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RANDOMIZED TRIAL

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# Lumbar Total Disc Replacement for Discogenic Low Back Pain: Two-year Outcomes of the activL Multicenter Randomized Controlled IDE Clinical Trial

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**Study Design.** A prospective, multicenter, randomized, controlled, investigational device exemption (IDE) noninferiority trial.

**Objective.** The aim of this study was to evaluate the comparative safety and effectiveness of lumbar total disc replacement (TDR) in the treatment of patients with symptomatic degenerative disc disease (DDD) who are unresponsive to nonsurgical therapy.

**Summary of Background Data.** Lumbar TDR has been used to alleviate discogenic pain and dysfunction while preserving segmental range of motion and restoring stability. There is a paucity of data available regarding the comparative performance of lumbar TDR.

**Methods.** Patients presenting with symptomatic single-level lumbar DDD who failed at least 6 months of nonsurgical management were randomly allocated (2:1) to treatment with an investigational TDR device (activL®, n = 218) or FDA-approved control TDR devices (ProDisc-L or Charité, n = 106). The hypothesis of this study was that a composite effectiveness outcome at 2 years in patients treated with activL would be noninferior (15% delta) to that in controls.

**Results.** The primary composite endpoint of this study was met, which demonstrated that the activL TDR was noninferior to control TDR ($P < 0.001$). A protocol-defined analysis of the primary composite endpoint also confirmed that activL was superior to controls ($P = 0.02$). Radiographic success was higher with activL versus controls (59% vs. 43%; $P < 0.01$). Mean back pain severity improved by 74% with activL and 68% with controls. Oswestry Disability Index scores decreased by 67% and 61% with activL and controls, respectively. Patient satisfaction with treatment was over 90% in both groups at 2 years. Return to work was approximately 1 month shorter ($P = 0.08$) with activL versus controls. The rate of device-related serious adverse events was lower in patients treated with activL versus controls (12% vs. 19%; $P = 0.13$). Surgical reintervention rates at the index level were comparable (activL 2.3%, control 1.9%).

**Conclusion.** The single-level activL TDR is safe and effective for the treatment of symptomatic lumbar DDD through 2 years.

**Key words:** activL, artificial disc, back pain, degenerative disc disease, motion preservation, randomized controlled trial, total disc replacement.

**Level of Evidence:** 2

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The device(s)/drug(s) that is/are the subject of this article is/are being evaluated as part of an ongoing FDA-approved investigational protocol (IDE) or corresponding national protocol for treatment of single-level degenerative disc disease (DDD) of the lumbar spine (L4 to S1) in patients who have been unresponsive to at least 6 months of prior conservative care. Aesculap Implant Systems, Inc. (Center Valley, PA, USA) grant funds were received in support of this work.

Relevant financial activities outside the submitted work: board membership, consultancy, expert testimony, payment for lectures, patents, royalties, stocks, payment for development of educational presentations, travel/accommodations/meeting expenses.



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Low back pain is one of the most common health complaints worldwide with a point prevalence of 18% and a 1-year prevalence of 38%.[1] The etiology of low back pain is multifactorial with several potential pain generators including the intervertebral discs and the facet joints. Accurate identification of the pain generators is critical, particularly when discogenic pain is suspected, so

that intervention may be properly targeted. In patients with progressively symptomatic degenerative disc disease (DDD), significant pain and quality of life limitations can be associated with a substantial economic burden.[2]

Traditionally, management of lumbar DDD was limited to either nonsurgical treatment or fusion of the affected level. During the last decade, surgical treatment for lumbar DDD has increased 2.4-fold in the United States.[3] However, reoperation rates of 12–19% over 5 years follow-up have been reported due to complications such as pseudarthrosis, adjacent segment degeneration, and incomplete pain relief.[4] Fusion necessarily sacrifices motion at the treated level and places increased stresses on adjacent levels. Considerable research has focused on the development of total disc replacements (TDR) as a motion-preserving alternative to fusion.

The goal of TDR is to alleviate the pain and dysfunction associated with symptomatic DDD while preserving segmental range of motion and restoring stability. On the basis of randomized controlled trials comparing TDR to fusion surgery, two lumbar artificial discs (Charité, DePuy Spine and ProDisc-L, Synthes Spine) have been approved by the FDA in the United States.[5–7] However, the comparative safety and effectiveness of lumbar TDRs are not well characterized.[8,9] The purpose of this randomized controlled trial was to evaluate the safety and effectiveness of a novel lumbar TDR in comparison to FDA-approved TDRs through 2 years follow-up.

