CLINICAL INVESTIGATIONAL PLAN (CIP)

EVALUATION OF SAFETY AND EFFECTIVENESS OF LOBSTER DYNAMIC INTERSPINOUS SPACER IN LUMBAR SPINAL STENOSIS: A SINGLE ARM, PROSPECTIVE, MUTLI-CENTER STUDY

Protocol Number:*LB2CT01*

Version: 1.0

Date: 08-09-2022

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REVISION HISTORY

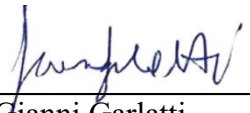
Version	Date	Summary of Changes
1.0	08-09-2022	Original Version

PROTOCOL APPROVAL SIGNATURE PAGE

Protocol Number: LB2CT01
Protocol Name: Evaluation of Safety and Effectiveness of Lobster Dynamic Interspinous Spacer in Lumbar Spinal Stenosis: A Single Arm, Prospective, Mutli-Center Study
Protocol Version: 1.0
Protocol Date: 08-09-2022

This protocol has been read and approved by:

SPONSOR:



09 / 08 / 2022

Gianni Garlatti
General Manager
Diametros Medical srl

Date (dd/mmm/yyyy)

INVESTIGATOR PROTOCOL SIGNATURE PAGE

I have read and understand this protocol and will conduct the study in accordance with this protocol. I will work consistently with the ethical principles that have their origin in the Declaration of Helsinki and that are consistent with good clinical practices, ISO14155 norm, ICH-GCP as far as applicable, and the local legally applicable requirements.

In my formal capacity as Investigator, my duties include ensuring the safety of the study subjects enrolled under my supervision and providing Diametros Medical with complete and timely information, as outlined in the protocol. It is understood that all information pertaining to the study will be held strictly confidential and that this confidentiality requirement applies to all study staff at this site.

Protocol Number: LB2CT01

Protocol Title: Evaluation of Safety and Effectiveness of Lobster Dynamic Interspinous Spacer in Lumbar Spinal Stenosis: A Single Arm, Prospective, Mutli-Center Study

Protocol Version: 1.0

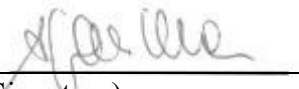
Protocol Date: 08-09-2022

Principal investigator at the local investigational site and PI Deputy and any additional required signatories:

Investigator:

STEFANO MARCIA

(Print Name)



(Signature)

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Upon signing, send a copy of this page to the Sponsor and retain a copy for your files.

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LIST OF ABBREVIATIONS

AE	Adverse Event
AIDS	Acquired Immunodeficiency Syndrome
AP	Anteroposterior
ASTM	American Society for Testing and Materials
CDRH	Center for Devices and Radiological Health
CEC	Clinical Events Committee
CFR	Code of Federal Regulations
CRF	Case Report Form
CRO	Contract Research Organization
CT	Computed Tomography or CAT Scan
DDD	Degenerative Disc Disease
DEXA	Dual-Energy X-ray Absorptiometry or Bone Density test
DHHS	U.S. Department of Health and Human Services
DSMB	Data and Safety Monitoring Board
EC	Ethics Committee
eCRF	Electronic Case Report Form
EDC	Electronic Data Capture
ELI	Extra Low Interstitials
EMG	Electromyography
EOB	Explanation of Benefits
FDA	U.S. Food and Drug Administration
GCP	Good Clinical Practice
HIPAA	Health Insurance Portability and Accountability Act
HIV	Human Immunodeficiency Virus
ICF	Informed Consent Form
ICH	International Conference on Harmonization of Technical Requirements for Registration of Pharmaceuticals for Human Use
IDE	Investigational Device Exemption
IFU	Instructions for Use
IMM	Independent Medical Monitor
ISO	International Organization for Standardization
LSS	Lumbar Spinal Stenosis
LTFU	Lost to Follow-Up
MRI	Magnetic Resonance Imaging

OUS	Outside United States
PF	Physical Function
PG	Performance Goal
PHI	Personal Health Information
PI	Principal Investigator
PMA	Premarket Approval
PRO	Patient Reported Outcome
SAE	Serious Adverse Event
SAP	Statistical Analysis Plan
SAP	Superior Articulating Process
SF-12	12-Item Short Form Survey
SOC	Standard of Care
SOP	Standard Operating Procedure
SSED	Summary of Safety and Effectiveness
SSI	Secondary Surgical Interventions
UADE	Unanticipated Adverse Device Effect
VAS	Visual Analog Scale
ZCQ	Zurich Claudication Questionnaire

1. STUDY SUMMARY

Study Full Title	Evaluation of Safety and Effectiveness of Lobster Dynamic Interspinous Spacer in Lumbar Spinal Stenosis: A Single Arm, Prospective, Mutli-Center Study
Study Sponsor	Diametros Medical srl
Study Number	LB2CT01
Protocol Version and Date	1.0, 08-09-2022
STUDY OVERVIEW	
Study Design	Prospective,multi-center study of the Lobster System in patients with moderate lumbar spinal stenosis.
Purpose	To demonstrate the safety and effectiveness of the Lobster device in comparison to an SSED-based performance goal.
Expected Study Duration	2 years, including enrollment and post-operative follow-up
Number of Subjects & Sites	Estimated 210 investigational subjectsin up to 3 sites in Italy will be enrolled.
Treatment	All enrolled subjects will be assigned to treatment with the Lobster device
Evaluation Schedule	Subjects will be evaluated at the following timepoints: • Pre-operation • 6 weeks • 3 months • 6 months • 12 months • 24 months, and annual thereafter until final subject reaches 12 months
ELIGIBILITY CRITERIA	
Intended Subject Population	Lobster Implantable Dynamic Interspinous 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 lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, MRI and/or CT evidence by a thickened ligamentum flavum, narrowed lateral recess, and/or central canal or foraminal narrowing. Patients must also meet all study inclusion and none of the study exclusion criteria.
Main Inclusion Criteria	In order to be eligible to participate in this study, subjects must meet all of the following criteria:

	1. Male or female subjects ≥ 45 years of age. 2. Persistent leg/buttock/groin pain, with or without back pain, that is relieved by flexion activities (example: sitting or bending over a shopping cart). 3. Subjects who have been symptomatic and undergoing conservative care treatment for at least 6 months. 4. Diagnosis of degenerative spinal stenosis of the lumbar spine, defined as the narrowing of the midline sagittal spinal canal (central) and/or narrowing between the facet superior articulating process (SAP), the posterior vertebral margin (lateral recess), and the nerve root canal (foraminal). 5. Radiographic confirmation of at least moderate spinal stenosis which narrows the central, lateral, or foraminal spinal canal at one or two contiguous levels from L1-L5. Moderate spinal stenosis is defined as 25% to 50% reduction in lateral/central foramen compared to the adjacent levels, with radiographic confirmation of any one of the following: a) Evidence of thecal sac and/or cauda equina compression. b) Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements. c) Evidence of hypertrophic facets with canal encroachment. Note: All imaging studies used to confirm LSS are to be completed within 3 months prior to enrollment. Radiographic (imaging) confirmation of LSS included MRI and/or CT. In the case of a transitional L5/L6 segment with a sufficiently prominent L6 spinous process, these subjects may be included by a deviation request from the applicant. 6. Must present with moderately impaired Physical Function (PF) defined as a score of > 2.0 of the Zurich Claudication Questionnaire (ZCQ). 7. Must be able to sit for 50 minutes without pain and to walk 15 meters (50 feet) or more . 8. Subjects who are able to give voluntary, written informed consent to participate in this clinical investigation and from whom consent has been obtained. 9. Subjects, who, in the opinion of the Clinical Investigator, are able to understand this clinical investigation, cooperate with the investigational

	procedures and are willing to return for all the required post-treatment follow-ups.
Main Exclusion Criteria	Subjects who meet any of the following criteria will be excluded from participating in this study: 1. Axial back pain only. 2. Fixed motor deficit. 3. Diagnosis of lumbar spinal stenosis which requires any direct neural decompression or surgical intervention other than those required to implant the control or investigational device. 4. Unremitting pain in any spinal position. 5. Significant peripheral neuropathy or acute denervation secondary to radiculopathy. 6. Lumbar spinal stenosis at more than two levels determined pre-operatively to require surgical intervention. 7. Significant instability of the lumbar spine as defined by ≥ 3mm translation or ≥ 5° angulation. 8. Sustained pathologic fractures of the vertebrae or multiple fractures of the vertebrae and/or hips. 9. Spondylolisthesis or degenerative spondylolisthesis greater than grade 1 (on a scale of 1-4). 10. Spondylolysis (pars fracture). 11. Degenerative lumbar scoliosis with a Cobb angle of > 10° at treatment level. 12. Osteopenia or osteoporosis. To confirm eligibility, at the Clinical Investigator's discretion, the following subjects may have a DEXA scan performed: i. Women 65 or older ii. Postmenopausal women < age 65 iii. Subjects with major risk factors for or diagnosed with osteoporosis or osteopenia iv. If DEXA is required, exclusion is defined as a DEXA bone density measurement T score ≤ -2.5 13. Morbid obesity, defined as Body Mass Index (BMI) greater than 40kg/m2. 14. Insulin-dependent diabetes mellitus. 15. Significant peripheral vascular disease (diminished dorsalis pedis or tibial pulses). 16. Prior surgery of the lumbar spine. 17. Cauda equina syndrome (defined as neural compression causing neurogenic bowel or bladder dysfunction).

	18. Infection in the disc or spine, past or present. 19. Evidence of active (systemic or local) infection at time of surgery. 20. Active systemic disease such as AIDS, HIV, hepatitis, etc. 21. Paget's disease at involved segment or metastasis to the vertebra, osteomalacia, or other metabolic bone disease. 22. Currently undergoing immunosuppressive therapy or long-term steroid use. 23. Known allergy to titanium or titanium alloys. 24. Tumor in the spine or a malignant tumor except for basal cell carcinoma 25. Known or suspected history of alcohol and/or drug abuse. 25. Prisoner or transient. 26. Life expectancy less than two years. 27. Angina, active rheumatoid arthritis, or any other systemic disease that would affect the subject's welfare or outcome of the clinical investigation. 28. Any significant mental illness (e.g., major depression, schizophrenia, bipolar disorder, etc.) that could impair the consent process or ability to complete subject self-report questionnaires. 29. Involved in pending litigation of the spine or worker's compensation related to the back. 30. Enrolled in the treatment phase of another drug or device clinical investigation (currently or within past 30 days). 31. Congenital defect of the spine. 32. Pregnant or lactating. 33. Any further contraindications and limitations of the device as described in the instructions for use (IFU).
STUDY ENDPOINTS	

Primary Endpoint	Subjects will be evaluated at the 12-month follow-up for the primary endpoint.
	
	Efficacy success will be evaluated as a two-prong composite endpoint:
	• ZCQ Responder (at least two of the three ZCQ domains)
	  ○ ≥0.5 point improvement in physical function.
	  ○ ≥0.5 point improvement in symptom severity
	  ○ Mean satisfaction ≤2.5 points.

	• No secondary surgical intervention (SSI) including re-operations, revision, removals or supplemental fixation or clinical significant confounding treatments (i.e., epidural steroid injections at the index level, spinal cord stimulators or rhizotomies) through 12 months. Safety success will be evaluated using precision-based statistics to characterize the incidence of major device- or procedure-related complications, including: • Device integrity failure (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.
Secondary Endpoints	• Oswestry Disability Index (ODI) • Visual Analogue Scale (VAS) (Back and Leg) • SF-12 Short Form Survey (Physical Function and Mental Health) • Patient satisfaction survey • Neurologic status
STATISTICAL CONSIDERATIONS	
Sample Size	Mimimum of 191 subjects- maximum of 250 subjects
Primary Effectiveness Hypothesis	The primary effectiveness hypothesis is that the composite success rate for the Lobster device is larger than the performance goal of 61.1%.
Compliance statement	This investigation will be conducted in compliance with the CIP, the current version of the Declaration of Helsinki, ISO14155, ICH-GCP (as far as applicable) as well as all national legal and regulatory requirements.

2. INVESTIGATION ADMINISTRATION

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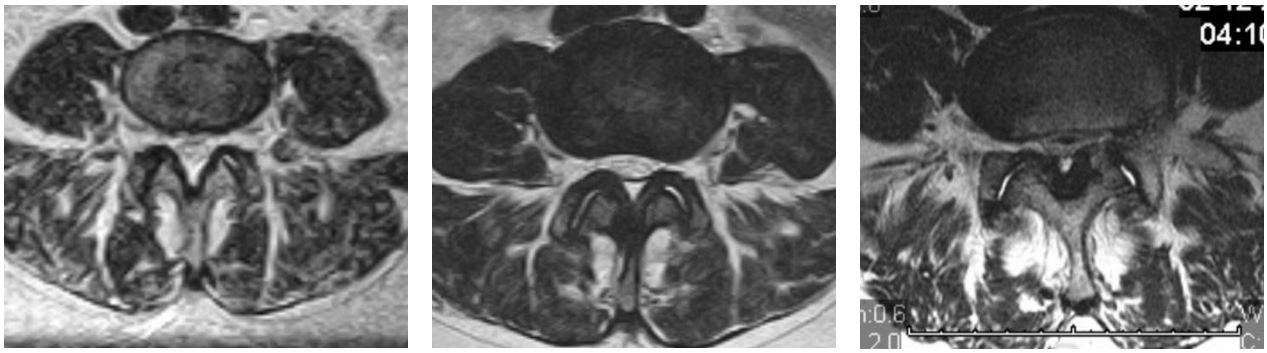
Study Sites	An updated list of all principal investigators and investigation sites is maintained and kept separately from the CIP.

