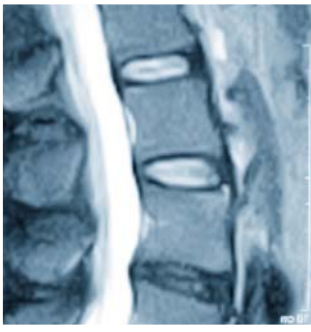
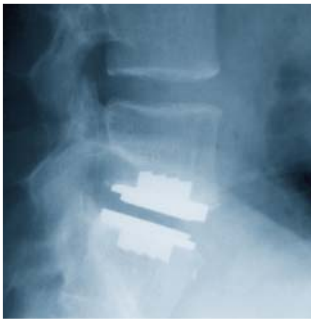
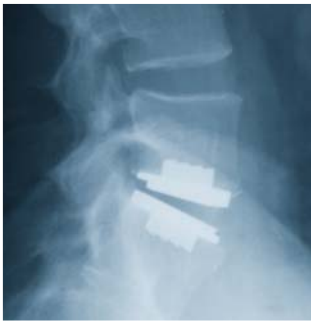
ProDisc-L Total Disc Replacement.
IDE Clinical Study.

A multi-center, prospective, randomized clinical trial.







SYNTHES® Spine

Instruments and implants approved by the AO Foundation

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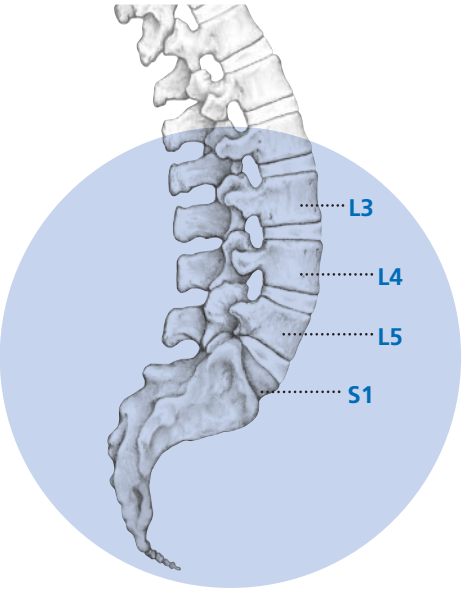
Indications, Contraindications and Warnings

Indications

The ProDisc-L Total Disc Replacement is indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one level from L3 to S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies. These DDD patients should have no more than grade 1 spondylolisthesis at the involved level. Patients receiving the ProDisc-L Total Disc Replacement should have failed at least six months of conservative treatment prior to implantation of the ProDisc-L Total Disc Replacement.



Contraindications

The ProDisc-L Total Disc Replacement should not be implanted in patients with the following conditions:

- Active systemic infection or infection localized to the site of implantation
- Osteopenia or osteoporosis defined as DEXA bone density measured T-score < -1.0
- Bony lumbar spinal stenosis
- Allergy or sensitivity to implant materials (cobalt, chromium, molybdenum, polyethylene, titanium, tantalum)
- Isolated radicular compression syndromes, especially due to disc herniation
- Pars defect
- Involved vertebral end plate dimensionally smaller than 34.5 mm in the medial-lateral and/or 27 mm in the anterior-posterior directions
- Clinically compromised vertebral bodies at affected level due to current or past trauma
- Lytic spondylolisthesis or degenerative spondylolisthesis of grade > 1

Warnings

Correct placement of the device is essential to optimal performance. Use of the ProDisc-L Total Disc Replacement should only be undertaken after the surgeon has become thoroughly knowledgeable about spinal anatomy and biomechanics, has had experience with anterior approach spinal surgeries, and has had hands-on training in the use of this device.

Study Objective and Design

Study Objective

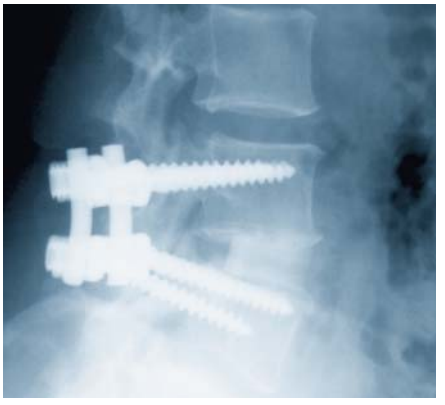
The study objective was to evaluate the safety and effectiveness of the ProDisc-L Total Disc Replacement compared to circumferential spinal fusion surgery for the treatment of discogenic pain associated with degenerative disc disease (DDD) at one level between L3 and S1.