## METHODS

### Study Design

This was a prospective, multicenter, randomized, single-blind, controlled investigational device exemption (IDE) trial approved by the FDA and the institutional review board at each participating site. Patients provided written informed consent before any study-related procedures were performed. The trial was prospectively registered at ClinicalTrials.gov (NCT00589797).

### Patients

Eligible patients reported lumbar pain due to a radiographically confirmed diagnosis of DDD at L4-L5 or L5-S1 despite at least 6 months of nonsurgical management. Key study inclusion and exclusion criteria are provided in Table, Supplemental Digital Content 1. http://links.ww.com/BRS/B46

### Devices

The activL Artificial Disc is a modular prosthesis comprised of an inferior cobalt–chromium plate anchored in the endplate of the caudal vertebral body, an ultrahigh molecular weight polyethylene (PE) inlay located on the inferior component, and a superior cobalt–chromium component, which is anchored in the endplate of the cranial vertebral body. The PE inlay permits a limited amount of translational motion in the sagittal plane, allowing the center of rotation to remain mobile, thereby potentially increasing range of motion while reducing stress on the facet joints (Figure 1). Endplates feature a spike or central keel, based on surgeon choice and patient anatomic characteristics, to anchor the device to the vertebral bodies (Figure 2). Secondary fixation of the prosthesis to the vertebral bodies is achieved by convex endplates and an osteointegrative Plasmapore™ titanium coating with a bioactive calcium phosphate layer. The activL TDR is designed to be inserted as a single unit and therefore does not require a second distraction step.

### Procedures

Pretreatment evaluations included a medical history, physical and neurological examination, and assessment for study eligibility based on predefined inclusion/exclusion criteria. Radiographic assessments included 6-view x-rays and magnetic resonance imaging of the lumbar spine. All TDR implants were placed via an anterior retroperitoneal approach. Patients returned for follow-up visits at 6 weeks, 3 months, 6 months, and annually thereafter. A physical

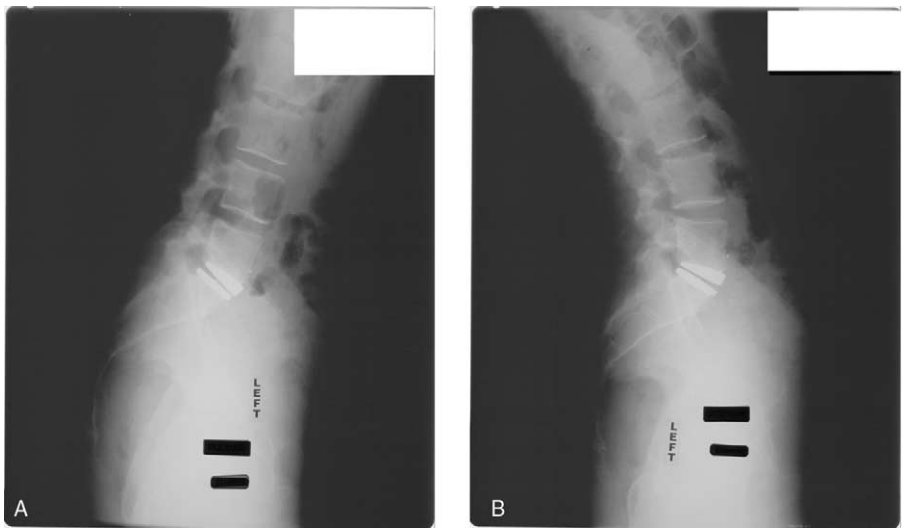


**Figure 1.** Flexion (left) and extension (right) radiographs demonstrating normal L5-S1 range of motion 1 year after activL total disc replacement implant.

