

Results of the Prospective, Randomized, Multicenter Food and Drug Administration Investigational Device Exemption Study of the ProDisc®-L Total Disc Replacement Versus Circumferential Fusion for the Treatment of 1-Level Degenerative Disc Disease

Jack Zigler, MD,* Rick Delamarter, MD,† Jeffrey M. Spivak, MD,§§§
Raymond J. Linovitz, MD, FACS,§ Guy O. Danielson, III, MD,|| Thomas T. Haider, MD,¶
Frank Cammisa, MD,# Jim Zuchermann, MD,** Richard Balderston, MD,††
Scott Kitchel, MD,‡‡ Kevin Foley, MD,§§ Robert Watkins, MD,|||| David Bradford, MD,¶¶
James Yue, MD,## Hansen Yuan, MD,*** Harry Herkowitz, MD,††† Doug Geiger, MD,‡‡‡
John Bendo, MD,§§§ Timothy Peppers, MD,§ Barton Sachs, MD,* Federico Girardi, MD,#
Michael Kropf, MD,† and Jeff Goldstein, MD,§§§

Study Design. A prospective, randomized, multicenter, Food and Drug Administration-regulated Investigational Device Exemption clinical trial.

Objective. To evaluate the safety and effectiveness of the ProDisc®-L (Synthes Spine, West Chester, PA) lumbar total disc replacement compared to circumferential spinal fusion for the treatment of discogenic pain at 1 vertebral level between L3 and S1.

Summary of Background Data. As part of the Investigational Device Exemption clinical trial, favorable single center results of lumbar total disc replacement with the ProDisc®-L have been reported previously.

Methods. Two hundred eighty-six (286) patients were treated on protocol. Patients were evaluated before and after surgery, at 6 weeks, 3, 6, 12, 18, and 24 months. Evaluation at each visit included patient self-assessments, physical and neurologic examinations, and radiographic evaluation.

Results. Safety of ProDisc®-L implantation was demonstrated with 0% major complications. At 24 months, 91.8% of investigational and 84.5% of control patients reported improvement in the Oswestry Low Back Pain Disability Questionnaire (Oswestry Disability Index [ODI]) from preoperative levels, and 77.2% of investigational and 64.8% of control patients met the $\geq 15\%$ Oswestry Disability Index improvement criteria. Overall neurologic success in the investigational group was superior to the control group (91.2% investigational and 81.4% control; $P = 0.0341$). At 6 weeks and 3 months follow-up time points, the ProDisc®-L patients recorded SF-36 Health Survey scores significantly higher than the control group ($P = 0.018$, $P = 0.0036$, respectively). The visual analog scale pain assessment showed statistically significant improvement from preoperative levels regardless of treatment ($P < 0.0001$). Visual analog scale patient satisfaction at 24 months showed a statistically significant difference favoring investigational patients over the control group ($P = 0.015$). Radiographic range of motion was maintained within a normal functional range in 93.7% of investigational patients and averaged 7.7°.

Conclusions. ProDisc®-L has been found to be safe and efficacious. In properly chosen patients, ProDisc®-L has been shown to be superior to circumferential fusion by multiple clinical criteria.

Key words: lumbar spine, total disc replacement, artificial disc, circumferential fusion, randomized study, Investigational Device Exemption clinical trial, ProDisc®-L. **Spine 2007;32:1155–1162**

From the *Texas Back Institute/Texas Health Research Institute, Plano, TX; †The Spine Institute at Saint John's Health Center, Santa Monica, CA; ‡Hospital for Joint Diseases, New York, NY; §CORE Orthopaedic Medical Center, Encinitas, CA; ||Texas Spine and Joint Hospital, Tyler, TX; ¶Haider Spine Center Medical Clinic, Inc., Riverside, CA; #Hospital for Special Surgery, New York, NY; **St. Mary's Spine Center, San Francisco, CA; †† Pennsylvania Hospital, Philadelphia, PA; ‡‡Orthopedic Spine Associates, LLC, Eugene, OR; §§Semmes-Murphey Neurological & Spine Institute, Methodist University Hospital, University of Tennessee, Memphis, TN; |||LA Spine Surgery Institute, Los Angeles, CA; ¶¶University of California at San Francisco, San Francisco, CA; ##Yale University, New Haven, CT; ***SUNY Syracuse, Syracuse, NY; †††William Beaumont Hospital, Royal Oak, MI; ‡‡‡Michigan Brain & Spine Institute PC, MI Orthopaedic Center, Ypsilanti, MI; and §§§New York University Medical Center/Hospital for Joint Diseases Spine Center, New York, NY.

