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CLINICAL TRIAL REPORT

24-Month Outcomes of Indirect Decompression Using a Minimally Invasive Interspinous Fixation Device versus Standard Open Direct Decompression for Lumbar Spinal Stenosis: A Prospective Comparison

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Video abstract

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Purpose: An early-stage, multi-centre, prospective, randomised control trial with five-year follow-up was approved by Health Research Authority to compare the efficacy of a minimally invasive, laterally implanted interspinous fixation device (IFD) to open direct surgical decompression in treating lumbar spinal stenosis (LSS). Two-year results are presented.

Patients and Methods: Forty-eight participants were randomly assigned to IFD or decompression. Primary study endpoints included changes from baseline at 8-weeks, 6, 12 and 24-months follow-ups for leg pain (visual analogue scale, VAS), back pain (VAS), disability (Oswestry Disability Index, ODI), LSS physical function (Zurich Claudication Questionnaire), distance walked in five minutes and number of repetitions of sitting-to-standing in one minute. Secondary study endpoints included patient and clinician global impression of change, adverse events, reoperations, operating parameters, and fusion rate.

Results: Both treatment groups demonstrated statistically significant improvements in mean leg pain, back pain, ODI disability, LSS physical function, walking distance and sitting-to-standing repetitions compared to baseline over 24 months. Mean reduction of ODI from baseline levels was between 35% and 56% for IFD ($p<0.002$), and 49% to 55% for decompression ($p<0.001$) for all follow-up time points. Mean reduction of IFD group leg pain was between 57% and 78% for all time points ($p<0.001$), with 72% to 94% of participants having at least 30% reduction of leg pain from 8-weeks through 24-months. Walking distance for the IFD group increased from 66% to 94% and sitting-to-standing repetitions increased from 44% to 64% for all follow-up time points. Blood loss was 88% less in the IFD group ($p=0.024$) and operating time parameters strongly favoured IFD compared to decompression ($p<0.001$). An 89% fusion rate was assessed in a subset of IFD participants. There were no intraoperative device issues or re-operations in the IFD group, and only one healed and non-symptomatic spinous process fracture observed within 24 months.

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Conclusion: Despite a low number of participants in the IFD group, the study demonstrated successful two-year safety and clinical outcomes for the IFD with significant operation-related advantages compared to surgical decompression.

Keywords: lumbar spinal stenosis, surgical decompression, posterior lateral arthrodesis, patient reported outcomes, minimally invasive spine, interspinous fixation device

Introduction

Lumbar spinal stenosis (LSS) is characterized by pain or abnormal sensations in the lower back, legs, buttocks, thighs and feet. These sensations are aggravated by walking (neurogenic claudication) and relieved by forward flexion, sitting, or recumbency. LSS can be congenital or more commonly primarily caused by degenerative changes which decrease the total area of the spinal canal, lateral recesses or neural foramina in the lumbar spine, and can compress nerve roots and leading to lumbar or sacral radiculopathy.[1,2] LSS can present in isolation, with or without associated disk bulging or herniation, and can be associated with degenerative disc disease, facet hypertrophy, spondylolisthesis or scoliosis.[2] Surgical treatment for LSS aims to decompress nerve structures and can be combined with spinal fusion to provide increased stability for the decompressed segment and prevent the recurrence of stenosis. Although surgical decompression seems effective for LSS,[3] surgical decompressions are not without serious risks and complications including post-surgical transfusions, dural tears, and recurrent stenosis requiring reoperation.[3,4]

Interspinous device surgeries are a less invasive treatment option for LSS which may present advantages over conventional surgical decompression. Minimally invasive surgery (MIS) techniques have been shown to preserve musculoskeletal tissues, reduce the risk of dural tissue damage, provide for shorter operative times and post-surgical rehabilitation,[5] and possibly provide a treatment option for those unable to have surgery with general anaesthesia by providing an option that may be done with moderate sedation and local anaesthetic.

Interspinous spacer devices (ISDs) are a subset of interspinous devices that aim to alleviate painful symptoms of LSS by distracting the spinous processes and allowing flexion but limiting lateral bending and axial rotation and preventing extension at the treated lumbar segment. Promising short- and medium-term findings have been observed with ISDs, including improvements in LSS symptoms, quality of life, the proportion of patients achieving a clinically significant improvement and patient satisfaction with treatment outcomes as compared with non-operative treatments.[6–11] Although ISDs may be equally as effective as surgical decompression at improving LSS symptoms,[6,12,13] some studies have reported ISD reoperation rates between 21% and 29% and high costs.[13–15] The reoperation rate associated with ISDs may have left a negative perception of all interspinous devices as a treatment option for LSS. At the same time, national health care guidelines in the United Kingdom (UK) have recommended against using epidural steroid injections for spinal stenosis (NICE NG59[16]). Consequently, there remains a need to establish safe and effective treatments for LSS. In addition, the approach used by different interspinous fixation devices (IFDs) needs to be evaluated since the potential for differences in safety, efficacy and fusion exists with a lateral approach to arthrodesis as compared to the classic direct interspinous approach. The lateral approach which spares the supraspinous ligament could potentially reduce posterior migration, a common cause of revision surgeries for previous generations of ISD devices.

IFDs, sometimes referred to as interspinous fusion devices, provide distraction of spinous processes using MIS techniques similar to interspinous spacers. Unlike interspinous spacers, IFDs provide rigid posterior fixation to the joint. The aim is to provide sufficient cranial-caudal distraction to relieve pain by reducing central canal and lateral recess stenosis and opening narrowed neural foramina. The study by Oliveira et al in 2010[17] demonstrated a link between these stenosis regions when indirect decompression procedures are used, noting that distraction procedures avoid the resection of posterior elements and morbidities that are associated with these techniques. In addition, IFDs are designed to provide sufficient motion restriction and biomechanical stability for arthrodesis to occur similar to pedicle screw constructs. Recent research in patients with LSS has demonstrated that IFDs reduce pain, pain-related disability and LSS symptoms, improve quality of life, result in high fusion rates (94%,[18] 92%,[19] 84%[20]), and have a good safety profile with comparable or lower rates of device migration and reoperation when compared to ISDs.[18–26] Despite this evidence, there is a lack of prospective data from randomized controlled trials for IFDs as compared to the standard of care surgical decompression, and there is no previous controlled clinical trial data for the minimally invasive lateral IFD used in this study.

This was an early-phase, prospective, multi-centre randomized controlled trial with a five-year follow-up designed to investigate and compare the clinical outcomes of the Minuteman® IFD to standard open surgical decompression in patients with LSS (NCT01455805). This IFD is a novel minimally invasive device designed to provide interspinous distraction, stabilization and interspinous-interlaminar fusion of the lumbar spine. A cadaveric biomechanical study demonstrated that the minimally invasive IFD provided multidirectional lumbar joint stabilization.[27] Creation and maintenance of indirect decompression under combined compression and flexion-extension loading was found to be comparable to conventional posterior instrumentation constructs. The surgical procedure for IFD is less invasive than surgical decompression, and it utilizes a lateral approach, unlike ISDs and surgical decompression.[6] There is no dissection or stripping of muscles, bones or nerves, and there is sparing of anatomical structures such as the supraspinous ligament and most of the interspinous ligament and the amount of soft tissue disruption is minimal. Preservation of the posterior ligamentous complex has been demonstrated to significantly contribute to lumbar joint stability.[28] Additionally, the minimally invasive lateral approach can be more efficient than surgical decompression, and implantation can be performed with less anaesthetic risk including the option of moderate sedation and/or local anaesthesia. These attributes as compared to open decompression may lead to lower costs to the health care system and fewer risks. The device uses bone graft material packed into the threaded cylinder to aid a fusion which can result in long-term stability. The device gained CE Mark approval in May 2011. This report contains the 24-month results from the first controlled clinical assessment of this device.

Materials and Methods

Study Design

This was a prospective, multi-centre, randomised controlled trial with a five-year follow-up undertaken by four National Health Service (NHS) Trusts in the UK. This study is registered with ClinicalTrials.gov and the 24-month follow-up results are reported here. The final amended study protocol assumed the recruitment of 25 participants per group with an expected drop-out rate of 25% over the course of the study. De-identified individual participant data that support the findings of this study are available from the first author upon reasonable request within three years of publication of this article. Available data include participant demographic and baseline data, surgery related data, scans and reported outcomes. Other study documents, including the study protocol and the patient informed consent form, are available upon reasonable request.

Patients were screened according to study inclusion and exclusion criteria, and informed consent was obtained. They attended a baseline visit where demographic and medical details were recorded, a neurological examination performed, vital signs assessed, and questionnaires and physical function assessments completed. Questionnaires included the visual analogue scale (VAS) for leg and back pain, Oswestry Disability Index (ODI) for pain-related disability, the physical function component of the Zurich Claudication Questionnaire (ZCQ) for LSS physical function, the functional status questionnaire for activities of daily living (ADL), analgesic and concomitant medication use and employment status. Physical function was also assessed using a walking distance test (distance walked in five minutes) and a sitting-to-standing test (number of repetitions completed from sitting to standing in one minute).

