vertiflex®

Product Approval Documentation

February 2019

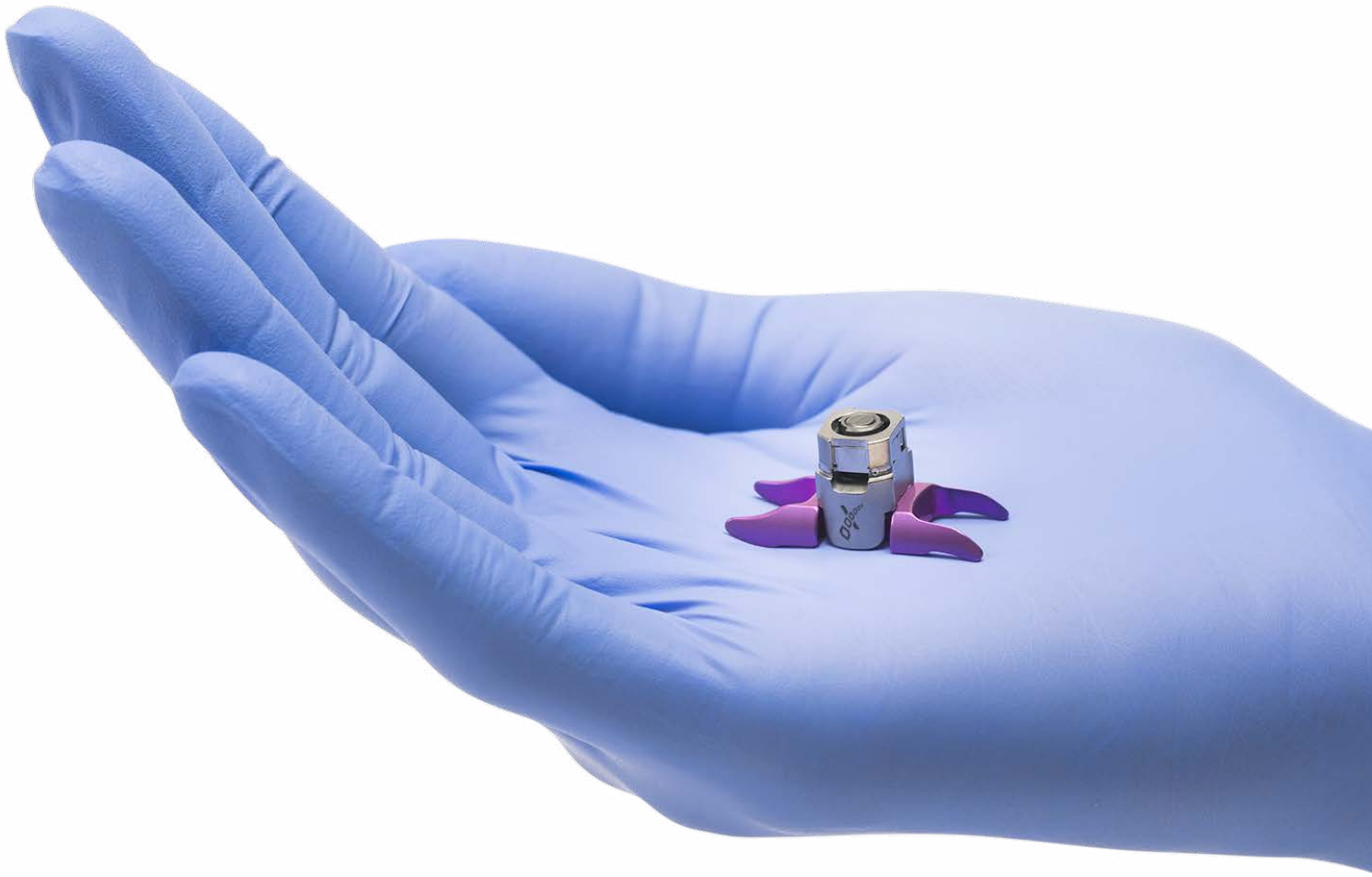


Table of Contents

Patient Education Guide

superion®
Indirect Decompression System

Life can cause spinal stenosis. Take yours back with Superion.®

Superion can help you take back your life with a simple new procedure.

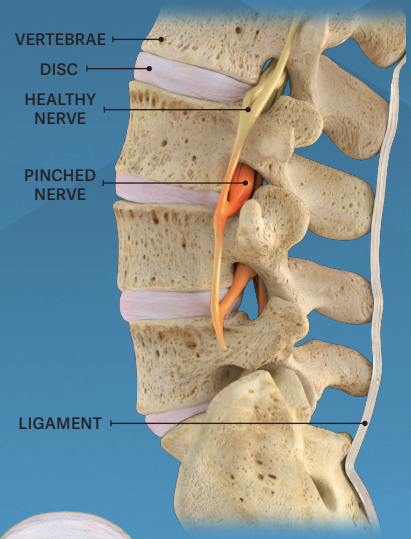
vertiflex®

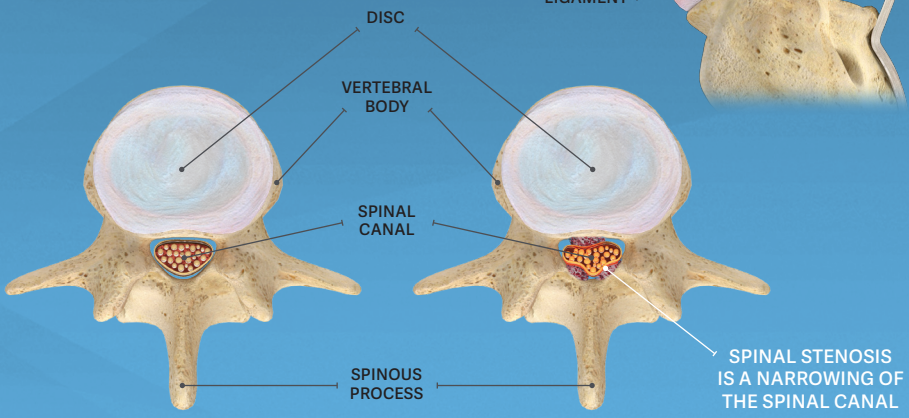
What is spinal stenosis?

Your spine is made up of a flexible column of 24 bones called vertebrae. Soft tissue "discs" are between each of the vertebrae. The vertebrae join together like links in a chain to support your head and body while the discs act as "shock absorbers."

Inside the spine, there is a channel called the spinal canal. It is surrounded by the vertebrae. This canal protects a cylinder of nerves called the spinal cord.

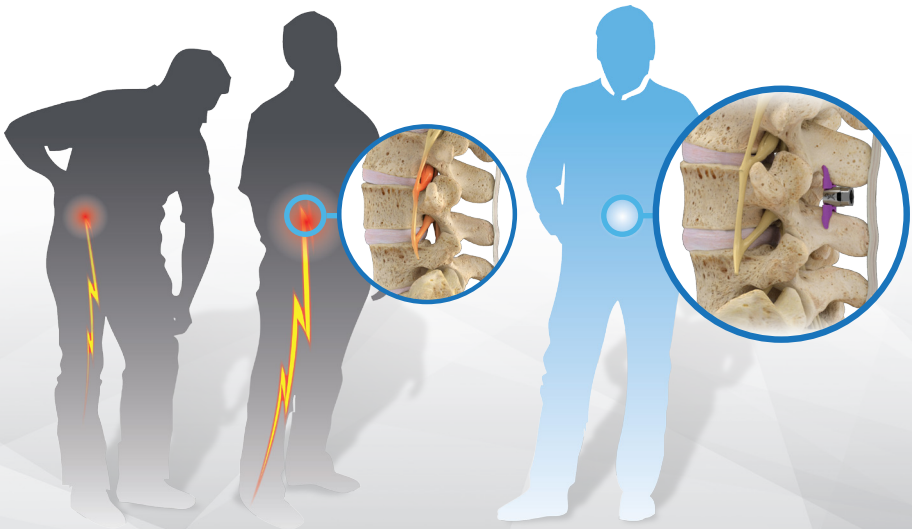
Spinal stenosis is the result of aging and "wear and tear" on the spine from everyday activities. These changes cause the spinal canal to narrow which can "pinch" the nerves in the lower back and may cause pain and or nerve damage. This is called lumbar spinal stenosis (LSS).





What are the symptoms?

- Decreased endurance during physical activities
- Weakness and/or loss of balance
- Symptoms improve when you sit, lean forward, lie on your back, or sit with your feet raised
- Numbness or a “tingling” feeling in your legs, calves, or buttocks
- Aching, dull back pain radiating (spreading) to your legs
- Neurogenic Claudication



A positive outcome for you.

The Superion system offers a safe and effective alternative to other more invasive surgical options, such as open surgical decompression. It is a minimally invasive procedural option. It has been thoroughly tested to ensure it can successfully treat leg pain symptoms associated with moderate spinal stenosis.

Among those patients in the clinical trial that were followed up through sixty months after surgery, almost all expressed overall satisfaction with the Superion implant.

Functional improvement & patient satisfaction at 60 months*

	24 Months	36 Months	48 Months	60 Months
Physical Function	73%	80%	80%	81%
Symptom Severity	77%	84%	84%	75%
Patient Satisfaction	**84%**	**92%**	**87%**	**90%**

*Responders

In the future, if your stenosis progresses from moderate to severe, your doctor may consider other procedures. The Superion procedure is reversible and will not remove the structure (bones or tissue) of the spine. All future treatment options will still be available.

Your doctor has recommended a simple procedure to insert a Superion implant. Your doctor has recommended this based on your total medical history. This may help relieve the leg pain you feel as a result of moderate lumbar spinal stenosis.

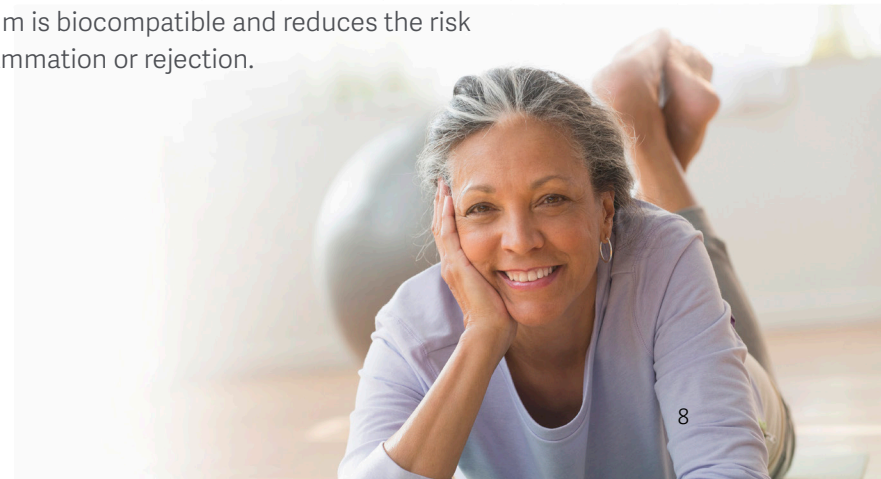
Superion is the appropriate first surgical option.

Superion was developed for patients with moderate spinal stenosis who have tried six months of conservative care treatment without finding relief from their pain. It is also for patients whose medical history shows that Superion may be their best treatment option because traditional spinal surgery could be too demanding.

People who will benefit the most from the Superion implant are those whose symptoms are relieved when bending forward, such as when pushing a shopping cart. Leaning forward causes the spinal canal to open, which relieves pressure on the nerves. The Superion implant produces the same effect—relieving pressure on the nerves—without leaning forward.

Superion shown at actual size.

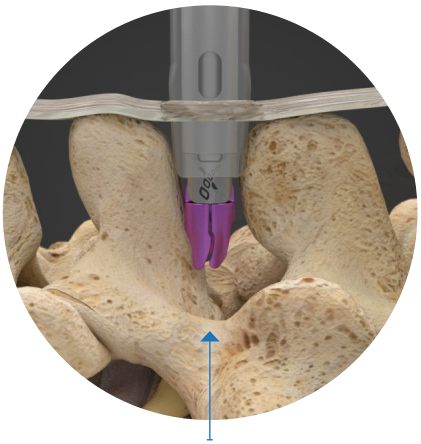
Superion is a small implant, available in different sizes to best match your spinal anatomy. It is made of titanium, a material used for medical implants because it is lightweight with great strength. Titanium is biocompatible and reduces the risk of inflammation or rejection.



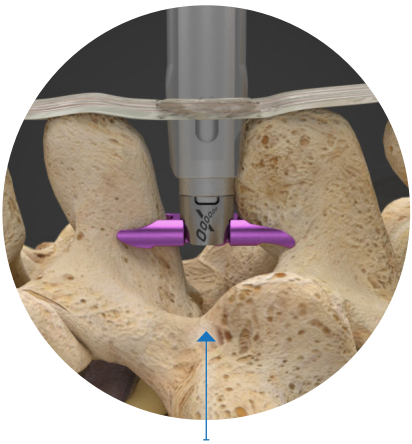
A simple, short procedure.

Placing the Superion typically takes about thirty minutes. It is implanted through a small incision in your lower back. The procedure can be performed in either the hospital operating room or an outpatient surgical center. The procedure involves no tissue or bone damage and minimal blood.

The Superion is designed to preserve your mobility while still providing the stability your spine requires.



Superion is placed between the vertebrae and holds them open. This relieves the pressure on the nerves in the spinal canal.



When the Superion is placed, the device arms are opened and surround the spinous process. This ensures that the Superion will not dislodge.

After the procedure, you may enjoy significant reduction in leg pain within the first few days. All post-operative care instructions should be prescribed by your physician. Your doctor will also talk to you about limiting your activity levels immediately after the procedure, and how to increase activities as you heal. Certain risks are associated with the use of the Superion. Consult your doctor for full information regarding these risks.

Post-Operative Care Guidelines and FAQs

How do I care for the surgical site post-operatively?

Most surgical site wounds will have a few stitches or staples that should be kept clean and dry until the first follow-up visit, usually scheduled in 7-14 days after having the procedure. Avoid scrubbing the surgical site for 72 hours. Do not take baths. Clean the site with soap and water and change the bandage daily and/or any time the bandage gets wet. Report any changes in the wound such as redness, bleeding or swelling to your physician.

Are there any restrictions to activity?

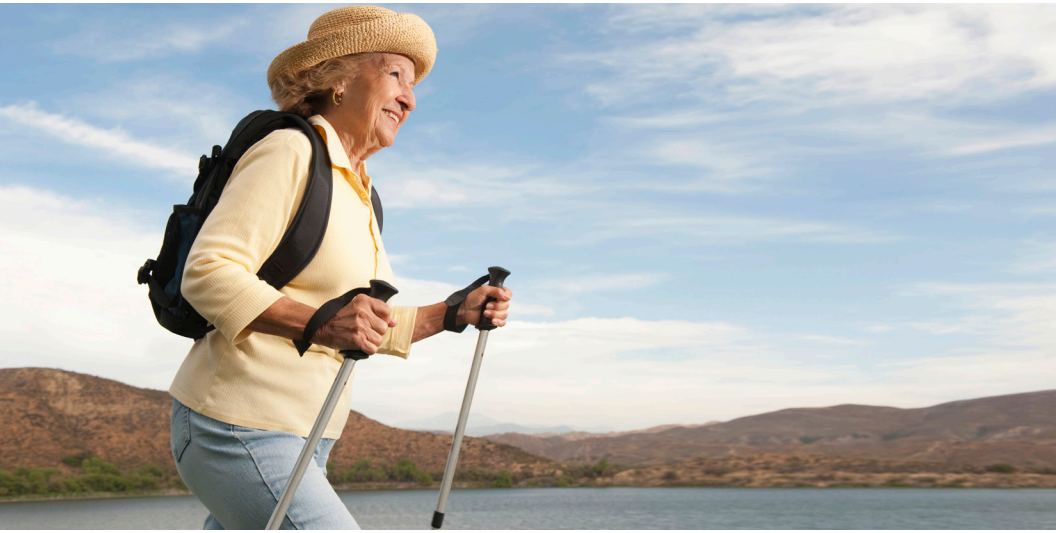
All patients have different needs therefore it is important to always follow the treating physician's instructions regarding recommended activity restrictions. For 6 weeks following your procedure, limit all lifting bending and strenuous activity including: lifting any weight over 10-15lbs. Any deep bending or twisting of the spine. Strenuous activities such as swimming, golf, tennis, racquetball, running, jogging or sexual activity.

superion®
Indirect Decompression System

Less pain, more movement!

If you have been living with leg pain from moderate LSS, you know the toll it can take on your day-to-day life. Today, there is a minimally invasive medical solution that may help: it is the Superion Indirect Decompression System.

Superion is a new medical treatment that may allow you to have a more active future. **Start enjoying your day-to-day life again.**



vertiflex®

Reimagining Lumbar Stenosis Treatments.

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Comprehensive Brochure

superion®
Indirect Decompression System

Proven. Preferred. Published.

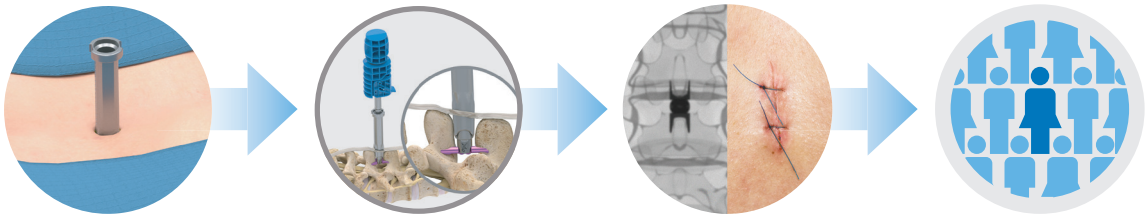
The new standard for lumbar stenosis.

vertiflex®

Same pain, new innovative solution.

Designed with patient safety and comfort in mind.

The Superion® Indirect Decompression System (IDS) is minimally disruptive to tissue and requires no resection of anatomical structures. The device is delivered through a small cannula about the size of a dime and deployed in a single step. The delivery of this device produces minimal blood loss and can be completed in an outpatient setting under monitored anesthesia care (MAC). The procedural kit is provided sterile to minimize infection risk for maximum patient safety. Through Superion®, patients are offered a new alternative in the fight against Lumbar Spinal Stenosis (LSS).



TISSUE SPARING MIDLINE APPROACH

SINGLE STEP IMPLANT DEPLOYMENT

OUTPATIENT FRIENDLY

PATIENT-FOCUSED OUTCOMES

Benefits of an ergonomic design.

The device was designed to be delivered in an undeployed position, to then be deployed and locked in situ in a single step. This streamlined approach allows for patients to benefit from a smaller incision, minimal blood loss, and a shorter recovery time than traditional decompression methods may offer. Superion® is made of titanium and is available in 5 sizes to best match your patients' spinal anatomy.

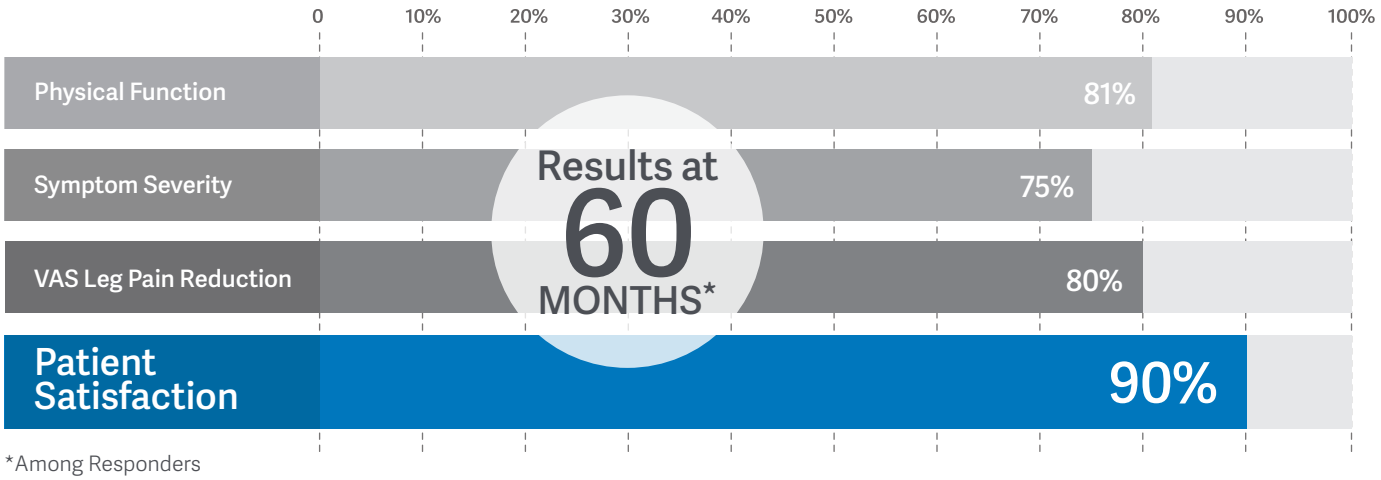
The results are clear.

The most extensive device clinical trial on lumbar spinal stenosis.

Our claim to clinically proven efficacy is backed by Level One Evidence generated by the most extensive device clinical trial on lumbar spinal stenosis: prospective, randomized, controlled, multicenter trial with 470 patients at 29 sites; plus, a 24-month follow-up and annually thereafter through 60 months.

Superion® is durable and effective.

Superion® has continued to deliver consistent and long-term relief. Among those patients in the clinical trial that were followed up through 60 months after surgery, almost all expressed overall satisfaction and significant reduction in clinical symptoms.



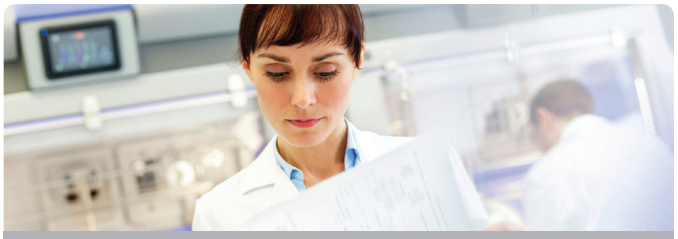
*Among Responders

CAT 1 CPT

Superion® received FDA approval for commercialization in 2015 and Category 1 CPT Code in 2017.

The Superion® IDS is covered by Medicare in all 50 states. The following CPT® codes should be used to report the insertion of Superion® at one or two contiguous levels.

CPT® Code	Description
22869	Insertion of interlaminar/interspinous process stabilization/distraction device without open decompression or fusion, including image guidance when performed, lumbar; single level
+22870	Second level (list separately in addition to code for primary procedure, 22869)



0% Early re-hospitalizations

0% Infections

0% Migrations/Dislodgements

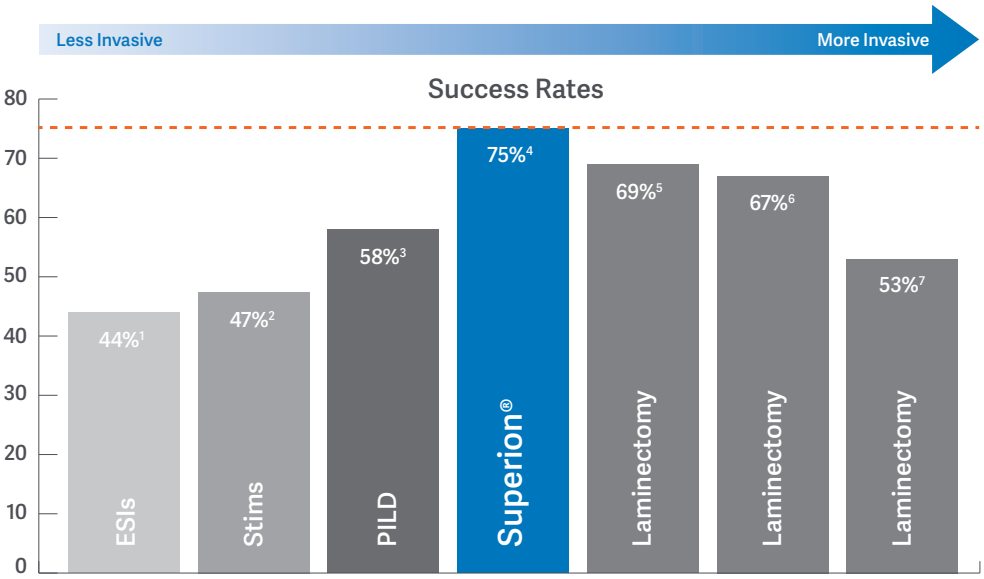
These results are representative of our clinical trial. We continue to track the safety of our device through commercialization.

Superion® sets a new standard.

Superion® was developed to provide patients with spinal stenosis a safe and durable alternative when conservative treatment has failed and laminectomy is too aggressive. When it comes to effectiveness, Superion® holds its own against the "gold standard" laminectomy and other treatments in the continuum of care.

Successful reduction in leg pain among treatment options.

Leg pain severity improvement with LSS Therapies



References

[1]Manchikanti; Leg Pain @ 2 yrs. (Pain Physician, 2012)

[2]North; Leg Pain @ 3 yrs. (Neurosurg, 2005)

[3]Benyamin; Leg Pain @ 1 yr. (Pain Physician, 2016)

[4]Superion® PMA P140004 (Leg Pain @ 5 yrs.)

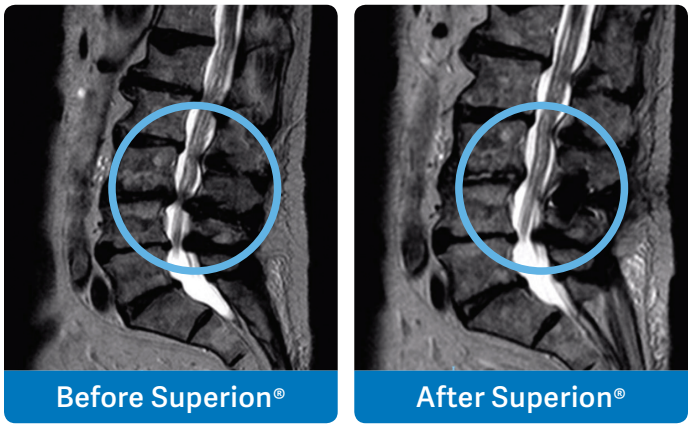
[5]Davis; Leg Pain @ 2 yrs. (Spine, 2013)

[6]Stromqvist; Leg Pain @ 2 yrs. (Spine, 2013)

[7]Malmivvaara; Leg Pain @ 2 yrs. (Spine, 2007)

The Superion® Effect.

Superion® limits extension, relieving pressure on the affected nerves.

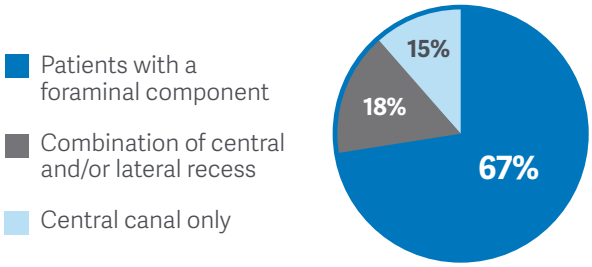


Sagittal MRI, Superion® at L3-4

Course of treatment was determined by the treating physician based on a combination of patient history, clinical presentation of symptoms, and comprehensive imaging.

Superion® is the complete solution for LSS.

In the clinical IDE trial, Superion® was found to be effective in treating all 3 types of stenosis—central, foraminal, and lateral recess.



67% of the entire trial population of 190 patients had some foraminal component, either by itself or in combination with central and/or lateral recess.

Filling the gap in the treatment continuum.

The Superion® IDS represents a new, minimally invasive approach to treating lumbar stenosis that fills a gap in the continuum between conservative care and invasive surgery. This device is FDA approved and was designed as a first/earlier line of defense against the effects of LSS pain. It is also for those patients whose medical history shows that traditional open decompression surgery could be too demanding.

Is Superion® right for your patient?

Appropriate patient selection is essential for a successful outcome. The following points represent key criteria when determining who may be a candidate for Superion®:

- Diagnosis of lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, MRI, and/or CT evidence of thickened ligamentum flavum, narrowed lateral recess, and/or central canal or foraminal narrowing
- Persistent pain, numbness, and/or cramping in the legs (neurogenic intermittent claudication)
- Moderately impaired physical function with relief in flexion from symptoms of leg/buttock/groin pain
- Subjects who have been symptomatic and undergoing conservative treatment for at least 6 months
- Operative treatment is indicated at no more than two levels

*For a comprehensive list of indications and contraindications refer to the Superion® Surgical Technique Manual (www.vertiflexspine.com)

About Vertiflex®

At Vertiflex®, we are relentlessly focused on providing the most advanced, least invasive treatments for lumbar stenosis.

We believe patients deserve an alternative to pain management solutions, and that they have a less invasive option when they are not ready or able to have traditional surgery. Vertiflex® fills this gap, allowing patients to take back their lives with new products and procedures that are simple, safe, and clinically proven to be effective.

We're a data-driven company.

In an effort to continue to collect data on the safety and efficacy of our product, we are currently participating in a commercial registry and a post-commercialization clinical trial.

PRESS Registry

Postmarket Registry for the Evaluation of the Superion® Spacer

Prospective, single arm, multi-center registry for an evaluation at 24 months' post treatment.

ASCEND Trial

Assessing Superion® Clinical Endpoints vs. Decompression

A 2- and 5-year comparative evaluation of clinical outcomes in the treatment of moderate lumbar spinal stenosis with the Superion® Indirect Decompression System vs. direct decompression surgery for FDA Actual Conditions of Use Study.

For more information, email **clinical@vertiflexspine.com**.

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U.S. Price List
Reimbursement Overview
MRI Compatability

SUPERION® INDIRECT DECOMPRESSION SYSETM

Superion® Indirect Decompression Implants

ITEM #	DESCRIPTION	UOM	LIST PRICE
100-9808	Indirect Decompression Implant, 8mm	EA	$12,495
100-9810	Indirect Decompression Implant, 10mm	EA	$12,495
100-9812	Indirect Decompression Implant, 12mm	EA	$12,495
100-9814	Indirect Decompression Implant, 14mm	EA	$12,495
100-9816	Indirect Decompression Implant, 16mm	EA	$12,495
101-9808	Indirect Decompression Implant, 8mm	EA	$12,495
101-9810	Indirect Decompression Implant, 10mm	EA	$12,495
101-9812	Indirect Decompression Implant, 12mm	EA	$12,495
101-9814	Indirect Decompression Implant, 14mm	EA	$12,495
101-9816	Indirect Decompression Implant, 16mm	EA	$12,495

Superion® Single Use Instruments

ITEM #	DESCRIPTION	UOM	LIST PRICE
102-9800	Superion SUI Kit	EA	$845.00
140-9800	Vertiflex Instrument Platform Kit	EA	$695.00

Superion® Reimbursement Overview

These Category 1 CPT® codes were developed by the American Medical Association to describe this procedure and are to be reported by physicians, ASCs, and hospital outpatient departments. The 2019 Medicare national average fee schedule payment rates for these codes by provider type are listed below.

2019 Coding and Medicare Reimbursement

CPT® Code(s)	**22869**: Insertion of interlaminar/interspinous process stabilization/distraction device without open decompression or fusion, including imaging guidance when performed, lumbar; single level **+22870**: second level (list separately in addition to code for primary procedure, 22869) **Medicare:** **C1821** Interspinous Process Distraction Device (implantable) For hospital outpatient reporting purposes only, to describe the Superion Indirect Decompression System. No separate payment available-payment is bundled into payment for procedure.
Physician Payment	**Medicare:** **22869** Work RVU: 7.03 PE RVU: 5.24 PLI RVU: 0.98 TOTAL: 13.25 **$476.99 One-level Superion procedure** **+22870** Work RVU: 2.34 PE RVU: 1.00 PLI RVU: 0.28 TOTAL: 3.62 **$230.32 additional level** **$607.31 Two-level Superion procedure** *2019 final Conversion Factor (CF): $36.04 **Non-Medicare:** Payment based on coverage guidelines and terms of contracts with commercial payers
ASC Payment	**Medicare:** $12,597 regardless if one level or two **Non-Medicare:** Payment based on coverage guidelines and terms of contracts with commercial payers
Hospital Outpatient Payment	**Medicare:** $15,402 regardless if one level or two **Non-Medicare:** Payment based on coverage guidelines and terms of contracts with commercial payers

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VF-LD-0095-H

Superion®

MRI COMPATIBILITY

Non-clinical testing has demonstrated that the VertiFlex Superion® Interspinous Spacer is MR Conditional. It can be scanned safely under the following conditions:

- Static magnetic field of 1.5-Tesla (1.5 T) or 3.0-Tesla (3.0 T).
- Spatial gradient field of up to:
  - 7,480 G/cm (74.80 T/m) for 1.5 T systems.
  - 3,740 G/cm (37.40 T/m) for 3.0 T systems.
- Maximum whole body averaged specific absorption rate (SAR) of:
  - 2.0 W/kg for 15 minutes of scanning in Normal Operating Mode at 1.5T.
  - 2.0 W/kg for 15 minutes of scanning in Normal Operating Mode at 3.0T.

1.5T RF heating

In non-clinical testing with body coil excitation, the VertiFlex Superion® Interspinous Spacer produced a temperature rise of less than 4.0 ºC at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg, as assessed by calorimetry for 15 minutes of scanning in a 1.5 T Siemens Espree (MRC30732) MR scanner with SYNGO MR B17 software.

3.0T RF heating

In non-clinical testing with body coil excitation, the VertiFlex Superion® Interspinous Spacer produced a temperature rise of less than 5.0 ºC at a maximum whole body averaged specific absorption rate (SAR) of 2.0 W/kg, as assessed by calorimetry for 15 minutes of scanning in a 3.0 T Siemens Trio (MRC20587) MR scanner with SYNGO MR A30 4VA30A software.

Caution: The RF heating behavior does not scale with static field strength. Devices that do not exhibit detectable heating at one field strength may exhibit high values of localized heating at another field strength.

MR Artifact

In testing with gradient-echo sequencing, the shape of the image artifact follows the approximate contour of the device and extends radially up to 2.6 cm from the implant.

Published Journal Articles

Spine

SPINE Volume 40, Number 5, pp 275-282

RANDOMIZED TRIAL

OPEN

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

Vikas V. Patel, MD,* Peter G. Whang, MD,† Thomas R. Haley, DO,‡ W. Daniel Bradley, MD,§ Pierce D. Nunley, MD,¶ Raphael P. Davis, MD,‖ Larry E. Miller, PhD,**†† Jon E. Block, PhD,†† and Fred H. Geisler, MD, PhD‡‡

Study Design. Prospective, multicenter, randomized, controlled, investigational device exemption noninferiority trial.

Objective. To determine 2-year outcomes in patients with intermittent neurogenic claudication secondary to moderate lumbar spinal stenosis (LSS) who were treated with the Superion interspinous process spacer.

Summary of Background Data. 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.

Methods. Patients presenting with intermittent neurogenic claudication secondary to moderate LSS who failed at least 6 months of nonsurgical management were randomly allocated to treatment with the Superion spacer or a control spacer (X-Stop) and followed for 2 years.

Results. A total of 391 randomized patients were implanted with Superion (n = 190) or control (n = 201) spacers at 29 sites in the United States 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 endpoint of this study was met, which demonstrated that the Superion spacer was noninferior 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 ≥20 mm) at 2 years. Back pain clinical success (improvement ≥20 mm) was 68%, with no differences between groups. Oswestry Disability Index clinical success (≥15% point improvement) was achieved in 65% of patients. The rates of complications and reoperations were similar between groups.

Conclusion. The Superion interspinous process spacer relieves symptoms of intermittent neurogenic claudication secondary to moderate LSS in the majority of patients through 2 years.

Key words: implant, indirect decompression, intermittent neurogenic claudication, interspinous process spacer, lumbar spinal stenosis, randomized controlled trial, Superion.

Level of Evidence: 2

Spine 2015;40:275–282

From the *University of Colorado Hospital, Denver, CO; †Department of Orthopaedic and Rehabilitation, Yale University School of Medicine, New Haven, CT; ‡Performance Spine and Sports Physicians, P.C., Pottstown, PA; §Texas Back Institute, Denton, TX; ¶Spine Institute of Louisiana, Shreveport, LA; ‖Stony Brook University, Stony Brook, NY; **Miller Scientific Consulting, Inc., Asheville, NC; ††The Jon Block Group, San Francisco, CA; and ‡‡McLaren Hospital, Petoskey, MI.

Acknowledgment date: October 10, 2014. Revision date: November 3, 2014. Acceptance date: December 3, 2014.