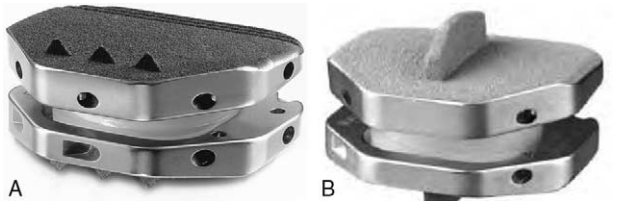


**Figure 2.** activL total disc replacement. Implant features a spiked (left) or keeled (right) cobalt–chromium endplate with an ultrahigh molecular weight polyethylene inlay.

examination, neurological assessment, and 6-view x-rays were performed at all follow-up visits.

### Outcomes

The primary endpoint of this study was a composite treatment success outcome at the 2-year follow-up visit. Treatment success required patients to meet all of the following criteria: a) ≥15 point improvement in Oswestry Disability Index (ODI), b) maintenance or improvement in neurological status, c) maintenance or improvement in range of motion at the index level, d) freedom from revision, reoperation, removal, or supplemental fixation at the index level, and e) freedom from serious device-related adverse events (AEs). Secondary outcomes included back pain severity, ODI, health-related quality of life assessed with the SF-36 questionnaire, patient satisfaction, return to work, range of motion at the index level, radiographic evaluations of device status, AEs, and reoperations. A serious AE was defined as any event that was fatal, was life-threatening, required prolonged hospitalization, resulted in permanent anatomic or physiological impairment, caused a malignant tumor, or resulted in distress, congenital anomaly, or death of a fetus. Serious device-related AEs were those specifically caused by the TDR.

### Hypotheses

The primary hypothesis was that the composite treatment success outcome at 2 years in patients treated with the activL disc would be noninferior to controls. A noninferiority margin of 15% was specified in the protocol. The FDA subsequently requested to also use a 10% noninferiority margin. A test for superiority was specified *a priori* if noninferiority was met.[10]

### Sample Size

Sample size was estimated using an O'Brien–Fleming group sequential spending function. Assumptions included a 65% success rate in each group, one-sided alpha = 0.05, power = 80%, 15% noninferiority margin, 2:1 allocation ratio, 10% loss to follow-up, and an interim analysis when at least 70% of patients in each group completed 2-year follow-up. A sample size of 194 activL patients and 97 controls was calculated using EAST version 5 (Aptiv Solutions, Reston, VA).

### Randomization

Patients were randomly allocated to implant with activL or control artificial discs using a 2:1 permuted block randomization scheme at each site. In patients randomized to the activL group, a spike or keel endplate was selected based on surgeon's preference. In patients allocated to the control group, choice of TDR (ProDisc-L or Charité) was also based on surgeon's preference. In general, ProDisc-L users selected the activL keel design and Charité users selected the activL spike design due to comparable endplate fixation characteristics.

### Blinding

Patients were blinded to treatment assignment through 2 years post-treatment. The Clinical Events Committee (CEC) was blinded to treatment assignment and patient outcomes to the extent possible. Investigators were aware of treatment assignment. All statistical analyses were performed in a blinded fashion.

### Data Quality

Data were monitored by an independent contract research organization. A CEC reviewed AEs and secondary surgical interventions to ensure consistency in reporting, and adjudicated all AEs. An imaging core laboratory independently reviewed radiographic endpoints.

### Statistical Methods

Continuous data were reported as mean ± standard deviation and categorical data were reported as frequencies and percentages. Comparisons of baseline characteristics were performed with independent samples t-test, Wilcoxon signed rank test, or Fisher's exact test, as appropriate. Main outcomes were reported using an intent-to-treat population (ITT), which included all randomized patients regardless of actual treatment. Superiority assessments of the primary endpoint utilized an O'Brien–Fleming sequential spending function, which included an interim analysis tested at $P < 0.019$ and, if noninferiority was not established at the interim analysis, a final analysis including complete 2-year follow-up, tested at $P < 0.044$. Sensitivity analyses were performed for the primary endpoint in order to assess the impact of missing data under a variety of plausible assumptions.

## RESULTS

### Participant Flow and Accountability

A total of 324 patients (218 activL, 106 control) were randomized at 14 sites between January 2007 and December 2009 (figure in Supplemental Digital Content 1 http://links.lww.com/BRS/B46). Through the 2-year follow-up period, follow-up compliance was 83% with activL and 80% with control.

