

# Prodisc-L Lumbar Total Disc Replacement. US IDE clinical study design and results.

A multi-center, prospective, randomized clinical trial.



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# Introduction

This brochure summarizes the design and results of the IDE clinical study. As a mandatory requirement for FDA approval in the United States, the IDE clinical study was successfully conducted to evaluate safety and effectiveness of the Prodisc-L lumbar total disc replacement. This US study design was restricted to DDD in one vertebral level from L3 to S1. A two level study is currently running in the US. **Note that outside the United States, single and multi-level use of Prodisc-L from L1 to S1 has been successfully released since 1990.**

Due to the fact that the complete text in the following chapters originates from US documents related to that study, some terms and definitions can be found that are not entirely common outside the United States. The most important FDA terminology is listed below.

## Premarket Approval (PMA)

PMA is the FDA process of scientific, regulatory, and quality system review to evaluate the safety and effectiveness of Class III medical devices. Class III devices are categorized by the FDA as devices that support or sustain human life, are of substantial importance in preventing impairment of health, or which present a potential risk of illness or injury. PMA is the most stringent type of device marketing application required by FDA. PMA approval is based on a determination that the PMA contains sufficient valid scientific evidence to assure that the device is safe and effective for its intended use.

## Investigational Device Exemption (IDE)

To obtain US clinical data on a class III device, an investigational device exemption (IDE) must be filed with FDA. An IDE allows the investigational device to be used in clinical trials to obtain safety and effectiveness data to support a PMA application. FDA reviews existing data on the device (lab tests, clinical data from outside the US, etc.) and determines if there is evidence to support initiation of an IDE clinical trial. FDA reviews and approves all IDE study protocols prior to beginning a clinical study. IDE studies are tightly bound by the approved protocols.

## 510(k)

A 510(k) application is typically used to seek FDA clearance for class I or II medical devices (instruments, bone grafts, plates, etc.). Class III medical devices (pacemakers, cardiovascular stents, total disc replacements, etc.) cannot use the 510(k) application process and instead must submit a PMA.

## Investigational Device

An investigational device is a device that has not received marketing clearance from the FDA and is undergoing study. Prodisc-L was classified as an investigational device prior to FDA approval. Prodisc-C is still classified as an investigational device.

## Multi-center

Multi-center refers to more than 1 investigational site.

## Prospective

Prospective refers to a study that was designed before any patients received implantations. Prospective studies begin tracking patients prior to receiving a treatment. A protocol guides the study and ensures pertinent data collection. A prospective study is widely accepted as the most rigorous design.

## Retrospective

Retrospective refers to a study which relies on going back and collecting and reviewing data on cases which have already been completed. Data may often be incomplete due to the variation of statistics, parameters, and information collected at the time of the procedure along with a lack of protocol associated with the procedure at the time it was performed.

## Randomized

Enrolled patients are randomly assigned to treatment groups. Patients in the Prodisc-L study were randomized 2:1 to fusion: for every 2 patients that were treated with Prodisc-L, 1 patient was treated with the fusion control.

# 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.

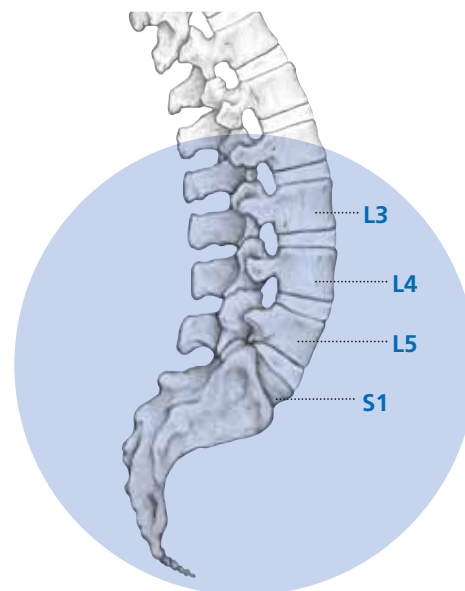
## Contraindications

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)
- 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