The device(s)/drug(s) that is/are the subject of this manuscript is/are being evaluated as part of an ongoing FDA-approved investigational protocol (IDE) or corresponding national protocol for [state the intended use on a separate page and attach].: Superion Interspinous Process Spacer for Intermittent Neurogenic Claudication Secondary to Moderate Lumbar Spinal Stenosis.

VertiFlex Inc. San Clemente, CA, funds were received in support of this work.

Relevant financial activities outside the submitted work: consultancy, grants pending, payment for lectures, royalties, payment for development of educational presentations, other, board membership, travel accommodations, stock.

Address correspondence and reprint requests to Larry E. Miller, PhD, Miller Scientific Consulting, Inc., 1854 Hendersonville Rd, # 231, Asheville, NC 28803; E-mail: larry@millerscientific.com

DOI: 10.1097/BRS.0000000000000735

Lumbar spinal stenosis (LSS) with intermittent neurogenic claudication represents a challenging therapeutic dilemma. Interspinous process spacers are a less-invasive alternative to surgical decompression in patients who have failed nonsurgical management. The mechanism of action is thought to be distraction of the spinous processes and/or limiting extension of the lumbar spine, which lessens the mechanically induced stenosis associated with lumbar extension, thus relieving claudicatory symptoms. In 2005, the X-Stop Interspinous Process Decompression System (Medtronic Inc., Minneapolis, MN) became the first Food and Drug Administration (FDA)-approved interspinous process spacer for treatment of neurogenic claudication secondary to LSS.[1] Since

then, no other interspinous process spacers have received FDA approval. The Superion InterSpinous Spacer (Vertiflex Inc., San Clemente, CA) was designed to be implanted between contiguous spinous processes *via* a less-invasive approach compared with the X-Stop spacer. The purpose of this randomized controlled trial was to compare 2-year outcomes in patients with intermittent neurogenic claudication secondary to moderate LSS who were treated with the Superion spacer or a control spacer (X-Stop).

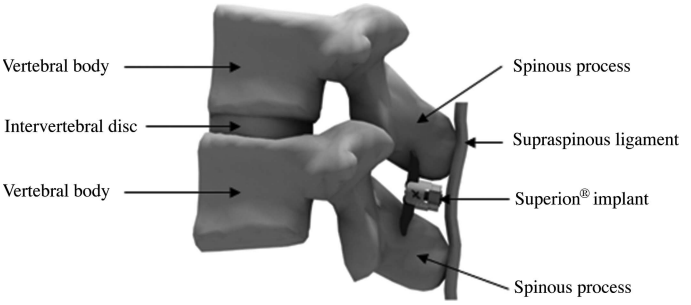

Figure 1. The Superion InterSpinous Spacer in spine model.

MATERIALS AND METHODS

Ethics

This was a prospective, multicenter, randomized, controlled investigational device exemption trial approved by the United States FDA. This study was approved by the institutional review board at each participating site and patients provided written informed consent before any study-related procedures were performed. The trial was prospectively registered at ClinicalTrials.gov (NCT00692276).

Patients

Patients presenting with neurogenic intermittent claudication symptoms were screened for study eligibility. Eligible patients were at least 45 years of age and reported symptoms of intermittent neurogenic claudication secondary to a confirmed diagnosis of LSS at 1 or 2 contiguous levels from L1 to L5, despite at least 6 months of nonsurgical management. Key study inclusion and exclusion criteria are provided in Table, Supplemental Digital Content 1 available at http://links.lww.com/BRS/A948.

Procedures

Pretreatment evaluations included a physical and neurological examination, medical history, and assessment for study eligibility based on predefined inclusion/exclusion criteria. Radiographical assessments included radiographs (standing anteroposterior, lateral lumbar, flexion/extension lateral lumbar) and magnetic resonance images or computed tomographic scans of the lumbar spine.

The Superion interspinous process spacer (Figures 1, 2) is a titanium implant delivered through a cannula and deployed between the spinous processes of the involved vertebral levels. The device consists of an implant body and 2 cam lobes that rotate during deployment to encompass the lateral aspects of the superior and inferior spinous processes. Device sizes range from 8 to 16 mm, with each size corresponding to the magnitude of desired distraction between the 2 spinous processes (Figure 3). Comprehensive descriptions of the Superion[2] and X-Stop[3] interspinous process spacers and operative technique have been previously reported.

Outcomes

Subjects were followed through hospital discharge and returned for visits at 6 weeks and 3, 6, 12, 18, and 24 months. A physical and neurological assessment was performed at all follow-up visits; neurological success was defined by freedom from new or worsening motor or sensory function. Radiographical evaluations included standing anteroposterior, lateral, and flexion/extension lateral lumbar radiographs. The primary endpoint of this study was a composite treatment success outcome at the 2-year follow-up visit, defined as: (1) clinically significant improvement in at least 2 of 3 Zurich Claudication Questionnaire (ZCQ)[4] domain scores compared with baseline (physical function $\geq$0.5-point decrease, symptom severity $\geq$0.5-point decrease, patient satisfaction score $<$2.5), (2) freedom from reoperation, revision, removal, or supplemental fixation at the index level, (3) freedom from epidural steroid injection or nerve block at the index level within 12 weeks of the 2-year visit, (4) freedom from rhizotomy or spinal cord stimulator at any level, and (5) freedom from major implant or procedure-related complications. Secondary outcomes included leg and back pain severity assessed on a 100-mm visual analogue scale, Oswestry Disability Index (version 2),[5] patient satisfaction questions rated on a 5-point Likert scale ranging from very satisfied to very dissatisfied, radiographical evaluations, and adverse events classified by seriousness and relationship to the device and/or procedure.

Hypotheses

The primary hypothesis was that the composite treatment success outcome at 2 years in patients treated with Superion would be noninferior to that of patients treated with X-Stop. A noninferiority margin of 10% was determined

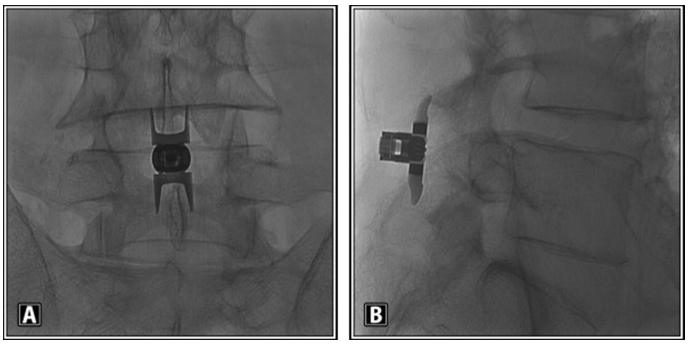

Figure 2. A, A/P and **B**, lateral radiographical image showing a properly placed Superion InterSpinous Spacer. A/P indicates anteroposterior, VAS, visual analogue scale; SD, standard deviation.

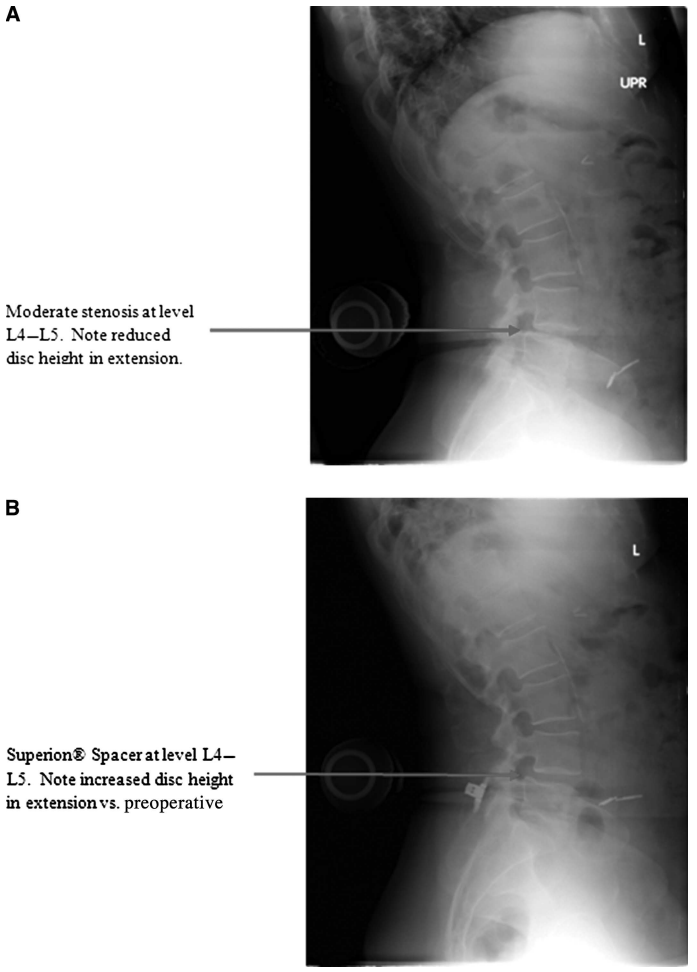

Figure 3. A, Preoperative lateral view of moderate stenosis at L4–L5. **B**, Lateral extension at 6 months postoperative in patient treated with Superion.

to be a clinically nonsignificant difference. Using a Bayesian approach, noninferiority would be claimed if the posterior probability of the null hypothesis was 95.8% or more, a value that was selected to ensure that the type I error remained less than 0.05.

Sample Size

A prospectively defined Bayesian adaptive sample size approach was used, which specified a total evaluable sample size ranging from 250 to 350 patients. An interim analysis was scheduled when patient accrual reached 250, 300, and 350. At each interim period, patient enrollment was either scheduled to stop if trial success was determined (posterior probability of the null hypothesis ≥95.8%) or continue to the next planned interim analysis, up to a maximum of 350 patients.

Randomization and Blinding

Patients were randomly allocated (1:1) to implant with Superion or X-Stop interspinous spacers and stratified by sex and number of index levels at each site. A web-based electronic data capture system was used to obtain treatment assignment before each patient was enrolled. Treatments were not concealed to investigators, outcome assessors, or trial participants.

Data Quality

This clinical trial was conducted per Good Clinical Practice guidance. Prior to commencing any study activity at any site, each investigator was trained in Good Clinical Practice, the study protocol, and the surgical technique for both interspinous process spacers. Data were regularly monitored by the sponsor and an independent contract research organization. Electronic data capture was handled by an independent firm (MedNet Solutions, Minnetonka, MN). A core radiographical laboratory (Medical Metrics Inc., Houston, TX) independently reviewed radiographs for evidence of spinous process fracture, and device disassembly, dislodgement, or migration.

Statistical Methods

Statistical analysis was performed by independent biostatisticians, who received all data for analysis directly from the electronic database. All outcomes were reported using a modified intent-to-treat population, which included all randomized patients who began anesthesia on the implant date. Continuous data were reported as mean ± standard deviation and categorical data were reported as frequencies and percentages. Comparisons of baseline characteristics were performed with independent samples *t* test, the Wilcoxon signed rank test, or Fisher exact test, as appropriate. Longitudinal changes in clinical outcomes between groups were assessed with unpaired *t* tests. Minimal clinically important changes in symptom severity were defined as 20 -mm or more improvement in pain scores[6,7] and a 15%-point or more improvement in Oswestry Disability Index.[6,8] The Kaplan-Meier method and log-rank tests were used to analyze freedom from reoperation through 2 years. The primary endpoint was assessed using a Bayesian approach that specified a posterior probability of the null hypothesis at 95.8% or more. Details of the Bayesian methodology were specified in a separate statistical analysis plan.

RESULTS

Participant Flow and Accountability

A total of 440 patients were randomized at 29 sites between August 2008 and December 2011 (Figure, Supplemental Digital Content 2 available at http://links.lww.com/BRS/A948). A total of 49 patients (Superion 28, control 21) were discontinued before treatment, most commonly due to withdrawal of informed consent. Ultimately, 391 were implanted with Superion (n = 190) or control (n = 201) spacers. During the 2-year follow-up period, 111 patients (Superion 54, control 57) were withdrawn from the study due to a protocol-defined secondary intervention, including device explant, revision surgery at the index level without explant, rhizotomy, rehospitalization for deep infection, or lumbar injection at the index

TABLE 1. Baseline Patient Characteristics

Variable	Superion (n = 190)	X-Stop (n = 201)
Demographics		
Age, yr	67 ± 9 (47–88)	66 ± 10 (46–89)
Male sex, n (%)	110 (58)	129 (64)
Body mass index, kg/m^2	30 ± 5 (16–40)	30 ± 5 (20–40)
Medical history*		
Spine, n (%)	170 (90)	178 (89)
Musculoskeletal, n (%)	151 (80)	163 (81)
Cardiovascular, n (%)	148 (78)	150 (75)
Gastrointestinal, n (%)	109 (57)	123 (61)
Tobacco history, n (%)	101 (53)	100 (50)
Genitourinary, n (%)	99 (52)	101 (50)
Endocrine/metabolic, n (%)	80 (42)	101 (50)
Allergy, n (%)	80 (42)	75 (37)
Neurological, n (%)	69 (36)	66 (33)
Respiratory, n (%)	47 (25)	59 (29)
Psychiatric, n (%)	47 (25)	49 (24)
Dermatological, n (%)	36 (19)	36 (18)
Symptoms		
Oswestry Disability Index	39 ± 13 (9–74)	40 ± 12 (7–80)
Back VAS	55 ± 28 (0–93)	55 ± 27 (0–100)
Leg VAS†	67 ± 24 (0–100)	68 ± 24 (0–95)
ZCQ Physical Function	2.6 ± 0.4 (1.6–3.6)	2.7 ± 0.4 (1.8–3.8)
ZCQ Symptom Severity	3.3 ± 0.6 (1.6–5.0)	3.4 ± 0.6 (2.0–5.0)

Continuous data reported as mean ± standard deviation (minimum–maximum).

**Variables reported with frequency more than 10% in either group.*

†Leg with highest pain severity used for calculation.

ZCQ indicates Zurich Claudication Questionnaire; VAS, visual analogue scale; SD, standard deviation.

TABLE 2. Operative Details

Variable	Superion (n = 189)	X-Stop (n = 199)
Anesthesia type, n (%)		
General	156 (82.1)	179 (89.1)
Conscious sedation	25 (13.2)	18 (9.0)
Local	14 (7.4)	11 (5.5)
Surgical approach, n (%)*		
Open	0	299 (100)
Miniopen	149 (53.2)	0
Percutaneous	131 (46.8)	0
Device size, n (%), mm		
6	NA	2 (0.7)
8	2 (0.7)	9 (3.0)
10	36 (12.9)	71 (23.8)
12	95 (33.9)	131 (43.8)
14	117 (41.8)	79 (26.4)
16	30 (10.7)	7 (2.3)
No. of treated levels, n (%)		
1	99 (52.4)	99 (49.7)
2	90 (47.6)	100 (50.3)
Concomitant procedures, n (%)	11 (3.9)	16 (5.4)
Soft-tissue removal	6 (2.1)	13 (4.4)
Osteophyte removal	3 (1.1)	3 (1.0)
Facet debulking	0	2 (0.7)
Laminectomy	0	1 (0.3)
Other	2 (0.7)	1 (0.3)
Operative time, min†	52 (12–193)	43 (10–110)
Blood loss, mL†	5 (0–100)	25 (0–300)
Hospital stay, d†	1 (1–11)	2 (1–10)

**Levels treated. †Median (minimum–maximum),*

NA indicates not available; ZCQ, Zurich Claudication Questionnaire.

level. Of the remaining patients, follow-up visit compliance was excellent (Superion 96.7%, control 94.7%).

Subject Characteristics

Baseline patient characteristics, including demographics, medical history, and symptom severity, were comparable between groups (Table 1). Only one baseline characteristic (ZCQ Physical Function) was statistically different between groups although this was not deemed a clinically important difference. Baseline radiographical findings are shown in Table, Supplemental Digital Content 3 available at http://links.lww.com/BRS/A948. Spinal stenosis was most frequently identified at L3–L4 or L4–L5. The incidence of low-grade spondylolisthesis was 32% at L4–L5, 9% at L3–L4, 1% at L2–L3, and 0% at L1–L2.

Operative Details

Interspinous process spacer implant success was 99.5% with Superion and 99.0% with control. Approximately 50% of patients were implanted at 1-level (typically L4–L5) and 50% at 2 levels (typically L3–L4/L4–L5). An important distinction between devices is that the X-Stop requires an open surgical

approach, whereas access is gained percutaneously (47%) or with a miniopen incision (53%) with the Superion spacer (Table 2). Blood loss (median: 5 *vs*. 25 mL, $P < 0.001$) and hospital stay (median: 1 *vs*. 2 days, $P < 0.05$) favored patients treated with Superion.

Primary Endpoint: Composite Treatment Success Outcome

Using a Bayesian approach, the posterior probability that the composite treatment success outcome through 2 years with Superion was no less than the 10% noninferiority margin compared with X-Stop was 0.993. This posterior probability exceeded the *a priori* criterion of 0.958, providing evidence that Superion is clinically noninferior to X-Stop. A number of sensitivity analyses were performed that corroborated the findings of the primary analysis. A tipping point analysis confirmed that the Bayesian posterior probability exceeded 0.958 in 92% of simulations.

Patient-Reported Symptoms

Leg pain severity decreased by 70% in both the Superion and control groups, with mean values of 20 ± 30 and 20 ± 26 at 2 years, respectively (Figure 4). At 2 years, leg pain clinical success was 76% with Superion and 77% with control. Back pain severity decreased by 65% in the Superion group and 69% with the control spacer, with mean values of 20 ± 26 and 18 ± 23 at 2 years, respectively (Figure 5). At 2 years, back pain clinical success was comparable (Superion 67%, control 68%, $P = 0.90$). Back-specific disability improved 51% with the Superion and 55% with the control spacer, with mean values of 20 ± 18 and 18 ± 15 at 2 years, respectively (Figure 6). At 2 years, Oswestry Disability Index clinical success was 63% with Superion and 67% with control ($P = 0.61$). ZCQ subdomain scores through 2 years were comparable between groups (Figure, Supplemental Digital Content 4 available at http://links.lww.com/BRS/A948). For symptom severity, mean improvement was 1.15 for Superion and 1.28 points for the control spacer. For physical function, mean improvement was 0.89 points for Superion and 1.09 points for control. At 2 years, mean ZCQ Patient Satisfaction scores were also comparable (Superion, 1.66; control, 1.52). Overall, patient-reported outcomes at 2 years were comparable in patients with and without spondylolisthesis (Table 3) and in patients with central *versus* lateral stenosis (Table 4).

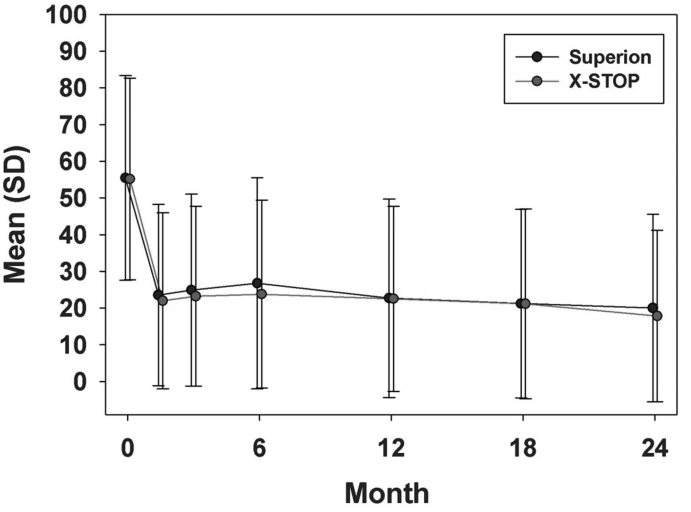

Figure 5. Changes in back pain severity during 2 years. VAS indicates visual analogue scale; SD, standard deviation.

Patient Satisfaction

The percentage of patients who were "satisfied" or "somewhat satisfied" with their treatment at 2 years was 86% with Superion and 89% with control. Similarly, 83% and 84% of patients, respectively, reported that they would "definitely" or "probably" undergo the same treatment again.

Radiographical Findings

There were no instances of device component fracture, disassembly, or collapse in either group as reported by independent radiographical assessment. Device dislodgement or

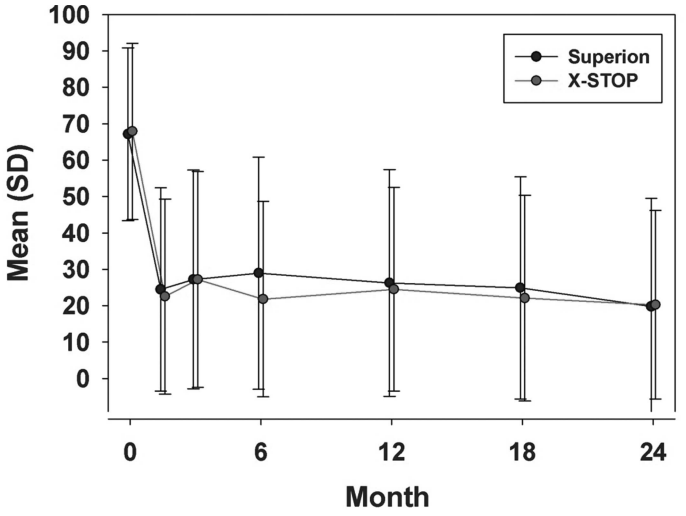

Figure 4. Changes in leg pain severity during 2 years. VAS indicates visual analogue scale; SD, standard deviation.

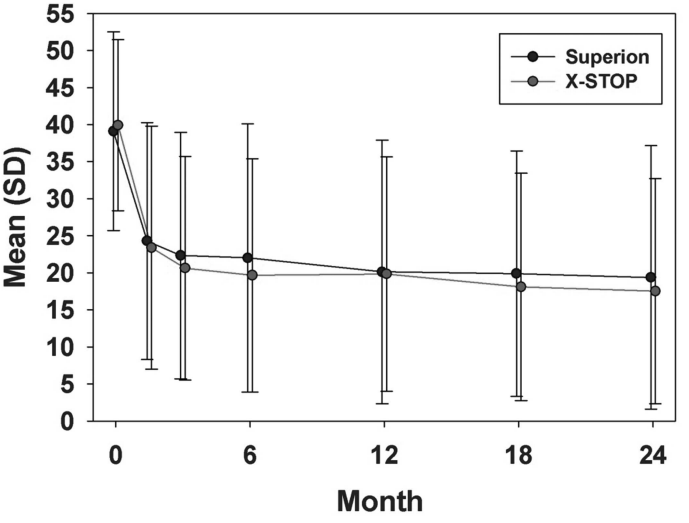

Figure 6. Changes in ODI during 2 years. ODI indicates Oswestry Disability Index; SD, standard deviation.

TABLE 3. Clinical Success Rates at 2 yr: Grade I Spondylolisthesis *vs.* no Spondylolisthesis

	Grade I Spondylolisthesis		No Spondylolisthesis	
Variable	Superion (n = 50)	X-Stop (n = 62)	Superion (n = 81)	X-Stop (n = 71)
Leg pain severity	74	76	77	79
Back pain severity	74	66	63	70
Oswestry Disability Index	64	65	63	69
ZCQ Physical Function	72	81	73	80
ZCQ Symptom Severity	80	79	75	82
ZCQ Patient Satisfaction	88	94	82	90

Values are percentages of patients achieving clinical success threshold for each outcome.
ZCQ indicates Zurich Claudication Questionnaire.

migration was identified in 0% of patients with Superion and 11.9% of control patients. At 2 years, the incidence of nonhealed spinous process fracture was 11.1% with Superion and 5.0% with the control spacer; healed spinous process fracture incidence was 5.3% with Superion and 3.5% in the control group. Approximately, 80% of spinous process fractures were identified by the 6-week follow-up visit in each group. Spinous process fractures were largely asymptomatic and had no influence on clinical effectiveness of either device.

Reoperations

There were a total of 44 (23.2%) reoperations or revisions in the Superion group compared with 38 (18.9%) in the control group ($P = 0.32$). Similar rates of decompression and device removal (11.6% Superion *vs.* 9.5% control, $P = 0.51$) and device removal and fusion (6.8% Superion *vs.* 5.5% control, $P = 0.68$) were observed. Comparing Superion to control, the frequency of other interventions was 0.5% *versus* 1.0% for device removal, 2.1% *versus* 0% for supplemental decompression, and 0.5% *versus* 1.0% for intraoperative complication preventing implantation. No patient was treated with a spinal cord stimulator at the index level and only 1 patient (control) received rhizotomy. During the 2-year follow-up period, 13.2% of patients with Superion and 16.4% of control patients received an epidural steroid injection or nerve block at the level(s) of surgery ($P = 0.40$). The Kaplan-Meier estimate of freedom from reoperation, revision, or epidural injection through 2 years was 72% (Figure 7). The main reasons for reoperation in each group were inadequate pain relief or return of symptoms.

Adverse Events

The incidence of adverse events was similar between the groups (Table 5). The incidence of serious adverse events classified as device or procedure-related was 8.4% with Superion and 9.5% with control ($P = 0.86$). Through 2 years, 6 (3.2%) deaths were reported in the Superion group and 5 (2.5%) in the control group ($P = 0.77$). No device- or procedure-related deaths were reported during follow-up. The rate of neurological complications was similar for both Superion (3.7%) and control (2.5%) groups.

DISCUSSION

The results of this randomized controlled trial demonstrate that the Superion interspinous process spacer provides

TABLE 4. Clinical Success Rates at 2 yrs: Central *vs.* Lateral Stenosis

	Central Stenosis		Lateral Stenosis	
Variable	Superion (n = 43)	X-Stop (n = 34)	Superion (n = 12)	X-Stop (n = 11)
Leg pain severity	74	88	75	64
Back pain severity	74	79	42	55
Oswestry Disability Index	70	68	75	64
ZCQ Physical Function	74	82	75	73
ZCQ Symptom Severity	84	82	67	64
ZCQ Patient Satisfaction	86	91	83	91

Values are percentages of patients achieving clinical success threshold for each outcome. Patients presenting with central and lateral stenosis not included in analyses.
ZCQ indicates Zurich Claudication Questionnaire.

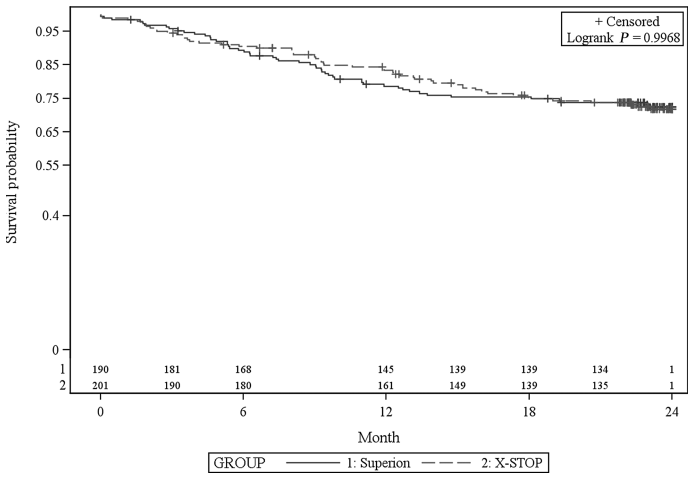

Figure 7. Freedom from reoperation, reintervention, and epidural through 2 years.

clinically meaningful relief of intermittent claudication symptoms due to LSS through 2 years. Furthermore, patient outcomes were comparable with those observed with the X-Stop, an FDA-approved interspinous spacer. The primary endpoint of this clinical trial was met, demonstrating noninferiority of the Superion spacer compared with the X-Stop spacer.

Despite the similarities in mechanism of action as well as clinical and radiographical outcomes, there are distinct differences in device design and surgical placement technique between these spacers that warrant further discussion. Both devices are inserted through a posterior incision and require initial distraction. However, the X-Stop requires much greater surgical exposure whereas the Superion device uses a minimally invasive approach, such that the device is inserted through a cannula about the size of a dime placed between adjacent spinous processes and, therefore, requires no surgical dissection of the spinal musculature. We attribute the smaller blood loss and shorter hospital stay associated with Superion to these procedural differences. The minimally invasive nature of the Superion spacer is also advantageous compared with the larger incision required for the control spacer in patients who later require secondary surgery because larger exposures generate scar tissue, making future reoperations more difficult.

In addition to the operative benefits, there are also biomechanical characteristics that may favor the Superion device. On the basis of the radiographical data, there were a significant number of dislodgements and migrations with the X-Stop device whereas none were observed in the Superion group. These events may occur because the open procedure results in greater disruption of anatomic structures, which may lead to a greater propensity for the X-Stop to dislodge or migrate. In addition, the slender wings of the X-Stop device may provide less stability between the spinous processes. The patients with dislodgements in the X-Stop group not only exhibited greater pain and loss of function, but also required a higher rate of additional surgical procedures.

In this study, the core laboratory also identified spinous process fractures in both groups. Most fractures were asymptomatic and the adverse event rate associated with spinous process fractures was not significantly higher than in patients without fractures. The long-term significance of these fractures is unknown; however, radiographical follow-up suggests healing is common. Potentially, spinous process fracture risk can be lowered by bone density screening to identify individuals with osteoporosis, exclusion of patients with high-grade spondylolisthesis deformities, accurate device sizing, proper patient positioning, and avoidance of overdistraction of the interspinous space.[9]

Data from this investigation as well as from previous studies suggest that the midterm treatment effectiveness of interspinous spacers is at least comparable with that of open decompression surgery. Leg pain, which is the primary complaint in this patient population, decreased by approximately 70% during 2 years in this study. According to published literature, leg pain severity generally decreases by 43% to 69% after laminectomy.[10–17] Furthermore, interspinous spacers are appealing to patients because of the less-invasive nature of this procedure relative to surgical decompression. For example, in the Spine Patient Outcomes Research Trial trial,[18] procedural outcomes included blood loss more than 300 mL, procedure time more than 2 hours, and hospitalization more than 3 days. In contrast, interspinous spacers result in minimal blood loss (5–25 mL) with reductions in procedure time and hospital stay of approximately 50%. Regardless, proper patient selection, meticulous surgical technique, and familiarity with relevant anatomy are prerequisites for favorable outcomes with interspinous process spacers.

Despite the strengths of this study that include a randomized design with rigorous study entry criteria and excellent patient follow-up rates using validated outcome measures, there were several limitations. The long-term durability of interspinous

TABLE 5. Adverse Events Through 2 Years

Variable	Superion (n = 190)	X-Stop (n = 201)	*P*
Any adverse event, n (%)	180 (94.7)	184 (91.5)	0.24
Back pain	49 (25.8)	61 (30.3)	
Leg pain	33 (17.4)	45 (22.4)	
LSS symptoms at index level	26 (13.7)	28 (13.9)	
Spinous process fracture	23 (12.1)	13 (6.5)	
Buttock/groin pain	19 (10.0)	12 (6.0)	
Any serious adverse event, n (%)	88 (46.3)	92 (45.8)	0.92
LSS symptoms at index level	16 (8.4)	13 (6.5)	
Leg pain	11 (5.8)	10 (5.0)	
Spinous process fracture	10 (5.3)	5 (2.5)	
Back pain	8 (4.2)	13 (6.5)	

Adverse events reported with frequency more than 5% in either group.
LSS indicates lumbar spinal stenosis.

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 brings into question the mechanisms of mechanical action of these devices. Finally, a comparison of interspinous process spacers with nonsurgical treatment or surgical decompression was not performed so this randomized study provides no information on these interesting questions.

CONCLUSION

The Superion and X-Stop interspinous process spacers both relieve symptoms of intermittent neurogenic claudication secondary to moderate LSS. In addition, the safety profiles of these devices were comparable. The Superion device may represent a reasonable treatment option for this patient population.

➢ Key Points

- ❑ A total of 391 patients with moderate LSS who failed at least 6 months of nonsurgical management were treated with the Superion (n = 190) or a control (n = 201) interspinous process spacer as part of a multicenter, randomized, controlled trial.
- ❑ During 2 years, the implantation of an interspinous spacer resulted in a 70% reduction in leg pain severity with high patient satisfaction.
- ❑ The Superion interspinous process spacer relieves symptoms of intermittent neurogenic claudication secondary to moderate LSS in the majority of patients through 2 years.

Supplemental digital content is available for this article. Direct URL citations appearing in the printed text are provided in the HTML and PDF version of this article on the journal's web site (www.spinejournal.com).

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ORIGINAL RESEARCH

Superion® InterSpinous Spacer for treatment of moderate degenerative lumbar spinal stenosis: durable three-year results of a randomized controlled trial

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Vikas V Patel[1]
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Thomas R Haley[4]
W Daniel Bradley[5]
Raphael P Davis[6]
Jon E Block[7]
Fred H Geisler[8]

[1]The Spine Center, University of Colorado Hospital, Denver, CO, [2]Spine Institute of Louisiana, Shreveport, LA, [3]Department of Orthopaedics and Rehabilitation, Yale University School of Medicine, New Haven, CT, [4]Performance Spine and Sports Physicians, PC, Pottstown, PA, [5]Texas Back Institute, Denton, TX, [6]Department of Neurological Surgery, Stony Brook Medicine, Stony Brook, NY, [7]Jon Block, Ph.D. San Francisco, CA, [8]McLaren Hospital, Petoskey, MI, USA

Purpose: This report provides the 3-year clinical outcomes from the randomized, controlled US Food and Drug Administration Investigational Device Exemption trial of the Superion® for the treatment of moderate degenerative lumbar spinal stenosis.

Patients and methods: 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 lumbar spinal stenosis at one or two contiguous levels from L1 to L5. Patients were treated between June 2008 and December 2011 at 31 investigational sites. Three hundred ninety-one subjects were included in the randomized study group consisting of 190 Superion® and 201 X-STOP® control subjects. The primary composite endpoint was individual patient success based on four components: improvement in two of three domains of the Zurich Claudication Questionnaire, no reoperations at the index level, no major implant/procedure-related complications, and no clinically significant confounding treatments.

Results: At 3 years, the proportion of subjects achieving the primary composite endpoint 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 endpoint in the Superion® group (range: 81%–91%). Improvements in back and leg pain severity as well as back- and disease-specific functional outcomes were also maintained through 36 months.

Conclusion: The 3-year outcomes from this randomized controlled trial demonstrate durable clinical improvement consistently across all clinical outcomes for the Superion® in the treatment of patients with moderate degenerative lumbar spinal stenosis.

Keywords: InterSpinous Spacer, lumbar spinal stenosis, Superion®, neurogenic claudication

Introduction

On May 20, 2015, the US Food and Drug Administration (FDA) approved the Superion® InterSpinous Spacer (ISS) (Superion®) for commercial distribution in the United States. Not requiring concomitant surgical decompression, this is the second "stand-alone" interspinous device approved by the FDA. This pivotal regulatory decision substantiates the graduation of the Superion® device from experimental to an acceptable clinical practice modality for the treatment of intermittent symptoms of neurogenic claudication secondary to moderate degenerative lumbar spinal stenosis.

Lumbar spinal stenosis is the manifestation of arthritic degeneration of the spine resulting in bony and ligamentous encroachment of the central canal and foramina

Correspondence: Jon E Block
Jon Block, Ph.D. 2210 Jackson Street, Suite 401, San Francisco, CA 94115, USA
Tel +1 415 775 7947
Email jb@drjonblock.com

causing classic claudicant symptoms.[1–3] These symptoms are often exacerbated during ambulation, standing, and trunk extension. It is estimated that 1.2 million individuals are diagnosed with lumbar spinal stenosis every year, with surgical hospitalizations increasing by 30% from 2000 to 2009.[4] Over 175,000 surgeries are performed to treat spinal stenosis annually, making it the number one reason for spine surgery in the elderly population.[5] In fact, stenosis is the most common indication for spine surgery in patients older than 65 years, and its prevalence is expected to rise 59% to 64 million elderly adults by the year 2025.[6]

The Superion® is designed for the treatment of symptoms of intermittent neurogenic claudication secondary to moderate degenerative lumbar spinal stenosis and is implanted by minimally invasive methods through a cannula.[7] In contrast to direct decompression procedures, such as laminectomy or laminectomy with fusion, where the soft and bony tissues compressing the neural elements are surgically removed through an open surgical exposure, the Superion® provides minimally invasive, indirect decompression of spinal nerves, and functions by serving as a spinal extension blocker to prevent compression of neural elements in extension without the removal of tissue adjacent to the nerves.

