CLINICAL INVESTIGATION

# Efficacy of an interspinous decompression device versus nonoperative treatment for lumbar spinal stenosis: an example for a randomized, controlled trial

**Clin. Invest.** (2012) 2(12), 1163–1169

**Background:** Lumbar spinal stenosis (LSS) with neurogenic intermittent claudication (NIC) is one of the most common degenerative spinal diseases in the elderly. One treatment option for LSS/neurogenic intermittent claudication is conservative management with oral analgesics, injections and physical therapy. Another relatively new operative alternative is interspinous process decompression. To date, there is no convincing evidence that these devices provide any patient benefits. **Methods:** This study is intended as a prospective, randomized, pilot-study to compare the safety and effectiveness of a minimally invasive, percutaneously implanted interspinous process decompression device with nonoperative treatment of LSS. Patients are randomized for surgical or nonsurgical treatment. The surgical group will undergo percutaneous implantation of an interspinous device (Aperius™ PercLID, Medtronic). The control group will receive nonoperative treatment with oral nonsteroidal anti-inflammatories, injections such as epidural steroid and facet joint injections, as well as intensive physical therapy. Follow-up examinations will take place immediately after treatment during the hospital stay, after 6 weeks, and 6, 12, 24, and 36 months post-treatment. A total of 11 patients will be included in each therapy group. Outcome measurements will include objective parameters such as pain-free-walking distance and frequency of pain-medication use. The Zurich Claudication Questionnaire, a Visual Analog Scale, SF-36 scores, patients' overall status, and clinical examinations will be assessed. **Summary:** As new surgical techniques are developed for the treatment of LSS, it is important to evaluate the effectiveness of competing strategies. With this study, not only patient-based scores, but also objective assessments will be used to quantify patient-derived benefits of therapy.

**Keywords:** conservative treatment • interspinous spacer • lumbar spinal stenosis • neurogenic claudication • randomized controlled trial • trial protocol

**Thomas Kaulhausen*[1], Peter Knoell[1,2], Gregor Stein[1], Jan Siewe[1], Martin Hellmich[3], Christina Otto[1], Annika Sayar[1], Ayla Yagdiran[1], Frank Beyer[1], Kourosh Zarghonni[1], Peer Eysel[1] & Rolf Sobottke[1]**

[1]Department of Orthopaedic and Trauma Surgery, University of Cologne, Kerpener Strasse 62, 50937 Cologne, Germany
[2]Clinical trials centre, University of Cologne, Kerpener Strasse 62, 50937 Cologne, Germany
[3]Institute of Medical Statistics, Informatics and Epidemiology, University of Cologne, Kerpener Strasse 62, 50937 Cologne, Germany
*Author for correspondence
Tel: +49 221 478 87294
Fax: +49 221 478 87296
E-mail: thomas.kaulhausen@uk-koeln.de

Lumbar spinal stenosis (LSS) with neurogenic intermittent claudication (NIC) is one of the most common degenerative spinal changes in the elderly [1–3]. NIC is a specific symptom in patients with LSS and is characterized by increasing leg, buttock or groin pain with or without lower back pain when walking a certain distance or reclining. Forward bending or sitting leads to rapid relief of the symptoms.

LSS is seen frequently in clinical practice. Of all patients consulting a general practitioner for lower back pain, 3–4% have degenerative changes, which leads to NIC. Nearly 15% of patients seeing a specialist for lower back pain have radiographically confirmed LSS [4]. Annual incidence rates of 5 per 100,000 have been reported [5]. In the USA, the annual cost of NIC to society from medical treatment and loss of productive work hours reaches tens of billions of dollars [6]. In Europe

FUTURE SCIENCE part of fsg

the annual cost of NIC to society may be as high as in the USA.

Nonoperative management is initially attempted with oral analgesics and physical therapy and the regimen can be intensified by adding epidural injections, whilst in a third of all patients, this therapy decreases symptoms sufficiently. In the remaining two-thirds of all cases, surgical treatment is necessary [7]. For patients over 65 years of age undergoing surgery, open decompression is most frequently performed [1,8,9]. One associated problem is surgical trauma to the osteoligamentous structures, which varies in severity depending on the extent of the operation performed.

