Assietti R, Beretta F, Arienta C. Two-level cervical discectomy and cage-assisted fusion without plates. Neurosurg Focus. 2002;12(1):E3.
4. Bärlocher CB et al. Comparative evaluation of microdiscectomy only, autograft fusion, polymethylmethacrylate interposition, and threaded titanium cage fusion for treatment of single-level cervical disc disease: A prospective randomized study in 125 patients. Neurosurg Focus. 2002;12(1): E4.
5. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Artificial intervertebral disc arthroplasty for treatment of degenerative disc disease of the cervical spine. TEC Assessment Program. Chicago, IL: BCBSA; April 2014;28(14).
6. Buyuk AF, Onyekwelu I, Gaffney CJ, et al. Symptomatic pseudarthrosis requiring revision surgery after 1- or 2-level ACDF

with plating: Peek versus allograft. J Spine Surg. 2020;6(4):670-680.

7. Caroli E, et al. Anterior cervical fusion with interbody titanium cage containing surgical bone site graft: Our institution's experience in 103 consecutive cases of degenerative spondylosis. J Spinal Disord Tech. 2007;20(3):216-220.
8. Celik SE, Kara A, Celik S. A comparison of changes over time in cervical foraminal height after tricortical iliac graft or polyetheretherketone cage placement following anterior discectomy. J Neurosurg Spine. 2007;6(1):10-16.
9. Chiang CJ, et al. Anterior cervical fusion using a polyetheretherketone cage containing a bovine xenograftp: Three to five-year follow-up. Spine (Phila Pa 1976), 2008;33(23):2524-428.
10. Cho DY, Lee WY, Sheu PC. Treatment of multilevel cervical fusion with cages. Surg Neurol. 2004;61(5):378-385, Discussion 385-386.
11. D'Antonio N, Lambrechts MJ, Heard J, et al. Effect of interbody composition on the development of pseudarthrosis following anterior cervical discectomy and fusion. Asian Spine J. 2023;17(3):518-528.
12. Di Lorenzo N, Capozza M. Discectomy and fusion with autologous bone: obsolete? Rome Spine 2012, VII Annual Congress. Rome Italy, December 6-7. 2012. Available at: http://www.formazionesostenibile.it. Accessed March 10, 2014.
13. Epstein NE. Iliac crest autograft versus alternative constructs for anterior cervical spine surgery: Pros, cons, and costs. Surg Neurol Int. 2012;3(Suppl 3):S143-S156.
14. Epstein NE, Agulnick MA. Review of anterior cervical diskectomy/fusion (ACDF) using different polyetheretherketone (PEEK) cages. Surg Neurol Int. 2022;13:556.
15. Goldberg JL, Meaden RM, Hussain I, et al. Titanium versus polyetheretherketone versus structural allograft in anterior cervical discectomy and fusion: A systematic review. Brain Spine. 2022;2:100923.
16. Goz V, Buser Z, D'Oro A, et al. Complications and risk factors using structural allograft versus synthetic cage: Analysis 17783 anterior cervical discectomy and fusions using a national registry. Global Spine J. 2019;9(4):388-392.

17. Hacker RJ, et al. A prospective randomized multicenter clinical evaluation of an anterior cervical fusion cage. Spine. 2000;25(20):2646-2654.
18. Hauerberg J, et al. Anterior cervical discectomy with or without fusion with ray titanium cage: A prospective randomized clinical study. Spine (Phila PA 1976). 2008;33(5):458-464.
19. Hermansen A, Hedlund R, Vavruch L, Peolsson A. A comparison between the carbon fiber cage and the Cloward procedure in cervical spine surgery: A 10-13 year follow-up of a prospective randomized study. Spine (Phila Pa 1976). 2011;(36)12:919-925
20. Hwang SL, et al. Outcome analysis of interbody titanium cage fusion used in anterior discectomy with fusion for cervical degenerative disease. J Spinal Disord Tech.2005;18(4):326-331.
21. Hwang SL, et al. Three-level and four-level anterior cervical discectomies and titanium cage-augmented fusion with and without plate fixation. J Neurosurg Spine.2004;1(2):160-167.
22. Jacobs W, Willems PC, Kruyt M, et al. Systematic review of anterior interbody fusion techniques for single- and double-level cervical degenerative disc disease. Spine (Phila Pa 1976). 2011;36(14):E950-E960.
23. Jacobs W, Willems PC, van Limbeek J, et al. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. Cochrane Database Syst Rev. 2011;(1):CD004958.
24. Jacobs WC et al. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. Cochrane Database Syst Rev. 2004;(4):CD004958.
25. Jain A, Marrache M, Harris A et al; and AOSpine Knowledge Forum Degenerative. Structural allograft versus PEEK implants in anterior cervical discectomy and fusion: A systematic review. Global Spine J. 2020;10(6):775-783.
26. Kersten RF, van Gaalen SM, de Gast A, Öner FC. Polyetheretherketone (PEEK) cages in cervical applications: A systematic review. Spine J. 2015;15(6):1446-1460.
27. Krause KL, Obayashi JT, Bridges KJ, et al. Fivefold higher rate of pseudarthrosis with polyetheretherketone interbody device than with structural allograft used for 1-level anterior cervical discectomy and fusion. J Neurosurg Spine. 2018;30(1):46-51.
28. Marrache M, Bronheim R, Harris AB, et al. Synthetic cages associated with increased rates of revision surgery and higher

costs compared to allograft in ACDF in the nonelderly patient. Neurospine. 2020;17(4):896-901.

29. Menon N, Turcotte J, Patton C. Structural allograft versus synthetic interbody cage for anterior cervical discectomy and fusion: A comparison of 1-year outcomes from a national database. Global Spine J. 2021;11(8):1215-1222.
30. Miller LE, Block JE. Safety and effectiveness of bone allografts in anterior cervical discectomy and fusion surgery. Spine (Phila Pa 1976). 2011;36(24):2045-2050.
31. Moo IH, Kam CJW, Lai MWS, et al. A comparison of contiguous two-level anterior cervical discectomy and fusion using a structural allograft versus a polyetheretherketone (PEEK) cage: The results of a three-year follow-up. BMC Musculoskeletal Disorders. 2020;21:331.
32. Niu CC, et al. Outcomes of interbody fusion cages used in 1 and 2-levels anterior cervical discectomy and fusion: Titanium cages versus polyetheretherketone (PEEK) cages. J Spinal Disord Tech. 2010;23(5):310-316.
33. Park HW, et al. The efficacy of the synthetic interbody cage and Grafton for anterior cervical fusion. Spine (Phila Pa 1976). 2009;34(17):E591-E595.
34. Pechlivanis I, et al. Non-fusion rates in anterior cervical discectomy and implantation of empty polyetheretherketone cages. Spine (Phila Pa 1976). 2011;36(1):15-20.
35. Powers AY, Nin DZ, Chen YW, et al. Anterior cervical discectomy and fusion with structural allograft is associated with lower postoperative health care utilization and reoperations compared with cage implants. Oper Neurosurg (Hagerstown). 2023 Sep 14 [Epub ahead of print].
36. Qureshi SA, Hecht AC, Boden SD. Multilevel anterior cervical diskectomy and fuion: Bone-grafting options. Ch. 2. In: Best Evidence for Spine Surgery: 20 Cardinal Cases. R Jandial, SR Garfin, eds. Philadelphia, PA: Saunders Elsevier; 2012.
37. Raad M, Xu AL, Ortiz-Babilonia C, et al. A five-year cost-utility analysis comparing synthetic cage versus allograft use in anterior cervical discectomy and fusion surgery for cervical spondylotic myelopathy. Spine (Phila Pa 1976). 2023;48(5):330-334.
38. Rodrigues AJ, Varshneya K, Stienen MN, et al. Clinical outcomes and cost profiles for cage and allograft anterior cervical

discectomy and fusion procedures in the adult population: A propensity score-matched Study. Asian Spine J. 2023;17(4):620-631.

39. Ryken TC, Heary RF, Matz PG, et al.; Joint Section on Disorders of the Spine and Peripheral Nerves of the American Association of Neurological Surgeons and Congress of Neurological Surgeons. Techniques for cervical interbody grafting. J Neurosurg Spine. 2009;11(2):203-220.
40. Ryu WHA, Richards D, Kerolus MG, et al. Nonunion rates after anterior cervical discectomy and fusion: Comparison of polyetheretherketone vs structural allograft Implants. Neurosurgery. 2021;89(1):94-101.
41. Shamsaldin M, Mouchaty H, Desogus N, et al. Evaluation of donor site pain after anterior iliac crest harvesting for cervical fusion: A prospective study on 50 patients. Acta Neurochir (Wien). 2006;148(10):1071-1074; discussion 1074.
42. Shukla G, Matur AV, Tao X, et al. Synthetic interbody devices and traditional bone graft are associated with a similar rate of surgical complications after 1-2 level ACDFs. Spine (Phila Pa 1976). 2023 [Epub ahead of print].
43. Skeppholm M, Olerud C. Pain from donor site after anterior cervical fusion with bone graft: A prospective randomized study with 12 months of follow-up. Eur Spine J. 2013;22(1):142-147.
44. Teton ZE, Cheaney B, Obayashi JT, Than KD. PEEK interbody devices for multilevel anterior cervical discectomy and fusion: Association with more than 6-fold higher rates of pseudarthrosis compared to structural allograft. J Neurosurg Spine. 2020;32(5):696-702.
45. Thomas C, et al. A prospective randomized comparison of rectangular titanium cage fusion and iliac crest autograft fusion in patients undergoing anterior cervical discectomy. J Neurosurg Spine. 2006;4(10):1-9.
46. Townsend CM, Beauchamp RD, Evers BM, eds. Sabiston Textbook of Surgery: The Biologic Basis of Modern Surgical Practice. 18th ed. Philadelphia, PA: W.B. Saunders; 2007.
47. U.S. Senate, Committee on Finance. Staff report on Medtronic's influence on infuse clinical studies. Washington, DC: U.S. Government Printing Office; October 2012.

48. Vavruch K, et al. A prospective randomized comparison between the Cloward procedure and a carbon fiber cage in the cervical spine: A clinical and radiologic study. Spine (Phila PA 1976). 2002;27(16):1694-1701.
49. Villavicencio AT, Nelson EL, Rajpal S, et al. Prospective, randomized, blinded clinical trial comparing PEEK and allograft spacers in patients undergoing anterior cervical discectomy and fusion surgeries. Spine (Phila Pa 1976). 2022;47(15):1043-1054.
50. Wang M, Chou D, Chang CC, et al. Anterior cervical discectomy and fusion performed using structural allograft or polyetheretherketone: Pseudarthrosis and revision surgery rates with minimum 2-year follow-up. J Neurosurg Spine. 2019 Dec 13 [Epub ahead of print].
51. Wang X, et al. Anterior decompression and interbody fusion with BAK/C for cervical disc degenerative disorders. J Spinal Disord Tech. 2009;22(4):240-245.
52. Yang S, Yu Y, Liu X, et al. Clinical and radiological results comparison of allograft and polyetheretherketone cage for one to two-level anterior cervical discectomy and fusion: A CONSORT-compliant article. Medicine (Baltimore). 2019;98(45):e17935.
53. Zevgaridis D; Thomas C; Krauss JK. Prospective controlled study of rectangular titanium cage fusion compared with iliac crest autograft fusion in anterior cervical discectomy. Neurosurg Focus, 12(1): E2 2002.

Epiduroscopy

1. Amirikia AM, Scott IU, Murray TG, et al. Acute bilateral visual loss associated with retinal hemorrhages following epiduroscopy. Archiv Ophthalmol. 2000;118(2):287-289.
2. Australian Safety and Efficacy Register of New Interventional Procedures - Surgical (ASERNIP-S). Epiduroscopy. Rapid Review. New and Emerging Techniques - Surgical. North Adelaide, Australia: ASERNIP-S; June 2003.
3. Blomberg R. A method for epiduroscopy and spinaloscopy. Presentation of preliminary results. Acta Anaesthesiol Scand. 1985;29(1):113-116.
4. Blomberg RG, Olsson SS. The lumbar epidural space in patients examined with epiduroscopy. Anesth Analges. 1989:68(2):157-

160.

5. Blomberg RG. Epiduroscopy and spinaloscopy: Endoscopic studies of lumbar spinal spaces. Acta Neurochir. 1994;61:106-107.
6. Guerts JW, Kallewaard JW, Richardson J, et al. Targeted methylprednisolone acetate/hyaluronidase/clonidine injection after diagnosit epiduroscopy for chronic sciatica: A prospective, 1-year follow-up study. Reg Anesth Pain Med. 2002;27(4):343-352.
7. Igarashi TMD, Hirabayashi YMD, Shimizu RMD, et al. The fiberoscopic findings of the epidural space in pregnant women. Anesthesiology. 2000;92(6):1631-1636.
8. Jimenez-Leon JC. Neuroendoscopy: Diagnosis and therapeutic uses. Rev Neurol. 1997;25(142):941-945.
9. Kawauchi Y, Yone K, Sakou T. Myeloscopic observation of adhesive arachnoiditis in patients with lumbar spinal canal stenosis. Spinal Cord. 1996;34:403-410.
10. Krasuski P, Poniecka AW, Gal E, et al. Epiduroscopy: Review of technique and results. Pain Clinic. 2001;13(1):71-76.
11. National Institute for Clinical Excellence (NICE). Endoscopic epidural procedures. Interventional Procedure Consultation Document. London, UK: NICE; February 2004.
12. Ogon M, Maurer H, Wimmer C, et al. Minimally invasive approach and surgical procedures in the lumbar spine. Orthopade. 1997;26(6):553-561.
13. Richardson J, McGuran P, Cheema S, et al. Spinal endoscopy in chronic low back pain with radiculopathy: A prospective case series. Anaesthesia. 2001;56(5):454-460.
14. Ruetten S, Meyer O, Godolias G. Application of holmium:YAG laser in epiduroscopy: Extended practicabilities in the treatment of chronic back pain syndrome. J Clin Laser Med Surg. 2002;20(4):203-206.
15. Ruetten S, Meyer O, Godolias G. Endoscopic surgery of the lumbar epidural space (epiduroscopy): Results of therapeutic intervention in 93 patients. Minim Invasive Neurosurg. 2003;46(1):1-4.
16. Ruetten S, Meyer O, Godolias G. Epiduroscopic diagnosis and treatment of epidural adhesions in chronic back pain syndrome of patients with previous surgical treatment: First results of 31

interventions. Zeitschrift fur Orthopadie und Ihre Grenzgebiete. 2002;140(2):171-175.
17. Saberski LR, Kitahata LM, Direct visualization of the lumbosacral epidural space through the sacral hiatus. Anesth Analges. 1995;80(4);839-840.
18. Saberski LR, Kitahata LM. Review of the clinical basis and protocol for epidural endoscopy. Conn Med. 1996;60(2):71-73.
19. Shutse G, Kurtse G, Grol O, et al. Endoscopic method for the diagnosis and treatment of spinal pain syndromes. Anesteziol Reanimatol. 1996;4:62-64.

Epidural Injections for Lysis of Adhesions

1. Anderson SR, Racz GB, Heavner J. Evolution of epidural lysis of adhesions. Pain Phys. 2000;3(3):262-270.
2. Bigos S, Bowyer O, Braen G et al. Acute low back problems in adults. Clinical Practice Guideline No. 14. AHCPR Publication No. 95-0642. Rockville, MD: Agency for Health Care Policy and Research (AHCPR): December 1994.
3. Borg PA, Krijnen HJ. Hyaluronidase in the management of pain due to post-laminectomy scar tissue. Pain. 1994;58(2):273-276.
4. Bourne IHJ. Lumbo-sacral adhesive arachnoiditis: A review. J Royal Soc Med. 1990;83:262-265.
5. Chopra P, Smith HS, Deer TR, Bowman RC. Role of adhesiolysis in the management of chronic spinal pain: A systematic review of effectiveness and complications. Pain Physician. 2005;8:87-100.
6. Devulder J, Bogaert L, Castille F, et al. Relevance of epidurography and epidural adhesiolysis in chronic failed back surgery patients. Clin J Pain. 1995;11:147-150.
7. Fibuch EE. Percutaneous epidural neuroplasty: Cutting edge or potentially harmful pain management? [editorial]. Reg Anesth Pain Med. 1999;24(3):198-201.
8. Gelozer M, Wang G. Epidural adhesiolyis for the treatment of back pain. Health Technology Assessment. Olympia, WA: Washington State Department of Labor and Industries, Office of the Medical Director; July 13, 2004.
9. Gerdesmeyer L, Wagenpfeil S, Birkenmaier C, et al. Percutaneous epidural lysis of adhesions in chronic lumbar radicular pain: A

randomized, double-blind, placebo-controlled trial. Pain Physician. 2013;16(3):185-196.