Participants were randomly allocated to have IFD or decompression and attended as a day-case for either implantation of the IFD or to undergo decompression surgery. Operative data was collected on the day of surgery for both IFD placement and surgical decompression.

The IFD consists of a central threaded body with two deployable wings hinged near its distal end, and an end cap on the proximal side of the device (Figure 1). The cylindrical body of the device can provide indirect decompression of the joint and carry bone graft fusion material. Spinous process fixation is achieved through compression – on both lateral sides of the anterior portion of the superior and inferior spinous processes – between the spikes on the ends of the deployable wings and the multi-spiked end cap plate. The spiked end cap plate is tightened in place with a locking hex nut. Compression between the spiked deployable wings and spiked cap plate, in conjunction with bone graft fusion material placed in the body of the device, resists motion of the spinous processes and facilitates fusion. The assembled device is inserted into the non-cervical spine through a 2.5 cm lateral incision using fluoroscopic guidance. Device insertion is shown by intraoperative device insertion scans in Figure 2. Dilators are used to create a working channel to the interspinous space, eliminating the need to dissect muscle and preserving the supraspinous ligament. As this was

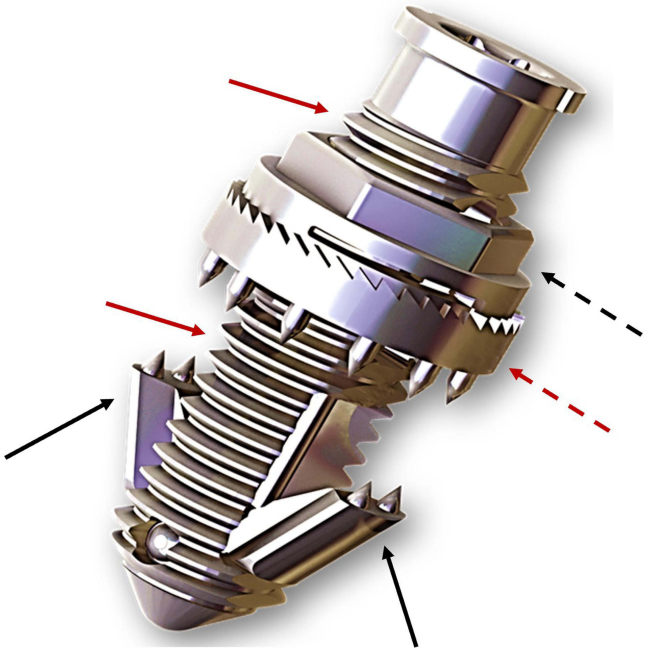

Figure 1 The Minuteman™ interspinous fixation device consists of a central threaded cylinder (solid red arrows) that has two deployable, spiked wings (solid black arrows) hinged near its distal end, and a multi-spiked end cap plate (dashed red arrow) that is located at the proximal side of the device and is tightened against the superior and inferior spinous processes with a locking hex nut (dashed black arrow). Compression between the spiked deployable wings and spiked end cap plate, in conjunction with bone graft material placed in the body of the device, resists motion of the spinous processes and facilitates fusion. The device is placed via a minimally invasive lateral approach.

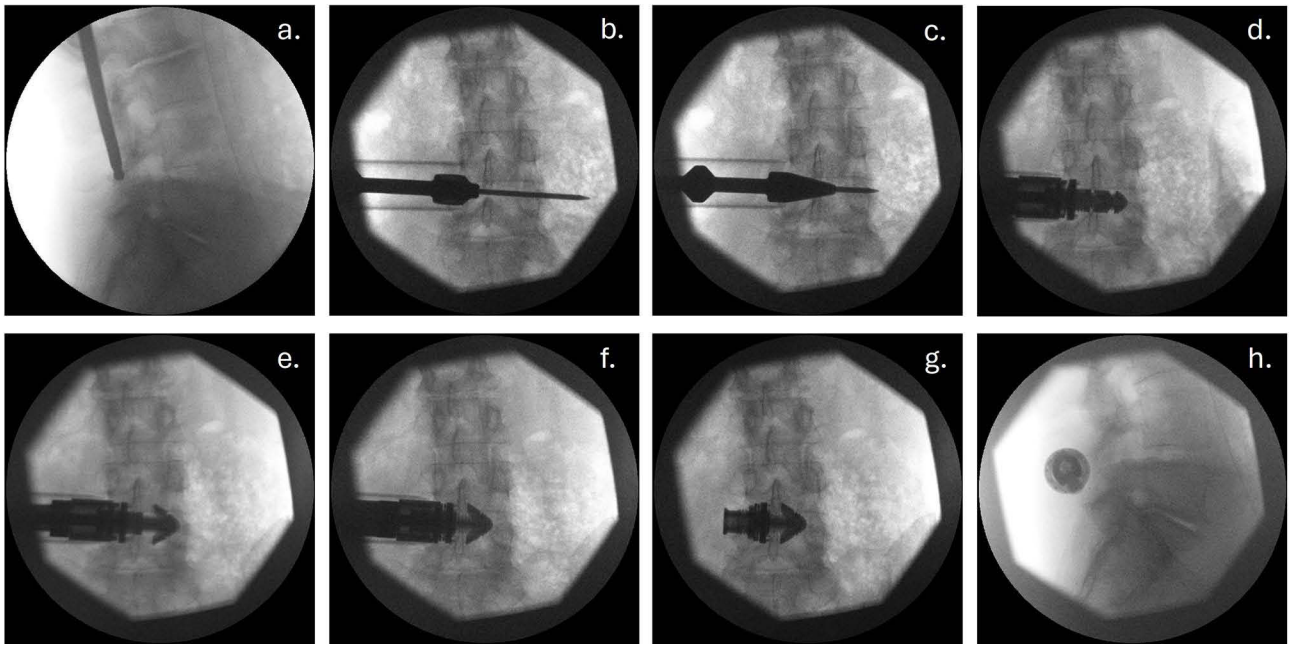

Figure 2 Intraoperative scans showing IFD implantation: (**a**) guidewire trajectory - lateral view, (**b**) and (**c**) decortication of the interspinous-interlaminar space and IFD sizing, (**d**) IFD insertion, (**e**) IFD wing deployment, (**f**) IFD fixation achieved by compression between spiked wings and plate, (**g**) Final IFD placement – A-P view, (**h**) Final IFD placement – lateral view.

a new procedure and a controlled environment was necessary, the initial IFD patient procedures were performed under general anaesthetic. Following the surgeon's familiarity with the procedure, the remaining implants were done using local anaesthetic and conscious sedation.

Lumbar surgical decompression was carried out under general anaesthesia. The decision on the appropriate non-instrumented decompression surgery was left to the operating surgeons and discussed in a spine multi-disciplinary team as is the standard practice. Decompression surgeries included one or more of laminectomy, foraminectomy, foraminotomy and flavectomy (see Table 1).

Participants in both groups attended follow-up visits at 8-weeks, 6-, 12-, 24-, 36-, 48- and 60-months post-op. At each follow-up visit, participants had a neurological examination, vital sign assessment, and completed the same questionnaires and physical function tests. Patient global impression of change (PGIC) and clinician global impression of change (CGIC) were also assessed. Adverse events were assessed from patient study entry to 30 days post-study completion or withdrawal.

Participants

Eligible Participants were aged 18 years or above and had a diagnosis of LSS with degenerative changes at one or two levels as confirmed by MRI or CT Myelogram (performed within the previous 12 months). They had leg pain with or without back pain relieved by either sitting or adopting a flexed posture and had completed at least six months of conservative treatment without obtaining adequate symptomatic relief or having worsening neurological symptoms. Exclusion criteria included spondylolisthesis greater than grade 1, diagnosis of scoliosis, previous lumbar spine surgery, body mass index (BMI) greater than 35, history of osteopenia or osteoporosis, and active infection or metabolic bone disease. Pre-operative pain and disability thresholds were: ODI of 20 or above; ZCQ Physical Function Domain of 2 or above; and VAS Leg Pain score of at least 40.

Research ethics committee approval was granted by NRES Committee Yorkshire and The Humber - Leeds West: 11/YH/0409. The study was conducted and reported following the protocol (NCT01455805), the International Conference on Harmonization Good Clinical Practice Guidelines standards, and the Declaration of Helsinki and local NHS Trust Research Office policies and procedures. Informed consent was obtained from each study participant before enrolment.

Randomization

Participants were randomized in a 1:1 ratio between IFD and decompression. Randomization codes were issued via a computerized random assignments generator program and the balanced randomization blocks were also randomized. After randomization codes were issued, they were individually placed in envelopes and sequentially numbered. Sealed envelopes were sent to each participating site in a block of 10. Site staff opened the next available sequential randomization envelope to facilitate surgical planning, and participants were informed of the randomized procedure post-operatively. Randomization effectiveness was assessed after enrolment based on patient demographics, baseline pain, disability, and physical function metrics for IFD and decompression groups.