3. INTRODUCTION

3.1 DISEASE STATE – MODERATE SPINAL STENOSIS

Spinal stenosis is defined as the narrowing of the central spinal canal, nerve root canals, and/or intervertebral foramina that leads to compression of the exiting or traversing spinal nerve roots[1]. Symptoms most often occur in patients > 50 years of age, and may therefore have a significant negative impact on the elderly population. Data from the Framingham Heart Study indicates that 1% of men and 1.5% of women already had evidence of stenosis at baseline (mean age of 54), increasing to 11% of men and 25% of women over the 25-year follow-up period[2].

A diagnosis of spinal stenosis can have varying degrees of severity, as well as other concomitant conditions. Figure 1 provides examples of varying severity of spinal stenosis, as observed radiographically.



(a) (b) (c)

Figure 1: Coronal MRIs Depicting Differing Severity of Central Spinal Stenosis
(a) Mild, (b) Moderate, and (c) Severe

At initial presentation, patients may complain of low back pain, buttock pain, leg pain, numbness, tingling, cramping, and/or trochanteric and posterior thigh pain that may radiate to the knee, lateral thigh, calves, and occasionally the feet[3]. In the earlier stages of the disease, these symptoms may be relieved by sitting or lying down and may be exacerbated by walking, especially downhill[4], an occurrence known as intermittent neurogenic claudication. While plain radiographs, three-dimensional imaging methods, and other radiographic measurements are useful in confirming the diagnosis of spinal stenosis, a careful clinical history is the necessary means for establishing the diagnosis[5]. In addition to leg/buttock pain, spinal stenosis patients may also complain of debilitating low back pain that is most commonly attributed to facet-based arthrosis, degenerative disc disease (DDD), or muscular strain.

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[1] Arnoldi CC, Brodsky AE, Cauchoix J, et al. Lumbar spinal stenosis and nerve root entrapment syndrome. Definition and classification. *Clin Orthop* 1976; 115:4-5.

[2] Treatment of Degenerative Lumbar Spinal Stenosis. Summary, Evidence Report/Technology Assessment: Number 32. AHRQ Publication No. 01-E047, March 2001. Agency for Healthcare Research and Quality, Rockville, MD. Available at http://www.ahrq.gov/clinic/epcsums/stenosum.htm.

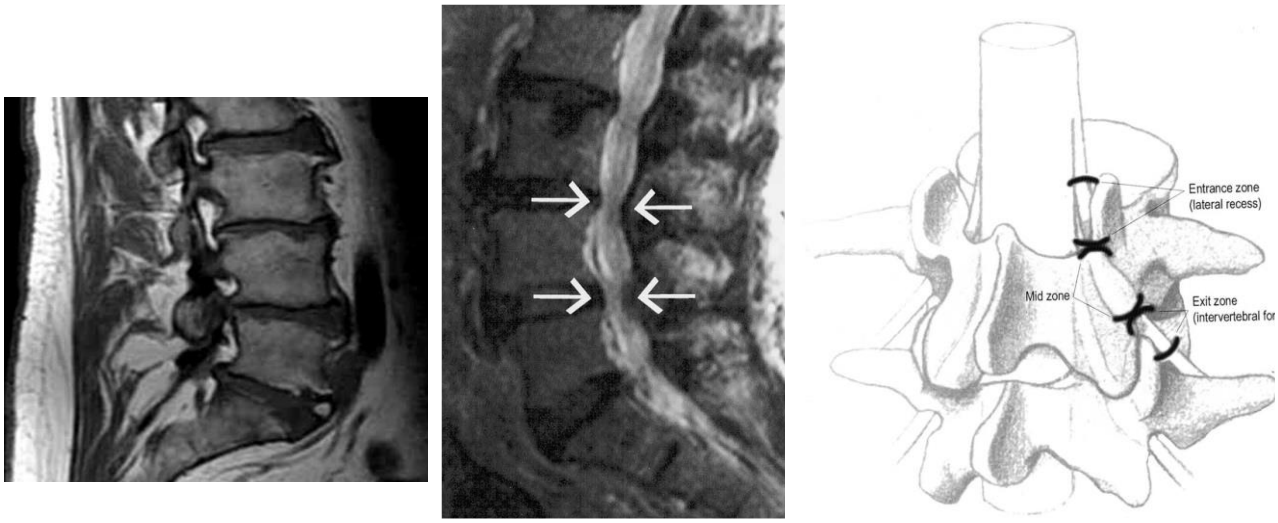
[3] Yong-Hing K, Kirkaldy-Willis WH. The pathophysiology of degenerative disease of the lumbar spine. *Orthop Clin North Am.* 1983;14:501-3.

[4] Delamarter RB, Howard M.: Lumbar spinal stenosis. Rehabilitation of the Spine, Science and Practice. Editors Hochschular S, Cotler H., Guyer R, Chapter 37, pp. 443-456, Mosby, 1993.

[5] Deyo RA, Rainville J, Kent DL. What can the history of physical examination tell us about low back pain? *JAMA* 1992;268:760-5.

While spinal stenosis can be congenital, it is most often the result of degenerative changes to the spine, typically those observed with aging. Degenerative spinal stenosis typically begins with degenerative changes of the nucleus pulposus portion of the intervertebral disc. As the disc degenerates and narrows, the vertebrae become more closely positioned to one another, which may result in ligament laxity and lead to intersegmental instability[6]. These changes can lead to osteophyte formation, which has the effect of temporarily restabilizing the unstable spinal segment. The presence of circumferential osteophytes, together with loss of disc space height, contribute to neural foraminal narrowing. As the degenerative changes progress, the ligamentum flavum shortens and buckles, producing thickening which may further reduce canal area and contribute to central spinal stenosis[7]. Finally, degenerative changes to the facet joints with secondary osteophyte formation may add a component of lateral recess stenosis.

Stenosis can be further classified by the location of neural impingement. Figure 2 presents images of foraminal, central, and lateral stenosis.



(a) (b) (c)

Figure 2: Types of Stenosis: (a) MRI Depicting Foraminal Stenosis (b) MRI Depicting Central Stenosis[2] (c) Diagram of Lateral Stenosis[8]

The initial diagnosis of spinal stenosis is usually based on patient history and physical examination, typically including a neurological examination. Confirmation of the diagnosis and delineation of both the degree of disease and its etiology may be accomplished by imaging methods such as plain radiograph, CT scan (with or without myelographic contrast), and MRI, and non-imaging tests such as electromyography (EMG)[9]. Many different parameters have been reported for objectively or semi-

[6] Fast A, Greenbaum M. Degenerative lumbar spinal stenosis. *Phys Med Rehabil St Art Rev* 1995; Oct. 9:673-82.
[7] Yong-Hing K, Kirkaldy-Willis WH. The pathophysiology of degenerative disease of the lumbar spine. *Orthop Clin North Am.* 1983;14:501-3.
[8] Botwin, KP, Gruber RD. Lumbar Spinal Stenosis: Anatomy and Pathogenesis. Phys Med Rehabil of Clin N Am 14 (2003) 1-15
[9] Delamarter RB, Howard M.: Lumbar spinal stenosis. Rehabilitation of the Spine, Science and Practice. Editors Hochschular S, Cotler H., Guyer R, Chapter 37, pp. 443-456, Mosby, 1993.

objectively evaluating the degree of spinal stenosis, most of which evaluate either the anterior to posterior (AP) dimension of the spinal canal, or its cross-sectional area[10].

The severity of spinal stenosis is often the driving factor in the treatment methodology. Severity can range from "mild" stenosis, where tissue impingement on spinal nerves and/or the spinal cord manifest symptoms that are generally are treated successfully with conservative (non-surgical) care, to "severe" stenosis, where significant amounts of impeding bone and ligamentum flavum need to be removed via direct surgical decompression with or without additional mechanical stabilization, to address symptoms. In addition, severe spinal stenosis is often associated with significant spondylolisthesis or retrolisthesis, creating instability in the spine once a decompression surgery is performed that may require stabilization with instrumentation.

It is recognized that spinal stenosis is a progressively degenerative condition that often continues to worsen as patients age. Non-surgical or conservative treatments, while effective in early and milder stages of the disease, may later prove ineffective as the stenosis worsens. Patients that have continued back and leg pain after conservative care has become ineffective are often diagnosed with "moderate" stenosis. These patients have progressed to a point where direct decompression is not yet required to achieve symptom relief, but where non-operative treatments are no longer effective.

Moderate stenosis is diagnosed clinically through patient symptomatology and is confirmed through radiographic criteria. The clinical hallmark of moderate stenosis is persistent leg, buttock, or groin pain, with or without back pain, that is relieved by placing the spine in flexion (e.g., leaning forward or bending over a shopping cart). These patients are generally no longer responsive to varying non-surgical treatments to relieve pain. In order to assess the extent of the pain and impaired function, validated scoring systems such as the Zurich Claudication Questionnaire can be used. In the clinical trials supporting PMA approval of the X-STOP® and VertiFlex Superion devices, moderate stenosis was further defined, in part, as patients who present with moderately impaired Physical Function (PF) defined as a score of ≥2.0 on the Zurich Claudication Questionnaire. When stenosis reaches a moderate severity and non-surgical care no longer mitigates symptoms, the only way to achieve sufficient pain relief is through surgical means.

Confirmation of moderate spinal stenosis is obtained by radiographic measurements, often defined as 25% to 50% reduction in lateral and/or central foraminal area compared to the adjacent levels. In addition, the patient can exhibit other radiographic evidence of moderate stenosis, including cauda equina compression, nerve root impingement, and hypertrophic facets with canal encroachment.

3.2 DIAGNOSIS AND CURRENT TREATMENT OPTIONS

An overall outline of the treatment continuum for spinal stenosis is included in Figure *3*. As shown by this figure, treatment options for spinal stenosis generally range from non-invasive, or conservative, treatments for conditions with milder symptoms, to invasive surgical options for moderate to severe stenosis, the latter often compounded by spinal instability. Surgical options range from indirect decompression devices (including VertiFlex Superion device) to decompression

[10] See, Treatment of Degenerative Lumbar Spinal Stenosis. Summary, Evidence Report/Technology Assessment: Number 32. AHRQ Publication No. 01-E047, March 2001. Agency for Healthcare Research and Quality, Rockville, MD. Available at http://www.ahrq.gov/clinic/epcsums/stenosum.htm.

procedures, with or without the coflex® device, to fusion procedures with stabilizing instrumentation. Increased surgical complexity and invasiveness is often associated with increased morbidity.

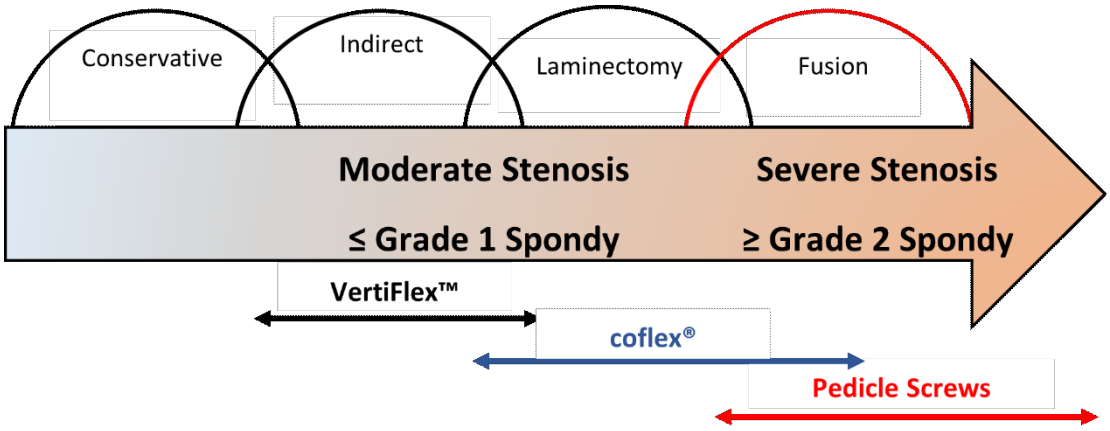


Figure 3: Stenosis Treatment Continuum

3.2.1 Conservative Care

As previously stated, in its early stages, spinal stenosis is primarily treated with physical therapy and other non-invasive methods of symptom management. As outlined in the North American Spine Society (NASS) guidelines for the treatment of spinal stenosis[11], initial treatments for spinal stenosis include modifications to daily living (bed rest, activity modification), bracing, medication (NSAIDs, opiates), and spinal manipulation. Of these, only bracing has demonstrated sufficient evidence of success in the literature, although there is no evidence that results are sustained once the brace is removed. For patients who do not respond to conservative care, an epidural steroid injection at the symptomatic level(s) is generally the next step in the treatment algorithm. NASS guidelines suggest epidural injections to provide short-term (two weeks to six months) symptom relief in patients with neurogenic claudication, although these treatments are still focused on symptom management and not on treating the underlying disease or pathology. If epidural treatment or pain management does not lead to an improved patient outcome, then surgical treatment is outlined as the next step in the care continuum. In patients with symptoms of moderate stenosis, non-surgical care has not been, or is no longer, effective in mitigating the symptoms of lumbar spinal stenosis.

3.2.2 Surgical Treatment

In the setting of lumbar spinal stenosis and degenerative spondylolisthesis recalcitrant to conservative treatment, surgical options have been shown in the recent NIH-funded SPORT trials to produce universally excellent results and superiority over non-operative treatment with results sustained at 4

[11] North American Spine Society. Clinical Guidelines for Multidisciplinary Spine Care: Diagnosis and Treatment of Degenerative Lumbar Spinal Stenosis. 2011.

years. The SPORT trials are Level 1 evidence and reflect the highest quality studies performed to date comparing conservative versus surgical treatment for spinal stenosis[12,13,14,15,16,17]. Depending on the nature of the pathology encountered, there are two types of decompression that can be considered: indirect and direct decompression (with the appropriate stabilization). When considering indirect decompression, the only currently marketed device is the VertiFlex Superion Indirect Decompression System (Boston Scientific). This device is indicated for the treatment of symptoms secondary to moderate stenosis and operates by the same mechanism as the subject Lobster device. The direct decompression options would consist of laminectomy, laminotomy, foraminotomy, decompression with stabilization with coflex® Interlaminar Technology, or laminectomy with posterior instrumentation and spinal fusion. Most of these options are indicated for moderate to severe spinal stenosis or stenosis in which instability exists.