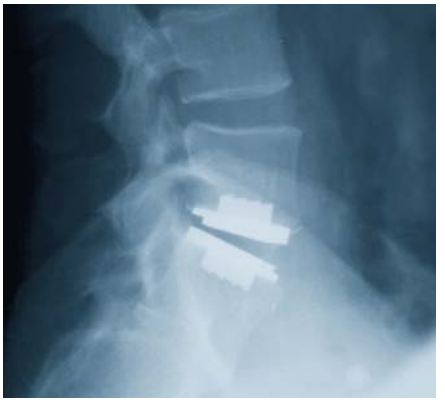
Study Design

The ProDisc-L Total Disc Replacement was compared to a circumferential fusion control consisting of an interbody fusion with a femoral ring allograft and a posterolateral fusion with autologous iliac crest bone graft combined with pedicle screw instrumentation.

ProDisc-L Total Disc Replacement vs. circumferential fusion:
– Multi-center, prospective, randomized trial
– 17 centers, 292 patients
  – 162 ProDisc-L patients
  – 80 fusion patients
  – 50 non-randomized ProDisc-L patients†
– Single level treatment (L3 to S1)
– 2:1 randomization (2 ProDisc-L:1 fusion)
– Follow-up at 6 weeks, and 3, 6, 12, 18 and 24 months

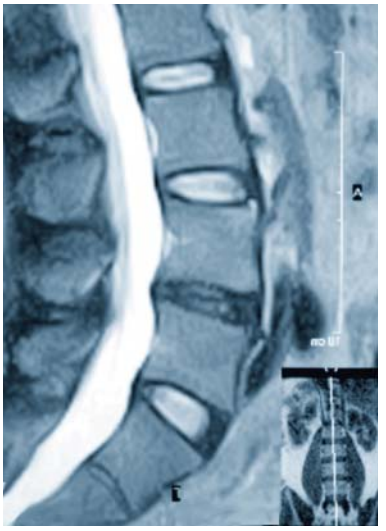
† All non-randomized patients (training cases) received ProDisc-L implants.





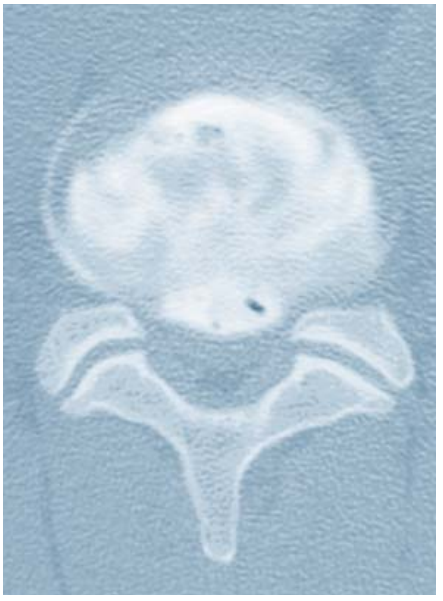
Study Inclusion and Exclusion Criteria

Inclusion Criteria:



- Degenerative Disc Disease (DDD) in one vertebral level from L3 to S1. Diagnosis requires:
  - Back and/or leg (radicular pain); and
  - Radiographic confirmation of any 1 of the following by CT, MRI, discography, plain film, myelography and/or flexion/extension films: instability (≥ 3 mm translation or ≥ 5° angulation); decreased disc height > 2 mm; scarring/thickening of annulus fibrosis; herniated nucleus pulposus; or vacuum phenomenon
- Age between 18 and 60 years
- Failed at least 6 months of conservative treatment
- Oswestry Low Back Pain Disability Questionnaire score of at least 40% (20/50 – interpreted as moderate to severe disability)
- Psychosocially, mentally and physically able to fully comply with this protocol including adhering to follow-up schedule and requirements and filling out of forms
- Signed informed consent

Exclusion Criteria:



- No more than 1 vertebral level may have DDD and all diseased levels must be treated
- Patients with involved vertebral end plates dimensionally smaller than 34.5 mm in the medial-lateral and/or 27 mm in the anterior-posterior directions
- Known allergy to titanium, polyethylene, cobalt, chromium or molybdenum
- Prior fusion surgery at any vertebral level
- Clinically compromised vertebral bodies at the affected level due to current or past trauma
- Radiographic confirmation of facet joint disease or degeneration
- Lytic spondylolisthesis or spinal stenosis
- Degenerative spondylolisthesis of grade > 1
- Back or leg pain of unknown etiology
- Osteopenia or osteoporosis: A screening questionnaire for osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation), used to screen patients to determine if a DEXA scan is required. If DEXA is required, exclusion will be defined as a DEXA bone density measured T score < -2.5.
- Paget's disease, osteomalacia or any other metabolic bone disease (excluding osteoporosis which is addressed above)
- Morbid obesity defined as a body mass index > 40 or a weight more than 100 lbs. over ideal body weight
- Pregnant or interested in becoming pregnant in the next 3 years
- Active infection – systemic or local
- Taking medications or 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, or hepatitis
- Active malignancy: A patient with a history of any invasive malignancy (except non-melanoma skin cancer), unless he/she has been treated with curative intent and there has been no clinical signs or symptoms of the malignancy for at least 5 years

Demographics and Intraoperative Data

Patient Demographics

– Patient demographics were similar for both the fusion and ProDisc-L groups.

Patients	Circumferential Fusion	ProDisc-L Randomized
Patients	80	162
Follow-up rate	88.5%	91.0%

Demographics		
Male	46.3%	51.2%
Female	53.8%	48.8%
Mean age (years)	40.2	39.6
Mean BMI (kg/m^2)	27.4	26.7

Intraoperative Data

– The ProDisc-L patient group demonstrated a statistically significant difference in mean operation time, blood loss and hospital stay compared to the fusion control group ($p < 0.05$).*

Treated Level	Circumferential Fusion	ProDisc-L Randomized
L3/L4	3.8%	1.9%
L4/L5	33.8%	33.3%
L5/S1	62.5%	64.8%

Intraoperative Data		
Mean operative time (min)	219	121*
Mean blood loss (cc)	451	203*
Hospital stay (days)	4.4	3.5*

* Statistically significant difference ($p < 0.05$), Wilcox rank sum test

Note: For complete ProDisc-L IDE study results, please see the *Summary of Safety and Effectiveness Data* at www.fda.gov.

Device Safety and Effectiveness

Intraoperative Complications
– Fusion and ProDisc-L patients experienced a low rate of complications.

	Circumferential Fusion	ProDisc-L Randomized
Clinically significant blood loss (>1500 cc)	2.5%	0.0%
Vessel damage/bleeding, major	1.3%	0.6%
Nerve root injury	0.0%	0.6%

Device Success
– Device success was demonstrated in 96.3% of the ProDisc-L patients at 24 months.

	Circumferential Fusion	ProDisc-L Randomized
Device Success†	97.3%	96.3%

† No reoperation, revision, removal or supplemental fixation

Neurological Success
– ProDisc-L patients demonstrated 91.2% neurological success at 24 months, which was statistically significantly different from the neurological success rate of fusion patients ($p < 0.05$).*

	Circumferential Fusion	ProDisc-L Randomized
Neurological Success††	81.4%	91.2%*

†† No decline in motor status, sensory deficit and reflexes
* Statistically significant difference ($p < 0.05$), Fisher's Exact Test

Patient Improvement in Pain and Disability

Oswestry Disability Index (ODI)

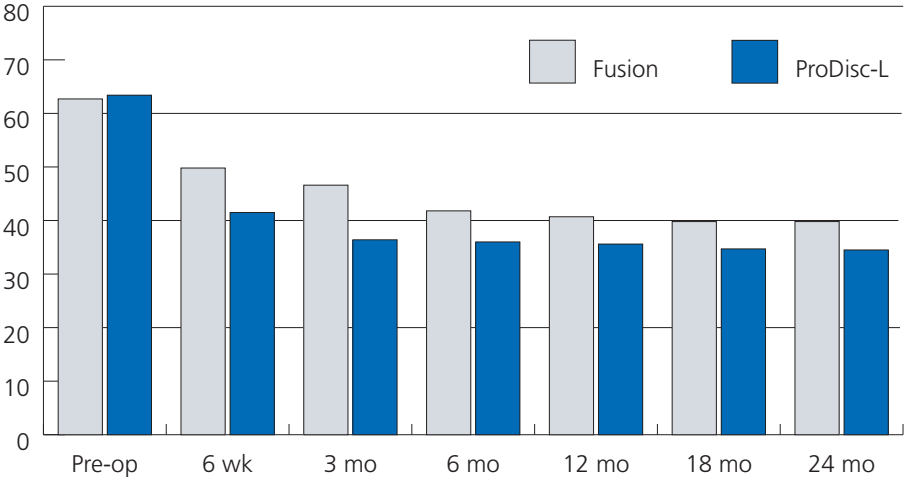
– ProDisc-L patients demonstrated a statistically significant difference in ODI improvement compared to fusion patients at 24 months ($p < 0.05$).*

