# Neurological complications of lumbar artificial disc replacement and comparison of clinical results with those related to lumbar arthrodesis in the literature: results of a multicenter, prospective, randomized investigational device exemption study of Charité intervertebral disc

Invited submission from the Joint Section Meeting on Disorders of the Spine and Peripheral Nerves, March 2004

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*Object.* Arthrodesis is the gold standard for surgical treatment of lumbar degenerative disc disease (DDD). Solid fusion, however, can cause stress and increased motion in the segments adjacent to the fused level. This may initiate and/or accelerate the adjacent-segment disease process. Artificial discs are designed to restore and maintain normal motion of the lumbar intervertebral segment. Restoring and maintaining normal motion of the segment reduces stresses and loads on adjacent level segments. A US Food and Drug Administration Investigational Device Exemptions multicentered study of the Charité artificial disc was completed. The control group consisted of individuals who underwent anterior lumbar interbody fusion involving BAK cages and iliac crest bone graft. This is the first report of Class I data in which a lumbar artificial disc is compared with lumbar fusion.

*Methods.* Of 304 individuals enrolled in the study, 205 were randomized to the Charité disc-treated group and 99 to the BAK fusion–treated (control) group. Neurological status was equivalent between the two groups at 6, 12, and 24 months postoperatively. The number of patients with major, minor, or other neurological complications was equivalent. There was a greater incidence of both major and minor complications in the BAK fusion group at 0 to 42 days postoperatively. Compared with data reported in the lumbar fusion literature, the Charité disc–treated patients had equivalent or better mean changes in visual analog scale and Oswestry Disability Index scores.

*Conclusions.* The Charité artificial disc is safe and effective for the treatment of single-level lumbar DDD, resulting in no higher incidence of neurological complications compared with BAK-assisted fusion and leading to equivalent or better outcomes compared with those obtained in the control group and those reported in the lumbar fusion literature.

KEY WORDS • lumbar spine • artificial disc replacement • neurological complication • metaanalysis

MANY procedures have been developed to treat abnormalities and degeneration in the intervertebral disc. The associated pathological entities include herniation of the nucleus pulposus, DDD, and seg-

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*Abbreviations used in this paper:* ALIF = anterior lumbar interbody fusion; BMP = bone morphogenetic protein; CoCrMo = cobalt-chromium-molybdenum; CT = computerized tomography; DDD = degenerative disc disease; FDA = Food and Drug Administration; FEA = finite element analysis; IDE = Investigational Device Exemptions; MR = magnetic resonance; ODI = Oswestry Disability Index; PLIF = posterior lumbar interbody fusion; ROM = range of motion; TLIF = transforaminal lumbar interbody fusion; VAS = visual analog scale; VB = vertebral body.

mental instability. In recent years, the diagnostic accuracy and description of these abnormalities have been aided by the development of water-soluble myelography, MR imaging, provocative discography, diagnostic blocks, and high-resolution CT scanning techniques with administration of both intravenous and intrathecal contrast. During the past 20 years, multiple therapeutic advances have been made to aid in the surgical management of lumbar DDD. These advances include rigid segmental pedicle screw fixation, titanium and polymer interbody cage fusion, and fusion involving preprocessed allograft interbody spacers. In addition to instrumentation and fusion devices, osteobiological materials have been developed to reduce or elim-

inate the need for iliac crest autograft while maintaining a high rate of solid arthrodesis. These include demineralized bone matrix, platelet-rich plasma, bone marrow aspirate, stem cell harvesting technology, BMPs, and numerous osteoconductive bone graft extenders.

Currently, multiple approaches to lumbar fusion have been reported with varying rates of success. It has become widely recognized that instrumentation-augmented posterolateral fusion is insufficient to manage the problems of lumbar DDD caused by discogenic pain in the anterior column. Although high arthrodesis rates have been reported after stand-alone ALIF,[5,8–10,27,28,35,40–42,50] circumferential fusion involving interbody stabilization and arthrodesis conducted via ALIF, PLIF, or TLIF has consistently demonstrated very high rates of arthrodesis.[4,7,17,18,22,32,34,36,44,46–49,52]

*Rationale for an Artificial Disc*

Fusion is designed to eliminate the normal motion of one or more lumbar segments. The inherent problem with surgical arthrodesis of the degenerative lumbar segment is that it merely masks the true disease process by eliminating the intervertebral motion and its normal physiological function. In using lumbar artificial disc technology, the restoration and maintenance of normal physiological motion are provided rather than the alternative—the elimination of motion.[3,14,15,20] Fusion is successful in many cases because the motion itself is the root cause of pain owing to inability of the degenerative segment to support the weight of the body comfortably. Thus, when the segment is fused, it no longer moves and therefore cannot cause pain. Solid fusion, however, can result in stress and increased motion in the segments adjacent to the fused level,[12,23] which may initiate and/or accelerate the degenerative disease process in adjacent segments. Hilibrand and colleagues[21] demonstrated this concept in the cervical spine. The premise of surgery involving a lumbar artificial disc is fourfold: 1) abnormal motion will be corrected; 2) intervertebral space height, lordosis, and the instantaneous axis of rotation will be restored; 3) the corrected normal intervertebral motion will be maintained over time; and 4) the patient will experience pain relief and return of function. If these goals are achieved, it stands to reason that the segments adjacent to the dynamically stable segment would not be subject to abnormal loads and motions, and therefore, deceleration or elimination of adjacent-level disc disease would follow.

*Rationale of Lumbar Artificial Disc Design*

Numerous artificial discs have been designed during the past 35 years, but most have never being produced.[33] There are four types of dynamic stabilization systems derived from artificial disc technology. First, nucleus pulposus replacements with a hygroscopic gel or fluid-filled cylindrical sacs are for use after standard discectomy in which the anulus maintains normal disc space height.[24,53,54] Second, posterior dynamic stabilization systems increase posterior-column stiffness.[16,43,45] Third, total lumbar joint replacement replaces both anterior and posterior lumbar segment components. Currently, no such devices are available in any US FDA trial, nor are any being used elsewhere in the world. Finally, total disc replacement is used to replace the entire lumbar disc. These devices require healthy facet joints as well as intact posterior ligaments and muscular

structures. In addition to hard implants having metal ends that attach to the osseous endplates, there are also some soft implants composed entirely of elastic with potential laminations or of a sac of fiber filled with some fluid or matrix.[25,26,29,51] Presently, none of the soft implants is being tested in US FDA trials.

An artificial lumbar disc should reproduce the biomechanical functions of a normal disc. Additionally, an artificial disc should reduce the mechanical forces transmitted to the adjacent segments, slowing or halting the degenerative changes. A total discectomy eliminates the chance of a disc herniation and would probably retard spondylosis, stenosis, and instability at the dynamically stabilized segment. By restoring the disc space height, an artificial disc should increase the exiting foraminal height and prevent compression on the exiting nerve roots at the stabilized level.