A less invasive alternative is the implantation of an interspinous process decompression device (IPD). The gold standard of surgical treatment (open spinal decompression) of degenerative lumbar spinal stenosis (DLSS) is more invasive than the investigated IPDs. Surgery time in the operating room is higher in comparison with the IPDs. Biomechanical studies have shown that IPDs significantly reduce intradiscal pressure as well as the facet load, and prevent narrowing of the spinal canal and neural foramina [10,11]. Previous studies have shown benefits for the use of implanted IPDs (e.g., X-Stop™) versus conservative therapy, especially with regards to quality of life [6,12].

For some patients with LSS, IPDs may be a viable alternative to the gold standard [13]. IPDs may be used either as 'stand alone' spacers or to augment open decompression by preventing instability [14]. The main idea behind their design is the limitation of dynamic extension in the affected segment [15]. Radiologic studies have demonstrated that the use of interspinous devices affects spinal alignment as well as the dimensions of the spinal canal and neural foramina [16–18].

The implantation of the IPDs can be done percutaneously through a 1.5 cm skin incision. This surgical approach is used for the Aperius™ PercLID device designed by Medtronic, Inc. A number of recently published studies have shown significantly better clinical outcome after implantation of the Aperius PercLID implant [19–23].

The aim of this study is to evaluate safety and efficacy of IPDs compared with conservative treatment of LSS. It is supported by the Faculty of Medicine, University of Cologne (Cologne, Germany), trial registration NCT01057641 [101].

## Material & methods

The study is designed as a randomized, therapy-controlled trial in an ambulatory care setting at a university hospital. Patients presenting to the outpatient clinic with degenerative LSS will be assessed against study inclusion and exclusion criteria. After patient informed consent and randomization, implantation of an IPD or conservative management will be implemented. Follow-up examinations will take place immediately after treatment during the hospital stay, and after 6 and 24 weeks, for a study duration of 6 months. Data will also be assessed after 12, 24, and 36 months for a supplemental study.

Experimental research in this trial will be carried out with the approval of the Ethics Committee of the Medical Faculty of the University of Cologne under the reference number 10–012. Research carried out in the trial will be in compliance with the Helsinki Declaration [24].

### Participants & recruitment

Patients over 50 years of age presenting to our outpatient clinic with symptoms of degenerative lumbar spinal stenosis are eligible for trial inclusion. IPD implantation is not indicated until after 3 months of conservative therapy. The main inclusion criteria is the radiographically and clinically confirmed symptomatic discoligamentous DLSS. Forward flexion leads to a rapid pain relief. The IPDs are not suitable for osseous DLSS and spondylolistesis greater then Meyerding 1. Patients with an absolute DLSS with a threshold diameter <10 mm will not be included. All inclusion criteria are summarized in **Box 1**.

Patients participating in parallel interventional studies as well as patients with lumbar scoliosis (>25° Cobb angle), spondylolisthesis > Meyerding 1, and/or systematic disease are excluded from this study. Further exclusion criteria are summarized in **Box 2**.

Prerequisite to inclusion is degenerative LSS according to symptoms and MRI. Determining the symptomatic level of LSS is one of the unsolved problems. If one or more high-grade stenotic level is evident, all levels will be treated.

One of the main problems in orthopedic clinical trials is that it is difficult to comparatively randomize conservative treatment and surgical treatment. In our opinion we developed a study that respects this issue by the inclusion criteria. We will receive a homogeneous patient population that shows symptomatic and radiographically confirmed DLSS with NIC, which can be be comparatively randomized.

Study subjects will be approached and recruited by experienced spine surgeons. An estimated 100 patients per year will be screened and a recruitment rate of 22 patients per year is anticipated **(Figure 1)**.

### Intervention

Patients will receive one of two treatments:

- Percutaneous implantation of an interspinous device ('spacer');
- Nonoperative treatment.

