

## Five-year Reoperation Rates, Cervical Total Disc Replacement versus Fusion,

### Results of a Prospective Randomized Clinical Trial

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### ABSTRACT

**Study Design.** Prospective randomized controlled trial (RCT).

**Objective.** Determine the reasons for, and rates of, secondary surgical intervention through 5 years at both the index and adjacent levels in patients treated with cervical total disc replacement (TDR) or anterior cervical discectomy and fusion (ACDF). TDR patients were treated with ProDisc-C.

**Summary of Background Data.** Several outcome-based prospective, randomized clinical trials have shown cervical TDR to be equivalent if not superior to fusion. The ability of TDR to allow decompression while maintaining motion has led many to suggest that adjacent level degeneration as well as reoperation rates may be decreased when compared to fusion.

**Methods.** A total of 209 patients were treated and randomized (103 TDR and 106 ACDF) at 13 sites. A secondary surgical intervention at any level was considered a reoperation.

**Results.** At 5 years, the ProDisc-C patients had statistically significant higher probability of no secondary surgery at the index and adjacent levels compared to the ACDF patients (97.1% vs 85.5%,  $p=0.0079$ ). No reoperations in ProDisc-C patients were performed for implant breakages or device failures. For ACDF patients, the most common reason for reoperation at the index level was pseudarthrosis, and for both ACDF and TDR patients the most common reason for adjacent level surgery was recurrent neck and/or arm pain.

**Conclusions.** 5-year follow-up of a prospective RCT revealed 5-fold difference in reoperation rates when comparing ACDF treated patients (14.5%) to TDR (2.9%). These findings suggest the durability of TDR, as well its potential to slow the rate of adjacent level disease.

**Key Words:** cervical disc arthroplasty, ProDisc-C, total disc replacement, ACDF, cervical fusion, randomized clinical trial, reoperation, re-operation

**Mini-Abstract:**

A multicenter prospective randomized control trial of 209 patients with symptomatic single level cervical disc disease compared surgical treatment with ProDisc-C to

traditional ACDF. Five-year results demonstrated statistically significantly lower rates of reoperations at both index and adjacent levels in patients randomized to treatment with ProDisc-C.

### **Key Points**

- Longer term follow-up of Level-1 study comparing TDR versus ACDF shows a 5-fold increase in the rate of reoperation for ACDF.
- No reoperations in the TDR group were due to implant breakages or device failures.
- TDR appears to be a robust technology and the theoretical advantages of maintaining or restoring motion appear to have a sparing effect on adjacent segment disease.

### **INTRODUCTION**

Anterior cervical discectomy and fusion (ACDF) is a well-accepted treatment for radiculopathy. It allows decompression and is generally accompanied by grafting of the interspace and anterior plate fixation. Although high success rates have been associated with this procedure, problems have included pseudoarthrosis with recurrent pain at the index level, which has been reported to range from 2.9% to 6.9% per year despite high fusion rates. Hilibrand, et al, investigated 338 patients and reported that adjacent segment disease occurred at a relatively constant incidence of 2.9% per year<sup>1</sup>.

Cervical total disc replacement (TDR) was designed to allow neural decompression similar to that performed in an anterior cervical discectomy and fusion, to maintain motion, along with the potential to minimize adjacent segment disease. Outcome-based, prospective randomized clinical trials for Prodisc-C, Prestige ST, and Bryan have shown cervical TDR to be equivalent if not superior to ACDF through 2

years.<sup>2,3,4</sup> For these three TDRs with FDA approval, longer term follow-up results have more recently become available.<sup>5,6,7</sup>

Several biomechanical studies have shown increased pressure in the disc spaces adjacent to an anterior cervical fusion, as well as increased range of motion in the adjacent discs.<sup>8,9,10</sup> These studies have also shown that TDR does not produce the similar increases in adjacent level disc pressure or range of motion. These in vitro studies suggest that discs adjacent to a fusion, showing increased range of motion and increased intra discal pressure, will have a higher incidence of degeneration and potential symptoms leading to surgical intervention compared to TDR.