10. He CJ, Nie HX, Ni JX. The application of percutaneous lysis of epidural adhesions in patients with failed back surgery syndrome. Acta Cir Bras. 2012;27(4):357-362.
11. Heavner JE, Racz GB, Raj P. Percutaneous epidural neuroplasty: Prospective evaluation of 0.9% NaCl versus 10% NaCL with or without hyaluronidase. Reg Anesth Pain Med. 1999;24(3):202-207.
12. Helm II S, Benyamin RM, Chopra P, et al. Percutaneous adhesiolysis in the management of chronic low back pain in post lumbar surgery syndrome and spinal stenosis: A systematic review. Pain Physician. 2012;15(4):E435-E462.
13. Kassenärztlichen Bundesvereinigung (KBV). Minimalinvasive wirbelsäulen-kathetertechnik nach Racz. Ein assessment der Bundesärztekammer und der Kassenärztlichen Bundesvereinigung. Köln, Germany: KBV; March 28, 2003. Available at: http://www.kbv.de/hta/. Accessed April 30, 2004.
14. Letter from Thomas J. Callahan, Center for Devices and Radiological Health, U.S. Food and Drug Administration (FDA), Bethesda, MD, to Donald R. Henderson, Medical Evaluation Devices and Instruments Corporation, Gloversville, NY, regarding section 510(K) notification of intent to market the Racz Epidural Catheter, 510(k) PMN No. K954584. Bethesda, MD: FDA; October 8, 1996.
15. Manchikanti L, Bakhit CE. Percutaneous lysis of epidural adhesions. Pain Phys. 2000;3(1):46-64.
16. Manchikanti L, Pakanati RR, Bakhit CE, et al. Role of adhesiolysis and hypertonic sline neurolysis in management of low back pain: Evoluation and modification of the Racz protocol. Pain Digest. 1999;9;91-99.
17. Manchikanti L, Pampati V, Bakhit CE, et al. Non-endoscopic and endoscopic adhesiolysis in post-lumbar laminectomy syndrome. Pain Phys. 1999;2(3):52-58.
18. Manchikanti L, Pampati V, Fellows B, et al. Role of one day epidural adhesiolysis in management of chronic low back pain: A randomized clinical trial. Pain Phys. 2001;4(2):153-166.
19. Manchikanti L, Rivera J, Pampati V, et al. Spinal endoscopic adhesiolysis in the management of chronic low back pain: A

preliminary report of a randomized, double-blind trial. Pain Phys. 2003;6:259-267.

20. Manchikanti L, Rivera JJ, Pampati V, et al. One day lumbar epidural adhesiolysis and hypertonic saline neurolysis in treatment of chronic low back pain: A randomized controlled trial. Pain Phys. 2004;7(2) (in press).
21. Manchikanti L, Singh V. Epidural lysis of adhesions and myeloscopy. Curr Pain Headache Rep. 2002;6(6):427-435.
22. Manchikanti L, Staats PS, Singh V, et al. Evidence-based practice guidelines for interventional techniques in the management of chronic spinal pain. Pain Phys. 2003;6:3-81.
23. Mississippi Workers Compensation Commission (MWCC). Pain Management Guidelines. Mississippi Workers Compensation Medical Fee Schedule. Jackson, MS: MWCC; June 2003.
24. National Institute for Clinical Excellence (NICE). Endoscopic division of epidural adhesions. Interventional Procedure Guidance 88. London, UK: NICE; September 2004.
25. National Institute for Health and Clinical Excellence (NICE). Therapeutic endoscopic division of epidural adhesions. Interventional Procedure Guidance 333. London, UK: NICE; February 2010.
26. Omoigui S. A safer technique utilizing an intravenous catheter introducer for epidural catheter lysis of adhesions. Reg Anesth Pain Med. 1998;23(4):427.
27. Park CH, Lee SH. Effectiveness of percutaneous transforaminal adhesiolysis in patients with lumbar neuroforaminal spinal stenosis. Pain Physician. 2013;16(1):E37-E43.
28. Racz GB, Heavner J. In response to article by Drs. Devulder et al. Clin J Pain. 1995;11(2):151-154.
29. Racz GB, Heavner JE, Raj PP. Percutaneous epidural neuroplasty: Prospective one-year follow-up. Pain Digest. 1999;9:97-102.
30. Racz GB, Heavner JE. Epidural phenol neurolysis using daily needle placements. Anesth Analg. 1986;65(7):822-823.
31. Racz GB, Holubec JT. Lysis of adhesions in the epidural space. In: Techniques of Neurolysis. GB Racz, ed. Boston, MA: Kluwer Academic Publishers; 1989:73-87
32. Racz GB, Noe C, Heavner JE. Selective spinal injections for lower back pain. Curr Rev Pain. 1999;3(5):333-341.

33. Veihelmann A, Devens C, Trouillier H, et al. Epidural neuroplasty versus physiotherapy to relieve pain in patients with sciatica: A prospective randomized blinded clinical trial. J Orthop Sci. 2006;11(4):365-369.
34. Viesca CO, Racz GB, Day MR. Special techniques in pain management: Lysis of adhesions. Anesthesiol Clin North Am. 2003;21(4):745-766, vi.

Endoscopic Transforaminal Percutaneous Discectomy

1. Ditsworth DA. Endoscopic transforaminal lumbar discectomy and reconfiguration: A postero-lateral approach into the spinal canal. Surg Neurol. 1998;49(6):588-597; discussion 597-598.
2. Hacker RJ, Miller CG. Failed anterior cervical foraminotomy. J Neurosurg. 2003;98(2 Suppl):126-130.
3. Stucker R, Krug C, Reichelt A. Endoscopic treatment of intervertebral disk displacement. Percutaneous transforaminal access to the epidural space. Indications, technique and initial results. Orthopade. 1997;26(3):280-287.

Percutaneous Polymethylmethacrylate Vertebroplasty and Kyphoplasty

1. Adelaide Health Technology Assessment (AHTA) on behalf of MSAC. Vertebroplasty and kyphoplasty for the treatment of vertebral compression fracture. Adelaide, SA: Adelaide Health Technology Assessment (AHTA) on behalf of MSAC; 2006.
2. Alberta Heritage Foundation for Medical Research (AHFMR). Vertebroplasty. Edmonton, AB: AHFMR; 1999.
3. Barr JD, Barr MS, Lemley TJ, et al. Percutaneous vertebroplasty for pain relief and spinal stabilization. Spine. 2000;25(8):923-928.
4. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis and malignancy. Technology Assessment Program. Chicago, IL: BCBSA; December 2004;19(12).
5. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Percutaneous vertebroplasty for vertebral fractures caused by osteoporosis and malignancy, or hemangioma.

Technology Assessment Program. Chicago, IL: BCBSA; December 2004;19(13).

6. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Percutaneous vertebroplasty and kyphoplasty for vertebral fractures caused by osteoporosis or malignancy. TEC Assessment Program. Chicago, IL: BCBSA; September 2008;23(5).
7. BlueCross BlueShield Association (BCBSA), Technology Evaluation Center (TEC). Percutaneous vertebroplasty or kyphoplasty for vertebral fractures caused by osteoporosis. TEC Assessment Program. Chicago, IL: BCBCA; April 2010; 24(7).
8. Bono CM, Heggeness M, Mick C, et al.; North American Spine Society. Newly released vertebroplasty randomized controlled trials: A tale of two trials. Spine J. 2010;10(3):238-240.
9. Buchbinder R, Osborne RH, Ebeling PR, et al. A randomized trial of vertebroplasty for painful osteoporotic vertebral fractures. N Engl J Med. 2009;361(6):557-568.
10. Centers for Medicare and Medicaid Services (CMS). Percutaneous kyphoplasty for vertebral fractures caused by osteoporosis and malignancy. Draft Technology Assessment. Medicare Coverage Database. Baltimore, MD: CMS; 2005.
11. Clark W, Bird P, Gonski P, et al. Safety and efficacy of vertebroplasty for acute painful osteoporotic fractures (VAPOUR): A multicentre, randomised, double-blind, placebo-controlled trial. Lancet. 2016;388(10052):1408-1416.
12. Clark W, Lyon S, Burnes J, et al. Trials of vertebroplasty procedures [letters]. N Engl J Med. 2009;361;2097-2100.
13. Cotten A, Bountry N, Cortet, B, et al. Percutaneous vertebroplasty: State of the art. Radiographics. 1998;18(2):311-323.
14. Danish Centre for Evaluation and Health Technology Assessment (DACEHTA). Percutaneous vertebroplasty. Pain management of osteoporotic vertebral fractures [summary]. Danish Health Technology Assessment. Copenhagen, Denmark; DACEHTA; 2004;6(2).
15. Dudeney S, Lieberman IH, Reinhardt MK, Hussein M. Kyphoplasty in the treatment of osteolytic vertebral compression fractures as a result of multiple myeloma. J Clin Oncol. 2002;20(9):2382-2387.
16. Fisher A. Percutaneous vertebroplasty: A bone cement procedure for spinal pain relief. Issues in Emerging Health Techologies.

Issue 31. Ottawa, ON: Canadian Coordinating Office of Health Technology Assessment (CCOHTA); May 2002.

17. Franck H, Boszczyk BM, Bierschneider M, Jaksche H. Interdisciplinary approach to balloon kyphoplasty in the treatment of osteoporotic vertebral compression fractures. Eur Spine J. 2003;12 Suppl 2:S163-S167.
18. Hardouin P, Fayada P, Leclet H, Chopin D. Kyphoplasty. Joint Bone Spine. 2002;69(3):256-261.
19. He SC, Teng GJ, Deng G, et al. Repeat vertebroplasty for unrelieved pain at previously treated vertebral levels with osteoporotic vertebral compression fractures. Spine. 2008;33(6):640-647.
20. Hijji FY, Narain AS, Kudaravalli KT, et al. Does the VAPOUR trial shed new light on the efficacy of vertebroplasty for acute painful osteoporotic fractures? AME Med J. 2017;2:32.
21. Institute for Clinical Systems Improvement (ICSI). Vertebroplasty and balloon-assisted vertebroplasty for the treatment of osteoporotic compression fractures. Technology Assessment Report #79. Bloomington, MN: ICSI; January 2004.
22. Jarvik JG, Kallmes DF, Deyo RA. Kyphoplasty: More answers or more questions? Spine. 2006;31(1):65-66.
23. Jensen ME, Evans AJ, Mathis JM, et al. Percutaneous polymethylmethacrylate vertebroplasty in the treatment of osteoporotic vertebral body compression fractures: Technical Aspects. Am J Neuroradiol. 1997;18(10):1897-1904.
24. Kaito T. Point of view. Spine. 2016;41(8):661.
25. Kallmes DF, Comstock BA, Heagerty PJ, et al. A randomized trial of vertebroplasty for osteoporotic spinal fractures. N Engl J Med. 2009;361(6):569-579.
26. Kallmes DF. If one vertebroplasty is good, two must be better. Spine. 2008;33(6):579-580.
27. Karliner L. Balloon kyphoplasty as a treatment for vertebral compression fractures. Technology Assessment. San Francisco, CA: California Technology Assessment Forum (CTAF); June 17, 2009.
28. Leigh BC, Skelly AC, Henrikson NB, et al. Vertebroplasty, kyphoplasty and sacroplasty. Health Technology Assessment. Prepared by Spectrum Research Inc. for the Washington State Healthcare Authority, Health Technology Assessment Program.

Olympia, WA: Washington State Healthcare Authority; November 4, 2010.

29. Levine SA, Perin LA, Hayes D, et al. An evidence-based evaluation of percutaneous vertebroplasty. Manag Care. 2000;9(3):56-60, 63.
30. Lieberman IH, Dudeney S, Reinhardt MK, Bell G. Initial outcome and efficacy of 'kyphoplasty' in the treatment of painful osteoporotic vertebral compression fractures. Spine. 2001;26:1631-1638.
31. Martin JB, Jean B, Sugiu K, et al. Vertebroplasty: Clinical experience and follow-up results. Bone. 1999;25(2 Suppl):11S-15S.
32. Medical Services Advisory Committee (MSAC). Review of kyphoplasty for the treatment of vertebral compression fracture and review of interim funded service: Vertebroplasty for the treatment of vertebral compression fracture. MSAC Reference No. 27. Canberra: ACT: Medical Services Advisory Committee (MSAC); 2011.
33. Muggli E. Safety and efficacy of percutaneous vertebroplasty in symptomatic osteoporotic vertebral compression fractures. Evidence Centre Evidence Report. Clayton, VIC: Centre for Clinical Effectiveness (CCE); 2002.
34. National Institute for Clinical Excellence. Balloon kyphoplasty for vertebral compression fractures. Interventional Procedure Guidance 20. London, UK: NICE; November 2003.
35. National Institute for Clinical Excellence. Percutaneous vertebroplasty. Interventional Procedure Guidance 12. London, UK: NICE; September 2003.
36. National Institute for Health and Clinical Excellence (NICE). Balloon kyphoplasty for vertebral compression fractures. Interventional Procedure Guidance 166. London, UK: NICE; 2006.
37. Ontario Ministry of Health and Long-Term Care (MAS), Medical Advisory Secretariat (MAS). Balloon kyphoplasty. Health Technology Literature Review. Toronto, ON: MAS; December 2004.
38. Ontario Ministry of Long-Term Care, Medical Advisory Secretariat (MAS). Balloon kyphoplasty for treatment of painful osteoporotic vertebral compression fractures: An evidence update. Toronto, ON: MAS; 2010;10(20).

39. Ortiz AO, Zoarski GH, Beckerman M. Kyphoplasty. Tech Vasc Interv Radiol. 2002;5(4):239-249.
40. Phillips FM, Pfeifer BA, Lieberman IH, et al. Minimally invasive treatments of osteoporotic vertebral compression fractures: Vertebroplasty and kyphoplasty. Instr Course Lect. 2003;52:559-567.
41. Pichon Riviere A, Augustovski F, Ferrante D, et al. Percutaneous vertebroplasty usefulness for vertebral fracture treatment [summary]. Report IRR No. 39. Buenos Aires, Argentina: Institute for Clinical Effectiveness and Health Policy (IECS); 2004.
42. Rousing R, Andersen MO, Jespersen SM, et al. Percutaneous vertebroplasty compared to conservative treatment in patients with painful acute or subacute osteoporotic vertebral fractures: Three-months follow-up in a clinical randomized study. Spine. 2009;34(13):1349-1354.
43. Rousing R, Lauritsen J, Thomsen K, et al. Percutaneous vertebroplasty as a treatment for osteoporotic vertebral fractures – a Health Technology Assessment. Copenhagen, Denmark: National Board of Health, Danish Centre for Health Technology Assessment; 2010;10(1).
44. Society of Interventional Radiology (SIR). Society of Interventional Radiology commentary on vertebroplasty and the August studies in the New England Journal of Medicine. SIR Commentary. Fairfax, VA: SIR; November 24, 2009.
45. Swedish Council on Technology Assessment in Health Care (SBU). Percutaneous vertebroplasty in severe back pain from vertebral compression fractures - early assessment briefs (Alert). SBU Alert Report No. 2007-02. Stockholm, Sweden: SBU; 2007.
46. Swedish Council on Technology Assessment in Health Care (SBU). Percutaneous vertebroplasty and balloon kyphoplasty in treating painful osteoporotic vertebral compression fractures. SBU Alert. Summary. Stockholm, Sweden: Swedish Council on Technology Assessment in Health Care (SBU); 2011.
47. U.S. Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH). Complications related to the use of bone cement and bone void fillers in treating compression fractures of the spine. FDA Public Health Web Notification. Rockville, MD: FDA; updated May 7, 2004.

48. Vlayen J, Camberlin C, Paulus D, Ramaekers D. Rapid assessment of emerging spine technologies: Intervertebral disc replacement and vertebro/balloon kyphoplasty. KCE Reports 39. Brussels, Belgium: Belgian Health Care Knowledge Centre (KCE); 2006.
49. Wardlaw D, Cummings SR, Van Meirhaeghe J, et al. Efficacy and safety of balloon kyphoplasty compared with non-surgical care for vertebral compression fracture (FREE): A randomised controlled trial. Lancet. 2009;373(9668):1016-1024.
50. Watts NB, Harris ST, Genant HK. Treatment of painful osteoporotic vertebral fractures with percutaneous vertebroplasty or kyphoplasty. Osteoporos Int. 2001;12(6):429-437.
51. Weinstein JN. Balancing science and informed choice in decisions about vertebroplasty. N Engl J Med. 2009;361(6):619-621.
52. Workers Compensation Board of British Columbia (WorkSafe BC), Evidence Based Practice Group. Percutaneous vertebroplasty for pain relief in the management of compressive vertebral fractures. Richmond, BC: WorkSafe BC; 2003.
53. Yang E-Z, Xu J-G, Huang G-Z, et al. Percutaneous vertebroplasty versus conservative treatment in aged patients with acute osteoporotic vertebral compression fractures: A prospective randomized controlled clinical study. Spine (Phila Pa 1976). 2016;41(8):653-660.

Sacroplasty

1. Frey ME, DePalma MJ, Cifu DX, et al. Efficacy and safety of percutaneous sacroplasty for painful osteoporotic sacral insufficiency fractures. Spine. 2007;32(15):1635-1640.

Vesselplasty

1. Cortet B, Cotten A, Boutry N, et al. Percutaneous vertebroplasty in patients with osteolytic metastases or multiple myeloma. Rev Rhum Engl Ed. 1997;64(3):177-183.
2. Flors L, Lonjedo E, Leiva-Salinas C, et al. Vesselplasty: A new technical approach to treat symptomatic vertebral compression fractures. AJR Am J Roentgenol. 2009;193(1):218-226.

