BlueCross BlueShield of Alabama

Name of Policy:

Artificial Intervertebral Disc

Policy #: 150
Category: Surgery

Latest Review Date: May 2014
Policy Grade: A

Background/Definitions:

As a general rule, benefits are payable under Blue Cross and Blue Shield of Alabama health plans only in cases of medical necessity and only if services or supplies are not investigational, provided the customer group contracts have such coverage.

The following Association Technology Evaluation Criteria must be met for a service/supply to be considered for coverage:

1. *The technology must have final approval from the appropriate government regulatory bodies;*
2. *The scientific evidence must permit conclusions concerning the effect of the technology on health outcomes;*
3. *The technology must improve the net health outcome;*
4. *The technology must be as beneficial as any established alternatives;*
5. *The improvement must be attainable outside the investigational setting.*

Medical Necessity means that health care services (e.g., procedures, treatments, supplies, devices, equipment, facilities or drugs) that a physician, exercising prudent clinical judgment, would provide to a patient for the purpose of preventing, evaluating, diagnosing or treating an illness, injury or disease or its symptoms, and that are:

1. *In accordance with generally accepted standards of medical practice; and*
2. *Clinically appropriate in terms of type, frequency, extent, site and duration and considered effective for the patient's illness, injury or disease; and*
3. *Not primarily for the convenience of the patient, physician or other health care provider; and*
4. *Not more costly than an alternative service or sequence of services at least as likely to produce equivalent therapeutic or diagnostic results as to the diagnosis or treatment of that patient's illness, injury or disease.*

Description of Procedure or Service:

Cervical Artificial Disc

Several prosthetic devices are currently available for artificial intervertebral disc arthroplasty (AIDA) of the cervical spine. AIDA is proposed as an alternative to anterior cervical discectomy and fusion (ACDF) for patients with symptomatic cervical degenerative disc disease (DDD).

Cervical degenerative disc disease (DDD) is a manifestation of spinal spondylosis that causes deterioration of the intervertebral discs of the cervical spine. Symptoms of cervical DDD include arm pain, weakness, and paresthesias associated with cervical radiculopathy. Disc herniation, osteophytes, kyphosis, or instability that compress the spinal cord can result in myelopathy, which is manifested by subtle changes in gait or balance, and in severe cases leads to weakness in the arms or legs, and numbness of the arms or hands. The prevalence of DDD secondary to cervical spondylosis increases with age. An estimated 60% of individuals older than 40 years have radiographic evidence of cervical DDD. By age 65, some 95% of men and 70% of women have at least one degenerative change evident at radiographic examination. It is estimated that approximately five million adults in the United States are disabled to an extent by spine-related disorders, although only a small fraction of those are clear candidates for spinal surgery. Cervical DDD is initially treated conservatively using noninvasive measures (e.g., rest, heat, ice, analgesics, anti-inflammatory agents, exercise). Surgical intervention may be indicated if symptoms do not improve or resolve after six or more weeks, or if they progress. Candidates for surgical intervention have chronic pain or neurologic symptoms secondary to cervical DDD and no contraindications for the procedure.

Anterior cervical discectomy and fusion (ACDF) is currently considered the definitive surgical treatment for symptomatic DDD of the cervical spine. The goals of ACDF are to relieve pressure on the spinal nerves (decompression) and to restore spinal column alignment and stability. Resolution of pain and neurologic symptoms may be expected in 80% to 100% of ACDF patients. ACDF involves an anterolateral surgical approach, decompression of the affected spinal level, discectomy, and emplacement of either autograft or allograft bone in the prepared intervertebral space to stimulate healing and eventual fusion between the vertebral endplates. A metal anterior cervical plate is attached to the adjoining vertebral bodies to stabilize the fusion site, maintain neck lordosis, and reduce the need for prolonged postoperative brace application that is needed following ACDF without an anterior plate. The choice of bone material for interbody fusion in ACDF has important clinical implications. Allograft bone has several drawbacks, including a small (albeit, unproven) risk of infectious disease transmission; possible immunologic reaction to the allograft, and possible limited commercial availability of appropriate graft material. In contrast, the use of autograft bone in ACDF has potentially substantial morbidities at the harvest site, generally the iliac crest. These morbidities include moderate-to-severe, sometimes prolonged pain; deep infection; adjacent nerve and artery damage; and increased risk of stress fracture. Although there may be slight differences between autograft and allograft sources in the postoperative rate of union, clinical studies demonstrate similar rates of postoperative fusion (90%-100%) and satisfactory outcomes for single-level, anterior-plated ACDF, using either bone source. Thus, the choice of graft material involves a trade-off between the risks specific to autograft harvest versus those specific to use of allograft material. Biomechanical modeling studies have suggested that altered adjacent segment

kinematics following fusion may lead to adjacent-level DDD; however, the clinical relevance of these changes has not been established.

Artificial intervertebral disc arthroplasty (AIDA) is proposed as an alternative to ACDF for patients with symptomatic cervical DDD. In AIDA, an artificial disc device is secured in the prepared intervertebral space rather than in bone. An anterior plate is not placed to stabilize the adjacent vertebrae, and postsurgical external orthosis is usually not required. It is hypothesized that AIDA will maintain anatomical disk space height, normal segmental lordosis, and physiological motion patterns at the index and adjacent cervical levels. The potential to reduce the risk of adjacent-level DDD above or below a fusion site has been the major rationale driving device development and use. Disc arthroplasty and ACDF for single-level disease have very similar surgical indications, primarily unremitting pain due to radiculopathy or myelopathy, weakness in the extremities, or paresthesia. However, the chief complaint in AIDA candidates should be radicular or myelopathic symptoms in the absence of significant spondylosis. Patients with advanced spondylosis or hard disc herniations have a separate pathologic condition and require a different surgical approach.

Lumbar Artificial Disc
Total disc replacement, using an artificial intervertebral disc designed for the lumbar spine, is proposed as an alternative to fusion in patients with persistent and disabling nonradicular low back pain.

When conservative treatment of degenerative disc disease (DDD) fails, a common surgical approach is spinal fusion; more than 200,000 spinal fusions are performed each year. However, the outcomes of spinal fusion have been controversial over the years, in part due to the difficulty in determining if a patient's back pain is related to DDD and in part due to the success of the procedure itself. In addition, spinal fusion alters the biomechanics of the back, potentially leading to premature disc degeneration at adjacent levels, a particular concern for younger patients. During the past 30 years, a variety of artificial intervertebral discs have been investigated as an alternative approach to fusion. This approach, also referred to as total disc replacement or spinal arthroplasty, is intended to maintain motion at the operative level once the damaged disc has been removed and to maintain the normal biomechanics of the adjacent vertebrae.

Potential candidates for artificial disc replacement have chronic low back pain attributed to DDD, lack of improvement with nonoperative treatment, and none of the contraindications for the procedure, which include multilevel disease, spinal stenosis, or spondylolisthesis, scoliosis, previous major spine surgery, neurologic symptoms, and other minor contraindications. These contraindications make artificial disc replacement suitable for a subset of patients in whom fusion is indicated. Patients who require procedures in addition to fusion, such as laminectomy and/or decompression, are not candidates for the artificial disc.

Use of a motion-preserving artificial disc increases the potential for a variety of types of implant failure. These include device failure (device fracture, dislocation, or wear), bone-implant interface failure (subsidence, dislocation-migration, vertebral body fracture), and host response to the implant (osteolysis, heterotopic ossification, and pseudotumor formation).

Policy:

Effective for dates of service on or after February 1, 2014:

FDA approved **cervical artificial intervertebral disc** as a treatment for degenerative cervical disc disease **meets** Blue Cross and Blue Shield of Alabama's medical criteria for coverage when:

- Performed at **one level** from C3-C7; **AND**
- Clinical record **documents cervical radiculopathy and/or myelopathy**; **AND**
- Patients have **failed at least six weeks of conservative** management*.

*Conservative management may include rest, application of heat/ice, physical therapy, exercise, pain and/or anti-inflammatory medications.

Cervical artificial intervertebral disc as a treatment for degenerative cervical disc disease **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and are considered **investigational**:

- In patients with **isolated axial neck pain without cervical radiculopathy or myelopathy**; **OR**
- When requested **adjacent to a prior fusion**; **OR**
- Used as part of a hybrid fusion: **OR**
- When **more than one level** is requested.

Lumbar artificial intervertebral disc as a treatment for degenerative lumbar disc disease **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational.**

Effective for dates of service prior to February 1, 2014:

Artificial Intervertebral Disc as a treatment for degenerative disc disease **does not meet** Blue Cross and Blue Shield of Alabama's medical criteria for coverage and is considered **investigational**.

Blue Cross and Blue Shield of Alabama does not approve or deny procedures, services, testing, or equipment for our members. Our decisions concern coverage only. The decision of whether or not to have a certain test, treatment or procedure is one made between the physician and his/her patient. Blue Cross and Blue Shield of Alabama administers benefits based on the member's contract and corporate medical policies. Physicians should always exercise their best medical judgment in providing the care they feel is most appropriate for their patients. Needed care should not be delayed or refused because of a coverage determination.

Key Points:

This policy includes updates of the literature using the MEDLINE database (most recently performed through November 20, 2013). Two-year results of the PCM, SECURE-C, and Mobi-C discs were also reviewed.

Cervical Artificial Disc

A number of meta-analyses have been published, with varying results. The most comprehensive was a 2013 Cochrane systematic review with a meta-analysis of nine studies (2400 patients) with one to two years of follow-up. Seven of the nine studies were conducted in the U.S. as FDA-regulated investigational device exemption (IDE) trials. The quality of the evidence was graded as very low to moderate, due in part to the non-blinded outcome measures. Results of the AIDA group were statistically better than the anterior cervical discectomy and fusion (ACDF) group for many of the primary comparisons, but differences were small (<10% of the scale) and not considered to be clinically relevant. No significant difference between AIDA and fusion was found for adjacent level surgery.

Prestige Cervical Disc

The Prestige disc received FDA marketing approval in 2007. Information on the Prestige cervical disc is available from a published report of the pivotal trial and from Medtronic's premarket approval (PMA) application to FDA. These documents report results from a randomized study of anterior cervical fusion (with allograft bone and plate stabilization) versus the artificial cervical disc for patients with nonaxial pain and other symptoms secondary to radiculopathy or myelopathy that did not improve with a minimum six weeks of conservative therapy. The study was designed as a randomized, non-blinded noninferiority trial with a 10% margin. Results for 137 investigational and 148 control patients who were evaluated at two years postsurgery were presented to FDA in the PMA application. These patients represented about half of the total population (276 and 265, respectively), while the peer-reviewed paper reported on about 75% of cases.

Three primary outcome variables were used in the Prestige trial: the Neck Disability Index (NDI), neurologic status, and functional spinal unit (FSU) height. The NDI is a validated multidimensional instrument that measures the effects of pain and disability on a patient's ability to manage everyday life. It is a modification of the Oswestry Low Back Pain Index, based on the response to ten questions that focus on neck pain intensity, personal care, lifting, reading, headaches, concentration, work, driving, sleeping, and recreation. The response to each question ranges from one to five, with a lower numeric score representing a better pain and disability status for that variable. A total NDI score is obtained by adding individual question scores and dividing by the maximum total of 50, if all questions are answered. Therefore, NDI scores range from 0% to 100%, with a lower percentage indicating less pain and disability. The neurologic status is a composite measure of motor function, sensory function, and deep tendon reflexes. It is used to judge if patients are within normal parameters for those categories based on physiologic measurement. Neurologic success in the Prestige trial was based on postoperative maintenance or improvement of condition as compared to preoperative status for each component. The anterior FSU height is a radiographic measure of intradiscal space. Comparison of the immediate postoperative FSU height with the six-week postoperative value shows whether or not the disc space has decreased, which indicates that graft or device subsidence has occurred. Secondary

outcome measures include the Medical Outcomes Study 36-Item Short Form Health Survey (SF-36) Mental and Physical Component Summary scores, neck and arm pain status, patient satisfaction, patient global perceived effect, gait assessment, foraminal compression test, adjacent level stability and measurements, return to work, and physician's perception.