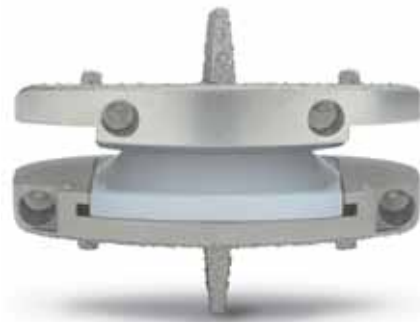
Correct placement of the device is essential to optimal performance. Use of the Prodisc-L Total Disc Replacement should only be undertaken after the surgeon has become thoroughly knowledgeable about spinal anatomy and biomechanics, has had experience with anterior approach spinal surgeries, and has had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

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## 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 one of the following by CT, MRI, discography, plain film, myelography and/or flexion/extension films: instability ( $\geq 3$  mm translation or  $\geq 5^\circ$  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



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**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.

| <b>Patients</b>               | <b>Circumferential Fusion</b> | <b>Prodisc-L Randomized</b> |
|-------------------------------|-------------------------------|-----------------------------|
| Patients                      | 80                            | 162                         |
| Follow-up rate                | 88.5%                         | 91.0%                       |
| <b>Demographics</b>           |                               |                             |
| Male                          | 46.3%                         | 51.2%                       |
| Female                        | 53.8%                         | 48.8%                       |
| Mean age (years)              | 40.2                          | 39.6                        |
| Mean BMI (kg/m <sup>2</sup> ) | 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 ( $p < 0.05$ ).\*

| <b>Treated Level</b>       | <b>Circumferential Fusion</b> | <b>Prodisc-L Randomized</b> |
|----------------------------|-------------------------------|-----------------------------|
| L3/L4                      | 3.8%                          | 1.9%                        |
| L4/L5                      | 33.8%                         | 33.3%                       |
| L5/S1                      | 62.5%                         | 64.8%                       |
| <b>Intraoperative Data</b> |                               |                             |
| Mean operative time (min)  | 219                           | 121*                        |
| Mean blood loss (cc)       | 451                           | 203*                        |
| Hospital stay (days)       | 4.4                           | 3.5*                        |

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

**Note:** For complete Prodisc-L IDE study results, please see the *Summary of Safety and Effectiveness Data* at [www.fda.gov](http://www.fda.gov).

# Device Safety and Effectiveness

## Intraoperative Complications

– Fusion and Prodisc-L patients experienced a low rate of complications.

|  | <b>Circumferential Fusion</b> | <b>Prodisc-L Randomized</b> |
|--|-------------------------------|-----------------------------|
| 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.

|                             | <b>Circumferential Fusion</b> | <b>Prodisc-L Randomized</b> |
|-----------------------------|-------------------------------|-----------------------------|
| Device Success <sup>†</sup> | 97.3%                         | 96.3%                       |

<sup>†</sup> 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 ( $p < 0.05$ ).<sup>\*</sup>

|                                    | <b>Circumferential Fusion</b> | <b>Prodisc-L Randomized</b> |
|------------------------------------|-------------------------------|-----------------------------|
| Neurological Success <sup>††</sup> | 81.4%                         | 91.2% <sup>*</sup>          |