3. Mathis JM, Wong, W. Percutaneous vertebroplasty: Technical considerations. J Vasc Interv Radiol. 2003;14(8):953-960.

Laser-Assisted Disc Decompression

1. American Academy of Orthopaedic Surgeons (AAOS). Use of lasers in orthopaedic surgery. Advisory Statement. Rosemont, IL: AAOS; July 1993.
2. Boult M, Fraser RD, Jones N, et al. Percutaneous endoscopic laser discectomy. Aust N Z J Surg. 2000;70(7):475-479.
3. Cambridgeshire Health Authority Board. Endoscopic laser spinal surgery. Policy 18. Cambridgeshire, UK: National Health Service (NHS); July 18, 2001.
4. Canadian Agency for Drugs and Technologies in Health (CADTH). Laser spine surgery for herniated discs and/or nerve root entrapment: A review of clinical effectiveness, cost effectiveness and guidelines. CADTH Rapid Response Report: Summary with Critical Appraisal. Ottawa, ON: CADTH; April 27, 2017.
5. Choy DSJ, Ascher PW, Saddekni S, et al. Percutaneous laser disc decompression. A new therapeutic modality. Spine. 1992;17(8):949-956.
6. Choy DSJ. Percutaneous laser disc decompression (PLDD): 352 cases with an 8½-year follow up. J Clin Laser Med Surg. 1995;13(1):17-21.
7. Gibson JNA, Grant IC, Waddell G. Surgery for lumbar disc prolapse (Cochrane Review). In: The Cochrane Library, Issue 2, 2002. Oxford, UK: Update Software.
8. Jordan J, Konstantinou K, Morgan TS, Weinstein J. Herniated lumbar disc. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; November 2006.
9. National Institute for Clinical Excellence (NICE). Interventional procedure overview of laser lumbar discectomy. Prepared by ASERNIP-S. London, UK: NICE; 2002.
10. National Institute for Clinical Excellence (NICE). Laser lumbar discectomy. Interventional Procedures Consultation Document. London, UK: NICE; September 2003.
11. National Institute for Clinical Excellence (NICE). Percutaneous endoscopic laser thoracic discectomy. Interventional Procedure

Consultation Document. London, UK: NICE; January 2004.
12. National Institute for Health and Clinical Excellence (NICE). Percutaneous endoscopic laser lumbar diskectomy. Interventional Procedures Consultation. London, UK: NICE; December 2008.
13. Ohnmeiss DD, Guyer RD, Hochschuler SH. Laser disc decompression. The importance of proper patient selection. Spine. 1994;19(18):2054-2059.
14. Quigley MR, Maroon JC. Laser discectomy: A review. Spine. 1994;19(1):53-56.
15. Quigley MR. Percutaneous laser discectomy. Neurosurg Clin N Am. 1996;7(1):37-42.
16. Sherk HH, Black J, Rhodes A, et al. Laser discectomy. Clin Sports Med. 1993;12(3):569-577.

Yeung Endoscopic Spinal Surgery (Y.E.S.S.) and Endoscopic Laser Diskectomy

1. Tsou PM, Yeung AT. Transforaminal endoscopic decompression for radiculopathy secondary to intracanal noncontained lumbar disc herniations: Outcome and technique. Spine J. 2002;2:41-48.
2. Yeung AT, Gore S. Evolving methodology in treating discogenic back pain by selective endoscopic discectomy (SED) and thermal annulplasty. J Minim Invasive Spinal Tech. 2001;1:8-16.
3. Yeung AT, Porter J. Minimally invasive endoscopic surgery for the treatment of discogenic pain. In: Pain Management: A Practical Guide for Clinicians. 6th ed. RS Weiner, ed. Boca Raton, FL: CRC Press; 2002; Ch. 87:1073-1078.
4. Yeung AT, Tsou PM. Posterolateral endoscopic excision for lumbar disc herniation. Surgical technique, outcome, and complications in 307 consecutive cases. Spine. 2002;27(7):722-731.

Microdiscectomy

1. Comité d'Evaluation et de Diffusion des Innovations Technologiques (CEDIT). La microdiscectomie par voie endoscopique. CEDIT les recommendations. Ref. 99.02.2. Paris, France: CEDIT; January 1, 2001.

2. Dent THS, Microdiscectomy for prolapsed intervertebral disc. STEER: Succinct and Timely Evaluated Evidence Review. DR Foxcroft and V Muthu, eds. Bazian, Ltd., and Wessex Institute for Health Research & Development, University of Southampton. STEER. 2001;1(3):1-7. Available at: http://www.signpoststeer.org. Accessed July 29, 2002.
3. Gibson JNA, Waddell G. Surgical interventions for lumbar disc prolapse. Cochrane Database Syst Rev. 2007;(2):CD001350.
4. Hanriksen L, Schmidt K, Eskesen V, Jantzen E. A controlled study of microsurgical versus standard lumbar discectomy. Br J Neurosurg. 1996;10:289-293.
5. Hermantin FU, Peters T, Quartararo L, Kambin P. A prospective, randomized study comparing the results of open discectomy with those of video-assisted arthroscopic microdiscectomy. J Bone Joint Surg. 1999;81:959-965.
6. Jordan J, Konstantinou K, Morgan TS, Weinstein J. Herniated lumbar disc. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; November 2006.
7. Lagarrigue J, Chaynes P. Etude comparative de la cirurgie discale avec et sans microscope. Neurochirurgie. 1994;40:116-120.
8. Malaysian Health Technology Assessment Unit (MHTAU). Minimal access surgery. Kuala Lumpur, Malaysia: MHTAU; 2005.
9. Norwegian Knowledge Centre for the Health Services (NOKC). Treatment of lumbar disc herniation. SMM-Report 1/2001. Oslo, Norway: Norwegian Knowledge Centre for the Health Services (NOKC); 2001.
10. Tullberg T, Isacson J, Weidenheilm L. Does microscopic removal of lumbar disc herniation lead to better results than the standard procedure? Results of a one year randomized study. Spine. 1993;18:24-26.

Pulsed Radiofrequency Treatment

1. Ahadian FM. Pulsed radiofrequency neurotomy: Advances in pain medicine. Curr Pain Headache Rep. 2004;8(1):34-40.
2. Binder A. Neck pain. In: BMJ Clinical Evidence. London, UK: BMJ Publishing Group; May 2006.
3. Mikeladze G, Espinal R, Finnegan R, et al. Pulsed radiofrequency application in treatment of chronic zygapophyseal joint pain.

Spine J. 2003;3(5):360-362.
4. Shah RV, Racz GB. Long-term relief of posttraumatic headache by sphenopalatine ganglion pulsed radiofrequency lesioning: A case report. Arch Phys Med Rehabil. 2004;85(6):1013-1016.
5. Van Zundert J, Brabant S, Van de Kelft E, et al. Pulsed radiofrequency treatment of the gasserian ganglion in patients with idiopathic trigeminal neuralgia. Pain. 2003;104(3):449-452.

Microendoscopic Discectomy

1. Khoo LT, Fessler RG. Microendoscopic decompressive laminotomy for the treatment of lumbar stenosis. Neurosurgery. 2002;51(5 Suppl):S146-S154.
2. Maroon JC. Current concepts in minimally invasive discectomy. Neurosurgery. 2002;51(5 Suppl):S137-S145.
3. Muramatsu K, Hachiya Y, Morita C. Postoperative magnetic resonance imaging of lumbar disc herniation: Comparison of microendoscopic discectomy and Love's method. Spine. 2001;26(14):1599-1605.
4. Nakagawa H, Kamimura M, Uchiyama S, et al. Microendoscopic discectomy (MED) for lumbar disc prolapse. J Clin Neurosci. 2003;10(2):231-235.
5. Perez-Cruet MJ, Foley KT, Isaacs RE, et al. Microendoscopic lumbar discectomy: Technical note. Neurosurgery. 2002;51(5 Suppl):S129-S136.
6. Toyone T, Tanaka T, Kato D, Kaneyama R. Low-back pain following surgery for lumbar disc herniation. A prospective study. J Bone Joint Surg Am. 2004;86-A(5):893-896.

Far Lateral Microendoscopic Diskectomy (FLMED)

1. O'Toole JE, Eichholz KM, Fessler RG. Minimally invasive far lateral microendoscopic discectomy for extraforaminal disc herniation at the lumbosacral junction: Cadaveric dissection and technical case report. Spine J. 2007;7(4):414-421.
2. Pirris SM, Dhall S, Mummaneni PV, Kanter AS. Minimally invasive approach to extraforaminal disc herniations at the lumbosacral junction using an operating microscope: Case series and review of the literature. Neurosurg Focus. 2008;25(2):E10.

Dynamic Stabilization

1. Chrobok J, Vrba I, Stetkarova I. Selection of surgical procedures for treatment of failed back surgery syndrome (FBSS). Chir Narzadow Ruchu Ortop Pol. 2005;70(2):147-153.
2. Grob D, Benini A, Junge A, Mannion AF. Clinical experience with the Dynesys semirigid fixation system for the lumbar spine: Surgical and patient-oriented outcome in 50 cases after an average of 2 years. Spine. 2005;30(3):324-331.
3. Hopf C, Heeckt H, Beske C. Indication, biomechanics and early results of artificial disk replacement. Z Orthop Ihre Grenzgeb. 2004;142(2):153-158.
4. Kanayama M, Hashimoto T, Shigenobu K, et al. A minimum 10-year follow-up of posterior dynamic stabilization using Graf artificial ligament. Spine (Phila Pa 1976). 2007;32(18):1992-1996; discussion 1997.
5. Korovessis P, Papazisis Z, Koureas G, Lambiris E. Rigid, semirigid versus dynamic instrumentation for degenerative lumbar spinal stenosis: A correlative radiological and clinical analysis of short-term results. Spine. 2004;29(7):735-742.
6. Kumar A, Beastall J, Hughes J, et al. Disc changes in the bridged and adjacent segments after Dynesys dynamic stabilization system after two years. Spine. 2008;33(26):2909-2914.
7. National Institute for Health and Clinical Excellence (NICE). Non-rigid stabilisation procedures for the treatment of low back pain. Interventional Procedure Consultation Document. London, UK: NICE; July 2005.
8. No authors listed. Dynamic Stabilization for lumbar spinal stenosis with Stabilimax NZ® Dynamic Spine Stabilization System. This study has been suspended. Verified by Applied Spine Technologies October 2008. Available at: http://www.spineuniverse.com/displayarticle.php/article4233.html. Accessed January 5, 2009.
9. Nockels RP. Dynamic stabilization in the surgical management of painful lumbar spinal diso rders. Spine. 2005;30(16 Suppl):S68-S72.
10. Noorani H, Topfer L. Graf ligament stabilization for degenerative lumbar disorders. Health Technology Inquiry Service (HTIS).

Ottawa, ON: Canadian Agency for Drugs and Technologies in Health (CADTH); August 18, 2006.

11. Pichon Riviere A, Augustovski F, Alcaraz A, et al. Device for Intervertebral Assisted Motion (DIAM) in spine instability. Report IRR No.97. Buenos Aires, Argentina: Institute for Clinical Effectiveness and Health Policy (IECS); 2006.
12. Putzier M, Hoff E, Tohtz S, et al. Dynamic stabilization adjacent to single-level fusion: Part II. No clinical benefit for asymptomatic, initially degenerated adjacent segments after 6 years follow-up. Eur Spine J. 2010;19(12):2181-2189.
13. Putzier M, Schneider SV, Funk J, Perka C. Application of a dynamic pedicle screw system (DYNESYS) for lumbar segmental degenerations - comparison of clinical and radiological results for different indications. Z Orthop Ihre Grenzgeb. 2004;142(2):166-173.
14. Putzier M, Schneider SV, Funk JF, et al. The surgical treatment of the lumbar disc prolapse: Nucleotomy with additional transpedicular dynamic stabilization versus nucleotomy alone. Spine. 2005;30(5):E109-E114.
15. Schwarzenbach O, Berlemann U, Stoll TM, Dubois G. Posterior Dynamic Stabilization Systems: DYNESYS. Orthop Clin North Am. 2005;36(3):363-372.
16. Sengupta DK, Mulholland RC. Fulcrum assisted soft stabilization system: A new concept in the surgical treatment of degenerative low back pain. Spine. 2005;30(9):1019-1029; discussion 1030.
17. U.S. Food and Drug Administration (FDA), Center for Devices and Radiological Health. Dynesys Spinal System Spinal Fixation System. 510(k) Summary. K043565. Rockville, MD: FDA; March 11, 2004.
18. Welch WC, Cheng BC, Awad TE, et al. Clinical outcomes of the Dynesys dynamic neutralization system: 1-year preliminary results. Neurosurg Focus. 2007;22(1):E8.

Inter-Spinous Distraction and Interlaminar Stabilization Procedures

1. Aggarwal N, Chow R. Real world adverse events of interspinous spacers using manufacturer and user facility device experience data. Anesth Pain Med (Seoul). 2021;16(2):177-183.

2. Anderson PA, Tribus CB, Kitchel SH. Treatment of neurogenic claudication by interspinous decompression: Application of the X STOP device in patients with lumbar degenerative spondylolisthesis. J Neurosurg Spine. 2006;4(6):463-471.
3. Bae HW, Lauryssen C, Maislin G, et al. Therapeutic sustainability and durability of coflex interlaminar stabilization after decompression for lumbar spinal stenosis: A four year assessment. Int J Spine Surg. 2015;9:15.
4. Belgian Health Care Knowledge Centre. The pre-market clinical evaluation of innovative high-risk medical devices. KCE reports 158C. Brussels, Belgium: KCE; 2011.
5. Bono CM, Vaccaro AR. Interspinous process devices in the lumbar spine. J Spinal Disord Tech. 2007;20(3):255-261.
6. Chou R, Baisden J, Carragee EJ, et al. Surgery for low back pain: A review of the evidence for an American Pain Society Clinical Practice Guideline. Spine (Phila Pa 1976). 2009;34(10):1094-1109.
7. Chou R. Subacute and chronic low back pain: Surgical treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed November 2013.
8. Christie SD, Song JK, Fessler RG. Dynamic interspinous process technology. Spine. 2005;30(16 Suppl):S73-S78.
9. Davis R, Auerbach JD, Bae H, Errico TJ. Can low-grade spondylolisthesis be effectively treated by either coflex interlaminar stabilization or laminectomy and posterior spinal fusion? Two-year clinical and radiographic results from the randomized, prospective, multicenter US investigational device exemption trial: Clinical article. J Neurosurg Spine. 2013b;19(2):174-184.
10. Davis RJ, Errico TJ, Bae H, Auerbach JD. Decompression and Coflex interlaminar stabilization compared with decompression and instrumented spinal fusion for spinal stenosis and low-grade degenerative spondylolisthesis: Two-year results from the prospective, randomized, multicenter, Food and Drug Administration Investigational Device Exemption trial. Spine (Phila Pa 1976). 2013a;38(18):1529-1539.
11. Deer TR, Grider JS, Pope JE, et al. The MIST Guidelines: The Lumbar Spinal Stenosis Consensus Group Guidelines for minimally invasive spine treatment. Pain Pract. 2019a;19(3):250-274.

12. Deer TR, Sayed D, Malinowski MN, et al. A review of emerging evidence for utilization of a percutaneous interspinous process decompression device to treat symptomatic lumbar adjacent-segment degeneration. Pain Med. 2019b;20(Suppl 2):S9-S13.
13. Doulgeris JJ, Aghayev K, Gonzalez-Blohm SA, et al. Biomechanical comparison of an interspinous fusion device and bilateral pedicle screw system as additional fixation for lateral lumbar interbody fusion. Clin Biomech (Bristol, Avon). 2015;30(2):205-210.
14. Falowski SM, Mangal V, Pope J, et al. Multicenter retrospective review of safety and efficacy of a novel minimally invasive lumbar interspinous fusion device. J Pain Res. 2021;14:1525-1531.
15. Forsth P, Ólafsson G, Carlsson T, et al. A randomized, controlled trial of fusion surgery for lumbar spinal stenosis. N Engl J Med. 2016;374(15):1413-1423.
16. Fuchs PD, Lindsey DP, Hsu KY, et al. The use of an interspinous implant in conjunction with a graded facetectomy procedure. Spine. 2005;30(11):1266-1272; discussion 1273-1274.
17. Ghogawala Z, Dziura J, Butler WE, et al. Laminectomy plus fusion versus laminectomy alone for lumbar spondylolisthesis. N Engl J Med. 2016;374(15):1424-1434.
18. Hartman J, Granville M, Jacobson RE, et al. The Use of Vertiflex® interspinous spacer device in patients with lumbar spinal stenosis and concurrent medical comorbidities. Cureus. 2019;11(8):e5374.
19. Hirsch C, Breque C, Ragot S, et al. Biomechanical study of dynamic changes in L4-L5 foramen surface area in flexion and extension after implantation of four interspinous process devices. Orthop Traumatol Surg Res. 2015;101(2):215-219.
20. Hsu KY, Zucherman JF, Hartjen CA, et al. Quality of life of lumbar stenosis-treated patients in whom the X STOP interspinous device was implanted. J Neurosurg Spine. 2006;5(6):500-507.
21. Kabir SM, Gupta SR, Casey AT. Lumbar interspinous spacers: A systematic review of clinical and biomechanical evidence. Spine (Phila Pa 1976). 2010;35(25):E1499-E1506.
22. Kim DH, Tantorski M, Shaw J, et al. Occult spinous process fractures associated with interspinous process spacers. Spine (Phila Pa 1976). 2011;36(16):E1080-E1085.
23. Kondrashov DG, Hannibal M, Hsu KY, Zucherman JF. Interspinous process decompression with the X-STOP device for lumbar spinal

stenosis: A 4-year follow-up study. Spinal Disord Tech. 2006;19(5):323-327.

24. Kong DS, Kim ES, Eoh W. One-year outcome evaluation after interspinous implantation for degenerative spinal stenosis with segmental instability. J Korean Med Sci. 2007;22(2):330-335.
25. Lauryssen C, Jackson RJ, Baron JM, et al. Stand-alone interspinous spacer versus decompressive laminectomy for treatment of lumbar spinal stenosis. Expert Rev Med Devices. 2015;12(6):763-769.
26. Lee J, Hida K, Seki T, et al. An interspinous process distractor (X STOP) for lumbar spinal stenosis in elderly patients: Preliminary experiences in 10 consecutive cases. J Spinal Disord Tech. 2004;17(1):72-77; discussion 78.
27. Lee SH, Seol A, Cho TY, et al. A systematic review of interspinous dynamic stabilization. Clin Orthop Surg. 2015;7(3):323-329.
28. Levin K. Lumbar spinal stenosis: Treatment and prognosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed February 2012; November 2020.
29. Lindsey DP, Swanson KE, Fuchs P, et al. The effects of an interspinous implant on the kinematics of the instrumented and adjacent levels in the lumbar spine. Spine. 2003;28(19):2192-2197.
30. Lonne G. Treatment of lumbar spinal stenosis; comparison of two different surgical methods; Mini-invasive decompression to X-stop (LSSS). ClinicalTrials.gov. Bethesda, MD: National Library of Medicine; 2013.
31. Lonne G, Johnsen LG, Rossvoll I, et al. Minimally invasive decompression versus x-stop in lumbar spinal stenosis: A randomized controlled multicenter study. Spine (Phila Pa 1976). 2015;40(2):77-85.
32. Medical Services Advisory Committee (MSAC). Minimally invasive, lumbar decompression and dynamic stabilisation using an interlaminar device, with no rigid fixation to the vertebral pedicles, of one or two lumbar motion. Public Summary Document. Canberra, ACT: MSAC; 2017.
33. Merkow J, Varhabhatla N, Manchikanti L, et al. Minimally invasive lumbar decompression and interspinous process device for the management of symptomatic lumbar spinal stenosis: A literature review. Curr Pain Headache Rep. 2020;24(4):13.

