Description

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).

Background

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 result in myelopathy, which is manifested by subtle changes in gait or balance, weakness in the arms or legs, and numbness of the arms or hands, in severe cases. 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 5 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). If symptoms do not improve or resolve after 6 weeks or more, or if they progress, surgical intervention may be indicated. 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 degenerative disc disease (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.

**Regulatory Status**

The Prestige® ST Cervical Disc (Medtronic) received U.S. Food and Drug Administration (FDA) premarket application (PMA P060018) approval as a Class III device on July 16, 2007. The Prestige ST Cervical Disc 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. The FDA has required the Prestige disc manufacturer to conduct a 7-year post-approval clinical study of the safety and function of the device and a 5-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, the FDA approval of ProDisc-C is conditional on 7-year follow-up of the 209 subjects included in the noninferiority trial (discussed in Rationale section), 7-year follow-up on 99 continued access subjects, and a 5-year enhanced surveillance study to more fully
characterize adverse events when the device is used under general conditions of use. The post-approval study reports are to be delivered to the FDA annually.

The Bryan® Cervical Disc (Medtronic Sofamor Danek) consists of 2 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 the 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 6 weeks of non-operative treatment prior to implantation of the Bryan cervical disc. As a condition for approval of this device, the FDA required the manufacturer to extend its follow-up of enrolled subjects to 10 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 5-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 2 post-approval studies. One study provides extended follow-up of the pre-market pivotal cohort out to 7 years. The second study provides 10-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 2 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 3 piece semi-constrained device with 2 metal (cobalt chromium molybdenum alloy) endplates and a polyethylene insert.
- The Mobi-C® (LDR Spine) received FDA approval in 2013. Mobi-C® is 3 piece semiconstrained device with metal (cobalt-chromium alloy) endplates and a polyethylene insert. The Mobi-C® is approved for 1 (P110002) or 2 level (P110009) disc replacement.

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

### Cervical Disc Prostheses under Investigation in the U.S.

<table>
<thead>
<tr>
<th>Prosthesis (Manufacturer)</th>
<th>Implant Composition</th>
<th>Articulation Design</th>
<th>Bearing Surface</th>
<th>Bearing Constraint</th>
<th>Fixation</th>
<th>FDA Status</th>
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<tr>
<td>Prestige® LP (Medtronic)</td>
<td>Titanium-ceramic composite</td>
<td>Ellipsoid saucer</td>
<td>MoM</td>
<td>Semi-constrained</td>
<td>Primary-dual rails; secondary-endplate ingrowth</td>
<td>FDA IDE clinical trial enrollment complete</td>
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<tr>
<td>Subject</td>
<td>Artificial Intervertebral Disc: Cervical Spine</td>
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**Kineflex C® Cervical Artificial Disc Implant (Spinal Motion)**
- **Material**: Cobalt-chromium molybdenum
- **Design**: Three-piece, metal core
- **Type**: MoM
- **Constraint**: Unconstrained
- **Design Features**: Primary-central keel; secondary-endplate ingrowth
- **Status**: FDA IDE clinical trial complete

**CerviCore ™ Intervertebral Disc (Stryker)**
- **Material**: Cobalt-chromium-molybdenum
- **Design**: Saddle
- **Type**: MoM
- **Constraint**: Unconstrained
- **Design Features**: Primary-dual rails; secondary-endplate ingrowth
- **Status**: Status unknown

**Discover (DePuy)**
- **Material**: Titanium-on-polyethylene
- **Design**: Three-piece, polyethylene core
- **Type**: MoP
- **Constraint**: Unconstrained
- **Design Features**: Primary-Spike fixation; secondary-endplate ingrowth
- **Status**: FDA IDE clinical trial enrollment complete

**NeoDisc ™ (NuVasive)**
- **Material**: FDA IDE clinical trial complete

**Freedom® Cervical Disc (AxioMed)**
- **Material**: Titanium endplates and polymer core
- **Design**: Seven-piece, with endplates and nucleus, fibrous annulus and sheath
- **Type**: PMA
- **Constraint**: Unconstrained
- **Design Features**: FDA IDE clinical trial recruiting

**M6-C (Spinal Kinetics)**
- **Material**: Titanium endplates and polymer core
- **Design**: Seven-piece, with endplates and nucleus, fibrous annulus and sheath
- **Type**: PMA
- **Constraint**: Unconstrained
- **Design Features**: FDA IDE trial withdrawn prior to enrollment

IDE: investigational device exemption; MoM: metal-on-metal; MoP: metal-on-polyethylene; PMA: premarket approval; SS: stainless steel; UHMWPE: ultra-high molecular weight polyethylene

Updates to the regulatory status of these devices can be viewed at online site: [http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm](http://www.accessdata.fda.gov/scripts/cdrh/cfdocs/cfPMA/pma.cfm) using the FDA product code “MJO”.