Table 1 Types of Non-Instrumented Decompression Surgeries in the Study

Type Of Decompression Surgery	Number
Laminectomy	10
Foraminectomy	8
Laminectomy + Foraminectomy	1
Laminectomy+Foraminotomy	2
Hemi-laminectomy	1
Laminectomy via left paraspinal approach	1
Flavectomy	1
2-level laminectomy	1
TOTAL	25

Outcomes

The primary study endpoints were measures of clinical efficacy assessed at 8 weeks and up to 60 months post-procedure, including: VAS leg and back pain, ODI pain-related disability, physical function component of the ZCQ, and assessment of physical function by distance walked in five minutes and number of sitting-to-standing repetitions in one minute using a non-rolling armless chair with the participant's knees at 90 degrees and the subject not allowed to push on their knees when standing up. Distance walked in five minutes was calculated based on the number of laps of a five-meter distance walked by the participant. The primary clinical Outcomes for the new IFD were a change from baseline of leg and back pain, ODI, physical component of ZCQ, and physical function assessed by walking distance and sit-to-stand repetitions at 8-week, 6-months, 12-months, and 24-months follow-up time points.

The secondary study endpoints were measures of quality of life and safety assessed at 8 weeks and up to 60 months post-procedure, including change from baseline in functional status (ADL), PGIC, CGIC, employment status, and adverse events related to device and procedure. Additionally, differences in operative data including blood loss, skin-to-skin operative time and total theatre time were compared between the treatment groups.

Following a protocol amendment, three independent radiologists assessed CT scans from nine IFD participants according to the following fusion grading scale:

Grade 1: Definitely fused. Clear evidence of bridging bone through and/or around the device. No noticeable lucencies or areas of concern.

Grade 2: Probably fused. Evidence of bridging bone through and/or around the device (50–70% at least), but there may be minor lucencies or areas of incomplete bone bridging.

Grade 3: Probably not fused. Some minor evidence of bone formation within a portion of the device but may not fully extend through the device (less than 50%). There may be lucency around a portion of the device.

Grade 4: Definitely not fused. No clear evidence that appreciable bone formation has occurred and/or major lucencies indicating that the device is not solidly anchored in bone.

This fusion assessment grading was the same as what was recently published by Skoblar et al[19] and was developed by combining features from Vokshoor et al[18] and the 4-point Bridwell scale,[29] commonly used to grade lumbar interbody fusions using interbody cages and pedicle-screws. If discrepancies occurred between the assessments provided by the radiologists, they were resolved by discussion. The scans were obtained from the remaining participants in the IFD group based on the subject's willingness and availability for the additional CT scanning procedure.

Statistical Analysis

A power calculation that assumed a total sample size of 50 participants (25 in each group) and a 25% drop-out rate throughout the study is estimated to have 83% power to detect a difference in the change in leg pain VAS of 10 points (out of 100) between IFD and decompression. This was based on data from Moojen et al[13] (2013, SE ±3.1) and Kuchta et al[30] (2009, SE ±2.3) which demonstrated reductions in leg pain scores associated with interspinous spacers ranging from 22 to 37 points in comparison to a reduction of 12 to 18 points for surgical decompression. It was also considered clinically important to detect at least an 8-point difference in the change in ODI (range 0 to 100) between the IFD and surgical decompression. Based on data from Weinstein et al[3] and Kuchta et al[30] comparing surgical decompression (change from baseline at 12 months of −14.9, SE ±1.9) and an ISD (change of −17.3, SE ±2.0), this number provides 75% power to detect such a difference in the ODI. Calculations assumed a 5% significance level (α) and a correlation between measurements of 0.7.

To provide a conservative way to reduce potential bias while including all patients who received treatment, an intention-to-treat (ITT) and last value carried forward (LVCF) approach was selected. Mixed ANOVAs with Bonferroni pairwise comparisons was chosen to evaluate changes in primary endpoints: leg pain (VAS), back pain (VAS), pain-related disability (ODI), LSS physical function (ZCQ), sitting-to-standing repetitions and walking distance across the

visits. Normality was ascertained via the Shapiro–Wilk test. The Greenhouse-Geisser correction was used when data did not meet the sphericity assumptions.

Clinical success was defined as ≥30% improvement in leg pain (VAS),[31] ≥30% improvement in back pain (VAS),[31] ≥30% improvement in pain-related disability (ODI)[31] and ≥0.5-point improvement in LSS physical function (ZCQ).[32] Clinical success was ascertained for each primary clinical outcome measure at all time points separately and combined. A composite clinical success was defined as per participant outcomes satisfying all four of these individual outcome success criteria. Consequently, the composite clinical success numbers would necessarily be less than or equal to the individual outcome with the lowest clinical success value. Combining the individual clinical success measures and the composite clinical success measure, there was a total of five clinical success measures by which to evaluate the effectiveness of the IFD.

The Fleiss Kappa statistic (κ) was used to evaluate the interobserver variability in grading the interspinous fusions. Independent sample *t*-tests (or Mann–Whitney U non-parametric tests for non-normally distributed data) explored differences in operating parameters (blood loss, skin-to-skin operative time and total theatre time) between IFD and decompression.

This study represents the first clinical evaluation of the Minuteman minimally invasive device. Consequently, it was reasonably expected that there would be learning-curve related effects only in the IFD treatment arm, as well as some reluctance to treat more severe stenosis cases with a novel minimally invasive indirect decompression device when selected by randomization. Treatment unfamiliarity and non-adherence to randomization selections can lead to weaker analyses when comparing outcomes between the two treatment cohorts.

Noting the potential for low participant enrolment numbers and these adherence challenges to randomization assignments in this early-stage study, baseline demographic values for all subjects were compiled for an ad hoc evaluation of the randomization performance upon completion of enrolment. This randomization evaluation assessed the differences between IFD and decompression in demographic and baseline characteristics using independent sample *t*-tests (or Mann–Whitney *U*-tests for non-normally distributed data, or Chi-Square Goodness of fit test for nominal data). In the case of insufficient enrolment number or randomization adherence causing greater than 15% differences in baseline primary outcome metrics, the determination of treatment effect would be analysed accordingly. Confidence intervals within treatment groups using LVCF repeated measures Analysis of Variance (ANOVA) with Bonferroni correction for each primary IFD endpoint would be substituted for the planned intention-to-treat (ITT), Mixed ANOVAs noninferiority data analysis. To lower the probability of type I statistical errors, Bonferroni corrected significance levels (corrected α = α / number of tests) were used to assess statistically significant improvements of IFD primary endpoints at each of the four time points over baseline values. The Bonferroni corrected significance level (α) used for the comparisons to baseline at each of the four time points of a repeated measures ANOVA was 0.0125.

Role of the Funding Source

The sponsors of the study provided input towards the study design. They were not involved in collecting the data. However, they reviewed the data analysis and interpretation, participated in writing and the decision to submit the paper for publication.

Results

Baseline

Figure 3 summarises the patient flow in the trial up to 24 months. In total, 48 participants (n = 31 males; n = 17 females) were enrolled. Three participants randomly allocated to IFD and two randomly allocated to decompression withdrew consent before surgery. Of the remaining participants, 20 were randomly allocated to IFD and 23 to surgical decompression. Prior to surgery, two IFD participants (both males over the age of 70 years) received decompression (IFD: n = 18; decompression: n = 25). One crossover was due to the opinion of the treating physician that the degree of stenosis was too severe, making the patient ineligible to be treated with the IFD. The other crossover was due to the treating