Both data sources for the Prestige disc trial showed equivalent results. Thus, 81% of both groups showed at least a 15-point improvement for the NDI, demonstrating noninferiority to fusion but not superiority. Similarly, the FSU height measure also demonstrated evidence of noninferiority but not superiority. Neurologic status showed noninferiority and statistical superiority for the disc compared to fusion. This contributed to the overall success composite end point demonstrating superiority for the disc compared to fusion. While maintained or improved neurologic status was more frequent following AIDA, it was unclear whether examiners were blinded. The majority of secondary outcome measures for the disc were deemed non-inferior to ACDF. Perioperative results and adverse events were similar in both groups, with very few serious complications.

Sixty-month follow-up of participants in this clinical trial were reported by Burkus et al in 2010. All participants were followed up in this FDA-regulated postapproval study. Outcomes at 60 months were reported on approximately half of the original randomized controlled trial (RCT) participants. The majority of the remaining patients had not yet reached that point in their follow-up, rather than being lost to follow-up. About 18% of all participants were actually lost to follow-up at 60 months. The NDI improved by 38.4 points for the Prestige disc compared to 34.1 for ACDF (p=0.022). For most other clinical outcomes, the Prestige disc was similar to ACDF, with no significant difference between groups in improvement in neck pain score (56.0 vs 52.4) or arm pain score (52.5 vs 47.7, both respectively). There was a trend for greater neurologic success in the Prestige disc group (95% vs 89%, p=0.051). Need for additional surgery was similar between the two procedures, and there was no significant difference in the percentage of patients requiring adjacent-level surgery (2.9% vs 4.9% for ACDF). No implant migration was observed at up to 60 months. Bridging bone was observed in 3 of 94 patients (3.2%) with the Prestige disc.

ProDisc-C

Murrey et al reported two-year results from the pivotal FDA randomized noninferiority trial to determine the safety and efficacy of ProDisc-C in comparison with ACDF. In this trial, 103 patients received the ProDisc-C implant and 106 were treated with fusion; participants were blinded to intervention until following surgery. Follow-up between six weeks and two years was reported to be 85% in the summary of safety and effectiveness data presented to FDA. Reasons for the loss to follow-up were not described but appear to have included two patients in the ProDisc-C group who had the implant removed and five patients in the fusion group who had undergone additional surgical procedures to modify the original implant. Non-inferiority was achieved for the FDA-defined combined end point of neurologic examination, NDI, adverse events, and device success, with 72% of ProDisc-C and 68% of fusion patients achieving success in all four component end points. Clinical outcomes at 24 months' follow-up were reported to be similar in the ProDisc-C and fusion groups for the following components: neurologic success (91% vs 88%), neck disability index (21.4 vs 20.5 points), reduction in pain scores (e.g., 46-mm

vs 43-mm reduction in neck pain on a visual analog scale [VAS]), and patient satisfaction (83 mm vs 80 mm, respectively).

Four-year interim follow-up of participants in this clinical trial were reported by Delamarter et al 2010. All participants in the clinical trial were followed up in this FDA-regulated postapproval study. At 48 months, follow-up rates for ProDisc-C and ACDF were 63% and 46.2% respectively. It was not reported what proportion of these patients had not yet reached 48 months postsurgery or were truly lost to follow-up at that time point. Also included in this report was 24-month follow-up on 77% of 136 continued access patients who received the ProDisc-C after the clinical trial. Clinical outcomes were similar between the three groups, with point estimates in favor of ProDisc-C. The NDI at 48 months was 20.3 for ProDisc-C versus 21.2 for ACDF. Neurologic success was achieved in 88.9% of ProDisc-C patients in comparison with 74.4% of ACDF patients (p=0.067). There was a cumulative incidence of additional surgeries of 2.9% (three patients) in the ProDisc-C group and 11.3% (12 patients) in the ACDF group. Two patients were converted to fusion with removal of the device; one patient had decompression with supplemental fixation without removal of the device. At 48 months, five ProDisc-C patients (7.7%) were found to have bridging bone.

Five-year results of this trial were published in 2013 with follow-up rates of 72.7% for ProDisc-C and 63.5% for ACDF. Outcomes on the NDI were found to be similar (50%-60% improved), along with VAS for arm pain (18 for both groups) and scores on the SF-36. VAS for neck pain was modestly improved with ProDisc-C compared to ACDF (21 vs 30), although the proportion of patients who achieved a clinically significant improvement in neck pain was not reported. There were a lower percentage of patients with ProDisc-C who had secondary surgery at either the index or adjacent level (2.9% vs 14.5%).

Nabhan et al reported one-year clinical and radiologic results of 49 patients randomized to receive a ProDisc-C artificial disc or fusion. Measurements taken at 3, 6, 12, 24, and 52 weeks showed a decrease in segmental motion at the index level in both groups over the first 12 weeks after surgery; at 52 weeks, segmental translation (xyz axis) was about 1mm greater in the ProDisc-C group. Clinical results were similar in the two groups, with a 70% reduction in neck pain and 86% reduction in arm pain in the ProDisc-C group and a 68% reduction in neck pain and 83% reduction in arm pain in the ACDF group. As noted by the authors, longer follow-up is needed to determine the effect of this implant on cervical motion and stress at adjacent levels.

Bryan Cervical Disc

Two- and four-year results have been published from the IDE trial for the Bryan disc. The trial employed inclusion/exclusion criteria and a composite outcome identical to the ProDisc-C trial. A total of 582 patients were randomized to the Bryan disc (n=290) or ACDF (n=292). Thirty-seven patients declined surgery in the AIDA group; 80 patients declined surgery in the ACDF group. Twelve patients crossed over from AIDA to ACDF, one crossed over from ACDF to AIDA, and two patients were excluded from ACDF due to protocol violations, leaving 242 patients who underwent AIDA and 223 who underwent ACDF. In the AIDA and ACDF arms, mean age (44.4 and 44.7 years), sex (45.5% and 51.1% men) and NDI scores (51.4 and 50.2, all respectively) were similar. All but one patient who underwent AIDA and three patients in the ACDF arm had documented neurologic abnormalities. After two years' follow-up, data were

available for 230 (95%) patients from the AIDA group and 194 (87%) who underwent ACDF. The overall success outcome was achieved more often after AIDA (82.6% vs 72.7%), with a mean 4.1-point greater improvement in the NDI scores. As measured by the composite end point, AIDA was superior to ACDF. At 24 months, neck pain scores were lower following AIDA, while other secondary outcomes were similar. Adverse event rates were similar in the two arms—1.7% in AIDA and 3.2% in ACDF arms, requiring revision.

In 2011, four-year follow-up from the IDE trial was reported for 181 patients (75% of 242) who received the Bryan disc and 138 patients (62% of 223) who underwent ACDF. It was reported that 25% of AIDA and 38% of the ACDF patients failed to return for follow-up at 48 months, due in part to FDA and institutional review board approvals and the need for additional patient consent for the continuation study. Overall success was defined as an improvement of equal to or greater than 15 points in the NDI, neurologic improvement, no serious adverse events related to the implant or surgical implantation procedure, and no subsequent surgery or intervention that would be classified as a treatment failure. The four-year overall success rates were significantly greater in the Bryan (85.1%) than the ACDF (72.5%) group. This finding was driven largely by differences in the NDI success (90.6% of arthroplasty and 79.0% of ACDF). Neurologic success rates were not different between the groups. Arm pain improved from a baseline of 71.2 in both groups to 16.6 for the Bryan disc and 22.4 for ACDF, the difference between groups was statistically significant. The improvement in neck pain scores was also significantly better in the Bryan disc group (from 75.4 to 20.7) compared to patients with fusion (from 74.8 to 30.6). Improvement in the SF-36 physical component score was also significantly greater in the arthroplasty group (15.8 vs 13.1). There was no significant difference in additional surgical procedures at either the index (3.7% Bryan, 4.5% ACDF) or adjacent (4.1% Bryan, 4.1% ACDF) levels. FDA-required follow-up will continue for ten years after the index surgery.

A post hoc subgroup analysis of 199 participants with myelopathy from the Prestige ST (n=111) and Bryan (n=88) trials found similar improvement in postoperative neurologic status and gait at 24 months (Prestige ST: AIDA 90% [95% confidence interval (CI), 79% to 97%] and ACDF 81% [95% CI, 65% to 92%]; Bryan: AIDA 90% [95% CI, 76% to 97%] and ACDF 77% [95% CI, 76% to 97%]). The authors noted that "although short-term results of cervical disc arthroplasty appear encouraging, studies with at least five to ten years of follow-up are required before cervical disc replacement can be viewed as a standard treatment for disc-based cervical myelopathy."

In 2010, Goffin et al reported four- and six-year follow-up from Phase I and Phase II trials of the Bryan disc. The total potential patient population for long-term follow-up was 98 patients (89 with 1-level and nine with 2-level); 59 of the patients were at least six years postoperative. Although four patients from the Phase I study declined to participate in the extended follow-up study, their results were included in the safety data. Mean neck pain at four and six years postoperatively was 2.2 and 2.0, respectively. Mean arm pain at four and six years was 2.4 and 2.3, respectively. Six patients experienced events that were believed to be related to the device, including minor device migration, device removal, hoarseness, and vocal cord paralysis, while three of the six cases involved pain or neurologic symptoms. The prosthesis was removed from one patient at six years after the index surgery because of progressive spinal cord compression due to recurrent posterior osteophyte formation. About 90% of patients were classified as having

excellent or good outcomes at four and six years. The success rate estimated by Kaplan-Meier analysis was 94% at seven years following surgery.

Two-level Bryan Cervical Disc
In 2009, Cheng et al reported two-year follow-up from an RCT of the Bryan disc versus ACDF with autograft in 65 patients with 2-level disc disease. One patient from the arthroplasty group and two patients from the ACDF group were lost to follow-up. Neck pain and arm pain measured by VAS tended to be better in the Bryan group (1.8 and 1.9, respectively) than the ACDF group at 12-month follow-up (2.5 and 2.4, respectively) and continued to improve at two-year follow-up (Bryan, 1.5 and 1.4; ACDF, 2.6 and 2.7, respectively). NDI and SF-36 Physical Component Summary scores were also significantly better in the Bryan group at both 12- and 24-month follow-up. These results support the short-term safety of the Bryan disc in 2-level disc disease; longer-term results are needed to evaluate the safety and efficacy of this device in comparison with ACDF for 2-level disc disease.

Kineflex-C
In 2011, Coric et al reported the 24-month pivotal multicenter randomized IDE trial of the metal-on-metal Kineflex-C artificial disc (n=136), compared to ACDF performed with allograft and anterior plate (n=133). There were no significant differences between the Kineflex-C and ACDF groups for operative time, blood loss, length of hospital stay, or reoperation rate at the index level. The overall success rate was significantly greater in the Kineflex-C group (85%) compared with the ACDF group (71%). (Overall success was defined as a composite measure of neurologic evaluation, >20% improvement in NDI, no device failure, no reoperation at the index level, and no major device-related adverse event.) There were six index-level reoperations (5%) in the Kineflex-C group, including one case of metal sensitivity and two for device migration. There were seven index-level surgeries (7.6%) in the ACDF group, including three for pseudarthrosis and four for instrumentation failure (removal or revision of the original anterior plate and screw construct). There was no significant difference between groups in VAS pain scores or NDI. Although fewer Kineflex-C patients showed severe adjacent-level radiographic changes (9% vs 24.8%), there was no significant difference between the groups in the adjacent-level reoperation rate (7.6% for the Kineflex-C group and 6.1% for the ACDF group) at short-term follow-up.

An accompanying editorial notes that while the 24-month IDE trials of artificial discs have been well done, and these new motion-saving mechanical devices may potentially be better than ACDF, a number of complications can occur with arthroplasty that include dislodgement, vertical vertebral body fracture, device failure, and heterotopic ossification. Given that no mechanical device has an infinite lifespan, and we do not know the failure rate, timeframe, or consequences of failure of cervical arthroplasty devices, a longer period of scientific scrutiny was advised to determine the real efficacy of artificial cervical discs.