Because of the mechanical changes in the degenerative lumbar segment, the natural disease process places abnormal forces on the adjacent levels. The application of an artificial disc should restore normal motion, height, and lordosis, and the forces on the adjacent level(s) should be decreased. Thus, an artificial disc may have beneficial effects compared with those attendant on the natural history of the nonoperated degenerative state on the adjacent-level rate of progression.

The design of artificial lumbar discs has multiple, very strict requirements. These devices must have superb mechanical strength and endurance. They are designed to last several decades because many will be implanted in young individuals. The base materials need to be biocompatible without causing significant surrounding inflammatory reaction either due to the base material reaction or secondary to any wear-related debris. The base material or potential debris of these devices must not produce organotoxic or carcinogenic reaction.

The biomechanical functional movement requirements of an artificial lumbar disc are stringent because they need to replicate the full biomechanical functions of a normal disc. The normal motion of a lumbar segment includes independent translation and rotation in all three planes of motion (flexion–extension, lateral bending, and axial rotation). Normal motion is often represented as a factor of coupled motion in two planes. The implant-related geometrical configuration and materials would determine the static configuration, dynamic motion, schematics, and any constrained nature of the motion. The exact placement of the artificial lumbar disc in the disc space is determined by its biomechanical design. Different designs require different degrees of accuracy. Fixed pivot devices may require a higher placement precision than devices that include a sliding core or an elastopolymer.

Potential problems exist with regard to the choice of base materials with which to construct an artificial disc. In cases involving a hard artificial lumbar disc, there is the possibility of the load-bearing surfaces becoming worn during the clinical lifetime of the device. Broadly, the materials are categorized into three groups: metal-on-metal, metal/ceramic, and metal/plastic designs. Those composed of metal-on-metal material have the potential of metal and/or metal ionic debris. The ceramic component may shatter in metal/ceramic designs. Plastic wear or cold flow may occur in metal/plastic discs. The plastic components in the current artificial

hip and knee designs survive a mean of 10 years before requiring revision.[1,55] If an artificial lumbar disc were made of these same base materials, CoCrMo and ultra–high molecular-weight polyethylene, it may be inferred that the plastic component would also require replacement at a mean of 10 years following implantation. There are, however, three primary differences between total joint replacement and artificial disc replacement. First, with each step the hip and the knee move approximately 50°, whereas the lumbar spine only tilts a few degrees. This greatly decreases the so-called sandpaper effect by more than one order of magnitude. Second, in the artificial disc design, the high-density polyethylene moves to reduce the stresses, is not constrained, and has two opposite surfaces of contact that share the movement. This is in marked contrast to the hips, where the plastic is constrained in a ball/socket-type joint. In the hip joints, the high-pressure points that arise at the constrained metal–plastic interface greatly accelerate the plastic wear. Because of the unconstrained nature of the plastic in the lumbar application, there are no wear-accelerated pressure points. Furthermore, in a report from Europe, the authors noted the absence of plastic wear 10 years after implantation,[29] which implies that the estimation of the lifetime of the material is far greater than that used in the hips and knees.

Four different artificial disc designs have been the subject of US FDA IDE trials (Fig. 1), with enrollment in two still open. It is notable that these devices do not restore the posterior-column degenerative changes, nor do they augment them. In fact, a contraindication to application of any of these devices would be spondylolysis or significant spondylosis, with facet joint hypertrophy and potential for ongoing nerve root compression. These devices have either an unconstrained or a semiconstrained design with a fixed center of rotation.

The artificial ProDisc (Spine Solutions, Inc., New York, NY) was designed by Thierry Marnay in the late 1980s. The ProDisc has a spherical articulation with two CoCrMo endplates and an ultra–high molecular-weight polyethylene core fixed to the lower device endplate, yielding a semiconstrained system. This design provides for a fixed pivot that places the instantaneous axis of rotation within the caudal VB rather than the disc space. The ProDisc is affixed to the vertebral endplates by a central keel (or fin), which is driven into the vertebral endplates. Enrollment in the ProDisc IDE study has concluded, and the study is expected to be completed by the end of 2004 after a 2-year follow-up period. The FlexiCore artificial disc (SpineCore, Inc., Summit, NJ) is a metal-on-metal semiconstrained device with a CoCrMo load-bearing surface. It has a 13-mm ball-and-socket joint, which places the stationary center of rotation centrally between the endplates. It has teeth on the outer ring of the implant endplates for fixation to the outer ring of the vertebral endplates. The US FDA IDE trial of the FlexiCore artificial disc began in August 2003. The Maverick artificial disc (Medtronic Sofamor Danek, Inc., Memphis, TN) has a semiconstrained metal-on-metal design. Like the ProDisc, the Maverick implant has central keels that are driven into the vertebral endplates for fixation and stability. Enrollment in the Maverick US FDA IDE trial is currently ongoing.

*Charité Artificial Disc*

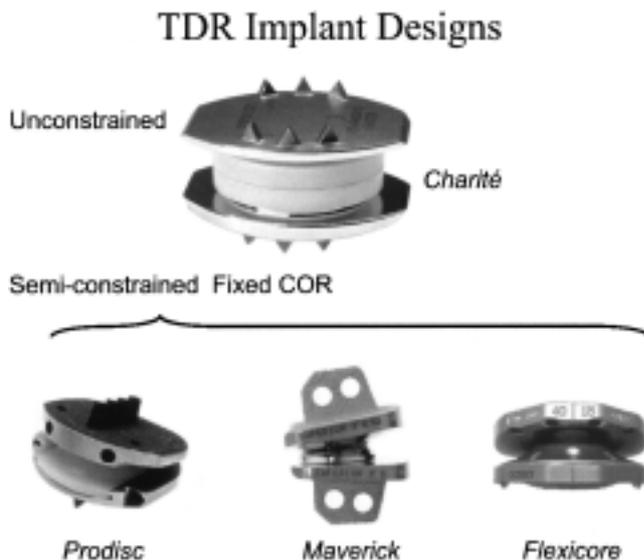The Charité artificial disc (Fig. 2) (DePuy Spine, Rayn-



FIG. 1. Photograph showing the four lumbar artificial discs, which can be classified into unconstrained and semiconstrained designs. The Charité artificial disc is the only unconstrained artificial disc. The Charité disc and the ProDisc are metal/plastic designs, whereas the Maverick and the FlexiCore discs are metal-on-metal–bearing surfaces.

ham, MA) was designed to duplicate the kinematics and dynamics of a normal lumbar motion segment[33,37] while restoring disc space height and motion segment flexibility. The Charité artificial disc is composed of two CoCrMo endplates and a free-floating ultra–high molecular-weight polyethylene core. The primary attachment of the plates is made possible by three anterior and posterior "teeth," which are forcefully implanted into the cranial and caudal vertebral endplates. Layers of plasma-sprayed porous titanium and calcium phosphate were added to the Charité disc in 1998. This coating provides for potential osseous ingrowth and long-term stability of the plates after implantation.[38] The coating is not a feature of the US version of the Charité disc but is expected to be incorporated into the design following FDA approval. The plates are currently available in five footprint geometrical configurations adaptable to the size of the vertebral endplates, each with four available angles (0, 5, 7.5, and 10°). This allows for built-in lordosis with variations of 0 to 20°.