### Control group: nonoperative treatment

The control group undergoes conservative management with oral nonsteroidal anti-inflammatories, other analgesics, physical therapy, and epidural pain treatment (3 × epidural injection). This is the gold standard for nonoperative therapy, and the current standard therapy in our hospital for this disease, when the patient is expressing moderate symptoms. The physical therapy is specifically tailored to NIC and consists of an isometric exercise program that is same for each patient. All patients will receive the same treatment, which consists of nonsteroidal anti-inflammatories (600 mg ibuprofen 3 per day) and physical therapy. This regimen will be carried out as an inpatient for 7 days. The physical therapy program will continue for 6 weeks (For schedule, see Tables 1 & 2).

### Intervention group: interspinous device

Patients of the experimental intervention group will receive the percutaneously implanted interspinous device. Insertion of the stand-alone spacer will be conducted under spinal or general anesthesia, with the patient placed in the prone position. The trocar will be introduced and pushed forward under position monitoring (X-ray) to the interspinous space. For optimal decompression, the trocar diameter can be increased. Once optimal diameter is identified, the spacer can be positioned between the spinous processes of the affected level and the wings of the spacer can then be unfolded. Patients will only be discharged after sufficient convalescence with an unremarkable wound. A hospital stay of 2–3 days will be necessary.

## Outcome measures & assessments

### Primary outcome measures: SF-36 physical component summary

Our investigation focuses on the subjective and objective benefits for the patient. Functional outcomes will be evaluated using the SF-36 score at 6 weeks and 6 months after treatment (evaluations at 12-, 24-, and 36-month follow ups will be performed in a supplemental study). The SF-36 is the most frequently used generic health status measure worldwide. Development of the physical component summary (PCS) and mental health component scores has eased interpretation as well as cross-cultural comparison of the instrument. In contrast to previous years, more recent investigations have focused on clinical, rather than technical, outcomes. To assess such parameters, more recent important clinical trials have used the SF-36, Oswestry Disability Index or Zurich Claudication Questionnaire (ZCQ). The scores of the experimental and control groups on the physical component summary of the SF-36 will be compared with objectively measured patient outcomes. It is assumed that LSS with NIC will mainly

**Box 1. Inclusion criteria.**

- Male or female ≥ 50 years of age
- One, two, or three segment degenerative lumbar spinal stenosis
- Symptoms of radiographically confirmed degenerative lumbar spinal stenosis, for example, leg, buttock or groin pain with or without back pain
- Absence of a peripheral motoric deficit
- Pain relief in forward flexion or sitting
- Ability to walk a distance of 50 m
- Unsuccessful conservative therapy for 3 months under outpatient conditions
- Informed consent
- Suitability for treatment with percutaneous interspinous spacer implantation as well as conservative therapy with physical therapy

**Box 2. Exclusion criteria.**

- Motor deficit
- Cauda equina syndrome
- Previous surgical intervention of the lumbar spine
- Relevant peripheral neuropathy
- Acute denervation subsequent to radiculopathy
- Scoliosis with Cobb angle >25°
- Spondylolisthesis, Meyerding grade >1
- General contraindication for elective lumbar spine surgery
- Morbid obesity (BMI > 40 kg/m$^2$)
- Pathologic fracture
- Osteoporosis with pathologic fracture
- Active systemic infection
- Rheumatic disease
- Disease of bone metabolism (e.g., Paget's Disease)
- Bone metastasis
- Local infection focus lumbar spine
- Seizure disorder
- Chronic ischemia Fontaine classification IIb–IV
- Severe heart insufficiency (New York Heart Association classification III–IV)
- Blood coagulation disorder or blood thinning therapy
- Cortisone intake more than one month in the 12 months before randomization
- Simultaneous participation in another clinical trial in the 30 days before randomization
- Known allergy or intolerance to the implants
- Dependency on investigator
- Lack of familiarity with the German language
- Placement in an institution by governmental or juridical advice
- Absent legal capacity
- Pregnancy