### Patient Characteristics

Baseline patient characteristics, including demographics, medical history, symptom severity, radiographic data, and neurological status were comparable between groups (Table 1). Mean age was 39 years and patients typically

**TABLE 1. Baseline patient characteristics**

| Variable | activL *n* = *218* | Control *n* = *106* |
|---|---|---|
| Demographics | | |
| Age, years | 39 ± 9 | 40 ± 9 |
| Male gender, n (%) | 116 (53) | 53 (50) |
| Body mass index, kg/m$^2$ | 27 ± 4 | 27 ± 4 |
| Medical history, n (%) | | |
| Current narcotic use | 184 (84) | 96 (91) |
| Musculoskeletal/connective tissue | 93 (43) | 41 (39) |
| Smoking history | 84 (39) | 43 (41) |
| Gastrointestinal | 67 (31) | 34 (32) |
| Cardiovascular | 67 (31) | 31 (29) |
| Neurologic | 55 (25) | 31 (29) |
| Previous lumbar surgery | 52 (24) | 30 (28) |
| Cervical pain | 42 (19) | 26 (25) |
| Pulmonary | 37 (17) | 17 (16) |
| Endocrine/metabolic | 22 (10) | 15 (14) |
| Renal | 20 (9) | 17 (16) |
| Hepatic/biliary | 14 (6) | 13 (12) |
| Symptoms | | |
| Oswestry Disability Index (ODI) | 57 ± 14 | 59 ± 14 |
| Back pain severity | 79 ± 15 | 79 ± 15 |
| Health-related quality of life | | |
| Physical Component Summary (PCS) | 30 ± 6 | 28 ± 6 |
| Mental Component Summary (MCS) | 39 ± 14 | 40 ± 15 |
| Radiographic characteristics, n (%) | | |
| Decreased disc height | 159 (73) | 71 (67) |
| Herniated nucleus pulposus | 152 (70) | 83 (78) |
| Facet joint degeneration | 52 (24) | 30 (28) |
| Facet joint/endplate osteophytes | 44 (20) | 17 (16) |
| LF, AF, or facet joint hypertrophy | 40 (18) | 18 (17) |
| Instability | 16 (7) | 10 (9) |
| Vacuum phenomenon | 13 (6) | 12 (11) |
| Range of motion* | | |
| Rotation (FE), degrees | 5.6 (−1.4 to 26.9) | 5.6 (−0.7 to 19.4) |
| Translation (FE), mm | 0.3 (−0.4 to 3.8) | 0.5 (−1.4 to 2.8) |
| Rotation (lateral), degrees | 0.5 (−2.3 to 12.5) | 0.6 (−3.3 to 10.0) |

*AF, annulus fibrosus; FE, flexion–extension; LF, ligamentum flavum.*

**Values are median (min–max).*

**TABLE 2. Operative details**

| Variable | activL *n* = *218* | Control *n* = *106* | *P* |
|---|---|---|---|
| Anterior surgical approach, n (%) | | | 0.66 |
| Retroperitoneal | 215 (99) | 104 (98) | |
| Transperitoneal | 3 (1) | 2 (2) | |
| Index level, n (%) | | | 0.52 |
| L5-S1 | 156 (72) | 72 (68) | |
| L4-L5 | 62 (28) | 34 (32) | |
| Operative time, minutes | 110 ± 43 | 119 ± 52 | 0.12 |
| Blood loss, cc* | 100 (10–900) | 100 (5–1,800) | 0.23 |
| Hospital stay, days | 2 ± 1 | 2 ± 1 | 0.95 |

