Investigator initiated, single center prospective study on the clinical and radiological outcome after FENIX ® Facet Resurfacing Implant insertion in patients with chronic non-specific low back pain

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Background

Chronic Low Back Pain (CLBP) is a major burden for the patient and society. The annual incidence of CLBP is 18.6% in an adult population. [1] Though in the majority of the cases it is difficult to identify the cause of CLBP, it is estimated that approximately 20% of CLBP can be attributed to degenerative disease of the lumbar facet joints. [2] Conventional management consists of rehabilitation, cognitive behavioral treatment and pharmacological treatment. When these treatment options fail to provide satisfactory pain relief, interventional pain treatment may be considered. These procedures mainly aim at blocking pain conduction by targeting the innervations of the facet joint. [3] In a thesis on the development of lumbar facet joint replacement, the different possible surgical treatments are described. [4] Facetectomy consists of removal of part of the facet joints and ligaments. The induced changes in kinematics may accelerate degeneration of adjacent levels. [5] Laminectomy is a decompression whereby the laminae are partially or completely removed. The failure rate of this treatment was reported to be as high as 48% and 10 to 20 % of patients have a poor outcome. Fusion surgery eliminates motion at the surgical levels. The increased stress and motion at the adjacent levels can result in adjacent disc degeneration in up to 52.5%. Total disc replacement is a motion preserving treatment requiring partial removal of the disc. The prosthesis is inserted between two metal plates applied to the vertebral endplates. This surgery is difficult and there is little tolerance for exact placement. Moreover, degeneration of the discs produces an increased load on the facets which can lead to facet arthrosis.[6, 7]
Joint replacement has been successfully used for the management of degenerative disease of the larger synovial joints such as the hip and the knee. [8] These interventions result in an immediate pain relief, apart from the recovery from the surgery, and more importantly in a recovery of the mobility. The same is true for smaller synovial joints such as the base of the thumb. [9]
The facet joints in the lumbar spine combine with the disc space to create a three-joint complex at each vertebral level. [3] The facet joint consists of two opposing bony surfaces covered with cartilage and there is some synovial fluid, held intra-articular by a joint capsule. The synovial fluid is lubricating the joint. The combination of the cartilage and the fluid allows the joint to move with little friction. However, facet joint osteo-arthritis causes the cartilage to break down and the joint movement is then associated with more friction and pain. The patient loses mobility and can develop non-specific CLBP [3].
In analogy with the hip, knee and thumb joint replacement, substituting the degenerated facet joint with an implant could provide pain relief and restore functionality. Total joint replacement with facet arthroplasty of the lumbar spine is a new concept in the field of spine surgery. The devices used are intended to replace both articulating processes of one

facet joint. [10] A master's thesis on the subject reported 11 patents for facet joint replacement. Up till now no reports in the literature about their use are found. [4]
The FENIX™ is a device for resurfacing the facet joint surfaces and is designed for reducing friction of the facet joint and restoring mobility. It is intended for the treatment of painful degenerative facet joint disease, with or without disc pathologies.
The facet joint resurfacing implant could provide a therapeutic option for patients suffering from CLBP attributable to degenerative facet joint(s). The treatment targets the cause of the pain as opposed to conservative pain treatment options currently available that are all symptomatic.

In March 2007, the FENIX™ device was approved for the sale under the criteria set out in MDD 42/1993 and received CE 1250 approval. In 2008, a pilot study of the FENIX™ device with Ethics committee approval, evaluated the efficacy, safety and function of the FENIX™ device. This pilot study yielded positive results in all the study's endpoints, but we recorded the dislocation of one implant in one patient.[11] Since then, all implants are secured with a screw or a locking system, preventing a dislocation.
The present study, to be carried out with the adapted implants, is an investigator initiated, prospective, observational study. The need for a surgical treatment of low back pain that preserves motion and reduces the load on the adjacent levels, is clearly illustrated by the difficulties and complications encountered with the standard surgical treatments.

This study aims at further evaluation of the FENIX™ device to continue assessment and verification of the clinical outcome in terms of safety, pain relief and improved functionality in the intended patient population.
The stability of the implants will also be controlled, as well as the mobility at the index level as measured by dynamic X-rays.

Study Purpose

The purpose of this study is to further evaluate the safety, the clinical and radiological performance of the FENIX™ Facet Resurfacing Implant when implanted in accordance with its approved surgical technique and in the intended patient population.

Research Question/Endpoint

Do the clinical and radiographic results of FENIX™ implantation at 2 years' follow-up outweigh the potential risks?

- The clinical outcome is defined as a significant improvement of pain and disability, measured respectively with Visual Analogue Scale (VAS), Oswestry Disability Index (ODI), reduced need of pain medication measured with the Medication Quantification Scale (MQS) and return to work.
- The radiological outcome is defined as stability of the implant (no dislocation) and maintenance/improvement of the mobility at the index level.
- The risk is judged based on the number of adverse events and severe adverse events, including implant dislocations or migration.

Adverse and Severe Adverse Events

The FENIX™ device is an implant manufactured from Cobalt Chromium alloy that is designed to replace the degenerated or otherwise diseased articulating surfaces of the lumbar facet joint in subjects with non-specific CLBP caused by osteo-arthritis of the facets of the lumbar spine (from L1 to S1).
These implants are designed for single use.
FENIX™ implantation in patients with a known Cobalt Chromium allergy should be avoided.
In the very exceptional case an allergic reaction should appear in a patient previously not known as allergic to this alloy, explantation should be offered.
In case of hardware failure such as loosening of implants and/or dislocation, revision surgery is possible, but the surgeon should also offer the possibility to convert the arthroplasty to an arthrodesis.
During preparation of the joint, the underlying nerve root and dural sac may be violated. Proper repair of dural tears should be carried out.

Device Description

The Implant:

FENIX™ consists of three primary components: the superior facet resurfacing implant, consisting of a locking base and an articulating surface, the inferior facet resurfacing implant and the translaminar locking mechanism, inclusive of the translaminar screw and the tightening nut.

The superior facet locking base implant is designed with a curved posterior surface to fit the anatomy of the articulating surface of the processus articularis superior. The articulating surface of this implant is designed to lock into its locking base by way of a morse taper connection. It articulates with the articulating surface of the corresponding inferior facet implant. (Fig 1-4)

Figure 1

Posterior aspect of the locking base for the superior articulating implant, covered with a plasma spray to facilitate ingrowth into the bony surface of the processus articularis superior

Figure 2

Anterior aspect of the locking base, showing the morse taper connection to the superior articulating implant

Figure 3

Posterior aspect of the superior articulating implant, showing the tapering that fits onto its locking base (Fig. 2).

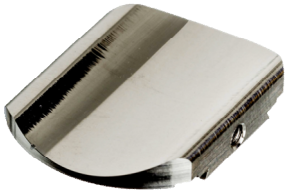


Figure 4

Articulating surface of the superior articulating implant

The inferior facet implant completely covers the resected aspect of the processus articularis inferior (i.e. partially resected lamina). The posterior aspect of this implant is tightly secured against the lateral aspect of the partially resected lamina (Fig 5 & 6)

Figure 5

Posterior aspect of the inferior articulating implant

Figure 6

Articulating aspect of the inferior articulating implant

The articulating surfaces of both implants are highly polished in order to facilitate unencumbered movement in an attempt to reduce or eliminate the chance for wear debris[12].

The non-articulating surface of the inferior facet implant features a plasma coated surface to facilitate long term bony ingrowth, and a slot for the acceptance of a trans laminar locking screw (Fig 5). Both the slot and the locking screw are designed to facilitate immediate fixation of the implant and subsequent long-term bony integration (Fig 7-8).

Figure 7
Translaminar locking screw to secure the inferior articulating implant. The screw is tightened with a nut that itself is fixed at the junction of the lamina and spinous process.

Figure 8
Cannulated screw to secure the locking base of the superior articulating implant

The non-articulating component of the superior facet implant (the locking base) features a roughened titanium surface with a screw hole, which is designed to facilitate immediate fixation of the implant until bony integration of the implant is achieved.
Through a translaminar approach, the locking base is secured at the prepared bony surface of the processus articularis superior by a 3.4mm cannulated screw (Fig.8)

The components of the FENIX ®implant are available in the following sizes:

IF 2401	FENIX® INFERIOR FACET IMPLANT 13mm x 16mm x 3mm
IF2402	FENIX® INFERIOR FACET IMPLANT 12mm x 15mm x 3mm
IF2403	FENIX® INFERIOR FACET IMPLANT 12mm x 14mm x 3mm
IF2411	FENIX® INFERIOR FACET IMPLANT 13mm x 16mm x 3.8mm - MIS
LS4203	FENIX® INFERIOR FACET TIGHTENING NUT
	TRANSLAMINAR LOCKING SCREWS
LS 5028	FENIX® Inferior facet locking screw 3mm x 28mm
LS 5030	FENIX® Inferior facet locking screw 3mm x 30mm
LS 5032	FENIX® Inferior facet locking screw 3mm x 32mm
LS 5034	FENIX® Inferior facet locking screw 3mm x 34mm
LS 5036	FENIX® Inferior facet locking screw 3mm x 36mm
LS 5038	FENIX® Inferior facet locking screw 3mm x 38mm
LS5130	FENIX® Inferior facet locking screw 3mm x 30mm
LS5135	FENIX® Inferior facet locking screw 3mm x 35mm

Study Objective

The overall objective of this study is to monitor patients who received the FENIX™ implant to confirm clinical performance and safety, the acceptability of identified risks and to detect emerging risks based on factual evidence.

Primary outcome measures:

1. To evaluate safety of the FENIX™ device in the defined patient population as determined by:

- Radiographic assessment:
  Antero posterior (AP) radiographic imaging in neutral standing position and under lateral left and right-sided flexion, to evaluate the implant location and mobility of the index segment. Lateral radiographic imaging will be performed in neutral standing position as well as in flexion and extension. All these images will be taken pre-operative and at 12, 26, 52 and 104 weeks post operatively.
- The surgical technique:
  Adverse events related to the surgical procedure will be collected and evaluated.

2. To evaluate clinical performance of the FENIX™ device in the defined patient population as determined by:

- Disability to be measured with the Oswestry Low Back Pain Questionnaire* at all assessment points compared to baseline.
- Change in back pain VAS* at all assessment points compared to baseline.