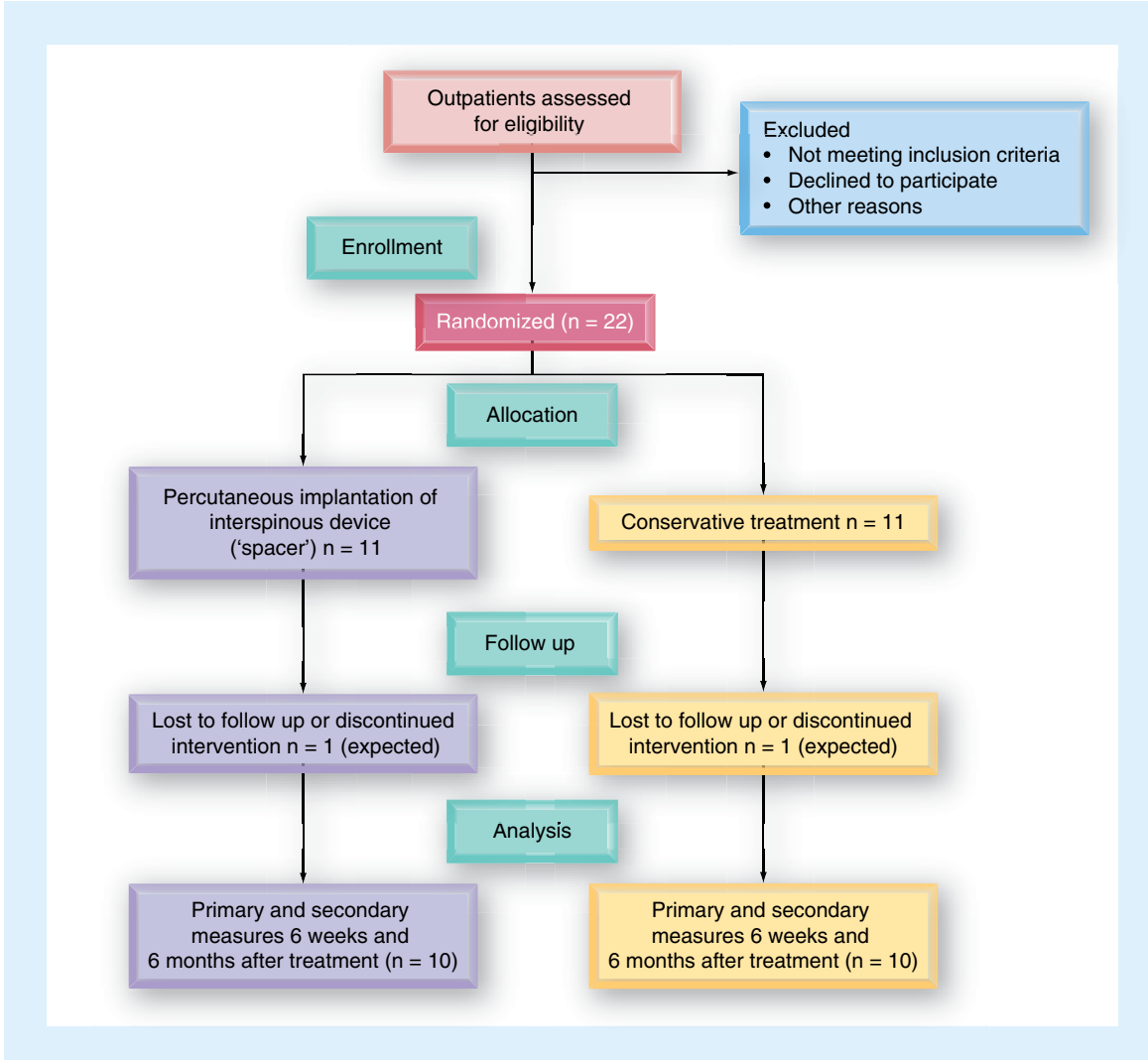


**Figure 1. Flowchart of trial procedures.**

affect the SF-36 dimensions of physical functioning, role-physical, and bodily pain, which contribute most to factor loadings of the PCS. Therefore we decided to use the SF-36 instead of the Oswestry Disability Index. The primary end point is the change from baseline to 6 weeks and 6 months. After this time, substantial dropout or conversion fraction is not expected, so that valid assessment should be possible. Of course, the follow up at 36 months will give essential information regarding long-term outcomes and the effects of conversion, in particular the number of patients in both groups eventually requiring open surgery.

