**2019 Position Statement from the International Society for the Advancement of Spine Surgery on Cervical and Lumbar Disc Replacements**

**Introduction:**

Cervical and lumbar degenerative disc disease are well known causes of neck and back pain in spine patients. The estimated 1-year incidence rate of neck pain and any episode of lower back pain is 10.4% to 21.3%1,2 and 1.5% to 36%3, respectively. Previous reports demonstrate significant socioeconomic effects of these common complaints.4,5 Currently, initial conservative treatment and ultimately fusion procedures are potential extremes of options for treatment of recalcitrant cervical and lumbar degenerative disc disease. Despite past reports of improved clinical outcomes with cervical and lumbar fusion procedures, there continues to be concerns of limiting motion at the affected segment and development of adjacent level degeneration and disease (ASD). Hilibrand et al. demonstrated that adjacent-segment disease occurred at a rate of 2.9% per year during the ten year postoperative period following anterior cervical fusion.6 Other studies have reported even higher adjacent segment degeneration and disease rates of 36%7 and 50%8 in the cervical spine. Past reports illustrate a wide range of the incidence rate (2.62%-34%) of adjacent segment degeneration and disease after lumbar fusion.9–11 These results led to the subsequent development of cervical and lumbar arthroplasty devices.

Despite the studies showing similar or improved clinical outcomes with cervical and lumbar arthroplasty, debate continues to exist over the potential benefits of total disc replacement (TDR) and potential complications with long-term device use. Currently, there are 8 Food and Drug Administration (FDA) approved cervical and 3 FDA approved lumbar TDR devices, not all of which are still commercially available. The aim of this review is to discuss the results of long-term follow-up studies, recent meta-analyses, newly approved devices, two-level use, and potential complications with cervical and lumbar TDR devices.

**Cervical Total Disc Replacement:**

**Historical Background:**

The first use of cervical total disc replacement (cTDR) dates back to the 1960s.12 Currently, 8 devices have been approved by the FDA for single level use in cervical arthroplasty including Prestige ST (Medtronic Inc.), ProDisc-C (DePuy Synthes; Johnson and Johnson), BRYAN (Medtronic Inc.), SECURE-C (Globus), PCM (Nuvasive), Mobic-C (Zimmer Biomet), Prestige LP (Medtronic Inc.), and M-6 cervical disc (Orthofix). Mobic-C and Prestige LP are also approved for two level use. The M6 device has moct recently received pre-market approval13(p6) and the Simplify disc has completed one and two level enrollment and is approaching FDA determination. The initial FDA investigational device exemption (IDE) trials for the currently approved cTDR devices demonstrated similar or greater improvement in outcomes of patients in the device group compared to ACDF.14–21 Similarly, meta-analyses of the these IDE trials illustrated similar improved outcomes with cTDR.22,23

**Long-term Follow-Up and Recent Meta-analyses:**

Initial prospective, randomized controlled IDE trials have demonstrated equivalent or improved functional outcome results of cTDR compared to ACDF.14–21 Mid and long-term follow-up have also demonstrated the overall positive success of arthroplasty compared to ACDF.24–28 In an 8-year follow-up study of twenty-one patients, Quan et al. reported that the majority of patients with the BRYAN disc continued to have favorable results.24 Burkus et al. reported that the arthroplasty group had improved or maintained neurologic status compared with ACDF at 5 year follow-up.25 Coric et al. reported significant, sustained improvement in range of motion in patients with cTDR (BRYAN disc or Kineflex-C) compared to ACDF at 4-year follow-up.26 In a 5 year follow-up study, Zigler et al. demonstrated that both groups (Prodisc-C and ACDF) had statistically significant improved clinical outcomes compared to baseline but patients with Prodisc-C had greater improvement in reported neck pain.27 At 4 year follow-up, Delamarter et al. reported improved visual analogue scale (VAS) neck score in patients with Prodisc-C compared to ACDF.28