**Related Policies:**

7.01.87 Artificial Intervertebral Disc: Lumbar Spine

**Policy**

*This policy statement applies to clinical review performed for pre-service (Prior Approval, Precertification, Advanced Benefit Determination, etc.) and/or post-service claims.*

Artificial intervertebral discs are considered **not medically necessary** for treatment of disorders of the cervical spine, including degenerative disc disease.
Rationale

Literature Review

This policy is based on Technology Evaluation Center (TEC) Assessments from 2007 through 2013 (1-4) with additional updates of the literature using the MEDLINE database. The 2009 TEC Assessments reviewed the 2-year follow-up of the trials for the FDA-approved Prestige ST discs (5) and ProDisc-C, (6) concluding that artificial intervertebral disc arthroplasty (AIDA) did not meet TEC criteria again due to insufficient evidence. (2) Neither the Prestige nor ProDisc-C trial provided adequate direct evidence over the relevant follow-up period (suggested to be 5 to 7 years) on subsequent adjacent-level degenerative disc disease (DDD) in control and investigational group patients. The 2011 and 2013 TEC Assessments reviewed mid-term outcomes at 4-5 years. (3, 4) These Assessments concluded that although results are consistent with continued noninferiority of artificial discs and lower cumulative reoperation rates, uncertainty remains due to the low follow-up rates. Two-year results of the PCM, SECURE-C, and Mobi-C discs were also reviewed.

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 9 studies (2,400 patients) with 1 to 2 years of follow-up. (7) Seven of the 9 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 U.S. Food and Drug Administration (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 the FDA. (5, 6) 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 non-axial pain and other symptoms secondary to radiculopathy or myelopathy that did not improve with a minimum 6 weeks of conservative therapy. The study was designed as a randomized, nonblinded noninferiority trial with a 10% margin. Results for 137 investigational and 148 control patients who were evaluated at 2 years post-surgery were presented to the 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. (9) It is a modification of the Oswestry Low Back Pain Index, based on the response to 10 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 1 to 5, 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 interdiscal space. Comparison of the immediate postoperative FSU height with the 6-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 summaries, 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 non-inferiority and statistical superiority for the disc compared to fusion. This contributed to the overall success composite endpoint 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 noninferior to ACDF, but none was statistically superior. 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. (10) All participants were followed up in this FDA-regulated post-approval 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 2 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 2-year results from the pivotal FDA randomized noninferiority trial to determine the safety and efficacy of ProDisc-C in comparison with ACDF. (11) 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 6 weeks and 2 years was reported to be 85% in the summary of safety and effectiveness data presented to the FDA. (12) Reasons for the loss to follow-up were not
described but appear to have included 2 patients in the ProDisc-C group who had the implant removed and 5 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 endpoint of neurologic examination, neck disability index, adverse events, and device success, with 72% of ProDisc-C and 68% of fusion patients achieving success in all 4 component endpoints. 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%, respectively), 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 analogue scale [VAS]), and patient satisfaction (83 mm vs. 80 mm all respectively).

Four-year interim follow-up of participants in this clinical trial were reported by Delamarter et al. 2010. (13) All participants in the clinical trial were followed up in this FDA-regulated post-approval 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 post-surgery 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 3 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% (3 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, 5 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. (14, 15) 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 1-year clinical and radiologic results of 49 patients randomized to receive a ProDisc-C artificial disc or fusion. (16) 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 1 mm 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 4-year results have been published from the IDE trial for the Bryan disc. (17, 18) 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, 1 crossed over from ACDF to AIDA, and 2 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 1 patient who underwent AIDA and 3 patients in the ACDF arm had documented neurologic abnormalities. After 2 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 endpoint, 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, 4-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. (18) 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 4-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 10 years after the index surgery.

In the discussion of this article, the authors comment that failure of other joint arthroplasty prostheses does not typically occur until at least 5 to 10 years postoperatively and that spinal arthroplasties also need to have serial assessments to determine whether complications such as wear-related failures, device fatigue, or spinal instability have developed. They conclude that as with any motion-sparing device, “longer-term follow-up is necessary for assessment of potential problems related to bearing surface wear.”

