Triangular Titanium Implants for Minimally Invasive Sacroiliac Joint Fusion: 2-Year Follow-Up from a Prospective Multicenter Trial

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Abstract

Background

Sacroiliac joint (SIJ) dysfunction is an underdiagnosed condition. Several published cohorts have reported favorable mid-term outcomes after SIJ fusion using titanium implants placed across the SIJ. Herein we report long-term (24-month) results from a prospective multicenter clinical trial.

Methods

One hundred and seventy-two subjects at 26 US sites with SI joint dysfunction were enrolled and underwent minimally invasive SI joint fusion with triangular titanium implants. Subjects underwent structured assessments preoperatively and at 1, 3, 6, 12, 18 and 24 months postoperatively, including SIJ pain ratings (0-100 visual analog scale), Oswestry Disability Index (ODI), Short Form-36 (SF-36), EuroQOL-5D (EQ-5D), and patient satisfaction. Adverse events were collected throughout follow-up. All participating patients underwent a high-resolution pelvic CT scan at 1 year.

Results

Mean subject age was 50.9 years and 69.8% were women. SIJ pain was present for an average of 5.1 years prior to surgical treatment. SIJ pain decreased from 79.8 at baseline to 30.4 at 12 months and remained low at 26.0 at 24 months ($p<.0001$ for change from baseline). ODI decreased from 55.2 at baseline to 31.5 at 12 months and remained low at 30.9 at 24 months ($p<.0001$ for change from baseline). Quality of life (SF-36 and EQ-5D) improvements seen at 12 months were sustained at 24 months. The proportion of subjects taking opioids for SIJ or low back pain decreased from 76.2% at baseline to 55.0% at 24 months ($p <.0001$). To date, 8 subjects (4.7%) have undergone one or more revision SIJ surgeries. 7 device-related adverse events occurred. CT scan at one year showed a high rate (97%) of bone adherence to at least 2 implants on both the iliac and sacral sides with modest rates of bone growth across the SIJ.

Conclusions

In this study of patients with SIJ dysfunction, minimally invasive SI joint fusion using triangular titanium implants showed marked improvements in pain, disability and quality of life at 2 years. Imaging showed that bone apposition to implants was common but radiographic evidence of intraarticular fusion within the joint may take more than 1 year in many patients.

This prospective multicenter clinical trial was approved by local or regional IRBs at each center prior to first patient enrollment. Informed consent with IRB-approved study-specific consent forms was obtained from all patients prior to participation.

KEYWORDS: SACROILIAC JOINT DYSFUNCTION, SACROILIAC JOINT FUSION, DEGENERATIVE SACROILIITIS, SACROILIAC JOINT DISRUPTIONS, MULTICENTER CLINICAL TRIAL

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Background

Pain emanating from the sacroiliac joint (SI joint) may explain 15-23% of chronic low back pain in the outpatient setting.[1,2] SI joint dysfunction (i.e., pain and disability resulting from abnormal function of the joint) may be even more prevalent (up to 40%) in patients with prior lumbar fusion.[3,4] The impact of SI joint pain on quality of life is substantial and often disabling, similar to that observed with other prominent orthopedic conditions such as lumbar spinal stenosis and degenerative hip arthritis.[5] Quality of life may be as or more depressed in preoperative SI joint fusion patients compared to those undergoing commonly performed lumbar spine surgeries.[6]

Substantial evidence points to the SI joint as a valid cause of pain. The SI joint is a richly innervated joint[7] and instillation of local anesthetic into the SI joint blocks pain provoked by joint pressurization.[8,9] Therapeutic evidence validates the SI joint as a cause of pain: blinded trials of both periarticular steroids[10,11] and radiofrequency (RF) ablation of the lateral branches of sacral nerve roots have shown (albeit temporary) pain relief.[12,13]

Commonly provided non-surgical treatments for SI joint pain include physical therapy, chiropractic manipulations, intraarticular SI joint steroid injections,[10,11,14] and RF neurotomy (ablation) of the dorsal ramus of L5 as well as the S1-S3 dorsal rami innervating the SI joint.[12,13] But for one 12-month study,[15] no high-quality evidence supports long-term pain relief from RF ablation, no study supports long-term pain relief associated with steroid injections, and no published high-quality evidence supports the effectiveness of physical therapy in SI joint pain unrelated to pregnancy.

Open SI joint arthrodesis, which was first reported in the 1920s,[16-18] is now infrequently performed for chronic non-traumatic pain, due primarily to relatively large incisions, lengthy hospital stays (3-5 days) and long recovery periods (often lasting months). Complication rates are high,[19] non-union relatively common[20-22] and patient satisfaction variable.[19] Minimally invasive alternatives to open SI joint fusion have gained popularity in recent years[23] and most published reports describe use of a series of triangular titanium implants coated with a porous titanium plasma spray (iFuse Implant System®, SI-BONE, Inc., San Jose, CA, USA).[24-30] Previously we reported 1-year outcomes from a prospective, multicenter clinical trial of this device in SI joint dysfunction due to degeneration and/or disruption of the joint.[31] Herein we report 24-month clinical and radiographic outcomes.

Methods

Sacroiliac Joint Fusion with iFuse Implant System (SIFI, NCT01640353) is a prospective, multicenter single-arm clinical trial. The study protocol was Institutional Review Board (IRB)-approved at each participating clinical site prior to patient enrollment. The study was sponsored by the device's manufacturer (SI-BONE, Inc., San Jose, CA, USA). All study data underwent both remote and on-site data monitoring, and all study data were 100% source-verified.

One hundred ninety-four patients were enrolled between August 2012 and December 2013 at 26 sites. Of these, 10 withdrew prior to SI joint fusion and data from 12 subjects at a single site were eliminated due to the site's persistent non-compliance with the study protocol, leaving 172 subjects enrolled and treated. Two additional sites were terminated more than 1 year into the study for protocol non-compliance, resulting in 3 additional subjects not having 24-month study follow-up.

Enrollment criteria were as follows. To participate, adult (age 21-70) patients had to have low back pain for at least 6 months inadequately responsive to conservative care, a baseline SI joint pain score of at least 50 on the 0-100 mm visual analog scale (VAS), an Oswestry Disability Index score of at least 30%, and diagnosed SI joint dysfunction due to degenerative sacroiliitis or sacroiliac joint disruption. Diagnosis was based on a history of pain at or near the SI joint,[8] positive provocative testing on at least 3 of 5 established physical examination tests,[32] and at least a 50% decrease in pain after image-guided injection/arthrogram into the SI joint with local anesthetic.[33-37] Patients had to have the necessary mental capacity to participate, be physically able to comply with study

protocol requirements and sign a study-specific informed consent form. Patients were excluded for the following reasons: severe back pain due to other causes (e.g., known hip or spine conditions), diagnosed sacral pathology of other origin, recent (<1 year) major trauma to the pelvis, metabolic bone disease (osteoporosis or other bone conditions), any chronic rheumatologic condition or chondropathy, allergy to titanium, use of medications that impair bone quality or soft-tissue healing, neurologic condition that would interfere with physical therapy, infection, pregnancy or planning to become pregnant, known or suspected drug abuse, psychiatric condition that could interfere with study participation, currently a prisoner or ward of the state, participation in another investigational study or involvement in litigation, on disability leave, or receiving workers' compensation related to their back or SI joint pain. All study sites obtained IRB approval for the study and patients who agreed to participate signed a study-specific informed consent form prior to any study-specific procedure.

Baseline (pre-surgery) assessments included a detailed medical history, physical examination, and several assessments, including VAS SI joint and lower back pain, disability as measured by Oswestry Disability Index (ODI),[38] and quality of life as measured by both EuroQoL-5D (EQ-5D)[39] and Short Form-36 (SF-36).[40] ODI is a validated ten-question survey for disability due to back pain. EQ-5D is a validated five-question broad quality of life measure that can be combined into a single index and represents the time trade-off (TTO) utility of current health using US norms. EQ-5D US norms (means and quantiles) were taken from population-based surveys.[41] SF-36 is a validated 36-question 8-subscaled generic quality of life measure. SF-36 physical component summary (PCS) summarizes overall physical health, with population norms with mean 50 and standard deviation of 10. Similarly, SF-36 mental component summary (MCS) summarizes overall mental health, with similar population norms.

Subjects underwent minimally invasive SI joint fusion under general anesthesia and fluoroscopic guidance, with placement of (typically three) implants, as described previously.[31] The iFuse implant, made from titanium with a titanium plasma spray (TPS) porous coating, is triangular in cross section, ranges from 30-70 mm in length and 4-7 mm in inscribed diameter. The implant's triangular shape is designed to minimize rotation and maximize surface area. The procedure incorporates an interference fit between the implant and adjacent osseous walls to reduce micromotion. The porous TPS coating allows for biological fixation in bone. The study protocol asked participating surgeons to perform the procedure according to the manufacturer recommendations, including placement of at least 2 implants across the SI joint. Subjects requiring treatment of both SI joints could undergo either bilateral same-day surgery or staged surgery within 60 days of the first. Subjects were discharged home at the surgeon's discretion. Intraoperative and postoperative measures included number and size of implants, procedure time, fluoroscopy time, blood loss and length of stay.

Postoperatively, subjects were asked to remain at heel-toe touch-down protected weight-bearing using a walker or crutches for three weeks followed by progressive increases in weight-bearing until fully ambulatory. Beginning 1-3 weeks postoperatively, subjects were asked to undergo individualized physical therapy at a recommended frequency of twice a week for 6 weeks. Post-operative physical therapy involved activity modification to minimize pain recurrence, mobility and stability exercises, as well as adjacent segment joint mobilization for stiffness and pain control, and general conditioning exercises. Direct manipulation of the treated SI joint was discouraged.