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Address correspondence and reprint requests to Jack Zigler, MD, Texas Back Institute/Texas Health Research Institute, Suite 200, 6020 W. Parker Road, Plano, TX 75093; E-mail: jzigler@texasback.com

Previous and ongoing prospective, randomized studies have shown that surgical intervention has benefits over conservative treatment for debilitating low back pain.^{1–3} There is some evidence over the past 80 years for spinal fusion as the surgical standard of care.^{4–7} This method may be successful in relieving pain, but it clearly changes the overall biomechanics of the spine.⁸

In 1990, Dr. Thierry Marnay implanted the first generation of ProDisc (Aesculap, Tuttlingen, Germany), a semiconstrained implant he developed in France. Between 1990 and 1993, 64 patients underwent single or

Table 1. Inclusion and Exclusion Criteria

Inclusion Criteria	Exclusion Criteria
Age 18–60 yr	No. vertebral levels with DDD >1
Single-level DDD at L3–S1. Diagnosis of DDD requires:	Patients with involved vertebral endplates dimensionally smaller than 34.5 mm in the medial-lateral and/or 27 mm in the anterior-posterior directions
1. Back and/or leg (radicular) pain; and	Known allergy to titanium, polyethylene, cobalt, chromium, or molybdenum
2. Radiographic confirmation of any 1 of the following by CT, MRI, diskography, plain film, myelography, and/or flexion/extension films:	Prior fusion surgery at any vertebral level
i. Instability (≥ 3 mm translation or $\geq 5^\circ$ angulation);	Clinically compromised vertebral bodies at the affected level due to current or past trauma
ii. Decreased disc height >2 mm;	Radiographic confirmation of facet joint disease or degeneration
iii. Scarring/thickening of anulus fibrosis;	Lytic spondylolisthesis or spinal stenosis
iv. Herniated nucleus pulposus; or	Osteoporosis. A screening questionnaire for osteoporosis, Simple Calculated Osteoporosis Risk Estimation, will be used to screen patients who require a DEXA bone mineral density measurement. If DEXA is required, exclusion will be defined as a DEXA bone density measured T score ≤ -2.5 (The World Health Organization definition of osteoporosis)
v. Vacuum phenomenon.	Back or leg pain of unknown etiology
Oswestry Low Back Pain Disability Questionnaire score ≥ 40 (20/50)	Paget's disease, osteomalacia, or any other metabolic bone disease (excluding osteoporosis addressed above)
Failed ≥ 6 mo of conservative treatment	Degenerative spondylolisthesis of grade >1
Psychosocially, mentally, and physically able to comply fully with protocol, including adhering to follow-up schedule and requirements, and filling out forms	Morbid obesity defined as a body mass index >40 or a weight more than 100 lb over an ideal body weight
Willing to give written informed consent	Pregnant or interested in becoming pregnant over the next 3 yr
	Active infection—systemic or local
	Taking any drug known to potentially interfere with bone/soft tissue healing (e.g., steroids)
	Rheumatoid arthritis or other autoimmune disease
	Systemic disease, including AIDS, HIV, hepatitis
	Active malignancy. A patient with a history of any invasive malignancy (except nonmelanoma skin cancer), unless treated with curative intent and there has been no clinical signs or symptoms of the malignancy >5 yr

AIDS indicates acquired immunodeficiency syndrome; CT, computed tomography; DDD, degenerative disc disease; DEXA, dual energy x-ray absorptiometry; HIV, human immunodeficiency virus; MRI, magnetic resonance imaging.

multilevel total disc replacement with ProDisc I. Marnay recently reported a 7–11-year follow-up on 95% of patients still living and found that 75% of them reported good-to-excellent results.⁹ The second-generation ProDisc, the ProDisc®-L (Synthes Spine, West Chester, PA), has design improvements such as a single centrally located keel, cobalt chromium molybdenum alloy/ultra-high molecular weight polyethylene (UHMWPE) articulation, and refined surgical technique and instrumentation.

The purpose of this report is to present the 2-year results of this prospective, randomized, multicenter Food and Drug Administration (FDA) Investigational Device Exemption (IDE) clinical trial to determine the safety and efficacy of the ProDisc®-L total disc replacement (investigational) *versus* the standard of care, circumferential spinal fusion (control) at a single level from L3 to the sacrum.

Materials and Methods

Study Design. Under an FDA-regulated IDE study (ProDisc®-L IDE No. G010133), 292 patients had surgery between October 2001 and June 2003 at 1 of 17 investigational sites across the United States. Approval was required from the institutional review board at each site before the study was initiated. Six patients were treated off-protocol and are not included in the analysis. The study population, thus, consisted of 50 nonrandomized training cases (3 per site: 51 enrolled, 50 treated) and 236 (161 investigational: 75 control) randomized cases. Treatment was unblinded to the patient after surgery. The randomization was weighted in a 2:1 ratio to receive either ProDisc®-L total disc replacement (investigational) or circum-

ferential fusion (control). The control group received anterior lumbar interbody fusion using commercially available femoral ring allograft and posterolateral fusion with autogenous iliac crest bone graft in combination with pedicle screws. The surgeon and surgical staff were not blinded due to preparation requirements for each procedure, as well as the difference in postoperative management (brace immobilization for the fusion patients *vs.* early mobilization for the arthroplasty patients). There were 38 surgeons involved in the study, most were fellowship trained, and all had clinical practices heavily based in adult spine. Inclusion/exclusion criteria (Table 1) were met before enrollment. The main inclusion criteria were that the patient had to have degenerative disc disease in 1 vertebral level between L3 and S1, have failed a minimum of 6 months of conservative treatment, have back and/or leg (radicular) pain, and demonstrate a minimum ODI score of $\geq 40\%$ (20/50) impairment.