**Values are median (min–max).*

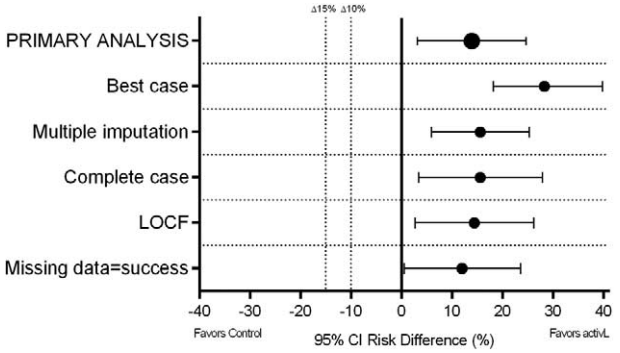


**Figure 3.** Primary and sensitivity analyses for composite endpoint at 2 years. Noninferiority with activL is demonstrated if the entire 95% confidence interval is greater than the prespecified noninferiority margin. Superiority with activL is demonstrated if the entire 95% confidence interval is greater than 0. In the primary analysis, treatment success was noninferior to controls at a 15% margin and a 10% margin (both $P < 0.001$) and also demonstrated superiority ($P = 0.02$). Sensitivity analyses corroborated the conclusions from the primary analysis. Primary analysis = all missing data conservatively counted as failure in each group; best case = missing data counted as success for activL and failure for control; multiple imputation = missing data replaced using multiple imputation procedures; complete case = missing data excluded from denominator; LOCF = last observation carried forward; missing data = success = all missing data counted as success in both groups.

presented with severe back pain, moderate/severe back-specific disability, and decreased disc height.

## Operative Details

A TDR was successfully placed in 100% of patients assigned to activL. One patient in this group erroneously received a control device; data from this patient were included in the activL group in accordance with ITT. Of the 106 controls, 64 received the ProDisc-L, 41 received the Charité artificial disc, and 1 patient did not receive a TDR due to an intraoperative posteroinferior rim fracture. A TDR was placed at L5-S1 in 70% of the patients and at L4-L5 in 30% of the patients. Operative time, procedural blood loss, and hospital stay were comparable between the groups (Table 2).

## Primary Endpoint: Composite Treatment Success Outcome

The overall treatment success rate at 2 years with activL was noninferior to controls using margins of 10% and 15% (both $P < 0.001$). Following establishment of noninferiority, the composite primary endpoint was tested for superiority, demonstrating a higher treatment success rate with activL versus controls ($P = 0.02$). A number of sensitivity analyses were performed that corroborated the findings of the primary analysis. Overall, the treatment success rate with activL remained superior to that with controls under all plausible scenarios (Figure 3). Components of the primary endpoint are presented in Table 3. Patients treated with the activL disc had higher rates of radiographic success (59% vs. 43%; $P < 0.01$) and ODI success (75% vs. 66%; $P = 0.08$) compared with controls.

## Secondary Effectiveness Outcomes

Most secondary outcomes at 2 years favored the activL group, although statistical significance between groups was not achieved. Over the 2-year follow-up period, back pain severity improved 74% ($79 \pm 15$ to $21 \pm 25$) with activL and 68% ($79 \pm 15$ to $26 \pm 30$) with controls, on average (Figure 4). Similarly, ODI improved 67% ($57 \pm 14$ to $19 \pm 18$) with activL and 61% ($59 \pm 14$ to $24 \pm 20$) with controls through 2 years (Figure 5). Health-related quality of life similarly improved over 2 years between the groups (Figure 6). The percentage of patients reporting improvement in back pain severity $\geq$20 mm (90% vs. 83%), ODI $\geq$15 points (88% vs. 81%), and Physical Component

**TABLE 3. Components of Primary Composite Endpoint at 2 Years**

| | Main Analysis* | | | Complete Case Analysis† | | |
|---|---|---|---|---|---|---|
| Type of Analysis | activL | Control | *P* | activL | Control | *P* |
| ODI success‡ | 75.2% | 66.0% | 0.09 | 87.4% | 80.2% | 0.14 |
| Neurological success§ | 80.3% | 76.4% | 0.47 | 92.9% | 93.0% | 1.0 |
| Radiographic success¶ | 58.7% | 42.5% | <0.01 | 69.2% | 52.9% | 0.01 |
| Device success‖ | 84.4% | 84.9% | 1.0 | 95.6% | 96.5% | 1.0 |
| Freedom from device-related serious AE** | 76.6% | 70.8% | 0.28 | 85.4% | 77.3% | 0.12 |

**Missing data counted as failure, denominators are 218 for activL and 106 for control.*

*†Missing data excluded from denominator, denominators range from 182 to 185 for activL and from 85 to 88 for controls.*

*‡Improvement ≥15 points in Oswestry Disability Index from baseline.*

*§Maintenance or improvement in neurological status compared with baseline.*

*¶Maintenance or improvement in range of motion at index level.*

*‖Freedom from device failure requiring revision, reoperation, removal, or supplemental fixation.*