This report provides the 3-year clinical outcomes from the randomized, controlled FDA Investigational Device Exemption trial of the Superion® for the treatment of moderate spinal stenosis.[8]

Materials and methods

Trial overview

The study was a prospective, multi-center, randomized controlled clinical trial comparing the Superion® to a control group consisting of the X-STOP® (X-STOP®), a legally marketed alternative with similar indications for use. The study methodology including eligibility criteria, randomization methods, sample size estimates, outcome measures, and statistical analyses have been detailed previously.[9,10] Briefly, the study evaluated the use of the Superion® in the treatment of subjects aged 45 years or older suffering from moderate symptoms of intermittent neurogenic claudication, secondary to a confirmed diagnosis of moderate degenerative lumbar spinal stenosis at one or two contiguous levels from L1 to L5. Patients were treated between June 2008 and December 2011 at 31 investigational sites. Three hundred ninety-one subjects were included in the randomized study group consisting of 190 Superion® ISS and 201 X-STOP® control subjects. FDA regulatory approval was based on the 24-month outcome data in this population.

This study was approved by the Institutional Review Board at each participating site and patients provided written informed consent before any study-related procedures were performed. The trial was prospectively registered at ClinicalTrials.gov (NCT00692276).

Approved indications for use

This device is indicated to treat skeletally mature patients suffering from pain, numbness, and/or cramping in the legs (intermittent neurogenic claudication) secondary to a diagnosis of moderate degenerative lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, magnetic resonance imaging, and/or computed tomography evidence of thickened ligamentum flavum, narrowed lateral recess, and/or central canal or foraminal narrowing. The Superion® is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, numbness, and/or cramping, with or without back pain, and who have undergone at least 6 months of nonoperative treatment. The Superion® may be implanted at one or two adjacent lumbar levels in patients in whom treatment is indicated at no more than two levels, from L1 to L5.

For this intended use, moderate degenerative lumbar spinal stenosis is defined as follows:

- A reduction of 25%–50% in the central canal and/or nerve root canal (subarticular and neuroforaminal) compared to the adjacent levels on radiographic studies, with radiographic confirmation of any one of the following:
  - Evidence of thecal sac and/or cauda equina compression
  - Evidence of nerve root impingement (displacement or compression) by either osseous or nonosseous elements
  - Evidence of hypertrophic facets with canal encroachment.
- And associated with the following clinical signs:
  - Presents with moderately impaired physical function defined as a score of ≥2.0 of the Zurich Claudication Questionnaire (ZCQ)
  - Ability to sit for 50 minutes without pain and to walk 50 feet or more.

Primary and secondary outcomes

The primary composite endpoint of the investigation as mandated by FDA was individual patient success, which required the patient to meet all of the following criteria at 24 months:

Table 1 Comparative 36-month success rates between Superion® and X-STOP® overall and for each primary endpoint component

	Number and percentage meeting criteria						*P*-value*
	Superion® ISS			X-STOP®			
	N	n	%	N	n	%	
1) ZCQ Responder (at least two of three ZCQ domains)	81	71	87.7	75	63	84.0	0.65
2) No reoperations, revisions, removals or supplemental fixation at the index level(s)	138	112	81.2	148	118	79.7	0.77
3) No major device- or procedure-related complications	138	125	90.6	148	126	85.1	0.21
4) No clinically significant confounding treatments	138	120	87.0	148	118	79.7	0.11
Composite clinical success	120	63	52.5	129	49	38.0	0.023

Note: *Fisher's exact test, two-tailed.
Abbreviations: ISS, InterSpinous Spacer; ZCQ, Zurich Claudication Questionnaire.

1. Clinically significant improvement in outcomes compared to baseline, as determined by meeting the criterion for at least two of three domains of ZCQ.
   - ≥0.5 point improvement in physical function
   - ≥0.5 point improvement in symptom severity
   - Score of ≤2.5 points on patient satisfaction domain
2. No reoperations, removals, revisions, or supplemental fixation at the index level(s).
3. No major implant or procedure-related complications.
   - No dislodgement, migration, or deformation
   - No new or persistent worsened neurological deficit at the index level
   - No spinous process fractures
   - No deep infection, death, or other permanent device attributed disability
4. No clinically significant confounding treatments:
   - No epidural injections, nerve block procedures at index level, spinal cord stimulators, or rhizotomies.

Secondary outcomes included leg and back pain severity assessed on a 100 mm visual analog scale, the Oswestry Disability Index (ODI), and the number of patients that required reoperation, revision or implant removal.

Three-year evaluation

The primary composite endpoint and all secondary outcomes were re-evaluated at the 36-month follow-up interval. In all, 90.2% and 91.4% of the Superion® and X-STOP® study subjects, respectively, were available at this interval. Statistical analysis was performed by an independent biostatistical firm who received all data for analysis directly from a study-specific electronic database. All outcomes were reported using a modified intention-to-treat population, which included all randomized patients who began anesthesia on the implant date. Minimal clinically important changes were defined as 20 mm or more improvement in pain scores and a 15% point or more improvement in ODI. Frequency distributions were compared between groups using Fisher's exact test, two-tailed.

Results

All subject background characteristics and operative details for the originally randomized inception cohort have been published previously.[9] Based on achieving the a priori specified 24-month primary endpoint, the two devices were demonstrated to be statistically noninferior as per the initial trial hypothesis, satisfying the FDA regulatory requirements for approval.

At 36 months, the proportion of subjects achieving the primary composite endpoint was greater for Superion® (63/120, 52.5%) than for X-STOP® (49/129, 38.0%) (*P*=0.023) (Table 1). The subjects implanted with the Superion® showed no degradation in clinical success compared to the 24-month endpoint analysis (53%), whereas

Table 2 Comparative 36 Month Success Rates between Superion® and X-STOP® for Primary and Secondary Clinical Outcomes

36-month clinical outcomes	Superion® ISS	X-STOP®	*P*-value*
Pain			
VAS back: ≥20 mm decrease	76.8% (63/82)	69.7% (53/76)	0.37
VAS leg (worse): ≥20 mm decrease	84.1% (69/82)	69.7% (53/76)	0.037
Back and stenosis-related outcomes			
ZCQ physical function: ≥0.5 point decrease	80.5% (66/82)	77.9% (60/77)	0.70
ZCQ symptom severity: ≥0.5 point decrease	82.9% (68/82)	75.3% (58/77)	0.25
ZCQ patient satisfaction: ≤2.5 points	91.5% (75/82)	88.3% (68/77)	0.60
ODI: ≥15 point decrease	69.5% (57/82)	71.4% (55/77)	0.86

Note: *Fisher's exact test, two-tailed.
Abbreviations: ISS, InterSpinous Spacer; ODI, Oswestry Disability Index; VAS, visual analog scale; ZCQ, Zurich Claudication Questionnaire.

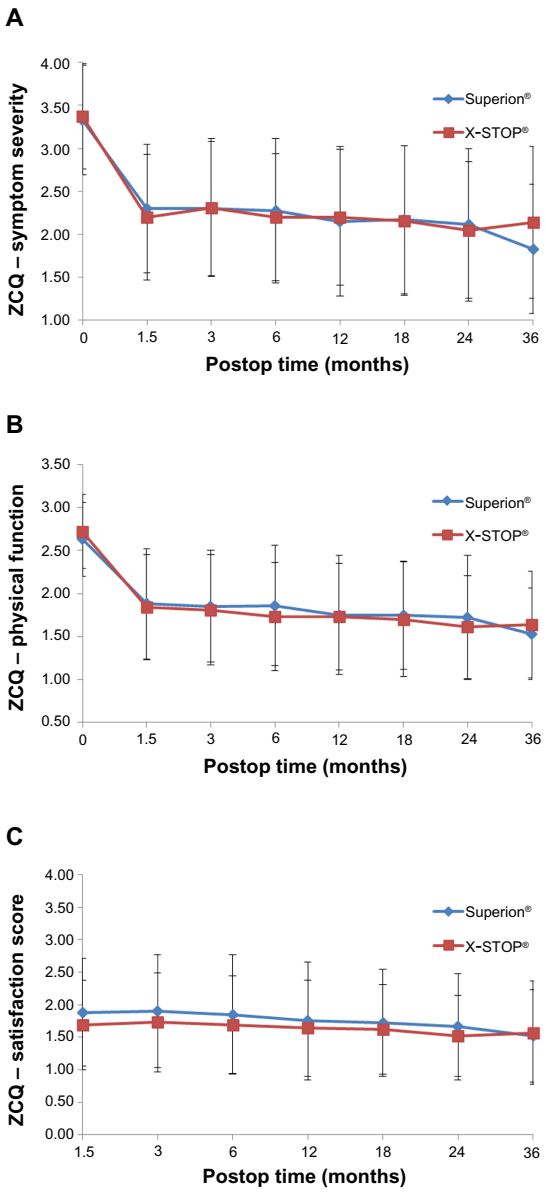

Figure 1 Time course of results for each sub-domain of the ZCQ.
Notes: (**A**) Symptom severity. (**B**) Physical function, and (**C**) Patient satisfaction.
Abbreviations: Postop, postoperative; ZCQ, Zurich Claudication Questionnaire.

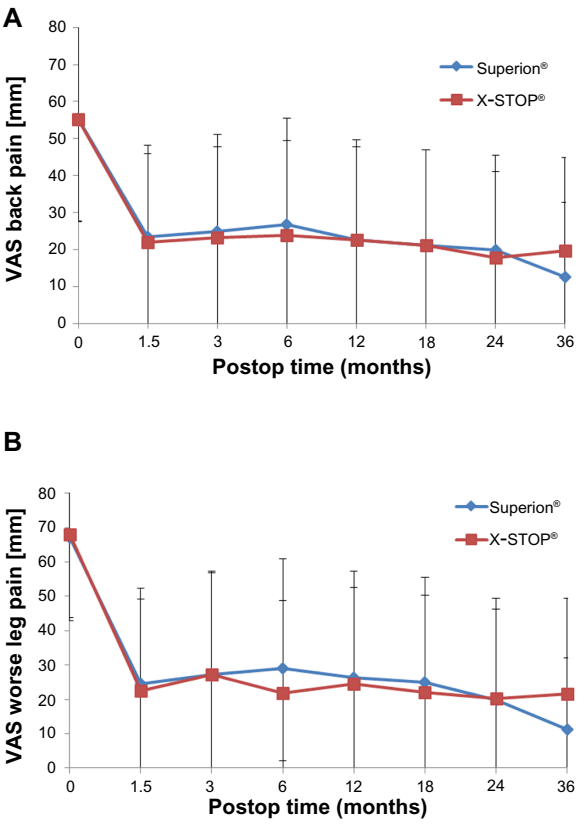

Figure 2 Time course of results for pain severity.
Notes: (**A**) Back pain. (**B**) Leg pain.
Abbreviations: VAS, visual analog scale; Postop, postoperative.

X-STOP® subjects showed a modest degradation over the same timeframe (50%). As shown in Table 1, the corresponding 36-month success rates exceeded 80% for each of the individual components of the primary endpoint in the Superion® group. Specifically, the success rates were 88%, 81%, 91%, and 87% for improvement in two of three domains of the ZCQ, no reoperations at the index level, no major implant/procedure-related complications, and no clinically significant confounding treatments, respectively.

Table 2 provides the 36-month success rates for pain severity as well as back- and disease-specific outcomes based on the minimal clinically important difference criteria for each variable. Five of six comparisons qualitatively favored treatment with the Superion® device; however, only the leg pain results achieved statistical significance. Inspection of the line graphs for each outcome captures both the durability of the Superion® results and the modest degradation in X-STOP® results between 24 and 36 months for the ZCQ (Figure 1) as well as for back and leg pain severity (Figure 2) and back function (Figure 3).

Comparing the 24-month data with the 36-month data, there was a higher increase in X-STOP® reoperations, revisions, and removals (n=15 out of 44 total) compared to the Superion® device (n=11 out of 49 total).

Discussion

With its recent regulatory approval, the Superion® becomes the only "stand-alone" interspinous device on the US market available to patients for the treatment of moderate spinal stenosis. While the X-STOP® received FDA regulatory approval in 2005, the manufacturer (Medtronic, Inc., Minneapolis, MN, USA) recently (2015) elected voluntarily to cease sale and distribution of the implant. This leaves the Superion® as

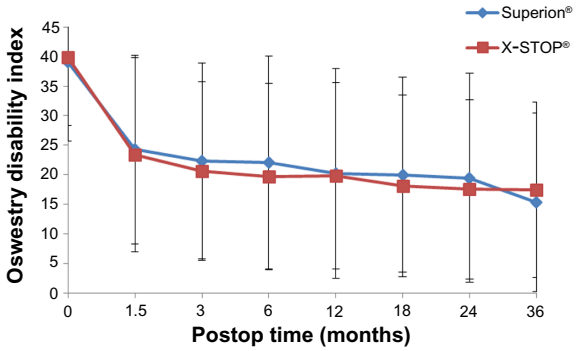

Figure 3 Time course of results for ODI.
Abbreviations: ODI, Oswestry Disability Index; Postop, postoperative.

the de facto clinical option for physicians and their patients seeking a minimally invasive alternative to laminectomy for claudicant symptoms refractory to conservative care.

Importantly, the Superion® implantation procedure does not cause substantial alterations or disruptions to the spinal anatomy which likely reduces the complexity of future surgical options in the event that revision becomes necessary to address progressive degenerative changes and/or reemergence of symptoms. If device removal is required, the implant can be removed via the same minimally invasive access as the original implantation procedure. This suggests that the Superion® device may be considered a reasonable "first line" option in the continuum of care for the treatment of moderate lumbar spinal stenosis.

The durable clinical results achieved with the Superion® in the current study are 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.[11] 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.

Conclusion

The 3-year outcomes from this randomized controlled trial demonstrate durable clinical improvement consistently across all clinical outcomes for the Superion® in the treatment of patients with moderate spinal stenosis. At this follow-up interval, a success rate in excess of 80% was maintained in all the four components of the primary endpoint.

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Author contributions

All authors contributed to the study design, conception, and execution as well as data interpretation, drafting of the manuscript, and provided critical revision of the manuscript for intellectual content. All authors read and provided final approval of the version to be published. All authors agree to be accountable for all aspects of the work in ensuring that questions related to the accuracy and integrity of any part of the work are appropriately investigated and resolved.

Disclosure

JB is an independent advisor to VertiFlex. The authors report no other conflicts of interest in this work.

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EXPERT REVIEWS

Stand-alone interspinous spacer versus decompressive laminectomy for treatment of lumbar spinal stenosis

Expert Rev. Med. Devices [Early online]

Carl Lauryssen[1], Robert J Jackson[2], Jeffrey M Baron[3], Richard A Tallarico[4], William F Lavelle[4], Harel Deutsch[5], Jon E Block[*6] and Fred H Geisler[7]

[1]*Neurosurgical Spine Institute, Lakeway, TX 78738, USA*
[2]*Orange County Neurosurgical Associates, Laguna Hills, CA 92653, USA*
[3]*Tucson Orthopaedic Institute, Tucson, AZ 85712, USA*
[4]*Upstate Bone and Joint Center, East Syracuse, NY 13057, USA*
[5]*Rush University Medical Center, Chicago, IL 60612, USA*
[6]*Independent Scholar, San Francisco, CA 94115, USA*
[7]*Chicago Back Institute, Chicago, IL 60625, USA*
**Author for correspondence: jb@drjonblock.com*

Objective: To compare the two-year clinical outcomes of a prospective, randomized controlled trial of an FDA-approved interspinous spacer with the compilation of published findings from 19 studies of decompressive laminectomy for the treatment of lumbar spinal stenosis. Methods: Back and leg pain, Oswestry disability index (ODI), and Zurich Claudication Questionnaire (ZCQ) values were compared between spacer- and laminectomy-treated patients preoperatively and at 12 and 24 months. Results: Percentage improvements between baseline and 24 months uniformly favored patients treated with the spacer for back pain (65% vs. 52%), leg pain (70% vs. 62%), ODI (51% vs. 47%) and ZCQ symptom severity (37% vs. 29%) and physical function (36% vs. 32%). Conclusion: Both treatments provide effective and durable symptom relief of claudicant symptoms. This stand-alone interspinous spacer offers the patient a minimally invasive option with less surgical risk.

Keywords: interspinous spacer • lumbar spinal stenosis • Superion • laminectomy

Introduction

One of the most profound societal ramifications of the increasing proportion of individuals living to advanced age is the impact and burden on the health care system associated with age-related degeneration of the musculoskeletal system. Indeed, the lumbar spine is particularly vulnerable to arthritic deterioration resulting in bony and ligamentous encroachment of the central canal and foramina, commonly referred to as lumbar spinal stenosis.[1] Radiographic stenosis is a common incidental finding in most advanced aged patients. Clinically significant lumbar stenosis that is refractory to nonoperative management is potentially treatable with surgical interventions. In fact, the SPORT trial showed that current nonoperative treatments provide only modest clinical benefit.[2] Stenosis is the most common indication for spine surgery in patients older than 65 with surgical hospitalizations increasing by 30% from 2000 to 2009.[3] Its prevalence is expected to rise 59% to 64 million elderly adults by the year 2025.[4]

The arthritic compression of the neural elements leads to classic intermittent symptoms of neurogenic claudication, leg pain and weakness, which are exacerbated during ambulation, standing and trunk extension. Symptoms are relieved with sitting or forward flexion. Given that the severity of spinal stenosis variably, but insidiously, progresses over time, patients require safe and effective treatment options to manage these symptoms.

Stand-alone interspinous spacers are designed for the treatment of symptoms of intermittent neurogenic claudication secondary to moderate lumbar spinal stenosis, and are implanted by minimally invasive methods through a cannula.[5] In contrast to direct surgical procedures, such as decompressive laminectomy, where the soft and bony tissues compressing the neural elements are surgically removed through an open operative exposure, spacers provide minimally invasive, indirect decompression of spinal nerves, and function by serving as a spinal extension blocker to

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prevent compression of neural elements in extension without the removal of tissue adjacent to the nerves.

This report provides a qualitative comparison of the published two-year clinical findings from the prospective, randomized controlled trial of a recently FDA-approved interspinous spacer [6] with the body of evidence for similar outcome measurements associated with the "gold standard" surgical treatment for lumbar spinal stenosis, decompressive laminectomy.[7]

Methods

This study was undertaken to compare the 2-year clinical outcomes of a randomized controlled investigational device exemption (IDE) trial of a stand-alone interspinous spacer (Superion®, Vertiflex, Inc. San Clemente, CA, USA) with the compilation of published findings on decompressive laminectomy for the treatment of claudicant symptoms associated with spinal stenosis. The IDE study methodology including eligibility criteria, randomization methods, sample size estimates, outcome measures and statistical analyses have been detailed earlier.[6,8] The findings of this trial supported the May 2015 regulatory approval of this device by the US Food and Drug Administration (FDA) and have been published previously.[6]

Articles were selected for inclusion in the laminectomy literature control group if they met the following criteria: inclusion of at least one patient-reported clinical outcome measurement consisting of back pain severity, leg pain severity, Oswestry disability index (ODI) or Zurich Claudication Questionnaire (ZCQ); outcome(s) measured preoperatively with at least one follow-up measurement at a minimum of 12 months, and surgical procedure consisted of complete ligamentous and bony decompression performed via open or endoscopic access. Articles reporting the outcomes of minimal decompression procedures (e.g., *mild*® procedure) and spinal fusion were excluded. Literature controls were identified from single-arm studies of laminectomy as well as from trials where laminectomy served as a "gold standard" comparator. Articles eligible for inclusion were identified through electronic key word searches of the PubMed database as well as through review of bibliographies of two recently published meta-analyses on the safety and effectiveness of decompressive laminectomy for spinal stenosis.[9,10]

For each clinical outcome, the median value (range) was computed from the contributing laminectomy study groups and compared graphically to the corresponding spacer mean value preoperatively as well as at 12 and 24 months. Additionally, the percentage improvement over baseline was estimated as the preoperative value compared to the final follow-up value for all outcomes. Back and leg pain scores were adjusted as necessary to correspond to a 100-mm visual analog scale. Only two of three ZCQ domains, symptom severity and physical function, were included in this comparative analysis as the patient satisfaction domain does not involve a baseline measurement. All data are presented as descriptive statistics.

Results

In all, 19 articles were identified that included a laminectomy study arm reporting at least one clinical outcome with a minimum 12 months of follow-up, representing 1045 patients (Table 1).[2,11–28] Fourteen laminectomy articles reported back pain severity (n = 618), 12 reported leg pain severity (n = 537), 12 reported ODI (n = 753) and 3 reported ZCQ values (n = 129). In the Superion® trial, 190 patients were randomly allocated to receive the device.[6]

Preoperatively, patients consistently presented with moderate to severe symptoms of neurogenic claudication irrespective of treatment, with laminectomy patients showing somewhat greater levels of chronic pain, functional impairment and condition-specific dysfunction (Figures 1–5). For example, prior to surgery, the average leg pain severity in the spacer group was 67 mm compared to a median value of 74 mm among laminectomy patients (range: 58–91 mm) (Figure 2).

Following treatment with either spacer or laminectomy, patients attained clinically substantial gains across all outcome measures at 12 months with durable improvement through 24 months, postoperatively (Figures 1–5). For back pain severity, patients realized an approximate 35-mm improvement following implantation with the spacer, reflecting an average percentage improvement of 65% (Figures 1 & 6). In comparison, laminectomy patients achieved an approximate 52% (range: 30–68%) improvement from a preoperative median score of 60 mm (range: 50–83 mm) to 27 mm (range: 21–39 mm) at 24 months, postoperatively (Figures 1 & 6).

For leg pain severity, the average percentage change with the spacer was 70%, exhibiting an improvement of approximately 47 mm over baseline (Figures 2 & 6). This improvement was slightly higher than the 62% median percentage improvement realized with laminectomy (range: 43–79%), reflecting a change from 74 mm (range: 58–91 mm) preoperatively to 29 mm (range: 19–37 mm) at 24 months, postoperatively (Figures 2 & 6).

With respect to back functional impairment as measured by ODI, overall percentage improvements were somewhat smaller for both spacer (51%) and laminectomy (47%, range: 36–83%) (Figure 6). Spacer patients showed an approximate 19 percentage point improvement through 24 months, whereas laminectomy patients improved from 43% (range: 31–74%) preoperatively to 20% (range: 12–25%) at 24 months, postoperatively (Figure 3).

Condition-specific dysfunction as measured by the ZCQ showed modest improvements for both treatments. For spacer, the symptom severity and physical function domains improved from 3.3 and 2.6 preoperatively to 2.1 and 1.6 at 24 months, reflecting gains of 37% and 36%, respectively (Figures 4–6). For laminectomy, the median preoperative scores for the symptom severity and physical function domains were 3.5 (range: 3.4–3.8) and 2.7 (range: 2.5–3.3) compared to 24-month median postoperative scores of 2.4 (range: 2.3–3.0) and 1.8 (range: 1.7–2.6), reflecting improvements of 29% (range: 21–34%) and 32% (range: 21–33%), respectively (Figures 4–6).

Table 1. Summary of studies of decompressive laminectomy.

Reference	Study design*	Sample size (n)	Procedure	Outcomes†
Fokter and Yerby (2006) [14]	Retrospective	38	Open decompression	ZCQ
Cavusoglu et al (2007) [12]	One-group pretest-posttest	50	Open decompression	BP, ODI
Malmivaara et al. (2007) [21]	RCT	50	Open decompression	BP, LP, ODI
Kim et al. [2007] [18]	Retrospective	31	Open decompression	BP, LP
Weinstein et al. (2008) [2]	RCT	278	Open decompression	ODI
Haro et al. (2008) [16]	One-group pretest-posttest	42	Open decompression	BP, LP
Pao et al. (2009) [23]	One-group pretest-posttest	50	Microendoscopic decompression	ODI
Celik et al. (2010) [13]	Retrospective	34	Open decompression	BP, LP, ODI
Jakola et al. (2010) [17]	Retrospective	101	Open decompression	BP, LP, ODI
Postacchini et al. (2011) [24]	Retrospective	35	Open decompression	ODI
Gurelik et al. (2012) [15]	RCT	26	Open decompression	ODI
Beyer et al. (2013) [11]	Two-group pretest-posttest	26	Microsurgical decompression	BP, LP, ODI
Son et al. (2013) [27]	Retrospective	31	Open decompression	BP, LP, ODI
Rajasekaran et al. (2013) [25]	RCT	23	Open decompression	BP, LP
Stromqvist et al. (2013) [28]	RCT	50	Open decompression	BP, LP, ZCQ
Liu et al. (2013) [19]	RCT	29	Open decompression	BP, LP
Richter et al. (2014) [26]	Two-group pretest-posttest	31	Microsurgical decompression	BP, ODI
Lonne et al. (2015) [20]	RCT	41	Microsurgical decompression	BP, LP, ODI, ZCQ
Moojen et al. (2015) [22]	RCT	79	Open decompression	BP, LP

* RCT indicates randomized controlled trial
† ZCQ, Zurich Claudication Questionnaire; BP, back pain; ODI, Oswestry disability index; LP, leg pain

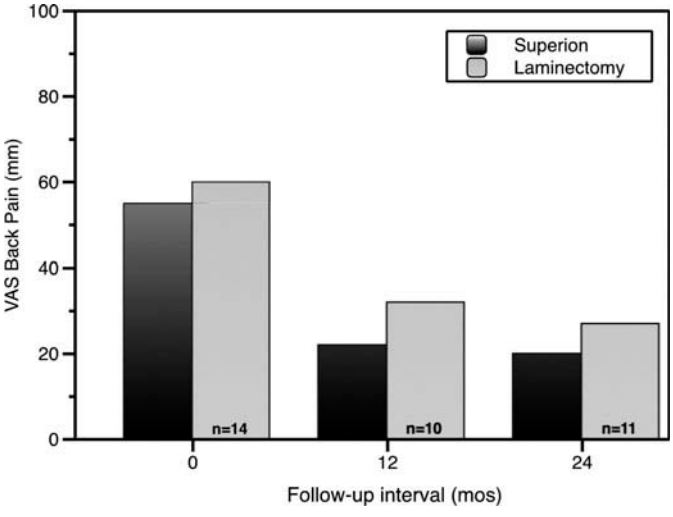

Figure 1. Back pain severity. Preoperative, 12- and 24-month scores for spacer (mean) and laminectomy (median); n refers to number of included studies.

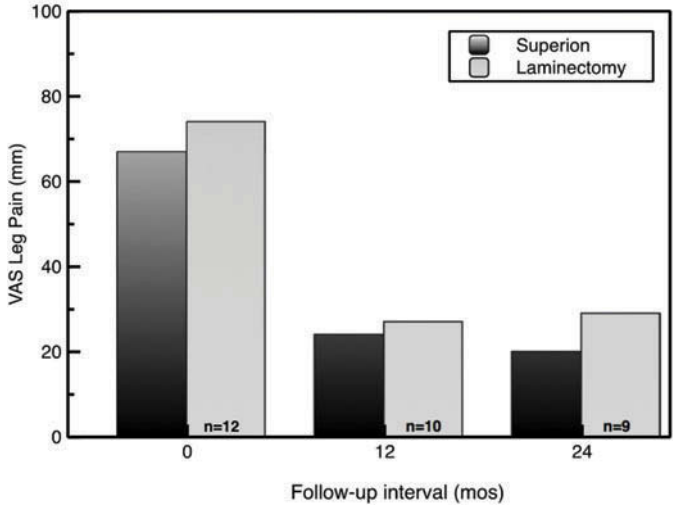

Figure 2. Leg pain severity. Preoperative, 12- and 24-month scores for spacer (mean) and laminectomy (median); n refers to number of included studies.

Discussion

Lumbar stenosis is an increasingly common disorder affecting our aging population with patients suffering from reduced mobility as well as chronic back and leg pain. Decompressive laminectomy is considered the "gold standard" surgical treatment when conservative options are exhausted.[7,29] The long-term results of the SPORT trial reported superiority of

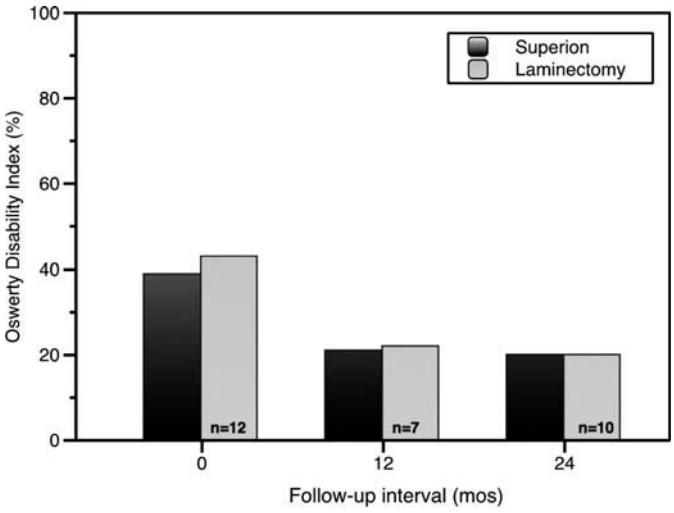

Figure 3. Oswestry disability index. Preoperative, 12- and 24-month scores for spacer (mean) and laminectomy (median); n refers to number of included studies.

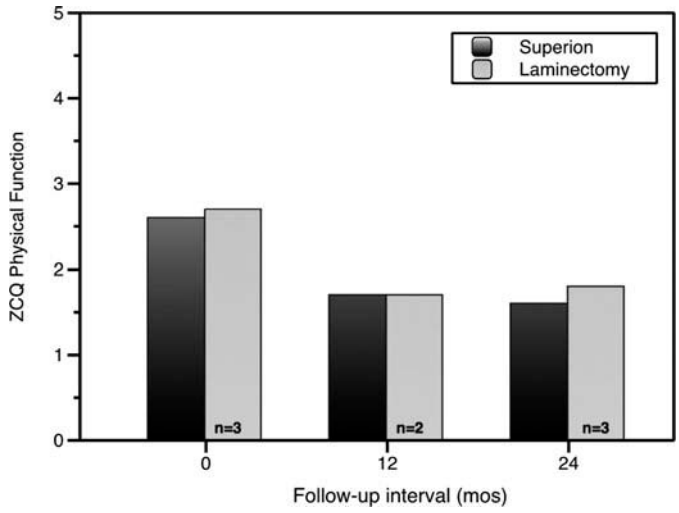

Figure 5. ZCQ physical function. Preoperative, 12 and 24 month scores for spacer (mean) and laminectomy (median); n refers to number of included studies.

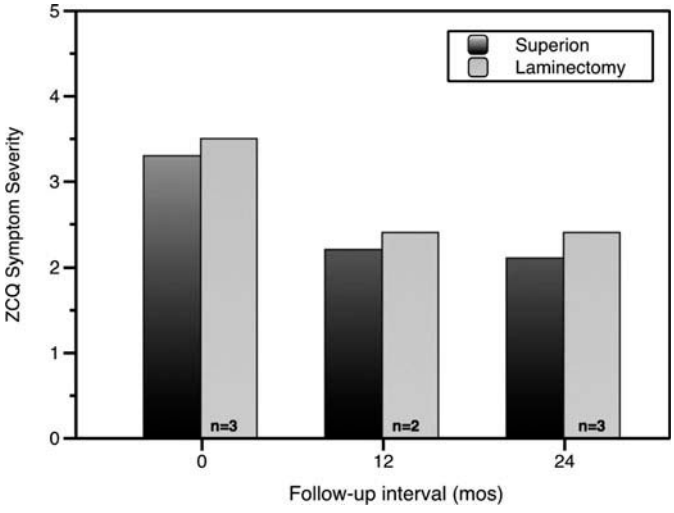

Figure 4. ZCQ symptom severity. Preoperative, 12- and 24-month scores for spacer (mean) and laminectomy (median); n refers to number of included studies.

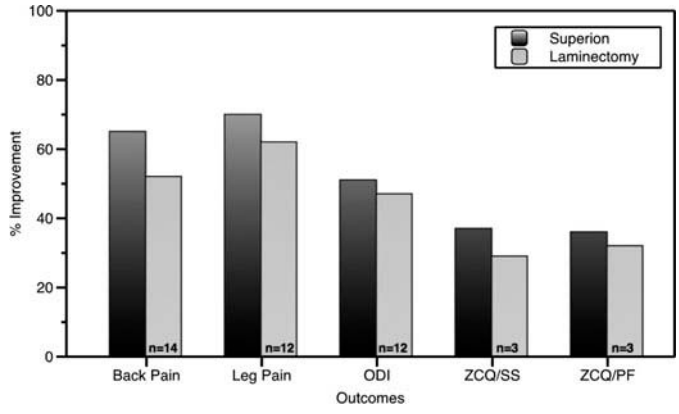

Figure 6. Percentage improvement by outcome measurement. ODI, Oswestry disability index; ZCQ/SS, Zurich Claudication Questionnaire Symptom Severity domain; ZCQ/PF, Zurich Claudication Questionnaire Physical Function domain. n refers to number of included studies.

laminectomy over continued nonoperative management.[2] Interspinous spacer devices offer a less invasive approach with the potential for decreased morbidity in the treatment of moderate lumbar stenosis.

This study demonstrated that intractable symptoms of neurogenic claudication are effectively ameliorated by treatment with an interspinous spacer or traditional decompressive surgery. Robust improvements were realized uniformly across all patient-reported outcomes through 24 months of follow-up for both treatments. These reported gains translate to tangible health benefits for the patient. In fact, in the spacer IDE study group, the percentage of patients that achieved the minimal clinically important level of improvement was 67% for back pain, 76% for leg pain, 63% for ODI and 82% for ZCQ.[6]

Not requiring concomitant surgical decompression, the Superion® is the second "stand-alone" interspinous spacer approved by the FDA and the only one currently available on the US market. Importantly, the implantation procedure does not cause substantial alterations or disruptions to the spinal anatomy which likely reduces the complexity of future surgical options in the event that revision becomes necessary to address progressive degenerative changes and/or reemergence of symptoms. Specifically, the epidural space is not surgically exposed during spacer insertion, whereas a laminectomy decompression

directly opens the epidural space. The surgical exposure of the epidural space is known to routinely produce epidural adhesions around the dural sac and exiting nerve roots, which can cause symptomatic problems.[30,31] Additional treatment and modification of subsequent surgical procedures may be necessary. If device removal is required, the implant can be explanted via the same minimally invasive access as the original implantation procedure. This suggests that interspinous spacers may be considered a reasonable "first-line" option in the continuum of care for the treatment of moderate lumbar spinal stenosis.

The minimization of iatrogenic insult associated with implantation of interspinous spacers significantly reduces the risk of operative adverse events. In a recent review of spinal devices in the Medicare population, higher perioperative complication rates were found in decompression surgeries compared to interspinous spacers.[32] Because of the minimally invasive nature of the surgery, implantation of spacers can be accomplished under local anesthesia or with sedation.

Despite similar levels of clinical effectiveness, two meta-analyses of treatments for spinal stenosis reported that reoperation rates were higher with interspinous spacers than with decompressive laminectomy.[9,10] However, these two interventions are not directly comparable in terms of their indications for use, target population or sequence in the continuum of care. Laminectomy is best reserved for more severely stenotic patients and, indeed, inspection of preoperative outcome scores in the current study consistently showed that patients treated with laminectomy presented with a higher degree of pain and functional impairment at baseline (Figures 1–5). Additionally, the revision procedure itself is notably different between these treatments with laminectomy requiring wide surgical exposure, dissection of extensive scar tissue with significant blood loss and operative risks, and conversion to fusion necessitating bone grafting and insertion of hardware. Alternatively, removal of the spacer can be accomplished with minimal tissue disruption and low surgical risk prior to conversion to a laminectomy. Thus, the spacer device, with its avoidance of epidural scarring, allows the patient to consider a wider choice of potential reoperations and their timing. The differences noted in reoperation rates may, in large part, reflect the ease of conversion (or lack thereof) to the next option in the continuum of care.

In conclusion, this recently FDA-approved stand-alone interspinous spacer offers an effective and safe treatment option for patients suffering from intermittent neurogenic claudication associated with moderate spinal stenosis. It is noteworthy that this review of the historical laminectomy literature failed to show that direct decompression provided superior clinical benefit compared to the indirect decompression provided by the spacer. Treatment with the spacer offers robust and durable symptom relief for at least two years postoperatively. It should be considered in the continuum of care prior to decompressive laminectomy, thereby minimizing the attendant surgical risks while allowing for multiple future options as the degenerative disease progresses.

Expert commentary

Interspinous spacers fill a distinct treatment gap in the continuum of care for patients with moderate degenerative lumbar spinal stenosis. These patients have exhausted conservative care but may be inappropriate candidates for or unwilling to undergo surgical decompressive laminectomy. Because spacers are implanted in a minimally invasive fashion without anatomical disruption, they can be easily removed and converted to laminectomy if symptoms reemerge. This study corroborates previous meta-analyses that found similar clinical benefit provided by both spacers and laminectomy, providing the patient with a minimally invasive option without compromising symptom relief.