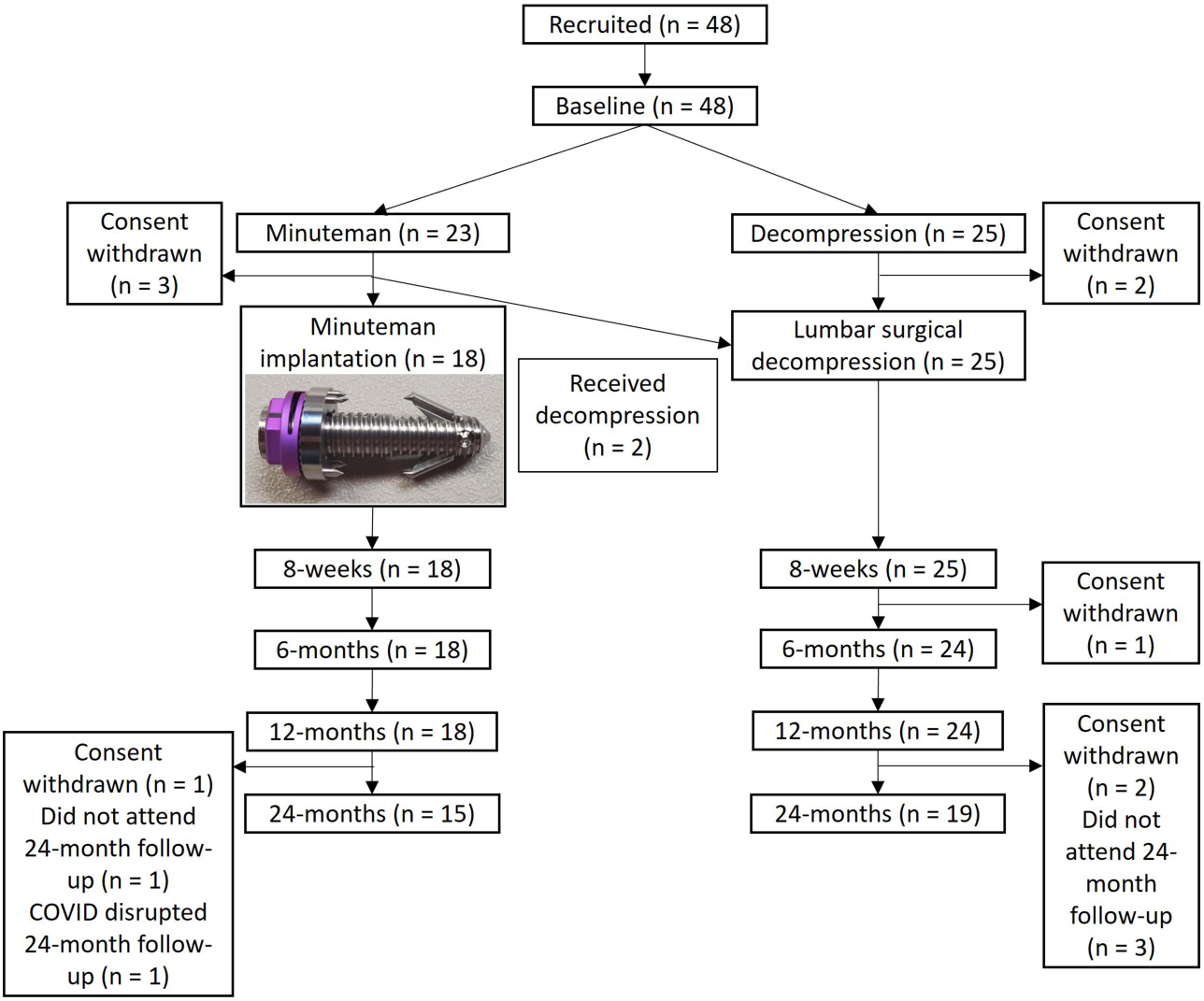

Figure 3 Patient flow through the first 24 months.

physician's inexperience with the procedure combined with the unavailability of a company advisor on the day of surgery. The types and numbers of non-instrumented decompression surgeries are listed in Table 1.

Typical preoperative and postoperative images for an IFD case are shown in Figure 4. Between the 8-week and 6-month follow-up visits, one decompression participant withdrew consent. Before the 24-month follow-up, one IFD and two surgical decompression participants withdrew consent, four participants failed to attend their 24-month follow-up, and the COVID-19 pandemic disrupted the 24-month follow-up for another participant. Three participants who attended the 24-month follow-up visit declined to perform the walking distance and sitting-to-standing physical tests.

The sexes were equally distributed between IFD and decompression (see Table 2). There were no clinically relevant differences in the following Baseline characteristics between IFD and decompression: age, BMI, presence of spondylosis or spondylolisthesis, leg pain, pain-related disability, LSS physical function, walking distance, and number of sitting-to-standing repetitions. However, the difference between groups in mean length of pain history and baseline VAS back pain were not within 15% of each other with mean baseline values of the decompression group being 23% and 31% higher than the IFD group respectively. The difference in baseline back pain was statistically significant (mean difference: −15.40; 95% CI: −28.99, −1.81; Welch *t*-test for unequal variances, p = 0.0281). Consequently, a clinically meaningful reduction of mean back pain in the decompression group could result

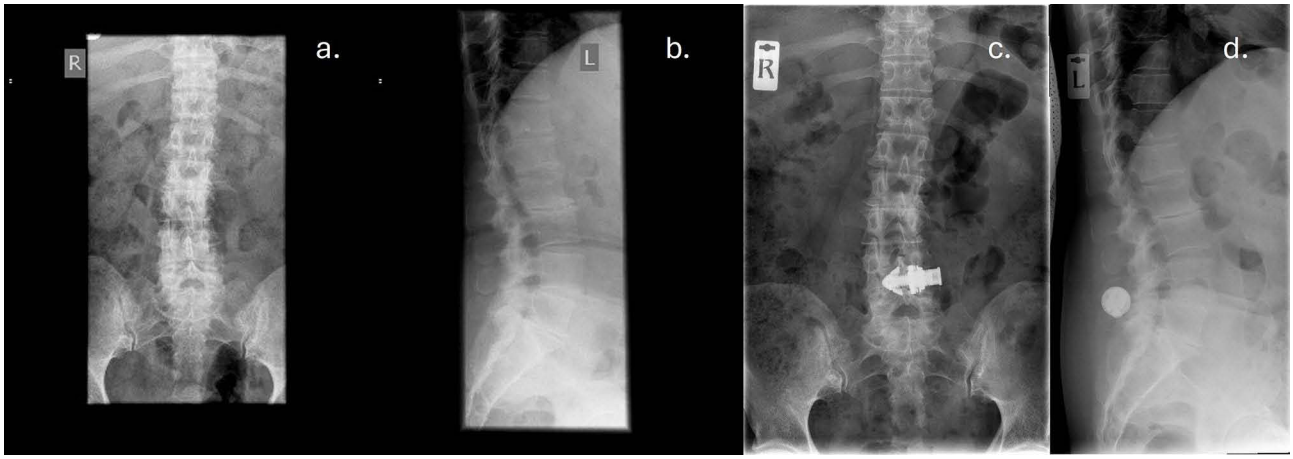

Figure 4 Preoperative and postoperative scans for one IFD participant: (**a**) preoperative A-P view, (**b**) preoperative lateral view, (**c**) postoperative A-P view, (**d**) postoperative lateral view.

in post-treatment mean back pain greater than the baseline back pain of the IFD group. Therefore, improvements in back pain due to treatment effects (ie reduction from baseline values) were not directly comparable between groups. It was noted that all 7 of the enrolled participants with VAS back pain below 40 (not an inclusion criterion) were assigned to the IFD group, and the one enrolled participant with VAS leg pain below the inclusion threshold of 40 was assigned to the IFD group. This IFD participant also had a baseline ZCQ less than the inclusion threshold of 2.0 (two additional IFD participants and one decompression participant also had baseline ZCQ below the inclusion threshold of 2.0). As randomization is intended to moderate baseline values between groups, these observations indicate that there was insufficient adherence to treatment assignments (2 known crossovers occurred) or the overall study sample size was inadequate to ensure mean differences of key baseline values between groups were within 15% of each other. While these differences do not degrade the evaluation of treatment efficacy for either group, they

Table 2 Demographic and Baseline Characteristics for IFD and Decompression. Data are Presented as Total Number for Target Levels, Raw and Percentage (%) for Sex, Presence of Spondylolisthesis and Spondylosis (Vertebral Hypertrophy), as the Mean ± Standard Deviation (n) for BMI and Length of Pain History, as the Mean ± Standard Deviation for Leg Pain, Back Pain, Pain-Related Disability, LSS Physical Function and Walking Distance, and Sitting-to-Standing Repetitions. Significance of Differences Between Groups is Also Presented. Difference in Baseline Back Pain Was Statistically Significant. BMI = Body Mass Index; VAS = Visual Analogue Scale; ODI = Oswestry Disability Index; ZCQ = Zurich Claudication Questionnaire

	IFD (n = 18)	**Decompression (n = 25)**	**Significance**
Sex (males/females)	10 (56%)/ 8 (44%)	17 (68%)/8 (32%)	p=0.258
Age (years)	61.89 ± 12.75	62.76 ± 12.93	p=0.828
BMI (kg/m^2)	27.56 ± 2.96 (n = 14)	28.35 ± 3.38 (n = 22)	p=0.466
Spondylosis	3/18 (17%)	7/25 (28%)	p=0.284
Spondylolisthesis	9/18 (50%)	12/25 (48%)	p=0.865
Length of pain history (months)	57.93 ± 45.82 (n = 14)	71.17 ± 60.92 (n = 24)	p=0.453
Leg pain (VAS, mm)	68.22 ± 19.97	66.16 ± 16.81	p=0.724
Back pain (VAS, mm)	50.06 ± 25.60	65.32 ± 12.22	**p=0.028**
Pain-related disability (ODI, %)	60.78 ± 15.40	59.36 ± 16.01	p=0.771
LSS physical function (ZCQ)	2.71 ± 0.59	2.84 ± 0.55	p=0.468
Walking distance (m)	148.83 ± 116.21	183.28 ± 82.99	p=0.291
Sitting-to-standing repetitions (n)	11.28 ± 7.46	11.60 ± 7.99	p=0.894
Target level	2/3(1), 3/4(3), 4/5(14)	3/4(7), 4/5(18)	

Notes: Bold significance value indicates statistically significant difference between groups with p<0.05.

reduce the reliability of outcomes comparisons between groups. With this ad hoc assessment indicating either insufficient adherence to treatment assignments or insufficient sample size or both, LVCF Repeated Measures Analysis of Variance (ANOVA) of IFD endpoints with no noninferiority hypothesis testing was substituted for the planned intention-to-treat (ITT), LVCF Mixed ANOVAs noninferiority data analysis.