Statistical Design. The sample size, based on a noninferiority design, was computed using the Blackwelder methodology, assuming that 85% of patients in both the investigational and control groups would have a successful result and that a clinically insignificant difference in success rates between groups (δ) was 12.5%. Choosing a type I error of 5% (1-sided) and 80% power, the sample size in the investigational group was 144 and 72 in the control group for a total of 216. Allowing for a potential dropout rate of 15%, total possible enrollment was 170 in the investigational group and 85 in the control group, for a total of 255 patients. Using a fixed randomization blocking method of 6 assignments per block, random allocations were generated in a 2:1 ratio. The randomization was held by the sponsor and disclosed to the site only after individual patient enrollment.

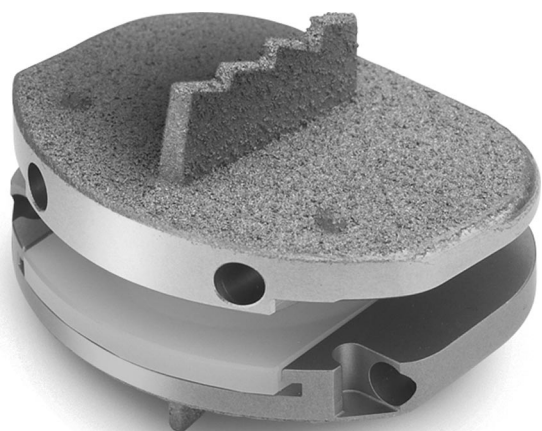


Figure 1. The ProDisc®-L total disc replacement. It is comprised of 2 cobalt-chromium molybdenum alloy endplates with central keels and an UHMWPE convex inlay.

Device Description. The ProDisc®-L design is based on a spherical joint articulation, 1 surface being metal and the other an UHMWPE. In the ProDisc®-L, the convex bearing surface is UHMWPE, and the concave highly polished bearing surface is cobalt chromium molybdenum alloy. Three components comprise this modular prosthesis. The design enables reconstruction of various heights, endplate lordosis angles, and vertebral endplate size (Figure 1).

Surgical Technique for ProDisc®-L. The patient is positioned in a supine, neutral position on a radiolucent operating table. Use of intraoperative fluoroscopy is mandatory. Exposure of the operative disc level is through a standard mini-open retroperitoneal approach. A complete discectomy is performed, possibly including removal of the posterior osteophytes and release of the posterior longitudinal ligament to ensure that the disc space has been mobilized. The cartilaginous endplates are carefully removed with curettes to maintain the integrity of the subchondral bony endplates.

The ProDisc®-L instrumentation set contains 12 implant sizes. Implant trials are placed into the disc space intraoperatively to determine the appropriate footprint size (medium or large), lordotic angle (6° or 11°), and disc height (10, 12, or 14 mm). Under lateral fluoroscopic control, the trial is advanced to the posterior margin of the vertebral bodies, the chisel is advanced into the vertebral bodies using a mallet until it is fully seated against the adjustable stop on the trial. The ProDisc®-L endplates are inserted in a collapsed fashion, with the keel following the slot cut by the chisel. Once the keel engages the slot, rotational and translational position is automatically maintained, and the disc space is visualized fluoroscopically as the surgeon determines the cephalad-caudad angulation and depth. This implant's modular nature requires only transient distraction for polyethylene insertion.

Clinical Outcome Measurements. Clinical status of each patient was evaluated before and after surgery, at 6 weeks, and 3, 6, 12, 18, and 24 months. All follow-up had a window for the patient visit according to the following schedule: 6-week and 3-month follow-up, (\pm) 2 weeks; 6-month follow-up, (\pm)

1 month; for all subsequent visits, (\pm) 2 months. Clinical evaluation at each visit included self-assessment ODI, SF-36 Health Survey [SF-36], pain on a 10-cm visual analog scale [VAS], and satisfaction on a 10-cm VAS), physical and neurologic examination, and radiographic evaluation. Physical and neurologic examinations evaluated range of motion (ROM), root tension, reflexes, muscle strength, and sensory deficits. Radiographic evaluation consisted of anteroposterior and lateral, flexion-extension, and coronal right and left lateral bending films. Medical Metrics Inc. (Houston, TX) performed an independent radiographic analysis on every film.

Clinical and Radiographic Outcomes and Determination of Success Criteria. There were 10 primary endpoints used to determine overall success for each patient: ODI, SF-36, device success, radiographic success (6 endpoints), and neurologic success. Rate of overall success was defined as the percentage of individual patients achieving success in all of these 10 endpoints. During the course of the study, the FDA required alternative definitions of 2 of the criteria, ODI and ROM. Thus, 2 analyses will be presented.