<sup>††</sup> No decline in motor status, sensory deficit and reflexes

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

# Patient Improvement in Pain and Disability

## Oswestry Disability Index (ODI)

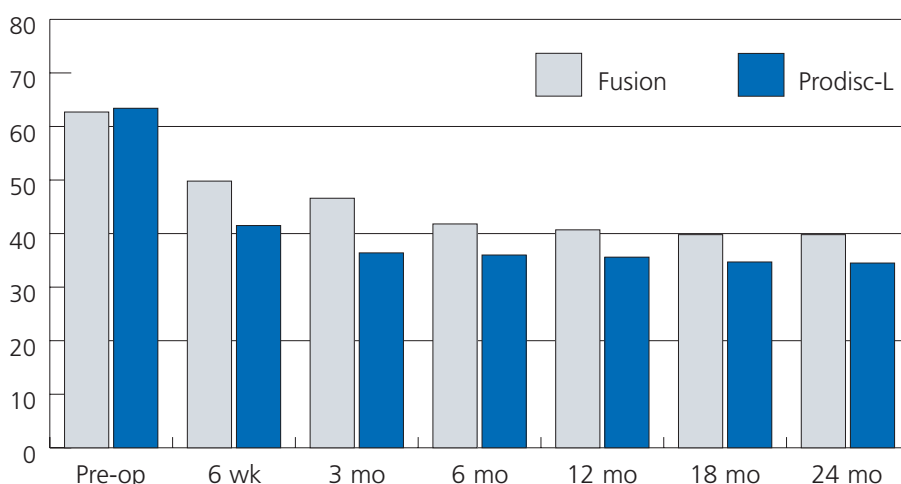
– Prodisc-L patients demonstrated a statistically significant difference in ODI improvement compared to fusion patients at 24 months ( $p < 0.05$ ).\*

– 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 ( $p < 0.05$ ), Wilcoxon rank sum test

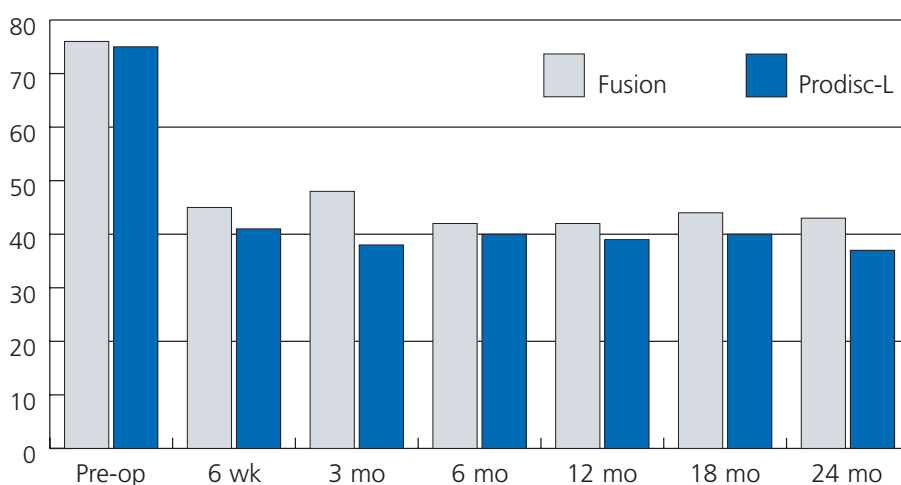
## Mean ODI Scores



## 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

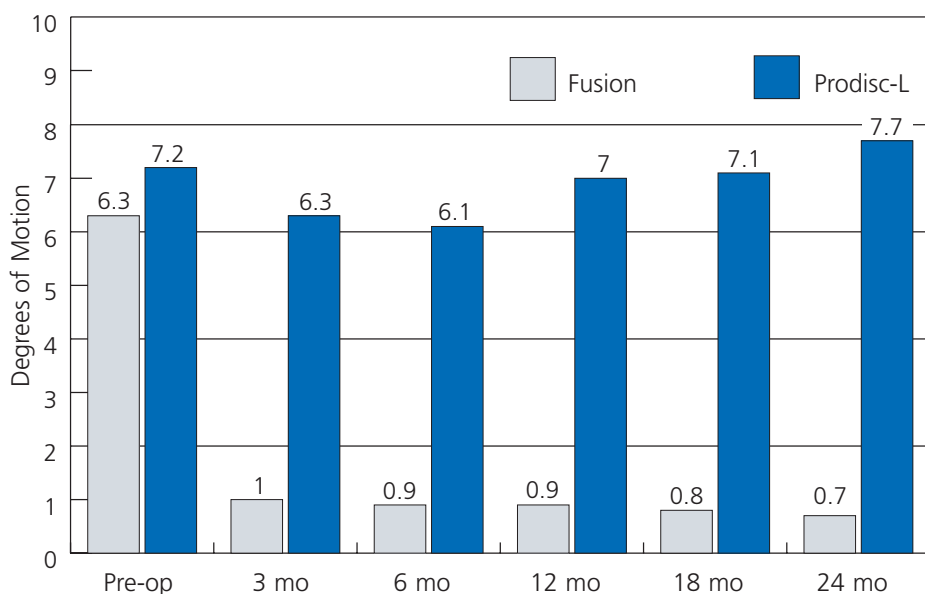
## Range of Motion (ROM)