- Frequency of pain periods as measured by a 5-point rating scale* at all assessment points compared to baseline.
- Analgesic medication use measured with the MQS score*[13]

** The scales used are described in detail under the heading 10 "Evaluation parameters"*

Secondary outcome measures

- Surgical parameters such as blood loss, duration of the intervention, technical problems during the intervention, and length of hospital stay.
- Duration of incapacity to work/need for help with daily activities post-surgery
- Patient social activities: return to work, sport performance.

Study Design

This study is a single-center; 30-patient, prospective, non-randomized, observational investigator-initiated study without concurrent or matched controls, conducted under an approved protocol. The study protocol is submitted for approval by a central authorized ethical committee (Antwerp University Hospital, Belgium) with approval of the local ethical committee (AZ Nikolaas, Belgium). All patients will receive complete information regarding the indication, the device, the technique and the study. They will be asked to sign a written informed consent.

Selection of Study Population

Subjects participating in this study will be recruited from the implanting surgeons' regular patient population. Subjects must meet all the following inclusion criteria and present none of the exclusion criteria.

Inclusion Criteria

1. Subject has a history of non-specific chronic low back pain (CLBP) for more than 6 months suggestive for "facet joint syndrome" (See clinical diagnosis in Attachment 1)
2. Subject age is between 20 and 70 years and is skeletally mature
3. Failed conservative treatment for 3 months, including rehabilitation treatment, pharmacological and minimal interventional treatment.
4. Positive diagnostic nerve block (See Section 10.3)
5. Condition involves at least one lumbar spine level between contiguous levels L1 to S1.
6. Back pain intensity of at least 5 on a scale of 10 (VAS).
7. Oswestry score > 40 (based on 100-point scale)
8. Pain frequency of at least 3 on a 5-point scale
9. Radiology features suggestive for facet joint pathology. (See Section 10.2 for definitions) That is, the patient must have radiographic evidence of facet joint degeneration on Magnetic Resonance Imaging, classified as 1 or 2 on the Weishaupt scale and the

SPECT-CT must show a hotspot level 2 at the facet joint, suspected to be the cause of low back pain [14]

Exclusion Criteria

1. Subject has any isthmic spondylolisthesis or degenerative spondylolisthesis >3mm detected on plain X-rays
2. Subject has had prior spine surgery at the index level
3. Subject has disc herniation that is not contained (3 or 4 on the Milette scale)[15, 16]
4. Subject has central spinal canal stenosis
5. Subject has Cauda Equina Syndrome
6. Subject's facet joints are absent or fractured.
7. Subject is morbidly obese, having a Body Mass Index (BMI) of 35 or greater
8. Kidney disease (serum creatinine >235 µmol)
9. Subject has an active systemic infection or at the operative site
10. Subject has a spinal tumor
11. Subject has a known Chrome-Cobalt allergy.
12. Subject is pregnant or plans to become pregnant during the study
13. Subject is at high risk for evolution to chronicity (StarT back screening tool)

Surgical Technique

An approved surgical technique manual is described below.

Exposure of the facet joints at the affected level.

- The patient is placed on a radiolucent operating table in neutral and prone position and is under general anesthesia.
- Avoid knee-chest position; the lumbar facet joints will subluxate. If FENIX™ is implanted in this position, the articulating surfaces will not properly correspond when the patient is in a normal upright position. The more pronounced the lumbar lordosis of the patient (pre-op evaluation by X-rays), the more important it becomes to respect this lordosis while implanting FENIX™.
- A pronounced lordosis at L4/5 may indicate a large distance between the skin and the facet joint. Have longer blades available to accommodate such an occurrence.
- The Quadrant retractor (Medtronic, Minneapolis, Minnesota, USA) can be used in nearly all approaches. It is sometimes necessary to use the longest tubes in cases of deep-seated facet joints.
- Before starting the procedure, ensure that fluoroscopy is properly installed and can offer you a clear lateral, oblique, AP and outlet view. (Figure 9)

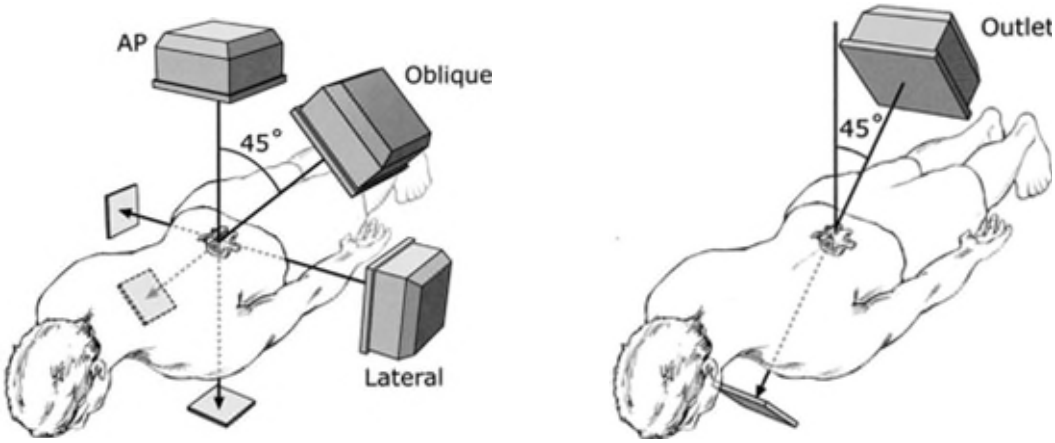


Figure 9:
Radiographic views for placement of trans-laminar screws include (top) antero posterior (AP), lateral, oblique and (right) outlet views.

- A small skin incision of 25-33mm is made centered on top of the facet joint and, in case of a minimal invasive approach, about 3 cm from the midline. The exact distance for an intermuscular Wiltse approach can be measured on pre-operative imaging (Figures 10-12).

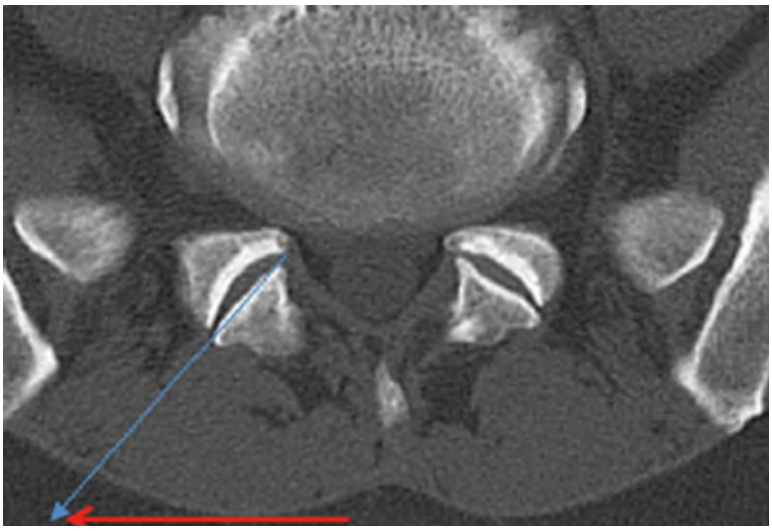


Figure 10:
On the pre-operative imaging, the obliquity of the index facet joint should be appreciated and the correct incision point can be calculated (red arrow).

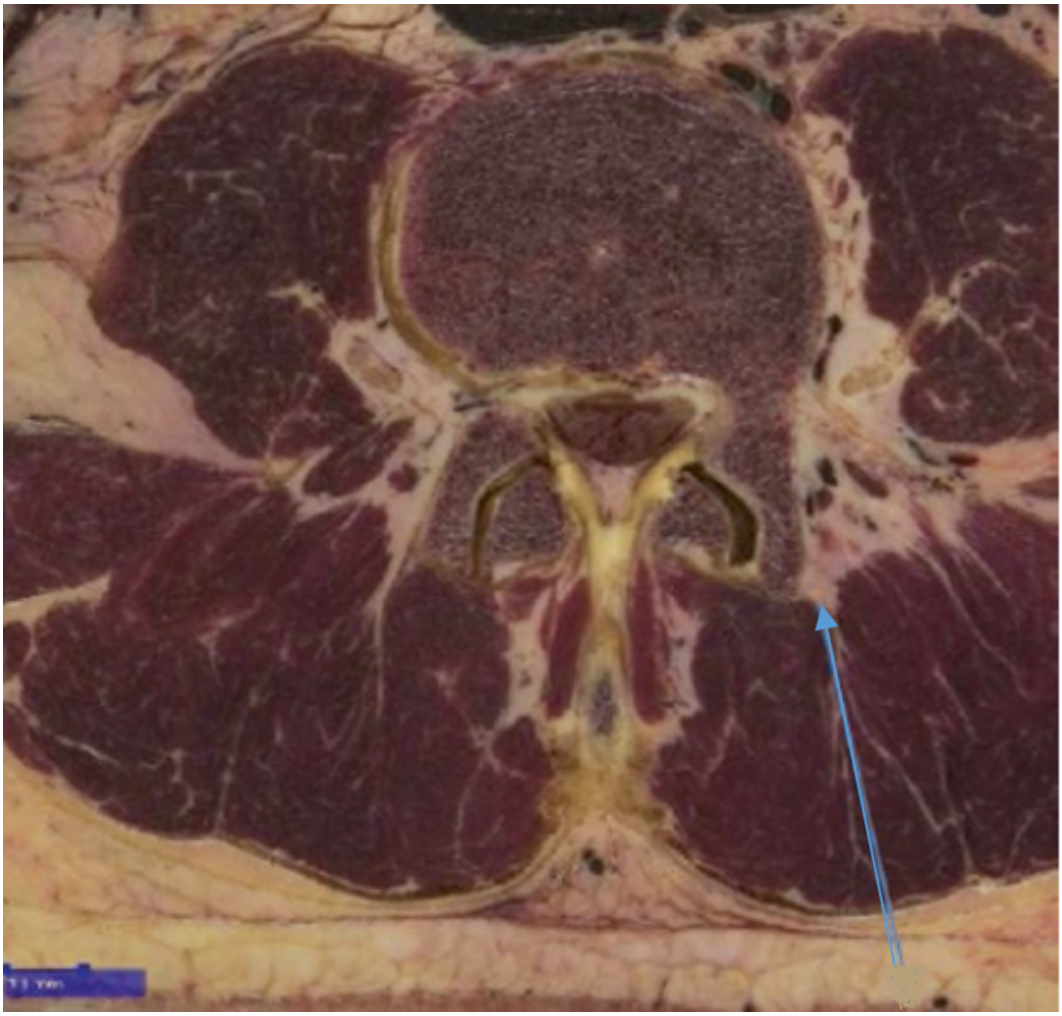


Figure 11:

Anatomical, axial view on the L4-L5 facet joints. Note the concavity of the superior articulating process, the obliquity of the orientation of the joint and the underlying ligamentum flavum, protecting the nerve roots and thecal sac. All preparation of the facet joint should be done with respect to the orientation of the articulating aspect of the superior articulating process. Note the route of the semi-Wiltse approach that starts about 3 cm off the midline (blue arrow). We do not prefer the rather bloody true transmuscular Wiltse approach, but rather prefer an approach that respects the muscles and looks for the fatty layers in between. It is important to always keep in mind the articular plane of the facet joint. Respecting this plane during preparation of the joint space will ensure a ¨natural¨ function of the joint after arthroplasty. (Courtesey Dr G. Groen)

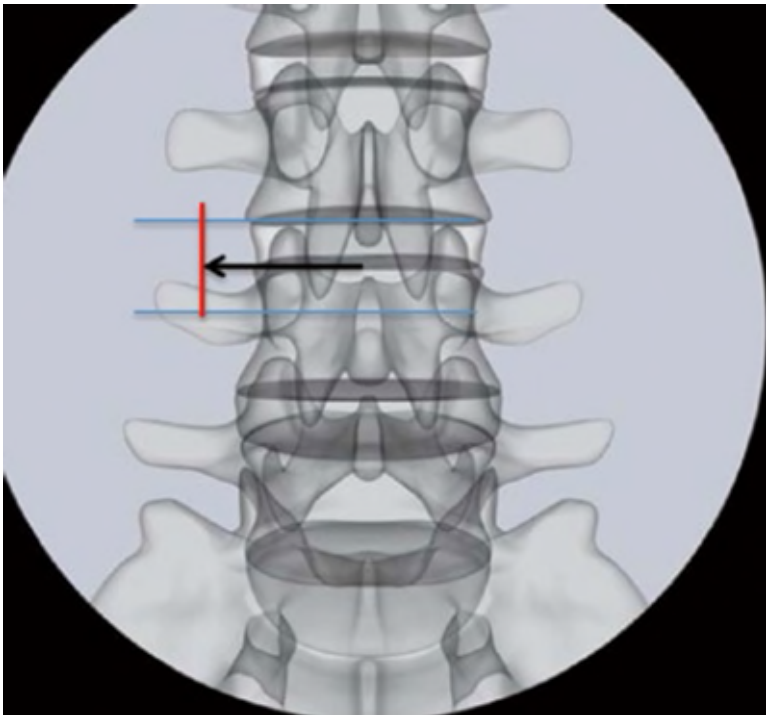


Figure 12:
Incision for a left sided L3-L4 approach (red line). The incision is on the AP view on top of the facet joint (two parallel blue lines) and about 3 cm lateral to the midline (black arrow).

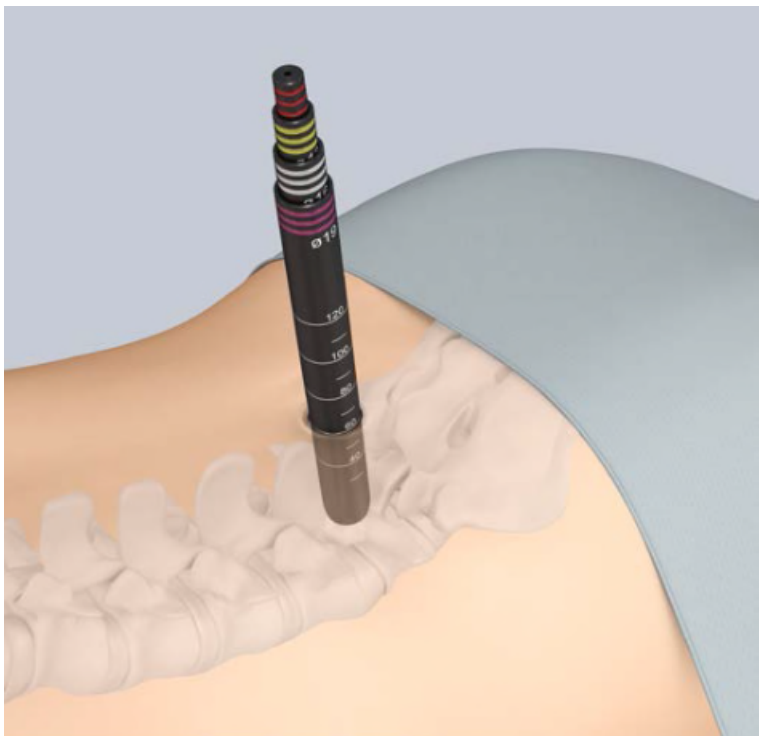


Figure 13:
Dilators targeted to the index facet joint (in this illustration L4-L5 left), facilitate blunt muscle dissection. After the largest dilator has been put in place, the ideal blade length can be measured and the Quadrant retractor (Medtronic, Minneapolis, Minnesota, USA) can be put in place and secured (Figure 14).

A B

Figure 14:
(A) The Quadrant retractor is in place and firmly secured. (B) Fluoroscopic AP image of the retractor in place, on top of the index facet joint. A Pennfield palpator marks the joint space.

The facet joint is accessed, directly through a working portal by a modified intermuscular Wiltse approach (the classical approach in a transmuscular one, but too bloody).[17-19] In case of bad illumination, video assisted endoscopy, blade illumination or the microscope can be used. An open approach is also possible; via a midline incision, the paravertebral muscles are retracted laterally, just enough to expose the capsule of the facet joint at the index level. After digital identification of the joint, verify with fluoroscopy that the correct level is approached.

- When securing a self-retaining retractor, make sure no metal frames cross the midline; imaging for the translaminar screw can be troublesome. Secure the retractor (if necessary), at the ipsilateral side of the affected joint.

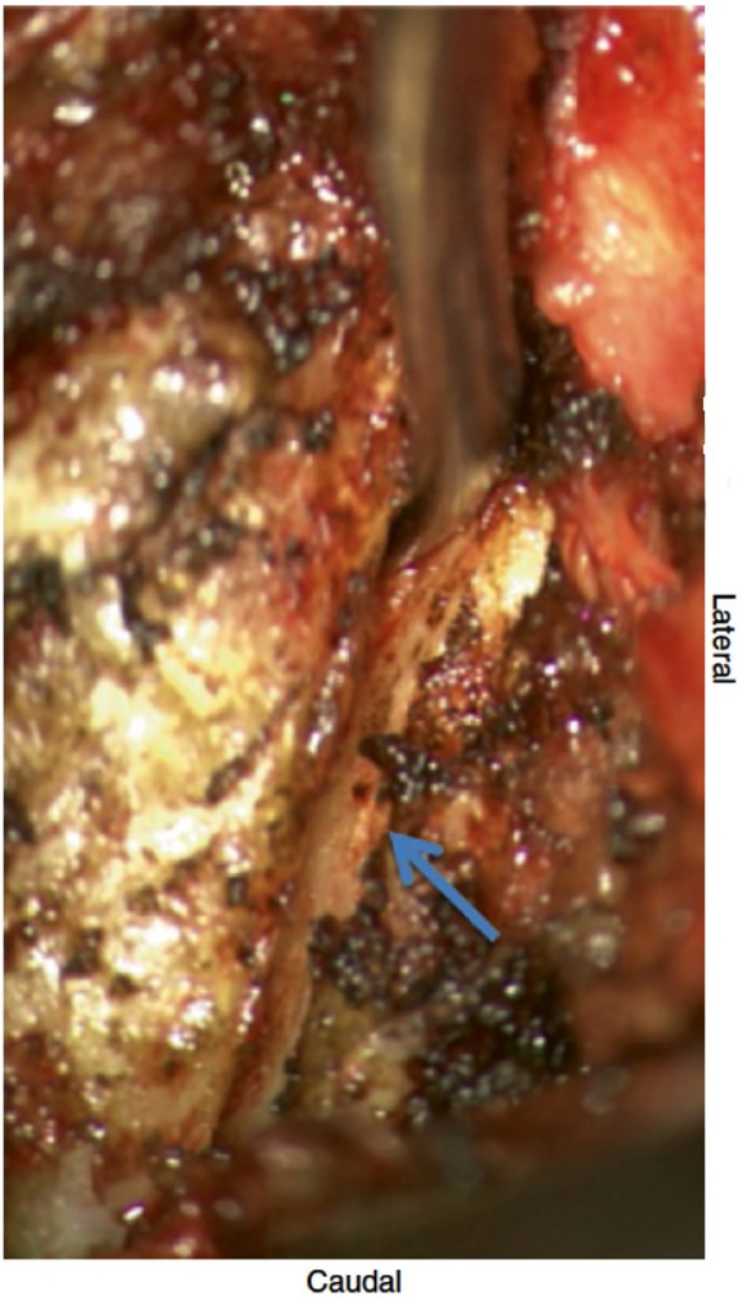


Figure 15:
Microscopic view of the right L4-L5 joint space, after resection by monopolar cautery of its capsule. The image is focused on the articulating surface of the superior articulating process (arrow).

- Once the facet joint is nicely and completely exposed (all soft tissue around the capsule and towards the lamina should be removed by monopolar cautery on the 'cutting' mode) remove the osteophytes and the facet joint capsule from cranial to caudal. This can be done with mono-polar cautery. The joint space can easily be identified (Figure 15)

Figure 16
Resection of the inferior articulating process, about 5 mm medial to its joint surface and parallel to the remaining superior articulating surface (arrow). Note the cutting blade of an ultrasonic tool on this saw bone model (blue arrow)

- The resection of the inferior articulating process should start, 5 mm medial to the articulating plane of the inferior articulating process. This large resection will facilitate the surgical procedure, especially when securing the inferior implant. If too much of the lamina is resected, this can be compensated by choosing a larger superior articulating implant surface component. (Figure 16)
- When resecting the inferior articulating process, take care to cut the lamina parallel to the articular plane of the remaining joint surface of the superior articulating process. (Figure 16) Care should be taken not to perforate or remove the Ligamentum Flavum initially. The Misonix ultrasound bone scalpel (Farmingdale, New York, USA) is recommended to do this job. It prevents from cutting the yellow ligament or underlying neural structures. It is important to create a smooth resection surface in order to fit the implant and promote bony ingrowth.