Mobi-C
Mobi-C is the only artificial disc that is approved for 1- or 2-level cervical disc disease. The 1-level Mobi-C trial randomized 169 patients to receive AIDA and 87 to ACDF. Patient characteristics were generally similar to the other trials. Patient with multilevel disease or previously treated cervical disease were excluded from the trial. At 24 months, the follow-up rate was 93%. Designed as a noninferiority trial, noninferiority criteria were met for NDI mean

improvement, percent NDI success (≥15-point improvement), and overall success. The overall protocol-specified success rate was higher in the Mobi-C group than the ACDF group (73.7% vs 65.3%), which met noninferiority criteria but did not meet superiority criteria. Cumulative subsequent surgical interventions at the index level were numerically lower in the AIDA group than the ACDF group (1.2% vs 6.2%).

Results from the 2-level Mobi-C IDE trial were reported by Davis et al in 2013. In this noninferiority trial, 225 patients received the Mobi-C device at two contiguous levels and 105 patients received 2-level ACDF. The follow-up rate was 98.2% for the AIDA group and 94.3% for the ACDF group at 24 months. Both groups showed significant improvement in NDI score, VAS neck pain, and VAS arm pain from baseline to each follow-up point, with Mobi-C meeting the noninferiority margin. Subsequent testing for superiority showed that AIDA patients had significantly greater improvement than ACDF patients in NDI at all-time points and had higher NDI success rates (78.2% vs 61.8%) and overall success rates (69.7% vs 37.4%). AIDA resulted in significantly greater improvement in VAS neck pain at three and six months postoperatively but not at 12 or 24 months. Arm pain scores did not differ between the groups. The Mobi-C group had a lower incidence of device-related adverse events (16.7% vs 34.3%), serious adverse events (23.9% vs 32.4%) and a lower reoperation rate (3.1% vs 11.4%). At 24 months, adjacent-level degeneration was observed in the superior segment in 13.1% of AIDA patients and 33.3% of ACDF patients. Adjacent-level degeneration was observed in the inferior segment in 2.9% of AIDA patients and 18.1% of ACDF patients.

Huppert et al compared outcomes between single- (n=175) and multilevel (2-4 levels, n=56) AIDA with the Mobi-C device in a prospective multicenter study from Europe. The age of the patients was significantly higher, and the time since symptom onset was significantly longer in the multilevel group. At two years, there was no significant difference between groups for the radicular VAS, cervical VAS, or NDI. Range of motion was similar in the two groups. The overall success rate was 69% for the single-level group and 69% for the multilevel groups. There was a trend for more patients in the single-level group to return to work (70% vs 46%), and for the return to work to occur sooner (4.8 months vs 7.5 months). A similar percentage of patients underwent adjacent-level surgery (2.3% for single-level and 3.6% for multilevel).

PCM Cervical Disc

Results of the two-year FDA-regulated multicenter randomized noninferiority trial of the PCM Cervical Disc were reported by Phillips et al in 2013. The investigator and surgical staff were not blinded to treatment assignment, and patients were informed of the treatment assignment after surgery. Of the 416 patients who were randomized (224 PCM, 192 ACDF), 340 (82%, 189 PCM and 151 ACDF) were per protocol for the 24-month primary end point of overall success. Overall success was defined as at least 20% improvement in NDI; absence of reoperation, revision, or removal; maintenance or improvement in neurological status; and absence of radiographic or major complications during the 24-month follow-up period. At 24 months, overall success was 75.1% in the PCM group and 64.9% in the ACDF group, which met both the noninferiority and superiority criteria. There was a trend toward a greater neurological success rate in the PCM group (94.7%) compared with ACDF (89.5%, p=0.10). There was no significant difference between the groups for VAS pain scores, SF-36 component scores, or implant- or surgery-related adverse events (5.2% PCM vs 5.4% ACDF). Patients with prior fusion were

included in this study. Overall success for the 2 subgroups in this analysis was similar (65.4% PCM and 64.3% ACDF).

SECURE-C

The FDA-regulated SECURE-C trial was a multicenter un-blinded noninferiority trial with151 patients randomized to receive AIDA and 140 patients randomized to ACDF. Patients with multilevel disease or previously treated cervical disease were excluded from the trial. Overall success was defined by FDA as a 15-point or more improvement in NDI; absence of reoperation, revision, or removal; stable or improved neurologic status, and absence of radiographic or major complications during the 24-month follow-up period. At 24 months, the follow up rate was 87%. Noninferiority criteria were met for NDI mean improvement, percent NDI success (89.2% vs 84.5%), neurologic success (96.0% vs 94.9%), and overall success (83.8% vs 73.2%, AIDA vs ACDF, all respectively) using FDA-defined criteria. The overall success rate as specified in the protocol at 24 months (>25% improvement in NDI, no removals and no complications) was also higher in the SECURE-C group than the ACDF group (90.1% vs 71.1%), which met both noninferiority criteria as well as superiority criteria. Cumulative secondary surgical interventions at the treated level were lower in the AIDA group than the ACDF group (2.5% vs 9.7%).

Adverse Events

Adjacent Segment Degeneration

A key question is whether cervical disc arthroplasty reduces adjacent segment degeneration, which is the hypothetical advantage of motion-preserving artificial discs. In a 2010 report, Jawahar et al evaluated the incidence of adjacent segment degeneration in 93 patients with 1- or 2-level cervical DDD who had participated in one of three FDA-regulated RCTs (Kineflex-C, Mobi-C, or Advent Cervical Disc). ACDF was performed using the modified Smith Robinson technique using cortical bone allograft. VAS pain scores, NDI, and cervical spine radiographs were collected at six weeks and at 3, 6, 12, 24, 36, and 48 months after surgery. Success was defined as a composite of reduction by more than 30 points in both VAS (100-point scale) and NDI, absence of neurologic deficits, and no further intervention at the index level. Patients developing new complaints pertaining to cervical spine were worked up for possible adjacent segment disease with repeat magnetic resonance imaging (MRI) of the cervical spine and electrophysiologic studies. Only those patients, who demonstrated clinical and radiologic stigmata of adjacent segment disease, and received active intervention for its management, were included in the statistical analysis.

At a median follow-up of 37 months (range, 24-49) 73.5% of ACDF and 71% of arthroplasty patients satisfied the criteria for clinical success. The median symptom-free survival period was 39.8 months for ACDF and 38.1 months for arthroplasty patients. There was no statistical difference between the groups for VAS or NDI at the final follow-up. The mean improvement in NDI was 43 points for ACDF and 45 points for arthroplasty; the mean improvement in VAS was 62 points for ACDF and 62 for arthroplasty. At final follow-up, 16% of arthroplasty patients and 18% of ACDF patients were treated for adjacent segment degeneration; these rates were not significantly different. The mean period of freedom from adjacent-level disease was 38 months for both groups.

In 2012, the same group of investigators published a report that included 170 patients (57 ACDF and 113 arthroplasty, with likely overlap in patients from the previous study) with a median follow-up of 42 months (range, 28-54). As in the earlier report, there was no significant difference in adjacent-level disease between ACDF and arthroplasty patients (14% vs 17%, respectively). The mean period of freedom from adjacent-level disease was 46 months after ACDF and 49 months after total disc arthroplasty. Osteopenia and lumbar DDD were found to significantly increase the risk of adjacent level disease.

In 2010, Coric et al reported outcomes from 98 patients with 1- or 2-level cervical disc disease who had participated in one of three IDE studies (Bryan, Kineflex/C and Discover cervical disc). Patients were evaluated with neurologic examinations, radiographs, and clinical outcome indices at 1, 3, 6, 12, 24, 36, 48, and 60 months. A minimum follow-up of 24 months (range, 24 to 67) was available for 90 patients (53 arthroplasty and 41 ACDF). Clinical success, defined as a composite measure consisting of five separate components (neurologic, 20% improvement in NDI, no adverse events, no reoperation at the index or adjacent level, no narcotic usage at 24-month follow-up) was achieved in 85% of arthroplasty and 70% of ACDF patients (p=0.035). Overall, angular motion was improved by 0.91° in the arthroplasty group and reduced by 7.8° in the ACDF group. In the arthroplasty group, there was a 5.6% incidence of bridging heterotopic ossification (three cases). There were a similar number of reoperations, with four (7.5%) in the combined arthroplasty group (one at the adjacent level) and three (8.1%) in the ACDF group (all at the adjacent level). A 2013 report from this group reported minimum 48-month follow-up (range, 48-108) of 74 patients who had received a Bryan or Kineflex cervical disc. There were no significant differences between the groups in the mean NDI or median VAS scores. There were three reoperations (7.3%) at the index (n=1) or adjacent levels (n=2) in the AIDA group and one (3%) adjacent level reoperation in the ACDF group.

Results on adjacent level degeneration from the 2-level Mobi-C IDE trial were reported in 2013 from 225 patients who received the Mobi-C device at two contiguous levels and 105 patients who received 2-level ACDF. At 24 months, adjacent-level degeneration was observed in the superior and inferior segments in 13.1% and 2.9% of AIDA patients, respectively. Adjacent-level degeneration was observed in the superior and inferior segments in 33.3% and 18.1% of ACDF patients, respectively.

Maldonado et al evaluated adjacent-level degeneration in a prospective cohort study of 85 patients treated with AIDA and 105 treated with ACDF for single-level DDD. The rationale for treatment allocation was not described. At three years after surgery, radiographic evidence of adjacent-segment disease was found in 10.5% of patients in the ACDF group and in 8.8% of subjects in the AIDA group (not significantly different). There was no significant difference between groups in VAS arm pain or NDI.

Cervical artificial intervertebral disc implantation after a prior fusion
Phillips and colleagues (2009) reported data from the prospective IDE trial of PCM artificial discs. Between 2005 and 2007, 126 individuals received TDR with the PCM cervical artificial disc as the primary procedure. Twenty-six individuals previously treated with a cervical fusion received the PCM device at an adjacent level. After surgery, both groups had significant improvements in the NDI and VAS neck ad arm pain scores (P=0.001) compared to baseline.

Surgical revisions were required by two participants in each group, with a rate of 1.6% in the primary procedure group and 7.7% in the adjacent-to-fusion group. The authors reported "The data suggests TDR adjacent to a prior fusion is a viable treatment option." However, limitations of this study include the small number of participants in the adjacent to fusion group and the short follow-up of two years. The authors concluded although the short-term clinical outcomes of TDR adjacent to a prior fusion are similar to primary TDR, longer follow-up is needed to determine if the functional scores change or the complications increase over time.

Device Failure
Reports of device failure may emerge with increased use of artificial discs and longer follow-up. One case report describes failure of a Bryan cervical disc due to a fatigue fracture of the flexible polyether urethane sheath at eight years after implantation. Degradation of the sheath, including surface fissures and full-thickness cracks, has been observed in 27% of retrieved Bryan discs. One case of anterior migration of the Mobi-C disc was reported. Another case was reported of fragmented fracture of the ceramic-on-ceramic Discocerv® Cervidisc Evolution at one month after implantation. This artificial disc is not available in the U.S.

Dysphagia
A lower incidence of dysphagia has been reported with cervical arthroplasty in comparison with ACDF. As part of the IDE trial for the porous-coated motion (PCM) device, patients who underwent arthroplasty (n=151) or ACDF (n=100) self-reported dysphagia severity using the validated Bazaz Dysphagia Score. The arthroplasty group showed a significantly lower incidence of dysphagia at all-time points (six weeks and 3, 6, 12, and 24 months after surgery). For example, at the six-week follow-up, moderate-to-severe dysphagia was reported in 18.7% of arthroplasty patients compared with 37.3% of ACDF patients, while at 12-month follow-up, moderate-to-severe dysphagia was reported in 4.3% of arthroplasty patients compared with 13.1% of ACDF patients.

Heterotopic Ossification
A meta-analysis of heterotopic ossification (McAfee Grade 3-4) after AIDA was published by Chen et al in 2012. Included in the meta-analysis were eight studies (617 patients). The pooled prevalence of any heterotopic ossification was 44.6% at 12 months after AIDA and 58.2% at 24 months after AIDA. The pooled prevalence of advanced heterotopic ossification was 11.1% after 12 months and 16.7% after 24 months. Although no publication bias was identified, there was significant heterogeneity in study results.