Five-year view

Current projections indicate a marked increase in the number of patients afflicted with spinal stenosis. Consequently, there remains a keen interest in minimally invasive treatment options that delay or obviate the need for invasive surgical procedures, such as decompressive laminectomy or fusion. Stand-alone interspinous spacers will likely fill a currently unmet treatment gap in the continuum of care and help to reduce the burden of this chronic degenerative condition on the health care system.

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Key issues

- Lumbar spinal stenosis is a progressively disabling condition that represents the leading cause for spinal surgery in older adults.
- Interspinous spacers offer a minimally invasive treatment option for patients with intermittent neurogenic claudication due to moderate spinal stenosis who have failed conservative care but where surgery is unwarranted or unwanted.
- Both spacer and laminectomy offer similarly robust and durable clinical improvements in claudicant symptoms.
- Use of the spacer may obviate the need for decompressive laminectomy in the majority of patients carefully selected in accordance with the approved indications for use.

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Cost-effectiveness of three treatment strategies for lumbar spinal stenosis: Conservative care, laminectomy, and the Superion interspinous spacer

Scott L. Parker, MD,[1] Louise H. Anderson, PhD,[2] Teresa Nelson, MS,[2] Vikas V. Patel MD, MA, BSME[3]

[1]Department of Neurosurgery, Vanderbilt University Medical Center, Nashville TN, [2]Technomics Research, Minneapolis MN, [3]University of Colorado Hospital, Denver CO

Abstract

Background

Lumbar spinal stenosis 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 adverse event (AE) rates. Interspinous spacers have been developed to offer a less-invasive alternative. The objective of this study was to compare the costs and quality adjusted life years (QALYs) gained of conservative care (CC) and decompressive surgery (DS) to a new minimally-invasive interspinous spacer.

Methods

A Markov model was developed evaluating 3 strategies of care for lumbar spinal stenosis. 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.

Results

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 (.28). The incremental cost-effectiveness ratios (ICER) for Spacers compared to CC was $16,300 and for DS was $15,200.

Conclusions

Both the Spacer and DS strategies are far below the commonly cited $50,000/QALY threshold and produced several times the QALY increase versus CC, suggesting that surgical care provides superior value (cost / effectiveness) versus sustained conservative care in the treatment of lumbar spinal stenosis.

KEYWORDS: COST EFFECTIVENESS, QALY, INTERSPINOUS SPACER, INTERMITTENT NEUROGENIC CLAUDICATION, LAMINECTOMY, LUMBAR SPINAL STENOSIS, DECOMPRESSIVE SURGERY, SUPERION

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Introduction

Lumbar spinal stenosis (LSS) is a condition in which the spinal canal becomes increasingly narrowed from degenerative changes such as facet arthropathy, disc degeneration, spondylolisthesis, and thickening/buckling of the ligamentum flavum; all of which result in compression of the thecal sac and contained nerve roots.[1] LSS is the most common indication for lumbar spine surgery and has an estimated annual incidence of 5 cases per 100,000 individuals.[2] Furthermore, LSS continues to increase in prevalence and is one of the most common reasons for surgery in elderly patients (>65 years old).[3-6] The cost to society in the United States resulting from this disease process has been estimated in the tens of billions of dollars annually.[7,8]

The initial treatment of LSS consists of various non-operative approaches including physical therapy,

pain medications (NSAIDs, mild opioids), and epidural steroid injections, referred to as conservative care (CC) in this study. There is no standardized paradigm for non-operative treatments in patients with LSS; and as such, approaches to management are often guided by clinical judgment of the treating physician. Patients with symptoms refractory to sustained (longer than 6 to 12 weeks) medical management warrant surgical consideration. Open lumbar laminectomy remains the gold standard for surgical decompression in patients with medically refractory LSS and has been shown to have good long-term efficacy.[5,9-13] However, open lumbar laminectomy has been shown to be associated with post-operative complication rates ranging from 12 to 29%, depending on comorbidity status, which is particularly important since LSS is predominantly a disease of the elderly, a demographic inherently associated with higher rates of comorbidities.[14-18]

As a result, less invasive surgical treatment strategies have been explored to manage patients with LSS refractory to conservative care. One such alternative is an interspinous device, which can be implanted between the spinous processes in the lumbar spine. These devices are designed to mechanically limit segmental lumbar extension and thereby maintain the diameter of the spinal canal and neuroforamen at the level of insertion.[19] The clinical effectiveness of an interspinous device compared to conservative care for the treatment of LSS has been previously demonstrated in a prospective, randomized clinical trial.[8] This study evaluates the cost-effectiveness of a next generation interspinous spacer (Superion®, VertiFlex, Inc.) that is significantly less invasive than previous spacers.

Markov models are frequently used for cost-effectiveness analysis.[20,21] The models assume that a patient is always in one of a finite number of discrete health states, called Markov states. Transitions from one state to another are used to represent patient events. Health care costs and utilities can be assigned at each state, and accumulated over the duration of the model. Because the Markov model can represent repetitive events and the time dependence of both probabilities and utilities, it can more accurately represent clinical settings than simpler models. In the current study, we developed a Markov micro-simulation model to compare the clinical effectiveness and cost-utility of comprehensive conservative care (CC), decompressive surgery by laminectomy without fusion (DS), and placement of the Superion interspinous device (Spacer) for the treatment of LSS.

Methods

A Markov model was developed to simulate costs, health outcomes, and incremental cost-effectiveness comparing three *strategies* for treatment of LSS. Each *strategy* included initial and follow-up *treatments*. Within a strategy, if the initial treatment failed, patients received a follow-up treatment. The initial treatments were conservative care (CC), decompressive surgery (DS) or interspinous spacer (Spacer). The index DS did not include fusion. DS with fusion was modeled only as a follow-up treatment after DS or Spacer failure, and only by a portion of patients with failure. The target population was assumed to have moderate symptoms of neurogenic claudication secondary to a confirmed diagnosis of LSS at one or two contiguous levels from L1 to L5, with or without Grade 1 spondylolisthesis, and have completed at least six months of conservative treatment. Data sources used to populate the model came from three sources. DS estimates were from a prospective spinal registry, from which patients that met the target population criteria and received DS without fusion were analyzed. CC estimates were from a previously published paper.[22] The spacer treatment data came from the pivotal FDA IDE trial of the Superion Interspinous Spacer System sponsored by VertiFlex, Inc.[23] The primary outcome measure analyzed was quality-adjusted life years (QALYs) gained. A payer perspective was taken. The payer reimburses the facility and physicians for procedures, but does not make separate reimbursement for implants. The model aggregates the cost of patient care, which includes the index procedure and any follow-up care or repeat procedures. Therefore, the model provides a more complete payer cost estimate than the cost of index procedures alone. All costs were in 2014 US dollars.

Model structure

Each strategy had a similar Markov process. The

Markov process for the CC strategy had seven states (Figure 1). Patients began the simulation in the Conservative Care state. Patients returned to that state in following cycles, although they had a probabilistic chance of treatment failure, which was followed by either DS or Spacer treatment. For patients receiving DS, if DS was successful, the patient moved to the Continue Post-DS state in the next cycle. If DS was unsuccessful, the patient returned to the DS state in the next cycle. Patients remained in the Continue Post-DS state, unless there was a DS failure, when they would return to DS. Similar transitions were followed for patients with Spacer treatment. However, the transition after failed Spacer treatment was to DS. Ninety percent of CC failures transitioned to DS in the base case analysis.

The Markov process for the Spacer strategy had four states (Figure 1, Spacer Model). Patients underwent Spacer Implant in the first cycle. If the implant was successful, the patient moved to the Continue Post-Spacer state in the next cycle. If the implant was unsuccessful, the patient moved to the DS state in the next cycle. Patients in the Continue Post-Spacer state returned to that state in following cycles, although they had a probabilistic chance of moving to DS due to implant failure. After DS, patients moved to the Continue Post-DS state or returned to DS.

Similarly, the Markov process for DS had two states (Figure 1, DS Model). Patients underwent DS in the first cycle. If the treatment was successful, the patient moved to the Continue Post-DS state in the next cycle. If the treatment was unsuccessful, the patient returned to the DS state in the next cycle. Patients in the Continue Post-DS state returned to that state in following cycles, although they had a probabilistic chance of moving to DS due to treatment failure.

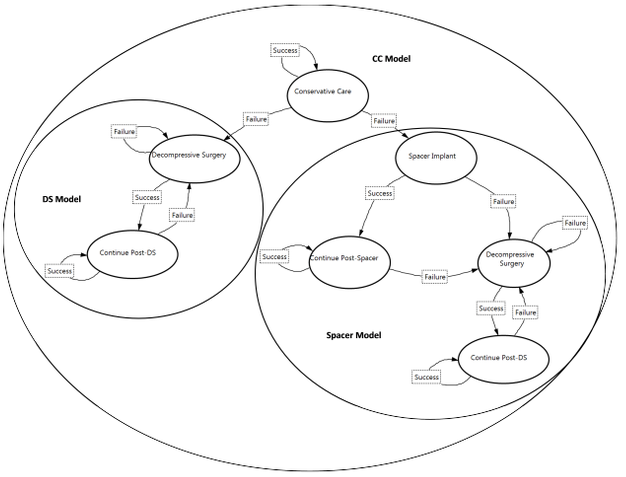

Fig. 1. Markov Models for Conservative Care (CC) Strategy, Spacer Strategy, and Decompressive Surgery (DS) Strategy.

Model Inputs

Estimates of treatment failure rates, adverse event rates, follow-up care utilization, and outcomes were from Parker et al, analysis of institutional registry data, and analysis of the Superion FDA trial data.[22,23] The registry included patient demographics, disease characteristics, and treatment variables assessed prospectively for each case. Baseline, three-month, one-year, and two-year Oswestry Disability Index (ODI), SF-12 quality of life, and follow-up utilization were assessed in phone interviews.[22] Similarly, the trial data included two-year follow-up after implant with the interspinous spacer. The details of this trial have been described in a previous publication.[23]

Costs

Costs included cost of procedures, complications, and follow-up utilization of healthcare resources (physical therapy, chiropractic therapy, epidural steroid injections, diagnostics, and medications). Procedure costs included reimbursements to the physician, anesthesiologist, and facility. CC and DS patient-reported resource utilization data over a two-year period were collected prospectively by telephone interviews. Self-reported instances of medical resource use were multiplied by unit costs for each cost component. Unit costs for office visits, hospitalizations, diagnostic tests, and DS procedures were based on 2012 Medicare national allowable payment amounts and inflated to 2014 using the medical consumer price index (CPI). Medication prices were based on 2012 average wholesale price and inflated to 2014.[22] Follow-up physical therapy utilization for Spacer patients was from the FDA trial data. Follow-up utilization for other services was assumed to be the same as DS patients. The unit costs applied for CC and DS follow-up utilization were applied for Spacer follow-up utilization.

Costs of Spacer and DS fusion procedures were

based on the appropriate DRG and CPT codes. The cost of DS fusion procedure was needed because a portion of patients who failed either their index DS or Spacer went on to have DS with fusion. All Spacer procedures were assumed to be performed in the hospital outpatient setting. Spacer CPT codes were 0171T and 0172T. Cost of DS with fusion was based on reimbursement for DRG 460 and CPT codes 22558, 22585, 22630, 22632, 22851, 22840, 22842. Anesthesiology costs for the Spacer procedure assumed 60 minutes and code 00670. Anesthesiology costs for DS without fusion assumed 180 minutes and code 00630, DS with fusion assumed 180 minutes and code 00670. All DS procedures were assumed to be performed as inpatient. Cost of inpatient rehabilitation was from the Medicare 2014 base rate adjusted for case-mix groups applicable to post-spine surgery patients (0501, 0601, 0901, 2001).[24] The cost was estimated as the average of the case-mix adjusted rates, assuming maximum function and minimum comorbidities.

Quality Adjusted Life Years (QALYs)

QALYs were measured using the SF-6D, estimated from the Mental Component Score (MCS) and Physical Component Scores (PCS) of the SF-12, age, and sex.[25] Individual level SF-12 MCS and PCS were available for the Spacer and DS patients. Summary data were used for the CC patients. For the model, QALYs gained during each quarter post-treatment were estimated by linear interpolation.

Analysis

Data analyses were performed using SAS version 9.4 (SAS Institute, Inc., Cary, NC). To recognize baseline differences in the patient populations that could affect outcomes, QALYs gained and failure rates for each surgical treatment were modeled as a function of baseline ODI and follow-up period. A repeated measures model was used to analyze QALY gains. If a significant relationship between baseline ODI and QALYs gained or failure rates was observed, baseline ODI was retained in the model. Exponential failure rates were estimated for Spacer; a life table method was used for DS. Modeling analyses were performed using TreeAge Pro Suite 2013 (TreeAge Software, Williamstown, MA). The micro-simulation had a two year time horizon, in quarterly cycles, and 10,000 hypothetical patients. Each simulated patient accumulated costs and health outcomes, which were discounted at 3% per year. Results were presented as mean costs, QALYs, and incremental cost-effectiveness ratios comparing surgical strategies to CC strategy. The primary endpoint for the cost-effectiveness analysis was the incremental cost-effectiveness ratio (ICER). To estimate the ICER, average total costs and average QALYs from baseline to 2-years were estimated for conservative care vs. surgical treatment groups. The ICER was defined as the difference in mean total costs between cohorts, divided by the difference in mean QALYs as follows: $ICER = (COST_{Strategy\ A} - COST_{Strategy\ B}) / (QALY_{Strategy\ A} - QALY_{Strategy\ B})$. Sensitivity analysis was conducted on single variables in the standard way, using the 95% confidence interval for the high and low values. Additionally, probabilistic sensitivity analysis, a standard method of integrating uncertainty about many variables simultaneously, was performed.[26]

Results

Patient Comparison

Baseline patient characteristics are shown in Table 1. CC patients had a higher level of disability as measured by ODI (57) compared to the DS cohort (47) and the Spacer cohort (39), $p<0.05$. Differences in ODI were found to be significant predictors of QALYs gained for the Spacer and DS patients, but had no effect on failure rates. QALYs gained for DS and Spacer treatments were estimated after adjusting for baseline ODI. For use in the model, a baseline ODI of 52 was assumed, the average ODI of the CC and DS patients. Age and gender of Spacer (66±9 years, 58% male) and DS (64±11 years, 59% male) patients were similar and assumed to have no significant relationship to QALYs gained or failure rates; therefore no covariate adjustment was performed. CC patients were slightly younger (58±12 years, $p<0.05$) and less likely to be male (40%, $p<0.05$) compared to the DS patients. The SF-12 PCS differed significantly among the groups. The differences were assumed to be highly correlated with the ODI score and therefore the ODI covariate adjustment sufficed to control for these differences. The SF-12 MCS scores were similar across patient groups. Approxi-

mately half of surgeries were one level and there was no difference in number of levels between Spacer and DS cohorts.

Base case values

Base case values of model estimates are shown in Table 2. Quarterly failure rate was highest among CC patients, 4.3% per quarter, and lowest among DS patients, 1.2% per quarter. Spacer patients had a 2.7% failure rate. No adverse events after Spacer implant generated reimbursement outside of the global 90-day payment. Five percent of DS patients experienced an adverse event leading to hospital readmission and nearly four percent were discharged to an inpatient rehabilitation facility after the initial procedure. For the patients requiring secondary decompressive surgery after DS or Spacer failure, the fusion rate was assumed to be 31%, based on the data from the FDA trial.

Probability of any healthcare, medication, or diagnostic utilization for CC patients approached 100% each quarter. In the quarter of the procedure, use of healthcare was lower for Spacer patients compared to DS patients, 45.2% vs. 76.2%, because fewer Spacer patients had outpatient physical therapy. In the quarter of the procedure, 94.4% of DS patients used medications and approximately one-fifth of DS patients had diagnostic testing. Use of medications during follow-up continued for nearly two-thirds of DS patients, but use of healthcare and diagnostic services decreased to 12.9% to 8.8% of patients.

Table 1. Baseline Characteristics

Characteristic	CC *	Spacer†	DS‡	Comparison p-value§		
				CC v Spacer	CC v DS	Spacer v DS
Number of patients	100	189	129	NA	NA	NA
Age, mean (SD)	58 (12)	66 (9)	64 (11)	<0.05	<0.05	NS
Male, %	40	58	59	<0.05	<0.05	NS
ODI, mean (SD)	57 (19)	39 (13)	47 (14)	<0.05	<0.05	<0.05
SF-12 PCS, mean (SD)	31.4 (8.1)	29.2 (8.4)	26.7 (9.4)	<0.05	<0.05	<0.05
SF-12 MCS, mean (SD)	49.2 (12.1)	49.9 (13.1)	48.2 (11.2)	NS	NS	NS
1 Level treated, %	NA	52	45	NS	NS	NS
2 Levels treated, %	NA	48	55			

SD: Standard deviation. *CC: Conservative Care, from Parker et al. 2014. Results from spondylolisthesis and stenosis patients were combined. †Spacer: from ISISS trial, Superion patients. ‡DS: Decompressive Surgery without fusion, from institutional registry. §For continuous variables, a two sample Z-test was used for the pairwise comparisons. For categorical variables, Fisher's exact test was used. A p-value of 0.05 was considered statistically significant. No corrections for multiplicity were applied.

Table 2. Base Case Values.

	Treatments		
	CC	Spacer	DS
Variable	Base Case	Base Case	Base Case
Failure rate, quarterly	4.3%	2.7%	1.2%
1 Level	NA	50.0%	50.0%
2 Levels	NA	50.0%	50.0%
Adverse event*	NA	0.0%	5.4%
Inpatient rehabilitation	NA	0.0%	3.9%
Fusion, secondary treatment[x]			31%
Probability of utilization - Qtr of Procedure			
Healthcare	NA	45.2%	76.2%
Medications	NA	94.4%	94.4%
Diagnostics	NA	22.2%	22.2%
Probability of utilization - FU Quarters			
Healthcare	94.0%	13.1%	12.9%
Medications	100.0%	64.3%	64.3%
Diagnostics	86.0%	8.8%	8.8%
Costs			
Procedure			
1 Level		$7,367	$7,883
2 Levels		$7,683	$8,155
1 Level, fusion[x]		NA	$26,118
2 Levels, fusion[x]		NA	$27,662
Anesthesiology	NA	$386	$454/$567[#]
Inpatient rehabilitation	NA	NA	$9,100
Qtr of Procedure			
Healthcare		$662	$774
Medications		$334	$334
Diagnostics		$333	$333
FU Quarters			
Healthcare	$289	$665	$1,060
Medications	$498	$337	$337
Diagnostics	$162	$870	$870
Adverse Event		NA	$6,770
QALY gained[‡]			
Baseline to 3 mo	0.008	0.111	0.091
3 mo - 6 mo	0.016	0.144	0.173
6 mo - 9 mo	0.016	0.144	0.162
9 mo - 12 mo	0.016	0.144	0.155
After 12 mo	0.016	0.144	0.151

*Adverse Events (AE) that generate additional reimbursement outside of the global payment. Healthcare includes non-surgeon physician visits, physical therapy, chiropractic care, acupuncture. Medications include narcotics, muscle relaxants, NSAIDs, and oral steroids. Diagnostics include MRI scans, CT scans, x-rays, spine injections, and EMGs. Superion patients assumed to have the same level of utilization for non-surgeon physician visits, medications, and diagnostics as decompressive surgery patients. [x]DS with fusion was received by a portion of patients after DS or Spacer failure. [#]Anesthesiology rate for DS without fusion / Anesthesiology rate for DS with fusion. [‡]QALY gained is an annual amount; one-fourth of the value is accumulated each quarter.

Utilities

After adjustment for baseline ODI, QALYs gained after 24 months were 0.016, 0.144, and 0.151 for CC, Spacer, and DS, respectively (Figure 2). The QALYs gained during each quarter after treatment applied in the model are shown in Table 2.

Base-Case Analysis

Average cost per patient was lowest for the CC Strategy ($10,540) and nearly identical for the Spacer and DS strategies ($13,947, $13,958) (Table 3). The CC strategy had the lowest QALY increase (0.06), while the QALY increase from the surgical strategies was 0.27 for the spacer cohort and 0.29 for the DS cohort. Consequently, the incremental cost effective ratios (ICERs) for the surgical strategies compared to CC were similar, $16,302 for the Spacer cohort and $15,231 for the DS cohort.

Sensitivity Analysis

One-variable sensitivity analyses (SA) value ranges and probabilistic sensitivity analysis (PSA) distributions are shown in Table 4. Results from one-variable SA showed that failure rates had the greatest influence on strategy costs. The average cost per patient in the CC strategy was $1100 above or below the base case at the upper and lower failure rates (Figure 3). The percentage of patients with fusion changed the average cost per patient by approximately $700 in either direction. None of the other variables changed the average cost by more than $300. Utility gained was affected by values of the CC and Spacer failure rates and CC and DS utility gain. Over all scenarios, CC strategy utility gain ranged from 0.04 to 0.08.

The average cost per patient in the Spacer strategy was $700 below or $900 above the base case at the upper and lower failure rates (Figure 4). The percentage of patients with fusion changed the average cost per patient by approximately $500 in either direction. None of the other variables changed the average cost by more than $200. Utility gained was affected only by values of the Spacer utility gain, when Spacer strategy utility gain ranged from 0.23 to 0.31. The average cost per patient in the DS strategy was $600 below or $1900 above the base case at the upper and lower failure rates (Figure 5). Adverse event and the inpatient rehabilitation rates changed the average cost per patient by approximately $300 in either direction. Utility gained was affected only by values of the DS treatment utility gain, when DS strategy utility gain ranged from 0.23 to 0.34.

Results of the PSA showed the average cost per patient for the CC strategy ranged from $9000 to $13000, while utility gained ranged from 0.05 to 0.09

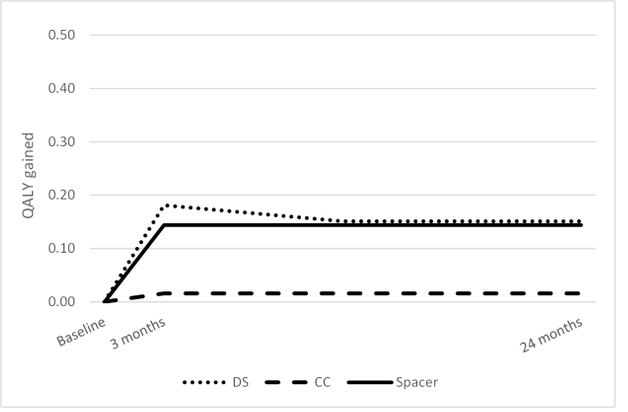

Fig. 2. QALYs gained at three months and 24 months.

Table 3. Base case results.

	Cost	Incremental Cost*	QALYs Gained	Incremental QALYs*	ICER*
CC Strategy	$10,540	NA	0.06	NA	NA
Spacer Strategy	$13,947	$3,408	0.27	0.21	$16,302
DS Strategy	$13,958	$3,418	0.29	0.22	$15,231

CC: Conservative Care; DS: Decompressive Surgery; Spacer: Interspinous spacer. *Compared to CC Strategy

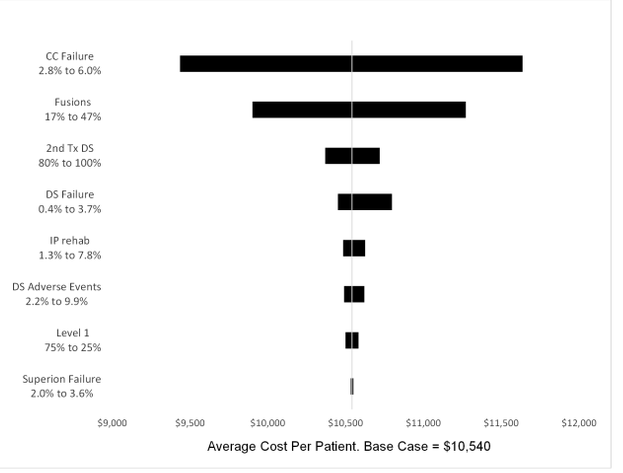

Fig. 3. Conservative Care Strategy one-variable sensitivity analysis.

(Figure 6). The average cost per patient ranged from $12500 to $16200 for the Spacer strategy and $12700 to $17000 for the DS strategy. Utility gained ranged from 0.21 to 0.34 for the Spacer strategy and 0.19 to 0.38 for the DS strategy. The cost-effectiveness plane plots the increase in cost versus the increase in utility gained of the surgery strategies compared to the CC strategy. The surgery strategies showed considerable overlap (Figure 7). On average, the surgeries cost $3400 more per patient than the CC Strategy, with greater QALYs gained of 0.21 to 0.22.

Table 4. One-variable and probabilistic sensitivity analyses, Ranges and Distributions.

	One-Variable Sensitivity Analysis			Probabilistic Sensitivity Analysis
Variable	Lower	Base case	Upper	Distribution (Parameters)
Failure				
CC	0.028	0.043	0.060	Beta (mean=.043, SE=.008)
Spacer	0.020	0.027	0.036	Beta (mean=.027,SE=.004)
DS	0.004	0.012	0.037	Beta (mean=.012,SE=.008)
DS AE rate	0.022	0.054	0.099	Beta (α = 7, β = 122)
IRF discharge rate	0.013	0.039	0.078	Beta (α = 5, β = 124)
Proportion 1 Level	0.25	0.50	0.75	Triangular (0.25,0.50,0.75)
Fusion rate	0.17	0.31	0.47	Beta (α = 11, β = 24)
DS after CC failure	0.80	0.90	1.00	Triangular (0.80,0.90,1.00)
Utility Increase				
CC	0.000	0.016	0.030	Fixed
Spacer	0.120	0.144	0.168	Normal (0.144, 0.013)
DS, 3 mo	0.154	0.181	0.207	Normal (0.181, 0.014)
DS, 12 mo	0.124	0.151	0.179	Normal (0.151, 0.014)

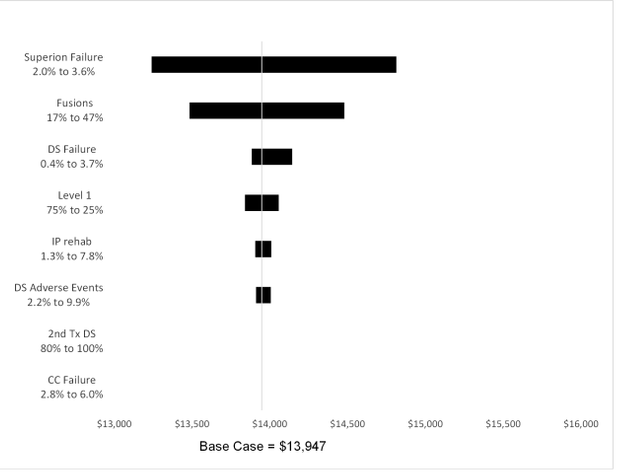

Fig. 4. Spacer Strategy one-variable sensitivity analysis.

Discussion

In the current study, we developed a Markov micro-simulation model to compare the clinical effectiveness and cost-utility of conservative care (CC), decompressive surgery (DS), and placement of a new minimally-invasive interspinous spacer (Spacer) in the treatment of lumbar spinal stenosis (LSS). We observed a significant and virtually identical improvement in quality of life for patients treated with either DS (0.151) or an interspinous spacer (0.144). On the other hand, patients undergoing CC did not

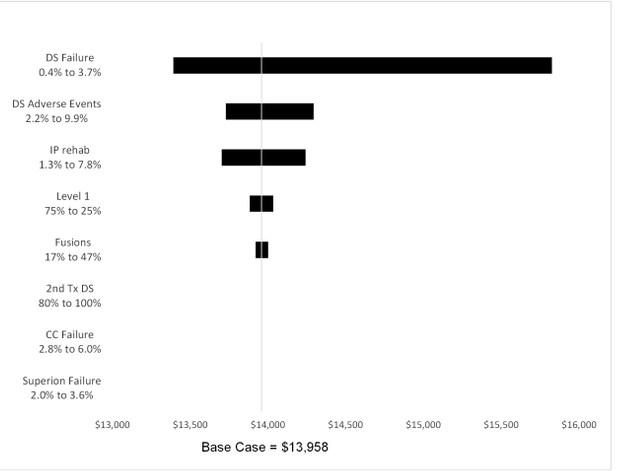

Fig. 5. Decompressive Surgery Strategy one-variable sensitivity analysis.

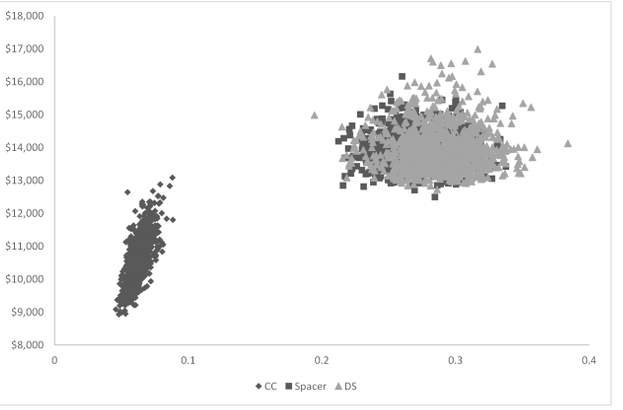

Fig. 6. Decompressive Surgery Strategy one-variable sensitivity analysis.

experience a significant improvement (0.016).

Furthermore, the cost per QALY gained in the DS and Spacer treatments were much lower than CC: $48,131/QALY gained with DS and $51,656/QALY gained with Spacer. Conversely, sustained CC had a very large cost/QALY gained value of $175,667. When directly compared to the CC cohort, both types of surgical management were found to be cost-effective strategies with an incremental cost-effective ratio (ICER) of $15,231 per QALY gained for DS and $16,302 per QALY gained for placement of an interspinous spacer. Compared to the often accepted cost-effective ICER threshold of $50,000/QALY, both of these surgical treatments represent very attractive strategies.

The findings of the current study are consistent with previous evidence reported in the literature pertaining to the cost effectiveness of surgical vs. conservative care treatment for LSS. Burnett et al. constructed a cost-effectiveness model based on a literature review of conservative treatment, decompressive surgery, and use of an interspinous spacer for the treatment of LSS.[27] The authors found both surgical treatments (laminectomy and interspinous spacers) to be more cost-effective than continued conservative care. Similarly, Skidmore et al. calculated the relative cost-effectiveness of the same three treatment strategies for LSS using clinical, quality of life, and economic data from various sources.[18] The authors demonstrated that in LSS patients with moderately impaired physical functioning, treatment with an interspinous spacer was cost-effective compared to conservative care (ICER = $17,894/QALY) and dominant to decompressive lumbar laminectomy (provided better improvement in quality of life and was less expensive).

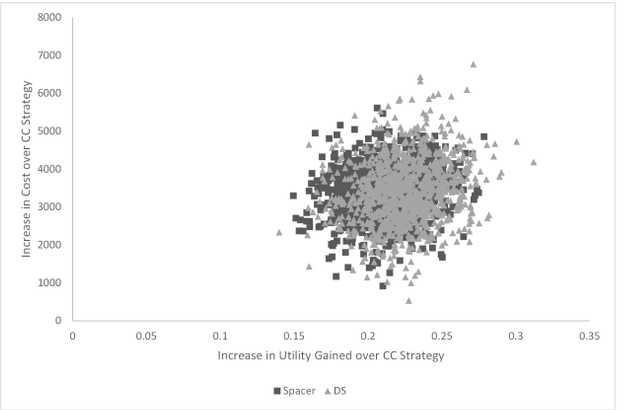

Fig. 7. Cost-effectiveness plane: Increase in cost versus increase in utility gained, Spacer and Decompressive Surgery (DS) Strategies compared to the Conservative Care (CC) Strategy.

In a prospective, randomized controlled trial (SPORT), Tosteson et al. demonstrated that laminectomy for stenosis was cost-effective when compared to medical management with an ICER of $77,600/QALY.[28] This study remains the sole Level 1 evidence for the cost utility of surgical vs. medical management of LSS; however, it should be noted that the high degree of treatment cross-over after randomization likely introduced significant bias into the cost-utility analysis, artificially elevating the mean reported QALY gained in the medical cohort and falsely decreasing the incremental QALY gain and cost-effectiveness of lumbar laminectomy.[29-31] Both of these factors would have the effect of decreasing the observed cost-utility of surgical vs. medical management in this patient population.

Decompressive lumbar laminectomy remains the gold standard surgical intervention for patients with medically refractory LSS; however, it is an open and invasive surgical procedure and has been shown to be associated with post-operative complication rates ranging from 12-29%.[18] As such, there has been substantial interest in developing less invasive treatment options. In a select subset of patients with LSS, placement of an interspinous spacer at the level of stenosis has been shown to be superior to sustained conservative care.[8]

The patient population in which an interspinous spacer may be most effective is those with medically refractory neurogenic claudication from LSS, whose symptoms are significantly relieved during flexion. Furthermore, it is most suitable for patients with moderate symptoms of neurogenic claudication who can still walk at least 50 feet. Patients with a fixed motor deficit, severe disability symptoms, bowel/bladder symptoms, greater than Grade I spondylolisthesis, or previous lumbar surgery at the affected level are not suitable candidates for consideration of an interspinous spacer. Therefore, in the continuum of treatment options for patients with LSS, placement

of an interspinous spacer can be an effective alternative to both sustained conservative care and decompressive surgery in patients with the above characteristics.

The limitations inherent in our study have significant implications for its interpretation. As in many studies using economic models, the treatments were not all randomized against one another. If outcomes are related to patient characteristics, this can cause bias in the comparisons. To address differences in patients at baseline, we 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 our model, do not in themselves cause bias, they do lead to more variable estimates of each treatment's effectiveness, and therefore more uncertainty in the comparisons. This may be especially true during the second year after the procedure, when the original sample size was somewhat reduced. However, our base case failure rates were within the range of other studies. For DS, our failure rate was 9.2% over two years, somewhat higher than 6.8% from Burnett, but similar to 8.9% (35/394) reported from the SPORT study.[27,28] In addition, results from our PSA were similar to the base case analysis, showing higher cost and greater QALYs gained for the surgical strategies compared to the CC strategy (Figure 6 & Figure 7).

Utility was estimated as a function of age, sex, SF-12 MCS and PCS scores. We did not recognize a utility decrement when a patient suffered an AE or incurred an IRF stay; but because these were short term events, they would have had minor impact on 2-year utility. Our QALYS gained by 2 years were also similar to previous studies. For Spacer, our QALY gained was 0.144 which compares to 0.14 from Skidmore and 0.15 from Burnett.[18,27] Similarly, our DS QALY gained was 0.15, which compares to 0.08 from Skidmore and 0.16 from Burnett and 0.17 from Tosteson.[18,27,28]

Finally, our analysis was limited to a two-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.

Conclusions

The current study adds to the evidence supporting decompressive surgery (DS) as a cost-effective strategy relative to sustained conservative care (CC) in treatment of lumbar spinal stenosis. In addition, we provide evidence to support a new Spacer treatment as cost-effective compared to CC and similar to DS in cost and QALYs gained. With ICERs of well under the generally accepted $50,000/QALY, these results suggest that surgical treatments provide superior value (cost / effectiveness) versus sustained conservative care in the treatment of patients with lumbar spinal stenosis.

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Disclosures

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Corresponding Author

Scott Parker MD, 1161 21st Ave. South T4224 MCN, Nashville, TN 37232. slparker7@gmail.com.