– ProDisc-L patients demonstrated a mean improvement in ODI scores of 46.1% from baseline to 24 months compared to 37.8% for fusion patients.

Oswestry Disability Index	Circumferential Fusion	ProDisc-L Randomized
Mean score, pre-op	62.9	63.4
Patients with 15 pt. improvement (24 mos.)	54.9%	67.8%*
Patients with 15% improvement (24 mos.)	64.8%	77.2%*

* Statistically significant difference ($p < 0.05$), Wilcox rank sum test

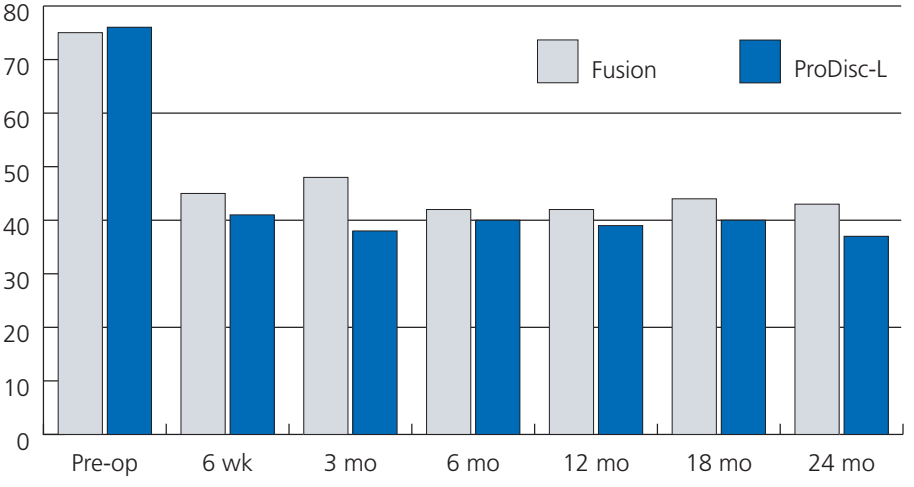
Mean ODI Scores



Visual Analog Scale (VAS) for Pain

– ProDisc-L patients demonstrated a mean decrease of 39 points from baseline to 24 months in VAS pain scores compared to 32 points for fusion patients.

Mean VAS Pain Scores



Radiographic Evaluation

Range of Motion (ROM)

– The ProDisc-L IDE clinical study is the first and only to assess ROM in a spinal arthroplasty device as a primary endpoint of overall success.

– 93.7% of the ProDisc-L patients had normal motion† at 24 months.

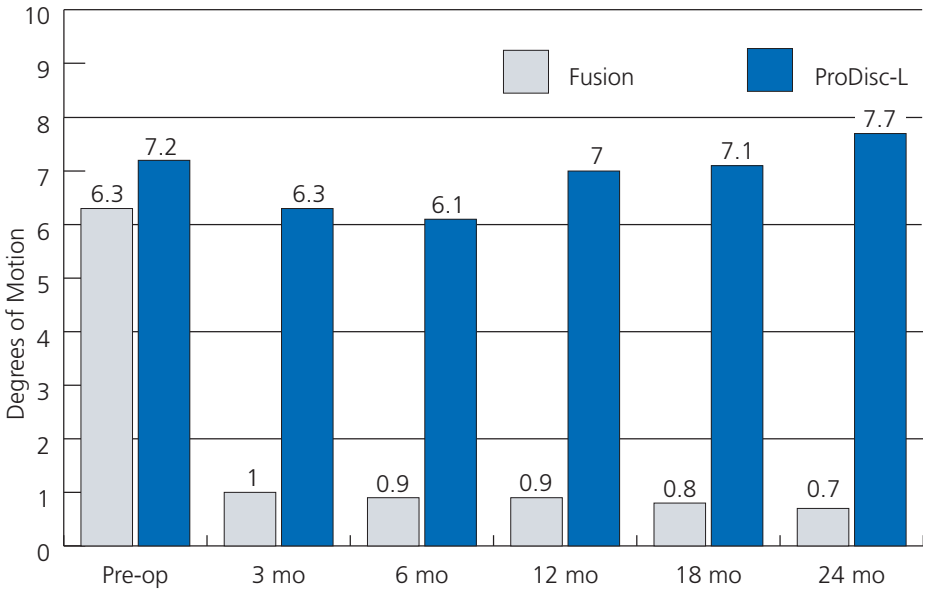
– ProDisc-L patients demonstrated a mean ROM of 7.7° at 24 months.