34. Mohi Eldin M. Coflex dynamic distraction stabilization device for lumbar degenerative disease. Cureus. 2014;6(1):e152.
35. Moojen WA, Arts MP, Brand R, et al. The Felix-trial. Double-blind randomization of interspinous implant or bony decompression for treatment of spinal stenosis related intermittent neurogenic claudication. BMC Musculoskelet Disord. 2010;11:100.
36. Moojen WA, Arts MP, Jacobs WC, et al; Leiden-The Hague Spine Intervention Prognostic Study Group. Interspinous process device versus standard conventional surgical decompression for lumbar spinal stenosis: Randomized controlled trial. BMJ. 2013;347:f6415.
37. Moojen WA, Bredenoord AL, Viergever RF, Peul WC. Scientific evaluation of spinal implants: An ethical necessity. Spine (Phila Pa 1976). 2014;39(26):2115-2118.
38. Musacchio MJ, Lauryssen C, Davis RJ, et al. Evaluation of decompression and interlaminar stabilization compared with decompression and fusion for the treatment of lumbar spinal stenosis: 5-year follow-up of a prospective, randomized, controlled trial. Int J Spine Surg. 2016;10:6.
39. National Institute for Health and Clinical Excellence (NICE). Interspinous distraction procedures for spinal stenosis causing neurogenic claudication in the lumbar spine. Interventional Procedure Consultation Document. London, UK: NICE; July, 2005.
40. National Institute for Health and Clinical Excellence (NICE). Interspinous distraction procedures for lumbar spinal stenosis causing neurogenic claudication. Interventional Procedure Guidance 165. London, UK: NICE; 2006.
41. Newton S, Hedayati H, Sullivan T, et al. Lumbar non-fusion posterior stabilisation devices. MSAC Application 1099. Adelaide, SA: Adelaide Health Technology Assessment (AHTA); 2008.
42. No authors listed. FDA approves implant for spinal pain. AP Health News. Blue Bell, PA: InteliHealth; November 23, 2005.
43. North American Spine Society (NASS). Diagnosis and treatment of degenerative lumbar spinal stenosis. Burr Ridge, IL: North American Spine Society (NASS); 2007.
44. North American Spine Society (NASS). Diagnosis and treatment of degenerative lumbar spinal stenosis. Burr Ridge, IL: North American Spine Society (NASS); December 2011.

45. North American Spine Society (NASS). Diagnosis and treatment of degenerative lumbar spondylolisthesis. Burr Ridge, IL: North American Spine Society; 2014.
46. Nunley PD, Deer TR, Benyamin RM, et al. Interspinous process decompression is associated with a reduction in opioid analgesia in patients with lumbar spinal stenosis. J Pain Res. 2018a;11:2943-2948.
47. Nunley PD, Patel VV, Orndorff DG, et al. Five-year durability of stand-alone interspinous process decompression for lumbar spinal stenosis. Clin Interv Aging. 2017b;12:1409-1417.
48. Nunley PD, Patel VV, Orndorff DG, et al. Interspinous process decompression improves quality of life in patients with lumbar spinal stenosis. Minim Invasive Surg. 2018b;2018:1035954.
49. Nunley PD, Patel VV, Orndorff DG, et al. Superion interspinous spacer treatment of moderate spinal stenosis: 4-year results. World Neurosurg. 2017a;104:279-283.
50. Parker SL, Anderson LH, Nelson T, Patel VV. Cost-effectiveness of three treatment strategies for lumbar spinal stenosis: Conservative care, laminectomy, and the Superion interspinous spacer. Int J Spine Surg. 2015;9:28.
51. Patel VV, Nunley PD, Whang PG, et al. Superion(®) interSpinous spacer for treatment of moderate degenerative lumbar spinal stenosis: Durable three-year results of a randomized controlled trial. J Pain Res. 2015b;8:657-662.
52. Patel VV, Whang PG, Haley TR, et al. Superion interspinous process spacer for intermittent neurogenic claudication secondary to moderate lumbar spinal stenosis: Two-year results from a randomized controlled FDA-IDE pivotal trial. Spine (Phila Pa 1976). 2015a;40(5):275-282.
53. Peul WC, Moojen WA. Fusion for lumbar spinal stenosis – safeguard or superfluous surgical implant? N Engl J Med. 2016;374(15):1478-1479.
54. Poetscher AW, Gentil AF, Ferretti M1, Lenza M. Interspinous process devices for treatment of degenerative lumbar spine stenosis: A systematic review and meta-analysis. PLoS One. 2018;13(7):e0199623.
55. Puzzilli F, Gazzeri R, Galarza M, et al. Interspinous spacer decompression (X-STOP) for lumbar spinal stenosis and

degenerative disk disease: A multicenter study with a minimum 3-year follow-up. Clin Neurol Neurosurg. 2014;124:166-174.

56. Reinhardt A, Hufnagel S. Longterm results of the interspinous spacer X-STOP. Orthopade. 2010;39(6):573-579.
57. Richards JC, Majumdar S, Lindsey DP, et al. The treatment mechanism of an interspinous process implant for lumbar neurogenic intermittent claudication. Spine. 2005;30(7):744-749.
58. Richter A, Schutz C, Hauck M, et al. Does an interspinous device (Coflex) improve the outcome of decompressive surgery in lumbar spinal stenosis? One-year follow up of a prospective case control study of 60 patients. Eur Spine J. 2010;19(2):283-289.
59. SFMT Europe B.V. X-Stop PK Interspinous Process Decompression (IPD) System. Driebergen, the Netherlands; SFMT; 2005. Available at: http://www.sfmt.com/sfmteuro/indications.html. Accessed December 21, 2005.
60. Siddiqui M, Smith FW, Wardlaw D. One-year results of X STOP interspinous implant for the treatment of lumbar spinal stenosis. Spine. 2007;32(12):1345-1348.
61. Stordeur S, Gerkens S, Roberfroid D. Interspinous implants and pedicle screws for dynamic stabilization of lumbar spine: Rapid Assessment . KCE Reports. Brussels, Belgium: Belgian Health Care Knowledge Centre (KCE); 2009.
62. Stromqvist BH, Berg S, Gerdhem P, et al. X-Stop versus decompressive surgery for lumbar neurogenic intermittent claudication: Randomized controlled trial with 2-Year follow-up. Spine. 2013;38:1436-1442.
63. Talwar V, Lindsey DP, Fredrick A, et al. Insertion loads of the X STOP interspinous process distraction system designed to treat neurogenic intermittent claudication. Eur Spine J. 2005 May 31.
64. Tekmyster G, Sayed D, Cairns KD, et al. Interspinous process decompression with the Superion ® spacer for lumbar spinal stenosis: Real-world experience from a device registry. Med Devices (Auckl). 2019;12:423-427.
65. Tram J, Srinivas S, Wali AR, et al. Decompression surgery versus interspinous devices for lumbar spinal stenosis: A systematic review of the literature. Asian Spine J. 2020;14(4):526-542.
66. Truumees E. Spinal stenosis: Pathophysiology, clinical and radiologic classification. Instr Course Lect. 2005;54:287-302.

67. U.S. Food and Drug Administration (FDA), Center for Devices and Radiological Health. X-Stop interspinous process distraction system. PMA Review Memorandum. Clinical Summary P040001. Rockville, MD; FDA; July 14, 2004.
68. U.S. Food and Drug Administration (FDA), Center for Devices and Radiological Health (CDRH). Orthopaedic and Rehabilitation Devices Panel Meeting Brief Summary for August 31, 2004. Rockville, MD: FDA; updated September 3, 2004.
69. Verhoof OJ, Bron JL, Wapstra FH, van Royen BJ. High failure rate of the interspinous distraction device (X-Stop) for the treatment of lumbar spinal stenosis caused by degenerative spondylolisthesis. Eur Spine J. 2008;17(2):188-192.
70. Welton L, Krieg B, Trivedi D, et al. Comparison of adverse outcomes following placement of Superion interspinous spacer device versus laminectomy and laminotomy. Int J Spine Surg. 2021;15(1):153-160.
71. Wiseman CM, Lindsey DP, Fredrick AD, Yerby SA. The effect of an interspinous process implant on facet loading during extension. Spine. 2005;30(8):903-907.
72. Yuan PS, Booth RE Jr, Albert TJ. Nonsurgical and surgical management of lumbar spinal stenosis. Instr Course Lect. 2005;54:303-312.
73. Yuan W, Su QJ, Liu T, et al. Evaluation of Coflex interspinous stabilization following decompression compared with decompression and posterior lumbar interbody fusion for the treatment of lumbar degenerative disease: A minimum 5-year follow-up study. J Clin Neurosci. 2017;35:24-29.
74. Zhao XW, Ma JX, Ma XL, et al. Interspinous process devices(IPD) alone versus decompression surgery for lumbar spinal stenosis(LSS): A systematic review and meta-analysis of randomized controlled trials. Int J Surg. 2017;39:57-64.
75. Zini C, Bellini M, Masala S, Marcia S. Percutaneous interspinous spacer in spinal-canal-stenosis treatment: Pros and cons. Medicina (Kaunas). 2019;55(7):381.
76. Zucherman JF, Hsu KY, Hartjen CA, et al. A multicenter, prospective, randomized trial evaluating the X STOP interspinous process decompression system for the treatment of neurogenic intermittent claudication: Two-year follow-up results. Spine. 2005;30(12):1351-1358.

Piriformis Muscle Resection

1. Kouvalchouk JF, Bonnet JM, de Mondenard JP. Pyramidal syndrome. Apropos of 4 cases treated by surgery and review of the literature. Rev Chir Orthop Reparatrice Appar Mot. 1996;82(7):647-657.
2. Papadopoulos EC, Khan SN. Piriformis syndrome and low back pain: A new classification and review of the literature. Orthop Clin North Am. 2004;35(1):65-71.
3. Solheim LF, Siewers P, Paus B. The piriformis muscle syndrome. Sciatic nerve entrapment treated with section of the piriformis muscle. Acta Orthop Scand. 1981;52(1):73-75.

Endoscopic Laser Foraminoplasty

1. Hafez MI, Zhou S, Coombs RR, McCarthy ID. The effect of irrigation on peak temperatures in nerve root, dura, and intervertebral disc during laser-assisted foraminoplasty. Lasers Surg Med. 2001;29(1):33-37.
2. Knight MT, Ellison DR, Goswami A, Hillier VF. Review of safety in endoscopic laser foraminoplasty for the management of back pain. J Clin Laser Med Surg. 2001;19(3):147-157.
3. National Horizon Scanning Centre (NHSC). Endoscopic laser foraminoplasty for low back pain - horizon scanning review. New and Emerging Technology Briefing. Birmingham, UK: NHSC; 2001.
4. National Institute for Clinical Excellence (NICE). Endoscopic laser foraminoplasty. Interventional Procedure Guidance 31. London, UK: NICE; 2003.
5. Takeno K, Kobayashi S, Yonezawa T, et al. Salvage operation for persistent low back pain and sciatica induced by percutaneous laser disc decompression performed at outside institution: Correlation of magnetic resonance imaging and intraoperative and pathological findings. Photomed Laser Surg. 2006;24(3):414-423.

Xclose Tissue Repair System

1. Anulx Technologies, Inc. Xclose Tissue Repair System [website]. Minnetonka, MN: Anulx Technologies, 2008. Available at:

http://www.anulex.com/. April 30, 2008.

Barricaid Annular Closure Device

1. Cho PG, Shin DA, Park SH, Ji GY. Efficacy of a novel annular closure device after lumbar discectomy in Korean patients: A 24-month follow-up of a randomized controlled trial. J Korean Neurosurg Soc. 2019;62(6):691-699.
2. Kienzler JC, Klassen PD, Miller LE, et al. Three-year results from a randomized trial of lumbar discectomy with annulus fibrosus occlusion in patients at high risk for reherniation. Acta Neurochirurgica. 2019;161:1389-1396.
3. Kienzler JC, Rey S, Wetzel O, et al. Incidence and clinical impact of vertebral endplate changes after limited lumbar microdiscectomy and implantation of a bone-anchored annular closure device. BMC Surg. 2021;21(1):19.
4. Miller LE, Allen RT, Duhon B, Radcliff KE. Expert review with meta-analysis of randomized and nonrandomized controlled studies of Barricaid annular closure in patients at high risk for lumbar disc reherniation. Expert Review of Medical Devices 2020.
5. Nanda D, Arts MP, Miller LE, et al. Annular closure device lowers reoperation risk 4 years after lumbar discectomy. Med Devices. 2019;12:327-335.
6. Peredo AP, Gullbrand SE, Mauck RL, Smith HE. A challenging playing field: Identifying the endogenous impediments to annulus fibrosus repair. JOR Spine. 2021;4(1):e1133.
7. Semlitsch T, Geiger-Gritsch S. Annulus dibrosus repair after lumbar discectomy, Executive Summary. Decision Support Document 65/ Update 2019. Vienna, Austria: Ludwig Boltzmann Institut, Health Technology Assessment; 2019.
8. Thome C, Kursumovic A, Klassen PD, et al; Annular Closure RCT Study Group. Effectiveness of an annular closure device to prevent recurrent lumbar disc herniation: A secondary analysis with 5 years of follow-up. JAMA Netw Open. 2021;4(12):e2136809.
9. Wang Y, He X, Chen S, et al. Annulus fibrosus repair for lumbar disc herniation: A meta-analysis of clinical outcomes from controlled studies. Global Spine J. 2023 Apr 17 [Online ahead of print].

Radiofrequency Denervation for Sacroiliac Joint Pain

1. American Society of Anesthesiologists Task Force on Chronic Pain Management, American Society of Regional Anesthesia and Pain Medicine. Practice guidelines for chronic pain management: An updated report by the American Society of Anesthesiologists Task Force on Chronic Pain Management and the American Society of Regional Anesthesia and Pain Medicine. Anesthesiology. 2010;112(4):810-833.
2. Cheng J, Pope JE, Dalton JE, et al. Comparative outcomes of cooled versus traditional radiofrequency ablation of the lateral branches for sacroiliac joint pain. Clin J Pain. 2013;29(2):132-137.
3. Cohen SP, Hurley RW, Buckenmaier CC 3rd, et al. Randomized placebo-controlled study evaluating lateral branch radiofrequency denervation for sacroiliac joint pain. Anesthesiology. 2008;109(2):279-288.
4. Cohen SP, Strassels SA, Kurihara C, et al. Outcome predictors for sacroiliac joint (lateral branch) radiofrequency denervation. Reg Anesth Pain Med. 2009;34(3):206-214.
5. Hansen HC, McKenzie-Brown AM, Cohen SP, et al. Sacroiliac joint interventions: A systematic review. Pain Physician. 2007;10(1):165-184.
6. Ho K-Y, Hadi MA, Pasutharnchat K, Tan KH. Cooled radiofrequency denervation for treatment of sacroiliac joint pain: Two-year results from 20 cases. J Pain Res. 2013;6:505-511.
7. Kapural L, Nageeb F, Kapural M, et l. Cooled radiofrequency system for the treatment of chronic pain from sacroiliitis: The first case-series. Pain Pract. 2008;8(5):348-354.
8. Kapural L, Rauck RL. First specifically designed comparative outcome study? Re: Cheng et al, Clin J Pain 2012. Clin J Pain. 2014;30(1):92.
9. Karaman H, Kavak GO, Tufek A, et al. Cooled radiofrequency application for treatment of sacroiliac joint pain. Acta Neurochir (Wien). 2011;153(7):1461-1468.
10. Patel N. Twelve-month follow-up of a randomized trial assessing cooled radiofrequency denervation as a treatment for sacroiliac region pain. Pain Pract. 2016;16(2):154-167.
11. Patel N, Cohen SP. Response to: Cheng et al. Comparative outcomes of cooled versus traditional radiofrequency ablation of

the lateral branches for sacroiliac joint pain. Clin J Pain 2013;29:132-137. Clin J Pain. 2013;29(12):1097-1098.
12. Patel N, Gross A, Brown L, Gekht G. A randomized, placebo-controlled study to assess the efficacy of lateral branch neurotomy for chronic sacroiliac joint pain. Pain Med. 2012;13(3):383-98.
13. Stelzer W, Aiglesberger M, Stelzer D, Stelzer V. Use of cooled radiofrequency lateral branch neurotomy for the treatment of sacroiliac joint-mediated low back pain: A large case series. Pain Med. 2013;14(1):29-35.