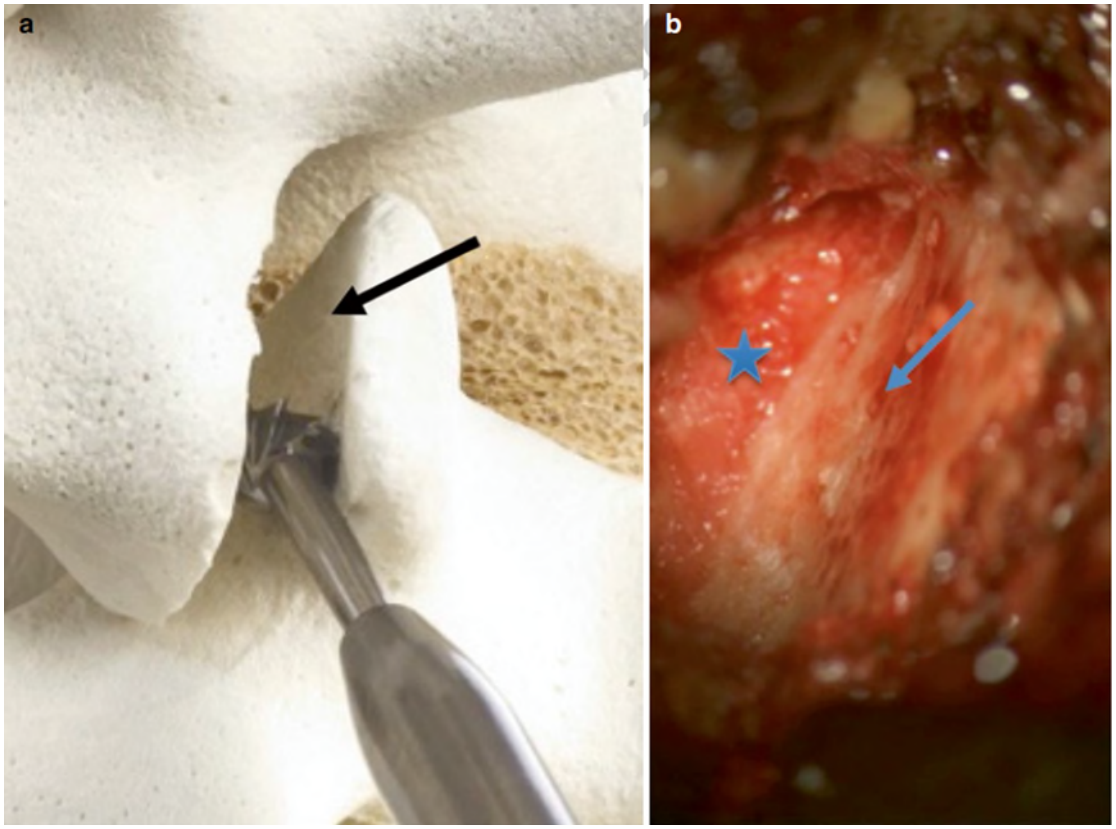


Figure 17:
Left. Drill resecting the remaining and damaged cartilage (black arrow) at the articulating surface of the superior articulating process.
Right. Intra-operative microscopic view. Mark the red spotting at the bony surface of the superior articulating joint (blue arrow), ready to accept the locking base. Notice the underlying yellow ligament (asterisk).

- With a high-speed drill, remove all cartilage from the articular aspect of the superior articulating process. Care must be taken to ensure preservation of the subchondral bone and not to weaken the cortical bony surface of the joint. (Figure 17)
- If required, foraminal decompression may be performed at this step of the procedure. At this stage, the yellow ligament may be resected with a small Kerrison punch, if necessary.
- By resecting this ligament, the neural structures will come into view and their decompression can be checked. This can only be accomplished with a proper view and illumination (i.e. operating microscope) and through a view parallel to the facet joint orientation (oblique). However, if no neural decompression is necessary, the yellow ligament must be left intact to protect the neural structures and to maintain as much as possible all stabilizing structures of the joint complex.

Preparation for Implantation:

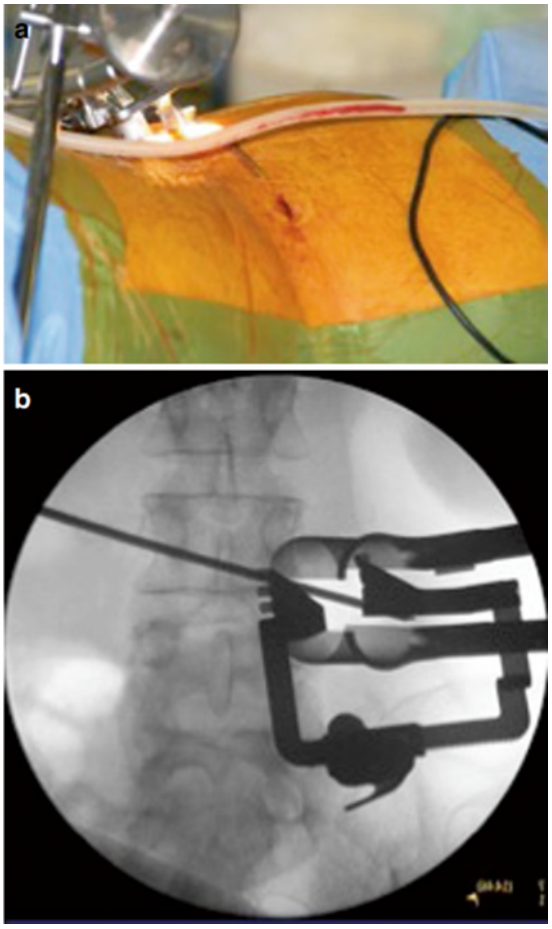


Figure 18
(A) Stab wound of 1 cm, contralateral to the implantation side and indicated by a proper AP view (B) Fluoroscopic AP view of the self-retaining retractor in place over the L3-L4 facet joint. A K-wire is presented on the skin and turned in a way its projection on this view marks exactly the translaminar trajectory. This will help identify the ideal contralateral stab wound for the translaminar approach

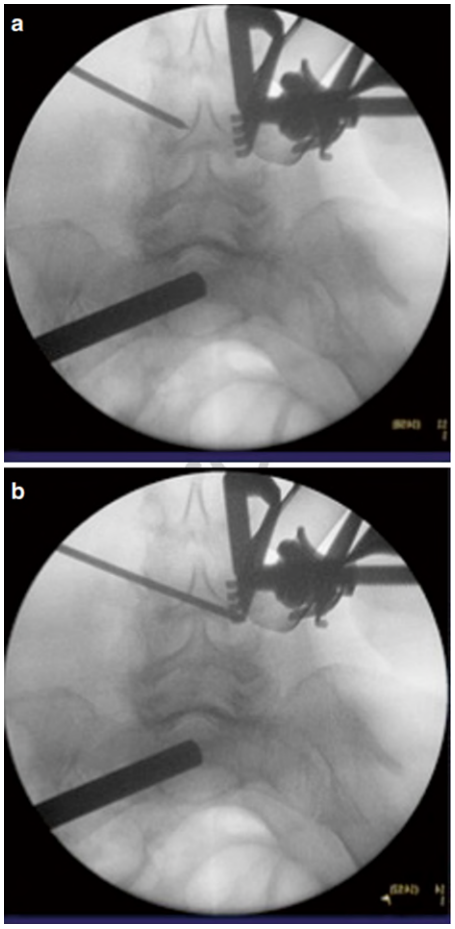


Figure 19
(A) Fluoroscopic outlet view with the starter needle at the junction between spinous process and L3 lamina. (B) Starter needle is advanced, stays inside the contour of the L3 lamina and ends at the partially resected joint space.

- Prior to the translaminar approach for both the cannulated screw for securing the locking base and the translaminar locking screw, the ideal contralateral stab wound of 1 cm should be made (Figure 18 A). A proper AP view of the lumbar spine showing the appropriate path for a translaminar screw tunnel indicates the exact location of the contralateral stab wound (Fig. 18 B).

- From the AP view shown in Figure 18 B, mark the desired trajectory on the patient's skin. This will aid in finding the correct contralateral entry point of the FENIX™ starter needle and proper placement of the working channel.
- Insert the starting needle into the stab wound and aim for the junction between the spinous process and the lamina on an outlet view. The ideal inclination of the needle must be checked in an AP view (cranio-caudal direction) and in the outlet view (ventral dorsal direction). Advance this starter needle, while checking your progress on alternating AP and oblique views. The needle should stay between the contours of the lamina. While doing so, it automatically will end in the partially resected joint space (Figure 18 A & 18 B, Figure 19).

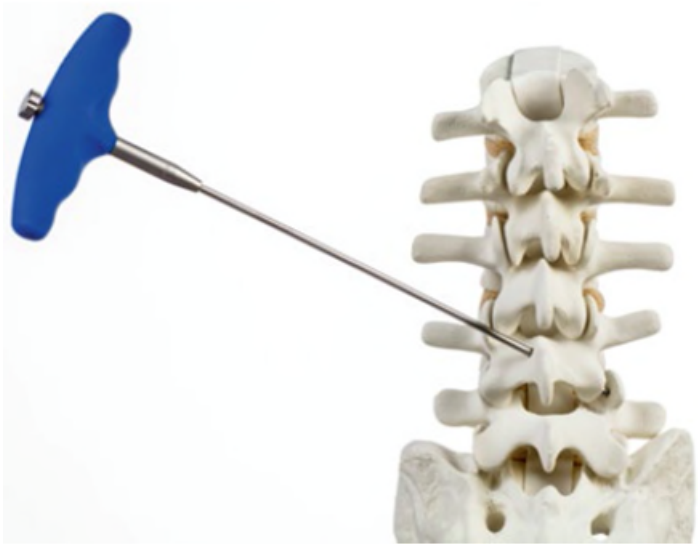


Figure 20
Representation on a saw bone of the translaminar placement of the starter needle.