Clinical and Radiographic Follow-up. Patient accountability reveals that follow-up at 24 months was 98.2%. There was no significant difference at 24 months between the investigational (98.6%) and control (97.1%) groups. Follow-up of patients with complete data for the purpose of calculating overall study success was 91% (investigational) and 88.5% (control) at 24 months.

■ Results

Demographics and Intraoperative Data

Overall patient demographics showed no statistically significant differences between treatment groups in age, gender, race, smoking status, body mass index, baseline ODI, surgical level, or prior surgical treatment (Table 2). Intraoperative data showed that the investigational group was statistically significantly lower with regard to operative time, estimated blood loss, and length of hospital stay ($P \leq 0.0001$; Table 2). Postoperative discharge was determined by the patient's ability to transfer and ambulate independently under oral pain management.

Clinical Outcomes

The sponsor's protocol criteria will be presented first followed by the additional FDA criteria and overall success.

ODI. Baseline preoperative ODI values between both treatment groups were not different (investigational 63.4 ± 12.6 and control 62.7 ± 10.3 ; $P = 0.6125$) but were 25.3% greater than seen in a similar, previously reported study of class I IDE data.¹⁰ Regardless of treatment, patients showed statistically significant improvement in ODI scores at all follow-up periods compared to baseline ($P < 0.0001$; Figure 2). At follow-up time points of 6 weeks, 3 months, and 6 months, the investigational group had statistically greater improvement than control patients ($P < 0.05$) and trended toward significance at 24 months ($P = 0.0551$). At 24 months, the mean score in the investigational group was 34.5 ± 24.8 points, for an

Table 2. Intraoperative Data and Patient Demographics

Variable	Fusion (n = 75)	ProDisc®-L (n = 161)	P*
Intraoperative data			
Implant size			
No. medium (%)	0 (0.0)	118 (73.3)	N/A
No. large (%)	0 (0.0)	43 (26.7)	
Implant level			
No. L3–L4 (%)	3 (4.0)	3 (1.9)	
No. L4–L5 (%)	22 (29.3)	54 (33.5)	0.5149
No. L5–S1 (%)	50 (66.7)	104 (64.6)	
Intraoperative time			
No.	75	160	<0.0001
Mean (SD)	229 min (75.9)	121 min (59.2)	
Estimated blood loss			
No.	73	160	<0.0001
Mean (SD)	465 cc (440.0)	204 cc (231.3)	
Length of hospital stay			
No.	75	161	0.0001
Mean (SD)	4.4 d (1.54)	3.5 d (1.29)	
Patient demographics			
Gender			
No. males (%)	34 (45.3)	82 (50.9)	0.4849
No. females (%)	41 (54.7)	79 (49.1)	
Age			
No.	75	161	0.1299
Mean (SD)	40.4 yrs (7.6)	38.7 yrs (8.0)	
Race			
No. Caucasians (%)	59 (78.7)	133 (82.6)	0.6239
No. African-Americans (%)	5 (6.7)	5 (3.1)	
No. Hispanics (%)	10 (13.3)	18 (11.2)	
No. Asian-Americans (%)	0 (0.0)	2 (1.2)	
No. others (%)	1 (1.3)	3 (1.9)	
Body mass index			
No.	75	161	0.4844
Mean (SD)	27.3 kg/m ² (4.3)	26.7 kg/m ² (4.2)	
Smoking status			
No. never (%)	34 (45.3)	87 (54.0)	0.1995
No. former (%)	17 (22.7)	40 (24.8)	
No. current (%)	24 (32.0)	34 (21.1)	
Prior surgical treatment†			
No. any (%)	23 (30.7)	57 (35.4)	0.5552
No. discectomy (%)	12 (16.0)	26 (16.1)	
No. IDET (%)	5 (6.7)	18 (11.2)	
No. laminectomy (%)	5 (6.7)	15 (9.3)	
No. laminotomy (%)	2 (2.7)	4 (2.5)	
No. other (%)	3 (4.0)	12 (7.5)	

*Continuous and ordinal variables were analyzed by a Wilcoxon rank sum test, and categorical variables were analyzed using Fisher's exact test between the fusion and ProDisc®-L patients.

†Patients may have been included in more than 1 category.

N/A indicates not applicable; SD, standard deviation.

average improvement from baseline of 28.9 points (46.1%), and the mean score in the control group was 39.8 ± 24.3 , for an average improvement from baseline of 22.9 points (36.0%).

ODI success was defined as $\geq 15\%$ improvement from baseline. The investigational group was found to be statistically superior to the control group at all follow-up time points except at 12 months ($P < 0.05$; Table 3). At 24 months, 77.2% of investigational and 64.8% of control patients met the 15% ODI improvement threshold. At 24 months, ODI success $\geq 25\%$ improvement was statistically different between groups ($P = 0.0396$), with

the investigational group at 69.1% and the control group at 54.9%. Overall, 91.8% of investigational and 84.5% of control patients reported improvement in ODI from preoperative levels at 24 months.