Subjects were asked to return for study-required follow-up visits at 1, 3, 6, 12, 18 and 24 months postoperatively. Follow-up assessments consisted of review of adverse changes in health, ambulatory and work status, medication use for SI joint or back pain, physical examination, pain, function and quality of life questionnaires. Subjects underwent pelvic lateral, inlet and outlet X-ray at 3, 6 and 24 months and CT scan at 12 months as part of the study.

Adverse events, defined as any negative change in health according to an international clinical trial standard (ISO14155:2011), were monitored continuously and assessed at all study visits. For each event, inves-

tigators were asked to rate severity and relatedness to the study device, the device placement procedure and, if present, pre-existing conditions. Relatedness was captured as definitely, probably, possibly, unlikely and unrelated to the device, procedure or pre-existing condition, and each event was categorized by body system.

Study endpoints and cohorts. The primary study endpoint, evaluated at six months after the most recent SI joint fusion (to accommodate subjects who underwent planned staged bilateral surgery), was a binary success/failure composite endpoint. A subject was considered a success if all of the following were met: reduction from baseline VAS SI joint pain by at least 20 points, absence of device-related serious adverse events, absence of neurological worsening related to the sacral spine, and absence of surgical re-intervention (removal, revision, reoperation, or supplemental fixation) for SI joint pain. The 20-point VAS threshold was selected as the minimum clinically important difference (MCID) in chronic lower back pain.[42,43] Various MCIDs for ODI in low back pain have been reported;[42,44-46] we selected a relatively conservative and commonly used threshold of 15. An intent-to-treat approach was used for the primary endpoint; success rates were calculated at subsequent time points using all available data but without imputing missing values. The impact of missing data on pain reduction and ODI was evaluated using a last observation carry forward (LOCF) approach. All other analyses used available data only. The study's secondary endpoints included an analysis of patient success rates at other time points as well as improvement from baseline in VAS SIJ Pain, ODI, SF-36 PCS and EQ-5D scores. All analyses included all enrolled subjects, including a small number of subjects who, during post-enrollment monitoring, were determined to be ineligible for the study. Pre-specified were the following subgroup analyses: underlying condition (degenerative sacroiliitis vs. sacroiliac joint disruption), history of prior lumbar fusion, smokers vs. non-smokers, and unilateral vs. bilateral SI joint fusion. Additional unplanned subgroup analysis was performed.

The study included detailed imaging analyses of 3, 6, and 24-month X-rays as well as a 12-month high-resolution pelvic CT scan. All CT scans were read independently by 3 non-conflicted bone radiologists subcontracted by an independent core radiographic laboratory (BioMedical Systems, Inc. St. Louis, MO). A "2 out of 3" approach was used to determine a consensus read for each endpoint, with the main reader adjudicating discrepancies. The primary imaging endpoint was the proportion of subjects showing at least 30% apposition of bone to both the iliac and sacral sides of at least 2 of 3 iFuse implants on 12-month CT scan. Primary safety parameters included: radiolucency (defined as lucency around the device consistent with possible loosening of the device), device failure/fracture, device breach (defined as presence of the distal end of the implant in the sacral foramen or outside the osseous envelope of the sacrum), device migration and adverse bone reaction. Additional radiographic endpoints included bridging bone across the SI joint (and extent thereof), positive bone remodeling response and heterotopic ossification. A single reader read inlet/outlet/lateral pelvic X-rays at months 3, 6 and 24, scoring a subset of the above-described endpoints.

Sample Size. Study sample size was determined by pre-planned interim analysis with a predictive enrollment stopping rule. Study enrollment was stopped in December 2013 with 172 subjects enrolled and treated as a result of a positive predicted success rate analysis.

Statistical analysis. For continuous variables, changes from baseline were compared using repeated measure analysis of variance. Confidence intervals for proportions were calculated using standard methods. Analysis of procedure-related variables focused on the index (first side) procedure only. All statistical analyses were performed using R.[47]

Results

Of 194 patients who were eligible and signed a consent form, 10 voluntarily withdrew prior to SI joint fusion. All data from 12 subjects at a single site were excluded due to persistent non-compliance with the study protocol, leaving 172 enrolled and treated subjects. Analysis excludes data from an additional 3 subjects, who were excluded after the month 12 visit

for persistent site non-compliance with the protocol. During post-enrollment monitoring, 21 patients (Supplementary Table 1) were found to not meet all eligibility criteria; as these subjects were already enrolled and treated, all were included in statistical analyses.

Baseline characteristics. Subjects averaged 50.9 years old, most (96.5%) were Caucasian and 69.8% were women. Baseline SI joint pain (mean 79.8 points, 0-100 scale) and Oswestry Disability Index (ODI, mean 55.2) levels were high. On average, pain had persisted for 5.1 years (range 0.43 to 41.08 years). Quality of life (QOL) was substantially diminished (mean EQ-5D TTO of 0.43 and mean SF-36 PCS of 31.7), values that are substantially lower than normal populations.[5] 131 (76.2%) subjects were taking opioid medications for SI joint or low back pain at baseline and many subjects (44.2%) had a history of prior lumbar fusion. SI joint pain persisted despite prior SI joint-focused physical therapy (64.5% of subjects), prior SI joint steroid injections (94.2%) and prior RF ablation of the SI joint (15.7%).

Procedure characteristics. Fourteen (8.1%) subjects underwent planned bilateral SI joint fusion. Procedure time averaged 46.6 minutes (range 13.0 to 111.0 minutes) and mean estimated blood loss was 51.0 cc (median 30 cc, range 5.0-800.0 cc, see Table 2). One subject, an outlier, had 800 cc of blood loss due to injury to the superior gluteal artery. Four implants were used in 12.8% cases; three were used in 83.7% of cases and 2 in 3.5% of cases. Subjects were discharged in a mean of 0.79 days (range 0 to 7 days); 164 (95.3%) were discharged either the same day or within 2 days.

Subject trial flow. Of the 172 participants, 167 (97.1%) had 6-month follow-up, 157 (91.3%) had 12-month follow-up and 149 (86.6%) had 24-month follow-up (Figure 1). Reasons for incomplete 24-month follow-up included the following: 5 had withdrawn consent to participate, 2 had died from causes unrelated to the SI joint, 10 were documented to be lost to follow-up, 5 were unavailable for other reasons, including termination of the site by the sponsor in 3 subjects and substance abuse in 1.

Primary endpoint. At month 6, 138 of 172 subjects met the study's success endpoint definition, for an

Table 1. Characteristics of enrolled subjects.

Characteristic	Value
Age, mean (range)	50.9 (23.5 - 71.6)
Women, n (% female)	120 (69.8%)
Race, n (%)	
White	166 (96.5%)
Hawaiian / Pacific Islander	1 (0.6%)
Black	2 (1.2%)
Other	3 (1.7%)
Ethnicity	
Hispanic or Latino, n (%)	7 (4.1%)
Body mass index, mean (range)	29.4 (17.2 - 51.0)
Smoking status, n (%)	
Current smoker	44 (25.6%)
Former smoker	49 (28.5%)
Never smoker	79 (45.9%)
Ambulatory without assistance (n, %)	154 (89.5%)
Work status (n, %)	
Working full time	64 (37.2%)
Working part time	9 (5.2%)
Not working, retired	35 (20.3%)
Not working due to back pain	60 (34.9%)
Not working, other reason	4 (2.3%)
Prior lumbar fusion (n, %)	76 (44.2%)
Underlying diagnosis	
Degenerative sacroiliitis	135 (78.5%)
Sacroiliac joint disruption	37 (21.5%)
Years of pain, mean (range)	5.1 (0.43-41.08)
Pain syndrome	
Pain began peripartum	20 (11.6%)
Pain radiates down leg	144 (83.7%)
Groin pain	96 (55.8%)
Pain worse with sitting	151 (87.8%)
Pain worse with rising	137 (79.7%)
Pain worse with walking	153 (89.0%)
Pain worse with climbing stairs	150 (87.2%)
Pain worse descending stairs	117 (68.0%)
Prior treatments	
Physical therapy	111 (64.5%)
Steroid SI joint injection	162 (94.2%)
RF ablation	27 (15.7%)
Taking narcotics (n, %)	131 (76.2%)
Proportion with lumbar stenosis (n, %)	42 (24.4%)
Proportion with hip diagnosis (n, %)	24 (14.0%)

intent-to-treat success rate of 80.2% (95% posterior credible interval 73.8-85.7%). Using available data only, the 12-month success rate was 127/159 (79.9%) and the 24-month success rate was 119/149 (79.9%). At all time points, the observed success rates exceeded the study's pre-determined threshold for success (Bayesian posterior probability of study success >0.999). Pre-specified subgroup analysis showed no statistically significant differences in 24-month success rates by underlying diagnosis, a history of prior lumbar fusion, smoking status, or unilateral vs. bilateral SI joint fusion surgery.