The largest study included in the meta-analysis evaluated rates of heterotopic ossification in 170 patients who had undergone cervical arthroplasty with one of three cervical discs (81 Bryan, 61 Mobi-C, 28 ProDisc-C) and had at least 12 months of follow-up. Heterotopic ossification was found in a total of 40.6% of patients; the median time without heterotopic ossification was 27.1 months. Heterotopic ossification occurred in 21% of Bryan patients, 52.5% of Mobi-C, and 71.4% of ProDisc-C patients. This study had several limitations. First, the investigators could not completely discriminate whether the newly developed bone was true heterotopic ossification or a bone mass from normal fusion of the prosthesis to bone. There was also a possibility of underestimating posterior or lateral heterotopic ossification due to limited sensitivity of plain radiographs. In addition, clinical outcomes were not assessed.

Tu et al assessed heterotopic ossification in a series of 36 patients (52 levels) who had received total disc replacement with the Bryan cervical disc and had completed clinical and radiological evaluations. Heterotopic ossification was observed in computed tomography (CT) images in 50% of the patients at a mean of 19 months' follow-up. However, only two treated levels (3.8%) showed a loss of segmental motion (<2°) by dynamic radiography. At a mean of 27 months' follow-up, clinical evaluation indicated a similar clinical success rate in patients who had heterotopic ossification compared with those who did not (94.4% in both groups).

Progressive spinal cord compression due to osteophyte formation has been observed with cervical disc arthroplasty.

The evidence on adverse effects of cervical AIDA raises questions on the overall risk/benefit ratio for these devices. The potential to reduce adjacent level DDD has been the major rationale driving device development and use of AIDA. Evidence to date has not demonstrated a reduction in adjacent level disease with use of artificial cervical discs.

Heterotopic ossification could potentially have a negative impact on the goal of mobility with AIDA. Studies to date indicate a high rate of heterotopic ossification at short-term follow-up. Longer follow-up with clinical outcome measures is needed to evaluate the clinical significance of heterotopic ossification following AIDA.

Hypersensitivity Reaction

The first reported case of a delayed hypersensitivity reaction to metal ions after disc arthroplasty was in 2009. Although no intracellular or extracellular metal alloy particles were detected in the tissue, the lymphocyte-dominated response was thought to be similar to reactions reported in patients with metal-on-metal hip prostheses. The patient had complete resolution of symptoms following implant removal and fusion. In 2011, Guyer et al reported four cases of a lymphocytic reaction to a metal-on-metal artificial disc (one Kineflex-C cervical disc and three lumbar) that required revision. The mode of failure was determined to be compression of neural tissue or other adjacent structures by a soft tissue mass. Three patients had a good outcome after the explantation and revision surgery; one patient continued to have residual symptoms related to the neural compression caused by the mass. No hypersensitivity reactions have been reported from devices with a polyethylene/polyurethane insert or from Prestige stainless steel implants, however, periprosthetic tissue explanted after one to seven years commonly showed focal metallosis.

Practice Guidelines and Position Statements

The 2011 guidelines from the North American Spine Society (NASS) on the diagnosis and treatment of cervical radiculopathy from degenerative disorders give a grade B recommendation that anterior cervical decompression with fusion and total disc arthroplasty are suggested as comparable treatments, resulting in similarly successful short-term outcomes, for single-level degenerative cervical radiculopathy.

The United Kingdom's National Institute for Health and Care Excellence (NICE) issued guidance on the artificial cervical disc in 2010. NICE concluded that "current evidence on the

efficacy of prosthetic intervertebral disc replacement in the cervical spine shows that this procedure is as least as efficacious as fusion in the short term and may result in a reduced need for revision surgery in the long term. The evidence raises no particular safety issues that are not already known in relation to fusion procedures. Therefore this procedure may be used provided that normal arrangements are in place for clinical governance, consent and audit. This procedure should only be carried out in specialist units where surgery of the cervical spine is undertaken regularly. NICE encourages further research into prosthetic intervertebral disc replacement in the cervical spine. Research outcomes should include long-term data on preservation of mobility, occurrence of adjacent segment disease and the avoidance of revision surgery."

Lumbar Artificial Disc

This policy was created in 2003 and has been periodically updated using the MEDLINE® database. The most recent literature update of this policy was performed through October 2013. Following is a summary of key literature to date.

When this policy was created in 2003, the only evidence available was several case series describing the international experience with the SB Charité device. In February 2005, TEC completed an assessment of artificial disc replacement, focusing on the Charité lumbar disc device. Only one completed randomized controlled trial (RCT) had evaluated the Charité artificial disc compared to the BAK fusion cage for the treatment of single-level degenerative disc disease (DDD). The ProDisc, FlexiCore, and Maverick devices were also undergoing investigation in similarly designed randomized trials. The 2005 TEC Assessment concluded that, compared with fusion or other treatments, evidence supporting the effectiveness of artificial vertebral discs in terms of pain relief and restoration of function among patients with chronic discogenic low back pain was insufficient. In August 2006 the ProDisc-L was approved by the U.S. Food and Drug Administration (FDA). An updated TEC Assessment in February 2007 reviewed the evidence on artificial lumbar disc replacement devices. The Assessment concluded that given what is known about fusion as a comparator treatment, neither of the noninferiority trials provided convincing evidence of efficacy. TEC concluded that the evidence supporting the effectiveness of the ProDisc-L and Charité artificial disc was limited and that there was no immediately discernible advantage to use of the artificial disc. In 2010, two systematic reviews concluded that high-quality RCTs with a relevant control group and long-term follow-up are needed to evaluate the effectiveness and safety of artificial lumbar disc replacement.

In 2012, a systematic review by Wang et al evaluated the risk of adjacent segment disease (ASD) with disc replacement versus fusion. Analysis of data from two randomized trials found a pooled risk of ASD treated surgically to be 1.2% following lumbar disc replacement and 7.0% following fusion. The number needed to harm was calculated to be 17. In one of the studies included in this systematic review, ASD was marginally reported, and the number of any reoperations did not differ between disc replacement and fusion. Limitations of the second trial are described below. A 2012 Cochrane review of seven studies concluded that while differences between disc replacement and fusion were statistically significant, they did not achieve clinically important differences for short-term pain relief, disability, or quality of life. Concerns included the highly selected population, the lack of proper assessment of the primary goal of prevention of adjacent-level disease and facet joint degeneration, and the potential for harm in the long term.

An updated TEC Assessment in 2013 evaluated the five-year follow-up from the pivotal trial of the ProDisc. The Assessment concluded that:

- Additional study of ProDisc in an appropriately powered clinical trial with minimum 5-year follow-up is needed to confirm the results of the investigational device exemption (IDE) trial in patients with single-level chronic symptomatic DDD unresponsive to conservative management.
- Questions remain about the durability of the disc, in particular the long-term effects on patient health of polyethylene wear debris. Surgical revision of a failed or dysfunctional disc may be complicated and dangerous to the patient, so the lifespan of a prosthetic device is a key issue.
- The main claim of the artificial disc—that it maintains range of motion and thereby reduces the risk of adjacent-level segment degeneration better than fusion—remains subject to debate.

Charité (INMOTION®)

The Charité device is no longer marketed under that name. The INMOTION artificial disc is a renamed and slightly modified version of the Charité. It is not currently marketed in the U.S.

Controlled Trials

The pivotal study for the Charité device consisted of an RCT comparing the artificial intervertebral disc with spinal fusion using a threaded fusion cage with autologous bone graft. Patients were randomly assigned in a 2:1 fashion, with 205 receiving the artificial disc and 99 undergoing fusion. In this trial's analysis of 267 patients followed up for up to 24 months, the Charité artificial disc had a success rate of 63% compared with a success rate of 53% for BAK (Bagby and Kuslich [BAK]) fusion, using a composite measure of outcomes that incorporated improvement of symptoms and absence of complications. The analysis showed noninferiority compared to BAK fusion using the composite measure of success but did not show statistically significant superiority in most outcome measures. The point estimate of 63% success did not show the artificial disc to be a highly successful treatment. In addition, the long-term effectiveness and health outcomes for artificial vertebral discs were uncertain.

In 2009, Guyer et al reported five-year follow-up of a subset of the patient cohort that had participated in the IDE trial of the Charité artificial disc (described above). Of the initial 14 sites, six declined participation in the five-year continuation study, and an additional eight patients were excluded from analysis, leaving 233 patients from the original randomized study. There were 133 cases included in the five-year assessment (57% from the eight sites). Based on a denominator of 375 patients originally enrolled in the IDE trial, this report represents 30% of the study population. Given the limitations of the original RCT and the50% to 70% loss to follow-up, results from the five-year follow-up cannot be interpreted.

Observational Studies

Mean 17.3 year (range, 14.5-19.2) follow-up was reported for Charité Types I-III intervertebral discs from the Charité hospital. For the 53 of 71 patients (75%) who were available for clinical and radiologic examination, there were 16 Type I discs (1984-1985), 25 Type II discs (1985-1987), and 22 Type III discs (1987-1989). Clinical evaluation at follow-up showed no significant difference between the three types of discs for the Oswestry Disability Index (ODI), visual

analog scale (VAS) for pain, or overall outcome score. Of the 53 patients, 12 (23%) had a segmental fusion during follow-up due to implant failure or pain. Seven of the 12 (58%) were due to implant fractures, and five underwent secondary operative instrumented spondylodesis. Of the remaining 41 patients, nine (17% of 53) showed no signs of heterotopic ossification or ankylosis at follow-up, while ankylosis was observed in 32 patients (60%) after 17 years. No signs of adjacent segment degeneration were found in the nine cases (17%) without signs of ankylosis, spondylodesis, or implant failure. Although no adjacent segment degeneration was observed in the small percentage of implants that remained functional (17%), these patients were significantly less satisfied than those with spontaneous ankylosis based on the ODI (52 vs 38) and VAS (6.1 vs 4.5). The authors, who had designed the prosthesis, concluded that this study demonstrated dissatisfying results after artificial disc replacement in the majority of the evaluated cases regarding clinical, as well as radiologic outcomes.

Scott-Young et al reported average 45-month follow-up (range, 2-10 years) from a consecutive series of 122 patients who received a single-level Charité disc. VAS back scores decreased from 78.2 preoperatively to 21.9 at final follow-up. ODI scores decreased from 51.1 to 16.2, and Roland-Morris Disability Questionnaire scores decreased from 16.7 to 4.2. Short Form-36 (SF-36) Physical Component Summary scores increased from 25.7 to 46.4, and SF-36 Mental Component Summary scores increased from 35.5 to 51.6. In this prospective study, 91% of patients rated their satisfaction with the surgery as “excellent” or “good” at two years. There were four (3.3%) complications that required revision with fusion. Heterotopic bone formation was reported in 6 cases (4.9%). This series is limited by loss to follow-up, with outcomes reported from 70 patients (57%) at two years, 18 patients (15%) at five years, and three patients (2%) at seven years.

Long-term follow-up in a larger number of patients is needed to answer questions regarding the potential for device failure, decay, wear, and facet degeneration.

ProDisc-L

Controlled Trials

The pivotal study for the ProDisc®-L was an unblinded RCT of 242 patients followed up for 24 months. Patients were originally randomized in a 2:1 ratio to ProDisc®-L artificial disc replacement (n=161) or circumferential fusion (n=75). Using an FDA-requested composite measure of outcome that incorporated symptom improvement and absence of complications, the ProDisc®-L had a success rate of 53.4% and fusion had a success rate of 40.8%. This met prespecified criteria for a noninferiority margin of 10% and just achieved statistical significance for a 1-sided statistical test of superiority with a p of 0.044. The calculations were based on between 88% and 91% of randomized patients—how or which patients were censored was not described. Two-year results from this trial were published in 2007, and five-year follow-up was reported in 2012. The published 24-month report included 236 patients but did not provide information about the number of patients lost to follow-up. The report included alternative definitions of overall success, which resulted in a greater difference between the two groups (experimental group 63.5%, control group 45.1%, p=0.005). Of an original 236 patients randomized, 186 (79%) were included in the five-year follow-up of clinical outcomes (134 ProDisc-L and 52 controls) and 166 (70%) (123 ProDisc-L and 43 controls) were included for radiographic outcomes. Results showed noninferiority, but not superiority of artificial disc

replacement, with 53.7% of ProDisc-L patients and 50.0% of fusion patients achieving overall success at five years. This change in overall success in ProDisc-L patients between two and five years (63.5%-53.7%, respectively) indicates a possible decrement in response over time with the artificial disc. This decrement in response rate was not observed in the standard fusion group and resulted in convergence of the primary outcome measures between groups over time. On post hoc analysis of radiographs, adjacent level degeneration was observed in fewer ProDisc-L patients (9.2% vs 28.6%, respectively). Adjacent level reoperations were not significantly different (1.9% ProDisc-L and 4% controls). There were six (3.7%) ProDisc-L device failures.