Recently, longer-term follow up (5 years or greater) studies continue to demonstrate successful results of arthroplasty compared to ACDFs.29–35 Janssen et al. reported that both groups (Prodisc- C and ACDF) continued to have improved patient satisfaction with surgery and neurologic status at 7 year follow-up.29 Both groups reported similar positive outcomes, however, less patients in the Prodisc- group (7%) had secondary surgery compared to those with ACDF (18%).29 In a 10 year follow-up of the IDE study, Gornet et al. reported stable results for the Prestige LP group with patient reported outcomes, neurological status, and overall success.30 The authors also reported that the average motion at the index and adjacent level was maintained at 10 year follow-up and concluded that the device continued to have safe and effective results.30 Lavelle et al. reported 10 year outcomes for patients with the BRYAN cervical disc.31 The authors reported statistically significant improvement in overall success (81.3% vs. 66.3%) and neck and disability index (NDI) score in patients with cTDR compared to the ACDF group.31 Although the results were not shown to be statistically significant, patients with the BRYAN disc had a lower rate of secondary surgeries compared to those with ACDFs.31 A 7 year follow-up of the FDA IDE trial for the PCM device demonstrated greater improvement with NDI, VAS neck pain, physical component score (PCS) and mental component score (MCS) of the Short Form-12 (SF-12).32 The authors also reported decreased trends in secondary surgeries (3.6% vs. 7.6%).32 Hisey et al. reported, at 5 year follow-up, similar improvements in NDI, VAS neck and arm pain, and SF-12 scores for both groups (Mobic-C and ACDF).33 Additionally at 7 year follow up for Mobic-C, Radcliff et al. reported improvement in patient reported outcomes (NDI, VAS neck/ arm pain, SF-12 MCS/ PCS scores) for both the cTDR and ACDF group.36 The authors reported a statistically significant greater patient satisfaction in the cTDR group compared to ACDF.36 Burkus et al. reported maintained or improved neurologic status in patients with cTDR (Prestige disc) compared to ACDF from a 5 to 7 year period.34 Vaccaro et al. reported statistical superiority in overall success (79.2% and 63.6%) and patient satisfaction (96% vs. 88.8%) in the SECURE-C investigational group compared to ACDF at 7 year follow-up.35

Previously in a meta-analysis, McAfee et al. demonstrated that patients who have undergone arthroplasty achieved greater overall clinical success compared to ACDF patients (77.6% vs. 70.8%).22 In a meta-analysis of 3 FDA IDE randomized controlled trials, Udaphyaya et al. reported greater neurological success and lower rate of secondary surgeries for the cTDR group compared to the ACDF group.23 More recently, Gao et al. reported improved neurologic success and neck/arm pain (VAS) scores, fewer secondary surgeries, and increased motion at the index level in patients with cTDR versus ACDF.37 Similarly, a meta-analysis conducted by Zhang et al. reported improved neurological success in the arthroplasty group compared to ACDF.38 The authors also reported superiority in NDI, neck and arm pain (Numeric Rating Scale [NRS]) scores, and fewer secondary surgical procedures at the index level.38

**Adjacent Segment Disease:**

Long-term follow-up has facilitated further understanding of radiographic adjacent segment degeneration and symptomatic adjacent segment disease with cervical arthroplasty. Phillips et al. reported more frequent radiographic adjacent segment degeneration with ACDF compared to cTDR.32 Hisey et al. demonstrated that adjacent segment degeneration at the superior level was significantly lower for cTDR patients than ACDF.33 Similarly, Burkus et. al reported lower rates of additional adjacent level surgeries in the cTDR group compared to ACDF.34 Vaccaro et. al also demonstrated that less SECURE-C patients (17%) reported symptoms related to the adjacent level(s) compared to ACDF patients (37.5%).35 Janssen et. al reported less surgical procedures involving the adjacent level(s) in the ProDisc-C group compared to the ACDF group.29 Results from Lavelle et al. and Gornet et al. also demonstrated lower rates of revision surgeries for the adjacent level in the cTDR group compared to the ACDF groups (BRYAN and Prestige LP, respectively).30,31