The unconstrained design allows the core to translate dynamically within the disc space during normal spinal motion, moving posteriorly in flexion and anteriorly in lumbar extension (Fig. 3). The mobile sliding core of the Charité disc works in a similar fashion to the mobile knee bearing in many of the contemporary knee implant designs. In essence, this could be considered a second-generation device or an advanced-type design over a fixed pivot, much like the mobile core in the knee is considered an advanced design over fixed bearings. The Charité design provides not only unloading of the posterior facet structures during this normal replication of motion but also allows forgiveness for slight off-center positioning of the implant.

In a cadaveric model, Cunningham and associates[12] demonstrated that the center of rotation for Charité close-
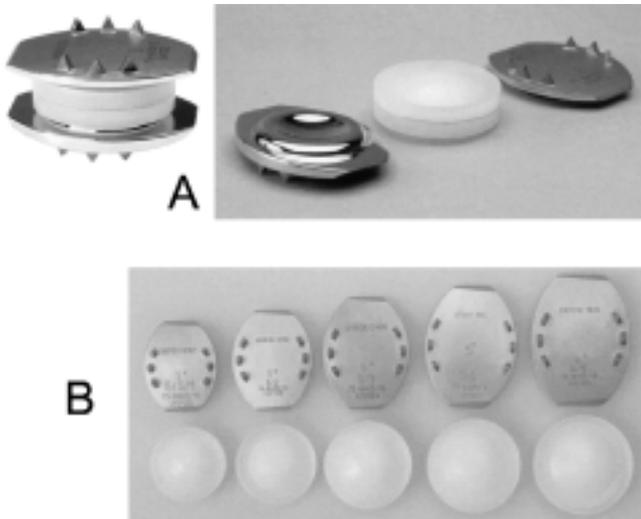
FIG. 2. Photographs. A: Constructed and disassembled parts of the two CoCrMo endplates and ultra–high molecular-weight polyethylene core of the Charité artificial disc. B: The various footprint sizes available for the Charité artificial disc. The metal endplates are available in a variety of angulations allowing for built-in lordosis of 0 to 20˚.
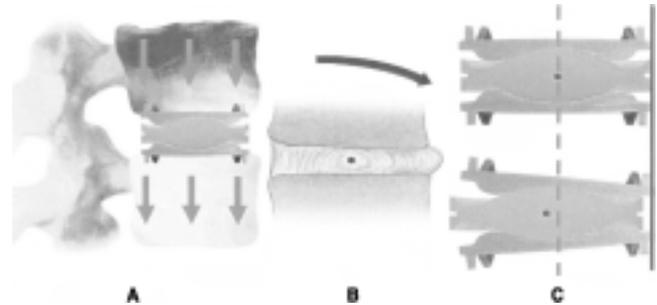


FIG. 3. Illustrations of the Charité artificial disc implanted in a spine model. Note the position of the device and how it transmits forces down the anterior column (A), the translation of a normal lumbar disc in flexion–extension motion (B), and the translation provided by the device's sliding core (C).

ly mimicked that of a normal lumbar disc at the level of implantation and at the superior adjacent level. Fusion, however, greatly distorted the center of rotation at the level of implantation and at the superior adjacent level (Fig. 4). In addition, compared with a normal intact segment, the Charité device did not adversely affect the ROM at adjacent levels while fusion caused a "marked increase" in adjacent-level motion. The FEA supports this concept. In a two-level three-dimensional nonlinear finite element mo-

del, Moumene and Geisler[39] described the effect of fusion compared with Charité disc–related treatment on the facet loading of the adjacent segment. In axial rotation, fusion increased the load on the facet joints at the adjacent level by 96% compared with the normal intact nonoperated segment. The Charité device decreased the facet joint load at the adjacent level by 50% compared with the normal intact nonoperated segment (Fig. 5).

### Clinical History of the Charité Artificial Disc

The third-generation Charité artificial disc has been used in Europe since 1987. Worldwide experience with this unconstrained anatomical replacement disc now comprises more than 7000 cases. In 1997, Lemaire and coworkers[31] described a series of 105 Charité disc–treated patients who underwent follow-up evaluation for 5 years. They reported 84.8% with good or excellent clinical outcome. In
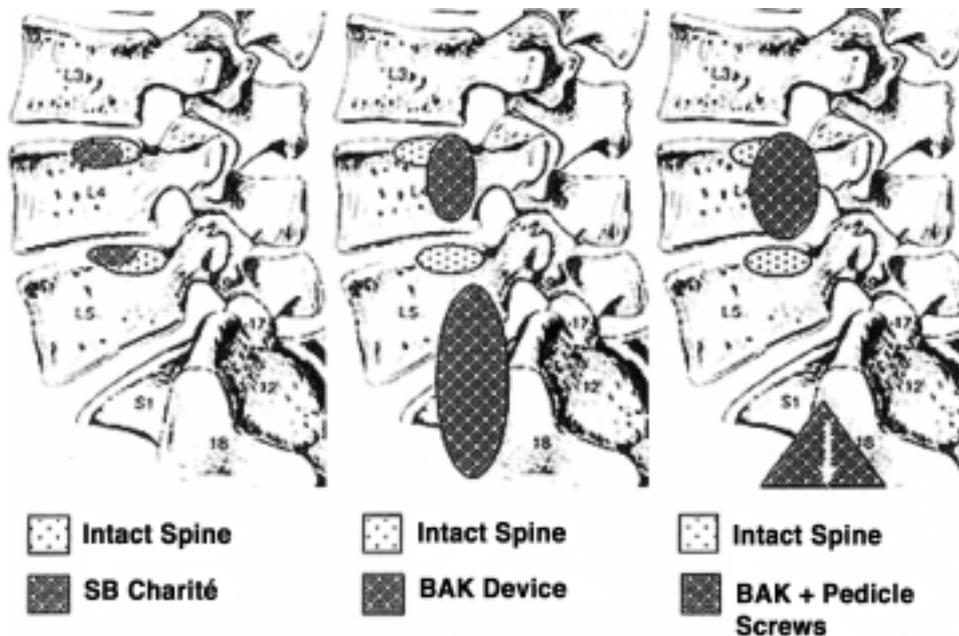