**Table 1. Schedule of conservative treatment, week 1: inpatient treatment.**

| Treatment | Day 1 | Day 2 | Day 3 | Day 4 | Day 5 |
|---|---|---|---|---|---|
| Body-stabilizing exercise | | x | | x | |
| Leg-strengthening exercises | x | | x | | x |
| Massage | | x | | x | |
| Fango (mudpack) application | | x | | x | |
| Relaxing lounger | x | | x | | x |
| Physical therapy | | x | | x | |

## Secondary outcome measures

This trial focuses on the subjective and objective benefits for the patient, therefore the following secondary end points will be analyzed:

- Patient satisfaction regarding treatment by both experimental and control groups as measured on the ZCQ comparing baseline values with those at

hospital discharge, at 6 weeks, and 6 months (for the supplemental study also 12, 24, and 36 months) after initiation of therapy;

- Average change in physical activity as measured on the ZCQ comparing baseline values with those at hospital discharge, at 6 weeks, and 6 months (for the supplemental study also 12, 24, and 36 months) after initiation of therapy;
- Average change of the symptom severity as measured on the ZCQ comparing baseline values with those at hospital discharge at 6 weeks and 6 months (for the supplemental study also 12, 24, and 36 months) after initiation of therapy;
- Walking distance according to treadmill measures comparing baseline values with those at hospital discharge, at 6 weeks, and 6 months (for the supplemental study also 12, 24, and 36 months) after initiation of therapy;
- Global patient health status as measured with the SF-36 comparing baseline values to those at hospital discharge at 6 weeks and 6 months (for the supplemental study also 12, 24, and 36 months) after initiation of therapy;
- Secondary end point: at each visit, patients will be asked to rate their subjective pain using a Visual Analog Scale;
- Treatment complications: general (e.g., deep venous thrombosis, pneumonia and urinary tract infection) and treatment-specific (e.g., implant failure, spinous process fracture, epidural hematoma and infection);
- Long-term effects of surgery (implant-loosening, accelerated degeneration of the adjacent segments) will be analyzed in the follow ups.

## Sample size

Our target recruitment is 22 patients. We assume a loss at follow up of 10%, leaving 20 patients available for the final analysis. The normalized form of the SF-36™ PCS (mean: 50; SD: 10) is assumed. With this number of patients, using a two-sided t-test, a normalized PCS score difference of 11 will be achieved. Two or more could be detected with a power of 80% and $\alpha = 0.05$. This trial is developed as a pilot trial to detect the difference between the two groups. After data analysis another study with a larger sample size will be designed to improve the statistic significance.

## Randomization

The randomization of patients into intervention and control groups is performed using blocks of randomly varied length in order to maintain balance of allocation while preventing predictability. Randomization is stratified by single or multisegmental disease. A container with the sequentially numbered, sealed envelopes is stored in a locked cupboard that only the investigator can open. The random allocation sequence and the sealed envelopes will be generated by the Institute of Medical Statistics, Informatics, and Epidemiology of the university conducting the trial. Enrollment and randomization will be executed by the investigator.

**Table 2. Schedule of conservative treatment, week 2–6: outpatient treatment.**

| Treatment | Week 2 | Week 3 | Week 4 | Week 5 | Week 6 |
|---|---|---|---|---|---|
| Body-stabilizing exercise | | x | | x | |
| Leg-strengthening exercises | | x | | x | |
| Massage | | x | | x | |
| Fango (mudpack) application | | x | | x | |
| Physical therapy | | x | | x | |

## Results

The primary analysis will be according to intention to treat. Repeated SF-36 subscores over time (primary: baseline, 6 weeks, 6, 12, 24, and 36 months) will be analyzed by mixed-effects models (using specific contrasts) with the variables: treatment, time and multiple segment DLSS according to intention to treat. The hypotheses on changes in bodily pain and physical function will be addressed in a fixed sequence (thus, no correction for multiplicity is required). Missing at random will be assumed and the impact of plausible missing mechanisms (i.e., missing not at random) will be explored within the study results. The analysis will be repeated according to treatment actually received (as treated). Subgroup analyses will be conducted according to gender and multiple segment DLSS (if this is possible with 22 randomized patients). Analysis of secondary end points will follow the same procedure (i.e., longitudinal regression). Safety analysis (complications/adverse events) will be descriptive, for instance, using tables and listings.