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Superion Interspinous Spacer Treatment of Moderate Spinal Stenosis: 4-Year Results

Pierce D. Nunley[1], Vikas V. Patel[2], Douglas G. Orndorff[3], William F. Lavelle[4], Jon E. Block[5], Fred H. Geisler[6]

OBJECTIVE: **To determine 4-year clinical outcomes in patients with moderate lumbar spinal stenosis treated with minimally invasive stand-alone interspinous process decompression using the Superion device.**

METHODS: **The 4-year Superion data were extracted from a randomized, controlled Food and Drug Administration investigational device exemption trial. Patients with intermittent neurogenic claudication relieved with back flexion who failed at least 6 months of nonsurgical management were enrolled. Outcomes 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 4-year follow-up, 89 of the 122 patients (73%) provided complete clinical outcome evaluations.**

RESULTS: **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 (>1.0): 1.49, 1.65, 1.42, 1.12, and 1.46 for ZCQss, ZCQpf, leg pain VAS, back pain VAS, and ODI.**

CONCLUSIONS: **Minimally invasive implantation of the Superion device provides long-term, durable relief of symptoms of intermittent neurogenic claudication for patients with moderate lumbar spinal stenosis.**

INTRODUCTION

Lumbar spinal stenosis is an increasingly common disorder affecting the aging population with patients experiencing reduced mobility and chronic leg and back pain.[1] Decompressive laminectomy is considered the gold standard surgical treatment when conservative options are exhausted.[2] Direct surgical decompression of the neural structures with laminectomy has been shown to offer superior clinical benefit compared with continued nonoperative care[3]; however, the procedure is not without risks. For example, laminectomy is routinely performed under general anesthesia. Although anesthesia-related morbidity and mortality are rare, the incidence of adverse events is markedly higher among the oldest age groups.[4] In studies that directly compared general anesthesia with monitored anesthesia care for the same surgical procedure, mortality was greater and perioperative complications were consistently worse with general anesthesia.[5-7]

As an alternative, interspinous process decompression is a minimally invasive procedure that builds on the concept that back extension is a seminal factor in the causative chain that instigates neurogenic claudication, the cardinal symptom of lumbar spinal stenosis. This procedure involves the implantation of a stand-alone interspinous spacer that functions by serving as a lumbar

Key words
- Decompression
- Interspinous spacer
- Lumbar spinal stenosis
- Neurogenic claudication
- Superion

Abbreviations and Acronyms
FDA: Food and Drug Administration
ODI: Oswestry Disability Index
pf: Physical function
ps: Patient satisfaction
ss: Symptom severity
VAS: Visual analog scale
ZCQ: Zurich Claudication Questionnaire

From the [1]Spine Institute of Louisiana, Shreveport, Louisiana; [2]The Spine Center, University of Colorado Hospital, Denver, Colorado; [3]Spine Colorado, Mercy Regional Hospital, Durango, Colorado; [4]Upstate Bone and Joint Center, East Syracuse, New York; [5]Private practice, San Francisco, California; and [6]Private practice, Chicago, Illinois, USA

To whom correspondence should be addressed: Jon E. Block, Ph.D. [E-mail: jb@drjonblock.com]

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vertebral joint extension blocker to prevent compression of neural elements in extension. The spacer blocks the extension motion without exposure or removal of tissue adjacent to the dura mater or exiting nerves. The implantation procedure does not cause substantial alterations or disruptions to the spinal anatomy adjacent to neural structures. Specifically, the epidural space is not surgically exposed during spacer insertion, whereas laminectomy decompression directly opens the epidural space. The surgical exposure of the epidural space puts the dura mater at risk of injury, and it is known to routinely produce epidural scar, adhesions, and tethering around the dural sac and exiting nerve roots, which can cause symptomatic problems.[8,9]

The Superion is the second "stand-alone" interspinous spacer approved by the U.S. Food and Drug Administration (FDA) and the only device currently available on the U.S. market. The Superion is the only spacer to receive approval from the Centers for Medicare and Medicaid Services for use in surgical procedures in ambulatory surgery centers under monitored care anesthesia. This article reports the 4-year clinical outcomes from the Superion arm of a multicenter, randomized controlled FDA investigational device exemption noninferiority trial of interspinous spacer treatment for moderate lumbar spinal stenosis.

MATERIALS AND METHODS

This study was approved by the institutional review board at each participating site, and patients provided written informed consent before any study-related procedures were performed. The trial was prospectively registered at ClinicalTrials.gov (ClinicalTrials.gov Identifier NCT00692276). The 4-year Superion clinical outcomes were extracted from an FDA investigational device exemption trial comparing 2 interspinous spacers: Superion (Vertiflex, Inc., Carlsbad, California, USA) and X-STOP (Medtronic, Minneapolis, Minnesota, USA). The study methodology, including eligibility criteria, randomization methods, sample size estimates, outcome measures, and statistical analyses, has been detailed previously.[10,11] Briefly, this investigational device exemption trial evaluated the use of interspinous process decompression in the treatment of subjects ≥45 years old with moderate symptoms of intermittent neurogenic claudication secondary to a confirmed diagnosis of moderate degenerative lumbar spinal stenosis at 1 or 2 contiguous levels from L1 to L5. Patients were treated between June 2008 and December 2011 at 31 investigational sites. The randomized study group comprised 391 subjects, including 190 Superion subjects and 201 X-STOP control subjects.

The comparative postoperative findings of the Superion and X-STOP spacers have been reported previously at 6 months,[12] 2 years,[11] and 3 years.[13] The 2-year clinical outcomes establishing noninferiority provided the basis for FDA regulatory approval for the Superion on May 20, 2015.[10] Concurrently in 2015, the X-STOP was withdrawn from commercial distribution in the United States. Owing to this lack of physician and patient availability, we restricted our current analysis to report only the Superion arm of the trial at the 4-year follow-up interval.

The Superion is indicated to treat skeletally mature patients experiencing pain, numbness, or cramping in the legs (intermittent neurogenic claudication) secondary to a diagnosis of moderate degenerative lumbar spinal stenosis, with or without grade 1 spondylolisthesis, confirmed by x-ray, magnetic resonance imaging, or computed tomography evidence of thickened ligamentum flavum, narrowed lateral recess, or central canal or foraminal narrowing. The Superion is indicated for patients with impaired physical function who experience relief in flexion from symptoms of leg, buttock, or groin pain, numbness, or cramping, with or without back pain, and who have undergone at least 6 months of nonoperative treatment.[14] The Superion may be implanted at 1 or 2 adjacent lumbar levels in patients in whom treatment is indicated at no more than 2 levels, from L1 to L5.

For this intended use, moderate degenerative lumbar spinal stenosis is defined as follows:

- 25%–50% reduction in the central canal and/or nerve root canal (subarticular, neuroforaminal) compared with the adjacent levels on radiographic studies, with radiographic confirmation of any one of the following:
  - Evidence of thecal sac and/or cauda equina compression
  - Evidence of nerve root impingement (displacement or compression) by either osseous or nonosseous elements
  - Evidence of hypertrophic facets with canal encroachment
- And associated with the following clinical signs:
  - Moderately impaired physical function (pf) defined as a score of ≥2.0 on the Zurich Claudication Questionnaire (ZCQ)
  - Ability to sit for 50 minutes without pain and to walk ≥50 feet

Of the 190 patients randomly assigned to receive treatment with Superion, 144 (75.8%) were free from reoperation, revision, or supplemental fixation at their index level at 4 years. Within the group of 46 patients requiring reoperation, 41 patients (89%) had the Superion device explanted. The remaining 159 patients (83.7%) were free from epidural steroid injections or nerve block procedures at 4 years. Of 190 patients, 128 (67.4%) were free from reoperation or steroid injection at 4-year follow-up. There were 6 patient deaths, leaving 122 patients with the Superion intact, with no intervening procedures, and actively participating in the postmarket period of this study. At the 4-year follow-up, 89 of the 122 patients (73%) provided complete clinical outcome evaluations, including the ZCQ, leg and back pain severity by visual analog scale (VAS), and the Oswestry Disability Index (ODI). These patients provide the basis for this report.

Responder rates for each outcome were calculated based on a priori definitions of the minimal clinically important difference: ≥0.5-point change for ZCQ symptom severity (ss) and pf, ≤2.5 points for ZCQ patient satisfaction (ps), ≥20 mm for pain VAS, and ≥15 percentage points for ODI. Additionally, improvement in each outcome measure at 4 years compared with preoperative values was assessed graphically and by computing the percentage improvement.

To gauge the practical clinical significance, we also computed the within-group (i.e., Superion arm only) effect size at the 4-year postoperative interval compared with baseline for each clinical outcome separately using the Cohen formula and thresholds.[15,16] The effect size is computed as the standardized

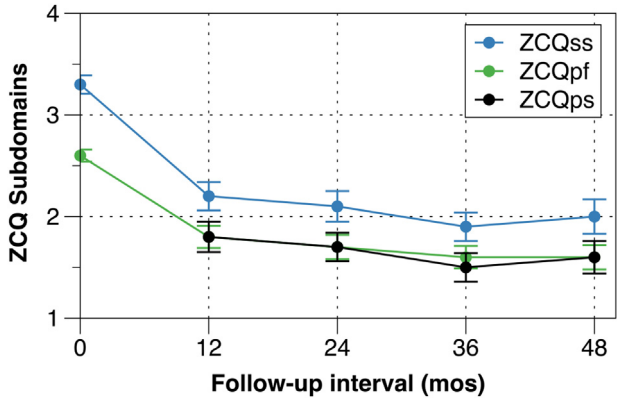

Figure 1. Time course of results for each subdomain of the Zurich Claudication Questionnaire (ZCQ): symptom severity (ss), physical function (pf), and patient satisfaction (ps). Results reported as mean (95% confidence interval).

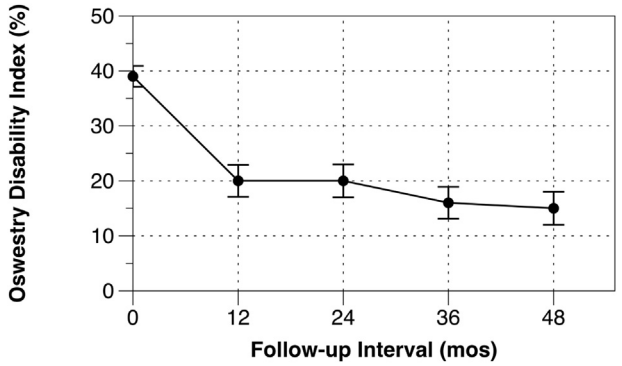

Figure 3. Time course results for Oswestry Disability Index. Results reported as mean (95% confidence interval).

difference between 2 means or, simply put, the mean score (preoperative) − mean score (follow-up)/SD of the change. Effect sizes are typically reported in the range from 0.0 (no effect) to >1.0 (very large effects) with the following thresholds: 0.2 (small effect), 0.5 (medium effect), 0.8 (large effect), >1.0 (very large effect). The effect size calculation provides some normalization for baseline and distribution imbalances.

RESULTS

At 4 years after the index procedure, 75 of 89 patients (84.3%) demonstrated clinical success on at least 2 of 3 ZCQ domains. The corresponding individual component responder rates were 83% (74 of 89), 79% (70 of 89), and 87% (77 of 89) for ZCQss, ZCQpf, and ZCQps; 78% (67 of 86) and 66% (57 of 86) for leg and back pain VAS; and 62% (55 of 89) for ODI. Consistently large improvements were also realized at each annual follow-up interval compared with baseline for the ZCQ (Figure 1), leg and back pain VAS (Figure 2), and ODI (Figure 3). Patients with Superion demonstrated percentage improvements over baseline of 41%, 40%, 73%, 69%, and 61% for ZCQss, ZCQpf, leg pain VAS, back pain VAS, and ODI (all $P < 0.001$) (Figure 4). Within-group effect sizes all were classified as very large (i.e., >1.0): 1.49, 1.65, 1.42, 1.12, and 1.46 for ZCQss, ZCQpf, leg pain VAS, back pain VAS, and ODI (all $P < 0.0001$) (Figure 5).

Long-term clinical follow-up information was also provided by 11 additional patients with Superion who had an intervening epidural steroid injection. Including the results of these patients did not measurably affect the overall clinical findings. For example, the responder rates were 82% (82 of 100), 77% (77 of 100), and 85% (85 of 100) for ZCQss, ZCQpf, and ZCQps. Similarly, responder rates were 77% (75 of 97) for leg pain VAS, 67% (65 of 97) for back pain VAS, and 61% (61 of 100) for ODI.

DISCUSSION

The clinical improvements achieved with Superion treatment reported here corroborate published results after 3 years of follow-up[13] and extend the durability to 4 years postoperatively.

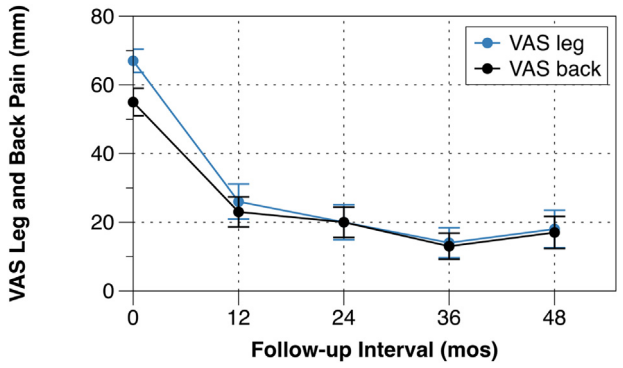

Figure 2. Time course of results for leg and back pain severity. Results reported as mean (95% confidence interval). VAS, visual analog scale.

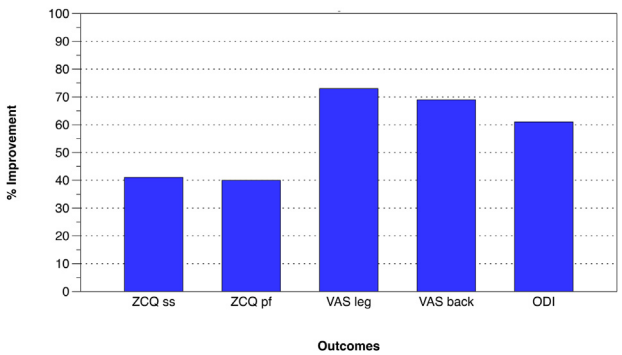

Figure 4. Percentage improvement for each outcome at 4 years compared with preoperative levels. All changes were statistically significant ($P < 0.001$). ZCQ, Zurich Claudication Questionnaire; ss, symptom severity; pf, physical function; VAS, visual analog scale; ODI, Oswestry Disability Index.

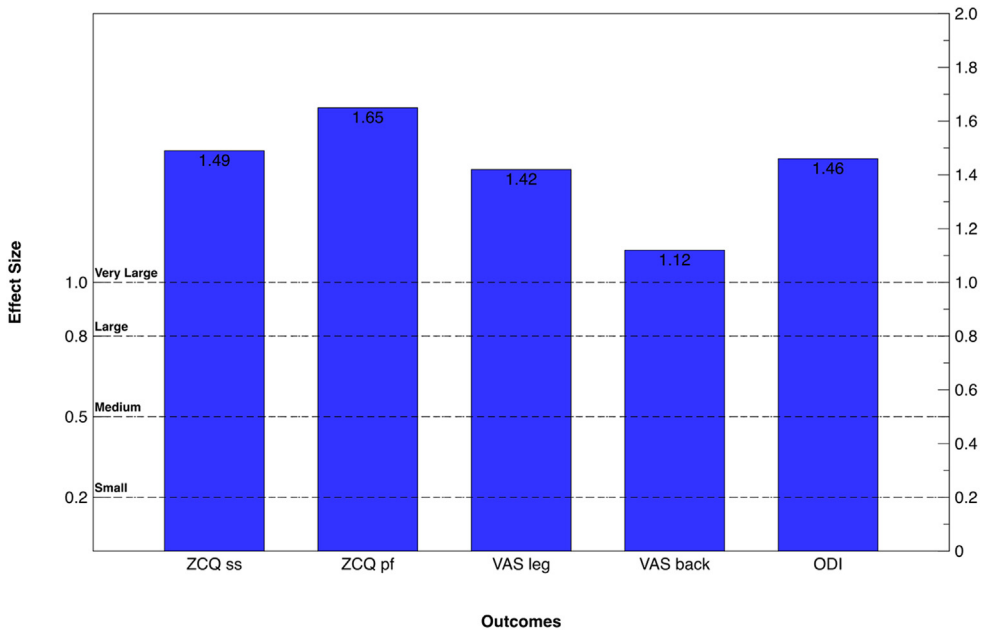

Figure 5. Within-group effect sizes for each outcome at 4 years. All effect sizes exceeded the very large threshold and were highly statistically significant ($P < 0.0001$). ZCQ, Zurich Claudication Questionnaire; ss, symptom severity; pf, physical function; VAS, visual analog scale; ODI, Oswestry Disability Index.

For every outcome, within-group effect sizes at 4 years were >1.0, representing very large effect sizes that were all highly statistically significant.

Approximately one quarter of patients randomly assigned to Superion treatment underwent a reoperation within the 4-year duration of this study. This reoperation rate is intermediate between recently published results from 2 randomized controlled trials of decompressive laminectomy.[17,18] Over a follow-up interval similar to the present study, Forsth et al.[17] reported that 21% of patients underwent revision surgery after decompressive laminectomy in a Swedish trial, whereas Ghogawala et al.[18] observed a reoperation rate of 34% in a U.S. trial.

Although a freedom from reoperation rate of approximately 76% with Superion compares favorably with direct surgical decompression, the revision procedure itself is notably different between these treatments, with laminectomy requiring wide surgical exposure, dissection of extensive scar tissue with significant blood loss and operative risks, and conversion to fusion necessitating bone grafting and insertion of instrumentation. Alternatively, removal of the Superion can be accomplished with minimal tissue disruption and low surgical risk before conversion to a laminectomy. Thus, the Superion device, with its avoidance of epidural exposure, allows the patient to consider a wider choice of potential reoperations and their timing.

At 4-year follow-up, the patients with Superion are now several years subsequent to achieving the primary FDA trial endpoint at 2 years. Consequently, maintaining compulsory patient adherence to annual outcome reporting becomes increasingly challenging, particularly among individuals who continue to do well clinically. That said, including data from 11 patients who had an intervening epidural steroid injection, we captured complete 4-year clinical outcomes in 100 of 190 Superion-treated patients. In contrast, in the X-STOP pivotal FDA trial, Zucherman et al.[19] reported a 93% (93 of 100) follow-up rate at the 2-year primary trial endpoint. However, by 4 years postoperatively, patient-reported outcomes were published for only 18 patients (18%).[20]

CONCLUSIONS

Interspinous spacers fill a distinct gap in the continuum of care for patients with moderate degenerative lumbar spinal stenosis. These patients have exhausted conservative care but may be inappropriate candidates for or unwilling to undergo surgical decompressive laminectomy. Because spacers such as the Superion are implanted in a minimally invasive fashion with relatively minor anatomic disruption, they can be easily removed and converted to a laminectomy if symptoms reemerge. Systematic reviews have found similar clinical benefit provided by both spacers and laminectomy,[21-23] giving patients a minimally invasive option without compromising symptom relief.

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ORIGINAL RESEARCH

Five-year durability of stand-alone interspinous process decompression for lumbar spinal stenosis

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Pierce D Nunley[1]
Vikas V Patel[2]
Douglas G Orndorff[3]
William F Lavelle[4]
Jon E Block[5]
Fred H Geisler[6]

[1]Spine Institute of Louisiana, Shreveport, LA, [2]The Spine Center, University of Colorado Hospital, Denver, CO, [3]Spine Colorado, Mercy Regional Hospital, Durango, CO, [4]Upstate Bone and Joint Center, East Syracuse, NY, [5]Independent Consultant, San Francisco, CA, [6]Independent Consultant, Chicago, IL, USA

Background: 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 treatment option for intermittent neurogenic claudication associated with spinal stenosis.

Methods: This study evaluated the 5-year clinical outcomes for IPD (Superion®) from a randomized controlled US Food and Drug Administration (FDA) noninferiority trial. Outcomes 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).

Results: At 5 years, 84% of patients (74 of 88) demonstrated clinical success on at least two of three 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 four of five clinical outcomes (ie, >1.0; all $P<0.0001$). Seventy-five percent of IPD patients were free from reoperation, revision, or supplemental fixation at their index level at 5 years.

Conclusion: After 5 years of follow-up, IPD with a stand-alone spacer provides sustained clinical benefit.

Keywords: interspinous spacer, lumbar spinal stenosis, Superion, neurogenic claudication, decompression

Introduction

Within 10 years, it is estimated that 64 million older adults will be afflicted with lumbar spinal stenosis, making it the most common indication for spine surgery in individuals older than 65 years.[1,2] This expanding population of patients requires a greater range of treatment options throughout the continuum of care, particularly in the elderly who may not be appropriate candidates for open surgical procedures with the associated risks of general anesthesia.[3] Interspinous process decompression (IPD) is a minimally invasive procedure that can be performed under monitored anesthesia care in an ambulatory surgery center and has been shown to provide comparable clinical performance to decompressive laminectomy for management of symptoms of spinal stenosis.[4,5]

Neurogenic claudication is the cardinal clinical feature of lumbar spinal stenosis, as it limits patients' walking ability and causes a major impact on their quality of life.[6] Intermittent neurogenic claudication is defined as unilateral or bilateral radicular pain

Correspondence: Jon E Block
2210 Jackson Street, Ste 401,
San Francisco, CA 94115, USA
Tel +1 415 775 7947
Fax +1 415 928 0765
Email jb@drjonblock.com

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during walking or standing that is relieved by sitting down or flexing the lumbar spine.[7] Stenotic arthritic degeneration of the lumbar spine causes bony and ligamentous compression of neural structures axially and laterally. Indeed, constriction and impingement of nerves traversing the lateral recess and exiting the foraminal aperture are highly contributory to the most pronounced and aggravating radicular symptoms of stenosis.[8]

IPD employs a stand-alone spacer that functions as an extension blocker to minimize the extent of compression of neural elements, particularly in the lateral recess and foramina.[9] Importantly, insertion of the spacer is performed percutaneously without surgical removal of tissue adjacent to the dura or exiting nerves. There is only one Food and Drug Administration (FDA)-approved stand-alone spacer commercially available in the USA. Herein, we provide the 5-year clinical outcomes for patients with moderate lumbar spinal stenosis treated with this IPD device.

Materials and methods

Clinical outcomes at the 5-year follow-up interval were obtained from the Superion® (VertiFlex, Inc., Carlsbad, CA, USA) treatment arm of a randomized controlled FDA noninferiority trial comparing two interspinous spacers. Methodological details of the study have been published previously.[10,11] This multicenter trial evaluated the use of stand-alone IPD in the treatment of subjects aged 45 or older with moderate symptoms of intermittent neurogenic claudication, secondary to a diagnosis of moderate degenerative lumbar spinal stenosis at one or two contiguous levels from L1 to L5. Three hundred ninety-one subjects met the trial eligibility criteria and were randomized to treatment. The comparative effectiveness of these two spacers and the FDA-approved indications for use for IPD have been reported previously.[12] The current 5-year analysis was restricted exclusively to the Superion arm of the trial.

This trial complied with all US regulatory requirements and was approved by the Institutional Review Board at each participating site (Table S1), and patients provided written informed consent before any study-related procedures were performed. The trial was prospectively registered at ClinicalTrials.gov (NCT00692276).

At the 5-year follow-up interval, 127 patients were free from reoperation (n=48) and/or epidural steroid injection (n=33), and there were 6 deaths, leaving 121 (64%) spacer patients actively participating in the post-market period of this study. Eighty-eight of 121 active spacer patients (73%) provided complete 5-year clinical outcome assessments by the Zurich Claudication Questionnaire (ZCQ), leg and back pain severity by visual analog scale (VAS), and the Oswestry Disability Index (ODI).

Clinical outcome data were analyzed in several ways. Success rates were calculated based on a priori definitions of the minimal clinically important difference: ≥0.5-point change for ZCQ symptom severity (ss) and physical function (pf), ≤2.5 points for ZCQ patient satisfaction (ps), ≥20 mm for pain VAS, and ≥15% points for ODI. Additionally, we computed the percentage improvement in each outcome measure at 5 years compared to preoperative values and displayed these results graphically.

The within-group effect sizes at the 5-year postoperative interval were computed and compared to baseline for each clinical outcome separately using Cohen's formula and thresholds.[13,14] Effect sizes were reported in the range from 0.0 (no effect) to >1.0 (very large effects) with the following thresholds: 0.2 (small effect), 0.5 (medium effect), 0.8 (large effect), and >1.0 (very large effect).

Results

Five years after the index procedure, 74 of 88 patients (84%) demonstrated clinical success on at least two of three ZCQ domains. The success rates for the individual ZCQ domains were 75% (66 of 88), 81% (71 of 88), and 90% (79 of 88) for ZCQss, ZCQpf, and ZCQps, respectively. For leg and back pain VAS, the success rates were 80% (68 of 85) and 65% (55 of 85), respectively, and the rate was 65% (57 of 88) for ODI.

There was substantial improvement at each annual follow-up interval compared to baseline for the ZCQ (Figure 1), leg and back pain VAS (Figure 2), and ODI (Figure 3). Spacer patients demonstrated percentage improvements over baseline

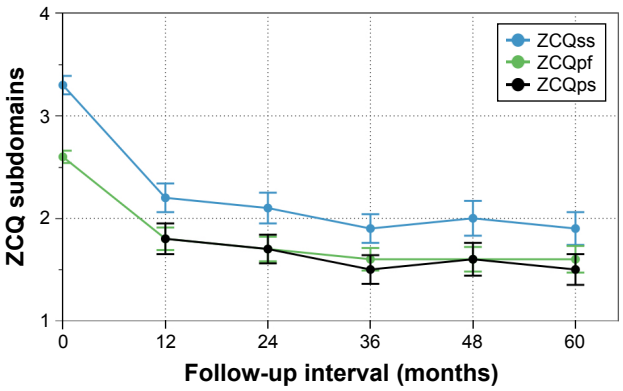

Figure 1 Time course of results for each subdomain of the ZCQ: ss, pf, ps.
Note: Results reported as mean (95% CI).
Abbreviations: pf, physical function; ps, patient satisfaction; ss, symptom severity; ZCQ, Zurich Claudication Questionnaire.

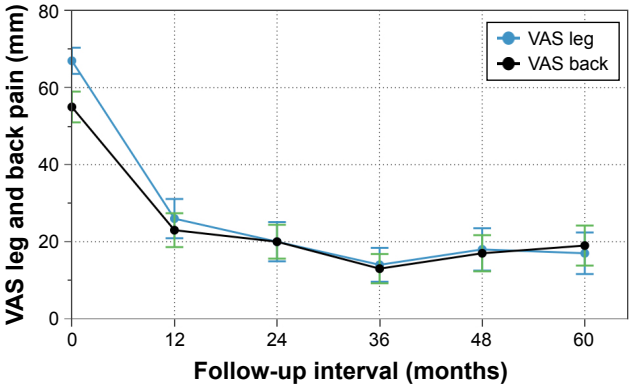

Figure 2 Time course of results for leg and back pain severity by VAS.
Note: Results reported as mean (95% CI).
Abbreviation: VAS, visual analog scale.

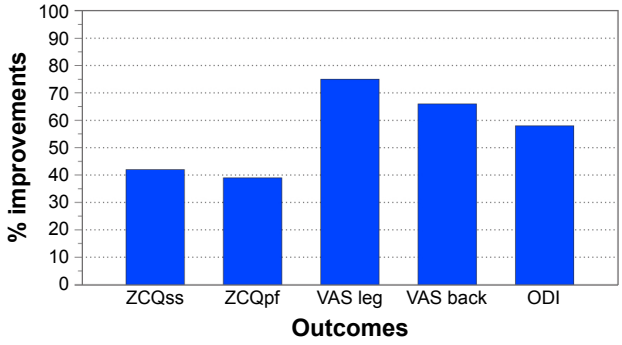

Figure 4 Percentage improvement for each outcome at 5 years compared to preoperative levels.
Note: All changes were statistically significant ($P<0.001$).
Abbreviations: ODI, Oswestry Disability Index; pf, physical function; ss, symptom severity; VAS, visual analog scale; ZCQ, Zurich Claudication Questionnaire.

of 42%, 39%, 75%, 66%, and 58% for ZCQss, ZCQpf, leg and back pain VAS, and ODI, respectively (all $P<0.001$), as shown in Figure 4. Within-group effect sizes were classified as very large for four of five clinical outcomes (ie, >1.0): 1.35, 1.40, 1.32, 0.97, and 1.37 for ZCQss, ZCQpf, leg and back pain VAS, and ODI, respectively (all $P<0.0001$), as shown in Figure 5.

Of the 190 patients randomized to receive treatment, 142 (75%) were free from reoperation, revision, or supplemental fixation at their index level at 5 years. Notably, there was a discernible trend toward decreasing risk of reoperation over time with the majority of revisions occurring during the initial 2 years of observation with annual percentage increments as follows: 27 (14.2%), 11 (5.8%), 3 (1.6%), 6 (3.2%), and 1 (0.5%) during years 1, 2, 3, 4, and 5, respectively.

Discussion

It has been estimated that ~40% of patients with lumbar spinal stenosis become refractory to conservative care and will ultimately require decompression surgery within 10 years to manage persistently worsening symptoms.[15] Moreover, while laminectomy effectively decompresses the offended neural elements providing symptom relief, it can destabilize the spine, eventually leading to re-emergence of symptoms requiring reoperation with instrumented fusion. A recent randomized controlled trial reported that one-third of laminectomy patients required reoperation with fusion within 4 years.[16] This rate of reoperation rate after laminectomy is comparable to a 28% rate reported from a large Washington state administrative database.[17] Treatment of recalcitrant symptoms of neurogenic claudication with an interspinous spacer may significantly delay or obviate completely the need for decompressive laminectomy as well as the downstream risk of revision surgery with instrumented fusion.

This is the first report to document the long-term clinical durability of stand-alone interspinous spacer decompression for lumbar spinal stenosis through 5 years of monitored follow-up. For the 75% of spacer patients who have remained free of reoperation with an intact implant, the clinical results

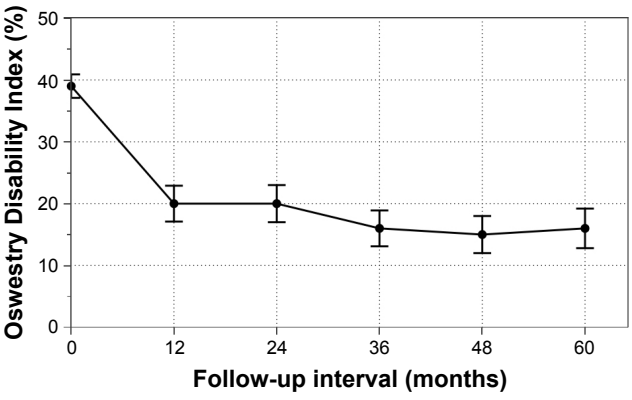

Figure 3 Time course results for the Oswestry Disability Index.
Note: Results reported as mean (95% CI).

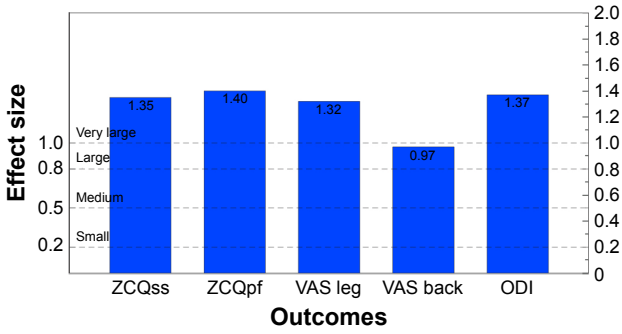

Figure 5 Within-group effect sizes for each outcome at 5 years.
Note: Effect sizes for four of five outcomes exceeded the very large threshold and all effect sizes were highly statistically significant ($P<0.0001$).
Abbreviations: ODI, Oswestry Disability Index; pf, physical function; ss, symptom severity; VAS, visual analog scale; ZCQ, Zurich Claudication Questionnaire.

continue to be impressive, with almost 85% of patients achieving success on at least two of three ZCQ domains. Leg pain symptom amelioration remains most notable with an average improvement of 75% at 5 years over preoperative values. This suggests that the spacer continues to offer sufficient indirect decompression of neural structures in the lateral recesses and foramina to suppress claudicant and radicular symptoms.

Thirty-eight of 48 (79%) spacer patients underwent reoperation within the initial 2 years of postoperative observation. Of the remaining 10 reoperations, only 1 occurred during the fifth year of observation, suggesting a decreasing risk of revision surgery with time. This implies that patients who demonstrate early clinical improvement with spacer implantation will maintain that benefit over time. Clinical failures after spacer treatment can be identified early in the postoperative time course and these patients can be offered other surgical options. In contrast, reoperation rates after laminectomy tend to increase with time.[16] Consequently, early clinical success may not be sustained in the long term, as outcomes eventually deteriorate due to the untoward effects of laminectomy-induced spinal instability, necessitating a complex instrumented fusion procedure to provide stabilization.

Because the IPD implantation procedure is performed in a minimally invasive fashion and causes only minor anatomic disruption, the full range of surgical options remains available if a revision becomes necessary to manage re-emergence of symptoms. Thus, with simplicity of the operative procedure, rapid patient recovery, low surgical risk of complications, and long-term clinical durability, IPD remains a viable treatment option for stenosis patients.

Conclusion

After 5 years of postoperative follow-up, IPD with a standalone spacer provides sustained clinical benefit. Its use is indicated for patients with intermittent neurogenic claudication associated with moderate lumbar spinal stenosis.

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Author contributions

All authors contributed toward data analysis, drafting and critically revising the paper and agree to be accountable for all aspects of the work.

Disclosure

JB is an independent advisor to VertiFlex. The authors report no other conflicts of interest in this work.