FIG. 4. Representations of the calculated centers of intervertebral rotation at the surgically treated and superior adjacent levels. The Charité artificial disc (left), stand-alone BAK fusion (center), and BAK fusion with transpedicular fixation (right) are compared. Reprinted with permission from Cunningham, et al.
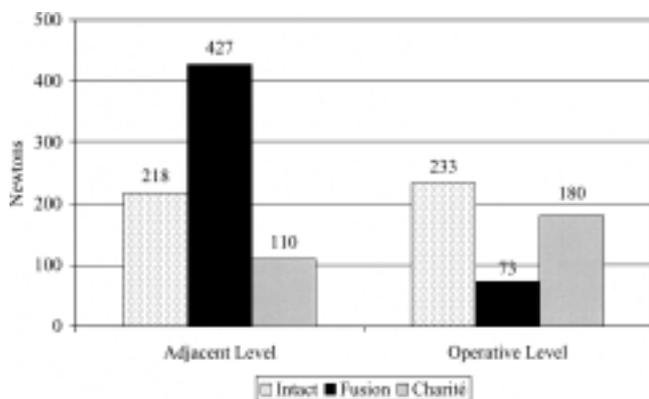
FIG. 5. Bar graph showing operative and adjacent-level facet loads derived from FEA in which Charité artificial disc replacement and L4–5 fusion data were compared.

2002, Lemaire[30] described 10-year results obtained in 100 patients in whom the Charité disc was implanted. He reported good or excellent clinical outcome in 90% and a return-to-work rate of 91%. Lemaire reported no device failures in this or an earlier series. David[13] reported good or excellent clinical outcome in 75% of his series of 92 patients with 5-year follow up. Zeegers, et al.,[56] discussed 50 patients in a Dutch series; the authors found good results in 70% of patients with a 2-year follow-up. Cinotti and colleagues[11] reported a 70% rate of good or excellent clinical outcome in 46 Italian patients.

## Clinical Material and Methods

The FDA IDE multicenter trial of the Charité artificial disc was performed at 14 centers (Appendix) across the US. The primary inclusion criteria included single-level DDD at L4–5 or L5–S1 confirmed by MR imaging and provocative discography, age 18 to 60 years, ODI score greater than or equal to 30, back pain VAS-rated score greater than or equal to 40 with no radicular component (referred leg pain was permitted), and failed nonoperative treatment of at least 6 months' duration. The primary exclusion criteria included previous thoracic or lumbar fusion, multilevel DDD, facet joint arthrosis, noncontained herniated nucleus pulposus, osteoporosis, spondylolisthesis slip greater than 3 mm, scoliosis greater than 11°, and midsagittal stenosis less than 8 mm.

Local institutional review board approval was obtained at each site. The study protocol indicated that participants at each site were to perform five training cases prior to randomization; 71 training cases were performed to implant the Charité device. Patients were then randomized into a Charité group and a BAK cage (Zimmer, Warsaw, IN) group (ALIF and iliac crest autograft). Two hundred five patients underwent placement of the Charité disc and 99 underwent BAK cage placement (2:1 ratio). Demographic features were not significantly different between the two groups with respect to age or sex. There was no intergroup difference with respect to levels treated: L4–5, 61 cases (29.7%) in the Charité group and 32 (32.3%) in the BAK group; L5–S1, 144 (70.3%) in the Charité group and 67 (67.7%) in the BAK group.

*Surgical Technique*

All surgeries were performed via an anterior retro- or transperitoneal approach, which was conducted by a general or vascular surgeon. The BAK cages were implanted according the manufacturer's instructions with two cages packed with iliac crest autograft at each treatment level. After the direct anterior approach (L4–5 or L5–S1) to the disc space is completed, the anterior longitudinal ligament is dissected to fit the width of the disc implant. A generous (complete) discectomy is performed, with care taken not to disturb the osseous endplates, although all of the cartilaginous endplates are removed. The discectomy is enlarged to expose the VB circumferential rim of cortical bone. Posterior osteophytes are removed using a 0.25-in chisel or a Kerrison punch. This disc space is prepared in anticipation for accepting the flat metal endplates of the Charité implant. Care is required during this stage not to damage the osseous endplates because these support the metal plates of the artificial disc. Additionally, especially at L5–S1, the anterior longitudinal ligament that is undergoing degenerative disease progression can be exceptionally thick (sometimes > 1 cm). The anterior longitudinal ligament needs to be removed to define clearly the anterior osseous margin so that after disc placement, its anterior cleats can be confirmed, fluoroscopically and visually, to be below the anterior cortical margin.

Once the disc material and cartilaginous endplates are removed, a sizer is used to measure the disc space fluoroscopically to choose the matching metal endplate footprint. A spreader is then placed into the disc space to produce parallel distraction, which is accomplished using a paint paddle–type instrument placed within the spreader; the posterior ligament is stretched and/or ripped to some extent, increasing the posterior height of the disc space. Once the disc space has been distracted, additional disc material that was contained within the buckled ligament within the neural canal is often delivered into the disc space. This is then removed using a Kerrison or biopsy punch. Next, the metal endplates of the artificial disc are inserted and tapped into position. Care is taken to have the centerline marked as determined fluoroscopically either using a burn mark or a self-drilling 4.5-mm screw (SLIM-LOC; DePuy Spine) placed within the VB cranially adjacent to the disc space. Because the screw is smooth on the top, it allows the great vessels to slide over if necessary and also provides an unambiguous unique visual and fluoroscopy marker. The metal endplates of the implant are impacted into the disc space, positioned posteriorly within it, and then parallel distraction is performed. During this expansion, it is essential that only the very lateral edges of the implant are touched with the distraction instrumentation to avoid scratching the inside of the cupped metal endplates—this would result in a very significant increase in the amount of plastic wear. Once the metal endplates have been placed, trial cores are used to size the distracted space and the final core is placed. The correct position of the plastic core is verified to ensure that it articulates with the cups and distraction is then fully removed. With a slight tapping on the core, the endplate sliders are removed (Fig. 6). The screw used for identifying the midline is removed before closure.