Several of the individual components of the primary outcome measure were also statistically better in the ProDisc-L group at two years, but were no longer significantly different at five years. For example, at five years ODI scores improved by 15% or more in 78.6% of ProDisc-L patients compared to 76.5% of controls. A similar percentage of patients maintained or improved SF-36 physical component scores compared with baseline (81.3% ProDisc-L and 74.0% fusion), and overall neurologic success was obtained in 88.8% of ProDisc-L patients and 89.6% of fusion patients. Secondary surgeries at the index level occurred in 8% of ProDisc-L patients and 12% of fusion patients (p value not reported). Device success, defined as the absence of any reoperation required to modify or remove implants and no need for supplemental fixation, was achieved in 96.3% of ProDisc-L patients and 97.3% of fusion patients. Analysis of VAS scores for pain excluded patients who had secondary surgical interventions (11 ProDisc-L and five fusions). For the ProDisc-L group, VAS improved from a mean of 75.9 at baseline to 37.1 at five years. Mean VAS for the fusion group improved from 74.9 at baseline to 40.0 at five years. There was no significant difference in VAS between the groups. Narcotic use decreased from a baseline of 84% to 44.6% in ProDisc-L patients and from 76% to 42.5% in fusion patients.

The ProDisc-L for 2-level lumbar degenerative disease was reported in 2011 from a multicenter randomized FDA-regulated noninferiority trial. All patients in the study had DDD at two contiguous vertebral levels from L3 to S1 with or without leg pain, a minimum of six months of conservative therapy, and a minimum ODI score equal to or greater than 40. A total of 237 patients were treated in a 2:1 ratio with total disc arthroplasty or open circumferential arthrodesis (performed through both anterior and posterior open incisions). Postoperative evaluations were performed at six weeks and at 3, 6, 12, 18, and 24 months postoperatively. The total disc replacement group had decreased operative times (160.2 vs 272.8 min), estimated blood loss (398.1 vs 569.3 mL), and length of hospital stay (3.8 vs 5.0 days). At 24 months, 58.8% patients in the ProDisc-L group and 47.8% patients in the arthrodesis group achieved the criteria for success, demonstrating noninferiority but not superiority. The ProDisc-L group showed significant benefit in percentage improvement in the ODI (52.4% vs 40.9%), a greater percentage of patients who achieved equal to or greater than 15-point improvement in the ODI (73.2% vs 59.7%), the SF-36 Physical Component Summary score (43.9 vs 39.2), and six-month neurologic success (87.3% vs 71.6%). A greater percentage of patients in the arthrodesis group required secondary surgical procedures (8.3% vs 2.4%). As noted in an accompanying commentary, there are a number of limitations to this study. Comparison with a procedure (open 360° fusion) that is not the gold standard precludes decisions on the comparative efficacy of this procedure to the standard of care. Other limitations include the relatively short follow-up and lack of blinding of both patients and providers.

Observational Studies

One case series was identified that followed up 55 patients for an average of 8.7 years after disc replacement with the ProDisc-L; 60% of patients report an excellent result. Additional publications report on the implantation of artificial discs at two levels in the lumbar spine.

Maverick

The Maverick disc is not marketed in the U.S.

In 2011, Gornet et al reported 24-month results from an FDA-regulated multicenter IDE randomized non-blinded trial of the metal-on-metal Maverick artificial disc. A total of 577 patients were randomized in a 2:1 ratio to the Maverick disc (n=405) or to anterior interbody fusion with INFUSE Bone Graft and tapered fusion cages (n=172). All patients underwent a single-level, open anterior surgical procedure between the L4 and S1 level. The Maverick group had longer surgical times (1.8 vs 1.4 hours) and greater blood loss (240.7 vs 95.2 mL). Hospitalization stays were similar for both groups (2.2 vs 2.3 days for fusion). At 24 months, radiographic fusion was observed in 100% of the control patients. Heterotopic ossification was observed in 2.6% of patients with the artificial disc.

The FDA-defined measure of overall success was a combination of a successful outcome in ODI, neurologic status, disc height, no additional surgery classified as failure, and no serious device or device/surgical procedure-related adverse events at the 24-month follow-up. Patients who received the Maverick artificial disc had superior outcomes in overall success (73.5% vs 55.3%) and in the component scores of ODI success (82.2% vs 74.6% improved), back pain (improvement of 53.4 vs 49 points), and SF-36 Physical Component Summary score (17.0 vs 14.3). Leg pain scores did not differ between the kit groups. Global perceived effect ("completely recovered" or "much improved") was higher in the Maverick group (78.1% vs 67.4%). The Maverick group had fewer implant or surgical procedure-related adverse events (1% vs 7%), and return-to-work intervals were reduced (median, 75 vs 96 days). The percentage of patients who were working at 24 months was similar (74.1% vs 73.4%). There were two implant removals in the Maverick Group. One implant was considered to be related to an allergic reaction. Longer follow-up with this two-piece metal-on-metal implant is needed; particularly in light of emerging complications (e.g., pseudotumor formation) with metal-on-metal hip implants.

FlexiCore

Preliminary results on the FlexiCore metal-on-metal intervertebral disc were presented in 2008 from two of the sites involved in the investigational device trial. Results were reported for 76 patients enrolled at the two sites (out of the entire study cohort of 401 patients) who had been randomly assigned with a ratio of 2:1 to either FlexiCore or fusion control; nine subjects did not receive the index surgery, 44 patients were treated with the artificial disc, and 23 patients were treated with fusion. Compared with fusion, placement of the artificial disc was associated with less blood loss (97 vs 179 mL, respectively), reduced operating time (82 vs 179 min, respectively), and reduced length of hospital stay (2 vs 3 days, respectively). ODI and VAS pain scores were not significantly different between the groups. At 24 months, the ODI scores had decreased from 62 to six in the FlexiCore group and from 58 to 12 in the fusion group. VAS scores decreased from 86 to 16 in the FlexiCore group and from 82 to 20 in the fusion group. Eight patients in each group had complications requiring interventional surgery.

Other

In 2009, Berg et al published two-year follow-up of an RCT of 1- and 2-level total disc replacement. Five-year follow-up of patients in this study was reported in 2013. Patients (n=152) with symptomatic DDD in one or two motion segments between L3 and S1, with lower back pain as a predominant symptom, were randomly assigned to one of three total disc replacement devices available in Sweden (Charité, ProDisc, or Maverick, n=80) or to instrumented fusion (posterolateral or posterior lumbar interbody fusion, n=72). The randomization was stratified for number of levels, with 56% of total disc replacement patients having 1-level surgery compared to 46% of fusion patients. Only patients who did not have a preference to the type of treatment were enrolled in the trial, and they were informed of the result of randomization on arrival at the hospital for surgery. No patient left the study when informed of the randomization. There was 100% follow-up at the one- and two-year assessments and 99.3% follow-up at the five-year assessment. The primary outcome, which does not appear to be a validated measure, was a global assessment of back pain consisting of "total relief," "much better," "better," "unchanged," or "worse." The percentage of patients in the disc replacement group who reported being pain-free was 30% at the one- and two-year follow-up, and 38% at 5-year follow-up. In the fusion group, 10% reported being pain-free at one year and 15% reported being pain-free at two and five years. At five years, a similar percentage of patients reported being either totally pain free or much better (72.5% for disc replacement and 66.7% for fusion). The total disc replacement group showed lower mean VAS for pain at one and two years (25.4 vs 29.2, respectively) and had better outcome scores on a quality-of-life scale (EQ-5D) and the ODI at one year (19.5 vs 24.9, respectively) but not the two-year follow-up (20.0 vs 23.0, respectively). At five years, the disc replacement group had modestly improved outcome scores for both VAS back pain (23 vs 31) and ODI (17 vs 23). The most common cause of reoperation in the disc replacement group was to fuse the index level that was believed to cause persistent or recurrent pain (5%). The most common cause of reoperation in the fusion group was operation at an adjacent level (7%). Twenty-two disc replacement patients underwent postoperative facet block due to remaining pain. Twenty fusion patients had their instrumentation removed due to persistent or recurrent pain. The investigators found no association between achievement of surgical goals (absence of mobility with fusion and maintenance of mobility with disc replacement) and clinical outcomes at two years.

The design of a U.S. multicenter clinical trial to evaluate the safety and effectiveness of the Aesculap Activ-L artificial disc has also been reported. The study is a single-blinded, randomized noninferiority trial comparing Activ-L with a control artificial lumbar disc (Charité or ProDisc-L) for single-level DDD of the lumbar spine. Following surgeon training with initial 90 patients, it is expected that 324 patients will be randomly assigned in a 2:1 ratio. The patients will be followed for five years posttreatment.

Adverse Events

Complications with artificial lumbar discs are emerging with longer-term follow-up. One study from Asia reported that clinical outcomes of both the Charité and the ProDisc were fairly good, but the facet joint of the index level and the disc at the adjacent level showed an aggravation of the degenerative process in a significant number of patients, regardless of the device used. Another study reported that progression of facet degeneration (29% of levels replaced with the ProDisc II) was associated with female gender, malposition of the prosthesis on the frontal plane,

and 2-level total disc replacement. Analysis of postoperative pain patterns in 58 patients of 175 (33%) implanted with the ProDisc II showed facet joint pain in 22 (13%) and sacroiliac joint pain in 21 (12%). Another report describes late complications in 75 patients who had received an earlier generation SB Charité prosthesis. As all of the patients had been originally treated by other surgeons, the percentage of implant failure cannot be determined from this report. The mean interval between insertion and retrieval of the prosthesis was eight years and 11 months (range, 3-16 years). The most frequent complications included subsidence (n=39), disc prosthesis too small (n=24), adjacent disc degeneration (n=36), degenerative scoliosis (n=11), facet joint degeneration (n=25), and metal wire breakage (n=10). The report indicated that good placement and good sizing of the disc prosthesis appeared problematic for many of the patients, adjacent-disc degeneration was seen in many patients, and polyethylene wear with inflammatory fibrous tissue containing wear debris was observed. The report concluded that wear mechanisms of artificial discs may be similar to artificial hips and knees and that, due to nearby vascular structures and scar tissue from the original surgery, retrieval of artificial disc prosthesis can be difficult and dangerous. Therefore, long-term health outcomes following disc implantation in young active patients may become a clinically significant issue.

In 2011, Guyer et al reported four cases of a lymphocytic reaction to a metal-on-metal artificial disc (one Kineflex-C cervical disc, two Kineflex-L lumbar discs, and one Maverick lumbar disc) that required revision. The mode of failure was determined to be compression of neural tissue or other adjacent structures by a soft-tissue mass. Three patients had a good outcome after the explantation and revision surgery; one patient continued to have residual symptoms related to the neural compression caused by the mass. Two other cases of a granulomatous mass (pseudotumor) with the metal-on-metal Maverick prosthesis have been reported. One caused iliac vein occlusion and spinal stenosis; the second resulted in spinal compression and paraplegia.

Summary

Overall, the available scientific evidence remains insufficient to permit conclusions concerning the effect of this technology on the net health outcome. The Charité has been withdrawn from the market and its successor, the INMOTION, is not marketed in the U.S. The five-year results of the ProDisc-L RCT provide evidence for the noninferiority of artificial disc replacement. Superiority of ProDisc-L to circumferential fusion was achieved at two, but not five years in this unblinded trial. At this time, the potential benefits of the artificial disc, such as faster recovery or reduced adjacent-level disc degeneration, have not been demonstrated. In addition, considerable uncertainty remains about whether response rates will continue to decline over longer time periods, as well as the potential for long-term complications with these implants.

Thus, evidence is insufficient to determine whether artificial lumber discs improve outcomes in the short term, and questions remain about potential long-term complications with these implants. While some randomized trials have concluded that this technology is non-inferior to fusion, the potential benefits of artificial lumbar disc that would make noninferiority sufficient to demonstrate clinical benefit have not been established.