Pain and quality of life outcomes. During follow-up, mean (SD) SI joint pain improved from a baseline of 79.8 (12.8) points to 26.0 (26.7) points at month 24 (see Figure 2); the reduction in pain was statistically significant (p<.0001) at every time point, including month 1. Similarly, mean (SD) Oswestry Disability Index score, a measurement of disability due to back pain, improved from a baseline of 55.2 (11.5) points to 30.9 (20.5) at month 24, with statistically significant reductions at each time point. For both VAS SI joint pain and ODI, there was no variation in response by preplanned subgroups (underlying diagnosis, history of prior lumbar fusion, smoking status, or bilateral vs. unilateral procedures). Additional subgroup analyses (e.g., age, race, ethnicity, number of postoperative rehabilitation visits, gender, years of SI joint pain, history of pain beginning during pregnancy or soon thereafter) showed no variation in response. Analyses that included imputation of missing data using the LOCF method showed only minimal differences in 24-month SI joint pain and ODI reductions resulting from missing data (-3.1 points [0-100 scale] for VAS SI joint pain and -1.6% for ODI [0-100% scale]). The proportions of subjects having VAS SI joint pain improvements ≥20 points at 6, 12 and 24 months were 82.2%, 81.8% and 83.9%, respectively. The proportions having ODI improvements ≥15 points were 65.7%, 66.7% and 69.1%, re-

Table 2. Index procedure characteristics (n=172). Only the index side procedure is reported.

Procedure duration, minutes, mean (SD), range	46.6 (16.1), 13-111
Fluoroscopy duration, minutes, mean (SD), range	2.7 (1.8), 0.3-13.5
Estimated blood loss, cc, mean (SD), range	51.0 (75.8), 5-800
Number of implants used, N (%)	
2	6 (3.5%)
3	144 (83.7%)
4	22 (12.8%)

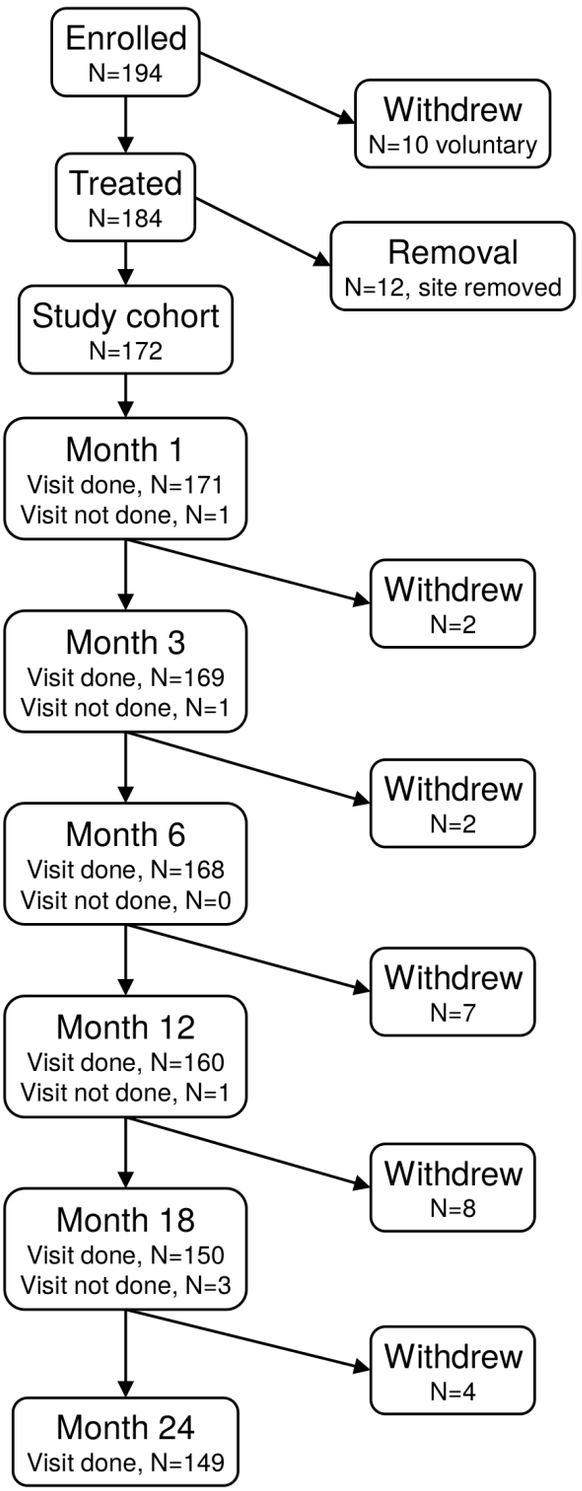

Fig. 1. Patient study flow.

spectively. The proportions of subjects with SI joint pain improvements of at least 40 points at months 6, 12 and 24 were 66%, 70% and 72%, respectively. The proportions with ODI scores <30 (indicating no or mild disability) were 46.2%, 50.3% and 46.3%, respectively. That is, the ODI improvement seen at 6 months was maintained at 2 years.

Quality of life was measured using EuroQOL-5D and SF-36, two commonly used global assessments. Over the 24-month follow-up period, EQ-5D time trade-off index, which was markedly depressed at baseline (mean 0.43) improved by 0.27 points (p<.0001, Table 3). Similarly, compared to baseline, all SF-36 subdomains improved at all time points assessed (Figure 3).

Other effectiveness outcomes. At each study visit, subjects were asked to report ambulatory and work status, and to compare current pain levels and ability to perform activities of daily living (ADLs) to their status prior to surgery (Figure 4). Prior to SI joint fusion, 89.5% of subjects were fully ambulatory. Recovery of loss of ambulatory status related to surgery was rapid (by month 3, Figure 4) and by month 24, the same proportion (89.2%) reported being fully ambulatory. Prior to SI joint fusion, 37.4% of subjects were not working due to back or other pain. By month 24, the proportion not working due to back or other pain decreased to 25.0% (McNemar test, p=0.0013). Throughout follow-up, subjects reported improved pain compared to baseline, with 88.5% reporting decreased pain at 24 months and only 4.1% reporting an increase in SI joint pain. Recovery of activities of daily living was also rapid: one month after surgery 53.2% reported less limitations of ADLs, and by month 24, 79.7% reported less limitation and only 6.1% reported more limitation.

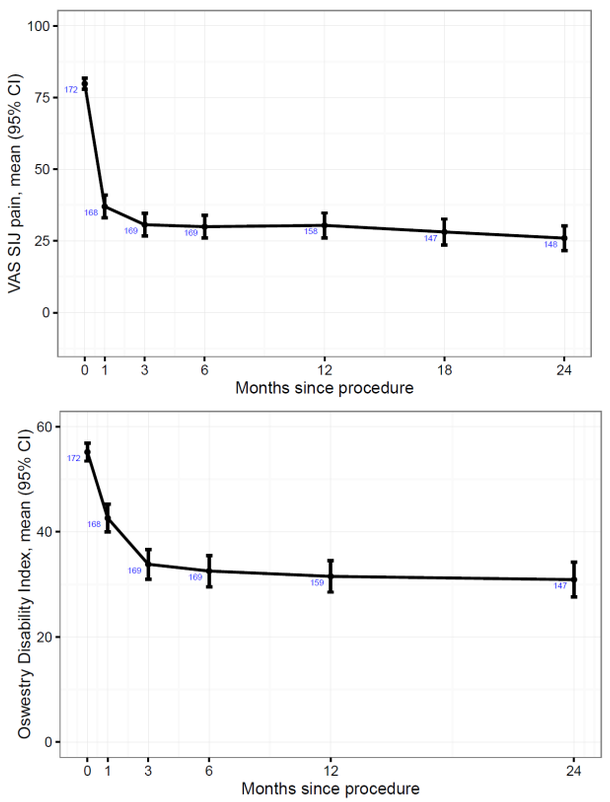

Fig. 2. Improvement in VAS SI joint pain (top) and Oswestry Disability Index (bottom). Numbers in blue indicate the number of subjects assessed. ODI was not assessed at month 18.

Table 3. Change over time in SI joint pain, Oswestry Disability Index, SF-36, and EQ-5D.

Time point	Mean (SD)	Improvement from Baseline, Mean (SD)	P-value*
VAS SI joint pain			
Baseline	79.8 (12.8)	-	
Month 1	37.0 (26.3)	42.7 (28.5)	
Month 3	30.7 (25.9)	49.2 (25.6)	
Month 6	30.0 (26.5)	49.9 (28.3)	<.0001
Month 12	30.4 (27.6)	49.3 (29.5)	
Month 18	28.1 (27.8)	51.5 (28.8)	
Month 24	26.0 (26.7)	53.3 (27.6)	
Oswestry Disability Index			
Baseline	55.2 (11.5)	-	
Month 1	42.6 (17.4)	12.5 (19.2)	
Month 3	33.8 (18.8)	21.3 (19.2)	<.0001
Month 6	32.5 (19.7)	22.7 (20.6)	
Month 12	31.5 (19.2)	23.8 (20.6)	
Month 24	30.9 (20.5)	24.5 (21.1)	
SF-36 PCS			
Baseline	31.7 (5.6)	-	
Month 6	40.1 (9.6)	8.3 (9.7)	<.0001
Month 12	40.5 (9.6)	8.8 (9.8)	
Month 24	40.7 (10.3)	8.9 (10.6)	
SF-36 MCS			
Baseline	38.5 (11.3)	-	
Month 6	47.8 (11.6)	9.3 (12.7)	<.0001
Month 12	48.2 (12.3)	9.5 (11.8)	
Month 24	49.0 (11.5)	10.1 (11.8)	
EQ-5D TTO			
Baseline	0.43 (0.18)	-	
Month 6	0.69 (0.21)	0.25 (0.24)	<.0001
Month 12	0.71 (0.20)	0.27 (0.24)	
Month 24	0.71 (0.22)	0.27 (0.26)	

*Repeated measures analysis of variance compared to baseline

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Satisfaction rates were high, with 78.1% reporting being very satisfied with SI joint treatment by month 24 and 93.8% being very or somewhat satisfied. 74.7% indicated they would definitely have the procedure again; 88.4% indicated they would probably or definitely have the procedure again.