Advance the K-wire through the starter needle and secure its threaded end into the superior articulating process. Remove the starter needle and use the muscle dilators over the K-wire, to install the working tube (Figure 21 A & 21 B, Figure 22)

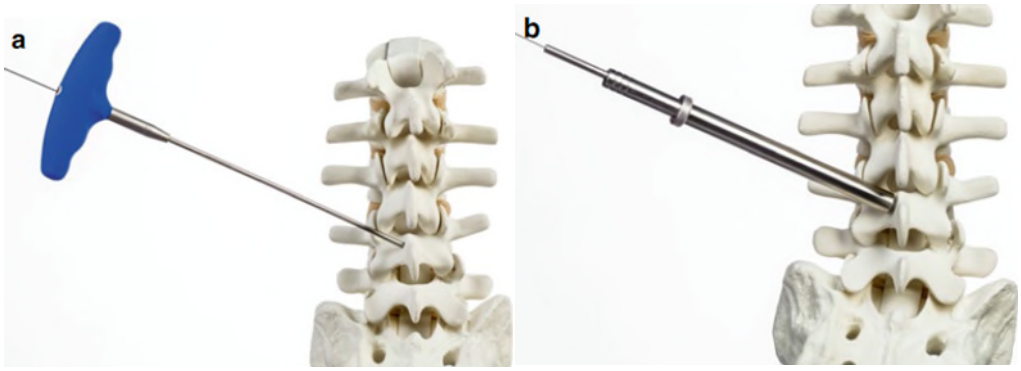
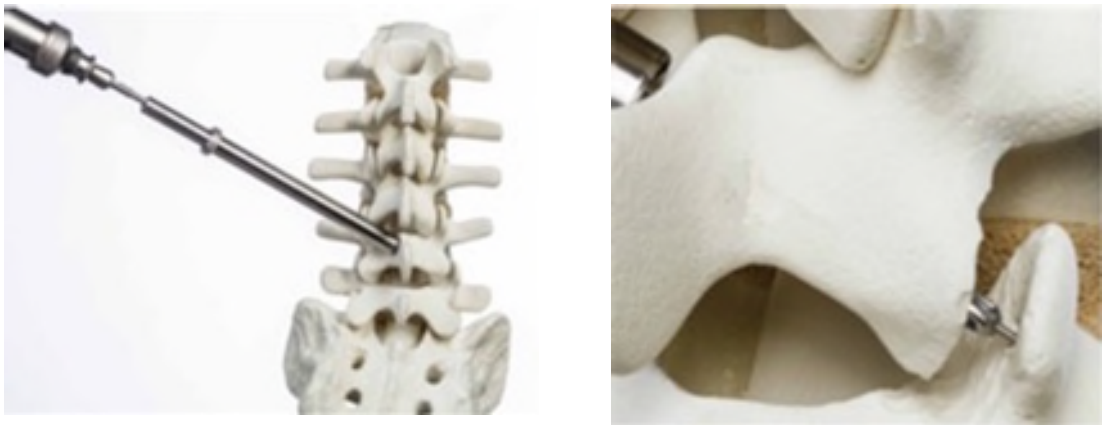


Figure 21
(A) K-wire is advanced in the starter needle. (B) Starter needle is removed and, over the muscle dilators, the working tube in inserted. Advance the working tube until it hits the bone.

Figure 22.
Ideal placement of the K-wire, locked at the center of the superior articulating process, after a proper translaminar (L4) course.

Drilling the trans-laminar channel:



A *B*

Figure 23:
(A) Mounted cannulated drill. (B) The drilling should stop before the superior articulating process.

- Place the 3.4mm cannulated drill over the K-wire; using the ¨spinal outlet¨ view, drill over the K- wire taking care to ensure the drill remains between the laminar cortices without entering the spinal canal (Figure 23).
- The freshly made trans laminar channel should exit ideally, in the center of the previously prepared facet joint (Figure 23). Do not advance the drill in the superior articulating process. This will prevent proper screw fixation of the locking base.

When drilling the contra lateral trans-laminar hole, be careful to offset the entry point to allow passage of the locking screw without interference with the previously prepared trans-laminar tunnel. Insertion of a k-wire or the starter needle in the previously prepared tunnel will help with orientation of a preferred starting point. The contralateral starting point will be somewhat lateral and more or less cephalad to the first entry point.

Figure 24
The contralateral starting point will be somewhat lateral and more or less cephalad to the first entry point in order to avoid that the translaminar locking screws hit each other at the spinous process-laminar junction

Implant insertion

Superior Implant Locking Base:

Figure 25
The superior implant locking-base in presented; smoothly slide it over the K-wire and check whether it fits properly to the articulating surface of the superior articulating process.

- Place the **Superior Implant locking-base** in the prepared space, using the implant introducer (Figure 25). Ensure the posterior aspect of this locking base fits perfectly with the prepared joint surface. This will allow proper bony ingrowth. If no perfect match is present, continue drilling the joint surface until a perfect fit is possible. However, while doing this, make sure not to harm the cortical bone. Just drill until bloody spotting of the cortex.

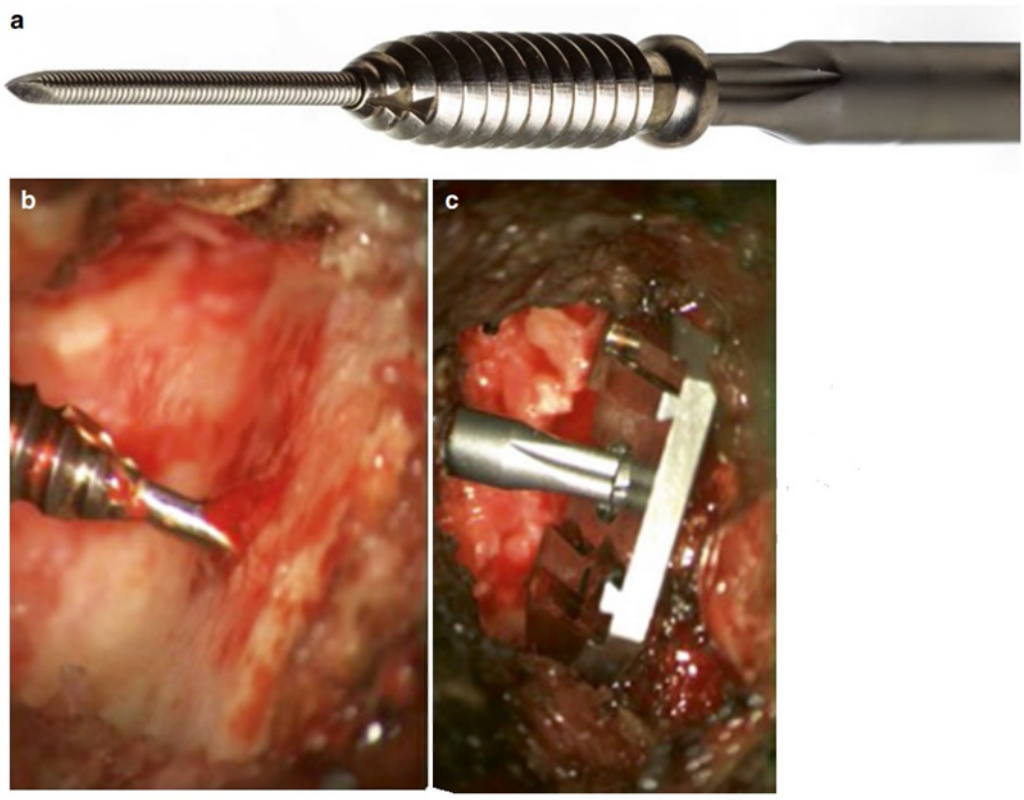
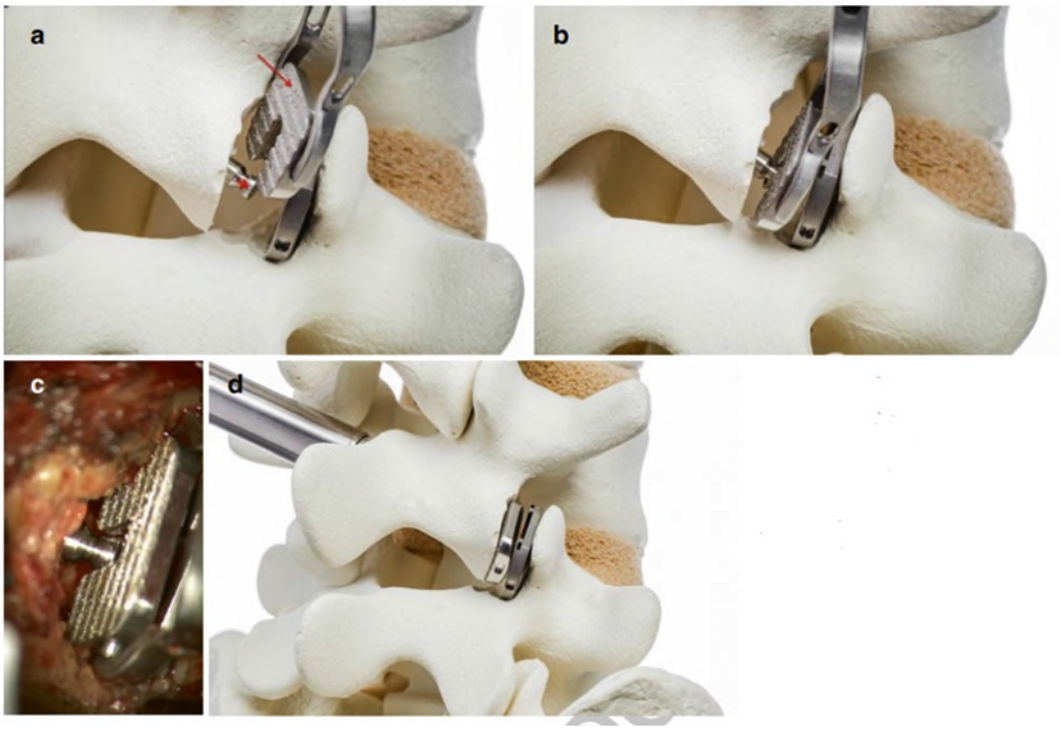


Figure 26
(A) Mount the screw for the locking base. As it is cannulated, it can be advanced over the K-wire by a proper screw driver. (B) Advance the screw until it becomes visible in the joint space of the partially resected facet joint. Note the K-wire, secured into the superior articulating process . (C) Intra-operative view of the cannulated screw driver, securing the locking base by advancing its screw.