In a review of 52,395 cases, Kelly et al. reported that secondary surgery was less common in the cTDR compared to the ACDF group within 90 days of surgery (2.04% vs. 3.35%), whereas there was no difference in rates at long term follow up (1,3,5, years postoperatively) between the two cohorts.39 Furthermore, the authors concluded that there was no protective benefits for single level degenerative disease with cTDR compared to ACDF.39

Various meta-analyses have been conducted in attempts to further clarify potential benefits of arthroplasty compared to ACDF.40–42 Verma et al. reported that although there were more patients in the ACDF group requiring adjacent-level surgery than cTDR (6.9% vs. 5.1%), the differences in rate of reoperation between the two groups was not statistically significant.40 In a meta-analysis of 32 studies, Shriver et al. reported an increased incidence of adjacent degeneration and disease in cervical arthroplasty with long-term follow up.41 Zhu et al. combined the results of 14 randomized controlled trials (RCTs) with long-term follow up (2 to 7 years) and reported that cTDR had lower rates of adjacent segment disease and fewer reoperations at the adjacent level.42 Although the meta-analysis by Luo et al. included fewer RCTs, the authors similarly concluded that cTDR had lower rates of adjacent segment disease compared to ACDF.43

**Approval for 2-level use:**

In 2013, Mobic-C was approved for two-level use. In the IDE trial conducted at 24 centers, results demonstrated significant, greater overall success of 2-level total disc arthroplasty with Mobic-C over ACDF.20 Since then, studies have demonstrated positive mid-term and long-term follow up for two-level cervical disc arthroplasty using the Mobic-C device.44,45 In a 4-year *post-hoc* comparison, Bae et al. reported that there were no statistical differences in clinical outcomes or overall success of the cTDR group compared to ACDF.46 In a 7 year follow-up study of the original IDE clinical trial, Radcliff et al. demonstrated that the two-level cTDR group had a significant improvement in NDI score, increased patient satisfaction rate, and decreased rate of re-operation at the index and adjacent level compared to ACDF.36

Prestige LP is also currently approved for two-level cervical disc arthroplasty. In the IDE randomized controlled trial, Gornet et al. demonstrated that the investigational group undergoing two level cervical disc arthroplasty had greater overall success than two level ACDF.47 Lanman et al. also demonstrated that the two-level Prestige LP group had statistically greater improvement in NDI score, neurological status, and overall success at 7 year follow-up.48 The investigational group also had preserved motion and fewer secondary surgeries than the ACDF group at long-term follow-up.48

**Devices with Recent Approval/ Currently in the FDA IDE Process:**

M6 recently received pre-market approval before the end point of the IDE trial. In a feasibility study, M6 demonstrated comparable results to other cervical total disc replacement devices.49 This device has an artificial annular (polyethylene weave) and nuclear (viscoelastic polyurethane core) component to better mimic the natural human intervertebral disc and range of motion.50 Reyes-Sanchez et al. demonstrated improved NDI score, neck/arm pain, and PCS of SF-36 with no serious adverse events at 24 months.51 The authors also reported that the mean range of motion returned to approximated pretreatment levels (12.2° vs 11.1°) by 24 months.51 Similarly, Thomas et al. also reported improved results for NDI, VAS, SF-36 scores in patients with the M6 device.52 With larger-scale distribution of the M6 implant, longer follow-up studies will be needed to continue to assess impact on clinical outcomes, patient range of motion, and potential adverse events.

The Simplify Disc™ is currently under investigation for FDA approval for one and two level use. Early results from Geisler et al. demonstrated improved NDI, VAS neck and arm pain for patients with the Simplify Disc.53 Two-level use studies with the Simplify disc have also recently completed patient enrollment.