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%]). (19) 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 4- and 6-year follow-up from Phase I and Phase II trials of the Bryan disc. (20) The total potential patient population for long-term follow-up was 98 patients (89 with 1-level and 9 with 2-level); 59 of the patients were at least 6 years postoperative. Although 4 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 4 and 6 years postoperatively was 2.2 and 2.0, respectively. Mean arm pain at 4 and 6 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 3 of the 6 cases involved pain or neurologic symptoms. The prosthesis was removed from 1 patient at 6 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 4 and 6 years. The success rate estimated by Kaplan-Meier analysis was 94% at 7 years following surgery.

Two-level Bryan Cervical Disc

In 2009, Cheng et al. reported 2-year follow-up from an RCT of the Bryan disc versus ACDF with autograft in 65 patients with 2-level disc disease. (21) One patient from the arthroplasty group and 2 patients from the ACDF group were lost to follow-up. Neck pain and arm pain measured by visual analog scores (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 2-year follow-up (Bryan, 1.5 and 1.4; ACDF, 2.6 and 2.7, respectively). The NDI and the SF-36 physical component 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 investigational device exemption (IDE) trial of the metal-on-metal Kineflex-C artificial disc (n=136), compared to anterior cervical discectomy and fusion (ACDF) performed with allograft and anterior plate (n=133). (22) 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 6 index-level reoperations (5%) in the Kineflex-C group, including 1 case of metal sensitivity and 2 for device migration. There were 7 index-level surgeries (7.6%) in the ACDF group, including 3 for pseudarthrosis and 4 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.

The need for longer-term studies remains to assess device failure and other long-term complications. 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. (23) 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. (24) Patient characteristics were generally similar to the other trials. Patient with multi-level disease or previously treated cervical disease were excluded from the trial. At 24 months, the follow-up rate was 93%. Designed as a non-inferiority trial, non-inferiority criteria were met for NDI mean improvement, percent NDI success (15-point or more 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 non-inferiority 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. (25) In this non-inferiority trial, 225 patients received the Mobi-C device at 2 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 non-inferiority 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 3 and 6 months post-operatively 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 multi-level (2-4 levels, n=56) AIDA with the Mobi-C device in a prospective multi-center study from Europe. (26) The age of the patients was significantly higher, and the time since symptom onset was significantly longer in the multi-level group. At 2 years, there was no significant difference between groups for the radicular VAS, cervical VAS, or NDI. Range of motion was similar in the 2 groups. The overall success rate was 69% for the single-level group and 69% for the multi-level 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 multi-level).
PCM Cervical Disc

Results of the 2-year FDA-regulated multicenter randomized non-inferiority trial of the PCM Cervical Disc were reported by Phillips and colleagues in 2013. (27) 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 endpoint 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 non-inferiority 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 sub-groups in this analysis was similar (65.4% PCM and 64.3% ACDF).

SECURE-C

The FDA-regulated SECURE-C trial was a multi-center un-blinded non-inferiority trial with 151 patients randomized to receive AIDA and 140 patients randomized to ACDF. (28) Patients with multi-level disease or previously treated cervical disease were excluded from the trial. Overall success was defined by the 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 degenerative disc disease (DDD) who had participated in 1 of 3 FDA-regulated RCTs (Kinflex-C, Mobi-C, or Advent Cervical Disc). (29) Anterior cervical discectomy and fusion was performed using the modified Smith Robinson technique using cortical bone allograft. VAS pain scores, NDI, and cervical spine radiographs were collected at 6 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 electrophysiological studies. Only those patients who demonstrated clinical and radiological 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 months) 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. There was no statistical difference between the groups for VAS or NDI at the final follow-up. 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 months). (30) 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 and colleagues reported outcomes from 98 patients with 1- or 2-level cervical disc disease who had participated in 1 of 3 IDE studies (Bryan, Kineflex/C and Discover cervical disc). (31) 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 5 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 degrees 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 (3 cases). There were a similar number of reoperations, with 4 (7.5%) in the combined arthroplasty group (1 at the adjacent level) and 3 (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 months) of 74 patients who had received a Bryan or Kineflex cervical disc. (32) There were no significant differences between the groups in the mean NDI or median VAS scores. There were 3 reoperations (7.3%) at the index (n=1) or adjacent levels (n=2) in the AIDA group and 1 (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 2 contiguous levels and 105 patients who received 2-level ACDF. (25) 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 artificial intervertebral disc arthroplasty (AIDA) and 105 treated with ACDF for single-level degenerative disc disease (DDD). (33) The rationale for treatment allocation was not described. At 3 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.