3.2.2.1 Indirect Decompression

For those patients that are demonstrating symptoms of neurogenic intermittent claudication secondary to moderate stenosis, the VertiFlex Superion Indirect Decompression System can also be considered a treatment modality. The VertiFlex Superion Indirect Decompression System has been approved to provide *indirect* neural decompression (i.e., decompression without surgical removal of soft or bony tissue impinging neural elements) by acting as an extension blocker, thus inhibiting compression of neural elements in extension. In this technique, a direct surgical decompression is not performed, and any neurologic recovery is contingent upon adequate indirect neuroforaminal decompression and restriction of extension (extension blocking).

3.2.2.2 Direct Decompression

The goal of most surgical treatments for stenosis is to decompress the nerve roots to relieve leg, groin, and/or buttock pain and other symptoms of neurogenic claudication secondary to lumbar spinal stenosis. A laminectomy procedure, with or without partial facetectomy, is a direct decompression, which removes the source of boney and ligamentous compression of the nerve roots. The treatment of spinal stenosis via laminectomy certainly has its place within a surgeon's armamentarium; however, for laminectomy to be a long term successful option, it has to be used for the proper patient. In addition, laminectomy procedures can be associated with significant adverse events related to the open surgical procedure, such as infection, as well as increased operative time and hospitalization following surgery when compared with interspinous spacer placement[18].

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[12] Birkmeyer NJ. Design of the Spine Patient outcomes Research Trial (SPORT). 2002.
[13] Pearson A. Degenerative spondylolisthesis versus spinal stenosis: does a slip matter? Comparison of baseline characteristics and outcomes (SPORT). 2010.
[14] Tosteson AN. The cost effectiveness of surgical versus nonoperative treatment for lumbar disc herniation over two years: evidence from the Spine Patient Outcomes Research Trial (SPORT). 2008.
[15] Weinstein JN. Surgical versus nonsurgical treatment for lumbar degenerative spondylolisthesis. 2007.
[16] Weinstein JN. Surgical compared with nonoperative treatment for lumbar degenerative spondylolisthesis. four-year results in the Spine Patient Outcomes Research Trial (SPORT) randomized and observational cohorts. 2009.
[17] Weinstein JN. Surgical Versus Nonoperative Treatment for Lumbar Spinal Stenosis Four-Year Results of the Spine Patient Outcomes Research Trial. 2010.
[18] 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.

The laminectomy/direct decompression procedure is often able to effectively remove the neurologic compression. However, it is well-accepted that decompression alone in patients with spinal stenosis and degenerative spondylolisthesis predisposes patients to progression of instability if not stabilized at the time of decompression[19,20,21]. Consequently, lumbar spinal fusion following decompressive laminectomy is commonly recommended for this patient cohort to facilitate both neural decompression and motion segment stabilization. Here also, the increased complexity and invasiveness of the procedure offers greater potential for morbidity.

The coflex® Interlaminar Technology was PMA approved (P110008) for the treatment of spinal stenosis. It's important to recognize coflex® is intended for patients with a greater progression of stenosis than the subject patient population (moderate to severe stenosis). coflex® is designed to be utilized in conjunction with a decompression surgery to provide additional stabilization.

Spinal fusion has well-documented shortcomings. Fusion surgery is more complex and invasive than a laminectomy in that the method for stabilization requires removal of the lamina bone and then implantation of pedicle screws and rods into the spine. Surgical dissection out to the tips of the transverse processes in order to achieve a posterolateral fusion requires extensive dissection and soft tissue trauma, which typically leads to more blood loss, longer operative times, significant scar tissue formation, and greater post-operative pain. Further, iliac crest bone graft harvest site pain following surgery is common and can be a persistent and debilitating source of continued pain in the post-operative period, despite having excellent relief from symptoms of spinal stenosis[22]. Long-term sequelae of the altered biomechanical environment may lead to progression of symptomatic disc degeneration at adjacent levels. The estimated rate of re-operation for symptomatic adjacent segment degeneration following lumbar spinal fusion is 36% at 10 years[23].

3.3 CLINICAL EVIDENCE TO DATE

Lobster device was certified with clinical evaluation (CER Rev.00 28-11-20) based on equivalence demonstrating its compliane with essential safety requirements (MDD 93/42/EEC), acceptable risk/benefit profile, and clinical performance.

The results of two post-market clinical investigation have been published in peer-reviewed journals and provided extensive clinical data on Lobster device.
Manfré 2020 et al. demonstrated the efficacy and safety of Lobster percutaneously implanted interspinous spacers for the relief of degenerative lumbar spinal stenosis (DLSS) in a cohort of 688 patients with chronic neurogenic claudication. In this cohort two sub-groups were compared: Lobster device only (group A) versus Lobster device plus polymethyl

[19] Herkowitz HN, Kurz LT. Degenerative lumbar spondylolisthesis with spinal stenosis. A prospective study comparing decompression with decompression and intertransverse process arthrodesis. J Bone Joint Surg Am. 1991 Jul;73(6):802-8.
[20] Johnsson KE, Redlund-Johnell I, Uden A, Willner S. Preoperative and postoperative instability in lumbar spinal stenosis. Spine 1989; 14(6): 591-593.
[21] Mardjetko SM, Connolly PJ, Shott S. Degenerative lumbar spondylolisthesis: A meta-analysis of literature 1970-1993. Spine 1994; 19(20S):2256S-2265S.
[22] Sasso RC, LeHuec JC, Shaffrey C; Iliac crest bone graft donor site pain after anterior lumbar interbody fusion: a prospective patient satisfaction outcome assessment. J Spinal Disord Tech. 2005 Feb;18 Suppl:S77-81.
[23] Ghiselli G, Wang JC, Bhatia NN, Hsu WK, Dawson EG Adjacent segment degeneration in the lumbar spine. J Bone Joint Surg Am. 2004 Jul;86-A(7):1497-503.

methacrylate augmentation (group). Only 11.3% of complications were observed in group A due to spinous process fractures and bone remodelling, and <1% in group B. Both groups showed marked improvement in the patients' ZCQ scores (3.2 to 1.3) and ODI scores (32 to 21) comparing pre-operative time with 12-months, with strong patient-reported ZCQ satisfaction results (1.7).

Huang et al. 2020 published a commentary on Manfré et al., highlighting how the Lobster devices implantation technique elevates the percutaneous approach beyond the minimally invasive alternatives of the past. Indeed, interspinous spacers offer an alternative for patients deemed challenging candidates for open decompression techniques. Spacers can be placed percutaneously and do not hinder future open surgical decompression or fusion. The commentary further highlighted that the sheer size of the study (covering a 9-year period) is impressive, providing a window for how that data might be improved in the long term, particularly for patients with osteoporosis. As a matter of fact, it is important to consider the spinous process fracture risk that can be limited with the spinoplasty. This is particularly important in eldery patients that may not be ideal surgical candidates; for this population documentation of fracture risk prior to the intervention with DEXA scans, or similar diagnostic studies, should be considered.
Pavan et al. 2022 showed that patients treated with this IPS (Lobster device) had significant improvement in clinical scores (VAS and ODI) at 3 months and significant increase in cross-sectional foraminal area at the treated level. Moreover, the study showed that the method of percutaneous device implantation carries high technical success with no contraindication for subsequent revision surgery if needed. Furthermore, the ability to place this IPS under sedation and local anaesthesia with limited reported complications indicates the feasibility for these types of minimally invasive procedures, which can be performed in interventional radiology departments for the treatment of symptomatic DLSS as a short-stay day-case procedure.

A post-market retrospective study is still on-going with the objective to follow-up 225 subjects with DLSS treated with Lobster percutaneous interspineous device for 2 years. At the moment, data at 6 months (LB2 Retrospective Study 2020) show improvement in pain control and functionality. Mean VAS score started at 7.8 before Lobster implantantion and decreased to 2.9 at 6 months. Disability assessed with ZCQ score showed that mean pre-operative ZCQ was 56.4 and decreased to 28.6 at 6 months. No major complications were described in this retrospective study, probably due to the complete percutaneous implantation technique avoiding surgical resection of the posterior ligaments. We did not record any recurrence, and the three device dislocations were treated with device retrieval and implantation of new Lobster device; only one procedure was not completed due to spinous process fracture. The retrospective study was performed on 3 different centers; a group of patients (n=172) received spinoplasty (introduction of cement inside the spinous processes) to reduce the possibility of spinous fractures, reporting better results both in terms of VAS and ZCQ. In conclusion, the results of this retrospective study suggests that Lobster is a safe and effective minimally invasive percutaneous procedure in DLSS."

Finally, the last Periodic Safety Update Report (Mod. 039-R02 PSUR_rev1) reported a high safety profile for the Lobster device without any reports of serious adverse events and complaints.

3.4 JUSTIFICATION FOR THE DESIGN OF THE CLINICAL INVESTIGATION

According to Clinical Evaluation Report (Rev 00 28-11-20), there is no necessity for further clinical investigations on Lobster device as there are no novel features to investigate and no critical aspects that need further investigation. However, the design of a new and prospective clinical investigation is needed for international registrations to provide additional clinical data not covered by EU requirements. Therefore, the clinical investigation is designed in compliance with ISO 14155:2020, according to last CER conclusions, and relevant post-market clinical data discussed in the previous paragraph to generate prospective, new, and accurate clinical data on Lobster performance and safety to support international registrations outside EU.

4. INVESTIGATIONAL DEVICE

Name of investigational device: Lobster Device
Class: IIb (Rule 8)

4.1 DESCRIPTION OF INVESTIGATIONAL DEVICE

The Lobster device is an implantable dynamic interspinous device, which is positioned between the spinous processes of the lumbar spine percutaneously, using a specific instrument set. It consists of a cylindrical central body (saddle) and at its ends it has four fins that open simultaneously using the internal central auger and limit the lateral movements of the device, preventing possible dislocations.

The whole device is made of medical grade titanium alloy (Ti-Al-4V ELI) compliant with ISO 5832-3 or ASTM F136 standards.

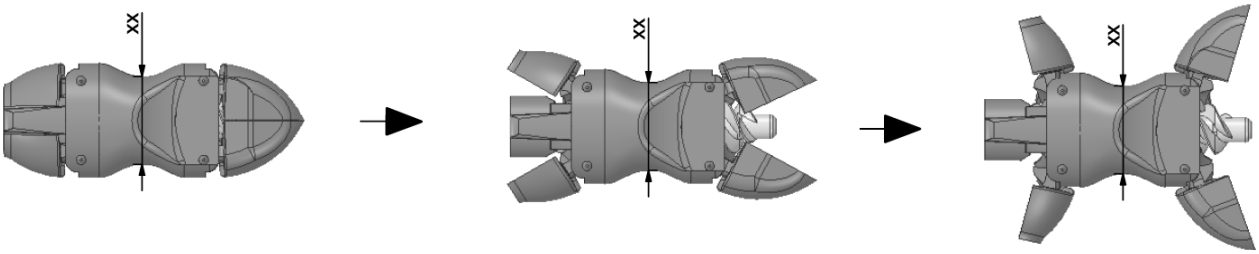

Figure 4-1: Lobster device IDS in closed (left) and open configurations (right)

The front of the device is pointed, designed to facilitate the introduction of the device between the spinous processes.

The Lobster device is available for this trial in multiple sizes, as outlined in **Table 4-1**.

Depending on the pathological status of the patient, treatment at one or two contiguous levels may be necessary.

Table 4-1: Lobster device IDS Available Sizes

Device Codes	Size
LBT08	Ø 8 mm
LBT10	Ø 10 mm
LBT12	Ø 12 mm
LBT14	Ø 14 mm
LBT16	Ø 16 mm

Figure 4-2: Alternate Views of Lobster IDS

The Lobster is supplied in a closed configuration, with the fins tightened. After measuring the size necessary for the distraction through the use of the probes supplied with the instrument set, the device of the chosen size is mounted on the implant holder and inserted in the patient between the two spinous processes. Once the saddle reaches center, the device is rotated by 90° and the fins are opened, as described in the IFU and in the operating technique, ensuring the stability of the Lobster between the spinous processes of the lumbar vertebrae.

The intervention is performed percutaneously using the dedicated instrument set.

The Lobster device works to relieve symptoms stemming from degenerative lumbar spinal stenosis by preserving foraminal height, reducing stress on the facet joints, and reducing pressure on the posterior annulus. As shown in figure, the device uses its four fins to fix itself in the interspinous space. A full surgical technique is attached.

The Lobster device instrument set is described in Table *4-2*.

Table 4-2: Lobster device Instrumentation

LOB-0101	Implant Holder	

LOB-0102	Opening tube for implant holder	
LOB-0103	Fixing shaft for implant holder	
LOB-0104	Quick connect cannulated handle	
LOB-0105	Guide Wire	
LOB-0108	Batting Support for dilation tube 03	
LOB-0201	Dilation Tube 01 with quick connect for handle	
LOB-0202	Dilation Tube 02	
LOB-0203	Dilation Tube 03 with 2 Tines	
LOB-0204	Dilation Tube 04 with 2 Tines	
LOB-0205	Dilation Tube 05	
LOB-0308	Implant Probe 8 mm	
LOB-0310	Implant Probe 10 mm	
LOB-0312	Implant Probe 12 mm	
LOB-0314	Implant Probe 14 mm	
LOB-0316	Implant Probe 16 mm	

More specifics can be found in the Investigator Brochure (IB) of the Lobster device.