Facet Joint Implantation

1. Carragee EJ, Hurwitz EL, Cheng I, et al. Treatment of neck pain: Injections and surgical interventions: Results of the Bone and Joint Decade 2000-2010 Task Force on neck pain and its associated disorders. J Manipulative Physiol Ther. 2009;32(2 Suppl):S176-S193.
2. Hegmann KT, ed. Low back disorders. In: Glass LS, et al., eds. Occupational medicine practice guidelines: Evaluation and management of common health problems and functional recovery in workers. 2nd Ed. Elk Grove Village, IL: American College of Occupational and Environmental Medicine (ACOEM); 2007.
3. North American Spine Society (NASS). Diagnosis and treatment of degenerative lumbar spinal stenosis. Burr Ridge, IL: North American Spine Society (NASS); January, 2007.
4. Work Loss Data Institute. Low back - lumbar & thoracic (acute & chronic). Corpus Christi, TX: Work Loss Data Institute; 2008.

Lateral Interbody Fusion

1. Bahtia NN, Timon S, Wieser ES, Wang JC. TLIF, XLIF or ALIF for adjacent segment degenerative disc disease. NASS SpineLine, May/June 2008.
2. Baker R. Re: Lateral interbody fusion (XLIF, DLIF) of the lumbar spine [letter]. Burr Ridge, IL: North American Spine Society (NASS); January 5, 2010.

3. Bergey DL, Villavicencio AT, Goldstein T, Regan JJ. Endoscopic lateral transpsoas approach to the lumbar spine. Spine. 2004;29:1681-1688.
4. Eck JC, Hodges S, Humphreys SC. Minimally invasive lumbar spinal fusion. J Am Acad Orthop Surg. 2007;15(6):321-329.
5. Karikari IO, Isaacs RE. Minimally invasive transforaminal lumbar interbody fusion: A review of techniques and outcomes. Spine (Phila Pa 1976). 2010;35(26 Suppl):S294-S301.
6. Knight RQ, Schwaegler P, Hanscom D, Roh J. Direct lateral lumbar interbody fusion for degenerative conditions: Early complication profile. J Spinal Disord Tech. 2009;22(1):34-37.
7. Mitchell W. Coding XLIF. Coding Q&A. SpineLine. July/August 2006:27.
8. National Institute for Health and Clinical Excellence (NICE). Lateral (including extreme, extra and direct lateral) interbody fusion in the lumbar spine. Interventional Procedure Guidance 321. London, UK: NICE; 2009.
9. Ozgur BM, Aryan HE, Pimenta L, Taylor WR. Extreme Lateral Interbody Fusion (XLIF): A novel surgical technique for anterior lumbar interbody fusion. Spine J. 2006;6(4):435-443.
10. Rodgers WB. Complications in 575 XLIF surgeries. Abstract Accepted for Podium Presention at the 16th International Meeting on Advanced Spine Techniques (IMAST), Vienna, Austria, July 15-18, 2009.
11. Shunwu F, Xing Z, Fengdong Z, Xiangqian F. Minimally invasive transforaminal lumbar interbody fusion for the treatment of degenerative lumbar diseases. Spine (Phila Pa 1976). 2010;35(17):1615-1620.
12. Smith W, Malone K. Complications in Extreme Lateral Interbody Fusion: One surgeon's experience with 566 patients and 1550 levels. Abstract P124. Proceedings of the NASS 24th Annual Meeting. Spine J. 2009;9:178S-179S.
13. Youssef JA, McAfee PC, Patty CA, et al. Minimally invasive surgery: Lateral approach interbody fusion: Results and review. Spine (Phila Pa 1976). 2010;35(26 Suppl):S302-S311.

Minimally Invasive/Endoscopic Cervical Laminoforaminotomy

1. Choi G, Lee SH, Bhanot A, et al. Modified transcorporeal anterior cervical microforaminotomy for cervical radiculopathy: A technical note and early results. Eur Spine J. 2007;16(9):1387-1393.
2. Epstein NE. Minimally invasive/endoscopic vs "open" posterior cervical laminoforaminotomy: Do the risks outweigh the benefits? Surg Neurol. 2009;71(3):330-331.
3. Holly LT, Moftakhar P, Khoo LT, et al. Minimally invasive 2-level posterior cervical foraminotomy: Preliminary clinical results. J Spinal Disord Tech. 2007;20(1):20-24.

Minimally Invasive Lumbar Decompression Procedures (including MILD)

1. Aldahshory AR, Mashaly H, El Molla ST, et al. Comparative study of minimally invasive lumbar decompression versus decompressive laminectomy with posterolateral transpedicular fixation for the treatment of degenerative Lumbar canal stenosis. Asian J Neurosurg. 2020;15(2):293-301.
2. Basu S. Mild procedure: Single-site experience prospective IRB study. Clin J Pain. 2012;28(3):254-258.
3. Benyamin RM, Staats PS. MiDAS ENCORE: Randomized controlled study design and protocol. Pain Physician. 2015;18(4):307-316.
4. Benyamin RM, Staats PS, for the MiDAS ENCORE investigators. MILD® is an effective treatment for lumbar spinal stenosis with neurogenic claudication: MiDAS ENCORE randomized controlled trial. Pain Physician. 2016;19(4):229-242.
5. Brown LL. A double-blind, randomized, prospective study of epidural steroid injection vs. the mild procedure in patients with symptomatic lumbar spinal stenosis. Pain Pract. 2012;12(5):333-341.
6. Centers for Medicare & Medicaid Services (CMS). Decision Memo for Percutaneous Image-guided Lumbar Decompression for Lumbar Spinal Stenosis (CAG-00433N). Baltimore, MD: CMS; January 9, 2014.
7. Chen H, Kelling J. Mild procedure for lumbar decompression: A review. Pain Pract. 2013;13(2):146-153.

8. Chopko B, Caraway DL. MiDAS I (mild Decompression Alternative to Open Surgery): A preliminary report of a prospective, multi-center clinical study. Pain Physician. 2010;13(4):369-378.
9. Chopko BW. A novel method for treatment of lumbar spinal stenosis in high-risk surgical candidates: Pilot study experience with percutaneous remodeling of ligamentum flavum and lamina. J Neurosurg Spine. 2011;14(1):46-50.
10. Chopko BW. Long-term results of percutaneous lumbar decompression for LSS: Two-year outcomes. Clin J Pain. 2013;29(11):939-43.
11. Connor C. Board and surgeon are close to truce. St. Petersburg Times, November 21, 2002.
12. Connor C. Pasco surgeon Bonati facing a 63-count state complaint. A doctor reviewing the records calls Alfred Bonati's practice 'a systematic abuse of patients.' St. Petersburg Times, December 6, 2001.
13. Deer T, Kim CK, Bowman RG 2nd, et al. Study of percutaneous lumbar decompression and treatment algorithm for patients suffering from neurogenic claudication. Pain Physician. 2012 15(6):451-460.
14. Deer T, Kim CK, Wahezi SE, et al. Objective real-world outcomes of patients suffering from painful neurogenic claudication treated with the mild® procedure: Interim 6-month report of a randomized controlled trial. J Pain Res. 2021;14:1687-1697.
15. Deer TR, Costandi SJ, Washabaugh E, et al. The MOTION Study: A randomized controlled trial with objective real-world outcomes for lumbar spinal stenosis patients treated with the mild® Procedure: One-year results. Pain Med. 2022;23(4):625-634.
16. Deer TR, Grider JS, Pope JE, et al. The MIST guidelines: The lumbar spinal stenosis consensus group guidelines for minimally invasive spine treatment. Pain Pract. 2019;19(3):250-274.
17. Deer TR, Kapural L. New image-guided ultra-minimally invasive lumbar decompression method: The mild procedure. Pain Physician. 2010;13(1):35-41.
18. Deer TR, Mekhail N, Lopez G, Amirdelfan K. Minimally invasive lumbar decompression for spinal stenosis. J Neurosurg Rev. 2011;1(S1):29-32.
19. Durkin B, Romeiser J, Shroyer AL, et al. Report from a quality assurance program on patients undergoing the MILD procedure.

Pain Med. 2013;14(5):650-656.

20. Fornari M, Robertson SC, Pereira P, et al. Conservative treatment and percutaneous pain relief techniques in patients with lumbar spinal stenosis: WFNS Spine Committee Recommendations. World Neurosurg X. 2020;7:100079.
21. Hagedorn JM, Yadav A, D'Souza RS, et al. The incidence of lumbar spine surgery following minimally invasive lumbar decompression and Superion indirect decompression system for treatment of lumbar spinal stenosis: A retrospective review. Pain Pract. 2022;22(5):516-521.
22. Haufe SM, Mork AR, Kunis CC. Surgical considerations of entire lumbar spine hardware removal via a minimally invasive approach. J Surg Orthop Adv. 2008;17(2):82-84.
23. Haufe SM, Mork AR. Complications associated with cervical endoscopic discectomy with the holmium laser. J Clin Laser Med Surg. 2004;22(1):57-58.
24. Haufe SM, Mork AR. Effects of unilateral endoscopic facetectomy on spinal stability. J Spinal Disord Tech. 2007;20(2):146-148.
25. Haufe SM, Mork AR. Intradiscal injection of hematopoietic stem cells in an attempt to rejuvenate the intervertebral discs. Stem Cells Dev. 2006;15(1):136-137.
26. Haufe SM, Mork AR.Sacroiliac joint debridement: A novel technique for the treatment of sacroiliac joint pain. Photomed Laser Surg. 2005;23(6):596-598.
27. Jain S, Deer T, Sayed D, et al. Minimally invasive lumbar decompression: A review of indications, techniques, efficacy and safety. Pain Manag. 2020;10(5):331-348.
28. Lawrence MM, Hayek SM. Minimally invasive lumbar decompression: A treatment for lumbar spinal stenosis. Curr Opin Anaesthesiol. 2013;26(5):573-579.
29. Levin K. Lumbar spinal stenosis: Treatment and prognosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed January 2021.
30. Levy RM, Deer TR. Systematic safety review and meta-analysis of procedural experience using percutaneous access to treat symptomatic lumbar spinal stenosis. Pain Med. 2012;13(12):1554-1561. 10.1111/j.1526-4637.2012.01504.x. Epub 2012 Nov 8. PMID: 23136978.

31. Lingreen R, Grider JS. Retrospective review of patient self-reported improvement and post-procedure findings for mild® (minimally invasive lumbar decompression). Pain Physician. 2010;13(6):555-560.
32. Mekhail N, Costandi S, Abraham B, Samuel SW. Functional and patient-reported outcomes in symptomatic lumbar spinal stenosis following percutaneous decompression. Pain Pract. 2012;12(6):417-425.
33. Mekhail NA, Costandi SJ, Armanyous S, et al. The impact of age on the outcomes of minimally invasive lumbar decompression for lumbar spinal stenosis. Med Devices (Auckl). 2020;13:151-161.
34. Mekhail B, Costandi S, Nageeb G, et al. The durability of minimally invasive lumbar decompression procedure in patients with symptomatic lumbar spinal stenosis: Long-term follow-up. Pain Pract. 2021; 21(8): 826-835.
35. Mekhail N, Vallejo R, Coleman MH, Benyamin RM. Long-term results of percutaneous lumbar decompression mild(®) for spinal stenosis. Pain Pract. 2012;12(3):184-193.
36. Merkow J, Varhabhatla N, Manchikanti L, et al. Minimally invasive lumbar decompression and interspinous process device for the management of symptomatic lumbar spinal stenosis: A literature review. Curr Pain Headache Rep. 2020;24(4):13.
37. National Institute for Health and Clinical Excellence (NICE). Percutaneous endoscopic laser lumbar diskectomy. Interventional Procedures Consultation. London, UK: NICE; December 2008.
38. Pope JE, Deer TR, Falowski SM, et al. A retrospective, single-center, quantitative analysis of adverse events in patients undergoing spinal stenosis with neurogenic claudication using a novel percutaneous direct lumbar decompression strategy. J Pain Res. 2021;14:1909-1913.
39. Pryzbylkowski P, Bux A, Chandwani K, et al. Minimally invasive direct decompression for lumbar spinal stenosis: Impact of multiple prior epidural steroid injections. Pain Manag. 2022;12(2):149-158.
40. Ricciardi L, Stifano V, Sturiale CL, et al. Minimally invasive decompression with posterior elements preservation versus laminectomy and fusion For lumbar degenerative spondylolisthesis: A systematic review and meta-analysis of

surgical, clinical and radiological outcomes. Surg Technol Int. 2020;36:457-463.

41. Schomer DF, Solsberg D, Wong W, Chopko BW. mild(®) lumbar decompression for the treatment of lumbar spinal stenosis. Neuroradiol J. 2011;24(4):620-626.
42. Staats PS, Benyamin RM, for the MiDAS ENCORE investigators. MiDAS ENCORE: Randomized controlled clinical trial report of 6-month results. Pain Physician. 2016;19(2):25-38.
43. Staats PS, Chafin TB, Golovac S, et al, MiDAS ENCORE Investigators. Long-term safety and efficacy of minimally invasive lumbar decompression procedure for the treatment of lumbar spinal stenosis with neurogenic claudication: 2-year results of MiDAS ENCORE. Reg Anesth Pain Med. 2018;43(7):789-794.
44. The Bonati Institute initiates ODI outcome study. Medical News Today, March 13, 2008.
45. Udeh BL, Costandi S, Dalton JE, et al. The 2-year cost-effectiveness of 3 options to treat lumbar spinal stenosis patients. Pain Pract. 2015;15(2):107-116.
46. U.S. Department of Health and Human Services (DHHS), Centers for Medicare & Medicaid Services (CMS). Decision memo for percutaneous image-guided lumbar decompression for lumbar spinal stenosis (CAG-00433N). Baltimore, MD: CMS; January 9, 2014.
47. Wang JJ, Bowden K, Pang G, Cipta A. Decrease in health care resource utilization with mild. Pain Medicine. 2013;14(5):657-661.
48. Wong WH. Mild interlaminar decompression for the treatment of lumbar spinal stenosis: Procedure description and case series with 1-year follow-up. Clin J Pain. 2102;28(6):534-538.
49. Zaina F, Tomkins-Lane C, Carragee E, Negrini S. Surgical versus non-surgical treatment for lumbar spinal stenosis. Cochrane Database Syst Rev. 2016;(1):CD010264.

Minimally Invasive Transforaminal Lumbar Interbody Fusion (MITLIF)

1. Deutsch H, Musacchio MJ Jr. Minimally invasive transforaminal lumbar interbody fusion with unilateral pedicle screw fixation. Neurosurg Focus. 2006;20(3):E10.

2. Isaacs RE, Podichetty VK, Santiago P, et al. Minimally invasive microendoscopy-assisted transforaminal lumbar interbody fusion with instrumentation. J Neurosurg Spine. 2005;3(2):98-105.
3. Park P, Foley KT. Minimally invasive transforaminal lumbar interbody fusion with reduction of spondylolisthesis: Technique and outcomes after a minimum of 2 years' follow-up. Neurosurg Focus. 2008;25(2):E16.
4. Scheufler KM, Dohmen H, Vougioukas VI. Percutaneous transforaminal lumbar interbody fusion for the treatment of degenerative lumbar instability. Neurosurgery. 2007;60(4 Suppl 2):203-212; discussion 212-213.
5. Villavicencio AT, Burneikiene S, Bulsara KR, Thramann JJ. Perioperative complications in transforaminal lumbar interbody fusion versus anterior-posterior reconstruction for lumbar disc degeneration and instability. J Spinal Disord Tech. 2006;19(2):92-97.

TruFuse Facet Fusion

1. American Association of Neurological Surgeons (AANS). Technical assessment of Tru-Fuse. Education and Meetings. Rolling Meadows, IL: AANS; 2010. Available at: http://www.aans.org. Accessed December 29, 2010.
2. miniSurg Corp. TruFuse facet fusion [website]. Clearwater, FL: miniSurg Corp; 2010. Available at: http://www.minsurg.com/index.aspx. Accessed December 29, 2010.
3. Williams AL, Gornet MF, Burkus JK. CT evaluation of lumbar interbody fusion: Current concepts. AJNR Am J Neuroradiol. 2005;26(8):2057-2066.

Nu-Fix

1. American Association of Neurological Surgeons (AANS). Technical Assessment of Nu-Fix. Education and Meetings. Rolling Meadows, IL: AANS; December 2009. Available at: http://www.aans.org. Accessed January 24, 2011.
2. NuFix, Inc. NuFix Precision Machined Allograft Antimigration Dowel. Advancing Fusion Through Medical Innovation [website].

Birmingham, AL: NuFix; 2010. Available at: http://nufix.org/. Accessed January 24, 2011.

Epidural Fat Graft during Lumbar Decompression Laminectomy/Discectomy

1. Gorgulu A, Simşek O, Cobanoglu S, et al. The effect of epidural free fat graft on the outcome of lumbar disc surgery. Neurosurg Rev. 2004;27(3):181-184.
2. Imran Y, Halim Y. Acute cauda equina syndrome secondary to free fat graft following spinal decompression. Singapore Med J. 2005;46(1):25-27.
3. MacKay MA, Fischgrund JS, Herkowitz HN, et al. The effect of interposition membrane on the outcome of lumbar laminectomy and discectomy. Spine (Phila Pa 1976). 1995;20(16):1793-1796.
4. Martin-Ferrer S. Failure of autologous fat grafts to prevent postoperative epidural fibrosis in surgery of the lumbar spine. Neurosurgery. 1989;24(5):718-721.
5. Urvoy P, Perlinski S, Berger M, et al. Cauda equina syndrome due to early postoperative migration of an adipose tissue flap following laminectomy. Acta Orthop Belg. 1990;56(2):513-516.

Interlaminar Lumbar Instrumented Fusion (ILIF)

1. Sharma AK, Kepler CK, Girardi FP, et al. Lateral lumbar interbody fusion: Clinical and radiographic outcomes at 1 year: A preliminary report. J Spinal Disord Tech. 2011;24(4):242-250.