***Adverse event attributable to the device that was fatal, was life-threatening, required prolonged hospitalization, resulted in permanent anatomic or physiological impairment, caused a malignant tumor, or resulted in distress, congenital anomaly, or death of a fetus.*

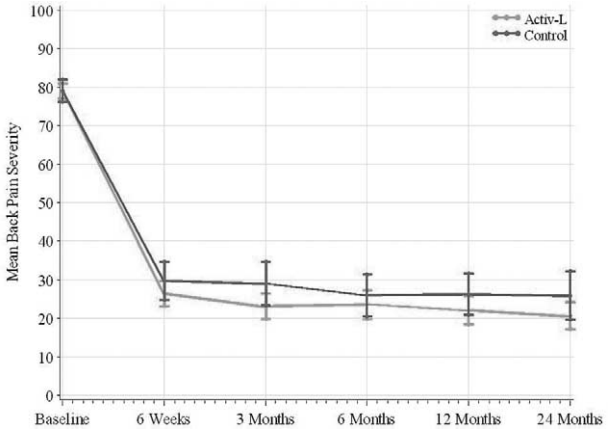


**Figure 4.** Back pain severity through 2 years. Values are mean ± 95% confidence interval.

Summary score ≥15% (88% vs. 81%) all favored the activL group. Patient satisfaction with treatment was over 90% in each group at 2 years (Table 4). The percentage of patients working full-time with no restrictions increased from 33% at pretreatment to 57% at 2 years with activL and from 33% to 49% with control ($P = 0.39$). Return to work was 1 month sooner ($P = 0.08$) with activL (68 days) compared with controls (97 days). Of patients who were not participating in recreational activities before TDR treatment, the percentage of those reporting regular participation at 2 years was 54% with activL and 39% with control ($P = 0.02$). The percentage of patients who regularly consumed narcotic medications decreased in each group over the 2-year follow-up period (activL: 65% to 31%, control: 61% to 33%; $P = 0.68$).

### Radiographic Findings

Two cases of subsidence and 1 case of device migration were identified through 2 years, all in the control group. Device disassembly was noted in 1 (0.5%) activL patient and 2 (2.3%) controls. Heterotopic ossification interfering with range of motion was identified in 1.6% and 1.1% of patients treated with activL and control, respectively. In each group, mean disc height increased from 8 ± 2 mm at baseline to 14 ± 2 mm at 2 years. The percentage of patients with disc height increase >3 mm was 94% with activL and 87% with controls ($P = 0.09$). Mean range of motion at the index level increased in all radiographic views with activL compared with baseline. Change in range of motion in lateral flexion–extension radiographs was statistically greater with activL compared with controls in segmental rotation (+0.9° vs. −1.4°; $P < 0.01$) and translation (+0.6 mm vs. +0.2 mm; $P < 0.001$) but not in lateral rotation on side-bending radiographs (+0.6° vs. +0.8°; $P = 0.52$).

### Complications

Serious AEs, regardless of cause, were less common in patients treated with activL versus controls through 2 years (30% vs. 43%; $P = 0.02$). Serious AEs related to the TDR were also less common with activL (12% vs. 19%; $P = 0.13$). The most commonly reported device-related serious AEs were lumbar/leg pain (6.9% vs. 15.1%) and implant subsidence (1.4% vs. 1.9%) (Table 5). The percentage of patients undergoing surgical reintervention at the index level was comparable between groups through 2 years (activL 2.3, control 1.9; $P = 1.0$). The reasons for reintervention were ongoing pain (4), device malposition (2), and lumbar spinal stenosis (1).

## DISCUSSION

The results of this randomized controlled trial demonstrate that the activL Artificial Disc provides clinically meaningful reductions in back pain and improvements in back-specific disability and health-related quality of life through 2 years. The primary composite treatment success endpoint with activL was statistically superior compared with FDA-approved TDRs.