4.2 DETAILS OF THE MANUFACTURER OF THE INVESTIGATIONAL DEVICE

Manufacturing Site:

Diametros Medical S.r.l.
Via Frà' Domenico Buonvicini n.17, 50132 Firenze (Italy)
Via di Terranuova 48/5, 52025 Montevarchi (AR), Italy
+ 39 055 980070
+39 055 3909868
info@diametrosmed.com
www.diametrosmed.com
15673341002

4.3 DEVICE APPROVAL STATUS

The procedure will be performed using the Lobester CE marked device. This study will evaluate the on-label use of Lobster for the treatment of moderate lumbar spinal stenosis. This device is to be used in accordance with the provided Instructions for Use (IFU).

4.4 INDICATIONS FOR USE

The Lobster device is indicated as follows:

Lobster Implantable Dynamic Interspinous 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 lumbar spinal stenosis, with or without Grade 1 spondylolisthesis, confirmed by X-ray, MRI and/or CT evidence by a thickened ligamentum flavum, narrowed lateral recess, and/or central canal or foraminal narrowing.

The Lobster device is indicated for those patients with impaired physical function who experience relief in flexion from symptoms of leg/buttock/groin pain, with or without back pain, who have undergone at least 6 months of non-operative treatment. The Lobster device may be implanted at one or two adjacent lumbar levels in patients in whom operative 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 120 of the Zurich Claudication Questionnaire (ZCQ)

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

4.5 DEVICE SUPPLY AND STORAGE

The medical device will be delivered in accordance with the provisions of the goods reception of the clinical investigation site and the contract between the Sponsor and the site. The Investigator is responsible for using the device in compliance with the Instructions for Use (IFU) provided and in accordance with this Clinical Investigation Plan (CIP). Documentation of receipt, disposition, and return of all device materials must be maintained by the investigator or his/her designee.

The packaging will be that of the commercialized products and storage should be in accordance with the IFU provided.

4.6 RETURN, ANALYSIS OR DESTRUCTION OF THE MEDICAL DEVICE

Return, disposal or destruction of the medical device are according to standard procedures.

In case of device deficiencies, including malfunction, usability issues, or inadequacy in the information supplied by the manufacturer including labelling, the devices will be returned to the sponsor for analysis as per standard procedures.

5. BENEFIT-RISK ANALYSIS

Diametros Medical is aware of the associated risks of lumbar spinal stenosis surgical treatment using interspinous process spacers. However, interspinous process spacers have been thoroughly investigated through clinical studies and literature. Further, Diametros Medical has taken multiple steps to mitigate these risks, namely non-clinical and preliminary clinical testing with positive results that support the safety and effectiveness of the investigational device.

5.1 RISKS

The potential risks for subjects enrolled in the trial include those related to surgery, lumbar spine surgery, interspinous spacers (including the Lobster device and other interspinous spacers) and instrumentation, or imaging for the study that are not standard of care. There is always a chance that unforeseen risks may occur.

Risks generally associated with any surgery include:

- Anesthetic medication reactions
- Surgery at the incorrect location, side or level
- Blood loss, blood vessel damage, phlebitis or hematoma
- Blood transfusion which may cause circulatory collapse, blood incompatibility, kidney damage, hepatitis, infection with HIV
- Myocardial infarction or circulatory problems
- Deep vein thrombosis, pulmonary embolism or thrombus formation in other vessels
- Stroke
- Fever or infection

- Pneumonia
- Injury to muscle, soft tissues or nerves
- Wound swelling, draining or delayed healing
- Discomfort and rehabilitation associated with recovery from surgery
- Inability to perform certain tasks, such as lifting, exercising etc.
- Death

Risks associated with lumbar spine surgery include:

- Damage to nerve roots or the spinal cord causing partial or complete sensory or motor loss (paralysis)
- Loss of bladder and/ or bowel functions
- Dural leaks (tears in the tissue surrounding and protecting the spinal cord)
- Instruments used during surgery may break or malfunction which may cause damage to the operative site or adjacent structures
- Fracture, damage or remodeling of adjacent anatomy, including bony structures or soft tissues during or after surgery
- New or worsened back or leg pain

Risks associated with lumbar spine implants (including the Lobster and other interspinous spacers) and associated instruments include:

- Sensitivity or allergy to the implant material
- Failure of the device/ procedure to improve symptoms and/ or function
- Pain and discomfort associated with the operative site or presence of implants
- Implant malposition or incorrect orientation
- Spinous process fracture
- Wear debris which may damage surrounding soft tissues including muscle or nerve
- Scar tissue may form at implant site
- Migration or dislodgement of the implant from the original position so that it becomes ineffective or causes damage to adjacent bone or soft tissues including nerves
- Implant may loosen, fatigue, deform, break or disassemble which may require another operation to remove the implant and may require another method of treatment
- Re-operation to remove or replace the implant

AEs that might reasonably occur because of placement or attempted placement of the investigational product or during follow-up were identified through a risk analysis. No interactions with concomitant medications are expected. The Risk Analysis in the device IFU lists clinical risks to the subject associated with study participation.

5.1.1 Risks associated with MRI, CT Scans, and X-rays

MRI scanners produce a strong magnetic field that will pull on magnetic materials and may cause unwanted movement of the medical device. The radiofrequency energy and magnetic fields may

cause heating of the implanted device and the surrounding tissue. X-rays and CT scans expose the patient to radiation. Exposure to radiation can add up over a patient's lifetime. The x-rays/CT scans obtained during this study are [as frequent/more frequent] than the number of x-rays/CT scans participants would undergo as standard of care for their medical condition. Specific counseling regarding radiographic imaging risk will be provided to the patient during the consent process.

5.1.2 Women of child-bearing potential

The investigator shall discuss specific risks associated with pregnancy and/or breastfeeding with women of child-bearing potential who are being considered as study subjects prior to study participation. A pregnancy test will be done to confirm the subject is not pregnant before treatment in this study. Subjects must immediately inform the investigator if they become pregnant during the study.

5.1.3 Unknown Potential Risks

While considerable pre-clinical biomechanical and biocompatibility tests have been performed, as well as pilot clinical studies to establish device safety, there is always the possibility of unforeseeable risks. Because this is a new type of device, other risks (such as risk to an embryo or fetus if a patient were to become pregnant) may also exist that are currently not foreseeable or are unknown.

5.2 RISK MITIGATION

Appropriate risk mitigation measures have been taken to initiate implantation of this subject population to the experimental device, as described below.

- Selection of only those subjects who meet the enrollment criteria
- Medical staff will carefully monitor subjects' post-treatment to ensure that any complications are detected early
- Consistent testing methods (i.e., study assessments) will be used by the investigational sites throughout the study follow-up period
- Data from the investigator will be reviewed to ensure an understanding of ongoing study results
- Operators will be trained on the surgical technique prior to site activation
- Medical staff will be trained on study procedures

An evaluation of the potential risks associated with use of the Lobster device has been performed to minimize the risks associated with the device. The following are some of the ways in which risks have been or will be minimized:

- Bench testing and sterilization validation
- Biocompatibility testing adhering to ISO 10993-1
- A retrospective, multi-centered OUS clinical study evaluating the safety and efficacy of the Lobster device in patients with neurogenic intermittent claudication (NIC) related to foraminal stenosis

5.3 ANTICIPATED BENEFITS

While there is no guarantee that a subject will benefit from taking part in this clinical trial, the information gained from this study may help others with this condition in the future. Below are the potential benefits from participating in this trial:

Implantation with the Lobster device may provide relief in leg and/ or back pain and other symptoms of lumbar spinal stenosis and the provision of motion of the lumbar spine, which may lead to increased functional capacity. The Lobster device may also help to relieve stress at other spinal levels when compared to a fusion procedure.

5.4 RISK-TO-BENEFIT RATIO

All applicable risks have been addressed through appropriate testing and clinical monitoring. Any residual risks are acceptable when weighed against the potential benefits to the subject. The device is appropriate for the intended use and is designed to protect the health and safety of the subject, user, and environment.

Therefore, the risk/benefit profile of the Lobster device in the intended use justifies the conduct of the proposed clinical investigation.

6. STUDY OBJECTIVES

6.1 PRIMARY OBJECTIVES

The primary objective of this study is to demonstrate the safety and effectiveness of the Lobster device in comparison to an SSED-based performance goal (PG). This clinical study is a prospective, multi-centered study with a historical control designed to support future international regulatory registrations

6.2 SECONDARY OBJECTIVES

Secondary objectives include documenting clinical outcomes such as low back pain, back and leg pain, physical function and mental health, neurological status and treatment satisfaction following surgical procedure with Lobster device.

Additionally, this study will evaluate device position and condition as well as integrity of the spinous processes via imaging studies.

7. STUDY DESIGN

Diametros is proposing a prospective multi-centre study with comparison to an SSED-based performance goal (PG). The proposed prospective clinical study will be actively and intentionally harmonized to previously cleared interspinous device studies, the Vertiflex Superion RCT (P140004). Prospectively defined evaluations of covariate balance and safety evaluations are included in the study design, supporting using a performance goal comparison for the primary endpoint. The proposed prospective clinical study is summarized in the table below. The inclusion/exclusion criteria, device indication, study population, study evaluations as well as follow-up intervals through 1-year are identical to that of the Superion RCT. This was done as part of the study design regime to promote and support the use of a Performance Goal comparison for the primary endpoint.

This clinical study is a prospective, multi-centered study using a historical control.

7.1 STUDY DURATION

The expected study duration is three (3) years, including enrollment (12 months) and post-operation follow-ups (24 months). The primary endpoint will be evaluated at 12 months as described in Section 7.4.

7.2 TREATMENT/CONTROL GROUPS

Enrolled patients meeting all inclusion and exclusion criteria will be treated with the Lobster device.

There is no active control group. The study will utilize a historical control based on publicly available SSED data for already-approved interspinous devices, namely Superion and X-Stop. Both Superion and X-Stop are approved interspinous devices, appropriate control comparators, and have been demonstrated to be non-inferior. Given that both arms arise from the same randomized and FDA-reviewed clinical trial and the similarity of outcomes, it would be reasonable to design a study where control patients are treated with either Superion or X-Stop devices.

7.3 METHODS FOR MINIMISING BIAS

Methods to minimize bias include use of validated questionnaires, review of imaging by an independent core laband safety review by independent Clinical Events Committee. This study is single-arm; therefore, there is no concern of bias from lack of randomization or blinding.

7.4 PRIMARY ENDPOINTS

Subjects will be evaluated at the 12-month follow-up for the primary endpoint.

Efficacy success will be evaluated as a two-prong composite endpoint:

- ZCQ Responder (at least two of the three ZCQ domains)
    - ≥0.5 point improvement in physical function
    - ≥0.5 point improvement in symptom severity
    - Mean satisfaction ≤2.5 points
- No secondary surgical intervention (SSI) including re-operations, revision, removals or supplemental fixation or clinical significant confounding treatments (i.e., epidural steroid injections at the index level, spinal cord stimulators or rhizotomies) through 12 months

Safety success will be evaluated using precision-based statistics to characterize the incidence of major device- or procedure-related complications, including:

- Device integrity failure (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

7.5 SECONDARY ENDPOINTS

- ODI
- VAS (Back and Leg)
- SF-12 Short Form Survey (Physical Function and Mental Health)
- Patient satisfaction survey

- Neurologic status

7.6 RADIOGRAPHIC ASSESSMENTS

An independent radiographic core laboratory will be used to provide an unbiased assessment of all x-rays and CT scans (pre-procedure through last follow-up assessment). All images will be evaluated in accordance with the Image Review Charter which is provided to the sites.

Radiographic evaluations include:

- Angular Range of Motion
- Translational Motion
- Device Condition
- Device Migration
- Device Dislodgement
- Bone-Implant Interface Changes
- Exuberant Bone Formation

Outside of this clinical investigation, in normal clinical practice, radiography or computed tomography is performed: before surgery, at the end of surgery, and as a follow-up at 6 months, 12 months, and 24 months. Consequently, the diagnostic activities at 6 weeks and 3 months are to be considered additional procedures to normal clinical practice and as such represent an increased risk. MRI scanners produce a strong magnetic field that attracts magnetic materials and can cause unwanted movement of the medical device. Radiofrequency energy and magnetic fields can cause heating of the implanted device and surrounding tissue. X-rays and CT scans expose the patient to radiation. Radiation exposure can accumulate over the patient's lifetime. The X-rays obtained during this study are more frequent than the number of X-rays participants would undergo as a standard of care for their medical condition. The patient will be given specific counseling about the risk of radiographic imaging during the consent process.

As discussed above, the diagnostic activities at 6 weeks and 3 months are to be considered additional procedures to normal clinical practice and as such represent an increased risk, however, these are essential procedures to meet the proposed objectives of this clinical investigation. All other diagnostic criteria in the clinical investigation are not considered burdensome and/or invasive.

8. SELECTION OF STUDY POPULATION

8.1 SUBJECT RECRUITMENT

Subjects participating in this study will be recruited from the investigators' standard patient populations. All patients presenting for treatment of lumbar spinal stenosis will be evaluated for study participation based on the inclusion/exclusion criteria listed below. Subjects must meet all of the following inclusion criteria and none of the exclusion criteria. The investigator maintains exclusive responsibility for the inclusion and exclusion of any potential study participant.

8.2 INCLUSION CRITERIA

In order to be eligible to participate in this study, subjects must meet all of the following criteria:

1. Male or female subjects ≥ 45 years of age.

2. Persistent leg/buttock/groin pain, with or without back pain, that is relieved by flexion activities (example: sitting or bending over a shopping cart)
3. Subjects who have been symptomatic and undergoing conservative care treatment for at least 6 months.
4. Diagnosis of degenerative spinal stenosis of the lumbar spine, defined as the narrowing of the midline sagittal spinal canal (central) and/or narrowing between the facet superior articulating process (SAP), the posterior vertebral margin (lateral recess), and the nerve root canal (foraminal).
5. Radiographic confirmation of at least moderate spinal stenosis which narrows the central, lateral, or foraminal spinal canal at one or two contiguous levels from L1-L5. Moderate spinal stenosis is defined as 25% to 50% reduction in lateral/central foramen compared to the adjacent levels, with radiographic confirmation of any one of the following:
    a. Evidence of thecal sac and/or cauda equina compression
    b. Evidence of nerve root impingement (displacement or compression) by either osseous or non-osseous elements
    c. Evidence of hypertrophic facets with canal encroachment

Note: All imaging studies used to confirm LSS are to be completed within 3 months prior to enrollment. Radiographic (imaging) confirmation of LSS on CT (or MRI if available in lieu of CT). In the case of a transitional L5/L6 segment with a sufficiently prominent L6 spinous process, these subjects may be included by a deviation request from the applicant.