Khan Kinetic Treatment (KKT)

1. Desmoulin GT, Yasin NI, Chen DW. Spinal mechanisms of pain control. Clin J Pain. 2007;23(7):576-585.
2. Desmoulin GT, Reno CR, Hunter CJ. Free axial vibrations at 0 to 200 Hz positively affect extracellular matrix messenger ribonucleic acid expression in bovine nucleus pulposi. Spine (Phila Pa 1976). 2010;35(15):1437-1444.

The OptiMesh Grafting System

1. Chi JH, Nunley PD, Huang KT, et al. Two-year outcomes from a prospective multicenter investigation device trial of a novel conformal mesh interbody fusion device. Int J Spine Surg. 2021;15(6):1103-1114.
2. Driver J, Huang KT, Krag M, et al. One-year outcomes from a prospective multicenter investigation device trial of a novel conformal mesh interbody fusion device. Spine (Phila Pa 1976). 2021;46(2):E126-E132.
3. Inamasu J, Guiot BH, Uribe JS. Flexion-distraction injury of the L1 vertebra treated with short-segment posterior fixation and Optimesh. J Clin Neurosci. 2008;15(2):214-218.
4. Lee JS, Yoon KB, Kim IK, Yoon DM. Pulsed radiofrequency treatment of pain relieving point in a soft tissue. Korean J Pain. 2011;24(1):57-60.
5. Tamimi MA, McCeney MH, Krutsch J. A case series of pulsed radiofrequency treatment of myofascial trigger points and scar neuromas. Pain Med. 2009;10(6):1140-1143.
6. Zheng X, Chaudhari R, Wu C, et al. Biomechanical evaluation of an expandable meshed bag augmented with pedicle or facet screws for percutaneous lumbar interbody fusion. Spine J. 2010;10(11):987-993.

Coccygectomy

1. Fletcher RH. Coccydynia (coccygodynia). UpToDate [online serial]. Waltham, MA: UpToDate; reviewed November 2012.
2. Patel R, Appannagari A, Whang PG. Coccydynia. Curr Rev Musculoskelet Med. 2008;1(3-4):223-226.
3. Trollegaard AM, Aarby NS, Hellberg S. Coccygectomy: An effective treatment option for chronic coccydynia: Retrospective results in 41 consecutive patients. J Bone Joint Surg Br. 2010;92(2):242-245.
4. Work Loss Data Institute. Low back - lumbar & thoracic (acute & chronic). Encinitas, CA: Work Loss Data Institute; 2011.

Oxygen-Ozone Therapy (Injection)

1. Costa T, Linhares D, Ribeiro da Silva M, Neves N. Ozone therapy for low back pain. A systematic review. Acta Reumatol Port. 2018;43(3):172-181.
2. Elawamy A, Kamel EZ, Hassanien M, et al. Implication of two different doses of intradiscal ozone-oxygen injection upon the pain alleviation in patients with low back pain: A randomized, single-blind study. Pain Physician. 2018;21(1):E25-E31.
3. Kallewaard JW, Terheggen MA, Groen GJ, et al. 15. Discogenic low back pain. Pain Pract. 2010;10(6):560-579.
4. Magalhaes FN, Dotta L, Sasse A, et al. Ozone therapy as a treatment for low back pain secondary to herniated disc: A systematic review and meta-analysis of randomized controlled trials. Pain Physician. 2012;15(2):E115-E129.
5. Rahimzadeh P, Imani F, Ghahremani M, Faiz SHR. Comparison of percutaneous intradiscal ozone injection with laser disc decompression in discogenic low back pain. J Pain Res. 2018;11:1405-1410.
6. Work Loss Data Institute. Low back - lumbar & thoracic (acute & chronic). Encinitas, CA: Work Loss Data Institute; 2011.

Sacroiliac Joint Fusion

1. Ackerman SJ, Polly Jr. DW, Knight T, et al. Comparison of the costs of nonoperative care to minimally invasive surgery for sacroiliac joint disruption and degenerative sacroiliitis in a United States Medicare population: potential economic implications of a new minimally-invasive technology. ClinicoEconomics and Outcomes Research 2013;5:575-587.
2. Al-Khayer A, Hegarty J, Hahn D, Grevitt MP. Percutaneous sacroiliac joint arthrodesis: A novel technique. J Spinal Disord Tech. 2008;21(5):359-363.
3. Araghi A, Woodruff R, Colle K, et al. Pain and opioid use outcomes following minimally invasive sacroiliac joint fusion with decortication and bone grafting: The Evolusion Clinical Trial. Open Orthop J. 2017;11:1440-1448.
4. Bornemann R, Roessler PP, Strauss A, et al. 2-year clinical results of patients with sacroiliac joint syndrome treated by arthrodesis

using a triangular implant system. Technol Health Care. 2017;25(2):319-325.

5. Buchowski JM, Kebaish KM, Sinkov V, et al. Functional and radiographic outcome of sacroiliac arthrodesis for the disorders of the sacroiliac joint. Spine J. 2005;5(5):520-528; discussion 529.
6. Capobianco R, Cher D; SIFI Study Group.. Safety and effectiveness of minimally invasive sacroiliac joint fusion in women with persistent post-partum posterior pelvic girdle pain: 12-month outcomes from a prospective, multi-center trial. Springerplus. 2015;4:570.
7. Centre for Reviews and Dissemination (CRD). Diagnostic validity of criteria for sacroiliac joint pain: A systematic review. Database of Abstracts of Reviews of Effectiveness (DARE). York, UK: Centre for Reviews and Dissemination, University of York; 2014.
8. Cher DJ, Polly DW. Improvement in health state utility after sacroiliac joint fusion: Comparison to normal populations. Global Spine J. 2016;6(2):100-107.
9. Chou R, Loeser JD, Owens DK, et al.; American Pain Society Low Back Pain Guideline Panel. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: An evidence-based clinical practice guideline from the American Pain Society. Spine. 2009;34(10):1066-1077.
10. Cross WW, Delbridge A, Hales D, Fielding LC. Minimally invasive sacroiliac joint fusion: 2-year radiographic and clinical outcomes with a principles-based SIJ fusion system. Sacroiliac Joint Fusion. Open Orthop J. 2018;12:7-16.
11. Cummings J Jr, Capobianco RA. Minimally invasive sacroiliac joint fusion: One-year outcomes in 18 patients. Ann Surg Innov Res. 2013;7(1):12.
12. Darr E, Meyer SC, Whang PG, et al. Long-term prospective outcomes after minimally invasive trans-iliac sacroiliac joint fusion using triangular titanium implants. Med Devices (Auckl). 2018;11:113-121.
13. Dengler J, Duhon B, Whang P, et al.; INSITE, iMIA, SIFI study groups. Predictors of outcome in conservative and minimally invasive surgical management of pain originating from the sacroiliac joint: A pooled analysis. Spine (Phila Pa 1976). 2017;42(21):1664-1673.

14. Dengler JD, Kools D, Pflugmacher R, et al. 1-year results of a randomized controlled trial of conservative management vs. minimally invasive surgical treatment for sacroiliac joint pain. Pain Physician. 2017;20(6):537-550.
15. Dengler J, Kools D, Pflugmacher R, et al. Randomized trial of sacroiliac joint arthrodesis compared with conservative management for chronic low back pain attributed to the sacroiliac joint. J Bone Joint Surg Am. 2019;101(5):400-411.
16. Duhon BS, Bitan F, Lockstadt H, et al; SIFI Study Group. Triangular titanium implants for minimally invasive sacroiliac joint fusion: 2-year follow-up from a prospective multicenter trial. Int J Spine Surg. 2016;10:13.
17. Duhon BS, Cher DJ, Wine KD, et al. Safety and 6-month effectiveness of minimally invasive sacroiliac joint fusion: A prospective study. Med Devices (Auckl). 2013;6:219-229.
18. Duhon BS, Cher DJ, Wine KD, et al; SIFI Study Group. Triangular titanium implants for minimally invasive sacroiliac joint fusion: A prospective study. Global Spine J. 2016;6(3):257-269.
19. Endres S, Ludwig E. Outcome of distraction interference arthrodesis of the sacroiliac joint for sacroiliac arthritis. Indian J Orthop. 2013;47(5):437-442.
20. Hansen H, Manchikanti L, Simopoulos TT, et al. A systematic evaluation of the therapeutic effectiveness of sacroiliac joint interventions. Pain Physician. 2012;15(3):E247-E278.
21. Hegmann KT, ed. Low back disorders. Occupational medicine practice guidelines: Evaluation and management of common health problems and functional recovery in workers. 3rd ed. Elk Grove Village, IL: American College of Occupational and Environmental Medicine (ACOEM); 2011.
22. Heiney J, Capobianco R, Cher D. A systematic review of minimally invasive sacroiliac joint fusion utilizing a lateral transarticular technique. Int J Spine Surg. 2015;9:40.
23. Kancherla VK, McGowan SM, Audley BN, et al. Patient reported outcomes from sacroiliac joint fusion. Asian Spine J. 2017;11(1):120-126.
24. Khurana A, Guha AR, Mohanty K, Ahuja S. Percutaneous fusion of the sacroiliac joint with hollow modular anchorage screws: Clinical and radiological outcome. J Bone Joint Surg Br. 2009;91(5):627-631.

25. Kim JT, Rudolf LM, Glaser JA. Outcome of percutaneous sacroiliac joint fixation with porous plasma-coated triangular titanium implants: An independent review. Open Orthop J 2013;7:51-56.
26. Ledonio CG, Polly DW Jr, Swiontkowski MF. Minimally invasive versus open sacroiliac joint fusion: Are they similarly safe and effective? Clin Orthop Relat Res. 2014;472(6):1831-1838.
27. Miller LE, Reckling WC, Block JE. Analysis of postmarket complaints database for the iFuse SI Joint Fusion System®: A minimally invasive treatment for degenerative sacroiliitis and sacroiliac joint disruption. Med Devices (Auckl). 2013;6:77-84.
28. National Institute for Health and Clinical Excellence (NICE). Minimally invasive sacroiliac joint fusion surgery for chronic sacroiliac pain. Interventional Procedures Guidance 578. London, UK: NICE; April 5, 2017.
29. Polly DW, Cher DJ, Wine KD, et al; INSITE Study Group. Randomized controlled trial of minimally invasive sacroiliac joint fusion using triangular titanium implants vs non-surgical management for sacroiliac joint dysfunction: 12-month outcomes. Neurosurgery. 2015;77(5):674-691.
30. Polly DW, Swofford J, Whang PG, et al. Two-year outcomes from a randomized controlled trial of minimally invasive sacroiliac joint fusion vs. non-surgical management for sacrioilac joint dysfunction. Int J Spine Surg. 2016;10(28).
31. Rappoport LH, Luna IY, Joshua G. Minimally invasive sacroiliac joint fusion using a novel hydroxyapatite-coated screw: Preliminary 1-year clinical and radiographic results of a 2-year prospective study. World Neurosurg. 2017;101:493-497.
32. Rudolf L, Capobianco R. Five-year clinical and radiographic outcomes after minimally invasive sacroiliac joint fusion using triangular implants. Open Orthop J. 2014;8:375-383.
33. Rudolf L. MIS fusion of the SI joint: Does prior lumbar spinal fusion affect patient outcomes? Open Orthop J. 2013;7:163-168.
34. Rudolf L.Sacroiliac joint arthrodesis-MIS technique with titanium implants: Report of the first 50 patients and outcomes. Open Orthop J. 2012;6:495-502.
35. Sachs D, Capobianco R, Cher D, et al. One-year outcomes after minimally invasive sacroiliac joint fusion with a series of triangular implants: A multicenter, patient-level analysis. Med Devices (Auckl). 2014;7:299-304.

36. Sachs D, Capobianco R. Minimally invasive sacroiliac joint fusion: One-year outcomes in 40 patients. Adv Orthop. 2013;2013:536128.
37. Sachs D, Capobianco R. One year successful outcomes for novel sacroiliac joint arthrodesis system. Ann Surg Innov Res. 2012;6(1):13.
38. Sachs D, Kovalsky D, Redmond A, et al. Durable intermediate-to long-term outcomes after minimally invasive transiliac sacroiliac joint fusion using triangular titanium implants. Med Devices (Auckl). 2016;9:213-222.
39. Schroeder JE, Cunningham ME, Ross T, Boachie-Adjei O. Early results of sacro-iliac joint fixation following long fusion to the sacrum in adult spine deformity. HSS J. 2014;10(1):30-35.
40. Shaffrey CI, Smith JS. Stabilization of the sacroiliac joint. Neurosurg Focus. 2013;35(2 Suppl):Editorial.
41. Smith AG, Capobianco R, Cher D, et al. Open versus minimally invasive sacroiliac joint fusion: A multi-center comparison of perioperative measures and clinical outcomes. Ann Surg Innov Res. 2013;7(1):14.
42. Soriano-Baron H, Lindsey DP, Rodriguez-Martinez N, et al. The effect of implant placement on sacroiliac joint range of motion: Posterior vs trans-articular. Spine (Phila Pa 1976). 2015;40(9):E525-E530.
43. Spain K, Holt T. Surgical revision after sacroiliac joint fixation or fusion. Int J Spine Surg. 2017;11:5.
44. Sturesson B, Kools D, Pflugmacher R, et al. Six-month outcomes from a randomized controlled trial of minimally invasive SI joint fusion with triangular titanium implants vs conservative management. Eur Spine J. 2017;26(3):708-719.
45. Szadek KM, van der Wurff P, van Tulder MW, et al. Diagnostic validity of criteria for sacroiliac joint pain: A systematic review. J Pain. 2009;10(4):354-368.
46. van Tilburg CWJ, Groeneweg JG, Stronks DL, Huygen FJPM. Inter-rater reliability of diagnostic criteria for sacroiliac joint-, disc- and facet joint pain. J Back Musculoskelet Rehabil. 2017;30(3):551-557.
47. Vanaclocha V, Herrera JM, Saiz-Sapena N, et al. Minimally invasive sacroiliac joint fusion, radiofrequency denervation, and

conservative management for sacroiliac joint pain: 6-year comparative case series. Neurosurgery. 2018;82(1):48-55.
48. Washington State Health Care Authority, Sacroiliac joint fusion. Agency Medical Director Comments. Olympia, WA: Washington State Health Care Authority; January 18, 2019.
49. Whang P, Cher D, Polly D, et al.Sacroiliac joint fusion using triangular titanium implants vs. non-surgical management: Six-month outcomes from a prospective randomized controlled trial. Int J Spine Surg. 2015;9:6.
50. Wise CL, Dall BE. Minimally invasive sacroiliac arthrodesis: Outcomes of a new technique. J Spinal Disord Tech. 2008;21(8):579-584
51. Work Loss Data Institute. Hip & pelvis (acute & chronic). Encinitas, CA: Work Loss Data Institute; 2011.
52. Work Loss Data Institute. Low back – lumbar & thoracic (acute & chronic). Encinitas, CA: Work Loss Data Institute; December 4, 2013.
53. Work Loss Data Institute. Low back – lumbar & thoracic (acute & chronic). Encinitas, CA: Work Loss Data Institute; 2011.
54. Zaidi HA, Montoure AJ, Dickman CA. Surgical and clinical efficacy of sacroiliac joint fusion: A systematic review of the literature. J Neurosurg Spine. 2015;23(1):59-66.

Cryoablation for the Treatment of Lumbar Facet Joint Pain

1. Barlocher CB, Krauss JK, Seiler RW. Kryorhizotomy: an alternative technique for lumbar medial branch rhizotomy in lumbar facet syndrome. J Neurosurg. 2003;98(1 Suppl):14-20.
2. Birkenmaier C, Veihelmann A, Trouillier H, et al. Percutaneous cryodenervation of lumbar facet joints: A prospective clinical trial. Int Orthop. 2007;31(4):525-530.
3. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2013.
4. Staender M, Maerz U, Tonn JC, Steude U. Computerized tomography-guided kryorhizotomy in 76 patients with lumbar facet joint syndrome. J Neurosurg Spine. 2005;3(6):444-449.
5. Wolter T, Deininger M, Hubbe U, Mohadjer M, Knoeller S. Cryoneurolysis for zygapophyseal joint pain: a retrospective

analysis of 117 interventions. Acta neurochirurgica. 2011;153(5):1011-1019.

Minimally Invasive Thoracic Discectomy

1. Chou R. Subacute and chronic low back pain: Surgical treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2013.
2. Kasliwal MK, Deutsch H. Minimally invasive retropleural approach for central thoracic disc herniation. Minim Invasive Neurosurg. 2011;54(4):167-171.
3. Regev GJ, Salame K, Behrbalk E, et al. Minimally invasive transforaminal, thoracic microscopic discectomy: Technical report and preliminary results and complications. Spine J. 2012;12(7):570-576.
4. Smith JS, Eichholz KM, Shafizadeh S, et al. Minimally invasive thoracic microendoscopic diskectomy: Surgical technique and case series. World Neurosurg. 2013;80(3-4):421-427.
5. Work Loss Data Institute. Low back - lumbar & thoracic (acute & chronic). Encinitas, CA: Work Loss Data Institute; 2011.

Total Facet Arthroplasty System

1. Phillips FM, Tzermiadianos MN, Voronov LI, et al. Effect of the Total Facet Arthroplasty System after complete laminectomy-facetectomy on the biomechanics of implanted and adjacent segments. Spine J. 2009;9(1):96-102.
2. Sjovold SG, Zhu Q, Bowden A, et al. Biomechanical evaluation of the Total Facet Arthroplasty System® (TFAS®): Loading as compared to a rigid posterior instrumentation system. Eur Spine J. 2012;21(8):1660-1673.