## Discussion

It is possible that IPDs improve the outcome of LSS. To date, however, there are few convincing published data regarding these percutaneously inserted implants. In an observational study, Galarza reported improvement in 40 patients after minimally invasive IPD implantation [21]. Patients were assessed by ZCQ and a Visual Analog Scale. Between 2007 and 2008, Nardi implanted IPDs in 152 patients and reported the postoperative

results [22]. No serious adverse events were recorded. In one case the IPD was not implanted because of hypertrophic facet joints, and in two cases therapeutic failure was observed. Visual Analog Scale and ZCQ scores improved significantly [22]. Van Meirhaeghe *et al.* could show that the safety and effectiveness of the Aperius device offer a minimally invasive option for the treatment of DLSS [25].

According to clinicaltrials.gov, two studies are ongoing and recruiting and each is comparing two different IPDs in a randomized trial [102,103]. In addition to an observational clinical follow-up study of the Aperius IPD that has finished recruiting [104], a feasibility study of NL-Prow™ Interspinous Spacer is ongoing, but not recruiting [105]. Finally, one observational long-term follow up of the X-STOP® IPD has been completed [106].

The aforementioned studies are encouraging for the use of IPDs. On the other hand Verhoof *et al.* reported on a high failure rate after short follow up in patients with spinal stenosis caused by degenerative spondylolisthesis, but did not recommend the IPDs for the treatment of spinal stenosis caused by degenerative spondylolisthesis [26].

However, to determine a superior effect of IPDs versus other treatment options for LSS/NIC, randomized clinical trials are indispensable. To our knowledge, no published or ongoing studies fulfill these conditions. Thus, we offer a randomized clinical trial comparing the Aperius IPD with conservative treatment.

On the other hand, our pilot study design has to be considered. The measurement of statistically significant effects and a large effect magnitude require large sample sizes. While obtaining our data, we recommend discussion of potential efficacy and if possible, further multicenter, randomized controlled trials (RCTs) to offer general recommendations for spine surgeons. The conservative treatment in this trial represents an intensified nonoperative treatment that we perform in our hospital. In this trial we want to see if the IPDs have the same clinical value such as the intensified conservative treatment.

## Future Perspective

There are specific difficulties to be faced when executing clinical trials related to surgical procedures (e.g., the learning curve of the surgeon, blinding). From our experience, recruitment in orthopedic trials including randomization is always challenging, especially comparing operative and nonoperative treatment. As a result, surgical RCT are underrepresented in the total number of RCTs and in the scientific literature. Evidence-based surgical therapy is essential for further development of a high quality surgical standard in spine surgery, which will also provide quality assurance in the future. First we want to analyze the new surgical treatment in comparison to the conservative treatment. The next step would be a RCT of IPDs versus open spinal decompression. Long-term effects of surgery (implant-loosening, accelerated degeneration of the adjacent segments) will be analyzed in the follow ups.

## Executive summary

- Lumbar spinal stenosis (LSS) with neurogenic intermittent claudication is one of the most common degenerative spinal diseases in the elderly.
- Another relatively new operative alternative is the use of interspinous process decompression (IPD).
- To date, there is no convincing evidence that these devices provide any patient benefits.
- Biomechanical studies have shown that IPDs significantly reduce intradiscal pressure, as well as the facet load, and prevent narrowing of the spinal canal and neural foramina.
- For some patients with LSS, IPDs may be a viable alternative to the gold standard.
- This study is intended as a prospective, randomized, pilot study to compare the safety and effectiveness of a minimally-invasive, percutaneously implanted IPDs with nonoperative treatment of LSS.
- Outcome measurements will include objective parameters such as pain-free walking distance and frequency of pain medication use. The Zurich Claudication Questionnaire, a Visual Analog Scale, SF-36 scores, patients' overall status, and clinical examinations will be assessed.
- One of the main problems in orthopedic clinical trials is that it is difficult to comparatively randomize conservative treatment and surgical treatment. In our opinion we developed a study that respects this issue by our inclusion criteria. We will receive a homogeneous patient population that shows symptomatic and radiographically confirmed degenerative LSS with neurogenic intermittent claudication, which can be comparatively randomized.
- As new surgical techniques are developed for the treatment of LSS, it is important to evaluate the effectiveness of competing strategies. With this study, not only patient-based scores, but also objective assessments will be used to quantify patient-derived benefits of therapy.