**Potential complications:**

Possible complications with cervical disc arthroplasty include heterotopic ossification, subsidence/migration, device wear and tear, and adjacent segment disease.54 Recent evidence continues to report low rates of reoperation at both the index and adjacent level.29,30,33,45,55–57 Past reports report a broad range (7.3-69.2%) for heterotopic ossification rate.58–60 In a meta-analysis evaluating adverse events of total disc replacements, Anderson et al. reported that there were no statistical differences in dysphagia, heterotopic ossification, or overall incidence of neurologic deterioration between cervical disc arthroplasty group and ACDF group.61 The authors also reported that the cTDR group had a lower relative risk of surgical-related neurologic events and secondary surgeries compared to ACDFs.61

**Lumbar Total Disc Replacement:**

**Historical Background:**

The first use of lumbar total disc replacement dates back to the 1960s.12,62 The first model of the Charité device was developed in the 1980s and subsequent models received FDA approval in 2004.63 Initial studies of this device reported improved clinical and radiographic success compared to fusion.64–66 Currently, activL Artificial disc (Aesculap Implant Systems) and Prodisc-L (Syntheses Spine) are the only two commercially available FDA-approved devices. Other lumbar devices had completed PMA studies (Maverick, Flexicore, Kineflex, but either withdrew before FDA consideration or declined to sell commercially in the US.

**Results of Current Approved Devices:**

Prodisc-L was approved by the FDA in 2006. This device consists of three components: upper and lower plates composed of cobalt-chrome molybdenium alloy (CoCrMo) and a monoconvex ultra-high molecular-weight polyethylene inlay.69 Combined, these components form a spherical articulating device resembling a ball and socket joint.69 In a randomized controlled FDA investigational device exemption (IDE) trial, Zigler et al. demonstrated that patients with Prodisc-L had improved patient reported outcomes (Oswestry Disability Index [ODI], SF-36, and VAS pain), and neurological success compared to patients with circumferential spinal fusion at 2 year follow-up.70 In a 5 year follow-up of the FDA IDE trial, Zigler and Delamarter reported that both groups maintained improved patient reported outcomes.71 The authors also reported fewer secondary surgeries at the index level and acceptable range of motion in the lumbar TDR group compared to the control group.71 With an alternate analysis including additional FDA parameters, 48.1% of TDRs and 41.1% of fusions were overall statistical successes using a complex success formula..71 In an RCT FDA IDE trial for two level use, Delamarter et al. reported that more patients in the lumbar TDR group (58.8%) reached statistical overall success than the fusion group (47.8%) at 2 year follow-up, using a similar complex success definition.72

ActivL artificial disc was recently approved in June 2015. This device consists of two metal endplates and one semi-constrained ultra-high molecular weight polyethylene inlay.73 The polyethylene core supports anterior and posterior translational direction, potentially reducing biomechanical stress at the facet joints and adjacent levels.73 In the randomized controlled FDA IDE trial, Garcia et al. reported that the device was non-inferior to the control devices (Charite or Prodisc-L).74 The authors also reported improved results for return to work, radiographic success (59% vs. 43%), and ODI success (75% vs. 66%) in the activL group compared to the control group at 2 year follow up.74 The activL group also had decreased serious adverse events related to the device (12% vs. 19%) and similar surgical re-intervention rates (2.3% vs. 1.9%) compared to controls, however, these results did not reach statistical significance.74 In addition, the activL group had improved range of motion with segmental rotation (0.9° vs.-1.4° ; p < 0.01) and translation (+0.6 mm vs. +0.2 mm; p < 0.001) but not with lateral rotation (+0.6 mm vs. + 0.8 mm, p= 0.52).74 Additionally, a greater percentage of patients with activL had an increase in disc height (> 3mm) than the control group (94% vs. 87%, p=0.09).74

Currently, there are limited reports on long-term follow-up for activL. In a randomized, controlled FDA IDE study with 5 year follow-up, Yue and Garcia reported improvement in back pain severity and patient satisfaction in the activL group compared to the control group, but these results did not achieve statistical significance.75 The authors also reported no significant differences observed with range of motion (flexion/extension, translation, and lateral rotation) or disc height between the two groups.75 Comparable results relating to serious adverse events were reported in both groups (58% vs. 40%, p<0.01).75