SF-36. SF-36 success was defined as any improvement from baseline in the composite score of the mental and physical components (Table 4). At the 6-week and 3-month follow-up, the investigational patients recorded scores significantly higher than the control group ($P = 0.018$; $P = 0.004$, respectively). At the 24-month time point, 79.2% of investigational and 70.0% of control patients demonstrated improvement relative to baseline, however, this was not statistically significant ($P = 0.094$).

Radiographic. Six radiographic outcomes were primary endpoints. Five of the components referred to device migration, device subsidence, disc height, fusion status, and radiolucency. Of patients reaching 24-month follow-up without reoperation, the ProDisc®-L group recorded 3 cases of device migration observed radiographically and 1 case of device subsidence (0.7%), although none were clinically significant. There were no reported incidences of radiolucency, loss of disc height, or spontaneous fusion. The control group reported 1 case of migration, 1 case of radiolucency, 2 cases failing to achieve fusion (3%), and 5 cases of loss of disc height (7.2%). Therefore, 97% of control patients were radiographically fused at 24 months.

The sixth radiographic outcome was flexion-extension ROM and was defined as restoration to a normal ROM at the implanted level (for L3–L4 and L4–L5 between 6° and 20° ; for L5–S1 between 5° and 20°). At 24 months, flexion-extension ROM averaged $7.7 \pm 4.67^\circ$ in the investigational group. The flexion-extension ROM criterion was met by 93.7% of investigational patients.

Device Success. Device success is defined as absence of any reoperation required to modify or remove implants and no need for supplemental fixation. Device success was achieved in 96.3% of investigational patients and 97.3% of control patients. There were 6 patients in the investigational group considered device failures, of whom 4 were categorized as migration failures. In 2 of these patients, the UHMWPE inlay dislodged in response to extreme trauma. In 1 patient, the UHMWPE inlay migrated anteriorly within 48 hours of surgery and was likely not locked correctly at time of surgery. The fourth case of migration was the only case that involved the entire implant. The smallest implant was inserted but was still relatively oversized, and resulted in removal and fusion. This event resulted in an addition to the exclusion criteria, requiring a minimum vertebral body endplate length in the sagittal plane. The 2 remaining device failure patients included 1 case of technical error where the UHMWPE inlay was inserted backwards, requiring reoperation

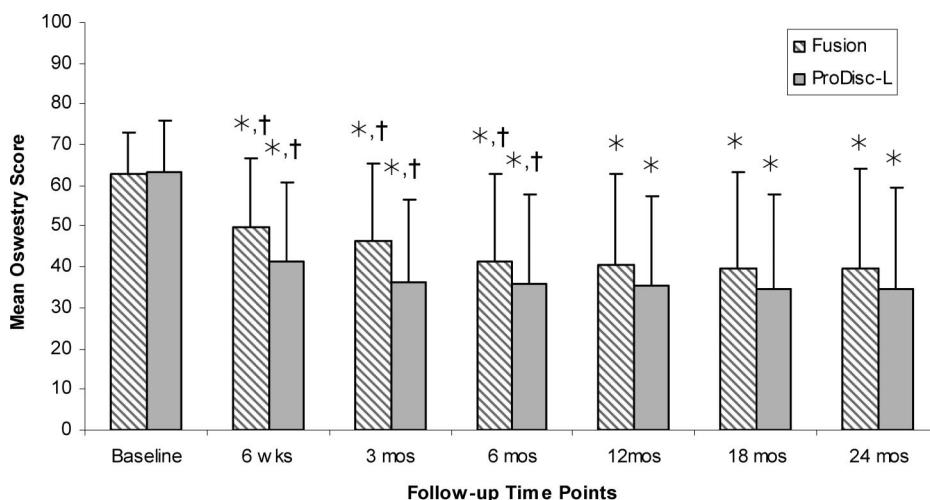


Figure 2. The mean ODI scores for each treatment over time. Error bars represent the standard deviation. Significance denoted by “*” represents difference from preoperative state within treatment group ($P < 0.0001$). Significance denoted by “†” represents difference between treatment groups at that specific time interval ($P \leq 0.02$).

and reinsertion of the inlay, and 1 case where a patient required supplemental fixation due to unresolved pain. There were 2 control patients who were considered device failures when both patients had unresolved pain requiring reoperation. Two additional patients in the control group had their posterior instrumentation routinely removed. Overall reoperation rate in the study was 3.7% for the investigational group and 5.4% for the control group.

Neurologic Success. Overall neurologic success was defined as the maintenance or improvement of patient responses to all neurologic evaluations, including sensory, motor, and reflex functions, and a straight leg raise test. At 24 months, the investigational group was statistically superior to the control group, with 91.2% success compared to 81.4% ($P = 0.0341$).