6. Must present with moderately impaired Physical Function (PF) defined as a score of > 2.0 of the Zurich Claudication Questionnaire (ZCQ)
7. Must be able to sit for 50 minutes without pain and to walk 50 feet or more
8. Subjects who are able to give voluntary, written informed consent to participate in this clinical investigation and from whom consent has been obtained
9. Subjects, who, in the opinion of the Clinical Investigator, are able to understand this clinical investigation, cooperate with the investigational procedures and are willing to return for all the required post-treatment follow-ups.

8.3 EXCLUSION CRITERIA

Subjects who meet any of the following criteria will be excluded from participating in this study:

1. Axial back pain only
2. Fixed motor deficit
3. Diagnosis of lumbar spinal stenosis which requires any direct neural decompression or surgical intervention other than those required to implant the control or investigational device
4. Unremitting pain in any spinal position
5. Significant peripheral neuropathy or acute denervation secondary to radiculopathy
6. Lumbar spinal stenosis at more than two levels determined pre-operatively to require surgical intervention
7. Significant instability of the lumbar spine as defined by ≥ 3mm translation or ≥ 5° angulation
8. Sustained pathologic fractures of the vertebrae or multiple fractures of the vertebrae and/or hips
9. Spondylolisthesis or degenerative spondylolisthesis greater than grade 1 (on a scale of 1-4)
10. Spondylolysis (pars fracture)

11. Degenerative lumbar scoliosis with a Cobb angle of > 10° at treatment level
12. Osteopenia or osteoporosis. To confirm eligibility, at the Clinical Investigator's discretion, the following subjects may have a DEXA scan performed:
    i. Women 65 or older
    ii. Postmenopausal women < age 65
    iii. Subjects with major risk factors for or diagnosed with osteoporosis or osteopenia
    iv. If DEXA is required, exclusion is defined as a DEXA bone density measurement T score ≤ -2.5
13. Morbid obesity, defined as Body Mass Index (BMI) greater than 40kg/m2
14. Insulin-dependent diabetes mellitus
15. Significant peripheral vascular disease (diminished dorsalis pedis or tibial pulses)
16. Prior surgery of the lumbar spine
17. Cauda equina syndrome (defined as neural compression causing neurogenic bowel or bladder dysfunction)
18. Infection in the disc or spine, past or present
19. Evidence of active (systemic or local) infection at time of surgery
20. Active systemic disease such as AIDS, HIV, hepatitis, etc.
21. Paget's disease at involved segment or metastasis to the vertebra, osteomalacia, or other metabolic bone disease
22. Currently undergoing immunosuppressive therapy or long-term steroid use
23. Known allergy to titanium or titanium alloys
24. Tumor in the spine or a malignant tumor except for basal cell carcinoma 25. Known or suspected history of alcohol and/or drug abuse
25. Prisoner or transient
26. Life expectancy less than two years
27. Angina, active rheumatoid arthritis, or any other systemic disease that would affect the subject's welfare or outcome of the clinical investigation
28. Any significant mental illness (e.g., major depression, schizophrenia, bipolar disorder, etc.) that could impair the consent process or ability to complete subject self-report questionnaires
29. Involved in pending litigation of the spine or worker's compensation related to the back
30. Enrolled in the treatment phase of another drug or device clinical investigation (currently or within past 30 days)
31. Congenital defect of the spine
32. Pregnant or lactating

8.4 STUDY ENROLLMENT PROCEDURES

8.4.1 Recruitment and screening

All subjects with lumbar spinal stenosis will be considered for screening into the study. Subjects expressing an interest in participation will proceed with the consent process as per Section10.1..

8.4.2 Patient Informed Consent

Potential patients will be asked to sign a consent form after verbal explanation of the study by the consenting PI or appropriate designee.

The PI explains to each subject the nature of the investigation, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each subject is informed that the participation in the investigation is voluntary and that he/she may withdraw from the investigation at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment. The subjects are informed that he/she can ask any question, and consult with family members, friends, their treating physicians or other experts before deciding about their participation in the investigation. Enough time is given to the subjects.

The subjects are informed that authorised individuals other than their treating physician may examine his/her medical records. All subjects a given a subject information sheet and a consent form describing the investigation and providing sufficient information for the subjects to make an informed decision about their participation in the investigation. The formal consent of a subject, using the approved consent form, is obtained before the subject is submitted to any investigation procedure. The subject should read, understand, and voluntarily agree before signing and dating the informed consent form, and is given a copy of the signed document. The consent form is signed and dated by the subject and the PI (or her/his designee). The signed consent form it is retained as part of the investigation records.

If new information becomes available that can significantly affect a subject's future health and medical care that information shall be provided to the subjects affected in written form. If relevant, all affected subjects shall be asked to confirm their continuing informed consent in writing.

Consent will not denote enrolment into the study. Subjects are enrolled at the time of incision.

8.4.3 Subject Identification

Subjects who consent to participate shall be assigned a unique Subject Identification Number to de-identify their information. This Subject Identification Number will be captured on the Screening & Enrollment Log and used to identify them on all source documents and eCRFs thereafter.

A record of all screened subjects will be maintained in a Screening/Enrollment Log. The date of screening, results of screening (included or not) and, if not eligible, the primary reason for excluding the subject, enrollment status (enrolled or not) and, if not enrolled, the primary reason will be recorded.

Please note, for purposes of the study population a subject is considered enrolled at the time of surgical incision.

8.5 SCREEN FAILURES

A screen failure subject is a consented subject that did not receive the index procedure/treatment due to withdrawing consent, being withdrawn from the study, or not meeting eligibility requirements for treatment.

If a subject signs the ICF but is found ineligible for inclusion in the study prior to or during the surgical procedure, the subject will not be advanced any further in this clinical investigation and will receive an appropriate alternative treatment as identified by the Investigator. The subject’s signed

ICF and completed inclusion/exclusion criteria will be retained by the Investigator, and the subject will be notified.

NOTE: If a subject does not meet the eligibility criteria during their initial screening, the subject cannot be re-evaluated for entry into the study later if deemed appropriate by the Investigator.
Screening data from the Pre-Op visit and Surgery visit (prior to incision/treatment), including the reason for exclusion, will be collected but may not be complete in cases where the subject is determined to be a screen failure early in the screening process. The subject's exclusion from the study, and reason for ineligibility, will be documented in the Screening & Enrollment Log.

8.6 SUBJECT TREATMENT ASSIGNMENT

Following screening, all subjects will be assigned to treatment with the Lobster device.

9. TECHNICAL AND TREATMENT FAILURES

Technical failures are subjects that are considered eligible for the study per the inclusion and exclusion criteria, enrolled at the time of incision, but did not complete the study treatment/ procedure due to safety concerns from the implanting surgeon (i.e., anatomical difficulties, issues noted during procedure, etc.).

These subjects will be included in the enrollment totals but will be withdrawn from the study and follow-up will be discontinued at the time of technical or treatment failure.

Treatment failures are subjects that must undergo a different procedure other than the study treatment (i.e. use of a different interspinous spacer or conversion to fusion) due to an intraoperative injury or damage to the investigational/ control device during an attempted implantation leading to safety concerns and a subsequent change in treatment. These subjects will be included in the enrollment totals but will be withdrawn from the study and follow-up will be discontinued at the time of technical or treatment failure. .

Patients that have not passed screening will not be enrolled in the study and further follow-up of these patients shall proceed according to the hospital standard procedures.

10. STUDY PROCEDURES

10.1 INFORMED CONSENT (ICF)

Potential patients will be asked to sign a consent form after verbal explanation of the study by the consenting PI or appropriate designee.

The PI explains to each subject the nature of the investigation, its purpose, the procedures involved, the expected duration, the potential risks and benefits and any discomfort it may entail. Each subject is informed that the participation in the investigation is voluntary and that he/she may withdraw from the investigation at any time and that withdrawal of consent will not affect his/her subsequent medical assistance and treatment. The subjects are informed that he/she can ask any question, and consult with family members, friends, their treating physicians or other experts before deciding about their participation in the investigation. Enough time is given to the subjects.

The subjects are informed that authorised individuals other than their treating physician may examine his/her medical records. All subjects a given a subject information sheet and a consent form describing the investigation and providing sufficient information for the subjects to make an informed decision about their participation in the investigation. The formal consent of a subject, using the approved consent form, is obtained before the subject is submitted to any investigation procedure. The subject should read, understand, and voluntarily agree before signing and dating the informed consent form, and is given a copy of the signed document. The consent form is signed and dated by the subject and the PI (or her/his designee). The signed consent form it is retained as part of the investigation records.

If new information becomes available that can significantly affect a subject's future health and medical care that information shall be provided to the subjects affected in written form. If relevant, all affected subjects shall be asked to confirm their continuing informed consent in writing.

Consent will not denote enrolment into the study. Subjects are enrolled at the time of incision.

10.2 SCREENING VISIT [*WITHIN 60 DAYS Of SURGERY*]

Upon successful documentation of informed consent, a preoperative screening visit will be performed within 60 days prior to the patient's surgery and will serve as a Standard of Care (SOC) evaluation by the Investigator to confirm patient eligibility.

NOTE: The subject recruitment and screening process should follow the study enrollment procedures outlined in Section 8.4. All Patient Reported Outcome Questionnaires (PRO) should be administered prior to any other study visit assessments or procedures being performed to prevent information from the examination biasing the subject's responses.

- Informed consent
- Inclusion/exclusion criteria review
- Demographics collection
- Medical history collection
- Physical examination
- Neurological examination
- Patient Reported Outcome (PRO) Questionnaires
    - VAS (back and leg)
    - ODI
    - SF-12
    - ZCQ
- Radiographic Imaging
    - X-rays
    - CT scans (or MRI if available in lieu of CT)

10.3 SURGERY/TREATMENT VISIT (DAY 0)

Upon successful completion of the Screening visit and confirmation of subject eligibility the subject will return on the day of surgery/treatment and undergo the following:

- Final review of inclusion/exclusion criteria
- Pregnancy determination
- Adverse events review
- Review postoperative rehabilitation regimen with the subject
  - CT scan to confirm device placement

Surgical Procedure

- The Investigator will perform the operation, as outlined in the Surgical Procedure/Technique Guide, with the investigational device
- Surgery start time will be recorded as the time of first incision
- Surgery stop time will be recorded as the time of skin closure
- The surgeon will consider the procedure to be successful once correct device placement is confirmed via postoperative radiographic evaluation.
- If the surgeon cannot complete the procedure for any reason, they should treat the patient per SOC.

Post-Surgical Procedures

- Record adverse events and device deficiencies, if applicable
- Review postoperative rehabilitation regimen with the subject
- Review of concomitant medications

10.4 6-WEEK (+/- 14 DAYS), 3-MONTH (+/- 14 DAYS), 6-MONTH (+/- 29 DAYS), 12-MONTH (+/- 60 DAYS), 24-MONTH (+/- 60 DAYS) POST-OPERATIVE VISIT

To allow the Investigator's assessment of the subject's progress, the subject will return for the 6-Week, 3-Month, 6-Month, 12-Month, and 24-Month visit and undergo the following:

NOTE: Surveys should be administered prior to performing any other study visit assessments or procedures to prevent information from these assessments or procedures biasing the subject's responses.

- PROs
  - VAS (back and leg)
  - ODI
  - SF-12
  - Patient satisfaction survey
  - ZCQ
- Neurological examination

- Record any new or updated adverse events and device deficiencies, if applicable
- Radiographic Imaging
  - X-rays
  - CT scans
- Review postoperative rehabilitation regimen with the subject

10.5 LATE AND MISSED VISITS

If a subject fails to return for a scheduled study visit within the visit window defined in the study protocol but completes the visit prior to the beginning of the next visit window, that visit is considered to have been completed late. A protocol deviation should be documented on the appropriate eCRF.

If a subject fails to return for a scheduled study visit within the visit window defined in the study protocol and the next scheduled study visit window opens, that visit is considered to have been missed. A protocol deviation should be documented on the appropriate eCRF.

All attempts should be made to schedule the subject for the study visit as soon as possible so that it is captured late rather than missed completely.

10.6 UNSCHEDULED VISITS

Subjects may be seen for unscheduled postoperative visits as needed. Data from unscheduled visits that relate to the index operation will be collected and reported as an Unscheduled Visit for this study. Unscheduled visits that do not relate to the index operation should be evaluated on a case-by-case basis by the Investigator to determine if they need to be reported as an Unscheduled Visit for this study.

For Unscheduled Visits relating to the index operation, the Investigator will assess the subject's progress and perform the following:

- PROs
  - VAS (back and leg)
  - ODI
  - SF-12
  - Patient satisfaction survey
  - ZCQ
- Neurological examination
- Record any new or updated adverse events and device deficiencies, if applicable
- Radiographic Imaging
  - X-rays
  - CT scans
- Review postoperative rehabilitation regimen with the subject

10.7 STUDY COMPLETION/DISCONTINUATION

The completion of this clinical investigation will be with the final follow-up visit (at 12 months) of the last enrolled patient. At the end of the study, further follow-up of these patients shall proceed according to the hospital standard procedures.

10.8 DATA COLLECTION SUMMARY

Table 10-1 below outlines the schedule of visits to be attended by the subject during his/ her participation in the study. The schedule spans the subject's enrollment to their last prescribed follow-up. Defined in the table are the tasks to be performed by the investigator and subject at each visit, including the examination(s) and imaging procedures as well as the types of information to be collected. Provided in parentheses next to each visit are the upper and lower acceptable bounds for the timing of the visit.