The control TDRs utilized in this study previously demonstrated favorable clinical outcomes versus single-level fusion surgery in FDA-IDE randomized controlled trials. Zigler and colleagues[7] evaluated the safety and effectiveness of the ProDisc-L TDR versus circumferential fusion for

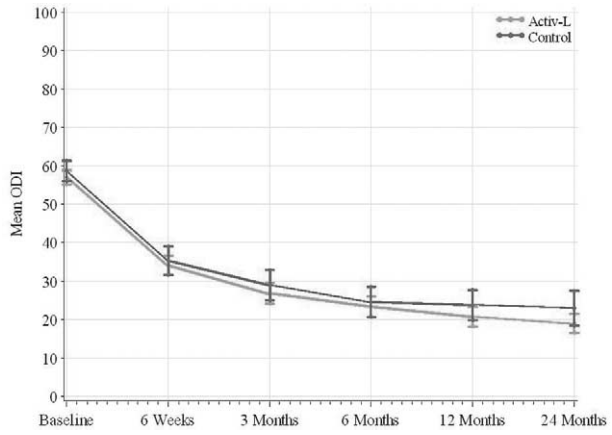


**Figure 5.** Oswestry Disability Index scores through 2 years. Values are mean ± 95% confidence interval.

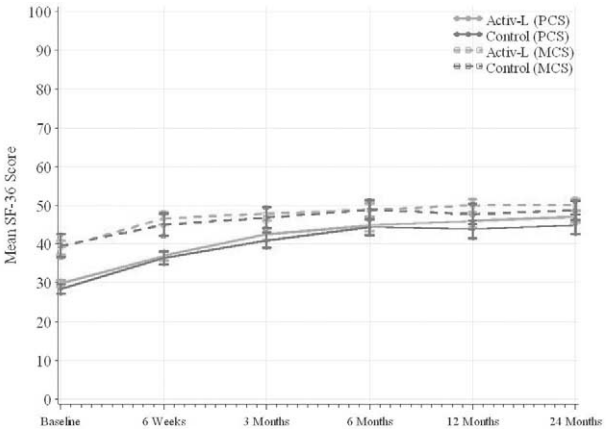


**Figure 6.** Health-related quality of life through 2 years. Values are mean ± 95% confidence interval. MCS, Mental Component Summary; PCS, Physical Component Summary.

**TABLE 4. Secondary Effectiveness Outcomes at 2 Years**

| Type of analysis | activL | Control | *P* |
|---|---|---|---|
| Back pain severity improvement ≥20 mm | 90.0% | 82.8% | 0.11 |
| ODI improvement ≥15 points | 87.7% | 80.5% | 0.14 |
| ODI improvement ≥15% | 90.9% | 88.5% | 0.52 |
| PCS improvement ≥15% | 86.7% | 80.2% | 0.20 |
| MCS improvement ≥15% | 56.1% | 55.8% | 1.00 |
| Very/somewhat satisfied with treatment | 94.1% | 93.1% | 0.79 |
| Definitely/probably would have surgery again | 91.4% | 94.3% | 0.48 |
| Treatment very/moderately effective in eliminating symptoms | 84.0% | 79.3% | 0.39 |

*MCS, Mental Component Summary; ODI, Oswestry Disability Index; PCS, Physical Component Summary; missing data excluded from denominator, denominators range from 180 to 187 for activL and from 86 to 87 for controls.*

single-level discogenic low back pain. Patients treated with the ProDisc-L TDR reported higher rates of ODI success, neurologic success, and patient satisfaction at 2 years. The FDA-IDE trial of the Charité TDR[5,6] randomized patients with single-level lumbar DDD to TDR or anterior lumbar interbody fusion. Patients treated with the Charité TDR had shorter hospitalization and reported lower levels of disability, lower reoperation rates, and higher rates of satisfaction at 2 years. These two FDA -IDE studies demonstrated that TDRs are effective treatments for single-level lumbar DDD in well-selected patients who have failed nonoperative treatment.