Primary Study Endpoints

Four participants did not have favourable outcomes throughout the 24-month post-surgical period, but there were no reoperations performed within this period. Three of these cases were decompression surgery and one was an IFD case. All participants received regular follow-up and additional intervention was available if symptoms got worse, or when requested by the participant (eg facet block). None of these four participants had additional interventions. An additional 5 subjects showed a loss of clinical benefit at the 2-year follow-up; 3 of these cases were IFD and 2 were decompression surgery.

Primary clinical outcome (leg and back pain, pain related disability and ZCQ physical function) mean values at each study time point for IFD and surgical decompression group are shown in Figure 5. The two primary physical function assessment endpoint (walking distance and sit-to-stand repetitions) mean values are shown at each study time point for IFD and decompression in Figure 6. Statistically significant improvements of IFD outcomes using Bonferroni corrected significance levels are indicated by asterisks in Figures 5 and 6 where appropriate.

Leg and Back Pain (VAS)

Mean Leg pain (Figure 5a, Table 3) at baseline was significantly higher for the IFD group than at all study time points: 8 weeks (mean difference: 50.9; 95% CI: 41.4, 60.4; repeated measures ANOVA: $p<0.0001$), 6 months (mean difference: 53.2; 95% CI: 42.8, 63.6; $p<0.0001$), 12 months (mean difference: 52.0; 95% CI: 41.1, 62.9; $p<0.0001$), and 24 months

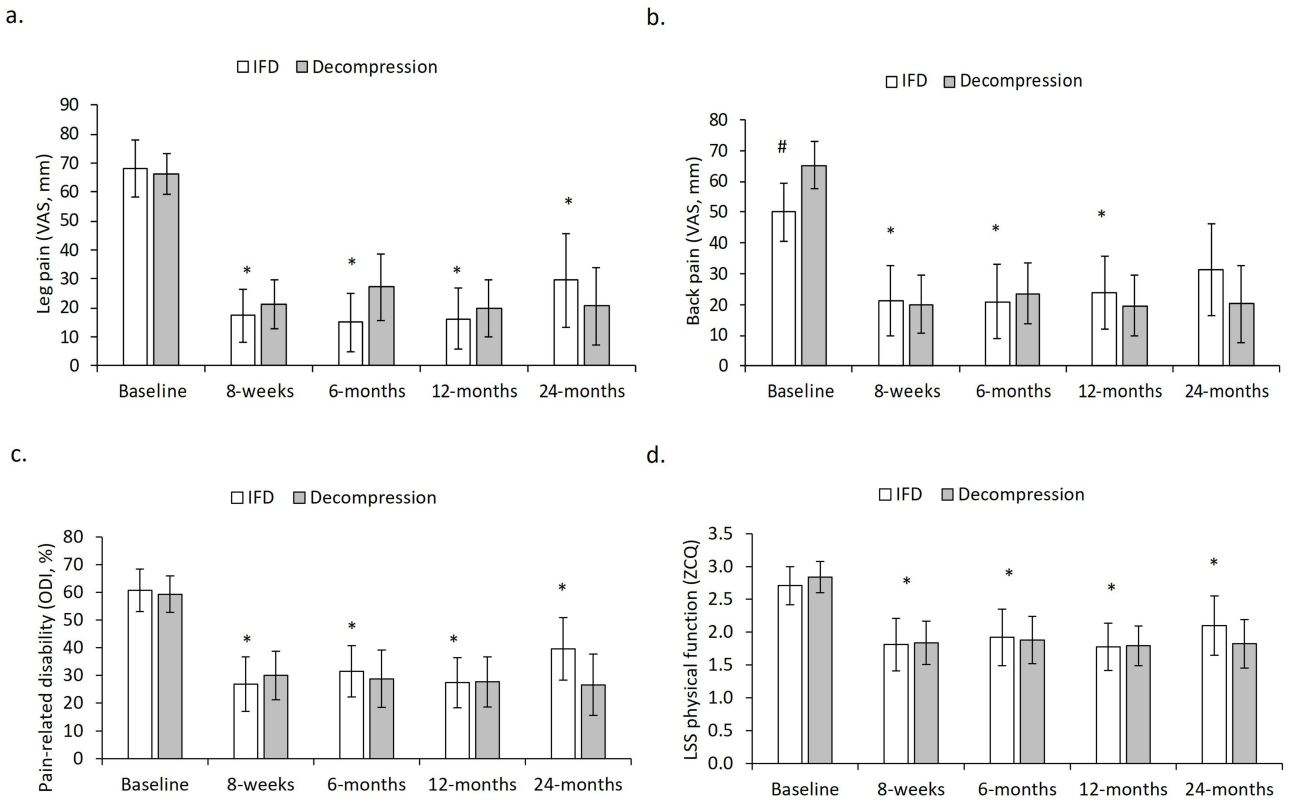

Figure 5 Bar graph showing measurements for leg pain (**a**), back pain (**b**), pain-related disability (**c**), and LSS physical function component of ZCQ for IFD and decompression for each visit. Improvements in IFD primary clinical outcomes (**a–d**) were assessed for statistical significance using a Bonferroni corrected significance level (α=0.0125) for each of the four follow-up time points. * = significantly different to baseline; # = significantly different to decompression baseline mean; VAS = Visual Analogue Scale; ODI = Oswestry Disability Index; ZCQ = Zurich Claudication Questionnaire. Data presented as the mean and 95% CI upper and lower limits.

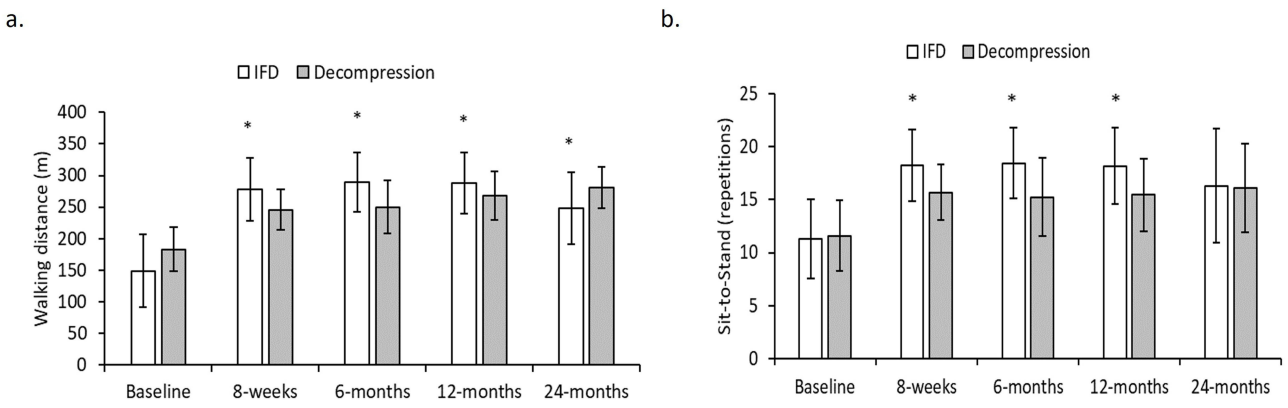

Figure 6 Bar graph showing measurements for walking distance (**a**) and sit-to-stand repetitions (**b**) for IFD and decompression for each visit. Improvements in IFD physical function endpoints were assessed for statistical significance using a Bonferroni corrected significance level (α=0.0125) for each of the four follow-up time points. * = significantly different to baseline. Data presented as the mean and 95% CI upper and lower limits.

(mean difference: 38.8; 95% CI: 22.0, 55.6; p<0.0001). The mean reduction of leg pain for the IFD group varied between 57% and 78% for all post-op time points. For the decompression group, the mean reduction of leg pain varied between 59% and 70% for all post-op time points.