Medication use. At each study visit, medications used for SI joint or low back pain were collected. The proportion of subjects taking opioid analgesics for SI joint or low back pain decreased from 76.2% immediately prior to surgery to 55.0% at month 24 (Figure 4). At month 24, 37 who were taking opioids at baseline had stopped taking them; in contrast, only 7 who were not taking opioids at baseline had started them by month 24 (McNemar test, p<.0001). Of those who began taking opioids, 2 had had contralateral SI joint fusion, one had recently undergone revision surgery, and 1 had back pain related to a fall 5 months after SI joint fusion.

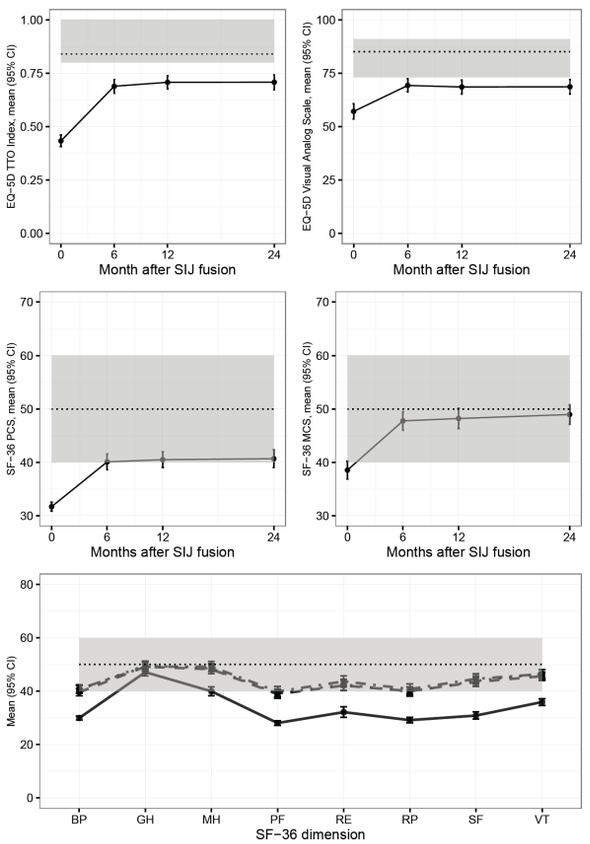

Fig. 3. Changes in EQ-5D time trade-off index and visual analog scale (top row), SF-36 PCS and MCS (middle row) and SF-36 individual dimensions (norm-based scale). Dotted lines show population medians (top row) or means (middle and bottom row) and 25th/75th percentiles (top row), 1 SD (middle and bottom row). In the bottom row, solid = baseline, dashed= 6 months, dotted=12 months, dot-dashed=24 months.

Device-related events. All negative changes in health were collected as adverse events, consistent with an international clinical trial standard (ISO 14155:2011). The number of adverse events was large (454 events in 153 subjects), but the majority were unrelated to the device or SI joint fusion procedure (a full listing of adverse events is provided in Supplementary Table 2). Four adverse events (2.4% of all subjects) were rated by the investigator to be definitely device-related (Table 4) and 3 (1.8%) were probably related. Neuropathic pain related to implant impingement on sacral nerve roots occurred in 3 cases (including one non-study-related case), all of which resolved with immediate repositioning of implants. In 4 cases, SI joint or hip pain was attributed to the presence of an implant or bone growth around the implant.

Procedure-related events. Twenty-six events were rated as probably or definitely related to the placement procedure (Table 4). The most common events were wound infection, irritation or drainage, SI joint pain related to implant malposition (described) above, and recurrent SI joint pain related to inadequate device placement. One subject had a deep wound infection that required surgical debridement.

Adverse event severity. Seventy-three events were noted to be severe, of which 1 was probably or definitely related to the device and 7 were probably or definitely related to the procedure. The device-related severe event was the above-described case of neuropathic pain related to suboptimal implant placement. The 6 procedure-related events were the above case plus: two cases of recurrent or persistent pain due to suboptimal implant position requiring revision surgery (described above), one case of postoperative surgical pain requiring brief hospitalization, one case of postoperative nausea/vomiting requiring prolonged hospitalization, and one case of deep wound infection requiring surgical wound debridement.

Revisions. Revision surgery of the index side(s) occurred in 8 cases (4.7%). In 2 cases, subjects awoke with new onset leg pain; pain resolved when implants were repositioned slightly. In 4 cases, SI joint pain improved only minimally after SI joint fusion

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and CT scan showed suboptimal implant placement, with the lower implants not placed sufficiently into the sacrum. In 1 case, radiolucencies along the implants were present on CT scan. All 4 underwent placement of additional devices with improvement in SI joint pain thereafter. One subject underwent staged bilateral SI joint fusion with initial pain relief on the index side followed by pain recurrence 6 months later. Workup showed bilateral labral tears and evidence of possible femoral acetabular impingement. Since repeat bilateral SI joint block provided temporary pain relief but intra-articular hip injections did not, he underwent traditional open SI joint arthrodesis followed by placement of one additional implant in each SI joint, which resulted in improved SI joint pain. Finally, one subject underwent L4-S1 fusion at a different institution approximately 13 months after right-sided SI joint fusion. A few months later, recurrent index-side SI joint pain developed. CT showed that the S1 screw was touching

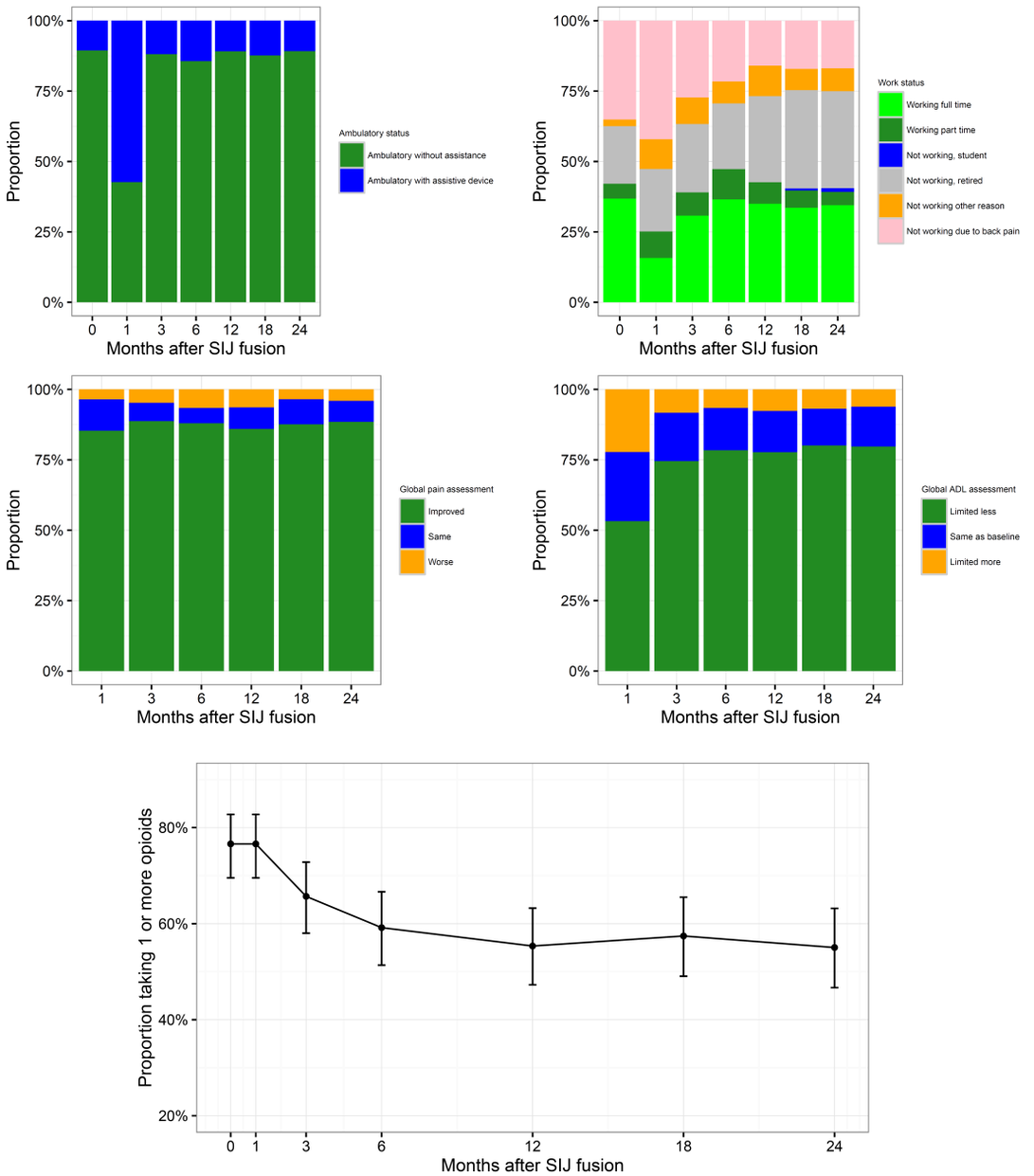

Fig. 4. Changes by month in ambulatory status (top left), work status (top right), global pain assessment (middle left), activities of daily living (middle right) and opioid use (bottom, proportion ± 95% confidence interval).

the proximal SI joint implant. Because the subject had pain relief with a repeat SI joint block, the subject underwent revision surgery in which the caudal implant was removed and an additional (non-iFuse) device placed across the joint. The investigator believed that recurrent SI joint pain could have been from additional stress transfer to the SI joint after the lumbar fusion, or possibly related to the S1 pedicle screw touching the proximal iFuse implant.