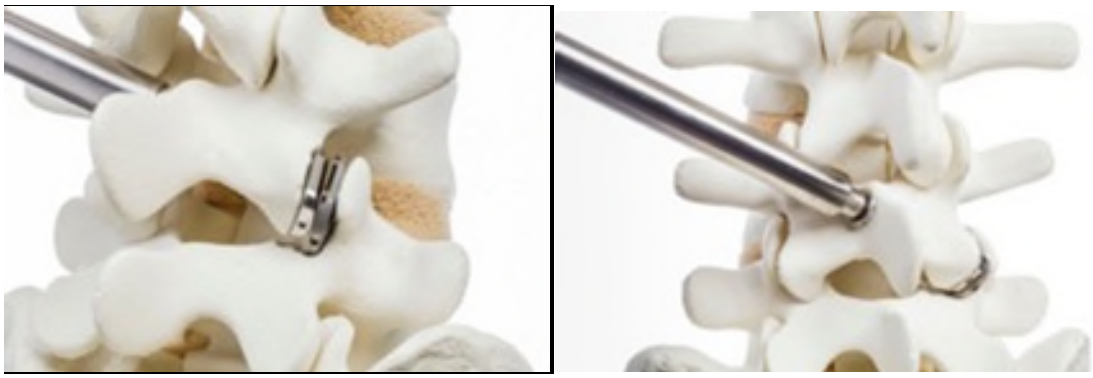
- The Superior Implant Locking Base is secured by advancing the 3.2mm cannulated bone screw over the K-wire, through the previously prepared trans laminar bone tunnel, directly through the hole in the tray. (Figure 26)
- Once the locking base is firmly secured, remove the K-wire, but hold the working channel firmly in place.
- Advance, through the working channel, the translaminar screw. Present the inferior implant and secure it by turning the mounted bolt (Figure 27)
- Ensure that the knobbed end of the trans laminar screw contacts the beginning of the track of the inferior component. Advance the inferior facet component over the trans laminar screw and lock it.



D’

Figure 27
(A) Note the translaminar locking screw (arrowhead) and the posterior aspect of the inferior implant (arrow). (B) Slide the inferior implant over the screw. (C) Intra-operative view (D) The inferior implant is locked against the partially resected lamina. (D) (D’) detail of figure D

- While holding the screw driver of the translaminar locking screw firmly in place, tighten the bolt, mounted on this locking screw, until the inferior implant fits perfectly against the partially resected lamina (Figure 28).



A ***B***

Figure 28

(A) By turning the bolt, mounted on the translaminar locking screw, the inferior implant is progressively secured against the resected part of the inferior articulating process. (B) The bolt is secured against the lamina.

- Use the sizing templates to get a proper fit between the two articulating implants (Figure 29). Sizing templates are provided in order to aid with the selection of the appropriate superior articulating implant. It is recommended that this step is used to ¨balance¨ the joint by ensuring tight contact and articular conformity between opposing articulating surfaces.

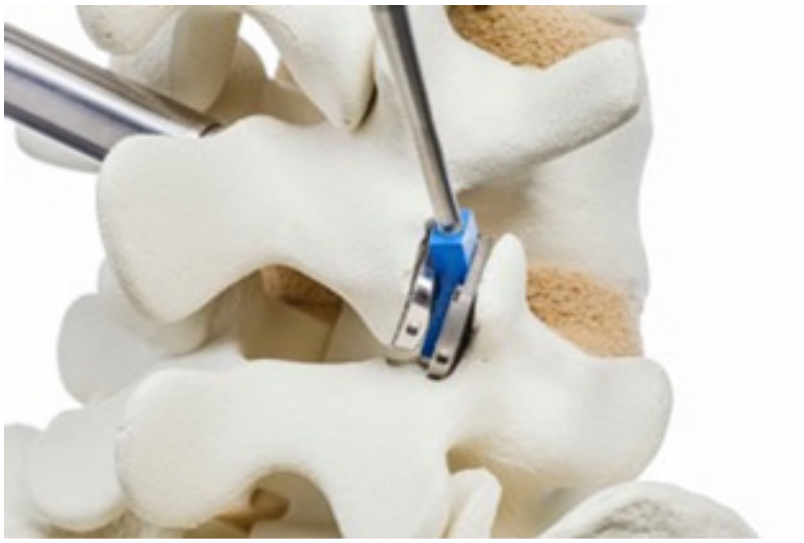


Figure 29
Sizing template in place to choose the correct superior implant.

- Slide the superior implant with correct size over its locking base (Figure 30)

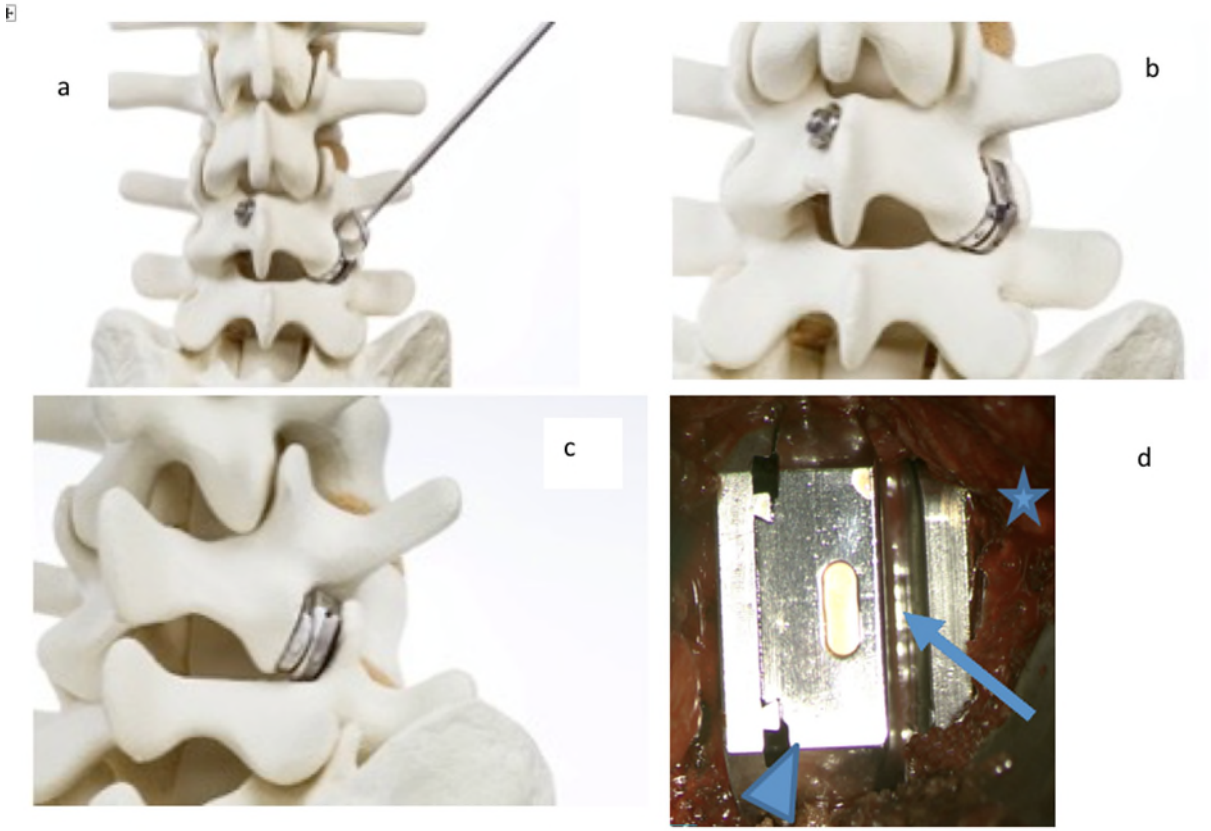


Figure 30
(A) Slide the superior implant over its locking base. (B) Detach the inserter; implantation of Fenix ® is completed. (C) Note the perfect fit between the two implants. (D) Intra-operative view on top of the assembled implants. Note the locking mechanism between the locking base (arrow head) and the superior articulating implant itself (arrow). Top of the inferior implant (asterisk).

- Closure of both wounds.

Exception

When, in the opinion of the implanting surgeon, the implant cannot be applied in a safe and proper manner at the affected level, the implanting surgeon may decide to abandon the procedure and convert to an alternative procedure, which in his/her opinion is suited to the patients' individual situation.

Evaluation parameters

Clinical diagnosis of facet pain

Patients report non-specific CLBP, possibly referred pain into the buttocks, the groin and anterior thigh (figure 31). The pain is worse when getting started, while sitting and standing. Pain is better when moving.

During the clinical exam, the LBP is getting worse on torsion, retroflexion and axial compression and there is no evidence for a radicular syndrome and patients experience paravertebral tenderness.

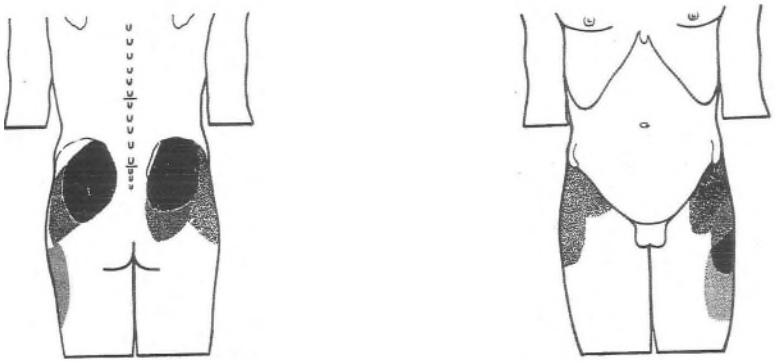


Figure 31: referral pattern of facet joint pain from McCall et al. [20]

Imaging

Radiography will be performed pre-operative and at 12, 26, 52 and 104 weeks post operatively

Antero posterior (AP) radiographic imaging will be performed in neutral standing position and under lateral left and right sided flexion.
Maintenance of motion
The degree of motion and translation will be measured in the lateral and AP radiographs, as described by Le Huec [21, 22]. Following parameters will be measured

1. ST—angle formed between the sacral endplate and the horizontal
2. PT—angle formed between the vertical plane and the line connecting the center of the hip to the center of the sacral endplate
3. Global lordosis—angle formed between the upper endplate of L1 and the sacral endplate
4. Segmental lordosis L4–L5—angle formed between the upper endplate of L4 and lower endplate of L5
5. Segmental lordosis L5–S1—angle formed between the upper endplate of L5 and the sacral endplate
6. Global kyphosis—angle between the upper endplate of T4 and lower endplate of T12

<u>MRI imaging</u>

MRI that allows interpretation of the facet joint synovitis performed (< 6 months) prior to inclusion in the study will be used to define the degree of facet joint synovitis. This will be interpreted according to the table 1

Table 1: Criteria for grading facet joint synovitis

0	No signal abnormality
1	Signal abnormality confined to joint capsule
2	Periarticular signal abnormality involving less than 50% of the perimeter of the joint*
3	Periarticular signal abnormality involving more than 50% of the perimeter of the joint*
4	Grade 3 with extension of signal abnormality into the intervertebral foramen, ligamentum flavum, pedicle, transverse process, or vertebral body

*Signal abnormality may extend into the articular pillar or lamina but does not contribute to the definition of the grade.