Practice Guidelines and Position Statements
In 2009, the American Pain Society's (APS) practice guidelines provided a recommendation of "insufficient evidence" to adequately evaluate long-term benefits and harms of vertebral disc replacement. The guideline was based on a systematic review commissioned by APS and conducted by the Oregon Evidence-Based Practice Center. The rationale for the recommendation was that although artificial disc replacement has been associated with similar outcomes compared to fusion, the trial results were only applicable to a narrowly defined subset of patients with single-level degenerative disease, and the type of fusion surgery in the trials is no longer widely used due to frequent poor outcomes. In addition, all trials had been industry-funded, and data on long-term (beyond two years) benefits and harms following artificial disc replacement were limited.

Guidance in 2004 from the United Kingdom's National Institute for Health and Clinical Excellence (NICE) concluded that evidence on the safety and efficacy of prosthetic intervertebral disc replacement in the lumbar spine appeared adequate to support the use of this procedure with audit and review; however, there was little evidence on outcomes beyond two to three years. In 2009, NICE updated the guidance on this procedure with studies reporting 13-year follow-up but with the majority of evidence from studies with shorter durations of follow-up. NICE concluded that evidence appeared adequate to support the use of this procedure, provided that normal arrangements are in place for clinical governance, consent, and audit. Clinicians were encouraged to continue to collect and publish data on longer-term outcomes, including information about patient selection and the need for further surgery.

Key Words:
Degenerative disc disease, spinal fusion, artificial intervertebral disc, total disc replacement, spinal arthroplasty, SB Charite III, ProDisc, Maverick™, Prestige Cervical Disc, Bryan Cervical Disc, ProDisc-L, ProDisc-C, Activ-L™ (Aesculap), INMOTION® lumbar artificial disc

Approved by Governing Bodies:
Cervical Artificial Disc
The Prestige® ST Cervical Disc (Medtronic) received U.S. Food and Drug Administration (FDA) premarket application (PMA) approval as a Class III device on July 16, 2007. The Prestige ST Cervical Disc is composed of stainless steel and is indicated in skeletally mature patients for reconstruction of the disc from C3-C7 following single-level discectomy. The device is implanted via an open anterior approach. Intractable radiculopathy and/or myelopathy should be present, with at least one of the following items producing symptomatic nerve root and/or spinal cord compression as documented by patient history (e.g., pain [neck and/or arm pain], functional deficit, and/or neurologic deficit) and radiographic studies (e.g., computed tomography [CT], magnetic resonance imaging [MRI], x-rays): herniated disc and/or osteophyte formation. FDA has required the Prestige disc manufacturer to conduct a seven-year postapproval clinical study of the safety and function of the device and a five-year enhanced surveillance study of the disc to more fully characterize adverse events in a broader patient population.

Another disc arthroplasty product, the ProDisc-C® (Synthes Spine) received FDA PMA approval in December 2007. As with the Prestige ST Cervical Disc, FDA approval of ProDisc-C is conditional on seven-year follow-up of the 209 subjects included in the noninferiority trial (discussed in Rationale section), seven-year follow-up on 99 continued access subjects, and a five-year enhanced surveillance study to more fully characterize adverse events when the device is used under general conditions of use. The postapproval study reports are to be delivered to FDA annually.

The Bryan® Cervical Disc (Medtronic Sofamor Danek) consists of two titanium-alloy shells encasing a polyurethane nucleus and has been available outside of the United States since 2002. The Bryan Cervical Disc was approved by FDA in May 2009 for treatment using an anterior approach of single-level cervical DDD defined as any combination of the following: disc herniation with radiculopathy, spondylotic radiculopathy, disc herniation with myelopathy, or spondylotic myelopathy resulting in impaired function and at least one clinical neurologic sign associated with the cervical level to be treated, and necessitating surgery as demonstrated using CT, myelography and CT, and/or MRI. Patients receiving the Bryan cervical disc should have failed at least six weeks of nonoperative treatment prior to implantation of the Bryan cervical disc. As a condition for approval of this device, FDA required the manufacturer to extend its follow-up of enrolled subjects to ten years after surgery. The study will involve the investigational and control patients from the pivotal investigational device exemption (IDE) study arm, as well as the patients who received the device as part of the continued access study arm. In addition, the manufacturer must perform a five-year enhanced surveillance study of the BRYAN® Cervical Disc to more fully characterize adverse events when the device is used in a broader patient population.

In more recent years, continued FDA approval requires completion of two postapproval studies. One study provides extended follow-up of the premarket pivotal cohort out to seven years. The second study provides ten-year enhanced surveillance of adverse event data. Continued approval is contingent on submission of annual reports, which include the number of devices sold, heterotopic ossification, device malfunction, device removal, or other serious device-related complications, and analysis of all explanted discs. The following have received FDA approval:

- The PCM [porous-coated motion] Cervical Disc® (NuVasive) received FDA approval in 2012 (P100012). The PCM® is a semi-constrained device consisting of two metal (cobalt-chromium alloy) endplates and a polyethylene insert that fits between the endplates.
- Secure®-C (Globus Medical) was approved in 2012 (P100003). The Secure®-C is a three piece semi-constrained device with two metal (cobalt chromium molybdenum alloy) endplates and a polyethylene insert.
- The Mobi-C® (LDR Spine) received FDA approval in 2013. Mobi-C® is three piece semiconstrained device with metal (cobalt-chromium alloy) endplates and a polyethylene insert. The Mobi-C® is approved for one (P110002) or two level (P110009) disc replacement.

A number of other devices are under study in FDA IDE trials in the United States:

- Prestige®LP (Medtronic)
- Kenefles C® cervical Artifical Disc Implant (Spinal Motion)
- CerviCore™ Intervertebral Disc (Stryker)
- Discover (Depuy)
- NeoDisc™ (NuVaisve)
- Freedom® Cervical Disc (AxioMed)

Lumbar Artificial Disc

While artificial intervertebral discs in the lumbar spine have been used internationally for more than ten years, only two devices (Charité® and ProDisc®-L) have received approval from the U.S. Food and Drug Administration (FDA). Because the long-term safety and effectiveness of these devices were not known, approval was contingent on completion of postmarketing studies. The Charité (DePuy) and ProDisc-L (Synthes Spine) devices are indicated for spinal arthroplasty in skeletally mature patients with degenerative disc disease (DDD) at one level; Charité is approved for use in levels L4–S1, and the ProDisc-L is approved for use in levels L3–S1. DDD is defined as discogenic back pain with degeneration of the disc confirmed by patient history and radiographic studies.

The INMOTION® lumbar artificial disc (DePuy Spine) is a modification of the Charité® device with a change in name under the same premarket approval. Production under the name Charité® was stopped in 2010. The INMOTION® is not currently marketed in the U.S. The Maverick™ artificial disc (Medtronic) is not marketed in the U.S. due to patent infringement litigation.

Other devices are currently under investigation in the U.S. as part of the U.S. Food and Drug Administration process of approval, including the FlexiCore® (Stryker Spine), and Activ-L™ (Aesculap) devices.

Benefit Application:

Coverage is subject to member's specific benefits. Group specific policy will supersede this policy when applicable.
ITS: Home Policy provisions apply
FEP contracts: FEP does not consider investigational if FDA approved and will be reviewed for medical necessity.

Current Coding:

CPT:	**0092T**	Total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophytectomy for nerve root or spinal cord decompression and microdissection), each additional interspace, cervical (list separately in addition to code for primary procedure)
	0095T	Removal of total disc arthroplasty (artificial disc), anterior approach, each additional interspace, cervical (list separately in addition to code for primary procedure)

0098T	Revision including replacement of total disc cervical arthroplasty, (artificial disc), anterior approach; each additional interspace, cervical (list separately in addition to code for primary procedure)
0163T	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), each additional interspace, lumbar (list separately in addition to code for primary procedure)
0164T	Removal of total disc arthroplasty, (artificial disc), anterior approach, each additional interspace, lumbar (list separately in addition to code for primary procedure)
0165T	Revision including replacement of total disc arthroplasty, (artificial disc), anterior approach, each additional interspace, lumbar (list separately in addition to code for primary procedure)
22856	Total disc arthroplasty (artificial disc), anterior approach, including discectomy with end plate preparation (includes osteophytectomy for nerve root or spinal cord decompression and microdissection), single interspace, cervical
22857	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), single interspace, lumbar
22861	Revision including replacement of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
22862	; lumbar
22864	Removal of total disc arthroplasty (artificial disc), anterior approach, single interspace; cervical
22865	Total disc arthroplasty (artificial disc), anterior approach, including discectomy to prepare interspace (other than for decompression), single interspace, lumbar
22899	Unlisted procedure, spine

Previous Coding

0090T	Total disc arthroplasty (artificial disc), anterior approach, including diskectomy to prepare interspace (other than for decompression); single interspace, cervical **(deleted 01/01/2009)**
0091T	Single interspace, lumbar **(deleted 01/01/2007)**
0093T	Removal of total disc arthroplasty, anterior approach; single interspace, cervical **(deleted 01/01/2009)**
0094T	Single interspace, lumbar **(deleted 01/01/2007)**
0096T	Revision of total disc arthroplasty, anterior approach; single interspace, cervical **(deleted 01/01/2009)**
0097T	Single interspace, lumbar **(deleted 01/01/2007)**

References:

1. Administration Investigational Device Exemption Study of the ProDisc-L total disc replacement versus circumferential fusion for the treatment of 1-level degenerative disc disease. Spine 2007, Vol. 32, No. 11, pp. 1155-1162.
2. Berg S, Tullberg T, Branth B et al. Total disc replacement compared to lumbar fusion: a randomized controlled trial with a 2-year follow-up. Eur Spine J 2009:18(10):1512-9.
3. Bertagnoli R, et al. Early results after ProDisc C cervical disc replacement. Journal Neurosurgery Spine, April 2005; 2(4): 403-410.
4. Bertagnoli R, et al. Lumbar total disc arthroplasty in patients older than 60 years of age: A prospective study of the ProDisc prosthesis with 2-year minimum follow-up period. Journal of Neurosurgery Spine, February 2006; 4(2): 85-90.
5. Bertagnoli R, et al. Lumbar total disc arthroplasty utilizing the ProDisc prosthesis in smokers versus nonsmokers: A prospective study with 2 year minimum follow-up. Spine, April 2006; 31(9): 992-997.
6. Bertagnoli R, et al. The treatment of disabling multilevel lumbar discogenic low back pain with total disc arthroplasty utilizing the ProDisc prosthesis: A prospective study with 2 year minimum follow-up. Spine, October 2005; 30(19): 2192-2199.
7. Bertagnoli R, et al. Treatment of symptomatic adjacent-segment degeneration after lumbar fusion with total disc arthroplasty by using the prodisc prosthesis: A prospective study with 2-year minimum follow up. Journal Neurosurgery Spine, February 2006; 4(2): 91-97.
8. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Artificial vertebral disc replacement. TEC Assessments 2005; Volume 20, Tab 1.
9. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Artificial lumbar disc replacement. TEC Assessments 2007; Volume 22, Tab 2.
10. Blue Cross and Blue Shield Association Technology Evaluation Center (TEC). Artificial lumbar disc arthroplasty for treatment of degenerative disc disease of the lumbar spine. TEC Assessments 2013; in press.
11. Blumenthal S, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemptions study of lumbar total disc replacement with the Charité artificial disc versus lumbar fusion: Part 1: Evaluation of clinical outcomes. Spine, July 2005; 30(14): 1565-1575.
12. Blumenthal SL, et al. Artificial intervertebral discs and beyond: A North American Spine Society Annual Meeting Symposium. The Spine Journal, November 2002; 2(6): 460-3.
13. Blumenthal SL, et al. Prospective study evaluating total disc replacement: Preliminary results. Journal of Spinal Disorders and Techniques, October 2003; 16(5): 450-4.
14. Bono CM, Ghiselli G, Gilbert TJ et al. An evidence-based clinical guideline for the diagnosis and treatment of cervical radiculopathy from degenerative disorders. Spine J 2011; 11(1):64-72.
15. Boselie TF, Willems PC, van Mameren H et al. Arthroplasty versus fusion in single-level cervical degenerative disc disease: a cochrane review. Spine (Phila Pa 1976) 2013; 38(17):E1096-107.
16. Burkus JK, Haid RW, Traynelis VC et al. Long-term clinical and radiographic outcomes of cervical disc replacement with the Prestige disc: results from a prospective randomized controlled clinical trial. J Neurosurg Spine 2010; 13(3):308-18.