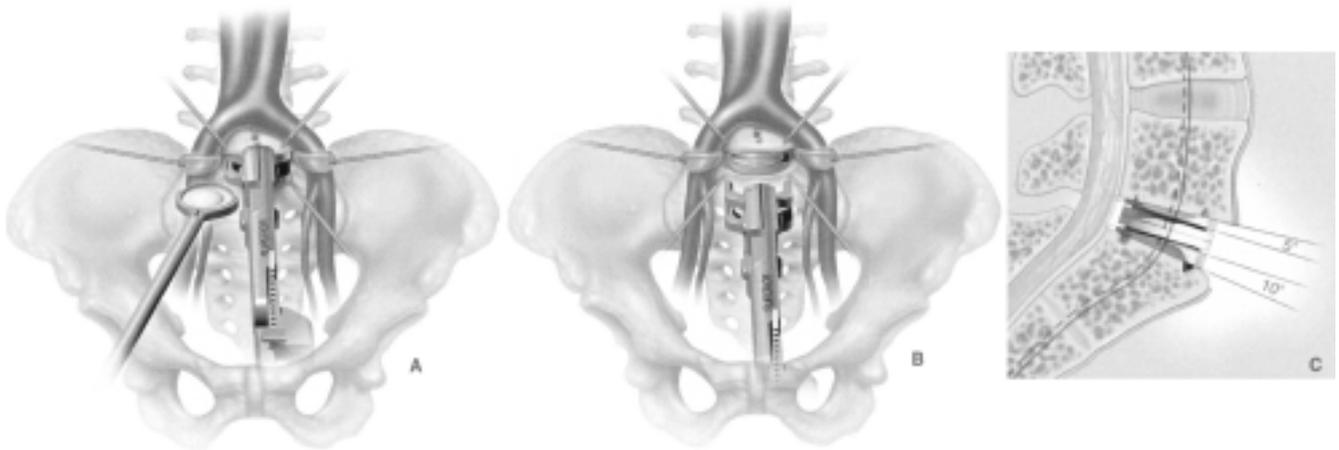In approximately two thirds of the cases during disc

Fig. 6. Schematic drawings.   A: Surgeon's view of the core insertion into the L5–S1 disc space after placement of distraction and the Charité metal endplates.   B: Surgeon's view of the final assembly of the L5–S1 Charité artificial disc. C: Lateral view cutaway of the L5–S1 Charité artificial disc. Note the angled endplates to match the lordosis in the distracted disc space.

space distraction, some epidural bleeding or significant bone bleeding along the posterior edge occurs. This is easily managed by placing strips of Avitene in the disc space and compressing them down against the remaining posterior longitudinal ligament area by using a standard 4 × 4–mm sponge. After allowing it to sit for 2 to 3 minutes, the sponge can be removed, leaving the thin layer of Avitene in place. This is easier to accomplish during the initial discectomy or after the metal endplates have been inserted than after the core is inserted. Anteroposterior and lateral fluoroscopy is used to aid in positioning the device and to provide final radiological verification. Visual verification is also required in the anterior plane to ascertain that the implant is recessed below the anterior cortical margin. A bone tamp is used on the sides of the metal endplates of the implant to make minor adjustments and also to impact the anterior cleats within the osseous structure. Patients in the BAK treatment group were required to wear a hard brace for 3 months following surgery; those in the Charité treatment group did not wear a brace. In both groups patients undertook activities progressively, as tolerated.

## Results

Patients in both groups underwent clinical and radiographic evaluation at 6 weeks and 3, 6, 12, and 24 months following surgery. Anteroposterior, lateral, and lateral flexion–extension radiographs were obtained at each time point. Patients responded to ODI, VAS, and Short Form–36 questionnaires preoperatively and at all postoperative time points according to the protocol.

### Neurological Adverse Events/Complications

Neurological status was assessed at 6, 12, and 24 months postoperatively. No significant intergroup difference with respect to neurological status was found when comparing baseline with 6-, 12-, or 24-month conditions (Table 1). There was no significant intergroup difference regarding neurological deterioration from baseline at 6 months (p =

0.4233), 12 months (p = 0.5765), or 24 months (p = 0.3242). Adverse neurological events were classified as major, minor, and other (see Table 2 for definitions). Major neurological events occurred in 10 (4.9%) of the Charité group patients and in four (4%) of the BAK fusion group patients; minor neurological events were observed in 20 (9.8%) of the former and eight (8.1%) of the latter. There were eight "other" neurological events (3.9%) in the Charité group and eight (8.1%) in the BAK fusion group (Table 2).

Neurological adverse events were also classified as related to the device or not related. There were three (1.5%) device-related neurological events in the Charité group and none in the BAK fusion group. In the Charité group one of three device-related events (nerve root injury) was classified as severe. Neurological adverse events were classified into four distinct time points (Table 3). Within 0 to 42 days following surgery the rate of major neurological events was 2.4% (five cases) in the Charité group and 5.4% (two cases) in the BAK fusion group. With respect to minor neurological events, the rate was 5.4% (11 cases) in the Charité group and 7.1% (seven cases) in the BAK fusion group.

### Clinical Results: Baseline to 24 Months Postoperatively

In the Charité group, the mean preoperative ODI score was 50.6, whereas at 24 months it was 25.8, which represented a mean change of −24.8. In the BAK fusion group, the mean preoperative ODI score was 52.1, whereas at 24 months it was 30.1, which was a mean change of −22. The second method of reporting the change in ODI scores is to sum the changes in ODI scores for all patients and calculate the mean. By this method, the mean change in ODI score from baseline to 24 months for the Charité disc was −24.2; for the BAK device it was −22.5. At all time points greater improvement in ODI scores was demonstrated in Charité disc–treated patients. Although the mean intergroup change in ODI was significantly different at all previous time points, it was not significantly different at 12 (p = 0.1388) and 24 months postoperatively (p = 0.5439).

TABLE 1
*Summary of neurological changes*

| Neurological Status: Change From Baseline | No. of Patients (%) | | |
|---|---|---|---|
| | Charité | BAK | p Value |
| 6 mos | | | |
| no change | 147 (77) | 67 (76) | 0.3644 |
| significantly improved | 6 (3) | 5 (6) | |
| slightly improved | 27 (14) | 9 (10) | |
| slightly deteriorated | 9 (5) | 4 (5) | |
| significantly deteriorated | 1 (1) | 3 (3) | |
| total | 190 | 88 | |
| missing | 15 | 11 | |
| 12 mos | | | |
| no change | 153 (82) | 61 (75) | 0.6258 |
| significantly improved | 5 (3) | 2 (2) | |
| slightly improved | 19 (10) | 12 (15) | |
| slightly deteriorated | 8 (4) | 6 (7) | |
| significantly deteriorated | 2 (1) | 0 | |
| total | 187 | 81 | |
| missing | 18 | 18 | |
| 24 mos | | | |
| no change | 141 (79) | 65 (82) | 0.7053 |
| significantly improved | 2 (1) | 0 | |
| slightly improved | 19 (11) | 10 (13) | |
| slightly deteriorated | 13 (7) | 3 (4) | |
| significantly deteriorated | 4 (2) | 1 (1) | |
| total | 179 | 79 | |
| missing | 26 | 20 | |
| overall no. | 205 | 99 | |

TABLE 2
*Summary of adverse neurological events in patients undergoing disc replacement or cage-assisted fusion**

| Factor | No. of Patients (%) | |
|---|---|---|
| | Charité | BAK |
| no. of NAEs | 38 | 20 |
| no. of patients w/ NAEs | 34 (16.6) | 17 (17.2) |
| major NAE | 10 (4.9) | 4 (4.0) |
| burning or dysesthetic leg pain | 5 (2.4) | 3 (3.0) |
| motor deficit in index level | 4 (2.0) | 1 (1.0) |
| nerve root injury | 1 (0.5) | 0 |
| minor NAE | 20 (9.8) | 8 (8.1) |
| numbness in index level | 20 (9.8) | 7 (7.1) |
| numbness in sacral nerve distribution | 0 | 1 (1.0) |
| other NAE | 8 (3.9) | 8 (8.1) |
| numbness in peripheral nerve or nonindex level | 5 (2.4) | 4 (4.0) |
| positive Waddell signs | 1 (0.5) | 1 (1.0) |
| reflex change | 2 (1.0) | 2 (2.0) |
| mechanical signs (SLRT) | 0 | 1 (1.0) |

* NAE = neurological adverse event; SLRT = straight leg–raising test.