Table 10-1. Clinical Visits – Scheduling and Requirements

Activity	Screening (within 60) days prior to surgery)	Index Procedure (Day 0)			6-week (+/- 14 days)	3-Mo (+/- 14 days)	6-Mo (+/- 28 days)	12-Mo (+/- 60 days)	Annual thereafter until final subject reaches 12-Mo (+/- 60 days)	Unscheduled
Informed Consent	X	-			-	-	-	-	-	-
Inclusion/Exclusion Criteria (including DXA, if needed)	X	X			-	-	-	-	-	-
Demographics	X	-			-	-	-	-	-	-
Medical History	X	-			-	-	-	-	-	-
Pregnancy Test	-	X			-	-	-	-	-	-
Radiographs (standing, lateral, neutral) and CT	X	X			X	X	X	X	X	X
ODI	X	-			X	X	X	X	X	X
ZCQ	X	X	X	-	X	X	X	X	X	X
VAS	X	-			X	X	X	X	X	X
Patient Satisfaction	-	-			X	X	X	X	X	X
SF-12	X	-			X	X	X	X	X	X
Physical Exam	X	-			X	X	X	X	X	X
Neurological Exam	X	-			X	X	X	X	X	X
Record/Review Concomitant Medications	X	X			X	X	X	X	X	X
Record/Review Adverse Events and Device Deficiencies	-	X			X	X	X	X	X	X

11. DESCRIPTION OF STUDY PROCEDURES

DEMOGRAPHICS
At screening, subject baseline characteristics including, but not limited to, age, race, and gender, will be recorded.

PAST MEDICAL HISTORY
At screening, each subject's past medical conditions and surgical procedures will be recorded.

PHYSICAL EXAMINATION
A standard physical examination, according to the site's SOC, will be conducted to assess subject's suitability for study participation based on the eligibility criteria.

PREGNANCY DETERMINATION
A pregnancy test will be performed on female subjects of childbearing potential prior to surgery to ensure that the subject is not pregnant before implanting the investigational device. The investigational site will conduct the pregnancy test according to its SOC.

NEUROLOGICAL ASSESSMENT
A neurological assessment is an evaluation of the subject's nervous system.

X-RAY IMAGING
X-ray views for this study include: Standing, lateral, and neutral.

CT SCAN
CT scans will be collected at each post-operative follow-up.

DEXA SCAN
To confirm eligibility, at the Clinical Investigator's discretion, some subjects may have a DEXA scan performed. For the purpose of this study, normal bone density is defined as a DEXA bone density T-score of >-1, osteopenia will be defined as a T-score ≤-1 and > -2.5, osteoporosis will be defined as a T-score ≤ -2.5 (The World Health Organization definition of osteoporosis).

PATIENT REPORTED OUTCOME QUESTIONNAIRES (PROS)
The following Patient Reported Outcome questionnaires will be completed by the subject and used to compare subject outcomes at follow-up time points compared to baseline:

Visual Analog Scale (VAS) Pain Assessments
VAS is a measurement instrument that measures the amount of pain that a subject feels ranges across a continuum from none to an extreme amount of pain. The VAS will be collected for: back, leg.

Oswestry Disability Index (ODI)
The ODI is used to quantify disability for low back pain. The self-reported questionnaire contains ten sections concerning intensity of pain, lifting, personal care, walking, sitting, sexual function, standing, social life, sleeping and traveling.

Zurich Claudication Questionnaire (ZCQ)
The ZCQ is a self-administered measure to evaluate symptom severity, physical function, and surgery satisvation in lumbar spinal stenosis.

SF-12
The SF-12 Health Survey uses 12 questions to measure functional health and well-being from the subject's point of view and is a validated instrument for collecting Quality of Life data. The survey asks subjects for their views about their general health including how they feel and how well they are able to perform their usual activities.

Treatment Satisfaction
Treatment Satisfaction is a self-reported questionnaire to measure the subject's satisfaction of the treatment under the protocol.

12. EARLY DISCONTINUATION FOR SUBJECTS

12.1 WITHDRAWALS

Subjects have the right to withdraw from the clinical investigation at any time and for any reason without prejudice to their future medical care by the investigation team or investigational site. The Principal Investigator will ask reason for their withdrawal and will record all information regarding the subject discontinuation.

A Subject may be withdrawn from the clinical investigation for the following reasons:

- Subjects may choose to withdraw from the clinical investigation under the terms of the Declaration of Helsinki and their consent documentation without having to give a reason;
- Any unanticipated adverse event which, in the opinion of the Principal Investigator, is related to the treatment and will endanger the well-being of the subject if treatment is continued;
- Development of any intercurrent illness(es), infection or condition(s) that might interfere with the clinical investigation;
- Non-compliance with the clinical investigation procedures deemed by the Principal Investigator to be sufficient to cause discontinuation;
- Any problem deemed by the Investigator to be sufficient to cause discontinuation.

Regardless of the reason for withdrawal, data available for the subject at the time of withdrawal, including the reason for withdrawal, will be entered on the Case Report Forms. All data obtained up to the date of withdrawal will be retained unless the patient explicitly requests complete deletion of the records, which should be documented by the site.

The Principal Investigator will treat all subjects discontinued from the investigation due to an unanticipated adverse event, directly related to the investigation, until the event resolves or no further improvement is expected. A Subject that has been withdrawn from the study after treatment will not be replaced.

12.2 LOST TO FOLLOW-UP (LTFU)

Subjects who miss the 24-month study visit will be regarded as Lost to Follow-Up. Site staff should perform and document a minimum of three attempts to contact them via phone, and one attempt to reach them via certified mail to bring them in for the final study visit prior to considering the subject LTFU. The staff should document the date and type of attempted communication.

All efforts should be made to have subjects complete all follow-up visits but only subjects that miss the 24-month visit will be considered LTFU.

12.3 DOCUMENTATION OF EARLY DISCONTINUATION

In every instance where a subject does not complete the study, the Investigator will document the primary reason for discontinuation in the subject's records.

All subjects are free to withdraw from participation at any time, for any reason, specified or unspecified, and without prejudice. However, if a subject expresses a desire to withdraw their consent for the study, the site should attempt to obtain written documentation for their study records.

For subjects that are discontinued by the Investigator, the Investigator must notify them of their discontinuation from the study in writing.

12.4 USE OF DATA FROM EARLY DISCONTINUATION CASES

Study data collected previously for subjects who withdraw from the study, are discontinued from the study by the Investigator or LTFU will be included in the data analysis and clinical study report.

12.5 ONGOING TREATMENT FOR EARLY DISCONTINUATION CASES

Subjects who withdraw voluntarily or are discontinued by the Investigator will remain eligible for SOC treatment by the Investigator and study staff.

13. STUDY SUSPENSION OR EARLY TERMINATION

13.1 PROCEDURE FOR SUSPENSION OR EARLY TERMINATION

The Sponsor may suspend or prematurely terminate this clinical investigation either at an individual investigational site or at all sites. The Sponsor may terminate the investigation prematurely according to certain circumstances, for example:

- Ethical concerns,
- Insufficient subject recruitment,
- When the safety of the subject(s) is doubtful or at risk, respectively,
- Alterations in accepted clinical practice that make the continuation of the investigation unwise,

- Early evidence of benefit or harm of the experimental intervention.

A Principal Investigator, IEC, or regulatory authority may suspend or prematurely terminate participation in this clinical investigation at the investigational sites for which they are responsible.

If suspicion of an unacceptable risk to subjects arises during the clinical investigation, or when so instructed by the EC or regulatory authorities, the Sponsor will suspend the clinical investigation while the risk is assessed. If an unacceptable risk is confirmed, the Sponsor will terminate the clinical investigation.

The Sponsor will consider terminating or suspending the participation of a particular investigational site or Investigator if monitoring or auditing identifies serious or repeated deviations on the part of an Investigator.

If suspension or premature termination occurs, the terminating party will justify its decision in writing and promptly inform the other parties with whom they are in direct communication.

If suspension or premature termination occurs:

The Sponsor will remain responsible for providing resources to fulfill the obligations from this protocol and existing agreements for following the subjects enrolled in the clinical investigation, and The site's Principal Investigator or authorized designee will promptly inform the enrolled subjects at his/her investigational site

If the study is terminated, Diametros Medical must comply with all applicable government regulations and the protocol-required subject follow-up. If discontinuation of the study should occur, the Principal Investigator must return all clinical investigation materials to the Sponsor and provide a written statement to the IEC and the regulatory authority(ies) explaining the reasons for the premature termination. All applicable clinical investigation documents shall be subject to the same retention policies, as detailed in Section 21.3.

13.2 PROCEDURE FOR RESUMING THE CLINICAL INVESTIGATION AFTER TEMPORARY SUSPENSION

When the Sponsor concludes an analysis of the reason(s) for the suspension, implements the necessary corrective actions, and decides to lift the temporary suspension, the Sponsor will inform the relevant parties of the rationale and provide them with the relevant data supporting this decision. Concurrence will be obtained from the ECs and, where appropriate, regulatory authorities before the clinical investigation resumes. If subjects have been informed of the suspension, the Principal Investigator or authorized designee will inform them of the reasons for resumption.

13.3 ROUTINE CLOSE-OUT

Routine close-out activities will be conducted to ensure that the Principal Investigator's records are complete, all documents needed for the Sponsor's files are retrieved, remaining clinical investigation materials are disposed of, previously identified issues have been resolved, and all parties are notified.

14. PROTOCOL DEVIATIONS

Conformance to the protocol is essential to the quality and integrity of the clinical study. Every effort should be made to avoid any deviation from the clinical protocol. A protocol deviation is an event whereby the clinical investigator or site personnel did not conduct the study according to the protocol.

Under emergency circumstances, deviations from the protocol to protect the rights, safety and well-being of human subjects may proceed without prior approval of the Sponsor and the EC. Such deviations shall be documented and reported to the Sponsor in the EDC within 5 days of knowledge. The EC and regulatory authorities should be notified of the deviation as required by EC reporting guidance.

All deviations will be reported in the eCRF and reviewed by the clinical study manager on a regular basis as outlined below. For the purposes of international regulatory submissions, deviations will also be reviewed by a Clinical Events Committee.

The patient must continue to be followed up for safety as described in Section 16. The decision regarding the patient's continuation in the study lies with the investigator.

Deviations include, but are not limited to the following list:

Major deviation:

Any deviation from patient inclusion and exclusion criteria or patient informed consent procedures.

- Failure to obtain proper informed consent (including patient writing the date of consent by themselves) prior to conducting study specific activities
- Inclusion/exclusion criteria not met
- Incorrect version of the ICF used

Minor deviation:

Deviation from a protocol requirement such as incomplete/inadequate patient testing procedures, follow-ups performed outside specified time windows, Adverse Events not reported by investigators in the required timeframe as specified in the protocol or source data permanently lost etc.

Site compliance with regard to deviations will be reviewed and analyzed by the clinical study manager on a regular basis and corrective and preventative actions will be put in place accordingly. In addition, all deviations from the protocol will be documented in the final report.

15. CONCOMITANT MEDICATIONS/THERAPIES

For the purposes of this clinical study, only medications taken or administered for the following will be recorded:

- Pain (any type);
- Inflammation (any type);

- Muscle relaxation;
- Numbness and/or tingling;
- Hormonal replacement therapy; and
- Other medications related to or given for the subject's lumbar spinal stenosis.

16. SAFETY REPORTING

16.1 DEFINITION AND ASSESSMENT OF (SERIOUS) ADVERSE EVENTS AND OTHER SAFETY RELATED EVENTS

AEs/DDs will be reported according to MDR Regulation (EU) 2017/745 and ISO 14155:2020, while recognizing and following other specific laws, regulations, directives, standards and/or guidelines, as appropriate, as required by the country(ies) in which the study is conducted.

The list of foreseeable AEs and anticipated adverse device effects, together with their likely incidence, mitigation or treatment are detailed in the Investigator Brochure (IB) and IFU of the medical device used in this study.

As detailed in the CIP, events of the following types are captured for all subjects throughout the study, between the start time of enrolment and the end of subject participation (i.e., completion of the study or withdrawal of consent).

16.1.1 Adverse Device Effect

Adverse event (1.2) related to the use of an investigational medical device
Note 1 to entry: This definition includes adverse events resulting from insufficient or inadequate instructions for use, deployment, implantation, installation, or operation, or any malfunction of the investigational medical device.
Note 2 to entry: This definition includes any event resulting from use error or from intentional misuse of the investigational medical device.
Note 3 to entry: This includes 'comparator' if the comparator is a medical device.
(ISO14155:2020,3.1)

16.1.2 Adverse Event (AE)

Any untoward medical occurrence, unintended disease or injury or any untoward clinical signs, including an abnormal laboratory finding, in subjects, users or other persons, in the context of a clinical investigation, whether or not related to the investigational device.
(MDR Article 2(57))

Note: Pre-Existing Medical Conditions; any medical conditions (including planned surgeries and planned hospitalizations) present at enrolment, which do not worsen in duration, severity or frequency during the study **are not adverse events (AE)**. These pre-existing medical conditions should be adequately documented in the patient's medical history in the eCRF. Medical conditions present at enrolment which worsen after exposure to study treatment will be recorded as an AE on the Adverse Event Form of the eCRF.
At each evaluation, patients should be interviewed in a non-directed manner to elicit potential AEs from the patient. The occurrence of an AE will be based on changes in the patient's physical

examination, laboratory results, and/or signs and symptoms at a clinical visit, otherwise based on information given by the patient over the telephone.