Alternative FDA Criteria

ODI Point Analysis. The FDA success criterion required ≥ 15 -point improvement. Using this definition, 67.8% of investigational and 54.9% of control patients were successful, and the investigational group was statistically superior to the control group at 24 months ($P = 0.0449$; Table 3).

Radiographic Flexion-Extension ROM Analysis. By the FDA definition, ROM success required greater motion at 24 months than at preoperative baseline for investigational

patients. Using this analysis, 89.5% of investigational patients were clinically successful.

Overall Success. Overall study success by criteria is presented in Table 5. Using the sponsor’s definition, 63.5% of investigational and 45.1% of control patients achieved overall study success, with the investigational group demonstrating a statistically significant advantage over the control group ($P = 0.0053$). Using the FDA definition, 53.4% of investigational and 40.8% of control patients were successful, with a statistically significant difference favoring the investigational group ($P = 0.0438$).

Additional Outcome Information

VAS Pain. VAS pain assessment showed statistically significant improvement from preoperative levels regardless of treatment ($P < 0.0001$; Figure 3). At 24 months, the mean VAS score was 37 ± 30.1 mm for a 39-mm average reduction (investigational) and 43 ± 31.6 mm for a 32-mm average reduction (control) from baseline and trended toward significance ($P = 0.08$).

VAS Patient Satisfaction. VAS patient satisfaction (Figure 4) at 24 months showed a statistically significant difference favoring the investigational patients with a mean of 76.7 ± 29.2 mm compared to 67.3 ± 31.5 mm in the control group ($P = 0.015$).

Surgery Again? Patients were asked whether they would have the same surgical treatment again (Figure 5). At 12

Table 3. ODI Success

Time Point	>15% Improvement			15-Point Improvement		
	Fusion	ProDisc®-L	P	Fusion	ProDisc®-L	P
Week 6	49.3%	72.1%	0.0007	35.6%	52.9%	0.0105
Month 3	60.6%	80.5%	0.0016	39.7%	58.6%	0.0061
Month 6	69.6%	81.8%	0.0346	44.8%	59.7%	0.0291
Month 12	68.9%	79.6%	0.0744	53.2%	57.7%	0.3329
Month 18	65.4%	81.4%	0.0189	50.9%	64.7%	0.0563
Month 24	64.8%	77.2%	0.0390	54.9%	67.8%	0.0449

Table 4. SF-36 Success Rate by Time Point

Time Point	Fusion	ProDisc®-L	P
Week 6	56.9%	72.1%	0.0183
Month 3	70.0%	86.6%	0.0036
Month 6	75.0%	80.4%	0.2333
Month 12	76.7%	81.0%	0.3024
Month 18	74.5%	79.1%	0.3170
Month 24	70.0%	79.2%	0.0943

Table 5. Overall Success Criteria at 24 Months

Endpoint	Sponsor Definition			FDA Definition		
	Fusion	ProDisc®-L	<i>P</i>	Fusion	ProDisc®-L	<i>P</i>
ODI 15% improvement	64.8%	77.2%	0.039			
ODI 15-point improvement				54.9%	67.8%	0.0449
Device success	97.3%	96.3%	1	97.3%	96.3%	1
Neurologic success	81.4%	91.2%	0.0341	81.4%	91.2%	0.0341
SF-36	70.0%	79.2%	0.0943	70.0%	79.2%	0.0943
Radiographic, no migration	98.6%	98.0%	1	98.6%	98.0%	1
Radiographic, no subsidence	100.0%	99.3%	1	100.0%	99.3%	1
Radiographic, no radiolucency	98.6%	100.0%	0.3165	98.6%	100%	0.3165
Radiographic, no loss of disc height	92.8%	100.0%	0.0029	92.8%	100%	0.0029
Radiographic, fusion status	97.1%	100.0%	0.0992	97.1%	100%	0.0992
Radiographic, ROM	98.6%	93.7%	0.2285	98.6%	89.5%	0.6724
Overall success	45.1%	63.5%	0.0053	40.8%	53.4%	0.0438

months, patients responded “yes” at a statistically significant higher rate in the investigational (81.6%) than the control group (63.8%) ($P = 0.0004$). At 24 months, investigational patients still responded “yes” at a higher rate (81%) than the control patients (69%) ($P = 0.1304$).

Narcotic Use. Before surgery, narcotic usage was 76% in the control group and 84% in the investigational group. Of patients achieving overall success at 24 months, only 31% of control and 39% of investigational patients remained on narcotics. In patients not achieving overall success, narcotic usage remained relatively unchanged (76% control and 79% investigational).

Work and Recreation Status. Status refers to percentage of patients partaking in the activity both full and part time. There was no difference before surgery between the control (78.1%) and investigational (83.5%) groups’ employment rate. However, at 24 months, the investigational group reported a statistical difference where 92.4% of patients were employed in comparison to 85.1% of control patients ($P = 0.0485$). Preoperative recreation status showed no difference (49.3% of control; 42.2% of investigational). At 24 months, recreation

status had increased significantly in both groups (77.3% of control and 87.4% of investigational; $P < 0.001$), and the investigational group was significantly different than the control ($P = 0.0307$).