Imaging findings. Imaging analysis was based on scheduled pelvic X-rays (inlet, outlet and lateral) at months 3, 6 and 24 and a 12-month high resolution pelvic CT scan. The study's primary radiographic endpoint was based on the 12-month CT scan.

X-ray analysis. 146 subjects (84.9%) underwent 1 or more scheduled pelvic X-rays (inlet, outlet and lateral) at months 3, 6 and 24. Of these, 128 (87.7%) had an X-ray at all 3 time points. Areas of lucency around one or more implants was present on the right side in 39 subjects and on the left side in 33 subjects. In the majority of cases (24 and 21 subjects, respectively) radiolucency was confined to the distal tip of the implant within the sacrum. In a minority of cases (15 and 12 subjects, respectively), radiolucency on the right or left side spanned a longer section of the implant within either the sacrum or ilium (Table 6).

Table 4. Device- or procedure-related events.

Event category	*n* (%)[b]
Related to device[a]	
Neuropathic pain related to device malposition	7
SI joint or buttock pain	3 (1.8%)
SI joint pain after fall associated with inadequate device placement	2 (1.2%)
Hip pain related to periosteal bone growth around implant	1 (0.6%)
	1 (0.6%)
Related to procedure[a]	26
Buttock pain	2 (1.2%)
Foot weakness related to anesthesia	1 (0.6%)
iFuse impingement	3 (1.7%)
Nausea/vomiting	3 (1.7%)
SI joint pain	5 (2.9%)
SI joint pain (inadequate stabilization)	3 (1.7%)
Urinary retention	1 (0.6%)
Vascular injury	1 (0.6%)
Wound drainage/irritation/infection	6 (3.5%)
Wound numbness	1 (0.6%)

[a]Number (rate) of events divided by number undergoing surgical procedure. Some events were related to both device and procedure. [b]Events rated as probably or definitely related to the device/procedure by the study site investigator.

CT analysis. Twelve month CT was done in 159 of 161 (98.8%) subjects still participating at month 12. Bone adherent/adjacent to placed implants covering >30% of the surface area of the implant was seen in >90% of implants (Table 5). Bony apposition to at least 30% of the implant surface area on both the iliac and sacral sides of 2 or more implants, the study's primary imaging endpoint, occurred in 97% of treated sides. Of the 3 cases where apposition could not be confirmed, the CT was technically inadequate in 2. Radiolucency was seen in 9 of 91 cases on the right and in 8 of 93 cases on the left. The degree of radiolucency was <15% in most cases and radiolucency was typically seen when the distal end of the implant was barely (e.g., <1 cm) into the sacrum. Breach of the implant into the sacral foramen was present in a small number of cases (4 on the right and 8 on the left). No patient had symptoms related to breach seen on the month 12 CT. No device failure or device migration was seen. Adverse bone reaction was generally absent; in 3 (right) and 6 (left) cases, small cystic changes or scattered erosions were seen. Bone remodeling was seen in >80% of treated SI joints. Bridging bone was seen in a minority of cases (20 on the right, 19 on the left) either adjacent to or distant from placed implants.

Discussion

Our study, the first prospective multicenter report of 2-year outcomes after minimally invasive SI joint fusion, provides strong evidence that patients can be diagnosed with SI joint dysfunction and successfully treated with triangular titanium implants placed during a minimally invasive surgical procedure. Study data show marked improvement in SI joint pain extending to 2 years, with parallel changes in disability as measured by ODI, and quality of life as measured by two commonly used instruments (SF-36 and EQ-5D). The proportion of subjects with clinically important (≥15 points) improvement in ODI was meaningful (about two-thirds). Quality of life improvements were substantial as measured by EQ-5D and approximately 1 SD for SF-36. We observed parallel improvements in self-rated global assessments of pain levels, limitations in activities of daily living,

and high rates of satisfaction and desirability of undergoing the procedure again. Full ambulatory status was preserved in the majority of patients. The proportion of subjects not working due to back pain decreased.

Results from our study are supported by several retrospective case series,[24-30] including some with up to 4.5- and 5-year follow-up,[49] as well as 12-month results from a prospective randomized trial that showed little response to non-surgical treatment in the same patient population.[50] As such, our trial pro-

Table 5. Findings from CT analysis.

12-Month CT Scan	Right (N=92 sides)		Left (N=93 sides)	
	Sacral	Iliac	Sacral	Iliac
Adherence of bone to implant on 30% or more				
Implant 1	88 (95.7%)	90 (97.8%)	91 (97.8%)	91 (97.8%)
Implant 2	89 (96.7%)	90 (97.8%)	90 (96.8%)	91 (97.8%)
Implant 3	83 (94.3%)	86 (97.7%)	86 (93.5%)	90 (97.8%)
Implant 4	7 (87.5%)	8 (100.0%)	15 (93.8%)	16 (100.0%)
At least 30% apposition on both iliac and sacral sides of at least 2 implants		90 (97.8%)		90 (96.8%)
Lucency in at least 1 implant				
Absent		80 (87.9%)		83 (89.2%)
Present		9 (9.9%)		8 (8.6%)
Unable to assess		2 (2.2%)		2 (2.2%)
Breach				
Absent		85 (93.4%)		83 (89.2%)
Present - anterior sacrum		1 (1.1%)		1 (1.1%)
Present - sacral foramen		3 (3.3%)		7 (7.5%)
Unable to assess		2 (2.2%)		2 (2.2%)
Device failure				
No		89 (97.8%)		91 (97.8%)
Yes		0 (0%)		0 (0%)
Unable to assess		2 (2.2%)		2 (2.2%)
Device migration*				
Absent		89 (97.8%)		91 (97.8%)
Present		0 (0%)		0 (0%)
Unable to assess		2 (2.2%)		2 (2.2%)
Adverse bone reaction				
Absent		86 (94.5%)		85 (91.4%)
Present		3 (3.3%)		6 (6.5%)
Unable to assess		2 (2.2%)		2 (2.2%)
Bone remodeling				
Absent		14 (15.4%)		10 (10.8%)
Present		75 (82.4%)		81 (87.1%)
Unable to assess		2 (2.2%)		2 (2.2%)
Bridging bone				
Absent		68 (74.7%)		72 (77.4%)
Present - adjacent and distant		2 (2.2%)		2 (2.2%)
Present - adjacent		14 (15.4%)		11 (11.8%)
Present - distant		4 (4.4%)		6 (6.5%)
Unable to assess		3 (3.3%)		2 (2.2%)

*Defined as movement ≥3 mm.

vides strong support for minimally invasive SI joint fusion as a standard treatment choice in patients with SI joint dysfunction unresponsive to non-surgical treatment. Our study also confirms that a minimally invasive surgical approach is associated with expected benefits of minimal blood loss, relatively short procedure times, a short hospital length of stay, and a low rate of adverse events.

SI joint pain has a marked impact on quality of life. Baseline quality of life scores in study subjects are consistent with a high burden of disease[5] and quality scores in our cohort were at least as depressed as those of other major orthopedic conditions commonly treated surgically, such as lumbar spinal stenosis and degenerative hip arthritis.[5] We observed marked improvements in quality of life after SI joint fusion with two commonly used quality of life instruments (EQ-5D and SF-36). The improvements seen in all measured parameters (pain, disability and quality of life) were impressive given the long duration of SI joint pain (on average 5 years) and the high rate of failure of prior therapies (64% had received physical therapy, 94% had received SI joint steroid injections and 16% had received RF ablation). In contrast to other studies of spine surgeries, in which patients with prior spine surgery are typically excluded, our study allowed patients with prior lumbar fusion to participate, as this is known to be a risk factor for SI joint degeneration,[51] possibly by increasing adjacent segment stresses.[52] Prior lumbar fusion was common (44.2%) and many patients had a history of concomitant spine and hip disease, making the observed improvement in pain and QOL all the more impressive. Interestingly, pre-specified subgroup analysis showed that subjects with a history of prior lumbar fusion responded similarly to those without such a history.

Outcomes observed in our trial were comparable to those of other accepted surgical spine treatments. In our study, 69.1% of subjects had 15 or more point improvement in ODI at 2 years, values similar to that observed after CHARITE artificial disc replacement (68%[53]). In an early study of lumbar fusion using recombinant bone morphogenetic protein, 83% of subjects had a 15-point or more improvement in ODI at month 24.[54] In another randomized trial of lumbar fusion with recombinant bone morphogenetic protein, 71% had 15-point improvements.[55] Mean improvement in ODI in our cohort (24.5 points) was about the same as that observed in SPORT's lumbar degenerative spondylolisthesis study (24 points[56]), slightly larger than that observed in SPORT's lumbar stenosis trial (20 points in the "as treated" analysis of the randomized and observational cohort[57]), and smaller than that observed in SPORT's lumbar disc herniation study (37.6 points[58]). Improvements in our cohort occurred despite the common finding of prior lumbar fusion (44.2%) and concomitant hip or spine disease (24.4% spinal stenosis, 14.0% hip problems, 9.3% prior sacral trauma), conditions that often result in exclusion from other clinical trials.