Dynamic (Intervertebral) Stabilization / Bioflex

1. Li DW, Ma YZ, Hu M, et al. Application of Bioflex dynamic stabilization system in treating multi-segment lumbar degenerative disease. Zhongguo Gu Shang. 2011;24(4):286-289.
2. Li Z, Li F, Yu S, et al. Two-year follow-up results of the Isobar TTL Semi-Rigid Rod System for the treatment of lumbar degenerative

disease. J Clin Neurosci. 2013;20(3):394-399.
3. Zhang L, Shu X, Duan Y, et al. Effectiveness of ISOBAR TTL semi-rigid dynamic stabilization system in treatment of lumbar degenerative disease. Zhongguo Xiu Fu Chong Jian Wai Ke Za Zhi. 2012;26(9):1066-1070.

Least Invasive Lumbar Decompression, Interbody Fusion

1. Osman S. Least invasive lumbar decompression, interbody fusion, and pedicle screw implantation - A case study report. March 2012. Available at: https://www.isass.org/pdf/sas11/2-Wednesday/MIS-I/76.pdf.

The Deuk Laser Disc Repair

1. Deukmedjian AJ, Cianciabella A, Cutright J, Deukmedjian A. Cervical Deuk Laser Disc Repair(®): A novel, full-endoscopic surgical technique for the treatment of symptomatic cervical disc disease. Surg Neurol Int. 2012;3:142.
2. Deukmedjian AJ, Jason Cutright ST, Augusto Cianciabella PC, Deukmedjian A. Deuk Laser Disc Repair(®) is a safe and effective treatment for symptomatic cervical disc disease. Surg Neurol Int. 2013;4:68.

Microsurgical Lumbar Sequestrectomy for the Treatment of Lumbar Disc Herniation

1. Azarhomayoun A, Chou R, Shirdel S, et al. Sequestrectomy versus conventional microdiscectomy for the treatment of a lumbar disc herniation: A systematic review. Spine (Phila Pa 1976). 2015;40(24):E1330-E1339.
2. Huang T, Tian Z, Li M, et al. Sequestrectomy versus microdiscectomy in the treatment of lumbar disc herniation: A meta-analysis. Int J Clin Exp Med. 2015;8(5):7261-7269.
3. Ran J, Hu Y, Zheng Z, et al. Comparison of discectomy versus sequestrectomy in lumbar disc herniation: A meta-analysis of comparative studies. PLoS One. 2015;10(3):e0121816.

Intradiscal Steroid Injections

1. Nguyen C, Boutron I, Baron G, et al. Intradiscal glucocorticoid injection for patients with chronic low back pain associated with active discopathy: A randomized trial. Ann Intern Med 2017;166(8):547-556.

Cooled Radiofrequency Ablation for Facet Denervation

1. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed October 2017.
2. Davis T, Loudermilk E, DePalma M, et al. Twelve-month analgesia and rescue, by cooled radiofrequency ablation treatment of osteoarthritic knee pain: Results from a prospective, multicenter, randomized, cross-over trial. Reg Anesth Pain Med. 2019;44:499–506.
3. McCormick ZL, Choi H, Reddy R, et al. Randomized prospective trial of cooled versus traditional radiofrequency ablation of the medial branch nerves for the treatment of lumbar facet joint pain. Reg Anesth Pain Med. 2019;44(3):389-397.
4. McCormick ZL, Walker J, Marshall B, et al. A novel modality for facet joint denervation: Cooled radiofrequency ablation for lumbar facet syndrome. A case series. Phys Med Rehabil Int. 2014;1(5):5.
5. Walega D, Roussis C. Third-degree burn from cooled radiofrequency ablation of medial branch nerves for treatment of thoracic facet syndrome. Pain Pract. 2014;14(6):e154-e158.

Intradiscal Injection of Platelet-Rich Plasma

1. Akeda K, Ohishi K, Masuda K, et al. Intradiscal injection of autologous platelet-rich plasma releasate to treat discogenic low back pain: A preliminary clinical trial. Asian Spine J. 2017;11(3):380-389.

Ultrasound Guidance for Sacroiliac Joint Injections

1. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA:

UpToDate; reviewed September 2017.
2. Perry JM, Colberg RE, Dault SL, et al. A cadaveric study assessing the accuracy of ultrasound-guided sacroiliac joint injections. PM R. 2016;8(12):1168-1172.
3. Soneji N, Bhatia A, Seib R, et al. Comparison of fluoroscopy and ultrasound guidance for sacroiliac joint injection in patients with chronic low back pain. Pain Pract. 2016;16(5):537-544.

Posterior Facet Cages

1. McCormack BM, Eyster E, Chiu J, Siemionow K. Minimally disruptive posterior cervical fusion with DTRAX Cervical Cage for single level radiculopathy - Results in 10 Patients at 1-Year. Spine Res. 2016;2(1):1-5.
2. Voronov LI, Siemionow KB, Havey RM, et al. Bilateral posterior cervical cages provide biomechanical stability: Assessment of stand-alone and supplemental fixation for anterior cervical discectomy and fusion. Med Devices (Auckl). 2016;9:223-230.

Expandable Cages

1. Alimi M, Shin B, Macielak M, et al. Expandable polyaryl-ether-ether-ketone spacers for interbody distraction in the lumbar spine. Global Spine J. 2015;5:169-178.
2. Hawasli AH, Khalifeh JM, Chatrath A, et al. Minimally invasive transforaminal lumbar interbody fusion with expandable versus static interbody devices: radiographic assessment of sagittal segmental and pelvic parameters. Neurosurg Focus. 2017;43:E10.
3. Kim CW, Doerr TM, Luna IY, et al. Minimally invasive transforaminal lumbar interbody fusion using expandable technology: A clinical and radiographic analysis of 50 patients. World Neurosurg. 2016;90:228-235.
4. Massie LW, Zakaria HM, Schultz LR, et al. Assessment of radiographic and clinical outcomes of an articulating expandable interbody cage in minimally invasive transforaminal lumbar interbody fusion for spondylolisthesis. Neurosurg Focus. 2018;44:E8.

Coflex

1. Chou R. Subacute and chronic low back pain: Surgical treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed October 2018.
2. Dong Y, Zheng X, Gu H, et al. Is the interspinous device (Coflex) outdated in the treatment of lumbar spinal stenosis? A seven-year follow-up. Spine Res. 2018;4(1):2.
3. Kleck CJ, Burger EL. Development of bilateral facet cysts causing recurrent symptoms after decompression and the placement of an intralaminar implant: A case report. JBJS Case Connect. 2018;8(1):e11.
4. Levin K. Lumbar spinal stenosis: Treatment and prognosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed October 2018.
5. Nomura H. A novel strategy of non-fusion instrumentation with coflex interlaminar stabilization after decompression for lumbar spinal stenosis. J Spine Surg. 2016;2(2):149-153.
6. Pan AX, Hai Y, Yang JC, et al. Radiographic study of Coflex interspinous device for lumbar spinal stenosis. Zhonghua Wai Ke Za Zhi. 2016;54(7):513-517.
7. Schmidt S, Franke J, Rauschmann M, et al. Prospective, randomized, multicenter study with 2-year follow-up to compare the performance of decompression with and without interlaminar stabilization. J Neurosurg Spine. 2018;28(4):406-415.
8. Zhang JX, Jing XW, Cui P, et al. Effectiveness of dynamic fixation Coflex treatment for degenerative lumbar spinal stenosis. Exp Ther Med. 2018;15(1):667-672.

Cementoplasty

1. Cazzato RL, Palussière J, Buy X, et al. Percutaneous long bone cementoplasty for palliation of malignant lesions of the limbs: A systematic review. Cardiovasc Intervent Radiol. 2015;38(6):1563-1572.
2. Guarnieri G, Masala S, Muto M. Update of vertebral cementoplasty in porotic patients. Interv Neuroradiol. 2015;21(3):372-380.

3. Iannessi A, Amoretti N, Marcy PY, Sedat J. Percutaneous cementoplasty for the treatment of extraspinal painful bone lesion, a prospective study. Diagn Interv Imaging. 2012;93(11):859-870.
4. Kim YI, Kang HG, Kim TS, et al. Palliative percutaneous stabilization of lower extremity for bone metastasis using flexible nails and bone cement. Surg Oncol. 2014;23(4):192-198.
5. Muto M, Guarnieri G, Giurazza F, Manfre L. What's new in vertebral cementoplasty? Br J Radiol. 2016;89(1059):20150337.
6. National Institute for Health and Care Excellence. Percutaneous cementoplasty for palliative treatment of bony malignancies. Interventional procedures guidance [IPG179]. Published date: June 2006.
7. Rollinghoff M, Hagel A, Siewe J, et al. Is height restoration possible with a comparatively smaller amount of cement in radiofrequency kyphoplasty using a monopedicle approach?. Z Orthop Unfall. 2013;151(2):156-162.
8. Scottish Intercollegiate Guidelines Network (SIGN). Control of pain in adults with cancer: A national clinical guideline. Edinburgh, Scotland; SIGN; November 2008.
9. Sun G, Jin P, Liu XW, et al. Cementoplasty for managing painful bone metastases outside the spine. Eur Radiol. 2014;24(3):731-737.

Intracept Procedure (Intra-Osseous Basivertebral Nerve Ablation) for the Treatment of Low Back Pain

1. Becker S, Hadjipavlou A, Heggeness MH. Ablation of the basivertebral nerve for treatment of back pain: A clinical study. Spine J. 2017;17(2):218-223.
2. Boody B, Sperry B, Harper K, et al. The relationship between patient demographic and clinical characteristics and successful treatment outcomes following basivertebral nerve radiofrequency ablation: A pooled cohort study of three prospective clinical trials. Pain Med. 2022;23(Suppl 2):S2-S13.
3. Chou R. Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2022.

4. Conger A, Burnham TR, Clark T, et al. The effectiveness of intraosseous basivertebral nerve radiofrequency ablation for the treatment of vertebrogenic low back pain: An updated systematic review with single-arm meta-analysis. Pain Med. 2022a;23(Supplement_2):S50-S62.
5. Conger A, Schuster NM, Cheng DS, et al. The effectiveness of intraosseous basivertebral nerve radiofrequency neurotomy for the treatment of chronic low back pain in patients with modic changes: A systematic review. Pain Med. 2021;22(5):1039-1054.
6. Conger A, Smuck M, Truumees E, et al. Vertebrogenic pain: A paradigm shift in diagnosis and treatment of axial low back pain. Pain Med. 2022b;23(Suppl 2):S63-S71.
7. Fischgrund JS, Rhyne A, Franke J, et al. Intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: A prospective randomized double-blind sham-controlled multi-center study. Eur Spine J. 2018;27(5):1146-1156.
8. Fischgrund JS, Rhyne A, Franke J, et al. Intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 2-year results from a prospective randomized double-blind sham-controlled multicenter study. Int J Spine Surg. 2019;13(2):110-119.
9. Fischgrund JS, Rhyne A, Macadaeg K, et al. Long-term outcomes following intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 5-year treatment arm results from a prospective randomized double-blind sham-controlled multi-center study. Eur Spine J. 2020;29:1925-1934.
10. Huang J, Delijani K, Jones J, et al. Basivertebral nerve ablation. Semin Intervent Radiol. 2022;39(2):162-166.
11. Khalil J, Smuck M, Koreckij T, et al. A prospective, randomized, multi-center study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain. Spine J. 2019;19(10):1620-1632.
12. Kim JY, Kim HS, Wu PH, Jang I-T. Alleviating paravertebral muscle spasm after radiofrequency ablation treatment of hypersensitive basivertebral and sinuvertebral nerves for chronic discogenic back pain. Pain Physician. 2021;24(6):E883-E892.
13. Koreckija T, Kreinerb S, Khalilc JG, et al; INTRACEPT Trial Investigators. Prospective, randomized, multicenter study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 24-month treatment arm results. N Am

Spine Soc J. 2021;8:100089. https://www.sciencedirect.com/science/article/pii/S266654842100041X.

14. Lorio M, Clerk-Lamalice O, Beall DP, Julien T. International Society for the Advancement of Spine Surgery Guideline -- Intraosseous ablation of the basivertebral nerve for the relief of chronic low back pain. Int J Spine Surg. 2020;14(1):18-25.
15. Lorio M, Clerk-Lamalice O, Rivera M, Lewandrowski KU. ISASS Policy Statement 2022: Literature review of intraosseous basivertebral nerve ablation. Int J Spine Surg. 2022;16(6):1084-1094.
16. Markman JD, Rhyne AL, Sasso RC, et al. Association between opioid use and patient-reported outcomes in a randomized trial evaluating basivertebral nerve ablation for the relief of chronic low back pain. Neurosurgery. 2020;86(3):343-347.
17. McCormick Z, Conger A, Smuck M, et al. Magnetic resonance imaging characteristics associated with treatment success from basivertebral nerve ablation: aA aggregated cohort study of multicenter prospective clinical trials data. Pain Med. 2022b;23(Suppl 2):S34-S49.
18. McCormick Z, Sperry B, Boody B, et al. Pain location and exacerbating activities associated with treatment success following basivertebral nerve ablation: An aggregated cohort study of multicenter prospective clinical trial data. Pain Med. 2022a;23(Suppl 2):S14-S33.
19. Michalik A, Conger A, Smuck M, et al. Intraosseous basivertebral nerve radiofrequency ablation for the treatment of vertebral body endplate low back pain: Current evidence and future directions. Pain Med. 2021;22(Suppl 1):S24-S30.
20. Sayed D, Naidu RK, Patel KV, et al. Best practice guidelines on the diagnosis and treatment of vertebrogenic pain with basivertebral nerve ablation from the American Society of Pain and Neuroscience. J Pain Res. 2022;15:2801-2819.
21. Schnapp W, Martiatu K, Delcroix GJR, et al. Basivertebral nerve ablation for the treatment of chronic low back pain: A scoping review of the literature. Pain Physician. 2022;25(4):E551-E562.
22. Smuck M, Khalil J, Barrette K, et al. Prospective, randomized, multicenter study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain: 12-month results. Reg Anesth Pain Med. 2021;46(8):683-693.

23. Tieppo Francio V, Sherwood D, Twohey E, et al. Developments in minimally invasive surgical options for vertebral pain: Basivertebral nerve ablation - A narrative review. J Pain Res. 2021;14:1887-1907.
24. Truumees E, Macadaeg K, Pena E, et al. A prospective, open-label, single-arm, multi-center study of intraosseous basivertebral nerve ablation for the treatment of chronic low back pain. Eur Spine J. 2019;28(7):1594-1602.
25. Urits I, Noor N, Johal AS, et al. Basivertebral nerve ablation for the treatment of vertebrogenic pain. Pain Ther. 2021;10(1):39-53.

Intradiscal Injections of Notochordal Cell-Derived Matrix for the Treatment of Intervertebral Disc Disease

1. Bach FC, Tellegen AR, Beukers M, et al. Biologic canine and human intervertebral disc repair by notochordal cell-derived matrix: From bench towards bedside. Oncotarget. 2018;9(41):26507-26526.

Transforaminal Endoscopic Discectomy

1. Gadjradj PS, van Tulder MW, Dirven CM, et al. Clinical outcomes after percutaneous transforaminal endoscopic discectomy for lumbar disc herniation: A prospective case series. Neurosurg Focus. 2016;40(2):E3.
2. Gibson JN, Cowie JG, Iprenburg M. Transforaminal endoscopic spinal surgery: The future 'gold standard' for discectomy? - A review. Surgeon. 2012;10(5):290-296.
3. Gibson JNA, Subramanian AS, Scott CEH. A randomised controlled trial of transforaminal endoscopic discectomy vs microdiscectomy. Eur Spine J. 2017;26(3):847-856.
4. Hoogland T, van den Brekel-Dijkstra K, Schubert M, Miklitz B. Endoscopic transforaminal discectomy for recurrent lumbar disc herniation: A prospective, cohort evaluation of 262 consecutive cases. Spine (Phila Pa 1976). 2008;33(9):973-978.
5. Jasper G, Francisco GM, Telfeian AE. Transforaminal endoscopic discectomy with foraminoplasty for the treatment of spondylolisthesis. Pain Physician, 2014;17(6):E703-E708.

6. Jasper GP, Francisco GM, Telfeian AE. A retrospective evaluation of the clinical success of transforaminal endoscopic discectomy with foraminotomy in geriatric patients. Pain Physician. 2013;16(3):225-229.
7. Jasper GP, Francisco GM, Telfeian AE. Clinical success of transforaminal endoscopic discectomy with foraminotomy: A retrospective evaluation. Clin Neurol Neurosurg. 2013;115(10):1961-1965.
8. Jasper GP, Francisoc GM, Choi DB, et al. Clinical benefits of ultra-minimally invasive spine surgery in awake obese patients in an outpatient setting: A retrospective evaluation of transforaminal endoscopic discectomy with foraminotomy. JSM Neurosurg Spine. 2014;2(5):1041.
9. Kamson S, Trescot A, Sampson P, Zhang Y. Full-endoscopic assisted lumbar decompressive surgery performed in an outpatient, ambulatory facility: Report of 5 years of complications and risk factors. Pain Physician 2017;20(2):E221-E231.
10. Kim HS, Paudel B, Jang JS, et al. Percutaneous full endoscopic bilateral lumbar decompression of spinal stenosis through uniportal-contralateral approach: Techniques and preliminary results. World Neurosurg. 2017;103:201-209.
11. Knight RQ, Scribani M, Krupa N, et al. Lumbar decompressive laminectomy or laminotomy for degenerative conditions: Outcome comparison of traditional open versus less invasive techniques. J Spine. 2013 S2:006. doi:10.4172/2165-7939.S2-006.
12. Pan Z, Ha Y, Yi S, Cao K. Efficacy of transforaminal endoscopic spine system (TESSYS) technique in treating lumbar disc herniation. Med Sci Monit. 2016;22:530-539.
13. Ren C, Li Y, Qin R, et al. Transforaminal endoscopic lumbar discectomy for lumbar disc herniation causing bilateral symptoms. World Neurosurg. 2017;106:413-421.
14. Ruetten S, Komp M, Merk H, Godolias G. Full-endoscopic interlaminar and transforaminal lumbar discectomy versus conventional microsurgical technique: A prospective, randomized, controlled study. Spine. 2008; 33(9):931-939.
15. Ruetten S, Komp M, Merk H, Godolias G. Surgical treatment for lumbar lateral recess stenosis with the full-endoscopic interlaminar approach versus conventional microsurgical

technique: A prospective, randomized, controlled study. J Neurosurg Spine. 2009;10(5):476-485.
16. Sanusi T, Davis J, Nicassio N, Malik I. Endoscopic lumbar discectomy under local anesthesia may be an alternative to microdiscectomy: A single centre's experience using thefar lateral approach. Clin Neurol Neurosurg. 2015;139:324-327.
17. Sclafani JA, Raiszadeh K, Laich D, et al. Outcome measures of an intracanal, endoscopic transforaminal decompression technique: Initial findings from the MIS prospective registry. Int J Spine Surg. 2015 Dec;9:69.