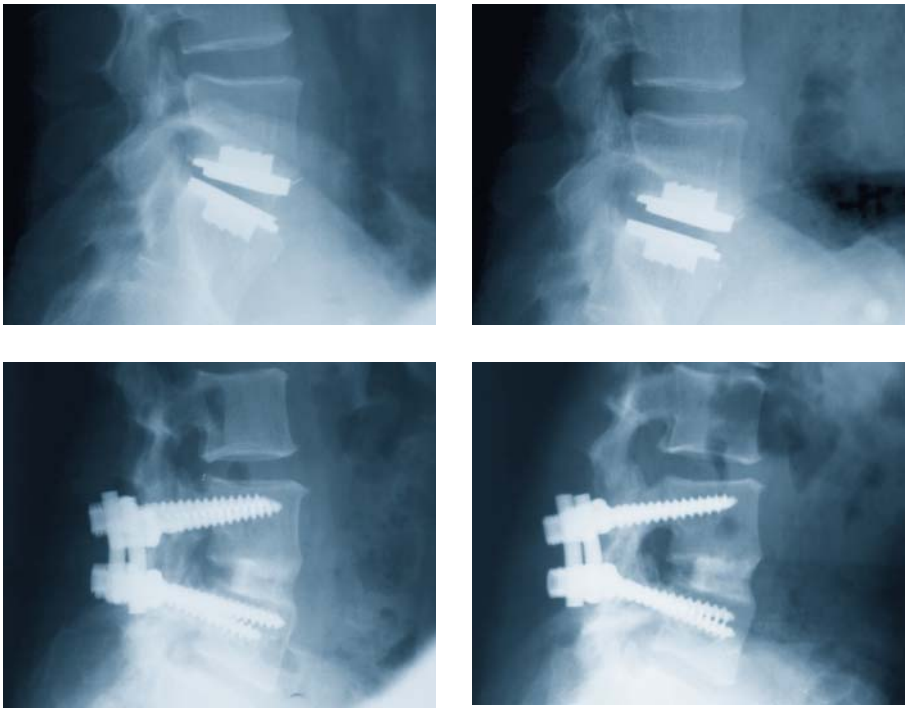
– No ProDisc-L patients showed evidence of bony fusion or loss of disc height at 24 months.

Fusion Success

– 97.1% of fusion patients demonstrated radiographic fusion success†† at 24 months.

Flexion/Extension ROM (Mean values)





† Normal motion defined as > 6° (with ± 3° measurement error applied) to 20° at L3/L4 or L4/L5, and > 5° (with ± 3° measurement error applied) to 20° at L5/S1

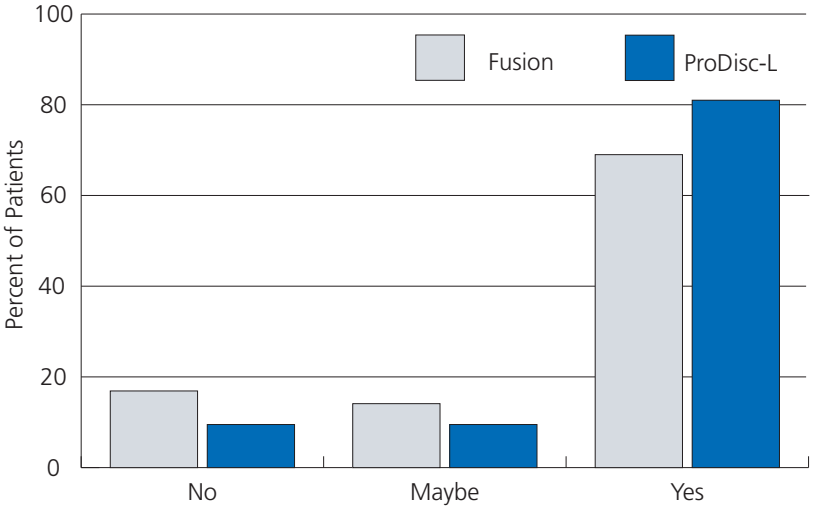
†† Strong evidence of fusion (> 50% trabecular bridging bone or bone mass maturation, increased or maintained bone density at site, and no visible gaps in the fusion mass)