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 8 years after implantation. (34) Degradation of the sheath, including surface fissures and full-thickness cracks, has been observed in 27% of retrieved Bryan discs. (35) One case of anterior migration of the Mobi-C disc was reported. (36) Another case was reported of fragmented fracture of the ceramic-on-ceramic Discocerv® Cervidisc Evolution at 1 month after implantation. (37) 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. (38) 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 (6 weeks and 3, 6, 12, and 24 months after surgery). For example, at the 6-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. (39) Included in the meta-analysis were 8 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 1 of 3 cervical discs (81 Bryan, 61 Mobi-C, and 28 ProDisc-C) and had at least 12 months of follow-up. (40) 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. (41) Heterotopic ossification was observed in CT images in 50% of the patients at a mean of 19 months’ follow-up. However, only 2 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. (20)

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 degenerative disc disease 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.

The rates of device failure and the need for reoperations due to device failure or malfunction are not well-defined. Reports of device failure that occur at time periods longer than the average follow-up in the clinical trials highlights the need for longer term studies to further define these adverse events.

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 case of a delayed hypersensitivity reaction to metal ions after disc arthroplasty was reported in 2009. (42) 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 4 cases of a lymphocytic reaction to a metal-on-metal artificial disc (1 Kineflex-C cervical disc and 3 lumbar) that required revision. (43) 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; 1 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 1 to 7 years commonly showed focal metallosis. (35)

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. (44)

The United Kingdom’s National Institute for Health and Care Excellence (NICE) issued guidance on the artificial cervical disc in 2010. (45) 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.”

The 2009 guidelines from the American Association of Neurological Surgeons (AANS) address anterior cervical discectomy (ACD) and anterior cervical discectomy and fusion (ACDF) for the treatment of cervical degenerative radiculopathy and cervical spondylotic myelopathy. These guidelines do not address the artificial cervical disc. (46, 47)

Summary

After 2 years of follow-up, trials of all the artificial cervical discs met non-inferiority criteria as measured by the NDI and overall success composite outcome. Longer term outcomes have only been reported on 3 of the devices (Prestige ST, ProDisc-C, and Bryan disks). The reports of long-term outcomes of these devices lack optimal follow-up rates. The trial results are consistent with continued non-inferiority of AIDA for all devices and lower cumulative reoperation rates at 4 to 5 years, but uncertainty remains because of the less than optimal follow-up rates. In addition, the reports of adverse effects of cervical artificial intervertebral disc arthroplasty (AIDA) raise questions on the overall risk/benefit ratio for these devices.

- The potential to reduce adjacent-level degenerative disc disease has been the major rationale driving device development and use of AIDA. Evidence to date has not consistently demonstrated a reduction in adjacent level disease with use of artificial cervical discs.

- The rates of device failure and the need for reoperations due to device failure or malfunction are not well-defined. Reports of device failure that occur at time periods longer than the average follow-up in the clinical trials highlights the need for longer term studies to further define these adverse events.

- 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.

At the present time, there is insufficient evidence to determine the impact of cervical arthroplasty devices on clinical outcomes over the long term. Results of trials that report 4-5 year outcomes are consistent with continued non-inferiority of AIDA, but uncertainty remains as to whether the benefits of these devices
outweigh the risks. Evidence to date has not shown a consistent beneficial effect of any cervical disc product on the development of adjacent level disease, whereas long-term complication rates with artificial discs remain unknown. The limited evidence on 4-5 year follow-up is inadequate to evaluate long-term results, in particular any effect of the device on adjacent level disc degeneration, device durability, adverse events, and revisions due to device malfunction. Longer term results are expected, given the FDA requirement for 7-10 year post-approval studies of the safety and function of the devices, and 5-10 year enhanced surveillance study of these discs to more fully characterize adverse events in a broader patient population. The longer follow-up is needed to better define the risk/benefit ratio of these devices.

Therefore, artificial intervertebral discs are considered not medically necessary for treatment of disorders of the cervical spine, including degenerative disc disease

Medicare National Coverage

A search of the online Medicare National Database (http://www.cms.gov/mcd/search.asp?from2=search.asp&) identified a national coverage decision on artificial intervertebral discs for the lumbar spine. There is no national coverage decision on artificial intervertebral discs for the cervical spine.

References


22. Coric D, Nunley PD, Guyer RD, Musante D, Carmody CN, Gordon CR, Lauryssen C, Ohnmeiss DD, Boltes MO. Prospective, randomized, multicenter study of cervical arthroplasty: 269 patients...


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ProDisc-C Total Disc Replacement  
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This policy was approved by the FEP® Pharmacy and Medical Policy Committee on March 14, 2014 and is effective April 15, 2014.

Signature on File  
Deborah M. Smith, MD, MPH