A recent meta-analysis conducted by Zigler et al. of 4 RCTs with long-term follow up demonstrated improved ODI scores, decreased risk of reoperation, and increased likelihood of patient satisfaction with TDR compared to fusion.76 This meta-analysis included three FDA IDE studies as well as one OUS non-IDE prospective randomized trial, all with five year follow-up. Rao et al. conducted a meta-analysis of 7 RCTs with 2 year follow-up. Similarly, the authors reported improvements in ODI score, in addition to improved VAS score and shorter length of hospitalization.77 Ding et al. reported conflicting results regarding the superiority of lumbar TDR after reviewing 5 overlapping meta-analyses. But, the authors also reported the potential of lumbar TDR as an alternative treatment to fusion based off of short-term results.78

Various devices that are approved outside of the US have published reports with long term-follow up. Although not a randomized controlled study, Aghayev reported improved VAS leg and back scores and quality of life improvement (EQ-5D) in patients with lumbar TDR at 5 year follow-up.79 Implants included in this study were ActivL, Charite, Maverick, and Prodisc-L.79 The authors also reported the overall rates of complications and adjacent segment degeneration as 23.4% and 10.7%, respectively.79

**Adjacent Segment Level Disease:**

Past reports have attempted to further clarify the potential incidence rate and prevalence of adjacent segment degeneration and disease after arthroplasty compared to fusion. Harrop et al. reported a significant decrease in incidence rate of adjacent segment degeneration (9% vs. 34%) and disease (1% vs. 14%) of lumbar TDR compared to fusion. 9 In analyzing data from a prospective multicenter study, Zigler et al. reported less changes in adjacent level degeneration in the lumbar TDR group compared to fusion (9.2% vs. 28.6%) at 5 year follow-up.80 The authors also reported a decrease in new findings of adjacent level degeneration (6.7% vs. 23.8%) and secondary surgery (1.9% vs. 4.0%) in the lumbar TDR group compared to fusion.80 In a meta-analysis of 13 studies, Ren et al. also demonstrated decreased prevalence and reoperation rate in the lumbar TDR group compared to fusion for short-term and long-term follow up.81

**Potential Complications:**

Implant-related complications can include collapse, subsidence, or dislocation.79,82,83 Additional concerns with lumbar arthroplasty include approach-related complications, osteolysis secondary to polyethylene wear, heterotopic ossification and reoperation at the index or adjacent level.84 Past reports demonstrate low or similar rates of reoperation with lumbar TDR compared to fusion. 70,71,74,76,77,85 In a meta-analysis conducted by Hiratzka et al., patients in the lumbar fusion group had a twofold increased risk of adverse events compared with lumbar TDR with 2 year follow-up but the relative risk remained stable at 5 year follow-up.86 Additionally, this pooled data was from a limited amount of RCTs due to a lack of consistency with reporting and describing adverse events in the various trials.86

**Conclusion:**

Currently, there is compelling level I and II evidence with long-term follow-up supporting the use of TDR as a viable alternative to fusion procedures. Although some of this is industry sponsored data, there are multiple layers of independent and governmental oversight, as well as peer-review prior to publication. Recent evidence and comparison with meta-analyses continue to demonstrate positive outcomes and benefits over time, even with with expanded two-level use in the cervical spine. Studies now following patients out to 5 to 10 years continue to show positive results for these novel devices.

Based on the above review of the available evidence-based scientific literature (much of it Level Ib or Level Ia), ISASS as a global organization of spine surgery professionals strongly supports both cervical and lumbar total disc replacements as safe and effective treatment alternatives to fusion in appropriately-selected patients, following FDA study guidelines for use.

ISASS Education Committee:

 Alex Vaccaro MD, PhD Chair

Greg Schroeder MD,

Divi,

Goyal,

Jack Zigler MD

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