Patient Satisfaction

Patient Satisfaction

– 81.0% of ProDisc-L patients would choose to have surgery again.

Would have surgery again?



– ProDisc-L patients demonstrated a statistically significant difference in mean VAS satisfaction scores compared to fusion patients at 24 months ($p < 0.05$).*

VAS satisfaction at 24 months	Circumferential Fusion	ProDisc-L Randomized
VAS satisfaction mean score	67	77*

* Statistically significant difference ($p < 0.05$), Fisher's Exact Test

Overall Success

Overall Success
A rigorous set of ten endpoints were used to define overall success at 24 months. A patient had to demonstrate success for all 10 endpoints to be considered an overall success in the study.

The IDE clinical study for the ProDisc-L Total Disc Replacement was not designed to demonstrate superiority; however, **there was a statistically significant difference in favor of the ProDisc-L group in the rate of overall success.***[1]

Criteria	Circumferential Fusion	ProDisc-L Randomized
ODI 15% improvement	64.8%	77.2%*
Device success	97.3%	96.3%
Neurological success	81.4%	91.2%*
SF-36 improvement	70.0%	79.2%
No migration	98.6%	98.0%
No subsidence	100.0%	99.3%
No radiolucency	98.6%	100.0%
No loss of disc height	92.8%	100.0%*
Fusion status success	97.1%	100.0%
ROM success	98.6%	93.7%
Overall Success	**45.1%**	**63.5%***

* $p < 0.05$, one-sided Fisher's Exact Test

1. *Summary of Safety and Effectiveness Data for the PRODISC-L Total Disc Replacement, Premarket Approval Application (PMA) Number: P050010*. Retrieved April 18, 2007, from http://www.fda.gov/cdrh/pdf5/p050010b.pdf

Non-Randomized (Training) Cases

Non-Randomized (Training) Cases
Each investigational site was required to enroll their first three ProDisc-L patients as non-randomized cases, with a total of 50 non-randomized, training patients treated.

Intraoperative Data
– ProDisc-L non-randomized patients had similar operative time, blood loss and hospital stay compared to randomized patients.

Device Safety
– ProDisc-L non-randomized patients experienced no device failures and no reoperations.

– The ProDisc-L Total Disc Replacement has a safe and reproducible surgical technique with a minimal learning curve.

Overall Success
– ProDisc-L patients in the non-randomized group demonstrated similar clinical results compared to the ProDisc-L patients in the randomized group for all endpoints.

Patients	**ProDisc-L Randomized**	**ProDisc-L Non-Randomized**
Patients	162	50
Intraoperative Data		
Mean operative time (min)	121	125
Mean blood loss (cc)	203	189
Hospital stay (days)	3.5	3.4

Criteria	**ProDisc-L Randomized**	**ProDisc-L Non-Randomized**
ODI 15% improvement	77.2%	85.4%
Device success	96.3%	100.0%
Neurological success	91.2%	83.3%
SF-36	79.2%	89.6%
No migration	98.0%	97.8%
No subsidence	99.3%	97.8%
No radiolucency	100.0%	100.0%
No loss of disc height	100.0%	100.0%
Fusion success	100.0%	100.0%
ROM	93.7%	97.8%
Overall Success	**63.5%**	**66.7%**

Conclusions

Conclusions
The ProDisc-L Total Disc Replacement is a safe and effective treatment for single-level discogenic back pain between L3–S1.

– The ProDisc-L Total Disc Replacement has a safe and reproducible surgical technique with a minimal learning curve.

– The ProDisc-L implant maintains motion.

– ProDisc-L patients were more satisfied than fusion patients.

The IDE clinical study for the ProDisc-L Total Disc Replacement was not designed to demonstrate superiority; however, **there was a statistically significant difference in favor of the ProDisc-L group in the rate of overall success.**[2]

2. Ibid.

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