16.1.3 Device deficiency (DD)

Any inadequacy in the identity, quality, durability, reliability, safety or performance of an investigational device, including malfunction, use errors or inadequacy in information supplied by the manufacturer.
(MDR Article 2(59))

16.1.4 Device Malfunction

Failure of an investigational medical device to perform in accordance with its intended purpose when used in accordance with the instructions for use or CIP, or IB.
(ISO 14155:2020, 3.33)

16.1.5 Incident

any malfunction or deterioration in the characteristics or performance of a device made available on the market, including use-error due to ergonomic features, as well as any inadequacy in the information supplied by the manufacturer and any undesirable side-effect.
(MDR Article 2(64))

16.1.6 Serious Adverse Device Effect (SADE)

Adverse device effect that has resulted in any of the consequences characteristic of a serious adverse event .
(ISO14155:2020, 3.44)

16.1.7 Serious Adverse Event (SAE)

Any adverse event that led to any of the following:
a) death,
b) serious deterioration in the health of the subject, that resulted in any of the following:
i. life-threatening illness or injury,
ii. permanent impairment of a body structure or a body function,
iii. hospitalisation or prolongation of patient hospitalisation,
iv. medical or surgical intervention to prevent life-threatening illness or injury or permanent impairment to a body structure or a body function,
v. chronic disease,
c) foetal distress, foetal death or a congenital physical or mental impairment or birth defect
(MDR Article 2(58))

16.1.8 Serious Incident

Any incident that directly or indirectly led, might have led or might lead to any of the following:
(a) the death of a patient, user or other person,

(b) the temporary or permanent serious deterioration of a patient's, user's or other person's state of health,
(c) a serious public health threat
(MDR Article 2(65))

16.1.9 Serious Public Health Threat

Means an event which could result in imminent risk of death, serious deterioration in a person's state of health, or serious illness, that may require prompt remedial action, and that may cause significant morbidity or mortality in humans, or that is unusual or unexpected for the given place and time
(MDR Article 2(66))

16.1.10 Unanticipated Serious Adverse Device Effect (USADE)

Serious adverse device effect which by its nature, incidence, severity or outcome has not been identified in the current risk assessment.
Note 1 to entry: Anticipated serious adverse device effect (ASADE) is an effect which by its nature, incidence, severity or outcome has been identified in the risk assessment.
(ISO14155:2020, 3.51)

16.1.11 Use Error

User action or lack of user action while using the medical device that leads to a different result than that intended by the manufacturer or expected by the user.
NOTE 1: Use error includes the inability of the user to complete a task.
NOTE 2: Use errors can result from a mismatch between the characteristics of the user, user interface, task or use environment.
NOTE 3: Users might be aware or unaware that a use error has occurred.
NOTE 4: An unexpected physiological response of patient is not by itself considered a use error.
NOTE 5: A malfunction of a medical device that causes an unexpected result is not considered a use error.
(ISO 14155:2020, 3.52)

16.2 CLASSIFICATION

16.2.1 Severity

Investigators will assess the severity of the AE and classify it according to the following definitions:

- MILD: The AE is transient or causes mild discomfort. There usually is no intervention/ therapy required and the AE does not interfere with the subject's normal activities.
- MODERATE: The AE causes some limitation in activity and some assistance may be needed. There is no or minimal medical intervention / therapy required.
- SEVERE: The AE causes marked limitation in activity. The subject's usual daily activity is interrupted. The subject may require medical intervention/ therapy, hospitalization is possible.

16.2.2 Relationship

Investigators will assess the potential relationship of the AE or SAE to the use of the Lobster device and classify the causality of the event according to the following definitions.

During causality assessment activity, clinical judgement shall be used and the relevant documents, such as the Investigator's Brochure (IB), the Clinical Investigation Plan (CIP) or the Risk Analysis Report shall be consulted, as all the foreseeable SAEs and the potential risks are listed and assessed there. The presence of confounding factors, such as concomitant medication/treatment, the natural history of the underlying disease, and other concurrent illness or risk factors shall also be considered.

The sponsor and the investigators will use the following definitions to assess the relationship of the SAE to the investigational device, the comparator or the investigation procedure.

Relationship

1) Not related: Relationship to the device, comparator or procedures can be excluded when:
   - the event has no temporal relationship with the use of the investigational device, or the procedures related to application of the investigational device;
   - the serious adverse event does not follow a known response pattern to the medical device (if the response pattern is previously known) and is biologically implausible;
   - the discontinuation of medical device application or the reduction of the level of activation/exposure - when clinically feasible - and reintroduction of its use (or increase of the level of activation/exposure), do not impact on the serious adverse event;
   - the event involves a body-site or an organ that cannot be affected by the device or procedure;
   - the serious adverse event can be attributed to another cause (e.g. an underlying or concurrent illness/ clinical condition, an effect of another device, drug, treatment or other risk factors);
     -the event does not depend on a false result given by the investigational device used for diagnosis, when applicable;

In order to establish the non-relatedness, not all the criteria listed above might be met at the same time, depending on the type of device/procedures and the SAE.

2) Possible: The relationship with the use of the investigational device or comparator, or the relationship with procedures, is weak but cannot be ruled out completely. Alternative causes are also possible (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or treatment). Cases where relatedness cannot be assessed, or no information has been obtained should also be classified as possible.

3) Probable: The relationship with the use of the investigational device or comparator, or the relationship
with procedures, seems relevant and/or the event cannot be reasonably explained by another cause.

4) Causal relationship: the serious adverse event is associated with the investigational device, comparator or with procedures beyond reasonable doubt when:

- the event is a known side effect of the product category the device belongs to or of similar devices and procedures;

- the event has a temporal relationship with investigational device use/application or procedures;
- the event involves a body-site or organ that
- the investigational device or procedures are applied to;
- the investigational device or procedures have an effect on;
- the serious adverse event follows a known response pattern to the medical device (if the response pattern is previously known);
- the discontinuation of medical device application (or reduction of the level of activation/exposure) and reintroduction of its use (or increase of the level of activation/exposure), impact on the serious adverse event (when clinically feasible);
- other possible causes (e.g. an underlying or concurrent illness/ clinical condition or/and an effect of another device, drug or
- treatment) have been adequately ruled out;
- harm to the subject is due to error in use;
- the event depends on a false result given by the investigational device used for diagnosis10, when applicable;

Where an investigator assessment of causality is not available and/or the causality classification of the SAE is still not clear with the information received, the event should be classified as "possible" and the reporting not delayed.

16.2.3 Adverse events categorization

The adverse events are categorized by the PI and the Sponsor using the following algorithm:
Does the AE meet the seriousness criteria?
o No, it is not serious
• Is the relationship to the device or the procedure possible, probable or causal?
No: non-related AE
Yes: ADE
o Yes, it is serious: SAE
• Is the relationship to the device or the procedure possible, probable or causal?
No: non-related SAE
Yes: SADE
o Is it anticipated (within expected type, severity and frequency of the complications)?
No: unanticipated SADE (USADE)
Yes: anticipated SADE (ASADE)

16.3 REPORTING PROCEDURES AND TIMELINES

16.3.1 Documentation

Device deficiencies (DD) and all adverse events (AE) including all serious adverse events (SAE) are collected, fully investigated and documented in the source document and appropriate case report form (CRF) during the entire investigation period, i.e. from the operating room when the initial incision(s)

is made to start the implantation procedure until the last CIP specific procedure, including a safety follow-up period.

- Documentation of AEs (including SAEs) by the PI includes diagnosis or symptoms, start and stop dates of event, event treatment, event resolution, assessment of severity, seriousness and causal relationship to device and/or investigation procedure.
- Documentation of DDs by the PI includes description of event, start date, investigational device information, action taken with regard to the investigational device, and whether the DD led to an AE. The Sponsor shall review all DDs and determine and document in writing.

The investigator will follow each subject who experiences an AE until the event resolves, resolves with sequelae, or no further improvement is expected. In the unusual circumstance that an AE has not resolved by the time of the subject's completion of the study, an explanation will be entered

16.3.2 Reporting of Safety related events to Sponsor

Any SAE/ADE/SADE/USADE/DD (including serious public health threat) must be recorded correctly in the electronic Case Report Form (eCRF) immediately, but no later than within 3 calendar days (CDs)/24h for serious public health threat after the investigation site study personnel has become aware of its occurrence even if not all the information is available. Other than reportable events should be reported within 30 calendar days after the investigation site study personnel's awareness of the event.

Table 16-1. Timelines for events reporting by Investigators to the Sponsor

Type of Event	Timeline for Reporting
ADE	Immediately but in any event no later than 3 CDs
SAE	Immediately but in any event no later than 3 CDs
SADE	Immediately but in any event no later than 3 CDs
USADE	Immediately but in any event no later than 3 CDs
All other AEs	In a timely manner, usually within 30 CDs
Device Deficiency	Immediately but in any event no later than 3 CDs
Serious Public Health threat	Immediately but in any event no later than 24 hours

Emergency Contact details for Adverse Events/Device Deficiencies/Serious health threat reporting:

Sponsor:
Moira Rossetti
Quality Manager
Diametros Medical srl
Via di Terranuoba 48/5
52025 Montevarchi -Arezzo- Italy
qualita@diametrosmed.com

+39 331 3553415

16.3.3 Reporting of Safety related events to Ethics Committee

The Sponsor or designee reports to the IEC promptly any SAE which has a causal relation with the device, comparator, or procedure/test method or where a causal relation appears to be possible.

In order to ensure prompt notification, the Sponsor may initially submit an incomplete notification.

If safety and health hazards that require measures must be taken immediately during the conduct of the investigation, the Sponsor notifies the IEC within 2 days of these measures and the circumstances which made them necessary.

16.3.4 Periodic Safety Reporting

An Annual Safety Report (ASR) is submitted by the Sponsor to the IEC, yearly. The ASR contains a list of all SADEs and DDs and a report on their degree of seriousness, causal relationship with the device and procedure and on subjects' safety.

16.3.5 Other reporting

Other reporting is done according to provisions of MD vigilance as per Art. 87-90 MDR.

16.3.6 Pregnancy Reporting

In order to ensure the safety of subjects who may become pregnant during the course of the study, subjects will be asked to return for all protocol-specified visits and will undergo all protocol-specified assessments at each follow-up visit, unless contraindicated, until the successful completion of the 24-month follow-up visit.

The Investigator will continue to follow the subject to report the outcome of the pregnancy to the Sponsor (i.e. live birth (full term or preterm birth), stillbirth, spontaneous abortion, and induced abortion.

16.4 TREATMENT OF AES

The Investigator will treat all subjects who experience an adverse event related to the device until the adverse event is resolved, resolved with sequelae, or no further improvement is expected. For all other adverse events, adverse event treatment and physician follow up will be dictated by standard of care.

16.5 SECONDARY SURGICAL INTERVENTIONS (SSIs)

The occurrence of the following SSIs will be documented for this study:

A **revision** is a procedure that adjusts or in any way modifies or removes part of the original implant configuration, with or without replacement of a component. A revision may also include adjusting the position of the original configuration.

A **removal** is a procedure where all of the original system configuration are removed with or without replacement.

A **reoperation** is any surgical procedure at the involved level(s) that does not removal, modification, or addition of any components to the system.

A **supplemental fixation** is a procedure in which additional instrumentation not under study in the protocol is implanted (e.g., supplemental placement of a rod/screw system or a plate/screw system).

16.6 SAFETY OVERSIGHT: CLINICAL EVENTS COMMITTEE (CEC)

A clinical event committee (CEC) will be established. The CEC is an independent committee consisting of three (3) spine surgeons with pertinent expertise who are not participants in the study and who do not have any other real or potential conflicts of interest. The CEC will meet periodically to review all adverse events, protocol deviations, SSIs, and neurological deterioration.

17. CLINICAL MONITORING

17.1 SITE MONITORING

The study will be monitored to ensure that it is conducted in conformance with the monitoring plan by the Sponsor to assess continued compliance with the protocol and to ensure and to ensure that applicable regulations and standards are followed. . In addition, the monitor verifies that study records are adequately maintained, that data are reported in a satisfactory manner with respect to timeliness, adequacy, and accuracy, and that the Investigator continues to have sufficient staff and facilities to conduct the study safely and effectively.

The study may also be subject to a quality assurance audit by the Sponsor or its designees, as well as inspection by appropriate regulatory authorities. It is important that the Investigator and relevant study personnel are available during on-site monitoring visits or audits and that sufficient time is devoted to the process.

The organization responsible for monitoring the study is:

Gianni Garlatti
General Manager
Email: g.garlatti@diametrosmed.com
Phone: +39 338 7845689
In addition to ensuring adequate communication between the Investigators and the Sponsor, the monitor's duties include on-site visits and review of study documents and reported data. The Monitor will be provided with appropriate device and protocol training prior to the study and will follow a Monitoring Plan for all study-related monitoring activities.

17.2 MONITORING ACTIVITIES

Monitoring visits include a pre-study Site Initiation Visit, periodic Interim Monitoring Visits, and a Close-Out Visit at the end of the site's participation in the study. The exact details of whether visits will be conducted on site or remotely shall be determined on an individual site basis as detailed in the Clinical Monitoring Plan,

Each site's Investigator will allocate adequate time for monitoring activities. The Investigator will also ensure that the monitor or other compliance or quality assurance reviewer is given access to the

study-related documents and study-related facilities and has adequate space to conduct the monitoring visit.

Monitoring visits will be documented on monitoring visit reports, and will aim to verify that:

- Compliance with the clinical protocol and applicable regulations is being maintained
- Source data is verified and signed-off upon as accurate
- Subject files are accurate and complete
- Subject withdrawal has been documented (if applicable)
- Subject non-compliance has been documented (if applicable)
- The Investigator and site staff are informed and knowledgeable of all relevant document updates concerning the clinical investigation
- Only authorized individuals are performing study-related functions
- The investigational device is being used according to the protocol and instructions for use
- Adequacy of staffing and facilities
- Signed and dated ICFs have been obtained from each subject
- eCRFs and queries are complete
- All adverse events and device deficiencies are reported to the Sponsor and the EC, as applicable
- All other required EC reports, notifications, applications, submissions, and correspondence are maintained in the Investigator's files and are accurate
- Corrective and preventive actions have been implemented (if applicable)

Monitoring activities related to eCRF, collected data, and reporting of adverse events will be done remotely through Smart-Trial software.