17. Cabraja M, Schmeding M, Koch A et al. Delayed formation of a devastating granulomatous process after metal-on-metal lumbar disc arthroplasty. Spine (Phila Pa 1976) 2012; 37(13):E809-13.
18. Caspi I, et al. Results of lumbar disk prosthesis after a follow-up period of 48 months. Israel Medical Association Journal, January 2003; 5(1): 9-11.
19. Cavanaugh DA, Nunley PD, et al. Delayed hyper-reactivity to metal ions after cervical disc arthroplasty: A case report and literature review. Spine, April 2009; 34(7): E262-265.
20. Chen J, Wang X, Bai W et al. Prevalence of heterotopic ossification after cervical total disc arthroplasty: a meta-analysis. Eur Spine J 2012; 21(4):674-80.
21. Cheng L, Nie L, Zhang L and Hou Y. Fusion versus Bryan Cervical Disc in two-level cervical disc disease: A prospective, randomised study. Int Orthop, October 2009; 33(5): 1347-1351.
22. Chou R, Baisden J, et al. Surgery for low back pain: A review of the evidence for an American Pain Society Clinical Practice Guideline. Spine, May 2009; 34(10): 1094-1109.
23. Chou R, Loeser JD, Owens DK, et al. Interventional therapies, surgery, and interdisciplinary rehabilitation for low back pain: An evidence-based clinical practice guideline from the American Pain Society. Spine, May 2009; 34(10): 1066-1077.
24. Chung, SS. Lumbar total disc replacement using ProDisc II: A prospective study with a 2 year minimum follow-up. Journal of Spinal Disorders Technology, August 2006; 19(6): 411-415.
25. Coric D, Cassis J, Carew JD et al. Prospective study of cervical arthroplasty in 98 patients involved in 1 of 3 separate investigational device exemption studies from a single investigational site with a minimum 2-year follow-up. Clinical article. J Neurosurg Spine 2010; 13(6):715-21.
26. Coric D, Finger F and Boltes P. Prospective randomized controlled study of the Bryan cervical disc: Early clinical results from a single investigational site. Journal of Neurosurgical Spine, January 2006; 4(1): 31-35.
27. Coric D, Kim PK, Clemente JD et al. Prospective randomized study of cervical arthroplasty and anterior cervical discectomy and fusion with long-term follow-up: results in 74 patients from a single site. J Neurosurg Spine 2013; 18(1):36-42.
28. David T. Long-term results of one-level lumbar arthroplasty: Minimum 10-year follow-up of the Charité artificial disc in 106 patients. Spine, March 2007; 32(6): 661-666.
29. David T. Revision of a Charité artificial disc 9.5 years in vivo to a new Charité artificial disc: Case report and explant analysis. European Spine Journal, June 2005; 14(5): 507-511.
30. Davis RJ, Kim KD, Hisey MS et al. Cervical total disc replacement with the Mobi-C cervical artificial disc compared with anterior discectomy and fusion for treatment of 2-level symptomatic degenerative disc disease: a prospective, randomized, controlled multicenter clinical trial. J Neurosurg Spine 2013; 19(5):532-45.
31. deKleuver M, et al. Total disc replacement for chronic low back pain: Background and a systematic review of the literature. European Spine Journal, April 2003; 12(2): 108-16.
32. Delamarter R, Zigler J, Spivak JM. Five year results of the prospective randomized multicenter FDA IDE ProDisc-L clinical trial. Spine (Phila Pa 1976) 2008; 8(62S-3S).
33. Delamarter R, Zigler JE, Balderston RA et al. Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement compared with circumferential arthrodesis for the treatment of two-level

lumbar degenerative disc disease: results at twenty-four months. J Bone Joint Surg Am 2011; 93(8):705-15.
34. Delamarter RB, et al. Clinical results of the ProDisc II lumbar total disc replacement: Report from the United States clinical trial. Orthopedic Clinics of North America, July 2005; 36(3): 301-313.
35. Delamarter RB, et al. ProDisc artificial total lumbar disc replacement: Introduction and early results from the United States clinical trial. Spine, October 2003; 28(20): S167-75.
36. Delamarter RB, Murrey D, Janssen ME. Results at 24 months from the prospective randomized multicenter investigational device exemption trial of ProDisc-C versus anterior cervical discectomy and fusion with 4-year follow-up and continued access patients. SAS Journal 2010; 4:122-28.
37. Delamarter RB, Zigler J. Five-year Reoperation Rates, Cervical Total Disc Replacement versus Fusion, Results of a Prospective Randomized Clinical Trial. Spine (Phila Pa 1976) 2013; 38(9):711-7.
38. Eijkelkamp MF, et al. Improving the fixation of an artificial intervertebral disc. International Journal of Artificial Organs, April 2002; 25(4): 327-33.
39. Eijkelkamp MF, et al. Requirements for an artificial intervertebral disc. International Journal of Artificial Organs, May 2001; 24(5): 311-21.
40. Fan H, Wu S, Wu Z et al. Implant failure of Bryan cervical disc due to broken polyurethane sheath: a case report. Spine (Phila Pa 1976) 2012; 37(13):E814-6.
41. Freeman BJ, et al. Total disc replacement in the lumbar spine: A systematic review of the literature. European Spine Journal, August 2006; 15 Suppl 3: S439-447.
42. Garrido BJ, Taha TA and Sasso RC. Clinical outcomes of Bryan cervical disc arthroplasty a prospective, randomized, controlled, single site trial with 48-month follow-up. J Spinal Disord Tech, August 2010; 23(6): 367-371.
43. Geisler FH, et al. 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. Journal of Neurosurgical Spine, September 2004; 1(2): 143-154.
44. Goffin J, Van Calenbergh F, van Loon J, et al. Intermediate follow-up after treatment of degenerative disc disease with the Bryan Cervical Disc Prosthesis: Single-level and bi-level. Spine, December 2003; 28(24): 2673-2678.
45. Goffin J, van Loon J, et al. A clinical analysis of 4- and 6-year follow-up results after cervical disc replacement surgery using the Bryan Cervical Disc Prosthesis. J Neurosurg Spine, March 2010; 12(3): 261-269.
46. Gornet MF, Burkus JK, Dryer RF et al. Lumbar disc arthroplasty with MAVERICK disc versus stand-alone interbody fusion: a prospective, randomized, controlled, multicenter investigational device exemption trial. Spine (Phila Pa 1976) 2011; 36(25):E1600-11.
47. Guyer RD, et al. Prospective randomized study of the Charite artificial disc: Data from two investigational centers. Spine Journal, Nov-Dec 2004; 4(6 Suppl): 252S-259S.
48. Guyer RD, McAfee PC, Banco RJ, et al. Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the CHARITÉ artificial disc versus lumbar fusion: Five-year follow-up. Spine Journal, May 2009; 9(5): 374-386.

49. Guyer RD, Shellock J, MacLennan B et al. Early failure of metal-on-metal artificial disc prostheses associated with lymphocytic reaction: diagnosis and treatment experience in four cases. Spine (Phila Pa 1976) 2011; 36(7):E492-7.
50. Hannibal M, Thomas DJ, Low J et al. ProDisc-L total disc replacement: a comparison of 1-level versus 2-level arthroplasty patients with a minimum 2-year follow-up. Spine (Phila Pa 1976) 2007; 32(21):2322-6.
51. Heller JG, Sasso RC, Papadopoulos SM, et al. Comparison of BRYAN cervical disc arthroplasty with anterior cervical decompression and fusion: clinical and radiographic results of a randomized, controlled, clinical trial. Spin, January 2009; 34(2): 101-107.
52. Hochschuler SH, et al. Artificial disc: Preliminary results of a prospective study in the United States. European Spine Journal, October 2002; 11 Suppl 2: S106-10.
53. Huang RC, et al. Correlation between range of motion and outcome after lumbar total disc replacement: 8.6 year follow up. Spine, June 2005; 30(12): 1407-1411.
54. Huppert J, Beaurain J, Steib JP et al. Comparison between single- and multi-level patients: clinical and radiological outcomes 2 years after cervical disc replacement. Eur Spine J 2011; 20(9):1417-26.
55. Jacobs WC, Anderson PG, et al. Single or double-level anterior interbody fusion techniques for cervical degenerative disc disease. Cochrane Database System Review, October 2004 (4): CD004958.
56. Jacobs W, Van der Gaag NA, Tuschel A et al. Total disc replacement for chronic back pain in the presence of disc degeneration. Cochrane Database Syst Rev 2012; 9:CD008326.
57. Jawahar A, Cavanaugh DA, Kerr EJ, 3rd et al. Total disc arthroplasty does not affect the incidence of adjacent segment degeneration in cervical spine: results of 93 patients in three prospective randomized clinical trials. Spine J 2010; 10(12):1043-8.
58. Kim WJ, et al. Treatment of juxtafusional degeneration with artificial disc replacement (ADR): Preliminary results of an ongoing prospective study. Journal of Spinal Disorders and Techniques, August 2003; 16(4): 390-7.
59. Kotani Y, et al. Artificial intervertebral disc replacement using bioactive three-dimensional fabric: Design, development, and preliminary animal study. Spine, May 2002; 27(9): 929-35.
60. Kurtz SM, Toth JM, Siskey R et al. The latest lessons learned from retrieval analysis of ultra-high molecular weight polyethylene, metal-on-metal, and alternative bearing total disc replacements. Semin Spine Surg 2011; 24(1):57-70.
61. Lemaire JP, et al. Clinical and radiological outcomes with the Charité artificial disc: A 10 year-minimum follow-up. Journal of Spinal Disorders Technology, August 2005; 18(4): 353-359.
62. Lemaire JP, et al. Intervertebral disc prosthesis. Clinical Orthopedics and Related Research, April 1997, No. 337, pp. 64-76.
63. Leviseth G, et al. Mobility of lumbar segments instrumented with a ProDisc II prosthesis: A two year follow up study. Spine, July 2006; 31(15): 1726-1733.
64. Maldonado CV, Paz RD, Martin CB. Adjacent-level degeneration after cervical disc arthroplasty versus fusion. Eur Spine J 2011; 20 Suppl 3:403-7.
65. Matthew P, et al. Bilateral pedicle fractures following anterior dislocation of the polyethylene inlay of a ProDisc artificial disc replacement: A case report of an unusual complication. Spine, June 2005; 30(11): E311-314.

66. Matz PG, Holly LT, Groff MW et al. Indications for anterior cervical decompression for the treatment of cervical degenerative radiculopathy. J Neurosurg Spine 2009; 11(2):174-82.
67. Mayer HM, et al. Minimally invasive total disc replacement: Surgical technique and preliminary clinical results. European Spine Journal, October 2002, 11 Suppl 2: S124-130.
68. McAfee PC, Cappuccino A, Cunningham BW et al. Lower incidence of dysphagia with cervical arthroplasty compared with ACDF in a prospective randomized clinical trial. J Spinal Disord Tech 2010; 23(1):1-8.
69. McAfee PC, et al. A prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of lumbar total disc replacement with the Charité artificial disc versus lumbar fusion: Part II: Evaluation of radiographic outcomes and correlation of surgical technique accuracy with clinical outcomes. Spine, July 2005; 30(14): 1576-1583.
70. McAfee PC, et al. Experimental design of total disk replacement-Experience with a prospective randomized study of the SB Charité. Spine, October 2003; 28(20): S153-62.
71. McAfee PC, et al. SB Charite disc replacement: Report of 60 prospective randomized cases in a U.S. center. Spine, January 2003; 28 Suppl: 424-33.
72. McAfee PC, Geisler FH, Saiedy SS, Moore SV, et al. Revisability of the CHARITE artificial disc replacement: Analysis of 688 patients enrolled in the U.S. IDE study of the CHARITE artificial disc. Spine, May 2006; 31(11): 1217-1226.
73. Mummaneni PV, Burkus JK, Haid RW, et al. Clinical and radiographic analysis of cervical disc arthroplasty compared with allograft fusion: A randomized controlled clinical trial. J Neurosurg Spine 2007; 6(3):198-209.
74. Mummaneni PV, Kaiser MG, Matz PG et al. Cervical surgical techniques for the treatment of cervical spondylotic myelopathy. J Neurosurg Spine 2009; 11(2):130-41.
75. Murrey DM, Janssen M, Delamarter R, et al. Results of the prospective, randomized, multi-center Food and Drug Administration investigational device exemption study of the ProDisc-C total disc replacement versus anterior discectomy and fusion for the treatment of 1-level symptomatic cervical disc disease. Article in press, 2008. Spine J 2009; 9(4);275-86.
76. Nabhan A, et al. Disc replacement using ProDisc C versus fusion: A prospective randomised and controlled radiographic and clinical study. European Spine Journal, March 2007; 16(3): 423-430.
77. National Institute for Health and Clinical Excellence (NICE). Prosthetic intervertebral disc replacement in the lumbar spine. 2010. Available online at: www.nice.org.uk/nicemedia/live/11157/48666/48666.pdf. Last accessed October 2013.
78. National Institute for Health and Clinical Excellence (NICE). Prosthetic intervertebral disc replacement in the cervical spine (IPG306). Available online at: www.nice.org.uk/nicemedia/pdf/IPG306Guidance.pdf. Last accessed November 2013.
79. Nguyen NQ, Kafle D, Buchowski JM et al. Ceramic fracture following cervical disc arthroplasty: a case report. J Bone Joint Surg Am 2011; 93(22):e132(1-4).
80. Nunley PD, Jawahar A, Kerr EJ, 3rd et al. Factors Affecting the Incidence of Symptomatic Adjacent Level Disease in Cervical Spine after Total Disc Arthroplasty: 2 - 4 Years Follow-Up of 3 Prospective Randomized Trials. Spine (Phila Pa 1976) 2011.