In the Charité group, the mean VAS scores were 72 and 30.6 at baseline and 24 months, respectively (mean change −41.4, mean decrease 57.5%). In the BAK fusion group, the mean VAS scores were 71.8 and 36.3 at baseline and 24 months, respectively (mean change −35.5, mean decrease 49.4%.) Using the second method for determining mean change for all patients, that for VAS score in the Charité group was −41.3, and for the BAK group was −35.1.

There is no established level of clinical significance attributed to a given decrease in ODI scores. Using a 25% improvement in ODI score as required in the protocol for FDA success, 62% of patients in the Charité group had a 25% improvement at 24 months and 49% of those in the BAK group had this same level of improvement (p = 0.0354). In a recent study, Hägg, et al.,[19] reported a 10-point improvement in ODI score (10% on a 0–100 scale because ODI scores are reported as a percentage of disability) as a clinically important difference. Figure 7 shows the percentage of patients at each follow-up time in whom improvement in ODI scores was 10 points or greater; note the initially faster rise in the percentage with significant meaningful recovery that is prolonged through the 2-year follow-up period, which was statistically significant at all time points (Fisher exact test).

Hägg, et al.,[19] also described an 18- to 19-point decrease in VAS scores as measurable clinical improvement. The FDA threshold for VAS score success is 20 points. At 24 months, 65% of Charité disc–treated patients had a decrease in VAS score of at least 20 points; in the BAK group this threshold of clinical success was observed in 56% (p = 0.1028).

The mean flexion–extension ROM at 24 months in the

Charité group was 7.4 ± 5.28° (mean ± standard deviation), whereas in the BAK group it was 1.1 ± 0.87° (Fig. 8).

*A Metaanalysis of Charité and Fusion Results*

One of the criticisms of this IDE study has been the use of stand-alone BAK fusion as the control. Some surgeons would argue that this lumbar fusion procedure is no longer state-of-the-art for the treatment of lumbar DDD. At the time the protocol was approved, however, the FDA recommended that the control group should consist of BAK cage–treated individuals. There was no other choice for the control group because IDE protocols do not allow for non-FDA–approved or off-label-use controls.

A metaanalysis of the lumbar fusion literature was conducted in an effort to compare the clinical results of this IDE study with other methods of lumbar fusion involving different implants. In March 2004, a Medline search of articles published between 1964 and the present was performed using the following search criteria: "Lumbar + Fusion or Fusions + Human + English Language − Biomechanics − Review"; 434 references were available for review. To be included in the analysis, the following were required: a minimum follow-up period of 2 years, baseline and 2-year or greater follow-up ODI and/or VAS scores (or report the mean change in either parameter), and a primary diagnosis in the data set of lumbar DDD. Because the use of VAS and ODI scores for clinical outcomes did not become prevalent until the late 1980s, these scales were not identified in the literature prior to 1992. Duplicate series were eliminated. The final analysis comprised 25 papers published between 1992 and 2004 and included 29 separate data sets, which were split into two groups: 360° fusion involving ALIF, PLIF, or TLIF[4,7,17,18,22,32,34,36,44,46–48,52] (Table 5) and stand-alone ALIF or PLIF[5,8–10,27,28,35,40–42,50] (Table 6).

The change in the mean VAS and ODI scores is reported because most investigators reported their results in this fashion. In the 360° fusion group, the weighted mean percent decrease in VAS was 49.1% compared with a mean

TABLE 3
*Summary of adverse neurological events stratified by postoperative time frame*

| | No. of Patients (%) | | | | | | | |
|---|---|---|---|---|---|---|---|---|
| | 0–2 Days | | >2– 42 Days | | >42–210 Days | | >210 Days | |
| Factor | Charité | BAK | Charité | BAK | Charité | BAK | Charité | BAK |
| no. of NAEs | 8 | 6 | 13 | 7 | 14 | 3 | 4 | 4 |
| no. of cases w/ NAEs | 6 (2.9) | 5 (5.1) | 12 (5.9) | 7 (7.1) | 11 (5.4) | 2 (2.0) | 4 (2.0) | 3 (3.0) |
| major NAE | | | | | | | | |
|   burning or dysesthetic leg pain | 0 | 2 (2.0) | 3 (1.5) | 0 | 2 (1.0) | 1 (1.0) | 0 | 0 |
|   motor deficit in index level | 1 (0.5) | 0 | 0 | 0 | 1 (0.5) | 1 (1.0) | 2 (1.0) | 0 |
|   nerve root injury | 1 (0.5) | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| minor NAE | | | | | | | | |
|   numbness in index level | 2 (1.0) | 2 (2.0) | 9 (4.4) | 4 (4.0) | 7 (3.4) | 0 | 2 (1.0) | 1 (1.0) |
|   numbness in lower sacral nerve distribution | 0 | 1 (1.0) | 0 | 0 | 0 | 0 | 0 | 0 |
| other NAEs | | | | | | | | |
|   numbness in peripheral nerve or nonindex level | 2 (1.0) | 0 | 0 | 3 (3.0) | 3 (1.5) | 0 | 0 | 1 (1.0) |
|   positive Waddell signs | 0 | 1 (1.0) | 1 (0.5) | 0 | 0 | 0 | 0 | 0 |
|   reflex change | 0 | 0 | 0 | 0 | 1 (0.5) | 1 (1.0) | 0 | 1 (1.0) |
|   mechanical signs (SLRT) | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 1 (1.0) |

decrease of 57.5% in the Charité IDE group. In the stand-alone fusion group, the mean percent decrease was 45.5%. In patients in the Charité IDE group the decrease in VAS-measured pain was greater than that in either approach to fusion. In regard to ODI, the mean change in the 360° fusion group was −20.6, whereas in the Charité IDE group it was −24.8. In the stand-alone fusion group, the mean change was −27.9, approximately 3% less disability as measured by ODI.