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Supplementary material

Table S1 Site list of institutional review board (IRB) information

Investigators/investigational sites				
Site	**Doctor**	**IRB site approved address**	**IRB address**	**IRB Chairman**
01	Pierce Nunley, MD 318-629-5555 (Site inactive)	Spine Institute of Louisiana 1500 Line Avenue, Suite 200 Shreveport, LA 71101 *Specialist Hospital of Shreveport 1500 Line Avenue, Suite 206 Shreveport, LA 71101	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
02	Robert Jackson, MD 949-588-5800 (Site inactive)	Orange County Neurosurgical Associates 23961 Calle de la Magdalena, Suite 504 Laguna Hills, CA 92563 *Saddleback Memorial Medical Center 24451 Health Center Drive Laguna Hills, CA 92563	Office of Research Administration Van Camp Center 2625 Pasadena Ave Long Beach, CA 90806 MHS Research Council-Mailing Address 2801 Atlantic Avenue Long Beach, CA 90806	Edward Quilligan, MD 562-933-9574
04	Warren Yu, MD 202-498-2105 (Site inactive)	George Washington University 2150 Pennsylvania Avenue, NW Suite 7-416 Washington, DC 20037	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Paul Newton 800-562-4789
08	Vikas Patel, MD 720-848-1980 (Site inactive)	Anschutz Outpatient Pavilion 1635 North Ursula Street MS F722, Box 6510 Aurora, CO 80045 *University of Colorado Hospital Anschutz Medical Campus 12605 East 16th Avenue Aurora, CO 80045 Lone Tree Health Center 9548 Park Meadows Drive Lone Tree, CO 80124	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
10	Vito Loguidice, MD 610-252-1600 (Site inactive)	Coordinated Health Inc., 3100 Emrick Blvd., Bethlehem, PA 18020 Orthopedic Associates of Greater Lehigh Valley 755 Memorial Parkway Phillipsburg, NJ 08865 *Warren Hospital 185 Roseberry Street Phillipsburg, NJ 08865	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115 Warren Hospital IRB 185 Roseberry Street Phillipsburg, NJ 08865 (IRB inactive)	Currien MacDonald 800-562-4789 Dr Frank Gilly 908-859-6700 inactive
11	Richard Ozuna, MD 978-818-6350 (Site inactive)	Sports Medicine North One Orthopedics Drive, 2nd Floor Peabody, MA 01960 *Orthopedic Surgical Center of the North Shore One Orthopedics Drive Peabody, MA 01960	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
13	Richard Tallarico, MD 315-464-8622 (Site inactive)	Upstate Bone and Joint Center 6620 Fly Road, Suite 200 East Syracuse, NY 13057 SUNY University of New York 750 East Adams Street, Syracuse, NY 13210-2375 *Upstate Orthopedics Ambulatory Surgery Center 6620 Fly Road, Suite 300 Syracuse, NY 13057	SUNY University of New York Institutional Review Board Office 750 East Adams Street, Syracuse, NY 13210-2375	Stephen L Graziano, MD 315-464-4317
14	Ralph Liebelt, MD 919-220-5255 (Site inactive)	Triangle Orthopedics Associates, PA 120 William Penn Plaza Durham, NC 27704 *Granville Medical Center 1010 College Street Oxford, NC 27565 North Carolina Specialty Hospital 3916 Ben Franklin Blvd., Durham, NC 27704 Triangle Orthopedic Associates, PA 103 Professional Park Drive Oxford, NC 27565	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
15	Thomas Haley, DO 610-275-7013 (Site inactive)	Performance Spine and Sports Physicians, PC 1603 East High Street, Suite C Pottstown, PA 19464 2 Lawnton Road, East Norriton, PA 19401	Pottstown Memorial Medical Center IRB 1600 East High Street, Pottstown, PA 19464	James T Guille, MD 610-327-7000 Main contact below

(*Continued*)

Table S1 (*Continued*)

Investigators/investigational sites				
Site	**Doctor**	**IRB site approved address**	**IRB address**	**IRB Chairman**
		*Pottstown Memorial Medical 1600 East High Street, Pottstown, PA 19464		Courtney Clemente IRB Coordinator 610-327-7000
17	Michael Hisey, MD 940-382-2204 (Current; Site inactive) William Bradley, MD 972-608-5000 (Previous)	Texas Back Institute 2817 South Mayhill Road, Suite 100 Denton, TX 76208 *Texas Back Institute, Plano 6020 West Parker Road, Suite 200 Plano, TX 75093 Texas Back Institute, Rockwall 1005 West Ralph Hall Parkway, Suite 227 Rockwall, TX 75032 Texas Back Institute 400 West Arbrook Arlington, TX 76014 Texas Back Institute, Mansfield 2800 East Broad Street, Suite 522 Mansfield, TX 76063 Texas Health Center for Diagnostics and Surgery 6020 West Parker Road, Plano, TX 75093	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Currien MacDonald 800-562-4789
18	Scott Kitchel, MD 541-284-0530 (Site inactive)	NeuroSpine Institute, LLC 74-B Centennial Loop, Suite 300 Eugene, OR 97401 *NeuroSpine Institute, LLC 74-B Centennial Loop, Suite 100 Eugene, OR 97401 NorthWest NeuroSpine Institute 74-B Centennial Loop, Suite 200 Eugene, OR 97401	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
19	Carl Lauryssen, MD 310-358-2490 (Site inactive)	Neurosurgical Spine Institute 8201 Beverly Hills Blvd., Suite 405 Los Angeles, CA 90048 *Olympia Medical Center 5900 West Olympic Boulevard Los Angeles, CA 90036	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Lucille Broberg 800-562-4789
20	Jeffery Roh, MD 206-302-0702 (Site inactive)	ProOrtho 901 Boren Avenue, Suite 900 Seattle, WA 98104 ProOrtho 12333 NE 130th Lane, Suite 400 Kirkland, WA 98104 Evergreen Medical Center 12040 Northeast 128th Street, Kirkland, WA 98034 *Orthopedics Intl. Ambulatory Surgery Center 600 Broadway, Suite 460 Seattle, WA 98122	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Currien MacDonald 800-562-4789
23	Reginald Davis, MD 443-849-4270 (Site inactive)	Greater Baltimore Neurosurgical Associates Physicians Pavilion North 6535 N Charles Street, Suite 600 Baltimore, MD 21204 *Greater Baltimore Medical Center Institutional Review Board 6701 North Charles Street Baltimore, MD 21704	Greater Baltimore Medical Center Institutional Review Board 6701 North Charles Street, Baltimore, MD 21704	Philip Levin, MD 443-849-2379
24	Bernard Guiot, MD 720-638-7500 (Site inactive)	Neurosurgery One 7780 S Broadway, Suite 350 Littleton, CO 80122 *Porter, Littleton, and Parker Adventist Hospital 2525 South Downing Street, Denver, CO 80210	Porter, Littleton, and Parker Adventist Hospital Joint IRB 2525 South Downing Street, Denver, CO 80210	Nathaniel Hibbs, DO 303-778-2554
26	Kevin Shrock, MD 954-764-8033 (Site inactive)	Shrock Orthopedic Research, LLC 1414 Southeast 3rd Avenue Ft. Lauderdale, FL 33316 Behnam Myers, DO 3850 Sheridan Street Hollywood, FL 33021	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Paul Newton 800-562-4789

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Table S1 (*Continued*)

Investigators/investigational sites				
Site	**Doctor**	**IRB site approved address**	**IRB address**	**IRB Chairman**
		Anthony Hall, MD 1222 South University Drive Plantation, FL 33324 *University Hospital and Medical Center 7201 North University Drive Tamarac, FL 33321		
27	Guy Lee, MD 215-588-1510 (Site inactive)	Abington Orthopedic Specialists, PC Rothman Institute (current) 2400 Maryland Road, Suite 20 Willow Grove, PA 19090 *Abington Memorial Hospital 1200 Old York Road, Abington, PA 19001-3788	Abington Memorial Hospital IRB 1200 Old York Road, Abington, PA 19001-3788	Chris Christensen III, DO. 215-481-7467
28	David Wiles, MD 423-232-8301 (Site inactive)	*East Tennessee Brain & Spine Center 701 Med Tech Parkway, Suite 300 Johnson City, TN 37604	East Tennessee State University VA Office for the Protection of Human Research Box 70565 Johnson City, TN 37614	George Youngbery, MD 423-439-6053
29	Edward Dohring, MD 602-953-9500 (Current; Site inactive) Daniel Lieberman, MD 602-256-2525 (Previous)	The Spine Institute of Arizona 9735 North 90th Place Scottsdale, AZ 85258 Arizona Center for Neurosurgery 3300 N. Central Avenue, Suite 2550 Phoenix, AZ 85020 Ali Araghi, DO The CORE Institute-North Phoenix 18444 North 25th Ave, Suite 210 Phoenix, AZ 85023 CORE Institute 14520 West Granite Valley Drive Sun City West, AZ 85375 *Surgical Specialty Hospital of Arizona 6501 North 19th Avenue Phoenix, AZ 85015	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnnette 800-562-4789
30	George Rappard, MD 232-913-4718 (Site inactive)	Brain and Spine Institute 6200 Wilshire Blvd., Suite 806 Los Angeles, CA 90048 *California Spine Institute 1001 Newbury Road Newbury Park, CA 91320 Glendale Adventist Medical Center 1509 Wilson Terrace Glendale, CA 91206 *Olympia Medical Center 5900 West Olympic Blvd., Los Angeles, CA 90036	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
31	Harold Hess, MD 913-491-3344 (Site inactive)	Johnson County Spine 8575 West 110th Street, Suite 205 Overland Park, KS 66210 *Menorah Medical Center 119th and Nall Overland Park, KS 66204	Patient Advocacy Council, Inc. 601 Bel Air Blvd., Suite 315 Mobile, AL 36606 251-479-5472	James V Roberts, Jr Attorney at Law Ph 251-479-5472
32	Peter Whang, MD 203-785-7132 (Site inactive)	Yale University Yale Physicians Building PO Box 208071 New Haven, CT 06520-8047 *Yale University 800 Howard Avenue New Haven, CT 06520-8071 48 Wellington Road, Milford, CT 06471	Human Investigational Committee 55 College Street, New Haven, CT 06510	Maurice Mahoney, MD, JD 230-785-4688
33	Douglas Orndorff, MD 970-882-9500 (Site inactive)	Durango Orthopedic Associates, PC Spine Colorado 1 Mercado Street, Suite 200 Durango, CO 81301 *Mercy Regional Medical Center 1010 Three Springs Blvd., Durango, CO 81301	Mercy Regional Medical Center 1010 Three Springs Blvd, Durango, CO 81301	John AK Boyd, MD
34	Mark Hollmann, MD 386-734-3710 (Site inactive)	Florida Research Associates, PA 740 West Plymouth Avenue Deland, FL 32720 Florida Orthopaedic Associates, PA 1053 Medical Center Drive, Suite 101 Orange City, FL 32763	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789

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Investigators/investigational sites				
Site	**Doctor**	**IRB site approved address**	**IRB address**	**IRB Chairman**
		*Florida Hospital Fish Memorial 1053 Medical Center Drive Orange City, FL 32763		
35	Jeffery Baron, MD 520-784-60276 (Site inactive)	Tucson Orthopaedic Institute, PC 5301 East Grant Road, Tucson, AZ 85712	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
		*Tucson Medical Center 5301 East Grant Road Tucson, AZ 85712	TMC Human Research Committee (IRB) 5301 East Grant Road, Tucson, AZ 85712	Carlos A Flores, MD 520-324-5512 inactive
36	Harel Deutsch, MD 312-942-6644 (Site inactive)	RUSH University Medical Center University Neurosurgery 1725 West Harrison, Suite 970 Chicago, IL 60612	RUSH University Medical Center Research and Clinical Trials Administration 1653 West Congress Parkway Chicago, IL 60612-3833	Allen Korenblit, MD, CIP 312-942-5498
		*RUSH University Medical Center 1653 West Congress Parkway, Chicago, IL 60612		
37	Kenneth Kopacz, MD 973-226-2725 (Site inactive)	Spine Care and Rehabilitation, Inc. 556 Eagle Rock Avenue Roseland, NJ 07068	Department of Medical Education St Barnabas Medical Center 94 Old Short Hills Road, Livingston, NJ 07039	Gregory J Rokosz, DO, JD 973-322-5048
		*St Barnabas Medical Center 94 Old Short Hills Road, Livingston, NJ 07039		
38	Richard Salib, MD 952-814-6600 (Site inactive)	Institute for Low Back and Neck Care 3001 Metro Drive, Suite 330 Bloomington, MN 55425	Schulman Associates, IRB 4445 Lake Forest Drive, Suite 300 Cincinnati, OH 45242	Julie Blasingim 513-761-4100
		*Allina Health System 800 East 28th Street Minneapolis, MN 55407	Allina Hospital & Clinics IRB 2925 Chicago Avenue Minneapolis, MN 55440	Yvonne Rumsey 612-262-4927 inactive
39	Raphael Davis, MD 631-444-7925 (Site inactive)	*SUNY Stony Brook HSC 12-80 Neurosurgery Stony Brook, NY 11794-8122	CORIHS Stony Brook University Stony Brook, NY 11794B Stony	Prof Harold Carlson 631-632-9036
40	Casey O'Donnell, DO 401-490-7530 (Site inactive)	New England Center for Clinical Research, Inc. 1681 Cranston Street, Suite C Cranston, RI 02920	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Theodore Schultz 800-562-4789
		*Our Lady of Fatima Hospital 200 High Service Avenue North Providence, RI 02919		
41	Timothy Deer, MD 304-347-6120 (Site inactive)	The Center for Pain Relief, Inc. 400 Court Street, Suite 100 Charleston, WV 25301	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Lucille Broberg 800-562-4789
		*Saint Francis Hospital 333 Laidley Street Charleston, WV 25301		
42	Robert Wailes, MD 760-941-2600 (Site inactive)	Pacific Pain Medicine Consultants 3998 Vista Way, Suite 106 Oceanside, CA 92056	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
		*Pacific Surgery Center 3998 Vista Way Oceanside, CA 92056		
43	John Regan, MD 310-881-3730 (Site inactive)	Spine Group of Beverly Hills 8929 Wilshire Blvd., Suite 302 Beverly Hills, CA 90211	Western Institutional Review Board (WIRB) 1019 39th Avenue, SE Suite 120 Puyallup, WA 98374-2115	Viveca Burnette 800-562-4789
		*Olympia Medical Center 5900 West Olympic Blvd., Los Angeles, CA 90036		

Notes: Primary treatment site, *denotes a secondary clinical site.

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CLINICAL TRIAL REPORT

Interspinous process decompression is associated with a reduction in opioid analgesia in patients with lumbar spinal stenosis

This article was published in the following Dove Press journal:
Journal of Pain Research

Pierce D Nunley[1]
Timothy R Deer[2]
Ramsin M Benyamin[3]
Peter S Staats[4]
Jon E Block[5]

[1]Spine Institute of Louisiana, Shreveport, LA 71101, USA; [2]Center for Pain Relief, Charleston, WV 25301, USA; [3]Millennium Pain Center, Bloomington, IL 61704, USA; [4]National Spine and Pain Centers, Rockville, MD 20852, USA; [5]Jon Block, San Francisco, CA 94115, USA

Background: Lumbar spinal stenosis (LSS) causes significant pain and functional impairment, and medical management has increasingly included the prescription of opioid-based analgesics. Interspinous process decompression (IPD) provides a minimally-invasive treatment option for LSS.
Methods: 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 (Vertiflex Inc., Carlsbad, CA USA). Data were obtained from the Superion-treatment arm of a randomized controlled noninferiority 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, we determined opioid-medication prevalence among subjects with a history of opioid use.
Results: 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.
Conclusion: Stand-alone IPD is 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.

Keywords: interspinous spacer, Superion, lumbar spinal stenosis, opioids, neurogenic claudication, indirect decompression

Introduction

Lumbar spinal stenosis (LSS) is a common degenerative condition that causes significant pain, disability, functional impairment, and diminished quality of life.[1–5] The clinical feature most commonly attributed to LSS is neurogenic claudication that involves leg symptoms encompassing the buttocks, groin, and anterior thigh, as well as radiating pain down the posterior aspect of the leg to the feet.[3,6] The discomfort associated with LSS is often described as a cramping or burning feeling. Symptoms of neurogenic claudication can be distributed unilaterally or bilaterally, and the patient may suffer concomitant back pain, although leg pain and discomfort are usually more bothersome.[7]

A distinguishing clinical attribute of neurogenic claudication is its relationship to the patient's posture, where lumbar extension increases and flexion decreases pain onset and severity. Symptoms progressively worsen when standing or walking, and are relieved

Correspondence: Jon E Block
Jon Block,
2210 Jackson Street, Suite 401,
San Francisco, CA 94115, USA
Tel +1 415 775 7947
Email jb@drjonblock.com

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by sitting and bending forward. In addition to the cardinal clinical feature of neurogenic claudication, patients often complain of symptoms that are more radicular in nature, with sharp lower-extremity pain. Leg pain is described as severe and radicular in distribution, and almost always presents with postural aggravation during lumbar extension.[6,8] LSS is the most common indication for spine surgery in older adults.

Conservative medical management of chronic spinal pain disorders, including LSS, has increasingly included the prescription of opioid-based analgesics.[9–11] This recommendation has been based on the belief that these medications can relieve pain and improve function and quality of life in selected patients.[12] In fact, opiates have become the most commonly prescribed class of drug for back pain, based on insurance-claim data.[13] Additionally, it has been estimated that more than half of regular opioid users report back pain as a primary complaint.[14]

Unfortunately, despite initial enthusiasm for opioid therapy, it has only recently been demonstrated that opioid analgesics offer little clinical benefit by way of pain reduction or functional improvement in patients with chronic musculoskeletal pain, including LSS.[15–20] Moreover, the odds of an opioid-related adverse event are three times that compared to placebo among older adults with musculoskeletal pain.[20] Specifically, Markman et al[19] failed to demonstrate any clinical benefit of opiates in older patients experiencing neurogenic claudication secondary to LSS.

Based on emerging evidence raising concerns over the ineffectiveness and possible hazards of opioid medications in the treatment of chronic low-back and leg pain, the British National Institute for Health and Care Excellence updated their recommendation for the assessment and management of low-back pain and sciatica.[21] They concluded, "Do not offer opioids for managing low back pain". Consequently, there is an urgent need to reverse the trend in opioid prescribing being a primary strategy for patients with LSS.

There is a growing body of published literature to support the safety and effectiveness of interspinous process decompression (IPD) with stand-alone interspinous spacers in the treatment of moderate LSS.[22,23] Spacers provide immediate symptom amelioration by serving as a spinal extension blocker to prevent the repetitive compression of neurovascular elements during back extension that is the primary source of LSS symptoms. Clinical follow-up from a US Food and Drug Administration (FDA) investigational device exemption (IDE) randomized controlled trial of the Superion device extends to 5 years of published findings.[24] Durable and clinically significant improvements have been demonstrated following spacer implantation in condition-specific impairment, leg- and back-pain severity, functional disability, and health-related quality of life. The degree of clinical improvement achieved with spacers appears to be strikingly similar to the improvement achieved with decompressive laminectomy, long considered the "gold standard" for surgical treatment of LSS.[25]

Owing to the magnitude, stability, and longevity of clinical benefit observed among LSS patients treated with IPD, we have undertaken additional analyses of ancillary variables in our IDE trial that may have a direct impact on health care utilization. This report examines and characterizes the opioid-medication-usage patterns among patients treated with stand-alone IPD through 5 years of postoperative follow-up.

Methods

Type, dosage, and duration of opioid medications through 5 years of postoperative follow-up were obtained from the Superion Indirect Decompression system (Vertiflex Inc., Carlsbad, CA, USA) treatment arm of a randomized controlled FDA IDE noninferiority trial comparing two interspinous spacers. Medication-prescribing history was documented and validated via electronic data-capture methods for all treated patients during their enrollment and participation as study subjects.

This multicenter trial evaluated the use of stand-alone IPD in the treatment of subjects aged 45 years or older with moderate symptoms of intermittent neurogenic claudication, secondary to a diagnosis of moderate degenerative LSS at one or two contiguous levels from L1 to L5. A total of 391 subjects met the trial-eligibility criteria and were randomized to treatment. The Superion was approved by the FDA in 2015 for commercial distribution based on the 2-year primary end-point analysis.[23] Additionally, condition-specific clinical outcomes have been reported through 5 years of follow-up.[24,26,27] Inasmuch as the control device (X-Stop IPD; Medtronic, Minneapolis, MN, USA) is no longer commercially available, the current opioid-medication analysis was restricted exclusively to the Superion arm of the trial.

This IDE trial complied with all US regulatory requirements and was approved by the institutional review board at each participating site, and patients provided written informed consent before any study-related procedures were performed. The trial was conducted in accordance with the Declaration of Helsinki and prospectively registered at ClinicalTrials.gov (NCT00692276).

Based on opioid-medication start date and duration of use, the prevalence of subjects using opiates was clas-

sified by postoperative follow-up in the same intervals as other previously reported clinical outcomes from this trial (ie, baseline, 6 weeks, and 3, 6, 12, 18, 24, 36, 48, and 60 months). Previous (ie, prestudy) opioid-medication use prior to a subject's enrollment in the trial was also captured based on entrance-eligibility interviews that queried medication history for LSS.

Our primary analysis included all 190 patients randomized to receive the Superion device to determine opioid-medication prevalence. At each follow-up, medication-usage data were provided only for subjects free of reoperation or revision at the index surgical level. Sample sizes were 190 (baseline), 181 (6 weeks), 173 (3 months), 174 (6 months), 163 (12 months), 150 (18 months), 150 (24 months), 125 (36 months), 106 (48 months), and 107 (60 months). A second subgroup analysis was also undertaken after excluding all subjects that had initiated opiates after surgery (n=92). In the remaining subgroup of 98 subjects, we determined opioid-medication prevalence in the same manner among subjects with a history of opioid use for LSS. Sample sizes in this subgroup were 98 (baseline), 90 (6 weeks), 87 (3 months), 87 (6 months), 84 (12 months), 74 (18 months), 79 (24 months), 66 (36 months), 54 (48 months), and 55 (60 months).

Results

Table 1 provides opioid-medication types and frequency of use among all study subjects through 60 months of clinical follow-up.

Among all study subjects, there was a marked year-on-year decrease in the proportion of patients prescribed opioid medications to manage LSS symptoms after Superion implantation (Figure 1). At baseline, almost 50% (94 of 190) of subjects were using opioid medication, with a spike in opioid use (64.1%, 116 of 181) at the 6-week follow-up interval. After this early postoperative interval, there was a sharp diminution 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. Overall, between baseline and 5 years, there was an 85% decrease in the proportion of subjects using opioids.

Table 1 Type and frequency of opioid medication usage

Medication name	n (%)
Buprenorphine	4 (1.27)
Codeine	10 (3.17)
Dextropropoxyphene	1 (0.32)
Fentanyl	2 (0.63)
Hydrocodone	94 (29.84)
Hydromorphone	37 (11.75)
Methadone	5 (1.59)
Morphine	7 (2.22)
Oxycodone	95 (30.16)
Oxymorphone	3 (0.95)
Tapentadol	1 (0.32)
Tramadol	56 (17.78)

Note: Data obtained from 190 Superion subjects prescribed multiple medication types (n=315).

A similar pattern of decreased opioid-medication usage was also observed among the subgroup of subjects with a history of opiates at trial entry (Figure 2). At enrollment, 67.3% (66 of 98) reported prior opioid usage to manage LSS symptoms. By week 6, usage had dropped to 48.9% (44 of 90). Opioid-medication prevalence was 27.4% (23 of 84) at 12 months, 15.2% (12 of 79) at 24 months, and 9.1% (5 of 55) at 60 months. In this subgroup, between baseline and 5 years, there was an 82% decrease in the proportion of subjects using opioids.

Discussion

It has recently been reported in patients aged ≥65 years with a new-back-pain visit that those filling two or more opioid prescriptions within 90 days of the visit had similar back-related outcomes, but an increased likelihood of filling opioid prescriptions 18–24 months later, compared with matched patients who did not fill early opioid prescriptions.[28] This finding suggests a dangerous opioid recidivism and underscores the need to reverse the trend in opioid-prescribing patterns among older patients with musculoskeletal pain syndromes, including LSS.

The large multicenter Spine Patient Outcome Research Trial (SPORT) trial of LSS reported opioid-usage prevalence of 27% at baseline prior to laminectomy.[29] In our IDE trial, we found that ~35% of patients randomized to receive Superion had a history of opioid use at enrollment in the study (Figure 1). We also noted that study subjects were perfunctorily prescribed opiates in the immediate postoperative period, raising the prevalence to 64% within 6 weeks of surgery.

However, after the early postsurgical period, we identified a marked diminution in the prevalence of opioid usage, dropping to 25% at 12 months and 13% by 24 months. These results compare favorably with opioid-prevalence estimates associated with other interventions for LSS. For example, in a randomized trial of repeated epidural steroid injections for LSS, Friedly et al[30] reported baseline opioid-usage prevalence of 38% and 12-month prevalence of 41%, confirming and extending previous research demonstrating lack of long-

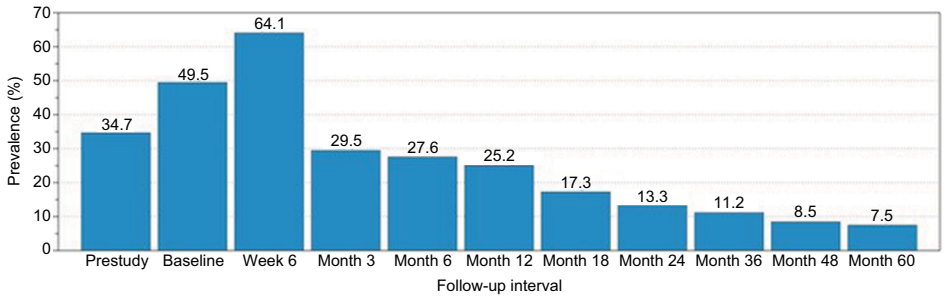

Figure 1 Opioid-medication prevalence (%) by follow-up interval for all study subjects (n=190).
Note: Sample sizes were 190 (prestudy, baseline), 181 (week 6), 173 (month 3), 174 (month 6), 163 (month 12), 150 (month 18), 150 (month 24), 125 (month 36), 106 (month 48), and 107 (month 60).

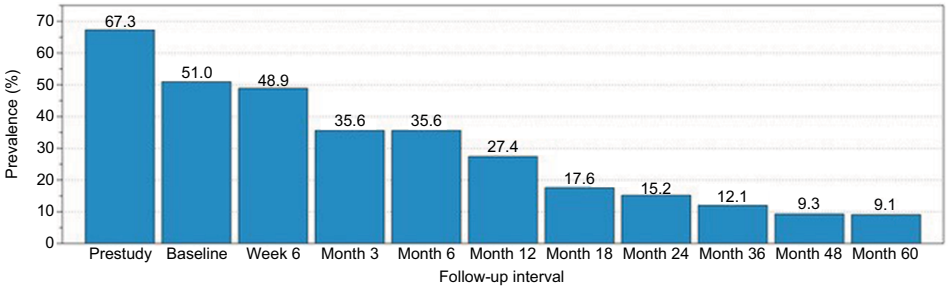

Figure 2 Opioid-medication prevalence (%) by follow-up interval for study subjects with opioid history (n=98).
Note: Sample sizes in this subgroup were 98 (prestudy, baseline), 90 (week 6), 87 (month 3), 87 (month 6), 84 (month 12), 74 (month 18), 79 (month 24), 66 (month 36), 54 (month 48), and 55 (month 60).

term effectiveness for epidural steroid injections for treating chronic LSS symptoms.[31,32]

Our results are also somewhat better than those realized after decompressive laminectomy. In a randomized controlled IDE trial, Schmidt et al[33] reported prestudy opioid-usage prevalence of 31%, spiking postsurgically to 67%, then decreasing to 19% at 12 months, and 23% by 24 months following laminectomy. In our trial, the prevalence of opioid usage continued to drop precipitously to 7.5% by 60 months. It is unknown whether postlaminectomy patients enjoy a similarly rapid decrease in opioid usage with longer-term follow-up. However, if laminectomy-associated instability ensues and symptoms reemerge, revision to fusion may be necessary, requiring reestablishment of opiate therapy.

Many patients expect spine surgery to eliminate the need for opioids. Indeed, prior to lumbar fusion surgery, over 90% of patients surveyed considered continued dependence on opioids neither an expected nor acceptable outcome.[34] In a retrospective cohort study of 2,492 patients having lumbar fusion surgery for degenerative conditions, including LSS, Deyo et al[35] found that more patients received long-term opioids postoperatively (n=1,094) than preoperatively (n=1,045). Additionally, opioid-naïve patients had a substantial risk of initiating long-term use.

Increasing utilization of opioid medications as part of a treatment regime to manage chronic pain has been associated with drug misuse, complications, and fatal overdoses.[36] This problem is even more acute in older adults, who are more susceptible to the adverse effects of opioids, such as disorientation, syncope, and falls.[37] We found that stand-alone IPD in older patients with LSS substantially reduced the need for opioid medication through 5 years of postoperative follow-up. This finding mirrors a similarly notable reduction in need for reoperation or revision following IPD. We previously reported that 75% (142 of 190) of IPD subjects were free of reoperation at their index level through 5 years of follow-up.[24] Importantly, among the 48 spacer subjects that had a reoperation, 38 (79%) subjects underwent their reoperation within the initial 24 months of follow-up. Only a single reoperation occurred during the fifth year of observation, suggesting a continuously decreasing risk of revision surgery with time. The compilation of results from this IDE trial demonstrates long-term durable improvements in condition-specific pain and functional outcomes, as well as marked reductions in the need for opioid medication and revision surgery with IPD through 5 years of follow-up.

This study has several limitations. In the absence of a nonsurgical control, we 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, our post hoc analysis was constrained to prevalence estimates within specified postoperative follow-up intervals and limited only to those patients who remained implanted with the study device and who were free of a reoperation at the index surgical level.

Conclusion

Stand-alone IPD is associated with a marked and sustained decrease in the need for opioid medications to manage symptoms related to LSS. This finding extends previous results showing long-term sustained clinical improvements, a reduction in symptoms of neurogenic claudication, and a decreasing requirement for revision surgery in this population.

Data sharing statement

Requests for data sharing can be made by contacting the corresponding author. Individual participant data that underlie the results reported in this article will be made available (after deidentification) from 9 to 36 months after article publication. Data sharing will be limited to investigators whose proposed use of the data has been approved by an independent review committee identified for this purpose.

Acknowledgments

The authors wish to thank Bob Hachadoorian for data-management support and conducting all statistical analyses. Graphic support was provided by Terry Meredith. Financial support for this work was provided by Vertiflex Inc. (Carlsbad, CA, USA).

Author contributions

All authors contributed to data analysis, drafting and revising the article, gave final approval of the version to be published, and agree to be accountable for all aspects of the work.

Disclosure

JEB is an independent advisor to Vertiflex Inc. and was remunerated for assistance in manuscript development. The other authors report no conflicts of interest in this work.

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FDA Approved Letter

DEPARTMENT OF HEALTH & HUMAN SERVICES Public Health Service

Food and Drug Administration
10903 New Hampshire Avenue
Document Control Center – WO66-G609
Silver Spring, MD 20993-0002

June 3, 2015

VertiFlex®, Incorporated
Mr. Steve Reitzler
Vice President, Clinical & Regulatory Affairs
1351 Calle Avanzado, Suite 100
San Clemente, California 92673

Re: P140004
Trade/Device Name: Superion® InterSpinous Spacer (ISS)
Filed: March 31, 2014
Amended: April 16, May 28, June 5, October 6, December 1 and December 12, 2014; January 20 and January 22, 2015
Product Code: NQO

Dear Mr. Reitzler:

This letter corrects our Approval Order letter of May 20, 2015.

The Center for Devices and Radiological Health (CDRH) of the Food and Drug Administration (FDA) has completed its review of your premarket approval application (PMA) for the Superion InterSpinous Spacer (ISS). This device is indicated to treat skeletally mature patients suffering from pain, numbness, and/or cramping in the legs (neurogenic intermittent claudication) secondary to a diagnosis of moderate degenerative lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, MRI and/or CT evidence of thickened ligamentum flavum, narrowed lateral recess, and/or central canal or foraminal narrowing. The Superion® ISS is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, numbness, and/or cramping, with or without back pain, and who have undergone at least 6 months of non-operative treatment. The Superion® ISS may be implanted at one or two adjacent lumbar levels in patients in whom treatment is indicated at no more than two levels, from L1 to L5. For this intended use, moderate degenerative lumbar spinal stenosis was defined as follows:

- 25% to 50% reduction in the central canal and/or nerve root canal (subarticular, neuroforaminal) compared to the adjacent levels on radiographic studies, with radiographic confirmation of any one of the following:
    - Evidence of thecal sac and/or cauda equina compression
    - Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements
    - Evidence of hypertrophic facets with canal encroachment

- AND associated with the following clinical signs:

    - Presents with moderately impaired Physical Function (PF) defined as a score of ≥ 2.0 of the Zurich Claudication Questionnaire (ZCQ)

    - Ability to sit for 50 minutes without pain and to walk 50 feet or more.

We are pleased to inform you that the PMA is approved. You may begin commercial distribution of the device in accordance with the conditions of approval described below.

The sale and distribution of this device are restricted to prescription use in accordance with 21 CFR 801.109 and under section 515(d)(1)(B)(ii) of the Federal Food, Drug, and Cosmetic Act (the act). The device is further restricted under section 515(d)(1)(B)(ii) of the act insofar as the labeling must specify the specific training or experience practitioners need in order to use the device. FDA has determined that these restrictions on sale and distribution are necessary to provide reasonable assurance of the safety and effectiveness of the device. Your device is therefore a restricted device subject to the requirements in sections 502(q) and (r) of the act, in addition to the many other FDA requirements governing the manufacture, distribution, and marketing of devices.

Expiration dating for this device has been established and approved at 5 years. This is to advise you that the protocol you used to establish this expiration dating is considered an approved protocol for the purpose of extending the expiration dating as provided by 21 CFR 814.39(a)(7).

Continued approval of this PMA is contingent upon the submission of periodic reports, required under 21 CFR 814.84, at intervals of one year (unless otherwise specified) from the date of approval of the original PMA. Two copies of this report, identified as "Annual Report" and bearing the applicable PMA reference number, should be submitted to the address below. The Annual Report should indicate the beginning and ending date of the period covered by the report and should include the information required by 21 CFR 814.84. This is a reminder that as of September 24, 2014, class III devices are subject to certain provisions of the final UDI rule. These provisions include the requirement to provide a UDI on the device label and packages (21 CFR 801.20), format dates on the device label in accordance with 21 CFR 801.18, and submit data to the Global Unique Device Identification Database (GUDID) (21 CFR 830 Subpart E). Additionally, 21 CFR 814.84 (b)(4) requires PMA annual reports submitted after September 24, 2014, to identify each device identifier currently in use for the subject device, and the device identifiers for devices that have been discontinued since the previous periodic report.

It is not necessary to identify any device identifier discontinued prior to December 23, 2013. For more information on these requirements, please see the UDI website, http://www.fda.gov/udi.

In addition to the above, and in order to provide continued reasonable assurance of the safety and effectiveness of the device, the Annual Report must include, separately for each model number (if applicable), the number of devices sold and distributed during the reporting period, including those distributed to distributors. The distribution data will serve as a denominator and provide necessary context for FDA to ascertain the frequency and prevalence of adverse events, as FDA evaluates the continued safety and effectiveness of the device.

In addition to the Annual Report requirements, you must provide the following data in post-approval study (PAS) reports for each PAS listed below, every 6 months during the first 2 years of these studies and annually thereafter. Two (2) copies of each report, identified as an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" in accordance with how the study is identified below and bearing the applicable PMA reference number, should be submitted to the address below.

1. ODE Lead PMA Post-Approval Study – "Superion® Post-Approval Clinical Evaluation and Review (SPACER)": The Office of Device Evaluation (ODE) will have the lead for this clinical study, which was initiated prior to device approval. The "Superion® Post-Approval Clinical Evaluation and Review (SPACER)" is described as follows:

   Based on the study plan received on May 1, 2015, you must perform a 60-month PAS to evaluate the longer term safety and effectiveness of the Superion® ISS as compared to the X-STOP® Interspinous Process Decompression (IPD®) System ("X-STOP® IPD®") by following all patients from the pivotal investigational device exemption (IDE) study G070118 with device survival to 24 months (137 Superion® ISS and 144 X-STOP® IPD® randomized patients had not died or terminally failed as of the 24-month visit) annually through 60 months at 25 study sites. Thus, the post-approval study duration is approximately 36 months, as all patients have reached 24 months prior to the start of this study.

   At each annual (±3 month) visit, you will collect the following data: Zurich Claudication Questionnaire (ZCQ); neurological status as determined by physical exam; radiographic information; maintenance of distraction; all adverse events regardless of cause; incidence of epidural injections regardless of the cause and spinal level injected; incidence of analgesic narcotics usage; reoperations, revisions, removals or supplemental fixation at the index levels; SF-12 Short Form Health Survey, Version 2; VertiFlex® Patient Satisfaction Survey; Visual Analog Scale (VAS); Oswestry Disability Index (ODI), return to work and to activities of daily living and rehabilitation utilization. In addition, you will report information on the length of hospital stay, operative time, estimated blood loss, and type of anesthesia.
   Radiographic information collected will include: standing anteroposterior and lateral lumbar radiographs, range of motion on lateral standing flexion/extension films (at implanted and adjacent level(s)), radiolucency, device displacement or migration, and radiographic

observations such as incidence of total and per patient spinous process fractures or heterotopic ossification. Adverse events will be evaluated by the Medical Monitor. Data will be evaluated for safety endpoints by an independent Clinical Events Committee (CEC).

The primary hypothesis of this extended follow-up post approval study is that performance of the Superion™ ISS remains clinically non-inferior to X-STOP® IPD® at 60 months post-surgery using the same non-inferiority margin (δ=-0.10) as was used at 24 months. An individual subject will be considered a success if they meet all of the following conditions at the 60-month follow-up:

Clinically significant improvement in outcomes compared to baseline, as determined by meeting the following:

- At least two of three domains of the Zurich Claudication Questionnaire (ZCQ)
    - Improvement in physical function by $\geq$ 0.5 points
    - Improvement in symptom severity by $\geq$ 0.5 points
    - "Satisfied" or "somewhat satisfied" as defined by a score of $\leq$ 2.5 points on the patient satisfaction domain
- No re-operations, revisions, removals or supplemental fixation at the index level(s)
- No major implant- or procedure-related complications:
    - No dislodgement, migration, or deformation
    - No new or persistent worsened neurological deficit at the index level
    - No spinous process fractures
    - No deep infection, death, or other permanent device attributed disability
- No clinically significant confounding treatments:
    - No epidural injections or nerve block procedures at index level, spinal cord stimulators or rhizotomies

The secondary study objective is to demonstrate the superiority of Superion® ISS to X-STOP® IPD® in effectively treating moderately impaired LSS patients as measured by 60 months postoperative overall success rates.

FDA will expect at least 85% follow-up at the 60-month time point to provide sufficient data to evaluate safety and effectiveness and sensitivity analysis to address missing data.

2. OSB Lead PMA Post-Approval Study - "Superion® New Enrollment Study": The Office of Surveillance and Biometrics (OSB) will have the lead for studies initiated after device approval. The "Superion® New Enrollment Study" is described as follows:

   You will recruit 358 subjects to ensure that at minimum 304 (152 per treatment group) patients will be followed through 60-months. Nine clinical visits will occur at the following intervals: screening (< 4 weeks before surgery), surgery, 6 weeks (±2 weeks), 6 months (±2 months), 12 months (±2 months), 24 months (±2 months), and annually (±4 months) thereafter through 60 months of follow-up. At each post-operative visit, you will collect the following data: ZCQ; neurological status as determined by physical exam; radiographic information; all adverse events regardless of cause; incidence of epidural injections regardless of the cause and spinal level injected; incidence of analgesic narcotics usage; reoperations, revisions , removals or supplemental fixation at the index levels; Patient Satisfaction Survey; VAS; ODI, return to work and to activities of daily living and rehabilitation utilization. In addition, you will collect information on the length of hospital stay, operative time, estimated blood loss, and type of anesthesia.