SPECT-CT imaging

Imaging will be performed on a dual-headed, hybrid SPECT (single photon emission computed tomography) /CT gamma camera (GE Discovery NM/CT 670) with a low energy high resolution (LEHR) collimator. Whole-body scintigraphy and SPECT/CT imaging will be performed 2-4h after IV administration of 700 MBq 99mTc-HDP.
SPECT images will be acquired in a 60-step (20 s/stop), 360° non-circular orbit and reconstructed in a 128 × 128 matrix using a three -dimensional ordered- subsets expectation maximization (OSEM) algorithm. Data will be reconstructed by Iterative Reconstruction using Flash-3D with four subsets and eight iterations, utilizing a Gaussian filter.
A CT transmission scan will be acquired after the SPECT study. The CT parameters used will be 120 kVp and automated exposure control. Reconstruction will be performed in a 512 × 512 matrix at slice thickness of 5 mm. The CT will be co- registered with the SPECT using the nuclear medicine workstation. CT attenuation correction will be applied to SPECT images. SPECT/CT studies will be viewed in the coronal, axial, and sagittal planes and in 3-dimensional mode. The CT-scan will be carried out, not as a diagnostic tool, but as a topographical one; it should help to correctly analyze the osteo-articular anatomy of the lumbar spine. As such, no analysis of soft tissue abnormalities will be done and for this study, the images obtained after this CT-scan will only be analyzed to grade the degree of facet joint degeneration.
The radiation exposure of the patient during the complete examination is estimated to be approximately 2.5 mSv. De CT-scan kan vergeleken worden met een klassieke C- scan van de lendenwervels.

The reading of the SPECT-image of each patient will be done by a nuclear medicine physician and consisted of a visual interpretation, without any quantification. The presence of hotspots will be recorded for, the lumbar facet joints. The reading and interpretation of the hotspots will be done according to the protocol described in table 2.
Table 2: Reading and interpretation of the SPECT-CT images with 3 levels: (see fig 1 and fig 2)

0 = normal (no active bone metabolism)
1 = slightly colored (moderate bone metabolism)
2= clear hotspot indicative for active bone metabolism

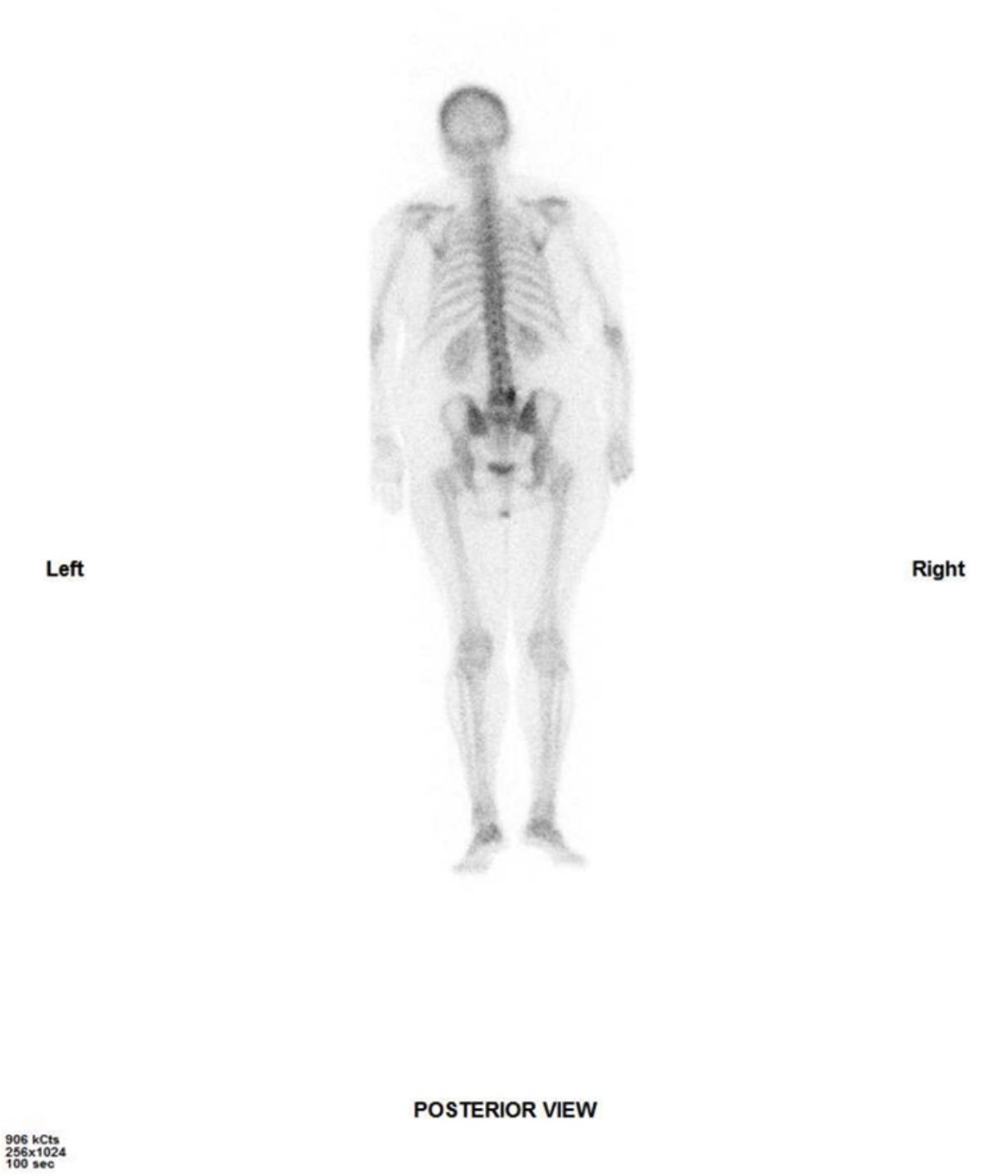


Figure 32: Whole body imaging bone scintigraphy clearly indicating a hot spot at the lower lumbar level on the right. When a hot spot is seen on this image, we classify it as a level two.

To identify the exact anatomical structure that is affected, the topographic CT-scan image is used (Fig. 33)

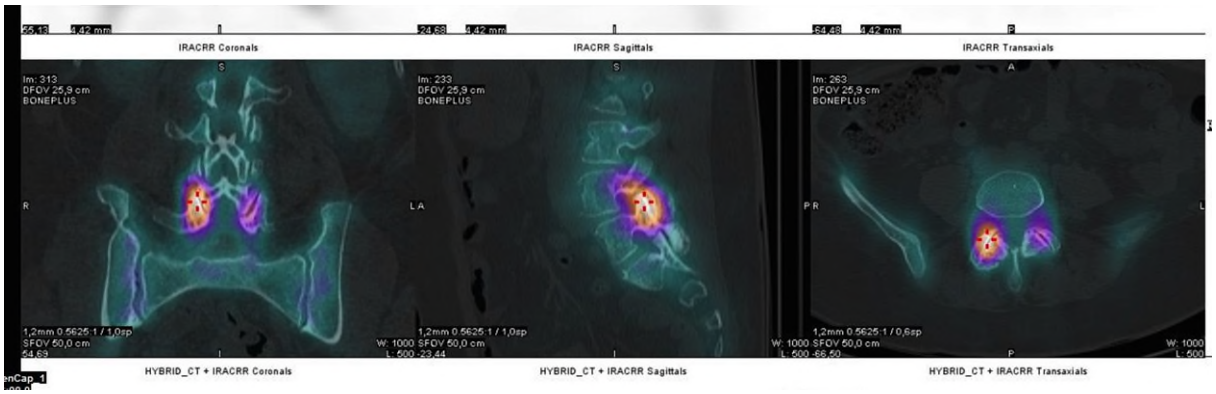


Figure 33: The upper images, the topographic CT-scan images in the three anatomical planes enable, after fusion with the SPECT images (the lower images the exact anatomical localization of the hot spot. This topographic CT image is not used to make a diagnosis on anatomical findings.
The lower images are the fusion images between the SPECT and CT-scan findings, confirming the hot spot detected in Fig 1 as altered bone metabolism at the right facet joint L4-L5. This lesion is classified as a level two hotspot. At the same level, to the left, there is a slightly colored spot at the facet joints, not seen on the whole-body imaging, which is therefore classified as a level one. All other anatomical locations analyzed (facet joints, endplates and both the SIJ) are classified a "zero" for this patient.

Diagnostic/confirmative block

A positive diagnostic block (≥50% pain relief), targeting the medial branch of the posterior primary ramus, was documented to be predictive for success of radiofrequency denervation, considered the reference treatment for pain originating from the facet joints. [23] The primary objective is to identify/confirm the causal level.
The neurosurgeon will perform the diagnostic block under fluoroscopic control at the level found during the clinical examination and confirmed by the medical imaging as most probable cause of CLBP. In view of the innervation of the facet joints from at least two spinal levels, the diagnostic nerve blocks will be performed at three levels for each joint. A 22-gauge needle will be placed under fluoroscopic control, which serves as orientation for the second and third needle. Each target will be injected slowly with 0.75 ml lidocaine 1%. Patients will be asked to score the effect of the injection in a four-step Likert scale, during 30 min follow-up. (table 3) When the patient reports good pain relief the targeted level will be

the level for surgery.