17.3 FREQUENCY OF VISITS

To ensure that the study is conducted in accordance with the terms of the clinical protocol, study monitors must visit each investigational site at routine intervals throughout the duration of the study. The exact frequency of visits shall be determined on an individual site basis as detailed in the Clinical Monitoring Plan, and shall depend upon the following factors:

- Rate of subject enrollment
- Experience of the Investigator in conducting clinical studies
- Record of previous site compliance

18. AUDITS AND INSPECTIONS

Participation as an Investigator in this study implies acceptance of potential inspection by government regulatory authorities. The Investigator must also be prepared to permit study-related audits and inspections by the Sponsor, CRO, EC and the site's institutional compliance and quality assurance

groups. The Investigator will ensure the capability for inspections of applicable study-related facilities, records, and reports.

The investigators will be available to the Sponsor, EC or other regulatory authorities to discuss study issues as requested. All involved parties must keep the subject data strictly confidential.

In the event that an Investigator is contacted by a Regulatory Agency in relation to this clinical trial/investigation, the Investigator will notify the Sponsor immediately and IEC as appropriate.

19. STATISTICAL METHODS

19.1 ANALYSIS SETS

The analysis data sets will be defined in a way that mirrors the Superion P140004 study.

The primary analysis cohort for this study will be the Modified Intent-to-Treat Cohort, defined as: Modified Intent-to-treat patient population (mITT): The mITT patient population will include all patients having an anesthesia start time. Subjects with an anesthesia start time but that do not receive the device will be failures.

Confirmatory analysis will be performed in the Per Protocol Cohort, defined as: Per protocol (PP) Population: The PP patient population will include all subjects with 12-month follow-up data and no major protocol deviations and subjects that failed before 12 months

19.2 PRIMARY ENDPOINT

Subjects will be evaluated at the 12-month follow-up for the primary endpoint.

Effectiveness success will be evaluated as a two-prong composite endpoint:

- ZCQ Responder (at least two of the three ZCQ domains)
  - ≥0.5 point improvement in physical function.
  - ≥0.5 point improvement in symptom severity
  - Mean satisfaction ≤2.5 points.
- No secondary surgical intervention (SSI) including re-operations, revision, removals or supplemental fixation or clinically significant confounding treatments (i.e., epidural steroid injections at the index level, spinal cord stimulators or rhizotomies) through 12 months.

The primary effectiveness hypothesis is that the composite success rate for the Lobster device is larger than the performance goal of 61.1%. A detailed description of the how the performance goal was calculated will be provided in the statistical analysis plan (SAP).

Formally, the hypotheses to be tested are:

H_0: The expected proportion of patients with composite success at Month 12 (p_T) is less than or equal to the performance goal (PG) of 61.1%.

H_A: The expected proportion of patients with composite success at Month 12 (p_T) is greater than the performance goal (PG) of 61.1%.

These hypotheses may be symbolically represented as:

$$H_o: p_T \leq PG = 61.1\%$$
$$H_A: p_T > PG = 61.1\%$$

Where p_T is the composite success rate for subjects treated with the Lobster device.

A one-sided normal approximation binomial test with type 1 error set to α=0.05 will be used to demonstrate that the investigational device meets the performance goal.

19.3 SAMPLE SIZE ASSESSMENT

The sample size was determined in order to have at least as many subjects as the Superion arm in the P140004 study, which enrolled 190 subjects, and to show superiority to the performance goal calculated from the results of that study.

The pooled two-prong composite effectiveness at Month 12 in the P140004 study was 71.1%, so the reference rate is specified as 0.711. The reference margin is set to be 10%, which is the same non-inferiority margin used in the Superion study. The performance goal is then 71.1%-10%=61.1%.

The sample size was calculated assuming the same success in the Lobster arm that was seen in the Superion study, 71.1%. With type 1 error set to α=0.05 and power=85%, the study would need to enroll 162 subjects. Allowing for 15% loss to follow-up, the study would need to enroll at least 191 subjects.

This study will enroll a minimum of 191 subjects and a maximum of 250 subjects. The final sample size will be justified in the SAP.

Expected distribution of enrollment among site is: 50% Cagliari (main site), 25% Siena, 25% Catania. The enrollment cap for the main site is 105 patients.

19.4 SAFETY ANALYSES

Assessment of the safety of the investigational implant will include an evaluation of the incidence and severity of complications and adverse reactions associated with the treatment.
Adverse event rates will be summarized by type of AE and for specific AEs in two ways: 1) per patient incidence of specific AEs and classes of AEs and 2) by event, summarizing event counts by visit interval over time and in accordance with FDA Guidance. Device and procedure-related events will be summarized by severity and relatedness. Events listings that include details such as relatedness, severity, onset and resolution status will be provided for all events and relevant subsets of events such as serious events and related events. Primary safety comparisons will be performed using the mITT analysis set. The summary tables will show the adverse events (in coded terms), the total number of events, and the number and the percentage of subjects affected in each treatment group (“subject wise evaluation”) and stratified by relation to device and severity.

The event rates observed in the Superion SSED (P140004) will be used as clinical guideposts only. There is no formal statistical hypothesis test on these endpoints. Please note that the primary endpoint captures both safety and effectiveness, and therefore these events are considered interesting but appropriately evaluated in this framework. Additional details regarding the safety comparisons will be provided in the SAP.

19.5 SECONDARY EFFECTIVENESS

The secondary endpoints are:

- Oswestry Disability Index (ODI)
- Visual Analogue Scale (VAS) (Back and Leg)
- SF-12 Short Form Survey (Physical Function and Mental Health)
- Patient satisfaction survey
- Neurologic status

Secondary continuous endpoints will be subjected to descriptive analyses including summaries over time and as changes over time using descriptive statistics including means, standard deviations, median, minimum and maximum values. Secondary categorical endpoints will be summarized over time using counts and percentages. In some cases, nominal 95% confidence intervals may be displayed for secondary endpoints. Additional details regarding the analysis of secondary endpoints will be provided in the SAP.

19.6 MISSING DATA/SENSITIVITY ANALYSIS

Handling of missing data will be described in the SAP.

19.7 POOLING AND SUBGROUPS

Pooling of data and description of important subgroups will be described in the SAP.

20. ETHICS & REGULATORY ASPECTS

20.1 ETHICAL CONDUCT

The investigation will be carried out according to the CIP and with principles enunciated in the current version of the Declaration of Helsinki, the European Regulation on medical devices 2017/745 (MDR), the Norms ISO14155 and ISO14971, the ICH-guidelines of Good Clinical Practice (GCP) as applicable and with any applicable local or regional laws and regulations.

The clinical investigational plan, informed consent, any other study specific study documents as required by regulations and all amendments to these study documents will be reviewed and approved by the apprioate regulatory authority and appropriate IEC before enrollment of any patient. EC and regulatory authority will receive the Annual Safety Report (ASR) and interim reports and be notified about investigation stop/end in agreement with local requirements.

Additional requirements set by the IEC or regulatory authorities must be implemented.

20.2 REPORTING TO ETHICS COMMITTEE (IEC) AND COMPETENT AUTHORITY

The Sponsor will submit the investigation to the EC and regulatory authority (as applicable) and obtain EC and regaulatory authority approval before the start of the investigation. Each PI at each participating investigational site ensures that approval from the EC and regulatory authority is obtained and filed in Investigator site file before the investigation starts.

Amendments are reported accordingly as described in section 20.3. The regular or premature end of the investigation as well as the interruption of the investigation is reported to the IEC. The reasons for a premature end or an interruption have to be explained. Annual progress reports will be submitted , as required. A final report shall be submitted within one year after the regular end of the investigation and within 3 months after a premature end of the investigation.

20.3 STUDY AMENDMENTS

All changes to the protocol, that impact validity of data, scientific soundness, the rights safety, or welfare of the subjects, must be documented in the format of an amendment with justification statements in the cover letter to the EC and apprioate regulatory authorities.. All amendments must be submitted to the EC and regulatory authority for review and approval.
Sponsor will inform the investigator about any relevant changes in the protocol. They will be documented as an amendment to the protocol which will be signed by each investigator. No changes can be implemented by the investigator before a fully approved amendment is available

20.4 INSURANCE

The Sponsor has issued clinical trial insurance with appropriate coverage for the continuation of the entire study. A copy of the certificate is filed in each investigational site file and the Sponsor file.

21. DATA HANDLING AND RECORDKEEPING

Data Management procedures will be detailed in trial specific Data Management Standard Operating Procedure.

The handling of all data on the CRFs will be the responsibility of the Sponsor.

It will be the responsibility of the investigator to ensure the accuracy of all data entered in the CRFs. The delegation log will identify all those personnel with responsibilities for data collection and handling, including those who have access to the trial database.

21.1 EDC AND ECRFS

eCRFs will be completed in an electronic data capture (EDC) system for each patient enrolled into the clinical study. The study staff will enter the source data onto the eCRFs, and study monitors will verify that the source documents match the eCRFs. Once verified, the study monitor will perform the monitoring approval step.

All procedures for the handling and analysis of data will be conducted using good clinical data management practices within systems meeting the Norms ISO14155 and the ICH-guidelines of Good Clinical Practice (GCP) as applicable for the handling, storage, and analysis of data for clinical studies.

The Investigator will sign off on each patient's casebook to attest that all data entered on the eCRFs are complete and accurate. All of the above signatures will be completed digitally within the EDC system using validated digital signature system function.

Any required data clarifications will be handled within the EDC system's query management system. The EDC will be programmed to automatically place data clarification queries on missing values and values out of acceptable ranges. Study monitors and data managers will also be able to add data clarification queries to data points within the system. Study staff will have the opportunity to correct data and/or respond to the query for review by monitors and data managers.

21.2 DATA SECURITY, ACCESS AND BACK-UP

Data will be managed and viewed by investigators, sponsor data manager, and clinical monitor with different levels of privilege, according to Smart-trial software functionality and its internal security systems validated with ISO 14155:2020 and regulation (EU) 2016/679 .

21.3 ELECTRONIC AND CENTRAL DATA VALIDATION

When using electronic data handling or remote electronic trial data systems, the Sponsor or the Sponsor's representative will:

- Ensure and document that the electronic data processing system(s) conforms to the Sponsor established requirements for completeness, accuracy, reliability, and consistent intended performance (i.e., validation).
- Maintain SOPs for using these systems.
- Ensure that systems are designed to permit changes to the data in such a way that the data changes are documented and there is no deletion of any edited or entered data (i.e., maintains an audit trail).
- Maintain a security system to prevent unauthorized access to the data and to uniquely identify individuals who access the data entry system.
- Maintain a list of individuals authorized to make data changes.
- Maintain adequate data backup.
- Ensure that the database is properly locked before the analysis according to the sponsor SOP.
- Ensure that patient's privacy will be protected according to the GDPR
- Ensure the database freeze/lock will be done. After cleaning process and resolution of queries, lock checklist will be complete and data lock and data freeze will be performed. Test lock will be undertaken and the final datasets will be saved by the statistician.
- Esnure that any study data released shall be done according to the publication policy and in accordance with any local regulations.

Primary data collection based on source-documented hospital and /or clinic chart reviews will be performed clearly, timely, adequately, and accurately by site personnel trained on the protocol and eCRF completion.

21.4 CAPTURE OF PATIENT REPORTED OUTCOMES

There is no acquisition of directly patient-reported outcomes (PROs).

Should future amendments to the study involve the use of patient-reported outcomes (PROs), the following will be done. PROs will be collected via web browser and the data will be transmitted directly to the CED. As the data is transmitted directly to the EDC, it is considered an electronic source and the data is locked when it enters the EDC to ensure its security. In cases where the web browser is not available (connectivity problems), paper versions of PRO forms will be used, which are considered sources.

21.5 ARCHIVING OF ESSENTIAL CLINICAL INVESTIGATION DOCUMENTS

All the documents of the investigation must be archived for a minimum of 15 years after regular or premature termination of the investigation.

A list of the essential clinical investigation documents which should be maintained in the investigation site and sponsor file is given in ISO14155 Annex E.

21.6 STORAGE OF BIOLOGICAL MATERIAL AND RELATED HEALTH DATA

No biological material will be stored for further analysis.

21.7 PUBLICATION AND DATA SHARING POLICY

Data generated from the conduct of this study will be used to support an application by Diametros Medical as a supplement to an original Premarket Approval (PMA) from FDA. Publication of the results of the study will follow Diametros Medical's Publication and Presentation Policy.

The study will be registered on on a publicly accessible database (Clinicaltrials.gov). Results of the study, including an unanticipated early termination of the trial, will be posted to the Clinicaltrials.gov database at the conclusion of the study. In the event that the study is terminated early, the posting of these results will be completed within 30 days of completion of data analysis.

21.8 PARTICIPANT AND DATA CONFIDENTIALITY

Subject confidentiality will be maintained throughout the study in a way that ensures that data can always be tracked back to the source data. For this purpose, a unique subject identification code will be used that allows identification of all data reported for each subject without traceability back to the actual subject.

In addition, the Principal investigator must keep a separate list of all subjects entered into the clinical investigation showing each subject's name, date of birth and assigned subject number (for identification purposes). A Subject Identification Log will also be provided in the Investigation Site File to record the subject's initials and assigned subject number.

The Principal Investigator or institution shall provide direct access to source data during and after the clinical investigation for monitoring, auditing, EC review and regulatory authority inspections.

The duration of storage time of personal data at the investigational sites will be in accordance with national regulations.

Information obtained in the course of executing this study, including still and motion photography, may be presented for regulatory, clinical or educational purposes as long as no subject is identified. The data collected is the property of Diametros Medical.

21.9 SUBJECT RECORDS

- All Source Documentation Worksheets
- Supporting data (e.g., medical records, clinic charts)

22. FUNDING AND SUPPORT

The study is financed by Diametros Medical srl.

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