SI joint pain has often been called "controversial" and challenging to diagnose, especially because other conditions (e.g., lumbar disc disease, hip osteoarthritis) can mimic SI joint pain. Unfortunately, no imaging study finding currently available is pathognomonic of SI joint dysfunction. Similar to other painful conditions, there is no gold standard for the diagnosis of any pain generator, and the idea that SI joint dysfunction diagnosis is challenging may stem, in part, from this void. Nonetheless, the diagnostic algorithm used in our study, which includes a typical history of off-center buttocks or low back pain below L5 and a positive Fortin finger test,[59] positive findings on 3 or more physical examination provocative maneuvers that stress the SI joint and reproduce SI joint pain, and confirmatory diagnostic SI joint block, identified a patient population with a high response rate to definitive treatment, with high long-term positive response rates. The high response rate validates the diagnostic approach. The use of diagnostic blocks in other pain conditions is commonly performed, and confirmatory diagnostic SI joint block is recommended by multiple pain and anesthesia specialty societies.[33-37]

Opioid use in the US has been termed an epidemic[60,61] and concern remains about rising rates of prescribed opioid use for pain treatment. Chronic opioid use after lumbar fusion is common, occurring in >50% of patients in one study.[62] In this study, chronic opioid use was associated with less return to work, and chronic opioid use prior to lumbar fusion was associated with failed back syndrome, additional

surgery, depression and extended work loss. In a community-based comparison of surgical vs. non-surgical treatments for chronic low back pain, the proportion of patients taking opioids at 1 year decreased in non-surgical but not surgical patients.[63] In a prospective case series, the proportion of spine surgery patients who were taking opioids preoperatively and at 1 year did not change.[64] In the SPORT studies, the likelihood of opioid use amongst patients taking opioids at baseline decreased, while the incidence of new opioid use amongst non-users at baseline was modest.[65] Surgical treatment in SPORT was associated with a lower incidence of opioid use compared to non-surgical treatment, but the non-randomized nature of treatment selection severely limits the comparison. Moreover, the overall proportion of SPORT participants taking any opioids at each study visit was not reported. In our study, the incidence of opioid use at baseline was high (76.2%), which may reflect the underlying severity and chronicity of disease, and the reduction in opioid use was important (55.0% at 24 months, a reduction of 28.2%). This reduction was consistent with results from a randomized trial of SI joint fusion, showing a reduction of opioid use at 6 months in the SI joint fusion group but an increase in the non-surgical group.[50] We note that pain and disability did not resolve completely in our cohort, and the use of opioids remained high. Potential explanations include: 1) the presence of comorbid conditions that require opioid use, 2) the long duration of SI joint pain (average of 5 years in our cohort), which could itself limit pain and disability improvement due to social or psychological factors, and 3) complications from prior surgeries, especially lumbar fusion, which may have been provided to patients on the basis of misdiagnosis of lower back pain as coming from the spine instead of the SI joint.

Imaging findings in our study, read by radiologists at an independent core laboratory, were instructive. The titanium implants used to perform SI joint fusion were designed for biological fixation in bone, and the study's primary imaging endpoint, the proportion of subjects showing bony apposition to at least 30% of the implant surface area on both the iliac and sacral sides of 2 or more implants, occurred in 97% of treated sides, validating the implant's design. The presence of bone on the implants suggests good bony integration and permanent stabilization of the SI joint. The number of implants with radiolucencies suggestive of implant loosening were small. As noted above, 97% of patients showed adherence of bone to at least 2 implants on both the sacral and ilial sides. The significance of scattered radiolucencies on implants is therefore unclear. Lucencies were more apparent on X-ray; these were typically around the leading edge of the implants that were placed less than 1 cm deep into the target sacrum. While lucencies along the implant's length may suggest a risk for inadequate fixation, the clinical impact may be limited in the long term by fusion across the SI joint itself. To date, only 1 of 172 patients underwent implant revision as a result of symptomatic loosening that was apparent along a major portion of the implant. Implant breach into the sacral foramen or beyond the sacral cortical bone anteriorly or posteriorly were present in a small number of patients, most of whom were asymptomatic. No device failures or migration were seen. Adverse bone reaction was generally absent, with a small number of cases showing small cystic changes or scattered erosions. Bone remodeling, predominantly in the ilium, was seen in >80% of treated SI joints, suggesting a positive impact of stabilization on bone structure.

Bridging bone across the SI joint was seen in a minority (approximately 22%) of cases. Given that a five-year study using the same imaging technique (pelvic CT) showed bridging bone in most cases (87%),[49] it is apparent that the technique used in our study may require longer periods of time to produce radiographically visible full bony bridging across the joint. Whether alternative techniques aimed at accelerating bony fusion across the SI joint (e.g., intraoperative decortication) produce incremental patient benefits is unknown. What is clear is that both short- and long-term data from our study indicate excellent pain, disability and quality of life improvements with the current device and technique, providing strong evidence that placement of porous TPS-coated triangular titanium implants transarticularly across the SI joint through a lateral approach results in clinically important beneficial patient outcomes. Implants clearly blocked joint motion and produced positive clinical outcomes even without radiographically visi-

ble arthrodesis of the SI joint (at 1 year).

In our cohort, revision surgeries were required in a small number of cases. Early revisions were performed in 2 cases to address radicular symptoms related to implant malposition; radicular pain resolved rapidly in both subjects on repositioning of offending devices. In 4 cases, SI joint pain did not improve and CT scan showed poor implant placement with caudal implants not fully engaging the sacrum. Revision surgery in these cases, with placement of additional implants, resulted in improved symptoms. These findings highlight the importance of placing a sufficient number of devices across the SI joint. Multiple studies have demonstrated superior SI joint stability with two-screw constructs compared to a single screw for unstable pelvic fractures.[66-68] Moreover, biomechanical studies show that placement of 3 iFuse implants across a SI joint reduced motion in flexion-extension, lateral bending, and axial rotation, with larger reductions observed using a transarticular configuration when compared with an inline (posterior) configuration.[69] One subject had pain associated with radiolucencies around the implant. Finally, in one study subject, failure to improve may have been explained by competing pathology. Overall, the revision rate for minimally invasive SI joint fusion appears to be low (3.6% or less at 4 years)[70] compared to other lumbar spine surgical procedures.[71,72]

Table 6. Findings from X-ray analysis.

3-, 6- and 24-month X-ray	Month 3	Month 6	Month 24
Lucency: right			
Absent	65 (75.6%)	53 (60.9%)	47 (52.2%)
Present	14 (16.3%)	23 (26.4%)	39 (43.3%)
Not available*	7 (8.1%)	7 (8.0%)	0 (0%)
Lucency: left			
Absent	70 (80.5%)	65 (72.2%)	56 (60.9%)
Present	11 (12.6%)	17 (18.9%)	32 (34.8%)
Not available	6 (6.9%)	4 (4.4%)	92 (100.0%)
Positive bone reaction: right			
Absent	78 (91.8%)	73 (84.9%)	71 (78.9%)
Present	0 (0%)	2 (2.3%)	15 (16.7%)
Not available	7 (8.2%)	7 (8.1%)	0 (0%)
Positive bone reaction: left			
Absent	81 (91.0%)	80 (88.9%)	72 (78.3%)
Present	1 (1.1%)	2 (2.2%)	16 (17.4%)
Not available	7 (7.9%)	4 (4.4%)	0 (0%)
Device failures	None	None	None
Device migration	None	None	None
Adverse bone reaction	None	None	None

*Not available = X-ray not done.

All negative changes in health were collected as adverse events in our study, which resulted in a high number of reported events. However, because the study protocol used an international clinical trial standard (ISO14155:2011), which defines an adverse event as any negative change in health, most adverse events were unrelated to the study device or procedure. Only 7 events were deemed related to the study implant, of which 3 were related to poor implant placement causing nerve irritation and one was related to a fall associated with inadequate implant placement. 26 events were deemed related to the study procedure; the events were not unexpected and all resolved.

Several devices are now commercially available in the US and other geographies to perform minimally invasive SI joint fusion. Some of these devices are placed across the articular SI joint using a lateral-to-medial approach, as done in our study. Other devices (none of which are currently cleared by US FDA) are placed into the dorsal ligamentous portion of the SI joint via a posterior approach. The dorsal/posterior approach typically involves removal of a portion of the dense dorsal ligaments and the interosseous ligament, which may acutely destabilize the joint.[73,74] As no implants are placed across the SI joint with the dorsal technique, the biomechanics of the dorsal technique will differ from the lateral technique. Thus, while it is unknown whether the results of our study are applicable to other lateral transfixing devices, it is highly unlikely that our results are applicable to devices placed through a dorsal approach.

Our study has several advantages. First, participants were carefully screened against predetermined eligibility criteria and results represent the prospective experience of multiple surgeons. Second, the trial was executed according to an international clinical trial standard (ISO14155:2011). Third, study data were collected on electronic case report forms at predetermined postoperative time points and all data were rigorously monitored and source verified.

The study has two primary limitations: 1) lack of a concurrent control group undergoing non-surgical treatment and, 2) a 24-month follow-up rate that was not as high as desired. Regarding the control group, direct comparisons can be made to INSITE (NCT01681004), a companion, randomized clinical trial run contemporaneously with the current study. In INSITE, patients enrolled using identical eligibility criteria were randomized to receive either SI joint fusion using the same device/procedure as used herein or non-surgical management, consisting of medication management, physical therapy, SI joint steroid injections and radiofrequency ablation of the SI joint. Baseline characteristics of SIFI and INSITE were very similar.[50] 12-month results from INSITE indicated a profound difference in response between surgical and non-surgical care, with superior outcomes for all effectiveness parameters measured. Moreover, pain and disability responses to SI joint fusion were very similar between the two studies. INSITE's non-surgical group's response validates that the positive health effects seen in the current study are robust and distinct from the natural course of disease. Marked improvement in pain, disability and quality of life in the absence of a definitive intervention would not be expected anyway, given the long mean pain duration (>5 years on average) and the lack of prior response to physical therapy and steroid injections, which were common in the treated patient population and which have very little support in the literature as being effective.