## Financial & competing interests disclosure

*T Kaulhausen is supported by the German Federal Ministry of Research and Education (BMBF grant 01KN1106) and CHIR-Net-FKZ (01GH1001E) and Forschungspool 'Klinische Studien', Faculty of Medicine, University of Cologne (Cologne, Germany). The authors have no other relevant affiliations or financial involvement with any organization or entity with a financial interest in or financial conflict with the subject matter or materials discussed in the manuscript apart from those disclosed.*

*No writing assistance was utilized in the production of this manuscript.*

## References

Papers of special note have been highlighted as:
- ▪ of interest
- ▪▪ of considerable interest

1 Ciol MA, Deyo RA, Howell E, Kreif S. An assessment of surgery for spinal stenosis: time trends, geographic variations, complications, and reoperations. *J. Am. Geriatr. Soc.* 44, 285–290 (1996).

▪ **A good overview of lumbar spinal stenosis.**

2 Porter RW. Spinal stenosis and neurogenic claudication. *Spine* 21, 2046–2052 (1996).

3 Vogt MT, Cawthon PM, Kang JD, Donaldson WF, Cauley JA, Nevitt MC. Prevalence of symptoms of cervical and lumbar stenosis among participants in the osteoporotic fractures in men study. *Spine* 31, 1445–1451 (2006).

4 Hart LG, Deyo RA, Cherkin DC. Physician office visits for low-back-pain – frequency, clinical-evaluation, and treatment patterns from a US national survey. *Spine* 20, 11–19 (1995).

5 Schulte TL, Bullmann V, Lerner T *et al.* Lumbar spinal stenosis [article in German]. *Orthopade* 35(6), 693–94 (2006).

6 Zucherman JF, Hsu KY, Hartjen CA *et al.* A multicenter, prospective, randomized trial evaluating the X STOP interspinous process decompression system for the treatment of neurogenic intermittent claudication: two-year follow-up results. *Spine* 30(12), 1351–1358 (2005).

▪▪ **The first randomized, controled trial of interspinous process decompression devices (IPD) with 2-year follow up.**

7 Amundsen T, Weber H, Nordal HJ, Magnaes B, Abdelnoor M, Lilleas F. Lumbar spinal stenosis: conservative or surgical management? A prospective 10-year study. *Spine* 25, 1424–1435, discussion 35–36 (2000).

8 Katz JN. Lumbar spinal fusion: surgical rates, costs, and complications. *Spine* 20, S78–S83 (1995).

9 Katz JN, Lipson SJ, Chang LC, Levine SA, Fossel AH, Liang MH. Seven- to 10-year outcome of decompressive surgery for degenerative lumbar spinal stenosis. *Spine* 21, 92–97 (1996).

10 Swanson KE, Lindsey DP, Hsu KY, Zucherman JF, Yerby SA. The effects of an interspinous implant on intervertebral disc pressures. *Spine* 28, 26–32 (2003).

11 Wiseman CM, Lindsey DP, Fredrick AD, Yerby SA. The effect of an interspinous process implant on facet loading during extension. *Spine (Phila Pa 1976).* 30, 903–907 (2005).

12 Zucherman JF, Hsu KY, Hartjen CA *et al.* A prospective randomized multi-center study for the treatment of lumbar spinal stenosis with the X STOP interspinous implant: 1-year results. *Eur. Spine J.* 13, 22–31 (2004).

▪▪ **The first randomized, controled trial of IPD devices with 1-year follow up.**

13 Sobottke R, Rollinghoff M, Siewe J *et al.* Clinical outcomes and quality of life 1 year after open microsurgical decompression or implantation of an interspinous stand-alone spacer. *Minim. Invasive Neurosurg.* 53, 179–183 (2010).