   The imaging data will be collected during screening (< 4 weeks before surgery) and during all post-operative visits via x-rays in the following positions: anteroposterior, lateral, flexion and extension. In addition, standing anteroposterior and lateral lumbar radiographs will be taken at time of discharge of index surgery. Computed tomography (CT) imaging will be captured in lieu of x-rays at 24 months for all patients, pending individual IRB approval, in the Superion® cohort. CT imaging may be performed in lieu of x-rays for Superion® patients at 60 months per surgeon discretion. CT imaging will be utilized to observe spinous process fractures.

   - The primary objective of this study is to demonstrate that the composite clinical success (CCS) of Superion® device performance will be non-inferior (δ=-0.125) to decompression at 60 months. The CCS is defined as following:
     - A clinically significant improvement in at least two of the three domains of the ZCQ
     - No reoperations, revisions, removals, or supplemental fixation at the index level(s)
     - No ≥2 injections or series of injections for the treated level, or nerve block procedures performed to treat spinal stenosis for the index level(s), or a single injection within 12 months of the 60-month endpoint.

A secondary endpoint with alternative CSS for the primary objective will also be evaluated at 60 months where CSS is defined as above with the exception of point number three where success will be defined as:

- No injections or series of injections at any level at any time.

Be advised that the failure to conduct any such study in compliance with the good clinical laboratory practices in 21 CFR part 58 (if a non-clinical study subject to part 58) or the institutional review board regulations in 21 CFR part 56 and the informed consent regulations in 21 CFR part 50 (if a clinical study involving human subjects) may be grounds for FDA withdrawal of approval of the PMA. In addition, the results from any post approval study should be included in the labeling as these data become available. Any updated labeling must be submitted to FDA in the form of a PMA Supplement. For more information on post-approval studies, see the FDA guidance document entitled, "Procedures for Handling Post-Approval Studies Imposed by PMA Order" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm070974.htm).

Within 30 days of your receipt of this letter, you must submit a PMA supplement that includes complete protocols of your post-approval studies described above. Your PMA supplements should be clearly labeled as an "ODE Lead PMA Post-Approval Study Report" or "OSB Lead PMA Post-Approval Study Report" as noted above and submitted in triplicate to the address below. Please reference the PMA number above to facilitate processing. If there are multiple protocols being finalized after PMA approval, please submit each protocol as a separate PMA supplement.

Before making any change affecting the safety or effectiveness of the device, you must submit a PMA supplement or an alternate submission (30-day notice) in accordance with 21 CFR 814.39. All PMA supplements and alternate submissions (30-day notice) must comply with the applicable requirements in 21 CFR 814.39. For more information, please refer to the FDA guidance document entitled, "Modifications to Devices Subject to Premarket Approval (PMA) - The PMA Supplement Decision-Making Process" (http://www.fda.gov/MedicalDevices/DeviceRegulationandGuidance/GuidanceDocuments/ucm089274.htm).

You are reminded that many FDA requirements govern the manufacture, distribution, and marketing of devices. For example, in accordance with the Medical Device Reporting (MDR) regulation, 21 CFR 803.50 and 21 CFR 803.52, you are required to report adverse events for this device. Manufacturers of medical devices, including in vitro diagnostic devices, are required to report to FDA no later than 30 calendar days after the day they receive or otherwise becomes aware of information, from any source, that reasonably suggests that one of their marketed devices:

1. May have caused or contributed to a death or serious injury; or

2. Has malfunctioned and such device or similar device marketed by the manufacturer would be likely to cause or contribute to a death or serious injury if the malfunction were to recur.

Additional information on MDR, including how, when, and where to report, is available at http://www.fda.gov/MedicalDevices/Safety/ReportaProblem/default.htm

In accordance with the recall requirements specified in 21 CFR 806.10, you are required to submit a written report to FDA of any correction or removal of this device initiated by you to: (1) reduce a risk to health posed by the device; or (2) remedy a violation of the act caused by the device which may present a risk to health, with certain exceptions specified in 21 CFR 806.10(a)(2). Additional information on recalls is available at http://www.fda.gov/Safety/Recalls/IndustryGuidance/default.htm

CDRH does not evaluate information related to contract liability warranties. We remind you; however, that device labeling must be truthful and not misleading. CDRH will notify the public of its decision to approve your PMA by making available, among other information, a summary of the safety and effectiveness data upon which the approval is based. The information can be found on the FDA CDRH Internet HomePage located at http://www.fda.gov/MedicalDevices/ProductsandMedicalProcedures/DeviceApprovalsandClearances/PMAApprovals/default.htm. Written requests for this information can also be made to the Food and Drug Administration, Dockets Management Branch, (HFA-305), 5630 Fishers Lane, Rm. 1061, Rockville, MD 20852. The written request should include the PMA number or docket number. Within 30 days from the date that this information is placed on the Internet, any interested person may seek review of this decision by submitting a petition for review under section 515(g) of the act and requesting either a hearing or review by an independent advisory committee. FDA may, for good cause, extend this 30-day filing period.

Failure to comply with any post-approval requirement constitutes a ground for withdrawal of approval of a PMA. The introduction or delivery for introduction into interstate commerce of a device that is not in compliance with its conditions of approval is a violation of law.

You are reminded that, as soon as possible and before commercial distribution of your device, you must submit an amendment to this PMA submission with copies of all approved labeling in final printed form. Final printed labeling that is identical to the labeling approved in draft form will not routinely be reviewed by FDA staff when accompanied by a cover letter stating that the final printed labeling is identical to the labeling approved in draft form. If the final printed labeling is not identical, any changes from the final draft labeling should be highlighted and explained in the amendment.

All required documents should be submitted in 6 copies, unless otherwise specified, to the address below and should reference the above PMA number to facilitate processing.

U.S. Food and Drug Administration
Center for Devices and Radiological Health
PMA Document Control Center - WO66-G609
10903 New Hampshire Avenue
Silver Spring, MD 20993-0002

If you have any questions concerning this approval order, please contact Zane W. Wyatt, Ph.D. at 301-796-5650 or zane.wyatt@fda.hhs.gov.

Sincerely yours,

Lori A. Wiggins -S

for
Mark N. Melkerson
Director
Division of Orthopedic Devices
Office of Device Evaluation
Center for Devices and
Radiological Health

PMA Executive Summary

VertiFlex® Superion® Interspinous Spacer

PMA No. P140004

Executive Summary

This Executive Summary presents an abstract of the clinical trial conducted to support FDA approval of the **VertiFlex® Superion® Interspinous Spacer** PreMarket Approval (PMA) application, No. P140004. The Superion® implant is designed for the treatment of symptoms of neurogenic intermittent claudication secondary to moderate lumbar spinal stenosis.

For a complete Summary of Safety and Effectiveness Data (SSED) derived from the clinical trial supporting FDA approval of the Superion® PMA, please refer to the SSED posted on the FDA website at http://www.accessdata.fda.gov/cdrh_docs/pdf14/P140004b.pdf.

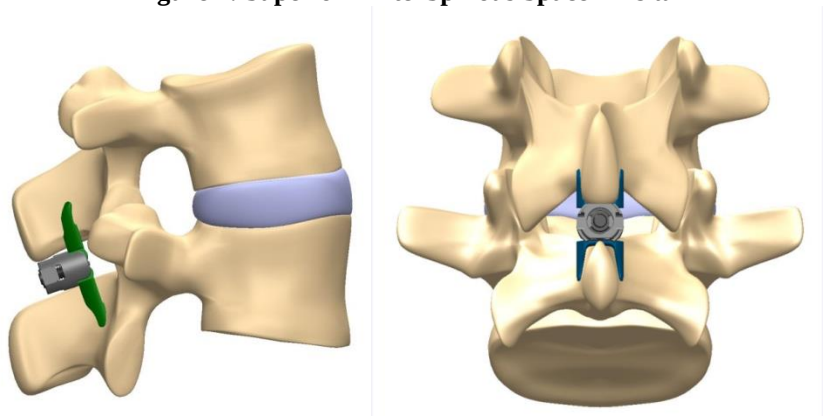
1. SUMMARY

The Superion® Interspinous Spacer (Superion® ISS) is a spinal implant designed to treat symptoms of intermittent neurogenic claudication secondary to moderate degenerative lumbar spinal stenosis, and is implanted by minimally-invasive methods through a cannula. The implant provides indirect decompression of spinal nerves, and functions as a spinal extension-blocker to prevent compression of neural elements in extension. The Superion® ISS was designed to treat a similar patient population as the FDA approved X-STOP® Interspinous Process Device (IPD®).

1.1 Device Description

The Superion® ISS is available in five (5) sizes, from 8mm to 16mm, in 2mm increments, to accommodate a range of spinal anatomy, and is composed entirely of Titanium 6Al-4V alloy conforming to ASTM Standard Specification F136, *Standard Specification for Wrought Titanium-6 Aluminum-4 Vanadium ELI (Extra Low Interstitial) Alloy for Surgical Implant Applications*. **Figure 1** depicts the implant in its final position after placement between the spinous processes.

Figure 1: Superion® InterSpinous Spacer *in situ*



Lateral View **A/P View**

The Superion® ISS can generally be described in two (2) "states": Undeployed (closed), and deployed (open). The implant is supplied in the undeployed state, and it is in this form that it is passed through a delivery cannula placed at midline, to the implantation site. Once delivered to, and located in, the interspinous space between the spinous processes at the selected level, the Superion® ISS is deployed to open the superior and inferior cam lobes. In doing so, these cam lobes rotate 90° from the implant axis to engage the lateral aspects of the superior and inferior spinous processes posterior to the lamina. **Figure 2** provides views of the implant as it transitions from the closed to open (or deployed) configuration.

Figure 2: Superion® ISS in Closed and Extended (Deployed) Position

The device may be implanted under general, or local (e.g., conscious sedation) anesthesia. The patient is placed prone with the spine in a flexed position. A percutaneous or mini-open approach is used for incision and placement of the cannula via sequential dilation, to allow cannula positioning in the interspinous space. Once the cannula is in place, a sizing tool is employed to determine the proper device size. The Superion® ISS is then inserted through the cannula and deployed under fluoroscopic guidance between adjacent vertebral spinous processes at the level to be treated. The insertion instrumentation is then removed, leaving the implant in place. The rigid implant serves thereafter to maintain the desired distraction between the spinous processes while still preserving motion. This maintains the intervertebral space and prevents narrowing of the canal by limiting extension at that level. Where a second, contiguous level is also symptomatic, the same procedure is used to place a Superion® ISS at that level.

1.2 Indications for Use

The Superion® InterSpinous Spacer is intended to treat skeletally mature patients suffering from pain, numbness, and/or cramping in the legs (neurogenic intermittent claudication) secondary to a diagnosis of moderate degenerative lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, MRI and/or CT evidence of thickened *ligamentum flavum*, narrowed lateral recess, and/or central canal or foraminal narrowing. The Superion® ISS is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, numbness, and/or cramping, with or without back pain. The Superion® ISS may be implanted at one or two adjacent lumbar levels in patients in whom treatment is indicated at no more than two levels, from L1 to L5.

For this intended use, moderate degenerative lumbar spinal stenosis is defined as follows:

- 25% to 50% reduction in the central canal and/or nerve root canal (subarticular, neuroforaminal) compared to the adjacent levels on radiographic studies, with radiographic confirmation of any one of the following:
  - Evidence of thecal sac and/or *cauda equina* compression
  - Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements
  - Evidence of hypertrophic facets with canal encroachment
- AND Associated with the following clinical signs:
  - Presents with moderately impaired Physical Function (PF) defined as a score of ≥ 2.0 of the Zurich Claudication Questionnaire (ZCQ)
  - Ability to sit for 50 minutes without pain and to walk 50 feet or more.

1.3 Contraindications

The Superion® Interspinous Spacer is contraindicated in patients with:

- an allergy to titanium or titanium alloy;
- spinal anatomy or disease that would prevent implantation of the device or cause the device to be unstable in situ, such as:
- significant instability of the lumbar spine, e.g., isthmic spondylolisthesis or degenerative spondylolisthesis greater than grade 1.0 (on a scale of 1 to 4);
- an ankylosed segment at the affected level(s);
- acute fracture of the spinous process, *pars interarticularis*, or laminae fracture (unilateral or bilateral);
- significant scoliosis (Cobb angle >10 degrees);
- *Cauda equina* syndrome defined as neural compression causing neurogenic bladder or bowel dysfunction;
- diagnosis of severe osteoporosis, defined as bone mineral density (from DEXA scan or equivalent method) in the spine or hip that is more than 2.5 S.D. below the mean of adult normals in the presence of one or more fragility fractures;
- active systemic infection, or infection localized to the site of implantation.

1.4 Clinical Study Design

The Superion® clinical trial was an FDA-approved study conducted under Investigational Device Exemption (IDE) number G070118. The trial was a prospective, randomized, multi-center, concurrently-controlled clinical study conducted to compare the Superion® ISS to an FDA-approved control, the X-STOP® IPD® device. A Bayesian statistical plan was employed to demonstrate non-inferiority. A total of 470 patients were enrolled in the study. 51 patients were post-consent screen failures prior to treatment. From the remaining 419 patients who met eligibility criteria, 28 non-randomized patients were assigned to a Superion® "training" cohort, while 391 patients were assigned to the randomized Intent-to-Treat (mITT) cohort. Of these patients, 190 were randomized to the Superion® arm, and 201 to the X-STOP® arm. Patients had follow up examinations at discharge, 6 weeks, 3 months, 6 months, 12 months, 18 months, and 24 months, with annual follow-up visits thereafter. Follow-up of patients will continue to 60 months as an FDA condition of approval.

1.4.1 Inclusion/Exclusion Criteria

The inclusion and exclusion criteria were designed to target a patient population having moderate degenerative stenosis, using criteria that would (a) include patients having sufficiently advanced stenosis (i.e., those who no longer benefit from conservative care) to require surgical treatment for spinal stenosis, while (b) excluding those patients with severe spinal stenosis likely to require more extensive intervention.

1.4.2 Patient Demographics

Baseline demographic information is presented in **Table 1** and **Table 2**.

Table 1: Baseline and Demographic Variables - Superion® and X-STOP® mITT Analysis Set

	Superion®					X-STOP®					p[1]	Effect
Demographics	**N**	**Mean**	**SD**	**Min**	**Max**	**N**	**Mean**	**SD**	**Min**	**Max**		**Size**
Age at surgery (yrs)	190	66.9	9.4	47.0	88.0	201	66.2	10.2	46.0	89.0	0.291	0.06
Height (inches)	190	67.2	4.2	57.1	76.0	201	67.9	3.8	59.1	77.2	0.088	-0.19
Weight (lbs)	190	189.7	36.5	89.1	288.8	201	195.8	36.9	114.9	284.4	0.105	-0.17
BMI (k/m^2)	190	29.5	4.6	16.4	40.0	201	29.7	4.6	19.8	39.5	0.667	-0.05
Baseline Functional Status	**N**	**Mean**	**SD**	**Min**	**Max**	**N**	**Mean**	**SD**	**Min**	**Max**		
Oswestry (ODI)	190	39.1	13.4	8.9	74.0	201	39.9	11.6	6.7	80.0	0.477	-0.06
Zurich Claudication Qx Severity	190	3.33	0.64	1.6	5.0	201	3.37	0.61	2.0	5.0	0.489	-0.07
Zurich Claudication Qx Physical	190	2.63	0.43	1.6	3.6	201	2.72	0.43	1.8	3.8	0.033	-0.22
SF-12 PCS (Physical)	189	29.4	8.1	12.1	52.4	201	28.5	6.9	12.7	55.0	0.285	0.11
SF-12 MCS (Mental Health)	189	50.0	12.7	15.6	73.7	201	48.9	12.2	19.6	73.8	0.381	0.09
VAS Back pain	190	55.4	27.9	0.0	93.0	201	55.1	27.4	0.0	100.0	0.809	0.01
VAS Leg pain (right leg)	190	55.0	31.3	0.0	100.0	201	52.9	32.5	0.0	100.0	0.533	0.07
VAS Leg pain (left leg)	190	49.6	31.8	0.0	100.0	201	50.8	31.7	0.0	100.0	0.758	-0.04

Notes: [1] Wilcoxon rank sum tests for interval variables and ordinal variables.

Table 2: Baseline and Demographic Variables - Superion® and X-STOP® Control mITT Analysis Sets

	Superion®		X-STOP®		p[1]
	n	%	n	%	
Number of subjects	190		201		
Males	110	57.9	129	64.2	0.214
Females	80	42.1	72	35.8	
Race	n	%	n	%	
White	177	93.2	196	97.5	0.020
Asian	0	0.0	1	0.5	
African American	8	4.2	1	0.5	
American Indian or Alaska Native	0	0.0	0	0.0	
Native Hawaiian or Other Pacific Islander	0	0.0	1	0.5	
Other	5	2.6	2	1.0	
Ethnicity	n	%	n	%	
Hispanic or Latino	5	2.6	11	5.5	0.204
Not Hispanic or Latino	185	97.4	190	94.5	
Use of nicotine products	n	%	n	%	
No	89	46.8	101	50.2	0.809
Current Use	24	12.6	24	11.9	.
Previous Use	77	40.5	76	37.8	.

Note: [1] Fisher's exact test (2-sided).

There were no differences in all but one baseline demographic parameter.

1.4.3 Patient Accountability

At the time of database lock for PMA submission (July 7, 2014), 94.6% (183 Superion® and 187 X-STOP® IPD®) of patients enrolled in the study were available for analysis at the study completion (24-month post-operative visit). The Superion® ISS cohort had a follow-up rate of 97.3% and the X-STOP® IPD® cohort had a follow-up rate of 94.9% through 24 months. Further, for patients theoretically due for 36 month follow-up at that time, the Superion® cohort had a follow-up rate of 90.2% and the X-STOP® cohort had a follow-up rate of 91.4%.

1.4.4 Primary and Secondary Endpoint Design

The primary endpoint of the investigation included effectiveness, safety, and risk-benefit criteria. Individual patient success required that a patient meet all of the following criteria at 24 months follow-up:

- Clinically significant improvement in outcomes compared to baseline, as determined by meeting the criterion for at least two of three domains of ZCQ
  - ≥ 0.5 point improvement in physical function
  - ≥ 0.5 point improvement in symptom severity
  - Score of ≤ 2.5 points on patient satisfaction domain
- No re-operations, removals, revisions, or supplemental fixation at the index level(s)
- No major implant or procedure related complications
  - No dislodgement, migration, or deformation
  - New or persistent worsened neurological deficit at the index level
  - Spinous process fractures
  - Deep infection, death, or other permanent device attributed disability
- No clinically significant confounding treatments:
  - No epidural injections or nerve block procedures at index level, spinal cord stimulators or rhizotomies

In addition, secondary outcomes included clinically significant decreases in leg pain and back pain (measured by ≥20mm decrease in Visual Analog Scale [VAS]), maintenance or improvement of SF-12, and clinically significant decrease (defined as ≥15 point decrease vs. baseline) in Oswestry Disability Index (ODI). Radiographic assessments were also performed for both groups by an independent radiographic core laboratory to determine qualitative and qualitative radiographic measures.

2. CLINICAL TRIAL OUTCOMES

2.1 Primary Endpoint Components

The percentage of subjects achieving success in each of the individual components of the composite primary endpoint at the 24 month follow-up are presented in **Table 3**:

Table 3: Primary Endpoint Component Success – 24 Months

Component Success Through 24 Months	Component Success	
	Superion®	X-STOP®
Clinical Success in any 2 of 3 ZCQ Domains	81.7%	87.2%
No Re-operations or Revisions	80.0%	86.6%
No Confounding Additional Treatments	86.3%	82.6%
No Major Related Complications	86.8%	83.1%

Importantly, success in these primary endpoint components remained durable at the 36 month follow-up, as shown in **Table 4**:

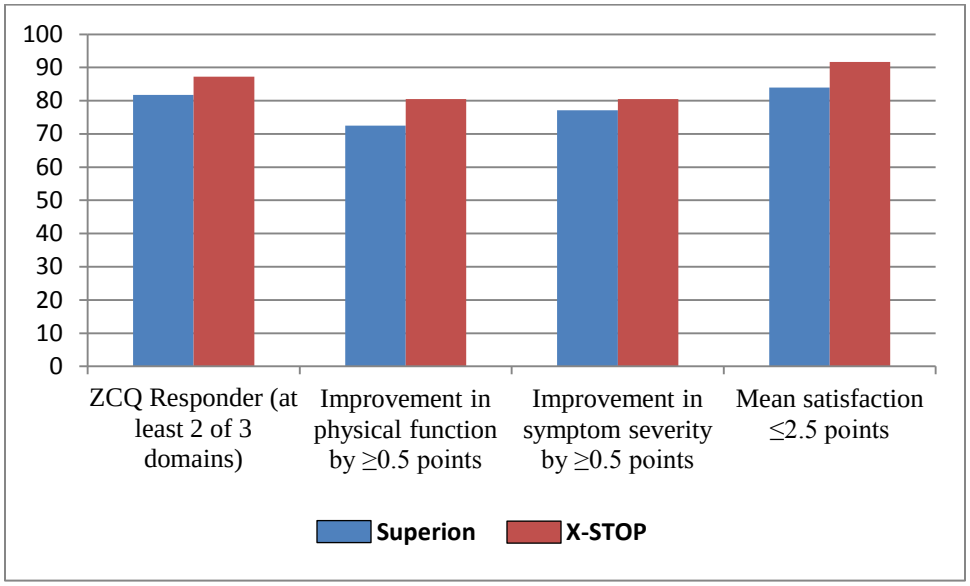
Table 4: Primary Endpoint Component Success – 36 Months

Component Success Through 36 Months	Component Success	
	Superion®	X-STOP®
Clinical Success in any 2 of 3 ZCQ Domains	87.7%	84.0%
No Re-operations or Revisions	81.2%	79.7%
No Confounding Additional Treatments	87.0%	79.7%
No Major Related Complications	90.6%	85.1%

2.1.1 Zurich Claudication Questionnaire (ZCQ)

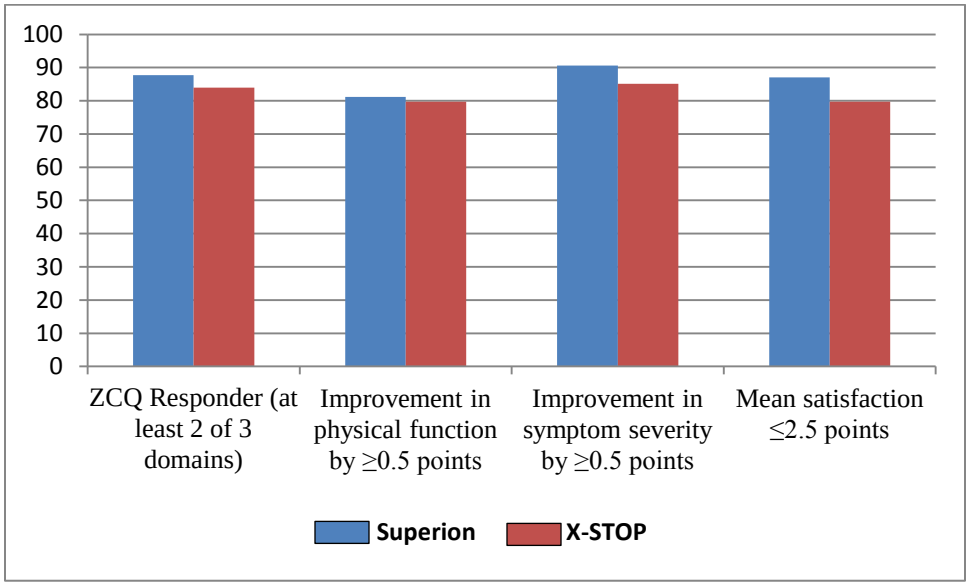
The Zurich Claudication Questionnaire (ZCQ) is a validated outcome measure for evaluating pain, function, and patient satisfaction in lumbar stenosis patients suffering from neurogenic intermittent claudication. The percentage of subjects in each arm whose scores reflect a clinically meaningful improvement over baseline at 24 months are shown below in **Figure 3**, and establish that, in a large majority of subjects, both the Superion® and X-STOP® devices provided significant improvement in pain and function, and a high degree of patient satisfaction with the procedure.

Figure 3: Success in ZCQ domains at 24 months



Notably, these outcomes proved durable through longer follow-up through 36 months, as shown in **Figure 4**:

Figure 4: Success in ZCQ domains at 36 months



2.1.2 Reoperations, Revisions, and Supplemental Fixations

In the modified intent-to-treat patient population (mITT), there were a total of 49 reoperations or revisions in the Superion® group (49/190, 25.8%) compared with 44 reoperations or revisions in the X-STOP® group (44/201, 21.9%, p = 0.365) through the last available follow-up, which included time points past 24 months for many patients, as shown in **Table 5**.

Through 24 months (as part of the primary endpoint), there were a total of 38 reoperations or revisions in the Superion® group (38/190, 20.0%) compared with 29 reoperations or revisions in the X-STOP® group (29/201, 14.4%, p = 0.179). Reoperations and revisions in patients prior to day 730 of treatment were considered to be failures in the primary endpoint although, as noted above, there was an increased number of reoperations and revisions in the X-STOP® arm, *vs*. the Superion® arm, at time points after 2 years.

Table 5: Reoperation and Revision Events – Intent-to-Treat (mITT) Population

Reoperation or Revision Type	Treatment Group	Event Time Course (months)								Total (events)	Reasons
		<1.5	1.5-3	3-6	6-12	12-24	24-36	36-48	48-60		
Decompression and Device Removal	Superion®	-	3	4	8	4	7	-	-	26	20 leg and/or low back pain, 2 bone-related fracture, 2 neurological decline, 1 device deployment issue, 1 facet cyst
Device Removal and Fusion	Superion®	1	-	-	4	5	2	1	-	13	9 leg and/or low back pain, 2 bone-related fracture, 1 neurological decline, 1 unknown
Device Removal	Superion®	-	-	-	1	-	-	-	-	1	1 leg and/or low back pain
Fusion (no device removal)	Superion®	-	-	-	1	1	1	-	-	3	2 leg and/or low back pain, 1 synovial cyst
Supplemental Decompression	Superion®	-	-	2	1	1	-	-	-	4	3 leg and/or low back pain, 1 synovial cyst
I&D and Device Removal	Superion®	1	-	-	-	-	-	-	-	1	1 dural tear
Intraoperative Failure	Superion®	1							-	1	1 dural tear
Decompression and Device Removal	X-STOP®	1	1	3	3	8	4	2	1	23	18 leg and/or low back pain, 3 device dislodgement, 1 neurological decline, 1 herniated disc
Device Removal and Fusion	X-STOP®	-	-	-	1	5	5	2	-	13	12 leg and/or low back pain, 1 bone-related fracture
Device Removal	X-STOP®	-	-	-	1	-	1	-	-	2	1 leg and/or low back pain, 1 bone-related fracture
Device Replacement	X-STOP®	-	1	-	1	-	-	-	-	2	2 leg and/or low back pain
Intraoperative Failure	X-STOP®	2	-	-	-	-	-	-	-	2	2 bone-related fracture
Irrigation and Debridement	X-STOP®	2	-	-	-	-	-	-	-	2	2 deep infection

The primary reason for reoperation or revision in both Superion® and X-STOP® patients was related to progression of, or failure to adequately relieve, the symptoms of spinal stenosis. One could consider these "treatment failures," as would be expected to be observed with any therapy. The subsequent surgical procedures following device removal performed in the Superion® clinical trial were consistent with consensus clinical standards. In particular, for subjects without grade I spondylolisthesis, surgical decompression was performed. For patients with grade I spondylolisthesis, surgical decompression with fusion was performed.

2.1.3 Neurological Outcomes

Neurologic success was defined by the presence of no new or worsening neurologic deficit with respect to motor or sensory function. The rate of neurologic failures was similar for both Superion® and X-STOP® groups. The Superion® patient population had seven (7) patients (3.7%) that had new or worsening persistent motor or sensory neurologic assessments at 24 months, while the X-STOP® population had five (5) failures (2.5%) of these criteria.

2.1.4 Additional Treatments (Epidural Injections, Rhizotomies, and Spinal Cord Stimulators)

Following index surgery, 25 of the 190 (13.2%) Superion® mITT subjects received an epidural steroid injection or nerve block at the level(s) of surgery prior to Month 24. In contrast, 33 of the 201 (16.4%) X-STOP® mITT subjects received an epidural steroid injection or nerve block at the level(s) of surgery prior to Month 24 (p=0.395). All patients who received such injections or nerve blocks at the level(s) of surgery prior to Month 24 and were considered study failures.

Following index surgery, none of the 190 (0.0%) Superion® mITT subjects received a rhizotomy at the level(s) of surgery prior to Month 24. One (1) of the 201 (0.5%) X-STOP® mITT subjects received a rhizotomy and was therefore considered a study failure (p = 1.000). No subject in either group received a spinal cord stimulator at the level(s) of surgery prior to Month 24.

2.1.5 Radiographic Observations

The incidence of radiographic observations is shown in **Table 6**.

Table 6: Subjects with Radiographic Observations in the Superion® IDE

Radiographic Observation	Superion® (n=190)		X-STOP® (n=201)	
	n	%	n	%
Spinous Process Fracture (any time)	31	16.3%	17	8.5%
Spinous Process Fracture (non-healed at 24 months)	21	11.1%	10	5.0%
Device Migration (>5mm)	0	0.0%	16	8.0%
Device Dislodgement	0	0.0%	20	10.0%
Any Radiographic Observation (any time)	31	16.3%	34*	16.9%
Any Radiographic Observation (24 months)	21	11.1%	28	13.9%

*Significant overlap was present in X-STOP® subjects having spinous process fractures, device migration, and device dislodgement.

The rate of spinous process fractures at 24 months for both groups was 11.1% and 5.0% for Superion® and X-STOP® patients, respectively. The rate of migrations and dislodgements was 0% in the Superion® group, but 11.9% in the X-STOP® group. In many cases these fractures and device movements were asymptomatic, and had no discernible effect upon the patient or their daily life through 24 months. It was observed that in some cases of dislodgement and migration in the X-STOP® arm clinical sequelae after the event were observed. As discussed below, those patients that had an X-STOP® migrate or dislodge showed an increase in VAS back pain scores (i.e., worsening pain) through 24 months, and in many cases had worse pain and function (ZCQ) scores at 24 months compared to those in whom the device did not migrate or dislodge.

While the incidence of spinous process fractures was higher in the Superion® group, the overall rate of radiographic observation was similar in both treatment groups (16.3% of Superion® vs. 16.9% of X-STOP®, p=0.690).

2.2 Secondary Endpoints

Patients in the Superion® group exhibited a similar success proportion at 24 months in all secondary endpoints when compared to the X-STOP® group (**Table 7**). Importantly, several of these secondary endpoints, such as pain measured by VAS, are arguably valid indicators of the device's effectiveness in relieving the neurogenic claudication symptoms that prompted patients to seek treatment.

Table 7: Secondary Endpoints at 24 Month Follow-Up in Superion® Clinical Trial

Outcome Measure	Superion® %	X-STOP® %	p-value[1]
ODI: ≥15 point decrease	63.4%	66.9%	0.606
VAS Back: ≥20mm decrease	67.2%	68.4%	0.895
VAS Leg (Worse): ≥20mm decrease	75.6%	77.4%	0.772
SF-12 Physical Function: Maintenance or Improvement	80.5%	89.5%	0.055
SF-12 Mental Health: Maintenance or Improvement	60.2%	66.9%	0.303

[1]Fisher's Exact Test

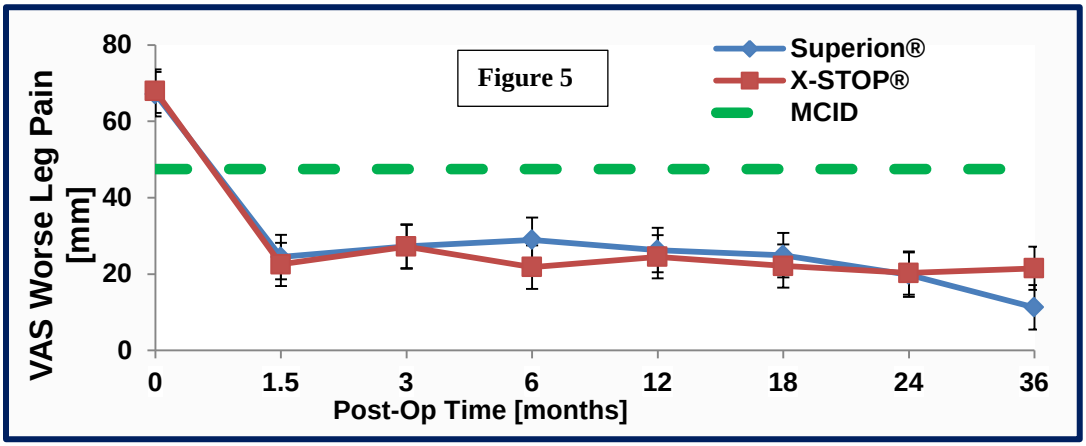
Here also, Superion® efficacy, as measured by secondary outcome metrics, remains durable at 36 months as shown in **Table 8**.

Table 8: Secondary Endpoints at 36 Month Follow-Up in Superion® Clinical Trial

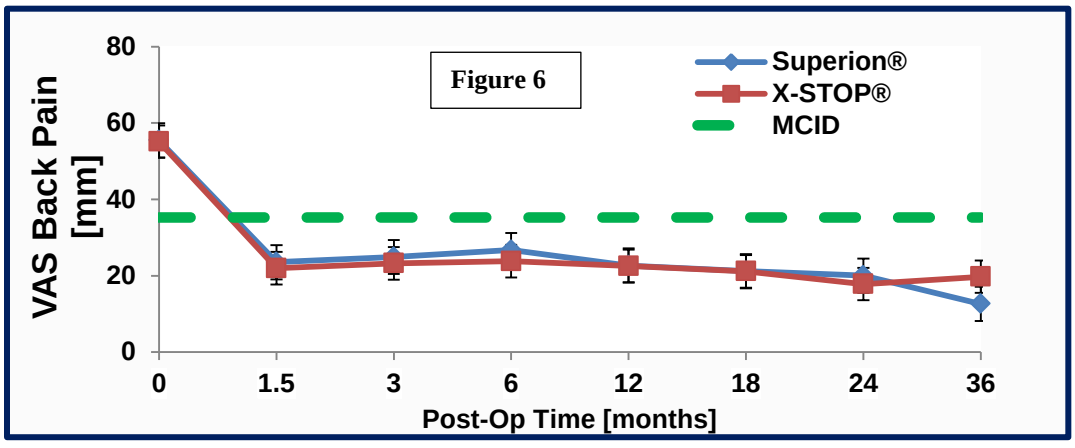
Outcome Measure	Superion® %	X-STOP® %	p-value[1]
ODI: ≥15 point decrease	69.5%	71.4%	0.863
VAS Back: ≥20mm decrease	76.8%	69.7%	0.369
VAS Leg (Worse): ≥20mm decrease	84.1%	69.7%	0.037
SF-12 Physical Function: Maintenance or Improvement	89.0%	86.8%	0.808
SF-12 Mental Health: Maintenance or Improvement	63.4%	60.5%	0.745

[1]Fisher's Exact Test

The time course of VAS – Leg Pain scores for each arm is indicated below in **Figure 5**, where mean scores for each arm are plotted through 36 months. The minimum clinically important difference (MCID) of 20 point improvement vs. baseline is also indicated. Relief of leg pain (shown here as the values corresponding to the worst of the two legs) was apparent at the first follow-up visit, and durable over the course of follow-up.



The time course of VAS – Back Pain scores for each arm are indicated below in **Figure 6**, where mean scores for each arm are plotted through 36 months. The minimal clinically important difference (MCID) of 20 point improvement vs. baseline is also indicated. Relief of back pain was apparent at the first follow-up visit, and durable over the course of follow-up.



2.3 Exploratory Analyses

Additional exploratory analyses were performed to demonstrate the poolability of several baseline patient cohorts and implantation procedures are presented in **Tables 9** and **10**. Baseline differences in covariates di not have an impact on the clinical success of patients in either group.