Table 3 Mean Change from Baseline for Primary Clinical Endpoints for Both Treatment Groups at Each Follow-Up Time Point. NS – Not Significant from Baseline Value Based on Bonferroni Adjusted Significance Level, α=0.0125 (IFD Group Only)

Treatment	Change@8-wks	Change@6-mo.	Change@12-mo.	Change@24-mo.
Leg pain (VAS)				
IFD	50.9 (−75%, p<0.001)	53.2 (−78%, p<0.001)	52.0 (−76%, p<0.001)	38.8 (−57%, p<0.001)
Decomp.	45.0 (−68%)	38.9 (−59%)	46.2 (−70%)	45.5 (−69%)
Back pain (VAS)				
IFD	28.8 (−58%, p=0.002)	29.2 (−58%, p<0.001)	26.3 (−53%, p=0.006)	18.8 (−38%, p=0.079 NS)
Decomp.	45.4 (−69%)	41.7 (−64%)	45.7 (−70%)	45.2 (−69%)
Pain-related disability (ODI)				
IFD	33.9 (−56%, p<0.001)	29.2 (−48%, p<0.001)	33.4 (−55%, p<0.001)	21.1 (−35%, p=0.001)
Decomp.	26.0 (−44%)	27.7 (−47%)	32.1 (−54%)	31.9 (−54%)
LSS physical function (ZCQ)				
IFD	0.9 (−33%, p<0.001)	0.8 (−31%, p<0.001)	0.9 (−34%, p<0.001)	0.6 (−22%, p=0.004)
Decomp.	1.0 (−35%)	1.0 (−34%)	1.1 (−37%)	1.0 (−36%)
Walking distance (m)				
IFD	129 (87%, p<0.001)	140 (94%, p<0.001)	139 (94%, p<0.001)	99 (66%, p=0.002)
Decomp.	63 (34%)	67 (36%)	85 (46%)	98 (53%)
Sit-to-stand (repetitions)				
IFD	6.9 (62%, p<0.001)	7.2 (64%, p<0.001)	6.9 (61%, p=0.001)	5.0 (44%, p=0.082 NS)
Decomp.	4.1 (35%)	3.6 (31%)	3.8 (33%)	4.5 (39%)

IFD cohort mean back pain (Figure 5b, Table 3) was significantly higher at baseline than at the primary outcome time points of 8 weeks (mean difference: 28.8; 95% CI: 16.9, 40.8; p = 0.002), 6 months (mean difference: 29.2; 95% CI: 19.2, 39.1; p<0.001), and 12 months (mean difference 26.3; CI: 13.6, 39.1; p=0.006), but not significantly higher at 24 months (mean difference: 18.8; 95% CI: 3.9, 33.8; p=0.075, Bonferroni corrected α=0.0125). As stated above, VAS mean baseline back pain was significantly lower in the IFD cohort than in the surgical decompression cohort. The mean reduction of back pain for the decompression group varied between 64% and 70% for all post-op time points.

Clinical success rates for leg pain at the 8-week, 6-month, 12-month and 24-month follow-up visits for IFD were 89%, 94%, 94% and 72% of subjects respectively. Clinical success rates for leg pain at the 8-week, 6-month, 12-month and 24-month follow-up visits for decompression were 84%, 84%, 88% and 76% respectively. Clinical success rates for back pain at the 8-week, 6-month, 12-month and 24-month follow-up visits for IFD were 72%, 78%, 67% and 56% of participants respectively. Clinical success rates for back pain at the 8-week, 6-month, 12-month and 24-month follow-up visits for decompression were 84%, 80%, 84% and 76% of subjects respectively. Differences in baseline values between groups may have distorted the assessment of back pain success rates. For the IFD participants not having clinical success in reducing back pain 30% or more, 65% were from the group with baseline back pain of 30 or less. All baseline back pain severity measurements for the decompression group were greater than 30. Likewise, the mean leg pain and back pain of those failing to have clinical success at 8-weeks or 6-months in the IFD group was 44.3 (range: 15–95), while in the decompression group the leg and back pain of those failing to have clinical success was 66.8 (range: 39–87) which is 51% higher than for the IFD group.

Pain-Related Disability (ODI)

Mean baseline ODI disability percentage (Figure 5c, Table 3) for the IFD group was significantly higher at baseline than at all study time points: 8 weeks (mean difference: 33.9; 95% CI: 23.7, 44.1; p<0.0001), 6 months (mean difference: 29.2; 95% CI: 19.7, 38.8; p<0.0001), 12 months (mean difference: 33.4; 95% CI: 24.0, 42.8; p<0.0001), and 24 months (mean difference: 21.1; 95% CI: 9.5, 32.8; p=0.001). The mean reduction of ODI percentage for IFD varied between 35% and 56% for all post-op time points. The mean reduction of ODI percentage for decompression varied between 49% and 55% for all post-op time points.

Clinical success rates for ODI disability at the 8-week, 6-month, 12-month and 24-month follow-up visits for IFD were 72%, 72%, 83% and 56% respectively. Clinical success rates for ODI disability at the 8-week, 6-month, 12-month and 24-month follow-up visits for decompression were 80%, 80%, 76% and 80% respectively.

LSS Physical Function (ZCQ)

Mean baseline physical function ZCQ (Figure 5d, Table 3) for the IFD group was significantly higher than at all follow-up time points: 8 weeks (mean difference: 0.90; 95% CI: 0.51, 1.29; p<0.0001), 6 months (mean difference: 0.79; 95% CI: 0.42, 1.16; p<0.0001), 12 months (mean difference: 0.93; 95% CI: 0.60, 1.27; p<0.0001), and 24 months (mean difference: 0.61; 95% CI: 0.19, 1.03; p=0.003). The mean reduction of physical function ZCQ for decompression varied between 0.96 and 1.05 points for all post-op time points.

Clinical success rates for physical function ZCQ at the 8-week, 6-month, 12-month and 24-month follow-up visits for IFD were 67%, 61%, 72% and 50% respectively. Clinical success rates for physical function ZCQ at the 8-week, 6-month, 12-month and 24-month follow-up visits for decompression were 68%, 64%, 72% and 80% respectively.

Composite Clinical Success Criteria

Composite clinical success rates at the 8-week, 6-month, 12-month and 24-month follow-up visits for IFD were 50% (9 of 18), 44% (8 of 18), 56% (10 of 18) and 50% (9 of 18) respectively. For decompression, composite success rates were 60% (15 of 25), 64% (16 of 25), 56% (14 of 25) and 72% (18 of 25) respectively.

Physical Function

The mean increase in walking distance (Figure 6a, Table 3) for IFD varied between 66% and 94% for all post-op time points. The mean increase in walking distance for decompression varied between 34% and 53% for all post-op time points. While the mean walking distance increase was larger for the IFD group than for the decompression group at all

time points, it was only at the 6-month time point that the difference was marginally significant using a Bonferroni adjusted significance level of 0.0125 (p=0.019, mean difference: 73.6, IFD 110% greater increased walking distance).

The mean increase in number of sitting-to-standing repetitions in one minute (Figure 6b, Table 3) for the IFD group varied between 44% and 64% for all post-op time points. The mean increase in number of sitting-to-standing repetitions in one minute for the decompression group varied between 31% and 39% for all post-op time points. While the mean sitting-to-standing repetitions increase was larger for the IFD group than for the decompression group at all time points, these differences were not statistically significant at any time points (0.105<0.972).

Secondary Study Endpoints

PGIC and CGIC

For PGIC, IFD participants reported or last reported improvements (very much improved, much improved, minimally improved) in symptoms at all time points (8 weeks: 94% [17 of 18], 6 months: 100% [18 of 18], 12 months: 94% [17 of 18], 24 months: 83% [15 of 18]). The percentage of participants reporting improvements for the decompression group were similar (8 weeks: 92% [23 of 25], 6 months: 84% [21 of 25], 12 months: 84% [21 of 25], 24 months: 80% [20 of 25]).

Similarly, clinicians reported high rates of patient improvement in symptoms for both IFD and decompression at all time points (8 weeks: IFD 100%, decompression 100%; 6 months: IFD 100%, decompression 84% [21 of 25]; 12 months: IFD 100%, decompression 88% [22 of 25]; 24 months: IFD 78% [14 of 18], decompression 84% [21 of 25]).

Safety

There were no intraoperative device issues or re-operations for IFD or decompression, and only one healed and non-symptomatic spinous process fracture for IFD within the first 24 months of the trial. There were 2 serious adverse events for the IFD group and 1 for the decompression group. None of the SAEs for the IFD group were device related. One SAE involved a post-operative haematoma requiring surgery to drain it which was probably procedure related. The other IFD group SAE involved unrelated humeral pain. The decompression group SAE involved hospitalization for a total knee replacement.

Additional Study Endpoints

Operating Parameters

Operating parameters all significantly favoured the IFD procedure. Blood loss ($p = 0.024$; mean difference: −60.86; 95% CI: −127.011, 5.29), skin-to-skin time ($p < 0.001$; mean difference: −44.49; 95% CI: −55.76, −33.21) and total theatre time ($p < 0.001$; mean difference: −44.70; 95% CI: −58.21, −31.19) were significantly lower for IFD than for surgical decompression (Figure 7).

Fusion

Of the nine IFD participants for whom Fusion was assessed (time-point median: 39 months, minimum: 13 months, maximum: 89 months), six were graded as definitely fused, two as probably fused and one as probably not fused (Table 4). A typical CT scan judged to be definitely fused is shown in Figure 8. According to the grading assessments by Vokshoor et al[18] and Skoblar et al[19] patients receiving a fusion assessment grade score of 1 or 2 were considered "fused" and those with 3 or 4 as "not fused", eight of the nine patients (89%) could be considered fused. The Kappa statistic for interobserver variability was 0.84 which represents almost perfect agreement between reviewers. It is important to note that there were no symptomatic spinous process fractures (only one healed and non-symptomatic spinous process fracture observed from CT scans), and no reoperations due to a fracture or device mechanical failure.