14 Schulte TL, Hurschler C, Haversath M *et al.* The effect of dynamic, semi-rigid implants on the range of motion of lumbar motion segments after decompression. *Eur. Spine J.* 17, 1057–1065 (2008).

15 Sobottke R, Schluter-Brust K, Kaulhausen T *et al.* Interspinous implants (X Stop, Wallis, Diam) for the treatment of LSS: is there a correlation between radiological parameters and clinical outcome? *Eur. Spine J.* 18, 1494–1503 (2009).

▪ **Interesting article concerning IPD.**

16 Lindsey DP, Swanson KE, Fuchs P, Hsu KY, Zucherman JF, Yerby SA. The effects of an interspinous implant on the kinematics of the instrumented and adjacent levels in the lumbar spine. *Spine* 28, 2192–2197 (2003).

17 Richards JC, Majumdar S, Lindsey DP, Beaupre GS, Yerby SA. The treatment mechanism of an interspinous process implant for lumbar neurogenic intermittent claudication. *Spine* 30, 744–749 (2005).

18 Siddiqui M, Karadimas E, Nicol M, Smith FW, Wardlaw D. Influence of X stop on neural foramina and spinal canal area in spinal stenosis. *Spine* 31, 2958–2962 (2006).

19 Assietti R, De Falco R. The first multicenter, prospective 6 month follow-up study of 21 patients treated with the Aperius™ PercLID™ system. Presented at: *13th European Congress of Neurosurgery*. Glasgow, Scotland, 2–7 September 2007.

▪ **First clinical results of the percutaneous IPDs.**

20 Collignon F, Fransen P. Treatment of symptomatic degenerative lumbar spinal stenosis by a percutaneous stand-alone lumbar interspinous implant. Preliminary experience with the Aperius device. *Neurochirurgie* 56, 3–7 (2010).

21 Galarza M, Fabrizi AP, Maina R, Gazzeri R, Martinez-Lage JF. Degenerative lumbar spinal stenosis with neurogenic intermittent claudication and treatment with the Aperius PercLID System: a preliminary report. *Neurosurg. Focus.* 28(6), E3 (2010).

▪▪ **First clinical results of the percutaneous IPDs.**

22 Nardi P, Cabezas D, Rea G, Pettorini BL. Aperius PercLID stand alone interspinous system for the treatment of degenerative lumbar stenosis: experience on 152 cases. *J. Spinal Disord. Tech.* 23, 203–207 (2010).

23 Fabrizi AP, Maina R, Schiabello L. Interspinous spacers in the treatment of degenerative lumbar spinal disease: our experience with DIAM and Aperius devices. *Eur. Spine J.* 20, 20–26 (2011).

24 Declaration of Helsinki. Ethical principles for medical research involving human subjects. *J. Indian Med. Assoc.* 107, 403–405 (2009).

▪▪ **The last clinical results of the percutaneous IPDs.**

25 Van Meirhaeghe J, Fransen P, Morelli D *et al.* Clinical evaluation of the preliminary safety and effectiveness of a minimally invasive interspinous process device APERIUS® in degenerative lumbar spinal stenosis with symptomatic neurogenic intermittent claudication. *Eur. Spine J.* doi:10.1007/s00586-012-2330-z (2012) (Epub ahead of print).

26 Verhoof OJ, Bron JL, Wapstra FH, van Royen BJ. High failure rate of the interspinous distraction device (X-Stop) for the treatment of lumbar spinal stenosis caused by degenerative spondylolisthesis. *Eur. Spine J.* 17(2), 188–192 (2008).

### ■ Websites

101 Clinical trials identifier: NCT01057641. www.clinicaltrials.gov

102 Clinical trials identifier: NCT00692276. www.clinicaltrials.gov

103 Clinical trials identifier: NCT01156675. www.clinicaltrials.gov

104 Clinical trials identifier: NCT00887744. www.clinicaltrials.gov

105 Clinical trials identifier: NCT01053364. www.clinicaltrials.gov

106 Clinical trials identifier: NCT00534092. www.clinicaltrials.gov