Table 9: Superion® IDE Composite Success Stratified by Demographic – Related Subgroups

	Superion®	X-STOP®	p-value
Age			
<67 Years	50.0% (44/88)	54.5% (54/99)	0.560
≥67 Years	53.7% (51/95)	44.3% (39/88)	0.237
BMI			
<29.5	55.9% (57/102)	46.7% (42/90)	0.247
≥29.5	46.9% (38/81)	52.6% (51/97)	0.547
Presence of Orthopedic Comorbidities			
Yes	50.9% (59/116)	48.8% (63/129)	0.799
No	53.7% (36/67)	51.7% (30/58)	0.859
Nicotine Use			
Yes	46.9% (45/96)	52.2% (47/90)	0.557
No	57.5% (50/87)	47.4% (46/97)	0.186

Table 10: Superion® IDE Composite Success Stratified by Indication – Related Subgroups

	Superion®	X-STOP®	p-value
Levels Treated			
1-level	55.2% (53/90)	48.4% (46/95)	0.386
2-level	48.3% (42/87)	51.1% (47/92)	0.766
Spondylolisthesis			
Grade 1 Spondylolisthesis	57.4% (39/68)	56.0% (42/75)	0.691
No Spondylolisthesis	48.7% (56/115)	45.5% (51/112)	1.000
Stenosis Type			
Central Only	53.1% (34/64)	44.8% (26/58)	0.691
Lateral Only	31.3% (5/16)	46.7% (7/15)	0.473
Mixed	54.4% (56/103)	52.6% (60/114)	0.892
Surgical Approach (Superion® Only)			
Mini-Open	51.1% (46/90)	-	-
Percutaneous	52.8% (47/89)	-	-

2.4 Adverse Events

The safety profile of the Superion® device is similar to that of the X-STOP® device when considering adverse event incidence.

Table 11 summarizes adverse events in the trial that occurred perioperatively or post-operatively, and those that were related to the device or procedure. No device-, or procedure-related deaths were reported in either group.

Table 11: Comparison of Summary Adverse Event Rates – Superion® and X-STOP®

	Superion® (I) (N=190)		X-STOP® (C) (N=201)		I vs. C		
	n	%	n	%	Diff	LB	UB
Any adverse event (per patient)	180	94.7	184	91.5	-3.2	-13.1	6.8
Any device related AE	22	11.6	15	7.5	-4.1	-14.0	5.8
Any procedure related AE	27	14.2	32	15.9	1.7	-8.2	11.6
Any serious AE	88	46.3	92	45.8	-0.5	-10.5	9.4
Serious AE that is either device or procedure related	16	8.4	19	9.5	1.0	-8.9	10.9
Deaths	6	3.2	5	2.5	-0.7	-10.6	9.3

Notes:
[1] Exact 95% confidence interval for the group difference.

Specific adverse events where the difference between Superion® and X-STOP® were more than 2% are indicated in **Table 12**.

Table 12: Specific Adverse Events in Superion® IDE

	Superion® (N=190)			X-STOP® (N=201)			I vs C
Adverse Event Type	No. of Events	No. of Pts.	% of Pts.	No. of Events	No. of Pts.	% of Pts.	p-value
Back pain	56	50	26.3	71	66	32.8	0.184
Cardiovascular	25	20	10.5	20	16	8.0	0.389
Device Migration	1	1	0.5	8	7	3.5	0.068
Device Subsidence	4	4	2.1	0	0	0.0	0.055
Dizziness	5	5	2.6	0	0	0.0	0.026
Genitourinary	25	22	11.6	17	17	8.5	0.317
Leg pain	41	37	19.5	54	47	23.4	0.389
Musculoskeletal	108	78	41.1	100	70	34.8	0.212
Neurological disorder	27	22	11.6	13	13	6.5	0.110
Other, specify	15	14	7.4	10	5	2.5	0.033
Pain - buttock or groin	23	21	11.1	13	13	6.5	0.150
Skin and Subcutaneous Tissue	2	2	1.1	10	8	4.0	0.106
Soft tissue damage	1	1	0.5	7	7	3.5	0.068
Spinous process fracture	24	22	11.6	14	13	6.5	0.110

There were no trends or statistical differences within any of the device-related or surgery-related categories of adverse events. Pain-related adverse events were distributed differently between the Superion® and X-STOP® groups. X-STOP® patients were more likely to have back pain or leg pain adverse events, while Superion® patients were more likely to have buttock or groin adverse events. In addition, X-STOP® patients were more likely to have events related to device migration, skin and subcutaneous tissue, and soft tissue damage. Superion® patients were more likely to have an adverse event related to spinous process fracture and neurological disorder. Overall, the adverse event rates between the Superion® and X-STOP® patients were similar, despite minor differences in type of events.

2.5 Study Summary

The Superion® IDE demonstrated reasonable assurance of safety and effectiveness through valid scientific evidence collected by means of a scientific study design, rigorous study conduct, and high level of patient accountability, and to establish non-inferiority of the device to the FDA-approved control device. Overall, the patients in both treatment groups demonstrated an immediate improvement in their stenosis symptoms, which was maintained in both groups through 24 months, and in the Superion® group through 36 months, as measured by ZCQ. In addition, there were similar safety profiles of both treatment groups.

3. COMPARISON OF STUDY RESULTS TO PRIOR STUDIES

For patients with moderate stenosis a number of treatments are available, depending on other concomitant pathologies present in the patient's spine. Each of these treatments has a different risk-benefit profile, and these risk-benefit profiles, along with the concomitant spinal pathologies, must be taken into consideration when comparing different treatment options.

3.1 Comparison to Direct Decompression

Direct decompression of the spine is utilized in many surgical procedures to treat moderate to severe lumbar spinal stenosis. A direct decompression surgery removes the osseous and soft tissues impinging upon the spinal nerve roots and column, thereby relieving a patient's spinal stenosis symptoms. Additional posterior stabilization in the form of posterolateral fusion with hardware (e.g., pedicle screw systems) or the coflex® Interlaminar Technology is often utilized in conjunction with a direct decompression, as the removal of bony tissue to relieve the patient's symptoms can create mechanical instability in the affected motion segment.

3.1.1 Perioperative Outcomes and Adverse Events

The major benefit of indirect decompression compared to surgical decompression with or without stabilization is the minimally-invasive nature of the procedure which lends itself to shorter surgeries and lower rates of perioperative adverse events, such as infection. These benefits can be quantified by comparing perioperative outcomes between studies of indirect decompression and decompression with or without posterior stabilization.

The coflex® IDE clinical trial utilized direct decompression for both treatment arms, followed by stabilization with coflex® or posterolateral fusion. A comparison of the Superion® trial results to the results from the coflex® trial[1] (for moderate to severe spinal stenosis with back pain) highlights the differences in perioperative outcomes (**Table 13**). Even though these devices are indicated for different patient populations, the blood loss and operative time data provide incremental benefit to the risk-benefit profile for indirect decompression.

Table 13: Perioperative Results from Superion® IDE and coflex® IDE (mean ± SD)

Operative Detail	Superion® IDE		coflex® IDE[1]	
	Superion®	X-STOP®	Decompression + coflex®	Decompression + Fusion
	(n=190)	(n=200)	(n=215)	(n=107)
Blood Loss (cc)	13.5 ± 15.9	38.7 ± 43.8	109.7 ± 120.0	348.6 ± 281.8
Hospital Length of Stay (days)	1.80 ± 1.5	1.90 ± 1.5	1.90 ± 1.08	3.19 ± 1.61
Operative Time (min)	56.3 ± 26.8	47.2 ± 18.8	98.0 ± 41.1	153.2 ± 55.5

As shown in the perioperative results from both Superion® and coflex® studies, indirect decompression surgeries with both Superion® and X-STOP® entailed significantly less blood loss and operative time than surgical decompression and stabilization with coflex® or fusion. While the severity of stenosis and baseline patient demographics in these two studies are different, the results demonstrate the differences in operative time and patient morbidity (based on estimated blood loss) between indirect decompression and decompression with stabilization using coflex® or posterolateral fusion.

In addition, the coflex® trial cited wound problems in 14.0% of decompression + coflex® patients (with irrigation and debridement required for 1.9% of decompression + coflex® patients), while the Superion® IDE cited infection in only 2.6% of Superion® patients (with irrigation and debridement required for 0.5% of Superion® patients and 1.0% of X-STOP® patients).

Other published studies demonstrate higher complication rates associated with direct decompression procedures compared to those demonstrated with interspinous spacers. A recently published retrospective study[2] comparing X-STOP® to a demographic-matched control of surgical decompression saw higher complication rates within 30 days of index surgery for surgical decompression (9.2%) compared to X-STOP® (3.4%), and an increase in mean index hospitalization for surgical decompression (2.49 days) compared with X-STOP® (1.58 days). Given that hospitalization and complication rates between the Superion® and X-STOP® devices were similar in the IDE trial, comparable comparisons can be extended to the Superion® device.Perioperative complication rates reported in the literature for direct decompression range from 10% to 29.6%[3,4,5], with greater complications associated when a fusion procedure is utilized for adjunctive stabilization[6]. These perioperative complications include infection, dural tear, hematoma, seroma, inflammatory reaction, pulmonary edema, urinary retention, and mechanical complications. A recent review of spinal devices in the Medicare population reported higher complication rates in decompression surgeries compared to interspinous spacers[7] (**Table 14**).

Table 14: Complication Rates Associated with Lumbar Spinal Stenosis Surgery, from Deyo et al. (2013)

	Interspinous Process Spacer	Interspinous Process Spacer + Decompression	Decompression Alone	Fusion
N for measures that include mortality	3,965	1,644	76,520	16,955
N for safety & utilization measures	3,912	1,617	75,310	16,623
Wound complications @ 30 days	30 (0.8%)	21 (1.3%)	1,343 (1.8%)	548 (3.3%)
Cardiopulmonary or stroke complications @ 30 days	39 (1.0%)	21 (1.3%)	1,192 (1.6%)	473 (2.9%)
Death w/in 30 days	7 (0.18%)	7 (0.43%)	240 (0.31%)	102 (0.60%)
Life-threatening complications (either of prior two rows)	45 (1.2%)	25 (1.6%)	1,351 (1.8%)	553 (3.3%)
All-cause rehospitalization within 30 days	175 (4.5%)	92 (5.7%)	4,985 (6.6%)	1,568 (9.4%)

3.1.2 Clinical Outcomes

While there have been no large scale randomized clinical studies comparing interspinous devices to direct decompression for the treatment of moderate stenosis, clinical outcome measurements presented in published clinical studies can be compared to the results from the Superion® trial to compare the effectiveness of these devices versus direct decompression. While these studies did not utilize a robust composite endpoint (as was utilized in the Superion® study), comparison of individual clinical outcomes is possible. Studies of direct decompression using the same ZCQ success criteria as the Superion® clinical trial are presented in **Table 15**.

[1]US Food and Drug Administration. Summary of Safety and Effectiveness Data – coflex® Interlaminar Technology. P110008. October 2012. Available at: http://www.accessdata.fda.gov/cdrh_docs/pdf11/P110008b.pdf.
[2]Patil CG, Sarmiento JM, Ugiliweneza B, Mukherjee D, Nuno M, Liu JC, Walia S, Lad SP, Boakye M. Interspinous device versus laminectomy for lumbar spinal stenosis: a comparative effectiveness study. Spine J. 2014; 14:1484-92
[3]Fokter SK, and Yerby SA: Patient –based outcomes for the operative treatment of degenerative lumbar spinal stenosis. Eur Spine J, 2006. 15:1661-1669.
[4]Ciol MA, et al.: An Assessment of Surgery for Spinal Stenosis: Time Trends, Geographic Variations, Complications, and Reoprations. J Am Geriatric Soc, 1996. 44(3): 1-10.
[5]Atlas SJ, et al.: The Maine Lumbar Spine Study, Part III: 1-Year Outcomes of Surgical and Nonsurgical Management of Lumbar Spinal Stenosis. Spine, 1996. 21(15)1: 1787-1794.
[6]Deyo RA, et al.: Morbidity and mortality in association with procedures on the lumbar spine. The influence of age, diagnosis, and procedure. J Bone Joint Surg Am, 1992. 74-A(4): 536-543.
[7]Deyo RA, et al.: Interspinous Spacers Compared With Decompression or Fusion for Lumbar Stenosis. Complications and Repeat Operations in the Medicare Population. Spine, 2013. 38(10): 865-872

These results demonstrate higher rates of perioperative complications associated with surgical decompression, with or without stabilization, compared to indirect decompression procedures such as Superion® and X-STOP®.

While direct comparison of these results with the Superion® trial are difficult due to differences in reporting, the results nonetheless align with the lower levels of wound-related complications shown in the Superion® trial compared with the results from the coflex® trial (which utilized decompression plus coflex® or posterolateral fusion).

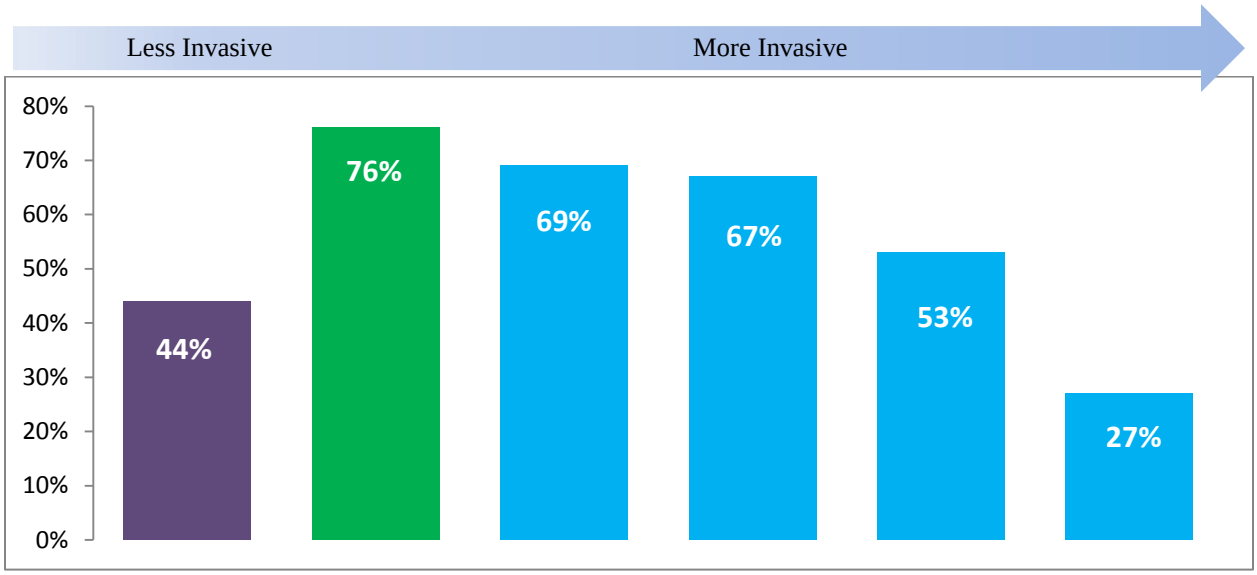
Table 15: Comparison of ZCQ Results of Decompression Studies to Superion® IDE

Article	n	Treatment	Time point	ZCQ Success (2 of 3)
Superion® IDE, Superion®	131	Superion®	24 months	81.7%
Superion® IDE, X-STOP®	133	X-STOP®	24 months	87.2%
Superion® IDE, Superion® (non-censored for injections)*	144	Superion®	24 months	80.6%
Superion® IDE, X-STOP® (non-censored for injections)*	156	X-STOP®	24 months	84.0%
Fokter et al., 2006[3]	58	Decompression	27 months (mean)	63.8%
Moojen et al., 2013[8]	79	Decompression	12 months	69%

*Subjects with epidural steroid or nerve root blocks are excluded from assessments of clinical outcome measurements due to the masking effects these procedures may have on the clinical outcome measurements. For direct comparison to results from the literature, subjects with injections are included in this assessment.

In comparison to these ZCQ results, both treatment arms in the Superion® trial achieved a higher rate of ZCQ success compared with patients undergoing decompression alone. In addition, leg pain improvement following laminectomy without posterior stabilization has been reported in 27-67% of subjects at 2 years[9,10,11], while 75.6% of Superion® subjects reported clinically significant leg pain improvement (>20mm VAS decrease vs. baseline) at 2 years. These data indicate that Superion® may perform at least similarly to direct decompression at 2 years postoperatively.

Comparing the results of the Superion® trial to those presented in published clinical literature (**Figure 7**) establishes that the Superion® device provides comparable clinical outcomes. Examining improvement in leg pain (a signal symptom associated with neurogenic claudication secondary to lumbar spinal stenosis), the improvement seen among Superion® trial patients compares favorably to both epidural steroid injections and surgical laminectomy when measured using the Visual Analog Scale (VAS):



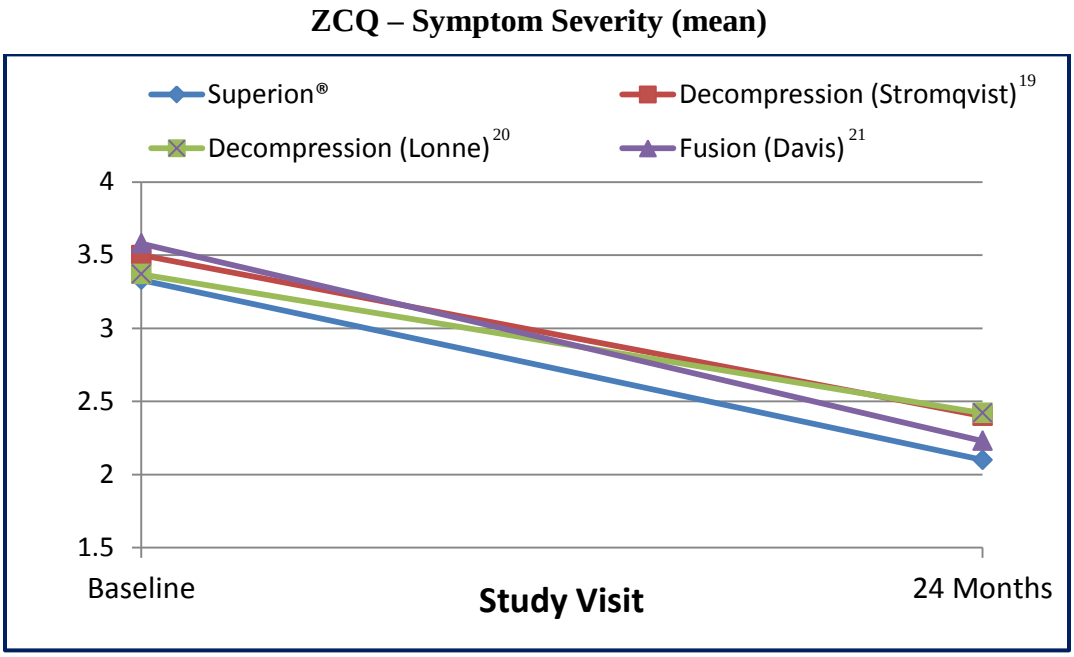
Author (Journal)	n		n	Author (Journal)	n
Manchikanti[12] (Pain Physician 2012)	**50**	**Superion® Trial Results**	**131**	**Davis[13] (Spine 2013)**	**86**
				Stromqvist[11] (Spine 2013)	**50**
				Malmivvaara[10] (Spine 2007)	**42**
				Haro[9] (Spine 2008)	**50**

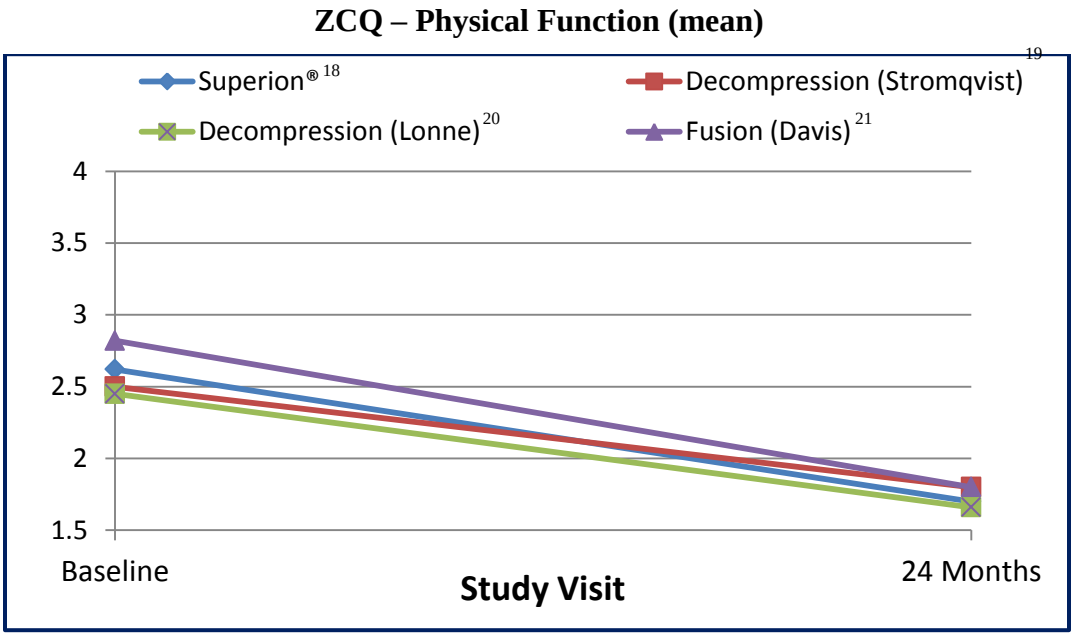
Figure 7: Comparison to Published Rates – Relief of Leg Pain (VAS)

Examining published outcomes of treatment for lumbar spinal stenosis, as measured by the Zurich Claudication Questionnaire (ZCQ), provides data for comparing the Superion® device to both decompression and fusion surgery. As shown in **Figure 8**, below, improvements in both the Physical Function and Symptom Severity domains of the ZCQ among patients treated with the Superion® device are similar to those seen among patients following decompression surgery, as well as fusion surgery.

[3]Fokter SK, Yerby SA. Patient-based outcomes for the operative treatment of degenerative lumbar spinal stenosis. Eur Spine J. 2006 Nov;15(11):1661-9.
[8]Moojen WA1, Arts MP, Jacobs WC, et al. Interspinous process device versus standard conventional surgical decompression for lumbar spinal stenosis: randomized controlled trial. BMJ. 2013 Nov 14;347:f6415.
[9]Haro H, Maekawa S, Hamada Y.: Prospective analysis of clinical evaluation and self-assessment by patients after decompression surgery for degenerative lumbar canal stenosis. Spine J. Mar-Apr 2008;8(2):380-384
[10]Malmivaara A, Slatis P, Heliovaara M, et al.: Surgical or nonoperative treatment for lumbar spinal stenosis? A randomized controlled trial. Spine (Phila Pa 1976). Jan 1 2007;32(1):1-8.
[11]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 (Phila Pa 1976). Aug 1 2013;38(17):1436-1442.
[12]Manchikanti L, et al.: Results of 2-Year Follow-Up of a Randomized, Double-Blind, Controlled Trial of Fluoroscopic Caudal Epidural Injections in Central Spinal Stenosis. Pain Physician 2012. 15:371-374.
[13]Davis et al., Spine 2013.

Figure 8: Comparison to Published ZCQ Outcomes





[19]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 (Phila Pa 1976). Aug 1 2013;38(17):1436-1442. [n=50]
[20]Lonne G, et al.: Comparing Cost-effectiveness of X-STOP With Minimally Invasive Decompression in Lumbar Spinal Stenosis. Spine, 2015. 40(8):514-520. [n= 41]
[21]Fusion: Davis et al., Spine 2013 [n=86]

3.1.3 Summary

Comparison of the results from the Superion® trial to other studies in the literature suggests that the Superion® ISS may provide similar rates of clinical success to other treatment options, but with a minimally-invasive surgical procedure and fewer perioperative complications. Further, the spinal anatomy is not altered significantly by the implantation procedure thereby offering the possibility of reducing the complexity of future surgical options in the event that reoperation becomes necessary to address return of symptoms as degenerative changes in the spine advance.

4 CONCLUSIONS

4.1 Device Design

Placement of the Superion® ISS between two adjacent spinous processes is intended to limit compression of the neural elements at the treated level by blocking extension motion of the affected spinal segment. This principal of "extension-blocking" is fundamental to the manner by which interspinous spacers such as the Superion® ISS achieve their intended effect. This mechanism of action is a function of the size of the implant placed, and maintenance of the device's position between the spinous processes.

The surgical technique by which the Superion® ISS is implanted uses a posterior, minimally-invasive approach, wherein the device is inserted through a narrow diameter cannula placed at midline, and which requires no surgical dissection of the spinal musculature. As such, device placement is minimally disruptive of surrounding and supporting tissues.

4.2 Clinical Study Results

4.2.1 Study Integrity

The Superion® cohort had a robust follow-up rate of 96.7% and the control X-STOP® cohort had a follow-up rate of 94.1% through 24 months, providing a very complete dataset upon which to base all clinical conclusions and to analyze the composite clinical success. In addition, 90.8% had 36 month data available. The use of Bayesian multiple imputation for the primary endpoint allowed those few patients who were lost to follow up to contribute data to the primary endpoint analysis. Lastly, the excellent follow-up rate and large number of study subjects allowed for poolability and sub-analysis of variable clinical populations, including 1- versus 2-level surgery, spondylolisthesis, different categories of stenosis, and baseline demographic differences, among others. The data clearly establish that the Superion® ISS is safe and effective when used at one or two levels.

4.2.2 Effectiveness Analyses

Based upon clinical outcome scores, implantation of the Superion® ISS provides a clear benefit for patients from at least 6 weeks post-operatively (the first post-operative study visit) though 24 months following implantation. Effectiveness, or benefit in reducing or eliminating symptoms of lumbar spinal stenosis, was measured by the primary endpoint and also by a number of secondary outcome metrics. The latter included Oswestry Disability Index (ODI), Visual Analog Scale (VAS) for both back pain and leg pain, and the SF-12 quality of life metric. Clinical data from 36 month visits indicate the treatment effect for Superion® is sustained as measured by these secondary outcomes measures.

The clinical benefits of the Superion® ISS are seen in a majority of patients, particularly in the relief from stenosis symptoms (as demonstrated by ZCQ symptom severity subdomain) and in relief from leg pain (as demonstrated by VAS Leg Pain measurement), which are the predominate expressions of neurogenic claudication attributable to lumbar stenosis. The ZCQ physical function domain also improved in these patients, albeit to a lesser degree than the ZCQ symptom severity. While stenosis manifests predominately as buttock, groin, and leg pain, there are patients with associated back pain and related functional limitations. Isolated back pain is often measured by ODI and VAS Back Pain scores. These measurements also demonstrated improvement, albeit to a lesser extent and with a more delayed effect.

4.2.4 Safety Evaluations

The primary safety endpoint was the absence of re-operations, revisions, or supplemental fixation. Through 24 months (as part of the primary endpoint), there were a total of 38 reoperations or revisions in the Superion® group (38/190, 20.0%) compared with 29 reoperations or revision in the X-STOP® group (29/201, 14.4%, p = 0.179). Through the last time point, however, which includes time points past 24 months, there were a total of 49 reoperations or revisions in the Superion® group (49/190, 25.8%) compared with 44 reoperations or revisions in the X-STOP® group (44/201, 21.9%, p = 0.365). The primary reason for reoperation or revision was lack of relief, or progression, of spinal stenosis symptoms, rather than an adverse reaction to, or caused by, the device or implantation procedure.

In addition to re-operations and revisions, the safety profile of the Superion® ISS is similar to the X-STOP® device when considering adverse event incidence. In almost every category, the event rate was similar in the Superion® cohort compared to the X-STOP® cohort. There were no unanticipated adverse events in either cohort.

Serious adverse events occurred in both arms of the trial at a comparable rate, in 46.3% of Superion® patients compared with 45.8% of X-STOP® patients. In addition, X-STOP® patients exhibited a slightly higher rate of serious adverse events that were device- or procedure-related (X-STOP®: 9.5%; Superion®: 8.4%). These device- or procedure-related serious adverse events primarily occur from the day of surgery through Month 3 postoperatively.

Overall, rates of re-operation and revision were similar in both groups. Adverse event rates between the Superion® and X-STOP® patients were similar, as well as the types of adverse events. Specifically, Superion® patients had more device-related adverse events, compared with X-STOP® patients, who had more procedure-related adverse events. The data demonstrated the safety of the Superion® ISS compared to an FDA-approved device (X-STOP®) for the same intended patient population.

4.2.5 Radiographic Analysis

The clinical effects of spinous process fractures, device migration, and device displacement identified by the independent radiographic core lab were reviewed. Following surgery, 16.3% of Superion® and 8.5% X-STOP® mITT subjects exhibited a spinous process fracture, while 0% of Superion® and 11.9% of X-STOP® subjects had a device migration and/or dislodgement.

Several observations from the data are notable from these radiographic observations. The majority of spinous process fractures in both arms was detected *only* by the radiographic core lab, and was not observed by the treating clinician. The fractures themselves were not symptomatic or otherwise noticed by the patient. Further, the rate of composite clinical success in Superion® subjects in whom a fracture was detected was comparable to the rate in subjects having no fracture, as was the rate of re-operations and removals in the Superion® population having a fracture to the rate observed in the entire Superion® randomized cohort (15.1% vs. 21.1%, respectively). Finally, many of the fractures were determined to have healed, or were healing, by the 24 month visit.

These data suggest that purely radiographic observations of spinous process fracture did not elicit undue or unexpectedly high rates of adverse clinical sequelae. Further, the secondary outcomes, and specifically those indicative of pain (VAS Back and Leg), were significantly improved in both the overall Superion® cohort, and in the sub-population of Superion® patients sustaining spinous process fractures.

Additional analyses identified demographic, radiographic, and intraoperative risk factors leading to increased incidence of spinous process fracture. Importantly, these factors, which included BMI, spinous process height and shape, and device positioning, are all readily managed and mitigated by labeling and appropriate surgeon training.

4.2.6 Risk/Benefit Profile

The clinical study established that the probable benefits of the Superion® ISS outweigh the probable risks for the treatment of moderate degenerative spinal stenosis, over the 24 month time period studied, with additional benefits noted in data through 36 months. In this population, the device was shown effective in relieving the symptoms of moderate spinal stenosis in the majority of patients treated, and the effectiveness proved durable through longer-term follow-up.

The minimally invasive nature of the Superion® surgery and smaller overall device size are novel, compared to both indirect and direct decompression options. This procedure provides lower patient morbidity than open direct surgical decompression, with or without additional stabilization, while offering comparable effectiveness in relieving symptoms. This conservative surgical option offers a benefit to patients whose overall health and existing co-morbidities preclude, or put them at increased risk of complications associated with a larger decompressive surgery. Surgeries requiring decompression or decompression with fusion also carry greater risk for adverse events, and recovery time is significantly longer, generally requiring extended hospital, post-surgical care and return to activities of daily living.

In addition, the device implantation procedure imposes no alteration of the spinal anatomy, thereby preserving potential future surgical options in the event of spinal disease progression. In comparison, direct decompression surgery can introduce spinal instability and require more serious interventions, such as spinal fusion, if the initial decompression is ineffective.

Further, the Superion® ISS demonstrated safe, with re-operations and revisions primarily due to lack of pain relief, potentially attributable to continued spinal degeneration and/or symptomatology arising from untreated spinal levels. Overall, approximately 4 of 5 subjects progressed to 3 or more years post-operatively without need for additional surgery to address unrelieved or worsening symptoms, thereby avoiding such surgery and the additional risks associated therewith.

In conclusion, valid scientific evidence demonstrate the safety and effectiveness of the Superion® ISS, and that the benefits of the Superion® ISS outweigh the risks of the device when used in accordance with instructions for use, contraindications, warnings, and precautions. Further, with Medtronic's decision to remove the X-STOP device from the market, Superion® ISS is the only FDA approved device indicated for indirect decompression available to physicians today and offers a safe and effective minimally invasive technological advancement for treatment of spinal stenosis.

Vertiflex, Inc. W-9

Form **W-9**
(Rev. November 2017)
Department of the Treasury
Internal Revenue Service

Request for Taxpayer Identification Number and Certification

▶ Go to *www.irs.gov/FormW9* for instructions and the latest information.

Give Form to the requester. Do not send to the IRS.

Print or type. See Specific Instructions on page 3.

1 Name (as shown on your income tax return). Name is required on this line; do not leave this line blank.

Vertiflex, Inc.

2 Business name/disregarded entity name, if different from above

3 Check appropriate box for federal tax classification of the person whose name is entered on line 1. Check only **one** of the following seven boxes.

☐ Individual/sole proprietor or single-member LLC ☑ C Corporation ☐ S Corporation ☐ Partnership ☐ Trust/estate

☐ Limited liability company. Enter the tax classification (C=C corporation, S=S corporation, P=Partnership) ▶ _____

Note: Check the appropriate box in the line above for the tax classification of the single-member owner. Do not check LLC if the LLC is classified as a single-member LLC that is disregarded from the owner unless the owner of the LLC is another LLC that is **not** disregarded from the owner for U.S. federal tax purposes. Otherwise, a single-member LLC that is disregarded from the owner should check the appropriate box for the tax classification of its owner.

☐ Other (see instructions) ▶

4 Exemptions (codes apply only to certain entities, not individuals; see instructions on page 3):

Exempt payee code (if any) _____

Exemption from FATCA reporting code (if any) _____

(Applies to accounts maintained outside the U.S.)

5 Address (number, street, and apt. or suite no.) See instructions.

2714 Loker Ave West, Suite 100

Requester's name and address (optional)

6 City, state, and ZIP code

Carlsbad, CA 92010

7 List account number(s) here (optional)

Part I Taxpayer Identification Number (TIN)

Enter your TIN in the appropriate box. The TIN provided must match the name given on line 1 to avoid backup withholding. For individuals, this is generally your social security number (SSN). However, for a resident alien, sole proprietor, or disregarded entity, see the instructions for Part I, later. For other entities, it is your employer identification number (EIN). If you do not have a number, see *How to get a TIN*, later.

Note: If the account is in more than one name, see the instructions for line 1. Also see *What Name and Number To Give the Requester* for guidelines on whose number to enter.

Social security number

			–			–				

or

Employer identification number

2	0	–	1	6	1	6	3	9	6

Part II Certification

Under penalties of perjury, I certify that:

1. The number shown on this form is my correct taxpayer identification number (or I am waiting for a number to be issued to me); and
2. I am not subject to backup withholding because: (a) I am exempt from backup withholding, or (b) I have not been notified by the Internal Revenue Service (IRS) that I am subject to backup withholding as a result of a failure to report all interest or dividends, or (c) the IRS has notified me that I am no longer subject to backup withholding; and
3. I am a U.S. citizen or other U.S. person (defined below); and
4. The FATCA code(s) entered on this form (if any) indicating that I am exempt from FATCA reporting is correct.

Certification instructions. You must cross out item 2 above if you have been notified by the IRS that you are currently subject to backup withholding because you have failed to report all interest and dividends on your tax return. For real estate transactions, item 2 does not apply. For mortgage interest paid, acquisition or abandonment of secured property, cancellation of debt, contributions to an individual retirement arrangement (IRA), and generally, payments other than interest and dividends, you are not required to sign the certification, but you must provide your correct TIN. See the instructions for Part II, later.

Sign Here Signature of U.S. person ▶ Jeffrey Lund Date ▶ 1/2/2018

General Instructions

Section references are to the Internal Revenue Code unless otherwise noted.

Future developments. For the latest information about developments related to Form W-9 and its instructions, such as legislation enacted after they were published, go to *www.irs.gov/FormW9*.

Purpose of Form

An individual or entity (Form W-9 requester) who is required to file an information return with the IRS must obtain your correct taxpayer identification number (TIN) which may be your social security number (SSN), individual taxpayer identification number (ITIN), adoption taxpayer identification number (ATIN), or employer identification number (EIN), to report on an information return the amount paid to you, or other amount reportable on an information return. Examples of information returns include, but are not limited to, the following.

- Form 1099-INT (interest earned or paid)
- Form 1099-DIV (dividends, including those from stocks or mutual funds)
- Form 1099-MISC (various types of income, prizes, awards, or gross proceeds)
- Form 1099-B (stock or mutual fund sales and certain other transactions by brokers)
- Form 1099-S (proceeds from real estate transactions)
- Form 1099-K (merchant card and third party network transactions)
- Form 1098 (home mortgage interest), 1098-E (student loan interest), 1098-T (tuition)
- Form 1099-C (canceled debt)
- Form 1099-A (acquisition or abandonment of secured property)

Use Form W-9 only if you are a U.S. person (including a resident alien), to provide your correct TIN.

If you do not return Form W-9 to the requester with a TIN, you might be subject to backup withholding. See What is backup withholding, *later.*

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866.268.6486 | info@vertiflex.com