Complications. There were no major complications (major vessel injury, neurologic damage, nerve root injury, or death) in the study. Two control group patients (2.5%) experienced clinically significant blood loss (>1500 cc). Retrograde ejaculation was reported in 2 patients (1.2%) in the investigational group. There were no infections reported in the investigational group and 2 infections reported in the control group. Three patients developed deep venous thrombosis after surgery (2 investigational; 1 control) and were successfully treated medically.

Discussion

This study presents class I data that show the safety and efficacy of the ProDisc®-L total disc replacement in individuals who had failed more than 6 months of conservative treatment for their chronic, disabling single-level lumbar disc disease. The safety of ProDisc®-L implanta-

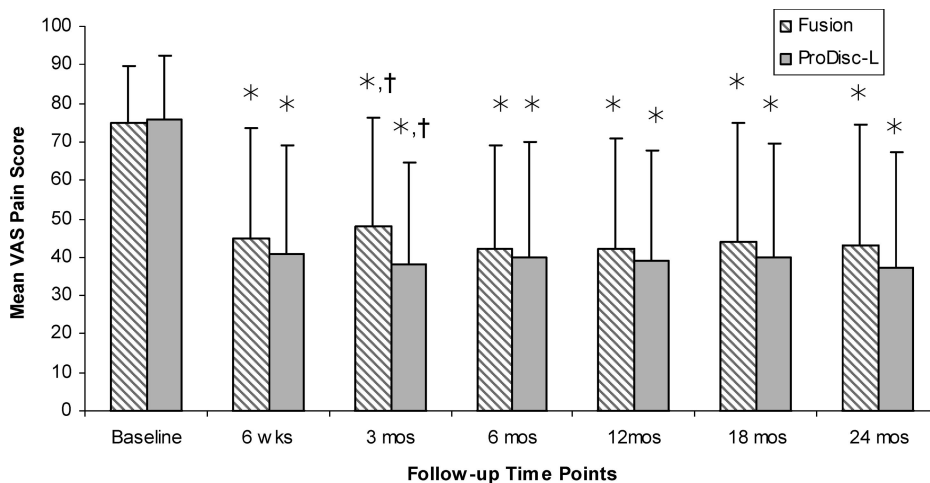


Figure 3. The mean VAS pain scores for each treatment over time. Error bars represent the standard deviation. Significance denoted by “*” represents difference from preoperative state within treatment group ($P < 0.0001$). Significance denoted by “†” represents difference between treatment groups at that specific time interval ($P = 0.0051$).

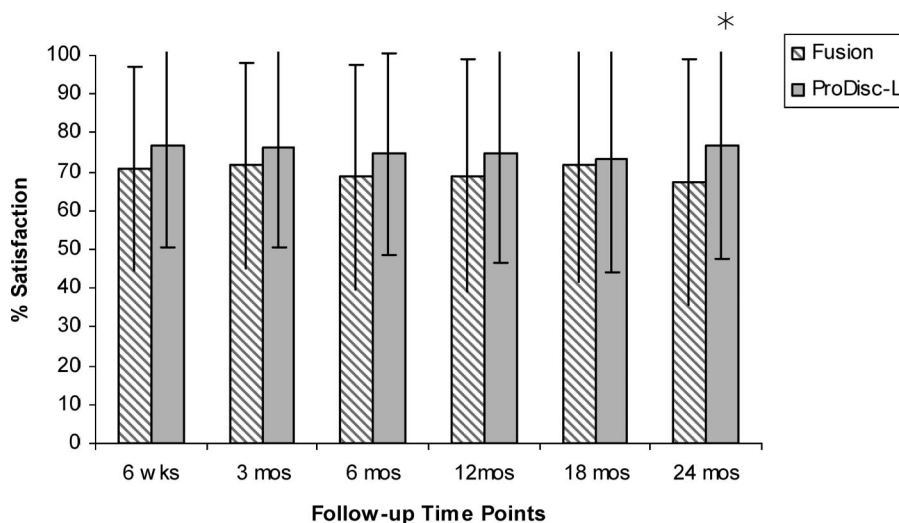


Figure 4. The mean VAS satisfaction scores for each treatment over time. Error bars represent the standard deviation. Significance denoted by "*" represents difference from preoperative state within the treatment group ($P = 0.0150$).

tion was demonstrated with 0% major complications in the study. The use of circumferential fusion as the control was a stringent outcome-based comparison, with a fusion rate of 97% at 24 months. Follow-up with complete data sets at 24 months was comparable between groups (89% control and 91% investigational). At 24 months, the ProDisc®-L group was found to be statistically significantly superior to the control group in multiple categories, including 15-point ODI improvement, 15% and 25% ODI improvement, neurologic success, and radiographic maintenance of disc height. At follow-up time points of 6 weeks, 3 months, and 6 months, the investigational group had statistically greater improvement than control patients ($P < 0.05$) and trended toward significance at 24 months ($P = 0.0551$), clearly showing better recovery in ProDisc®-L patients. Using the study success criteria, ProDisc®-L demonstrated overall study success at 64%

versus 45% for fusion by the sponsor's criteria, and 53% versus 41% by the secondarily required FDA criteria. Most importantly, regardless of definition, ProDisc®-L was statistically superior to circumferential fusion by the 10-point overall success criteria.