Discussion

This prospective, multi-center randomized controlled trial with five-year follow-up aimed to evaluate the effects of a novel minimally invasive IFD on LSS symptoms compared to standard surgical decompression surgery. As an early-stage investigation, the study design enabled initial clinical outcome comparisons between a minimally invasive treatment and a standard surgical treatment with a randomization process designed to avoid potential patient selection bias. However, randomization assignments were deviated from by at least two investigators lowering the sample size, especially in the IFD group, to an insufficient number to evaluate device noninferiority compared to the standard surgical decompression group. Sufficient patients from this early study did exist to assess the efficacy and Safety of this novel posterior lumbar arthrodesis device.

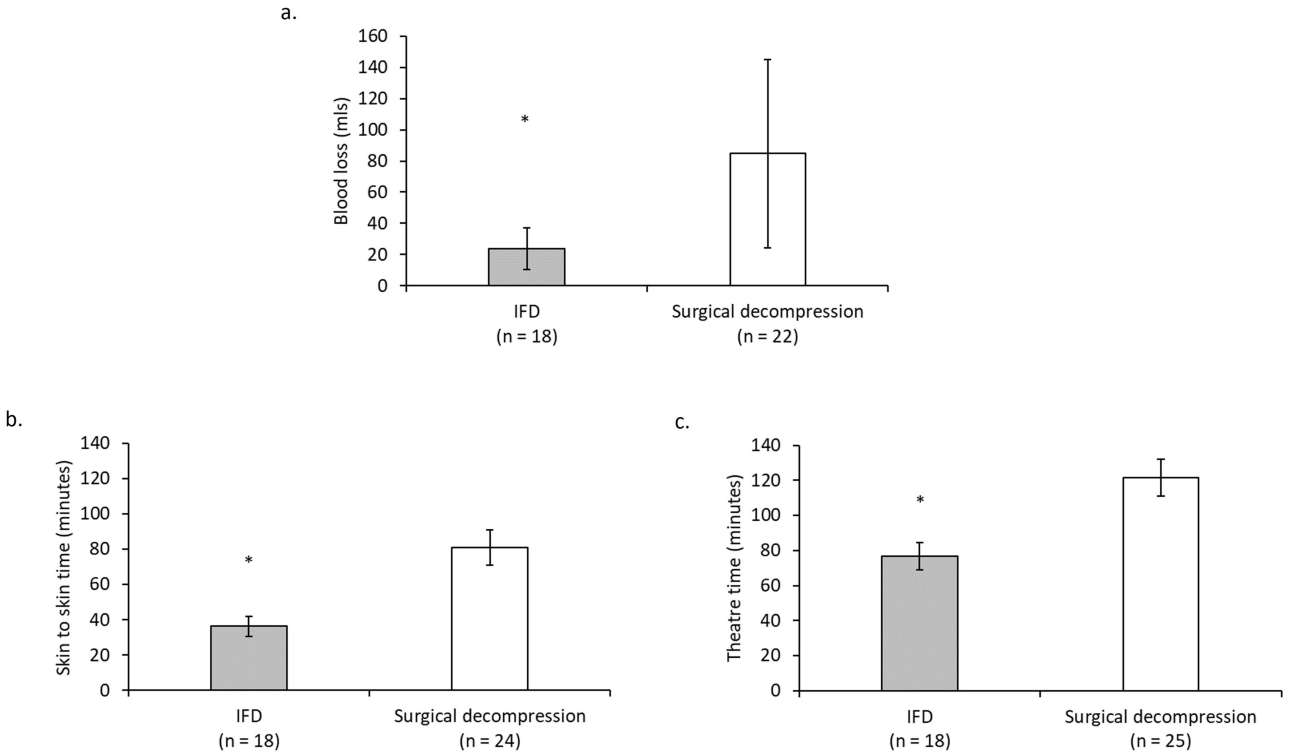

Figure 7 Operative parameters: blood loss (**a**) skin-to-skin operative time (**b**) and total theatre time (**c**) for IFD and decompression. * = significantly different to surgical decompression. Data presented as the mean and 95% CI upper and lower limits.

Effectiveness and Safety of IFD in LSS

Aside from back pain at 24 months, there were significant improvements compared to baseline in leg pain, back pain, pain-related disability (ODI) and physical function (physical function component of ZCQ) at 8 weeks through 24 months for the IFD. These outcomes were similar to surgical decompression. Additionally, improvements in LSS symptoms, ascertained by the PGIC and CGIC over the 24 months, demonstrated clinical improvements for most IFD patients (83%

Table 4 Summary of Fusion Assessment. Initial Radiologist Fusion Grades are Presented

Device	Radiologist 1	Radiologist 2	Radiologist 3	Comments
1	Grade 1	Grade 1	Grade 1	No fracture, no migration
2	Grade 2	Grade 2	Grade 2	No fracture, no migration
3	Grade 1	Grade 1	Grade 1	No fracture, no migration
4	Grade 1	Grade 1	Grade 1	No fracture, no migration
5	Grade 1	Grade 1	Grade 1	No fracture, no migration
6	Grade 2*	Grade 3	Grade 3	Healed fracture of L5 spinous process, no migration
7	Grade 1	Grade 1	Grade 1	No fracture, no migration
8	Grade 2	Grade 2	Grade 2	No fracture, no migration
9	Visual confirmation of fusion by surgeon who performed device removal (at 26 months). Pathology reports also support solid fusion.			Scans were not read by the radiologists because there was direct visual confirmation of fusion, no fracture, and no migration.

Notes: Grade 1 = Definitely fused; Grade 2 = Probably fused; Grade 3 = Probably not fused; Grade 4 = Definitely not fused. Percent overall agreement = 91.7%; Fleiss Kappa = 0.84. * - After Discussion with the other reviewers, this reviewer agreed with the rating of Grade 3.

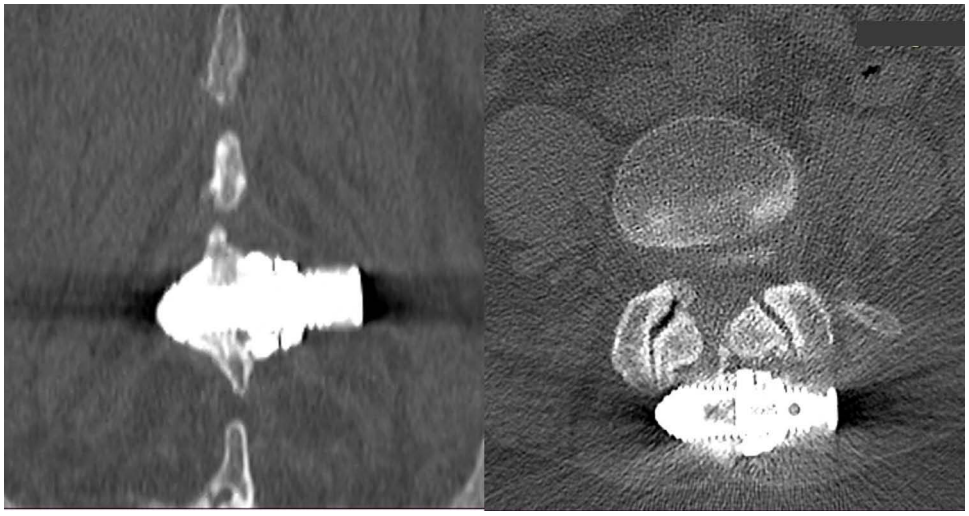

Figure 8 Representative CT scans of a fused segment.

and 78% respectively). Similarly, decompression surgery resulted in PGIC and CGIC improvements of 80% and 84% respectively. Operating parameters, including blood loss, skin-to-skin procedure time and total theatre time, were significantly lower for the IFD than decompression as could be expected for a minimally invasive procedure[12,32] suggesting the IFD may confer operation-related advantages compared to standard decompression surgeries. Independent radiologists confirmed probable or definite interspinous fusion in eight of nine participants (89%). This result is comparable to the 92% fusion rate reported in a separate prospective evaluation of 69 lateral IFD treated levels in 43 patients from a single US physician's practice.[21] The minimally invasive IFD appears to be a safe procedure, as evidenced by no serious adverse events, no intraoperative issues or re-operations, and only one healed, asymptomatic spinous process fracture observed within the first 24 months of this trial.

The ability of this minimally invasive IFD to provide adequate multiaxial rigid fixation has been demonstrated in a cadaveric biomechanics study.[27] The stand-alone MIS IFD provided comparable multiaxial stability to pedicle screw or facet screw posterior stabilization constructs. Foraminal heights were increased and maintained under combined compression and flexion-extension loading with the stand-alone MIS IFD and each of the other tested constructs in this study. It is reasonable to conclude that this stabilization contributes to the observed high rate of posterior fusion.

The predecessor to IFDs, ISDs, can improve pain, pain-related disability, LSS symptoms, quality of life, the proportion of patients achieving a clinically significant improvement and patient satisfaction with treatment outcomes.[6–11,32] However, ISDs do not provide biomechanical stabilisation in flexion initially or through the induction of osseous fusion. Retrospective research has shown that interspinous fixation/fusion devices can reduce pain, pain-related disability, and LSS symptoms, and improve quality of life in patients with LSS.[17–25] Interspinous devices have demonstrated the ability to enlarge the spinal canal and neural foraminal areas,[5,30,32–36] while the proposition that posterior element distraction can unload the posterior annulus is more speculative.[5] In addition to potentially reducing posterior disc bulging, posterior disc unloading may reduce mechanical stimulation of imbedded nociceptive nerve endings in the posterior portion of the disc.