Second, 13.4% of subjects were lost to follow-up during the study or did not have 24-month visits. Pain and ODI scores in exiting subjects were higher than subjects who continued to participate; however, the impact of missing values on pain and ODI scores were analyzed and found to be minor, and do not effect overall study conclusions. Recently published 24-month follow-up rates in spine surgery randomized trials conducted under investigational device exemption have shown similar long-term participation rates (83%/80%,[75] 89%/82%,[76] 98%/94%,[77] 91%/90%,[78] 81/82%,[79]) to that in our study (86.6%).

Combined with results from other studies, our study confirms that SI joint fusion with iFuse implants has proven to be safe and effective, and hence a reasonable surgical treatment option for patients with SI joint dysfunction not responsive to non-surgical care.

Conclusions

This prospective multicenter clinical trial provides strong evidence that minimally invasive SI joint fusion using triangular porous coated implants placed across the SI joint improved pain, disability and quality of life at 24 months in patients with SI joint dysfunction due to degenerative sacroiliitis and sacroiliac joint disruption, and was associated with a decrease in opioid usage for SI joint or low back pain. Imaging showed evidence of stabilization and early fusion of the SI joint.

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Supplementary Table 1. Patients included but who did not meet all study eligibility requirements.

Reason	N
Receiving disability payments	9
Involvement in litigation claims	3
Osteoporosis	3
Rheumatologic disease	1
Severe concomitant back pain	1
SI joint pain score too low	3
Age > 70	1
Total	21

Supplementary Table 2. Listing of adverse events by frequency.

Event	N	%
Contralateral SI joint pain	20	11.6
SI joint pain	14	8.1
Trochanteric bursitis	8	4.7
Buttock pain	7	4.1
Upper respiratory infection	7	4.1
Fall causing back pain	6	3.5
Pneumonia	6	3.5
SI joint pain	6	3.5
Urinary tract infection	5	2.9
Knee pain	4	2.3
Back pain	3	1.7
Fall causing SI joint pain	3	1.7
Fall causing shoulder pain	3	1.7
Sinusitis	3	1.7
Wound infection	3	1.7
Acute appendicitis	2	1.2
Avascular necrosis of hip	2	1.2
Basilar artery occlusion causing stroke	2	1.2
Bronchitis	2	1.2
Cataracts	2	1.2
Cholecystitis	2	1.2
Degenerative joint disease of shoulder	2	1.2
Facet arthropathy with low back pain	2	1.2
Fall causing SI joint pain	2	1.2
Fall causing buttock pain	2	1.2
Fall causing calf contusion	2	1.2
Fall causing contralateral SI joint pain	2	1.2
Fall causing hip pain	2	1.2
Fall causing humerus fracture	2	1.2
Hip pain due to osteoarthritis	2	1.2
Hypercalcemia	2	1.2
Hypercholesterolemia	2	1.2
Ischial tuberosity pain	2	1.2
Lateral epicondylitis	2	1.2
Low back pain of unknown cause	2	1.2
Lower back pain due to lumbar spine degeneration	2	1.2
Lumbar facet pain	2	1.2
Migraine headache	2	1.2
Motor vehicle accident	2	1.2
Nephrolithiasis	2	1.2
Postoperative iFuse neuropathy	2	1.2
Postoperative nausea	2	1.2
Rheumatoid arthritis	2	1.2
Abdominal and hip pain, cause unknown	1	0.6
Acid reflux / helicobacter infection	1	0.6
Acute bronchitis	1	0.6
Acute confusion, cause unknown	1	0.6
Acute sinusitis	1	0.6
Allergic dermatitis due to surgical tape	1	0.6
Allergic reaction to wound tape	1	0.6
Allergic rhinitis	1	0.6
Anaphylaxis	1	0.6
Ankle pain due to arthritis	1	0.6
Anterior thigh pain of unknown origin	1	0.6
Anxiety	1	0.6
Aortic aneurysm	1	0.6
Arm/leg pain due to cervical stenosis	1	0.6
Asymptomatic right leg weakness on physical exam	1	0.6
Atrial flutter	1	0.6
Avascular necrosis of hip (bilateral)	1	0.6
Back and PSIS pain unknown cause	1	0.6
Back and SI joint pain due to thoracolumbar intervertebral disc degeneration	1	0.6
Back and SI joint pain, possible piriformis syndrome	1	0.6
Back and contralateral SI joint pain	1	0.6
Back pain due to L4-5 degeneration	1	0.6
Back pain due to L5-S1 degeneration	1	0.6
Back pain due to degenerative disc disease	1	0.6

Back pain due to degenerative lumbar disc disease	1	0.6
Back pain due to degenerative lumbar scoliosis	1	0.6
Back pain due to disc degeneration	1	0.6
Back pain due to fractured pedicle screws	1	0.6
Back pain due to known degenerative disc disease	1	0.6
Back pain due to lumbar facet disorder and lumbar spondylosis	1	0.6
Back pain due to lumbar screw failure	1	0.6
Back pain due to lumbar strain	1	0.6
Back pain due to mild trauma	1	0.6
Back pain due to spondylolisthesis	1	0.6
Back pain due to spondylolysis and spondylolisthesis	1	0.6
Back pain due to trigger point injection	1	0.6
Back pain from L5/S1 pseudoarthrosis and screw breakage	1	0.6
Back pain from minor trauma resulting in thoracolumbar fusion	1	0.6
Back pain from severe L5/S1 disc herniation	1	0.6
Back pain from sneeze	1	0.6
Back pain possibly due to failed prior lumbar fusion	1	0.6
Back pain possibly due to prior L3/4 surgery	1	0.6
Back pain possibly related to a previous L4-L5 discectomy	1	0.6
Back pain related to DDD and facet arthritis	1	0.6
Back pain related to lumbar disc degeneration	1	0.6
Back pain related to prior lumbar fusion	1	0.6
Back/leg pain due to L4-5 stenosis and spondylolisthesis	1	0.6
Bacterial gastroenteritis	1	0.6
Bilateral SI joint pain requiring revision	1	0.6
Bilateral ear pain, suspected eustachian tube malfunction	1	0.6
Bilateral foot numbness of unknown cause	1	0.6
Bilateral hip labral tear on MRI	1	0.6
Bilateral leg neuropathic pain	1	0.6
Bilateral lower extremity edema	1	0.6
Bleeding from cervical fusion wound	1	0.6
Bothersome surgical pain pump	1	0.6
Bowel obstruction	1	0.6
Buttock and leg pain	1	0.6
Buttock pain due to lifting heavy object	1	0.6
Buttock pain from irritation of nerve root by disc herniation	1	0.6
Calf/heel pain	1	0.6
Car accident causing lateral epicondylitis	1	0.6
Cervical cancer recurrence	1	0.6
Cervical myelopathy	1	0.6
Cervical radicular pain	1	0.6
Cervical radiculopathy	1	0.6
Chest pain	1	0.6
Choledocholithiasis	1	0.6
Chondromalacia of knee	1	0.6
Chronic lymphocytic leukemia	1	0.6
Constipation	1	0.6
Contralateral SI joint pain requiring fusion redo	1	0.6
Contralateral back and buttock pain	1	0.6
Contralateral back pain related to prior L5/S1 fusion	1	0.6
Contralateral buttock pain due to PT	1	0.6
Contralateral buttocks pain	1	0.6
Contralateral calf pain	1	0.6
Contralateral hip/back pain	1	0.6
Contralateral knee pain	1	0.6
Contralateral knee stiffness	1	0.6
Contralateral leg numbness and pain	1	0.6
Contralateral neck/arm pain due to cervical arthritis	1	0.6
Corneal abrasion	1	0.6
Decreased ankle jerk on physical exam	1	0.6
Decreased sensation and strength in ipsilateral leg	1	0.6
Deep venous thrombosis	1	0.6
Deep wound infection related to SI joint fusino	1	0.6
Degenerative disc disease L1/L2	1	0.6
Dehydration after contralateral SI joint fusion	1	0.6
Diabetes mellitus	1	0.6
Diastasis Recti	1	0.6
Drug addiction rehabilitation	1	0.6