Table 3: Likert scale to be used for the assessment of the outcome of the medial branch block 30 minutes after the blocks are administered.

No pain relief	0-30% pain reduction
Moderate pain relief	30-50% pain reduction
Good pain relief	50-80% pain reduction
Pain free	80-100% pain reduction

Follow-up assessments

During and immediately after the intervention the hospital report will be filled out

Hospital Report

Implant Procedure

Surgical information is collected regarding date of surgery, implanted level, duration of surgery, blood loss, concomitant procedures performed, intraoperative findings that precluded implantation, implant size, implant lot number. This CRF will serve as the source document.

Discharge Report

Discharge information pertaining to duration of hospital stay and medication use is collected.

At each follow-up visit (12, 26, 52 and 104 weeks post operatively) following assessments will be performed.

Pain intensity

Pain intensity will be evaluated by the patient on a visual analogue scale (VAS) of 10 cm with 0 representing no pain and 10 the worst imaginable pain.

Frequency of pain

Patients will be asked to indicate according to the list below what applies best to their condition:

How frequent was your pain during the last week?

1. I had pain continuously
2. I had pain most of the time
3. I had pain regularly
4. I seldom had pain

5. I had no pain or only one flair-up of pain

Functional disability

Patients will be asked to fill out the Oswestry Disability Questionnaire for assessment of the functional disability [24-26]

Medication Use

The type and dose of medication used for the control of pain will be recorded at each visit. The evaluation of the pain medication will be done with the Medication Quantification Scale (MQS)[13]

Sample Size

Based on the outcome of the pilot study in 8 patients SPSS repeated anova shows highly significant improvement of ODI and VAS. Power calculation of the effect size shows that 30 patients are sufficient to show clinical effect. Therefore 30 subjects will be enrolled in the study.

Duration of Follow-up

The duration of the study is 24 months. It is anticipated that subject recruitment and enrollment will take approximately 1 year with an additional 24 months of subject follow-up and data collection. Follow-up of the subjects will continue until the last subject to receive the FENIX™ device has completed the 24th month follow-up visit.

Analysis of Results

Descriptive statistical analyses (mean, standard deviation, median, minimum and maximum) will be reported for Oswestry, VAS (back pain, and pain frequency) at the pre-operative and 12 weeks, 26 weeks, 52 weeks and 104 weeks follow-up visits. In addition, the 95% confidence intervals on the mean changes from the pre-operative result in Oswestry, VAS (back pain) will be computed and reported. Rates for adverse events will be reported as percentages of implanted subjects experiencing one or more events. Data will be reported in appropriate tabular or graphic formats.
At 1 year an interim evaluation of the radiological outcome will be performed.

Study Conduct

Informed Consent

The implanting surgeon or an individual designated by the implanting surgeon must obtain written study-specific informed consent from an eligible subject prior to subject enrollment in the study. The signed study-specific consent will indicate that (i) the subject agrees to participate in the evaluation of the FENIX™ device including follow-up examinations by the

implanting surgeon or an implanting surgeon-designated physician, (ii) the subject's clinical data will be stored in a data-base for further analysis and, (iii) if required, the clinical data will be made available to regulatory/health authorities.

Appendix 1 contains the recommended subject consent form text. The text of the informed consent is to be approved by the Ethics Committees

Ethical Considerations

A duly constituted Ethics Committee (Antwerp University Hospital, Belgium) representing the study site (AZ Nikolaas, Sint-Niklaas, Belgium) will review and approve the informed consent document, the protocol, and the implanting surgeon's participation in the study. This study will be conducted in accordance with applicable regulations, laws, good clinical practices, the Declaration of Helsinki and the Protocol.

Follow Up Visits and Data Reporting

To ensure data quality and completeness, all required data will be recorded on standardized case report forms (CRFs) (Appendix 2). The CRFs will be centralized at the principal investigator's site. Data will be entered into a validated database. The subject response (VAS) and Oswestry Low Back Pain Questionnaire will be completed by the subject directly on the appropriate CRFs, thereby making the CRF the source document. The implanting surgeon must sign and date all CRFs. Table 4 lists the various intervals at which data are to be collected, and the data forms to be completed at each interval.

The implanting surgeon will be responsible for ensuring that all associated personnel are properly trained to perform their assigned tasks.

Table 4: Data Collection Schedule

Case Report Forms	Baseline (within 8 weeks prior to surgery)	Day of Surgery	12 weeks ±2 weeks	26 weeks ±4 weeks	52 weeks ±8 weeks	104 weeks ±8 weeks
Consent Form	x*					
Clinical History	x					
MRI	x[a]					
SPECT –CT	x					
Subject Evaluation	x*					
Subject Evaluation (Postoperative)			x*	x*	x*	x*
Discharge Letter		x				
Adverse Event Initial Report		x	x	x	x	x
Flexion & Extension X-rays	x [a]			x	x	x
AP & Lateral X-rays	x [a]			x	x	x
Pain Medication	x		x	x	x	x
VAS	x		x	x	x	x
ODI	x		x	x	x	x
Work	x		x	x	x	x

*These forms: (VAS pain, Frequency of pain, Oswestry disability Index) are to be completed by the subject

a) May be performed outside the baseline period window, e.g., > 8 weeks prior to surgery with a maximum of 6 months in case of unchanged complaints

Evaluation (Baseline and Postoperative)

The CRF will contain the necessary documents relative to the evaluation parameters described above for the different evaluation time points:
Baseline (within 8 weeks prior to surgery), day of surgery and 12, 26, 52 and 104 weeks post-surgery.

Radiographic Analysis

Radiographic data (X-ray and MRI) will be evaluated by the neuro-radiologist, Prof. dr J.W.M. Van Goethem who will record the results in the specially designed section of the CRF. The SPECT-CT will be evaluated by Dr. K. Melis and also reported in the designed section of the CRF. This radiographic data will also be entered into a validated database. The radiographic CRF will serve as the source document.

Protocol Deviations

A protocol deviation is an event whereby the implanting surgeon or site personnel did not conduct the study according to the protocol or the study agreement.

Each protocol deviation should be recorded in the CRF. The principal investigator should be informed about the protocol deviation.

The implanting surgeon must notify the reviewing EC of any deviations from the protocol to protect the life or physical well-being of a subject. Such notice should be given as soon as possible, but no later than five working days after the deviation occurred.

Adverse Events

An adverse event (AE) is any undesirable clinical occurrence in a subject whether it is related to the FENIX™ device or its implantation. Any condition at baseline that is recorded as a pre-existing condition is not an AE unless it worsens in intensity or duration. The collection of AEs will begin in the operating room when the incision(s) is made that starts the implant procedure. All AEs that occur through completion of the final follow-up visit, whether observed by the implanting surgeon or reported by the subject, and whether thought to be device or procedure related, will be reported in detail on the appropriate CRF and followed to resolution. 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 on the appropriate CRF.

Additional information such as operative notes, discharge summaries, histopathology reports, and a physician's summary of the event, should be made available to the principle investigator.

Intensity
The implanting surgeon will evaluate the intensity of the adverse event using the following categories: mild, moderate or severe.

Relationship
The implanting surgeon will evaluate the relationship of the adverse event to the FENIX™ device or procedure using the following categories: not at all related, potentially related or definitely related based on his clinical experience

Serious Adverse Device Effect (SAE)
All SAE's must be reported to the principal investigator within 48 hours after having been made aware of the incident. An AE will be categorized as a SAE if it:

- results in death
- is life threatening
- is disabling
- requires medical intervention to prevent permanent impairment/damage

Unanticipated Adverse Device Effect (UADE)
An UADE is defined as "any serious adverse effect on health or safety or any life-threatening problem or death caused by, or associated with, a device, if that effect, problem, or death was not previously identified in nature, severity, or degree of incidence in the protocol or application, or any other unanticipated serious problem associated with a device that related to the rights, safety, or welfare of patient." All UADE's must be reported to the principal investigator by the implanting surgeon within 48 hours of his/her knowledge of the event.

Serious adverse events must be reported to the ethical committee of AZ Nikolaas, the ethical committee of UZA and Laterna

Records and Reports

Implanting Surgeon Records

The implanting surgeon must maintain adequate records on all aspects of the study including administrative records that include but are not limited to EC correspondence, EC approvals, and CVs, and subject records that include, but are not limited to, original CRFs, supporting data (e.g. medical records, clinic charts), queries and adverse event reports. All CRFs must be signed and dated by the implanting surgeon.

Implanting Surgeon Reports

The implanting surgeon is responsible for the timely preparation and submission of the reports cited in table 5.

Table 5: Implanting Surgeon Reports

Report	Sent To	Timing of Report
Unanticipated adverse device effect (UADE)	Principal investigator	UADE must be reported as soon as possible, but in no event later than 10 working days after the implanting surgeon first learns of the event
Withdrawal of EC approval	Principal investigators	Reported within 5 working days
Device use without informed consent	Principal investigator, EC	This deviation must be reported within 5 working days after the use occurs.
Other	EC	Upon request, accurate, complete, and current information about any aspect of the investigation must be reported.

Principal investigator's Records

The principal investigator will maintain accurate, complete, and current records including, but not limited to, all study correspondence, EC approval letters and rosters, required reports CVs for all implanting surgeons, protocol deviations, copies of all CRFs, supporting data, queries, and study related radiographs. All medical imaging should be made available for the central neuro-radiologist, Prof. dr J.W.M. Van Goethem.

Retention of Records

The implanting surgeon must retain all study records required by the applicable regulations in a secure and safe facility. The implanting surgeon must consult the principal investigator before disposal of any study records and must notify the principal investigator of any change in the location, disposition or custody of the study files. Study records are those that individually and collectively permit evaluation of the conduct of the study and the quality of the data produced. These documents must be retained permanently.

Publications

The principal investigator retains the right to the publication of the intermediate and final study results of the entire study population. He will be the first author of those publications. The other participants will be co-author. The order will be defined by consent.

Once the global study results have been published, other investigators may publish sub-sets of the data. Each publication should, however, be submitted to the principal authors for approval.

Appendix 3: Approvals

Approved: _____
Erik Van de Kelft
Principal investigator

Date:_____

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