As previously discussed, there is a second method for reporting decreases in ODI scores—determining the mean of the sum of changes obtained in each individual score. To compare this mean, it is necessary to know the standard deviation of each data set. The mean change in ODI score from baseline to 24 months was compared between the following four data sets: Charité, BAK fusion (patients from the same IDE), LT-Cage (Medtronic Sofamor Danek, Inc.) with BMP-2 IDE,[8] and LT-Cage with autograft[8] (Table 6). Because the 95% confidence intervals overlap

for the mean decrease in the ODI scores, there is no statistically significant difference among the four treatments. The four treatments are clinically equivalent.

## Discussion

### Neurological Complications

The rate of major neurological complications in both the Charité group and the BAK group was small—4.9 and 4%, respectively. Just three of the neurological events in the Charité group were device related. The intergroup rate of neurological complications was equivalent; however, the rate of all neurological events was 16.6% in the Charité group and 17.2% in the BAK fusion group. These rates may seem high, but under an IDE protocol, the tracking of adverse events/complications is very strict and dissimilar to the reporting of complications in Class II or Class III data sets. The rate of neurological events was
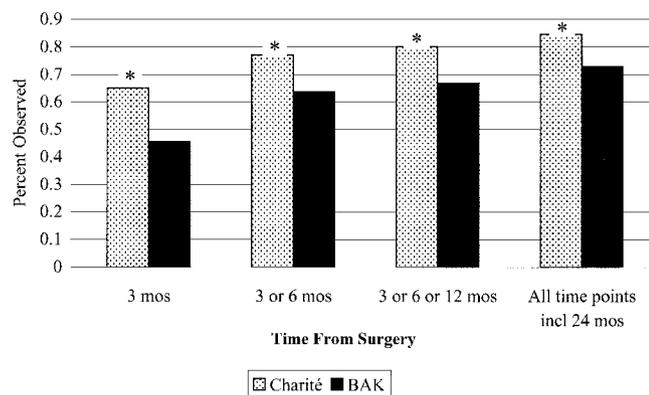


FIG. 7. Bar graph of the first incidence of 10-point ODI improvement in the Charité disc–treated group and the control BAK fusion–treated group. Note the initially faster rise in the number of patients with significant meaningful recovery, which is statistically significant at all time points (Fisher exact test). *p < 0.05.



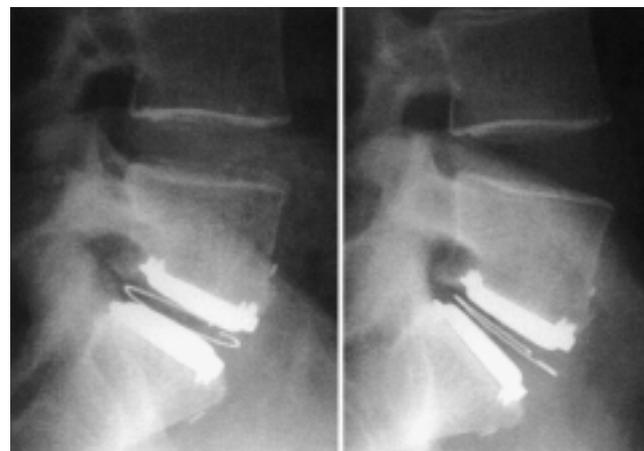FIG. 8. Radiograph of the L5–S1 Charité artificial disc in lateral flexion *(left)* and extension *(right)* at 24 months postoperatively. The measured ROM in flexion–extension was 12.9°.

TABLE 4

*Results of metaanalysis involving studies in which ODI and VAS scores were reported: 360° fusion via ALIF, PLIF, or TLIF\**

| Authors & Year | No. of Cases | Approach/ Instrumentation | % Change in Mean VAS (591 patients) | Change in Mean ODI (162 patients) |
|---|---|---|---|---|
| Soini, 1994 | 27 | FRALIF ExtPed | −47.9 | −19.0 |
| Gertzbein, et al., 1996 | 67 | FRALIF | −70.4 | |
| Hinkley & Jaremko, 1997 | 81 | AlloBDauto ALIF | −14.1 | |
| Gertzbein, et al., 1998 | 51 | FRALIF | −40.5 | |
| Whitecloud, et al., 1998 | 35 | mesh ALIF | −23.6 | |
| Leufven & Nordwall, 1999 | 29 | auto PLIF | | −61.6 |
| Tandon, et al., 1999 | 53 | Br PLIF | −12.1 | |
| Barrick, et al., 2000 | 18 | delayed FRALIF | −40.5 | −8.7 |
| Brantigan, et al., 2000 | 92 | Br PLIF | −60.0 | |
| Thalgott, et al., 2000 | 46 | mix ALIF | −56.0 | |
| Lowe, et al., 2002 | 40 | mesh TLIF | −61.4 | |
| Thalgott, et al., 2002 | 20 | 200 ALIF | −61.8 | −29.0 |
| Thalgott, et al., 2002 | 50 | mesh ALIF | −57.3 | |
| Madan, 2003 | 35 | mix PLIF | −52.4 | −36.0 |
| weighted mean | | | −49.1 | −20.6 |
| mean % change: Charité IDE cases | | | −57.5 | |
| change in means: Charité IDE cases | | | | −24.8 |

\* Allo = allograft; AlloBDauto = allograft bone dowels filled with autograft; auto = autograft; Br = Brantigan Cage; ExtPed = external transpedicular fixation; FRALIF = femoral ring allograft ALIF; mesh = titanium mesh cage; mix = mixed grafts.

markedly higher in the BAK group during the 0- to 42-day postoperative time frame, but not statistically significant. The risk of neurological complications due to the Charité device is no greater than in any ALIF procedure.

### Clinical Results and Metaanalysis

The argument that the use of BAK cage–augmented fusion as a control renders the study design inferior is undercut by results of the metaanalysis of the lumbar fusion literature. In terms of clinical outcome, the Charité procedure is equivalent to one-level BAK fusion in which iliac crest autograft is used. In comparison with 360° fusion approaches as well as stand-alone ALIF involving BMP-2 or autograft, both considered to be state-of-the-art techniques, the clinical outcomes following Charité device treatment are equivalent or better in terms of ODI and VAS scores at 24 months postoperatively.

### Surgical Experience and Training

The unconstrained design of the device is more forgiving in terms of placement than a semiconstrained design. When using fusion cages or allograft spacers, exact placement in the disc space is often unnecessary; however, precise placement is crucial to the proper functioning of the Charité prosthesis. For best results and to mimic the normal instantaneous axis of rotation of a normal intact disc, the Charité device must be placed approximately 2 to 3 mm posterior to the center of the disc space and as close to the exact center as possible in the coronal plane. Large deviations from this placement may yield less than ideal results.