Previous research investigating the efficacy of ISDs (eg, the X-STOP, Superion) suggests around 48% to 60% of the patients inclusive of reoperations report successful outcomes based on ZCQ scores.[9,10,37] Given the ZCQ evaluates LSS symptom severity, physical function and patient satisfaction with treatment, clinical success has most frequently been determined by using scores from this questionnaire. Other studies have explored how improvements in leg pain and pain-related disability can be used to determine whether a patient has had a successful outcome after placement of an interspinous device.[37] In line with these studies, and to generate a comprehensive account, we defined clinical success at each follow-up visit as ≥30% improvement in leg pain,[31] ≥30% improvement in back pain,[31] ≥30% improvement in ODI[31] and ≥0.5-point improvement in ZCQ scores.[32] The majority of IFD participants reported clinical success at the

follow-up visits when explored for each patient reported outcome variable separately, ranging from 50% to 94%, and when combined to form a composite clinical success index. Indeed, 50% of IFD participants achieved composite clinical success at 24 months with no reoperations. In addition, similar percentages of IFD and surgical decompression participants reported improvements in symptoms at all follow-up visits, where 83% of IFD and 80% of decompression participants reported improved symptoms at 24 months. Similar patterns were reported by clinicians, providing further support that the IFD device conferred similar clinical outcomes as decompression in this early-stage study.

The objective of the current prospective, multi-centre randomized controlled trial with five-year follow-up was to investigate the efficacy of a new minimally invasive lateral IFD and compare these initial Results to surgical decompression in a randomized controlled study. Clinically relevant improvements in leg and back pain, pain-related disability and LSS physical function component of ZCQ metrics were observed in both treatment groups. Mean improvements in walking distance and number of sitting-to-standing repetitions were larger for the IFD group than the decompression group at all follow-up time points, however the only marginally significant difference was seen in walking distance at the 6-month follow-up ($p=0.019$, Bonferroni adjusted $\alpha=0.0125$). Due to the insufficient adherence to treatment assignments in this early-stage study, noninferiority of the IFD relative to decompression surgery could not be established. In addition to clinically meaningful improvements in all outcome metrics, the strength of the device may rest on its more favourable operating parameters. Consistent with our expectations, blood loss, skin-to-skin operative time and total operative time were significantly lower for IFD than decompression. Additionally, although the earliest study follow-up was at 8-weeks post procedure, the study team also noted that IFD participants could return to normal activity more quickly in the immediate post-operative period than decompression participants, and most IFD patients were up and walking within 30 minutes of the procedure. This accelerated return to normal activities is rarely reported and should be included in future clinical studies of MIS decompression devices. The observed early return to normal activities was expected due to the unique MIS lateral approach associated with the IFD. There is no dissection of back muscles, bones or nerves, while conversely there is sparing of the surrounding anatomical structures, including the supraspinous ligament and some of the interspinous ligament. In addition to the reduction of postoperative pain, recovery time, and muscular atrophy, preservation of the posterior ligamentous complex (the supraspinous and interspinous ligaments) has been demonstrated to significantly contribute to lumbar joint stability[28] and may reduce destabilization and accelerated degeneration of the adjacent spinal level. Additionally, the minimally invasive procedure has significantly less intraoperative time as compared to surgical decompression which has been shown to reduce infection risks and overall surgical morbidity.[5,38,39] Furthermore, implantation can be performed under local anaesthetic and with or without conscious sedation, or if desired with general anaesthesia, giving the proceduralist additional treatment options and the potential for a reduction in costs and risks. This possibility for a difference in immediate post-operative recovery function between the two treatments should be explored using robust measures in future research.

Previous research has shown that interspinous fixation/fusion devices have a good safety profile with minimal device/procedure-related adverse events.[17–25] Within the first 24 months of this trial, there were no serious adverse events (SAEs), no intraoperative device issues and only one healed and non-symptomatic spinous process fracture observed with the IFD. Furthermore, there were no reoperations for the IFD or the decompression subjects. The finding that no IFD participant required reoperation stands in contrast to the high reoperation rates reported in previous literature utilizing ISDs (non-fixation).[15] ISDs have demonstrated a 19% to 29% reoperation/revision rate, and rates of SAEs of 8.4% to 9.5%.[13,15,37] Other IFDs have demonstrated a similar absence of reoperations or SAEs.[21] In addition, the IFD appears to have lower rates of spinous process fractures and device removals compared to other interspinous fixation/fusion devices.[17,19,22,23,25]

Fusion with Minimally Invasive IFD

The MIS IFD uses non-particulate bone material to facilitate bone fusion. The study by Skoblar et al[19] demonstrated the ability of the device to induce posterior arthrodesis for long-term stabilization in 93% of 69 MIS IFD treated levels with no reoperations or device-related complications. Although other IFDs have the same intended use as the tested IFD (ie, stabilisation and fixation of the spinous processes to develop fusion), there is currently limited radiographic evidence of these other devices providing fusion.[19,22,23] In a prospective cohort study of 25 patients with degenerative spondylolisthesis and treated with the Nuvasive Affix device, CT scans at 4 and 6

months showed that "certain" fusion occurred in 21 patients (84%), incomplete fusion in one (4%) and absent fusion in three (12%).[24] In a sub-cohort of 50 patients with the Zimmer Biomet Aspen device, CT scans taken at a mean of 182 days after surgery showed that 94% had Grade 3 (solid incorporation and bridging bone) or Grade 4 (solid fusion, with incorporation and obvious stability and maturity) fusion.[17]

In the current trial, an assessment of fusion in the CT scans of nine IFD participants by three independent radiologists concluded that 8 of 9 patients were fused (89%). The assessment of fusion in a random one-half of the IFD cohort was limited by the small number of patients in this cohort. However, this data points to a need for future research to systematically assess fusion when treating LSS with IFDs. In addition, an evaluation of the correlation between fusion and clinical outcomes would aid in understanding how fusion can play a role in improving patient outcomes, along with helping to determine the differences in outcomes between ISDs and IFDs.

Limitations and Future Directions

The randomized controlled design of this clinical trial, comparing a new IFD to a conventional treatment option along with the inclusion of physical mobility tests were the intended strengths of this study. However, low enrolment numbers and at least two cases of nonadherence to treatment assignments led to insufficient randomization and baseline differences in mean back pain and pain duration that limited the ability to make statistically meaningful comparisons between treatment groups. As previous evidence suggests, positive effects of an IFD (BacFuse) may be maintained up to five years post-implant.[22] The five-year results in the present study will be useful to examine whether the minimally invasive lateral IFD is also associated with favourable long-term outcomes and whether there is a correlation between fusion and long-term clinical outcomes. Future clinical studies should also quantify the accelerated return to normal activities associated with MIS IFD using earlier clinical follow-up time points. Although consumption of analgesic medication was a primary study endpoint, and functional status (ADL) and employment status were secondary study endpoints, the lack of early data points limited the ability to determine the change in these measures over the first 24 months. As previous research has shown high costs for ISDs,[13,14] a health economics comparison between this IFD and decompression would provide further information about the health utility of the MIS IFD as compared to surgical decompression and should be explored in follow-on research. Another area of potential concern in spinal arthrodesis is spinal positioning. A recent review article analysed the relationships between clinical outcomes and restoration of sagittal alignment, pelvic parameters and spinopelvic mismatch.[40] The data in the studies that this paper reviewed were quite varied and the perceived relationships between spinal positioning parameters and clinical outcomes were not well aligned. This resulted in no conclusions or guidelines coming out of an extensive analysis. Nonetheless, data linking spinal positioning parameters with clinical outcomes for the posterior arthrodesis device evaluated in this clinical trial would be valuable to include in future studies and could potentially elucidate best practices for this minimally invasive device.

Conclusion

This prospective, multi-centre randomized controlled trial with a five-year follow-up aimed to compare a new minimally invasive IFD with open surgical decompression in patients with LSS symptoms. This paper reports the 24-month results. Despite the low number of enrolled participants and non-adherence to randomization selections, findings showed that with the exception of 24-month back pain, IFD participants had clinically relevant outcomes characterized by statistically significant improvements in leg pain, back pain, pain-related disability and physical function at all follow-up time points. Key strengths of the IFD could rest with the favorable operating parameters compared to surgical decompression and the likelihood of bone fusion. The five-year follow-up period will help assess the long-term effectiveness and safety of treating LSS using a minimally invasive, muscle and ligament sparing IFD.

Data Sharing Statement

These clinical trial data can be requested by any qualified researchers who engage in rigorous, independent, scientific research, and will be provided following review and approval of a research proposal, statistical analysis plan, and

execution of a data sharing agreement. This would include access to anonymised, de-identified individual and trial-level data (analysis datasets).

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Disclosure

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