Lumbosacral Fusion for Bertolotti Syndrome

1. Holm EK, Bünger C, Foldager CB. Symptomatic lumbosacral transitional vertebra: A review of the current literature and clinical outcomes following steroid injection or surgical intervention. SICOT J. 2017;3:71.
2. Jancuska JM, Spivak JM, Bendo JA. A review of symptomatic lumbosacral transitional vertebrae: Bertolotti's syndrome. Int J Spine Surg. 2015;9:42.
3. Li Y, Lubelski D, Abdullah KG, et al. Minimally invasive tubular resection of the anomalous transverse process in patients with Bertolotti's syndrome: Presented at the 2013 Joint Spine Section Meeting: Clinical article. J Neurosurg Spine. 2014;20(3):283-290.
4. Santavirta S, Tallroth K, Ylinen P, Suoranta H. Surgical treatment of Bertolotti's syndrome. Follow-up of 16 patients. Arch Orthop Trauma Surg. 1993;112(2):82-87.

Discseel Procedure (Regenerative Spine Procedure)

1. Chou R. Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2019a.
2. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2019b.
3. Chou R. Subacute and chronic low back pain: Surgical treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2019c.

4. Kirchner F, Anitua E. Intradiscal and intra-articular facet infiltrations with plasma rich in growth factors reduce pain in patients with chronic low back pain. J Craniovertebr Junction Spine. 2016;7(4):250-256.

Intramuscular Steroid Injection for the Treatment of Neck Pain / Back Pain

1. Chou R. Subacute and chronic low back pain: Nonpharmacologic and pharmacologic treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed December 2021.
2. Friedman BW, Esses D, Solorzano C, et al. A randomized placebo-controlled trial of single-dose IM corticosteroid for radicular low back pain. Spine (Phila Pa 1976). 2008;33(18): E624-E629.
3. Knight CL, Deyo RA, Staiger TO, Wipf JE. Treatment of acute low back pain. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed December 2021.
4. Levin K, Hsu PS, Armon C. Acute lumbosacral radiculopathy: Treatment and prognosis. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed May 2021.
5. Nouged E, Dajani J, Ku B, et al. Local anesthetic injections for the short-term treatment of head and neck myofascial pain syndrome: A systematic review with meta-analysis. J Oral Facial Pain Headache. 2019;33(2):183–198.
6. Robinson J, Kothari MJ. Treatment and prognosis of cervical radiculopathy. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2019.
7. Treatment of neck pain. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2019.

Anterior Lumbar Interbody Fusion (ALIF)

1. Mobbs RJ, Phan K, Malham G, et al. Lumbar interbody fusion: Techniques, indications and comparison of interbody fusion options including PLIF, TLIF, MI-TLIF, OLIF/ATP, LLIF and ALIF. J Spine Surg. 2015;1(1):2-18.
2. Rao PJ, Loganathan A, Yeung V, Mobbs RJ. Outcomes of anterior lumbar interbody fusion surgery based on indication: A

prospective study. Neurosurgery. 2015;76(1):7-23; discussion 23-24.
3. Shah M, Kolb B, Yilmaz E, et al. Comparison of lumbar laminectomy alone, lumbar laminectomy and fusion, stand-alone anterior lumbar interbody fusion, and stand-alone lateral lumbar interbody fusion for treatment of lumbar spinal stenosis: A review of the literature. Cureus. 2019;11(9):e5691.
4. Vieli M, Staartjes VE, Eversdjik HAJ, et al. Safety and efficacy of anterior lumbar interbody fusion for discogenic chronic low back pain in a short-stay setting: Data from a prospective registry. Cureus. 2019;11(8):e5332.

DiscoGel (Intradiscal Alcohol Injection)

1. de Seze M, Saliba L, Mazaux J-M. Percutaneous treatment of sciatica caused by a herniated disc: An exploratory study on the use of gaseous discography and Discogel(®) in 79 patients. Ann Phys Rehabil Med. 2013;56(2):143-154.
2. Hashemi M, Dadkhah P, Taheri M, et al. Effectiveness of intradiscal injection of radiopaque gelified ethanol (DiscoGel ®) versus percutaneous laser disc decompression in patients with chronic radicular low back pain. Korean J Pain. 2020;33(1):66-72.
3. Kuhelj D, Dobrovolec A, Kocijancic IJ, et al. Efficacy and durability of radiopaque gelified ethanol in management of herniated discs. Radiol Oncol. 2019;53(2):187-193.
4. Papadopoulos D, Batistaki C, Kostopanagiotou G. Comparison of the efficacy between intradiscal gelified ethanol (Discogel) injection and intradiscal combination of pulsed radiofrequency and gelified ethanol (Discogel) injection for chronic discogenic low back pain treatment. A randomized double-blind clinical study. Pain Med. 2020;21(11):2713-2718.
5. Sayhan H, Beyaz SG, Ulgen AM, et al. Long-term clinical effects of DiscoGel for cervical disc herniation. Pain Physician. 2018;21(1):E71-E78.

SpineJack System

1. Arabmotlagh M, Nikoleiski SC, Schmidt S, et al. Radiological evaluation of kyphoplasty with an intravertebral expander after

osteoporotic vertebral fracture. J Orthop Res. 2019;37(2):457-465.

2. Baeesa S, Krueger A, Aragon FA, Noriega DC. The efficacy of a percutaneous expandable titanium device in anatomical reduction of vertebral compression fractures of the thoracolumbar spine. Saudi Med J. 2015;36(1):52-60.
3. Chang M, Zhang C, Shi J, et al. Comparison between 7 osteoporotic vertebral compression fractures treatments: Systematic review and network meta-analysis. World Neurosurg. 2021;145:462-470.
4. Chi J-E, Hsu J-Y, Chan RWY, et al. Kyphoplasty with an intravertebral reduction device for osteoporotic vertebral compression fractures with spinal canal encroachment. Formos J Surg. 2020;53(1):20-28.
5. Chiang CJ, Huang JW, Chen SM, et al. Kyphoplasty with intravertebral reduction devices associated with better height restoration and greater kyphosis correction than kyphoplasty with balloons. Sci Rep. 2021;11:5430.
6. Crespo-Sanjuan J, Ardura F, Hernandez-Ramajo R, Noriega DC, et al. Requirements for a stable long-term result in surgical reduction of vertebral fragility fractures. World Neurosurg. 2017;105:137-144.
7. Descamps J, Lamerain M, Chenguel Z, et al. Vertebral compression fractures treated in acute by instrumented kyphoplasty: Early and mid-term clinical and radiological results. BioMed Res Int. 2019;2019:1386510.
8. England RW, Gong A, Li T, et al. Clinical outcomes and safety of the SpineJack vertebral augmentation system for the treatment of vertebral compression fractures in a United States patient population. J Clin Neurosci. 2021;89:237-242.
9. Hasanein M, Shater MS. SpineJack system for percutaneous stabilization of osteoporotic vertebral compression fractures: Clinical and radiological results. Egyptian Spine J. 2019;32(1):33-44.
10. Huang C-C, Tai S-H, Lai C-H, Lee E-J. Comparison of an intravertebral reduction device and percutaneous vertebroplasty for anatomical reduction with single-level vertebral compression fractures. Formosan Journal of Surgery. 2020;53(3):101-108.
11. Jacobson RE. The use of SpineJack intravertebral implant for the correction of recurrent vertebral fracture after kyphoplasty.

Cureus. 2020;12(4):e7599.

12. Kerschbaumer G, Gaulin B, Ruatti S,et al. Clinical and radiological outcomes in thoracolumbar fractures using the SpineJack device. A prospective study of seventy-four patients with a two point three year mean of follow-up. Int Orthop. 2019;43(12):2773-2779.
13. Lin J-H, Wang S-H, Lin E-Y, Chiang Y-H. Better height restoration, greater kyphosis correction, and fewer refractures of cemented vertebrae by using an intravertebral reduction device: A 1-year follow-up study. World Neurosurg. 2016;90:391-396.
14. Lofrese G, Ricciardi L, De Bonis P, et al. Use of the SpineJack direct reduction for treating type A2, A3 and A4 fractures of the thoracolumbar spine: A retrospective case series. J Neurointerv Surg. 2022;14(9):931-937.
15. Long Y, Yi W, Yang D. Advances in vertebral augmentation systems for osteoporotic vertebral compression fractures. Pain Res Manag. 2020;2020:3947368.
16. Meyblum L, Premat K, Elhorany M, et al. Safety of vertebral augmentation with cranio-caudal expansion implants in vertebral compression fractures with posterior wall protrusion. Euro Radiol. 2020;30(10):5641-5649.
17. Munoz Montoya JE, Torres C, Ferrer ER, Munoz Rodríguez EE. A Colombian experience involving SpineJack, a consecutive series of patients experiencing spinal fractures, percutaneous approach and anatomical restoration 2016-2017. J Spine Surg. 2018;4(3):624-629.
18. Noriega D, Kruger A, Ardura F, et al. Clinical outcome after the use of a new craniocaudal expandable implant for vertebral compression fracture treatment: One year results from a prospective multicentric study. BioMed Res Int. 2015a; 2015:927813.
19. Noriega D, Maestretti G, Renaud C, et al. Clinical performance and safety of 108 SpineJack implantations: 1-year results of a prospective multicentre single-arm registry study. BioMed Res Int. 2015b;2015:173872.
20. Noriega DC, Crespo-Sanjuan J, Olan WJ, et al. Treatment of thoracolumbar type A3 fractures using a percutaneous intravertebral expandable titanium implant: Long-term follow-up results of a pilot single center study. Pain Physician. 2021;24(5):E631-E638.

21. Noriega DC, Ramajo RH, Lite IS, et al. Safety and clinical performance of kyphoplasty and SpineJack® procedures in the treatment of osteoporotic vertebral compression fractures: A pilot, monocentric, investigator-initiated study. Osteoporos Int. 2016;27(6):2047-2055.
22. Noriega DC, Rodríguez-Monsalve F, Ramajo R, et al. Long-term safety and clinical performance of kyphoplasty and SpineJack procedures in the treatment of osteoporotic vertebral compression fractures: A pilot, monocentric, investigator-initiated study. Osteoporos Int. 2019;30(3):637-645.
23. Renaud C. Treatment of vertebral compression fractures with the cranio-caudal expandable implant SpineJack: Technical note and outcomes in 77 consecutive patients. Orthop Traumatol Surg Res. 2015;101(7):857-859.
24. Vanni D, Pantalone A, Bigossi F, et al. New perspective for third generation percutaneous vertebral augmentation procedures: Preliminary results at 12 months. J Craniovertebr Junction Spine. 2012;3(2):47-51.
25. Venier A, Roccatagliata L, Isalberti M, et al. Armed kyphoplasty: An indirect central canal decompression technique in burst fractures. Am J Neuroradiol. 2019;40(11):1965-1972.
26. Yeh K-L, Wu S-H, Liaw C-K, et al. Outcomes of different minimally invasive surgical treatments for vertebral compression fractures: An observational study. World J Clin Cases. 2021;9(31):9509-9519.

Tendon Sheath injections for the Treatment of Back Pain

1. Cho JH, Jung SH, Yang SM, Park H. Atypical calcific tendinitis involving the long biceps tendon: A rare cause of hemiplegic shoulder pain. J Back Musculoskelet Rehabil. 2019;32(2):355-359.
2. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed November 2020.

Magnetic Resonance Imaging-Guided Focused Ultrasound (MRgFUS) for the Treatment of Lumbar Facet Joint Pain

1. Tiegs-Heiden CA, Lehman VT, Gorny KR, et al. Improved treatment response following magnetic resonance imaging-

guided focused ultrasound for lumbar facet joint pain. Mayo Clin Proc Innov Qual Outcomes. 2019;4(1):109-113.

LinQ Sacroiliac Joint Stabilization System

1. Deer TR, Rupp A, Budwany R, et al. Pain relief salvage with a novel minimally invasive posterior sacroiliac joint fusion device in patients with previously implanted pain devices and therapies. J Pain Res. 2021;14:2709-2715.
2. Kaye AD, Edinoff AN, Scoon L, et al. Novel interventional techniques for chronic pain with minimally invasive arthrodesis of the sacroiliac joint: (INSITE, iFuse, Tricor, Rialto, and others). Rheumatol Ther. 2021;8(3):1061-1072.
3. Kim D, Sayed D, Lamb C, et al. Initial experience with a minimally invasive sacroiliac fusion device, a retrospective case series. Tampa, FL: PainTEQ; 2020. Available at: https://painteq.com/doctors/news/2020/07/initial-experience-with-a-minimally-invasive-sacroiliac-fusion-device-a-retrospective-case-series/. Accessed October 31, 2022.
4. Sayed D, Balter K, Pyles S, Lam CM. A multicenter retrospective analysis of the long-term efficacy and safety of a novel posterior sacroiliac fusion device. J Pain Res. 2021;14:3251-3258.

Smoking Cessation and Spinal/SI Joint Fusion Outcomes

1. Connor M, Briggs RG, Bonney PA, et al. Tobacco use is associated with increased 90-day readmission among patients undergoing surgery for degenerative spine disease. Global Spine J. 2022;12(5):787-794.
2. Debono B, Wainwright TW, Wang MY, et al. Consensus statement for perioperative care in lumbar spinal fusion: Enhanced Recovery After Surgery (ERAS®) Society recommendations. Spine J. 2021;21(5):729-752.
3. Dengler J, Duhon B, Whang P, et al. Predictors of outcome in conservative and minimally invasive surgical management of pain originating from the sacroiliac joint: A pooled analysis. Spine (Phila Pa 1976). 2017;42(21):1664-1673.
4. Gatot C, Liow MHL, Goh GS, et al. Smoking is associated with lower satisfaction in nondiabetic patients undergoing minimally

invasive single-level transforaminal lumbar interbody fusion. Clin Spine Surg. 2022;35(1):E19-E25.
5. Khalid SI, Thomson KB, Chilakapati S, et al. The impact of smoking cessation therapy on lumbar fusion outcomes. World Neurosurg. 2022;164:e119-e126.
6. Nunna RS, Ostrov PB, Ansari D, et al. The risk of nonunion in smokers revisited: A systematic review and meta-analysis. Global Spine J. 2022;12(3):526-539.
7. Pearson RG, Clement RGE, Edwards KL, Scammell BE. Do smokers have greater risk of delayed and non-union after fracture, osteotomy and arthrodesis? A systematic review with meta-analysis. BMJ Open. 2016;6(11):e010303.
8. Phan K, Fadhil M, Chang N, et al. Effect of smoking status on successful arthrodesis, clinical outcome, and complications after anterior lumbar interbody fusion (ALIF). World Neurosurg. 2018;110:e998-e1003.
9. Zhuang T, Ku S, Shapiro LM, et al. A cost-effectiveness analysis of smoking-cessation interventions prior to posterolateral lumbar fusion. J Bone Joint Surg Am. 2020;102(23):2032-2042.

Cooled Radiofrequency Denervation for Sacroiliac Joint Pain

1. Candan B, Gungor S. Cooled-radiofrequency neurotomy for the treatment of chronic lumbar facet (zygapophyseal) joint pain: A retrospective study. Medicine (Baltimore). 2021;100(52):e28459.
2. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2022.
3. Kawamoto LF, Sakata RK, Campos JL, et al. Retrospective study of the analgesic effect of sacroiliac joint radiofrequency denervation. Pain Physician. 2021;24(5):E625-E629.
4. McCormick Z, Choi H, Reddy R, et al. Randomized prospective trial of cooled versus traditional radiofrequency ablation of the medial branch nerves for the treatment of lumbar facet joint pain. Reg Anesth Pain Med. 2019;44(3):389-397.
5. Shih C-L, Shen P-C, Lu C-C, et al. A comparison of efficacy among different radiofrequency ablation techniques for the treatment of lumbar facet joint and sacroiliac joint pain: A systematic review and meta-analysis. Clin Neurol Neurosurg. 2020;195:105854.

Trigger Point Injections with Normal Saline

1. Cho S-C, Kwon D-R, Seong J-W, et al. A pilot analysis on the efficacy of multiple trigger-point saline injections in chronic tension-type headache: A retrospective observational study. J Clin Med. 2022;11(18):5428.
2. Chou R. Subacute and chronic low back pain: Nonsurgical interventional treatment. UpToDate [online serial]. Waltham, MA: UpToDate; reviewed September 2022.
3. Kongsagul S, Vitoonpong T, Kitisomprayoonkul W, Tantisiriwat N. Ultrasound-guided physiological saline injection for patients with myofascial pain. J Med Ultrasound. 2019;28(2):99-103.
4. Roldan CJ, Osuagwu U, Cardenas-Turanzas M, Huh BK. Normal saline trigger point injections vs conventional active drug mix for myofascial pain syndromes. Am J Emerg Med. 2020;38(2):311-316.