81. Nunley PD, Jawahar A, Kerr EJ, 3rd et al. Factors affecting the incidence of symptomatic adjacent-level disease in cervical spine after total disc arthroplasty: 2- to 4-year follow-up of 3 prospective randomized trials. Spine (Phila Pa 1976) 2012; 37(6):445-51.
82. Papadopoulos S. The Bryan cervical disc system. Neurosurgical Clinics of North America, October 2005; 16(4): 629-636.
83. Park CK, Ryu KS and Jee WH. Degenerative changes of discs and facet joints in lumbar total disc replacement using ProDisc II: Minimum two-year follow-up. Spine, July 2008; 33(16): 1755-1761.
84. Phillips FM, Allen TR, Regan JJ, et al. Cervical disc replacement in patients with and without previous adjacent level fusion surgery: a prospective study. Spine (Phila Pa 1976). 2009; 34(6):556-565.
85. Phillips FM, Lee JY, Geisler FH et al. A Prospective, randomized, controlled clinical investigation comparing PCM Cervical disc arthroplasty with anterior cervical discectomy and fusion: 2-year results from the US FDA IDE Clinical Trial. Spine (Phila Pa 1976) 2013; 38(15):E907-18.
86. Punt HM, Visser VM, et al. Complications and reoperations of the SB Charité lumbar disc prosthesis: Experience in 75 patients. Eur Spine J 2008; 17: 36-43.
87. Punt IM, et al. Complications and reoperations of the SB Charite lumbar disc prosthesis: Experience in 75 patients. European Spine Journal, October 2007.
88. Putzier M, et al. Charité total disc replacement-clinical and radiographical results after an average follow-up of 17 years. European Spine Journal, February 2006; 15(2): 183-195.
89. Riew KD, Buchowski JM, Sasso R, et al. Cervical disc arthroplasty compared with arthrodesis for the treatment of myelopathy. Am J Bone Joint Surg, November 2008; 90(11): 2354-2364.
90. Robertson JT, Papadopoulos SM and Traynelis VC. Assessment of adjacent-segment disease in patients treated with cervical fusion or arthroplasty: A prospective 2 year study. Journal of Neurosurgical Spine, December 2005; 3(6): 417-423.
91. Sasso RC, Roulk DM and Hahn M. Prospective, randomized trial of metal-on-metal artificial lumbar disc replacement: Initial results for treatment of discogenic pain. Spine, January 2008; 33(2): 123-131.
92. Schoenfeld AJ. Commentary on an article by Rick Delamarter, MD et al.: "Prospective, randomized, multicenter Food and Drug Administration investigational device exemption study of the ProDisc-L total replacement compared with circumferential arthrodesis for the treatment of two-level degenerative lumbar disc disease. Results at twenty-four months". J Bone Joint Surg Am 2011; 93(8):e41.
93. Schroven I, et al. Intervertebral prosthesis versus anterior lumbar interbody fusion: One year results of a prospective nonrandomized study. Acta Orthopedics Belgium, January 2006; 72(1): 83-86.
94. Scott-Young MN, Lee MJ, Nielsen DE et al. Clinical and Radiological mid-term outcomes of lumbar single-level total disc replacement. Spine (Phila Pa 1976) 2011.
95. Shim CS, et al. Vertical split fracture of the vertebral body following total disc replacement using ProDisc: Report of two cases. Journal of Spinal Disorders Technology, October 2005; 18(5): 465-469.
96. Shim CS, Lee SH, Shin HD, et al. CHARITÉ versus ProDisc: A comparative study of a minimum 3-year follow-up. Spine, April 2007; 32(9): 1012-1018.

97. Siepe CJ, et al. Clinical results of total lumbar disc replacement with ProDisc II: Three year results for different indications. Spine, August 2006; 31(17): 1923-1932.
98. Siepe CJ, et al. Total lumbar disc replacement: Different results for different levels. Spine, April 2007; 32(7): 782-790.
99. Siepe CJ, Korge A, Grochulla F, et al. Analysis of post-operative pain patters following total lumbar disc replacement: Results from fluoroscopically guided spine infiltrations. Eur Spine J 2008: 17: 44-56.
100. Skold C, Tropp H, Berg S. Five-year follow-up of total disc replacement compared to fusion: a randomized controlled trial. Eur Spine J 2013.
101. Stieber JR. Early failure of lumbar disc replacement: Case report and review of the literature. Journal of Spinal Disorders Technology, February 2006; 19(1): 55-60.
102. The Hayes AIS Medical Technology Advisor. Artificial cervical discs. November 2007, Vol. 1, No. 2.
103. Thierry D. Long-term results of one-level lumbar arthroplasty. Spine 2007, Vol. 32, No. 6, pp. 661-666.
104. Traynelis VC. The Prestige cervical disc. Neurosurgical Clinics of North America, October 2005; 16(4): 621-628.
105. Tropiana P, et al. Lumbar total disc replacement. Surgical technique. Journal Bone Joint Surgery, March 2006; 88(Suppl 1, PH): 50-64.
106. Tropiano P, et al. Lumbar disc replacement: Preliminary results with ProDisc II after a minimum follow-up period of 1 year. Spine, January 2003; 28 Suppl: 362-8.
107. Tropiano P, et al. Lumbar total disc replacement. Seven to eleven year follow up. Journal of Bone Joint Surgery, March 2005; 87(3): 490-496.
108. Tsermoulas G, Bhattathiri PS. Anterior migration of prosthesis following cervical arthroplasty. Br J Neurosurg 2013; 27(1):132-3.
109. Tu TH, Wu JC, Huang WC et al. Heterotopic ossification after cervical total disc replacement: determination by CT and effects on clinical outcomes. J Neurosurg Spine 2011; 14(4):457-65.
110. U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health. Summary of Safety and Effectiveness Data: Mobi-C. 2013. Available online at: www.accessdata.fda.gov/cdrh_docs/pdf11/P110002b.pdf. Last accessed November, 2013.
111. U.S. Food and Drug Administration (FDA) Center for Devices and Radiological Health. Summary of safety and effectiveness data: SECURE-C. 2012. Available online at: www.accessdata.fda.gov/cdrh_docs/pdf10/P100003b.pdf. Last accessed November, 2013.
112. van den Eerenbeemt KD, Ostelo RV, van Royen BJ et al. Total disc replacement surgery for symptomatic degenerative lumbar disc disease: a systematic review of the literature. Eur Spine J 2010;19(8):1262-80.
113. Van Ooij A, et al. Polyethylene wear debris and long-term clinical failure of the Charité disc prosthesis: A study of 4 patients. Spine, January 2007; 32(2): 223-229.
114. Van Ooij A, Oner FC, Verbout AJ. Complications of artificial dis replacement: A report of 27 patients with the SB Charité disc. J Spinal Disord Tech 2003; 16(4): 369-383.
115. Vernon H and Mior S. The Neck Disability Index: A study of reliability and validity. September 1991; 14(7): 409-415.
116. Wang JC, Arnold PM, Hermsmeyer JT et al. Do lumbar motion preserving devices reduce the risk of adjacent segment pathology compared with fusion surgery? A systematic review. Spine (Phila Pa 1976) 2012; 37(22 Suppl):S133-43.

117. Yajun W, Yue Z, Xiuxin H et al. A meta-analysis of artificial total disc replacement versus fusion for lumbar degenerative disc disease. Eur Spin J 2010;19(8):1250-61.
118. Yi S, Kim KN, Yang MS et al. Difference in occurrence of heterotopic ossification according to prosthesis type in the cervical artificial disc replacement. Spine (Phila Pa 1976) 2010; 35(16):1556-61.
119. Yue JJ, Mo FF. Clinical study to evaluate the safety and effectiveness of the Aesculap Activ-L artificial disc in the treatment of degenerative disc disease. BMC Surg 2010:10:14.
120. Zigler JE, et al. Lumbar spine arthroplasty: Early results using the ProDisc II: A prospective randomized trial of arthroplasty versus fusion. Spine, January 2003; 28 Suppl: 352-61.
121. Zigler JE, Delamarter R, Murrey D et al. ProDisc-C and anterior cervical discectomy and fusion as surgical treatment for single-level cervical symptomatic degenerative disc disease: five-year results of a Food and Drug Administration study. Spine (Phila Pa 1976) 2013; 38(3):203-9.
122. Zigler JE, Delamarter RB. Five-year results of the prospective, randomized, multicenter, Food and Drug Administration investigational device exemption study of the ProDisc-L total disc replacement versus circumferential arthrodesis for the treatment of single-level degenerative disc disease. J Neurosurg Spine 2012; 17(6):493-501.
123. Zigler JE, Glenn J, Delamarter RB. Five-year adjacent-level degenerative changes in patients with single-level disease treated using lumbar total disc replacement with ProDisc-L versus circumferential fusion. J Neurosurg Spine 2012; 17(6):504-11.

Policy History:

Medical Policy Group, February 2004 **(2)**
Medical Policy Administration Committee, March 2004
Available for comment March 22-May 5, 2004
Medical Policy Group, January 2006 **(1)**
Medical Policy Group, June 2006
Medical Policy Group, August 2006 **(1)**
Medical Policy Administration Committee, August 2006
Medical Policy Group, September 2006 **(2)**
Medical Policy Group, April 2007
Medical Policy Group, July 2007 **(1)**
Medical Policy Administration Committee, August 2007
Medical Policy Group, October 2007 **(1)**
Medical Policy Group, March 2008
Medical Policy Group, May 2008
Medical Policy Group, August 2008 **(3)**
Medical Policy Group, June 2009 **(3)**
Medical Policy Administration Committee, July 2009
Medical Policy Group, October 2009 **(1)**
Medical Policy Group, October 2010 **(1):** Updated description, Key Points, no policy statement coverage change
Medical Policy Panel, October 2010

Medical Policy Group, January 2011 **(2)**
Medical Policy Group, November 2011 **(2)**: Updated Description, Key Points & References
Medical Policy Group, October 2013 **(2)**: Removed ICD-9 Procedure codes; Removed references related to Medical Policy Reference Manual; no change to policy statement.
Medical Policy Panel, October 2013
Medical Policy Panel, November 2013
Medical Policy Group, December 2013 **(2):** Updated Policy Statement with limited coverage for cervical artificial disc. Key Points, Approved by Governing Bodies, Key Words and References updated to reflect information found in latest literature search. Invalid web references deleted. Coding section corrected
Medical Policy Administration Committee, December 2013 and March 2014
Available for comment March 5 through April 16, 2014
Medical Policy Group, May 2014 **(4):** Updated Key Points and References No changes to the policy statement at this time.