**TABLE 5. Serious Adverse Events Through 2 Years**

| Type of Analysis | activL | Control | *P* |
|---|---|---|---|
| Serious AE | 30.3% | 43.4% | 0.02 |
| Device-related serious AE* | 12.4% | 18.9% | 0.13 |
| Lumbar/leg pain | 6.9% | 15.1% | 0.03 |
| Implant subsidence | 1.4% | 1.9% | 0.66 |
| Rheumatoid arthritis | 0.9% | 0% | 1.0 |
| Implant migration | 0.5% | 0.9% | 0.55 |
| Operative bleeding | 0.5% | 0% | 1.0 |
| Adjacent vertebral fracture | 0.5% | 0% | 1.0 |
| Ankylosing spondylitis | 0.5% | 0% | 1.0 |
| Facet joint deterioration | 0.5% | 0% | 1.0 |
| Spinal stenosis | 0.5% | 0% | 1.0 |
| Unilateral motor deficit, persistent | 0.5% | 0% | 1.0 |
| Unilateral motor deficit, transient | 0.5% | 0% | 1.0 |
| Implant expulsion | 0% | 0.9% | 0.33 |
| Nondevice-related serious AE† | | | |
| Cervical pain | 1.8% | 4.7% | 0.16 |
| Retrograde ejaculation | 1.8% | 2.8% | 0.69 |
| Bowel obstruction | 1.4% | 1.9% | 0.66 |
| Appendicitis | 1.4% | 0.9% | 1.0 |
| Substance dependence | 1.4% | 0.9% | 1.0 |
| Nonlumbar joint surgery | 1.4% | 0% | 0.55 |
| Cancer | 0.5% | 1.9% | 0.25 |
| Knee pain | 0% | 1.9% | 0.11 |
| Suicide ideation/attempt | 0% | 1.9% | 0.11 |
| Incisional hernia | 0% | 1.9% | 0.11 |

*AE = adverse event.*

**All device-related serious AEs listed.*

*†All nondevice-related serious AEs with incidence ≥1% in either group listed.*

A recent meta-analysis of randomized controlled trials reported that TDR improved physical function, reduced pain, and shortened hospital stay in relation to fusion, although no differences were noted for operating time, procedural blood loss, and long-term complication rates.[11] Additionally, the cost-effectiveness of TDR is reported to be at least comparable, if not superior, compared with fusion.[12] Data from the current investigation suggest that the effectiveness and safety of activL is superior to that of the control TDRs. Given the superiority of control TDRs versus fusion in historical studies and the favorable outcomes of activL versus control TDRs in the current study, it appears plausible that activL offers advantages in comparison to fusion surgery.

The design attributes of the activL disc may account for the improved patient outcomes compared with control TDRs. The primary design advancements of the activL TDR compared with control TDRs relate to device insertion technique and range of motion. Both control TDRs are designed so that the endplates are inserted and secured without the core. After endplate placement, the disc space is distracted to allow the core to be seated in the inferior endplate. By comparison, the activL disc is implanted as a single unit (inferior and superior endplates and PE inlay) and therefore does not require this second distraction step. Additionally, the ultrahigh molecular weight PE inlay permits limited translation of the inlay, which improves range of motion, mimics the native nucleus, and may protect the facets. This device attribute likely contributed to the superior ROM outcomes with activL versus control TDRs. The influence of specific device- and procedure-related differences on patient outcomes deserves further study.

This study had several limitations. First, the long-term durability of the activL TDR is unknown and requires further investigation. Recent studies with the ProDisc-L[4,13] and Charité[14] TDR devices have reported excellent patient outcomes through 5 years. Second, a TDR should only be used in patients with confirmed lumbar DDD refractory to nonsurgical treatment. Third, although patients, the CEC, and statisticians were blinded to treatment allocation and imaging was independently reviewed by a core laboratory, surgeons and clinical outcome assessors were not blinded, which may influence study results. Finally, this study was underpowered to evaluate activL in comparison to each control device separately. This limitation is partially mitigated by the fact that patient characteristics and main outcomes with the ProDisc-L and Charité devices were comparable (Table, Supplemental Digital Content 2 http://links.lww.com/BRS/B46). The strengths of this study included a randomized design, rigorous study entry criteria, and use of validated outcome measures.

## CONCLUSION

The activL TDR is safe and effective for the treatment of symptomatic lumbar DDD through 2 years with superior performance compared with FDA-approved TDRs.

### ➢ Key Points

- A total of 324 patients with single-level lumbar degenerative disc disease unresponsive to at least 6 months of nonsurgical management were randomized to treatment with the activL (n = 218) or control (n = 106) total disc replacement.
- The primary composite treatment success endpoint was statistically superior with the activL implant versus controls at 2 years ($P = 0.02$).
- Radiographic success, defined as maintenance or improvement in range of motion at 2 years, was significantly higher in activL (59%) versus controls (43%).
- Device-related serious adverse events were less common in patients treated with activL versus controls (12% vs. 19%).

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