- 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<sup>†</sup> 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<sup>\*\*</sup> at 24 months.

## Flexion/Extension ROM (Mean values)



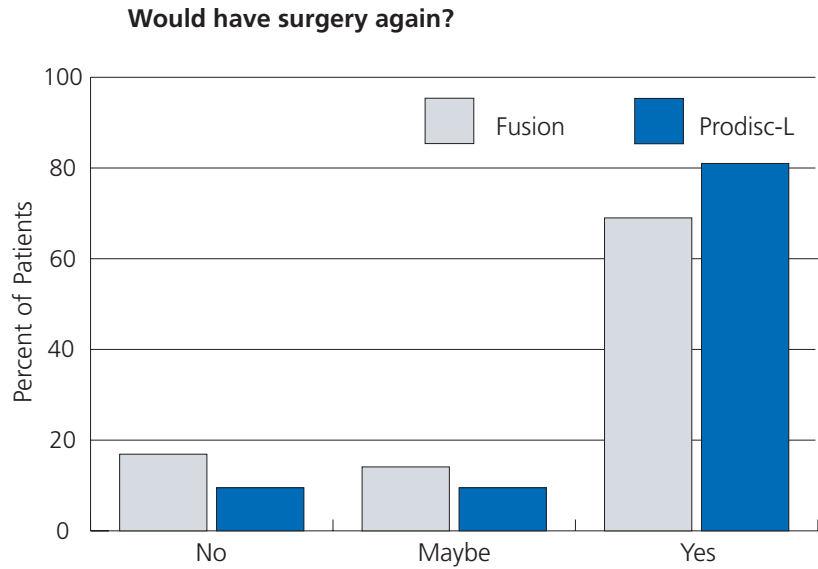
<sup>†</sup> Normal motion defined as > 6° (with ± 3° measurement error applied) to 20° at L3/L4 or L4/L5, and > 5° (with ± 3° measurement error applied) to 20° at L5/S1

<sup>\*\*</sup> 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.



– 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.

**Overall success of Prodisc-L Total Disc Replacement was determined to be noninferior to circumferential fusion ( $p < 0.0001$ ).\*\***

| 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%                |
| <b>Overall Success</b> | <b>45.1%</b>           | <b>63.5%**</b>       |

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

\*\* P-value  $< 0.0001$  for a test of non-inferiority using a non-inferiority margin of 12.5%.

# 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<br>Randomized | Prodisc-L Non-<br>Randomized |
|----------------------------|-------------------------|------------------------------|
| Patients                   | 162                     | 50                           |
| <b>Intraoperative Data</b> |                         |                              |
| Mean operative time (min)  | 121                     | 125                          |
| Mean blood loss (cc)       | 204                     | 189                          |
| Hospital stay (days)       | 3.5                     | 3.4                          |
| <b>Criteria</b>            |                         |                              |
| 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%                        |
| <b>Overall Success</b>     | <b>63.5%</b>            | <b>66.7%</b>                 |

# Conclusions

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## Conclusions

The Prodisc 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.

**Overall success of Prodisc-L Total Disc Replacement was determined to be noninferior to circumferential fusion ( $p < 0.0001$ ). \***

\* P-value  $< 0.0001$  for a test of non-inferiority using a non-inferiority margin of 12.5%.







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