Artificial disc replacement is one of the most challenging procedures in spine surgery in the senior author's experience. One cannot stress enough the importance of thorough knowledge of indications and contraindications for the Charité device as well as the anterior retroperitoneal approach, nor the associated potential complications. The learning curve will be longer for surgeons with little or no experience performing ALIF compared with those who perform it regularly. Surgeons who have not performed ALIF surgery or perform very few such procedures should resign themselves to performing multiple ALIF procedures before incorporating artificial disc technology. It is also essential that the spine surgeon work closely with a general or vascular surgeon during the approach as well

TABLE 5

*Results of metaanalysis involving studies in which ODI and VAS scores were reported: stand-alone ALIF or PLIF\**

| Authors & Year | No. of Cases | Approach/ Instrumentation | % Change Mean VAS (799 patients) | Change in Mean ODI (1186 patients) |
|---|---|---|---|---|
| Pfeiffer, et al., 1996 | 80 | ALIF w/ auto | | −35.7 |
| Tiusanen, et al., 1996 | 83 | ALIF w/ auto | | −18.3 |
| Kuslich, et al., 1998† | 299 | BAK ALIF + BAK/PLIF | −41.2 | |
| Kuslich, et al., 2000† | 185 | BAK ALIF + BAK/PLIF | −44.8 | |
| Madan & Boeree, 2001 | 27 | ALIF w/ HH | −31.4 | −26.4 |
| Burkus, et al., 2002A | 22 | AlloBDauto ALIF | −33.1 | −22.5 |
| Burkus, et al., 2002A | 24 | Allo BD BMP-2 ALIF | −54.6 | −33.5 |
| Burkus, et al., 2002B | 108 | LT auto ALIF | −50.9 | −31.3 |
| | 122 | LT BMP-2 ALIF | −53.8 | −33.4 |
| | 68 | ALIF w/ IntFix | | −21.6 |
| Pellise, et al., 2002 | 12 | ALIF w/ Br | | −69.2 |
| Beutler & Peppelman, 2003 | 104 | BAK ALIF | | −24.0 |
| Burkus, et al., 2003 | 285 | LT auto ALIF | | −26.3 |
| | 215 | LT BMP-2 ALIF | | −31.3 |
| Sasso, et al., 2004 | 48 | FRALIF | | −21.2 |
| weighted mean | | | −45.5 | −27.9 |
| mean % change: Charité IDE cases | | | −57.5 | |
| change in means: Charité IDE cases | | | | −24.8 |

\* HH = Harshill horseshoe cage; IntFix = internal fixation; LT = LT-Cage.
† Pain scale scores were converted to VAS score equivalent.

TABLE 6
*Summary of mean changes in ODI score from baseline to 24 months postoperatively, stratified by form of treatment\**

| | | LT-Cage | | |
|---|---|---|---|---|
| Variable | Charité | w/ BMP | w/ Autograft | BAK Cage |
| no. of patients | 178 | 122 | 108 | 79 |
| mean change | −24.2 | −29.0 | −29.5 | −22.5 |
| SD | 21.1 | 19.8 | 22.0 | 21.8 |
| 95% CI | (−27.3 to −21.1) | (−32.5 to −25.5) | (−33.6 to −25.4) | (−27.3 to −17.7) |

\* CI = confidence interval; SD = standard deviation.

throughout the surgery should vessel-related complications arise.

The availability of lordotic metal endplates makes it possible to create a lordosis of 0 to 20°. The use of the largest footprint prosthesis possible in the intervertebral space is preferable. At the time of publication, new third-generation instrumentation for implantation of the Charité device will allow for an intuitive, straightforward implantation of the prosthesis.

*Indications and Contraindications*

The indications for Charité artificial disc replacement studied as part of the IDE are narrow, considering all degenerative diseases of the lumbar spine. One-level DDD at L4–5 or L5–S1 is the indication tested in this FDA IDE study. One-level symptomatic DDD does not necessarily mean that a black disc will be observed on MR imaging. The discogenic pain component must be verified using provocative discography. Although discography may still be controversial in some circles, if performed correctly (injecting and verifying a nonpainful control disc first[2]), the rate of false-positive results can be decreased dramatically. Failure to perform discography in patients in whom artificial disc replacement is indicated may result in a misdiagnosis and improper use of not only the Charité artificial disc, but other total disc replacements as well. In most degenerative surgically treated discs that were diagnosed based on positive provocative discography, Modic endplate changes[6] are observed immediately adjacent to the painful disc.

If suspected, the facet joints should be precluded as a pain generator by using evocative facet blocks. In patients with severe facet joint degeneration or arthrosis Charité artificial disc replacement is contraindicated. Although FEA analysis showed that the Charité unconstrained design reduced load on the facet joints, there is no evidence that it helps to regenerate them, and no assumptions should be made that facet joint degeneration will improve following artificial disc replacement. Central canal stenosis, spondylolisthesis, scoliosis, kyphosis, and other deformity or instability are also contraindications for this procedure. Use of the Charité artificial disc in these patients may cause less than ideal results.

## Conclusions

The Charité intervertebral disc is safe and effective for the treatment of mechanical back pain caused by one-level DDD at L4-5 or L5–S1. Clinical outcomes at 2 years are equivalent to those resulting from one-level BAK fusion. Clinical outcomes are equivalent or better than those related to 360° or stand-alone interbody fusion reported in the literature; however, there is the added benefit of restoring and maintaining segmental motion 2 years postoperatively. The incidence of major neurological complications was exceedingly low and equivalent to those demonstrated in control individuals in the BAK fusion group. Accurate placement of the device within the intervertebral space is important for proper functioning of the prosthesis. The Charité artificial disc should be used in properly selected patients, and surgeon training is essential for good clinical and functional outcomes. Further follow-up evaluation beyond 2 years is recommended to corroborate the long-term results demonstrated in Europe.

## Disclosure

All authors have a financial interest in subject matter contained in this manuscript.

## United States Food and Drug Administration Disclosure

The Charité artificial disc is limited to investigational use in the US.

APPENDIX
*Summary of locations and investigators involved in the randomized, trial of the Charité disc*

| Site No. | City & State | Clinical Investigator |
|---|---|---|
| 1 | Plano, TX | Scott Blumenthal, M.D. |
| 2 | Towson, MD | Paul McAfee, M.D. |
| 3 | Louisville, KY | Richard Holt, M.D. |
| 4 | Aventura, FL | Rolando Garcia, M.D. |
| 5 | Baton Rouge, LA | Jorge Isaza, M.D. |
| 6 | Golden, CA | Doug Wong, M.D. |
| 7 | Columbus, OH | Bradford Mullin, M.D. |
| 8 | Franklin, TN | Michael McNamara, M.D. |
| 9 | Scottsdale, AZ | James Maxwell, M.D. |
| 10 | New York, NY | Fabien Bitan, M.D. |
| 11 | Chicago, IL | Fred Geisler, M.D., Ph.D. Noam Stadlan, M.D. |
| 12 | Los Angeles, CA | John Regan, M.D |
| 13 | Lockport, NY | Andy Cappucino, M.D. |
| 14 | Boston, MA | Robert Banco, M.D. |

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