This was the first and only FDA IDE study that used motion success as an endpoint. For this study of the ProDisc®-L motion device, motion was maintained within normal ranges in 94% of patients, averaging 7.7° per operated segment. Using the alternative FDA success criteria, 89.5% of investigational patients had greater motion at 24 months. However, it is the authors' belief that the sponsor's definition is more appropriate. By the FDA definition, failures would include a patient with 7° ROM before surgery at the index level that maintains 7° at 24 months or a hypermobile segment returned to a normal functional ROM, and successes would include improvement from 1° ROM before surgery to a nonfunctional 2°

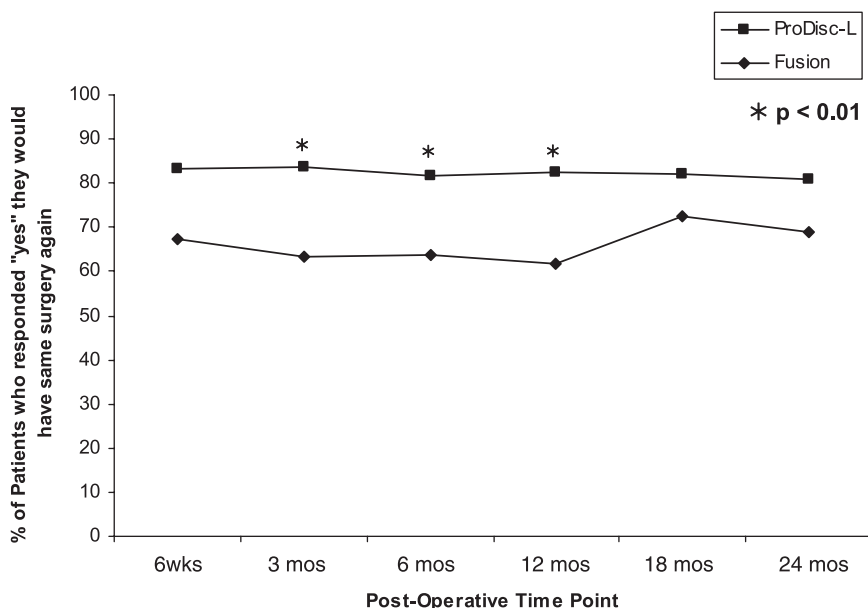


Figure 5. Comparison of responses as to whether the patient would choose the same treatment option again. At 24 months, 81% of investigational patients and 69% of control patients responded "yes," they would choose the same surgical procedure.

ROM after surgery. Maintaining a normal ROM is clearly evident with the use of ProDisc®-L, and longer term scrutiny is required to demonstrate the benefits of motion preservation for the deceleration of adjacent level degeneration.

The clinical results of this study should be reproducible among surgeons who select their patients following guidelines and do not expand on the IDE indications. The most important technical factor of the total disc replacement procedure is mobilization of the disc space. One of the greatest strengths of this multicenter trial is that it represents the combined class I data of 17 sites and 38 surgeons, proving the likelihood of achieving similar results in future-trained surgeons. The surgical technique is straightforward, and the implant is dependable.

Overall success is a mathematical measure and does not directly measure clinical success. We, as clinicians, believe that the focus should be on evaluating VAS pain, VAS satisfaction, ODI, response to whether the patient would have the procedure again, work status, and narcotic usage, as these parameters may have more clinical relevance. Results of this study demonstrated that at 24 months, the ProDisc®-L patients had 51% improvement in VAS pain, 46% improvement from baseline ODI, VAS satisfaction was statistically significantly higher, 81% of these patients would have the surgery again, and their neurologic status was statistically significantly superior to the fusion patients. Additionally, ProDisc®-L patients' work and recreation status were both statistically significantly higher than control patients. Finally, narcotics use decreased by over 50% in successful patients. This is 1 of the most rigorous studies ever reported in the field of spinal surgery. Maintaining a normal ROM is clearly evident with the use of ProDisc®-L, and longer term scrutiny is required to demonstrate the benefits of motion preservation for the deceleration of adjacent level degeneration.

■ Key Points

- ProDisc®-L total disc replacement has been shown to be safe and efficacious for the treatment of 1-level degenerative disc disease.
- These data represent class I data.
- ProDisc®-L total disc replacement was found to be superior to circumferential fusion by multiple clinical criteria.
- ROM was maintained within a normal functional range in 94% of ProDisc®-L total disc replacement patients.
- There were no major complications in either group in this study.

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