Drug allergy	1	0.6
Dry mouth causing tooth decay	1	0.6
Eczema flare-up	1	0.6
Elbow pain	1	0.6
Elevated liver enzymes of unknown etiology	1	0.6
Episode of shingles	1	0.6
Esophageal cancer	1	0.6
Facet degeneration at C4-5 and C5-6	1	0.6
Fall causing SI joint pain. Poor device placement.	1	0.6
Fall causing ankle pain	1	0.6
Fall causing back and sacral pain	1	0.6
Fall causing buttock and hip pain	1	0.6
Fall causing buttock, back and neck pain	1	0.6
Fall causing buttocks and hip pain	1	0.6
Fall causing contralateral SI joint and back pain	1	0.6
Fall causing dislocated shoulder	1	0.6
Fall causing foot and hand fracture	1	0.6
Fall causing foot fracture	1	0.6
Fall causing hip and back pain	1	0.6
Fall causing hip/leg pain	1	0.6
Fall causing knee meniscal injury	1	0.6
Fall causing knee pain	1	0.6
Fall causing pain in back, buttock and neck	1	0.6
Fall causing radial head fracture	1	0.6
Fall causing shoulder rotator cuff injury	1	0.6
Fall causing shoulder, body, hip and knee pain	1	0.6
Fall causing wrist fracture	1	0.6
Fall worsening pain related to lumbar hardware	1	0.6
Fatal myocardial infarction	1	0.6
Fatigue/generalized weakness of unknown cause	1	0.6
Fibromyalgia	1	0.6
Flexor sheath cyst on finger	1	0.6
Foot pain	1	0.6
Foot pain due to torn tendon	1	0.6
Gastrointestinal bleeding	1	0.6
Hair loss	1	0.6
Hammer toe	1	0.6
Hamstring tear	1	0.6
Hand arthritis	1	0.6
Heart failure due to ventricular septal defect	1	0.6
Hematuria of unknown cause	1	0.6
Hiatal hernia	1	0.6
Hip and buttock pain	1	0.6
Hip arthritis requiring hip replacement	1	0.6
Hip bursitis	1	0.6
Hip pain	1	0.6
Hip pain after hip replacement	1	0.6
Hip pain due to fibrosis	1	0.6
Hip pain due to hip joint osteoarthritis	1	0.6
Hip pain of unknown cause	1	0.6
Hip/leg pain, possible piriformis syndrome	1	0.6
Hypertension exacerbation due to medication non-compliance	1	0.6
Hypotension related to dehydration	1	0.6
Iliotibial band syndrome	1	0.6
Infection left arm related to flu shot	1	0.6
Infection of implanted pain pump	1	0.6
Inguinal pain of unknown origin	1	0.6
Injury from spousal physical abuse causing back pain	1	0.6
Intermittent contralateral hip and buttock pain	1	0.6
Intermittent hip and buttock swelling	1	0.6
Intracranial aneurysm	1	0.6
Intraoperative hemorrhage	1	0.6
Ipisilateral thigh pain	1	0.6
Ipsilateral buttock pain	1	0.6
Ipsilateral buttocks pain	1	0.6
Ipsilateral hip pain	1	0.6
Ipsilateral knee pain due to patellofemoral arthritis	1	0.6
Ipsilateral leg numbness possibly due to degenerative disc disease	1	0.6

Ipsilateral leg pain due to prior lumbar fusion	1	0.6
Jaw osteomyelitis	1	0.6
Knee pain due to twisting injury	1	0.6
Knee swelling of unknown cause	1	0.6
L3-4 vertebral fractures due to coughing	1	0.6
L5 radiculopathy due to lumbar disc bulge	1	0.6
L5 sensory neuropathy	1	0.6
Lateral thigh pain unknown cause	1	0.6
Left groin pain related to ”left groin pull”	1	0.6
Leg cellulitis	1	0.6
Leg edema due to pneumonia hospitalization	1	0.6
Leg numbness possibly related to OR positioning	1	0.6
Leg pain	1	0.6
Leg pain due to piriformis syndrome	1	0.6
Leg pain due to possible disc bulge	1	0.6
Leg pain possibly due to hip osteoarthritis or lumbar disc	1	0.6
Leg sensory exam deficit related to epidural stimulator	1	0.6
Leg weakness of unknown cause	1	0.6
Limited knee extension related to old injury	1	0.6
Loosening of wrist implants after wrist fusion surgery	1	0.6
Loss of balance causing fall	1	0.6
Loss of consciousness due to supraventricular tachycardia	1	0.6
Low back and buttock pain	1	0.6
Low back and hip pain	1	0.6
Low back and radicular pain possibly due to prior lumbar fusion	1	0.6
Low back due to degenerative disc disease, spinal stenosis and SI joint dysfunction	1	0.6
Low back pain	1	0.6
Low back pain due to degenerative disc disease (location not known)	1	0.6
Low back pain due to facet arthritis	1	0.6
Low back pain due to previously implanted hardware (not iFuse)	1	0.6
Low back pain related to prior lumbar fusion	1	0.6
Low back possibly related to mild disc bulge	1	0.6
Lower back pain due to DDD and annular tear	1	0.6
Lower back pain due to L5 disc degeneration	1	0.6
Lower back pain due to lumbar spinal stenosis	1	0.6
Lumbar myofascial pain	1	0.6
Lumbar radiculitis, with multiple potential causes	1	0.6
Lumbar radiculopathy	1	0.6
Lung cancer diagnosis	1	0.6
MVA causing back and neck pain	1	0.6
Medication side effect	1	0.6
Mid and low back pain related to prior lumbar fusion	1	0.6
Midback pain due to thoracic degenerative disc disease and T8/9 herniation	1	0.6
Morbid obesity	1	0.6
Motor vehicle accident causing elbow pain	1	0.6
Motor vehicle accident causing loss of consciousness	1	0.6
Muscle spasms of unknown etiology	1	0.6
Musculoskeletal chest pain	1	0.6
Narcotic-induced constipation related to surgery for esophageal cancer	1	0.6
Nausea/vomiting/constipation related to esophageal cancer and opioid use	1	0.6
Neck and back pain secondary to nausea and vomiting	1	0.6
Neck and upper/lower back pain	1	0.6
Neck pain due to cervical facet arthropathy / fall	1	0.6
Neck pain due to cervical stenosis	1	0.6
Neck pain due to herniated C5-6	1	0.6
Neck pain from cervical spondylosis	1	0.6
Neck pain possibly due to cervical stenosis	1	0.6
Neck pain related to cervical ACDF	1	0.6
Neck pain related to prior cervical fusion	1	0.6
Numbness around surgical wound	1	0.6
Numbness/tingling in foot	1	0.6
Osteoarthritis of wrist	1	0.6
Osteopenia	1	0.6
Osteoporosis	1	0.6
Osteoporotic vertebral body compression fracture	1	0.6
Painful diabetic neuropathy	1	0.6

Pericarditis	1	0.6
Piriformis syndrome	1	0.6
Possible hip pain	1	0.6
Postoperative iFuse neuropathy after contralateral SI joint fusion redo	1	0.6
Postoperative ileus	1	0.6
Postoperative nausea/vomiting	1	0.6
Postsurgical wound infection (not iFuse)	1	0.6
Prolapsing hemorrhoids	1	0.6
Pulmonary embolism	1	0.6
Pulmonary embolism and pneumonia	1	0.6
Radicular pain due to lumbar stenosis and previous lumbar surgeries	1	0.6
Radicular pain due to spinal stenosis	1	0.6
Radicular pain from L5/S1 degeneration	1	0.6
Radiculopathy due to L4-S1 foraminal stenosis	1	0.6
Radiculopathy due to L4/5 disc degeneration	1	0.6
Restless leg syndrome	1	0.6
Right L5 radicular pain and numbness	1	0.6
Right foot weakness due to nerve injury from regional anesthesia	1	0.6
Right knee buckling	1	0.6
Rotator cuff pain	1	0.6
Rotator cuff tear	1	0.6
SI joint and leg pain	1	0.6
SI joint pain due to inadequate placement	1	0.6
SI joint pain, possibly from periosteal growth around implant	1	0.6
SI joint pain due to inadequate stabilization	1	0.6
SI joint pain due to radiolucency around implant	1	0.6
SI joint pain from irritation of SI joint implant by screw placed during lumbar fusion	1	0.6
Scapular pain due to cervical radiculopathy/stenosis	1	0.6
Scapular pain due to prior thoracolumbar fusion	1	0.6
Shoulder injury due to pulling	1	0.6
Shoulder labral tear	1	0.6
Shoulder pain due to bone spur	1	0.6
Shoulder pain of unknown etiology	1	0.6
Sinus tachycardia related to WPW syndrome	1	0.6
Sinus tachycardia, unknown cause	1	0.6
Spontaneous abortion	1	0.6
Staple irritation	1	0.6
Suicide	1	0.6
Supraspinatus tear	1	0.6
Symptomatic cervical stenosis	1	0.6
Symptomatic renal calculus	1	0.6
Syncope/dizziness	1	0.6
Systemic viral infection	1	0.6
Tachycardia	1	0.6
Thigh and foot numbness due to contralateral SI joint dysfunction	1	0.6
Thigh numbness due to lumbar radiculopathy	1	0.6
Thigh pain related to DDD	1	0.6
Thoracic strain	1	0.6
Thoracolumbar numbness related to syringomyelia	1	0.6
Thumb laceration	1	0.6
Thumb pain due to arthritis	1	0.6
Tibial plateau stress fracture	1	0.6
Transient WBC elevation without infection	1	0.6
Transient ischemic attack	1	0.6
Trauma causing leg, hip and groin pain	1	0.6
Trauma to finger	1	0.6
Twisted foot	1	0.6
Type 2 diabetes mellitus	1	0.6
Unclear, SI joint degeneration vs. pain	1	0.6
Upper back pain due to thoracic disc degeneration	1	0.6
Urge incontinence	1	0.6
Urinary retention	1	0.6
Worsened aortic atherosclerosis found during lumbar fusion surgery	1	0.6
Worsened cervical myelopathy	1	0.6
Worsened chronic thoracic pain	1	0.6
Worsened contralateral SI joint pain	1	0.6
Worsened left ankle dorsiflexion	1	0.6

Worsening back pain due to known degeneration of L4-L5	1	0.6
Worsening fibromyalgia	1	0.6
Worsening lumbar radicular pain	1	0.6
Wound drainage	1	0.6
Wound infection after cervical fusion surgery	1	0.6
Wound seroma	1	0.6
Wrist injury from trauma	1	0.6
Xanax withdrawal	1	0.6

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