Multiple clinical studies have compared ACDF with cervical TDR and many have shown significant differences with increased motion at adjacent levels in the ACDF cohorts, as well as increased adjacent level degeneration.<sup>7,11-19</sup> More importantly, several studies comparing cervical TDR to ACDF have reported a 2 to 6 times higher rate of reoperation in the ACDF patients.<sup>2,5,13,17,20</sup>

The objective of this report is to determine the rates of secondary surgical intervention at both the index and adjacent levels through 5 years, comparing patients treated with cervical TDR versus the control group, ACDF.

## **MATERIALS AND METHODS**

### **Study Design**

This study provides 5-year results for the investigational device exemption (IDE), randomized control trial comparing results with ProDisc-C (Synthes USA Products LLC, Westchester, Pennsylvania) to ACDF previously described through two years (Murray 2009). As part of the FDA regulated post approval study, patients in the original study,

who consented, are being followed at annual intervals through seven years. This analysis provides an interim report of the secondary surgeries performed through 5 years. Institutional review board approval and patient informed consent were obtained for the initial and post approval studies. The clinical trial identification number is NCT00291018.

This design of the IDE trial with follow-up out to 2 years has been previously well described.<sup>1</sup> A total 209 patients were preoperatively randomized (1:1) to ProDisc-C or ACDF, and remained blinded to their treatment assignment until immediately after surgery. After FDA approval of ProDisc-C, consenting patients in the original study are being followed at annual intervals up to 7 years as part of an FDA-regulated post approval study. This analysis provides an interim assessment of the results through 5 years. Patients were evaluated preoperatively and postoperatively at six weeks, three months, six months, 12 months and then annually up to 5 years.

### **Patient Population**

The primary patient inclusion criteria included single level cervical disc disease causing debilitating radiculopathy from a single vertebral segment between C3 and C7, unresponsive to nonoperative treatment for at least six weeks, and a neck disability index score of 15/50 (30%) or more.

### **Study Interventions**

The ProDisc-C is based on a ball and socket principle and is comprised of three components. There are two endplates manufactured from a cobalt chromium molybdenum alloy with a midline keel fixation, titanium plasma-sprayed coating for bony ongrowth, and an ultra-high-molecular-weight-polyethylene (UHMWPE) inlay.

The upper endplate design allows for a highly polished concave bearing surface that articulates with a convex UHMWPE spherical dome. The design for the caudal endplate allows for the UHMWPE inlay to snap lock into the plate, thus providing the convex bearing surface. For the ProDisc-C, this is pre-assembled during manufacture. This design enables reconstruction utilizing various heights and vertebral endplate sizes (Figure 1).

For the control group, after similar discectomy, allograft bone spacers (either surgeon cut or commercially prepared) were used and, when available, local bone was also packed around or within the allograft. No other bone substitutes were applied. An anterior cervical fixed angle plate was placed over the graft and secured in the adjacent vertebral bodies with four screws.

For both treatment groups, the standard Smith-Robinson anterior approach was used to expose the cervical spine with exposure limited to the operative level. The postoperative care regimen, including an appropriate rehabilitation program, was at the discretion of the surgeon. All patients began ambulating immediately postoperative, and many were done on an outpatient basis. A hard or soft collar was used if deemed necessary by the surgeon.

### **Study Outcomes**

A secondary surgical intervention of any type, at any level, was considered a reoperation. Reoperations included any subsequent surgical procedure to the cervical spine, including posterior procedures such as a decompressive laminectomy or foraminotomy.

### **Statistical Analysis**

Based on the Cox Proportional Hazards model, the Andersen-Gill model was used to compare the rate of index and adjacent level related reoperations between treatment groups. The Andersen-Gill model is most appropriate when modeling multiple failure-time data. In this case, subjects can experience multiple reoperations at different time intervals. In that respect, it is superior to a more traditional survival analysis model, such as Kaplan-Meier, as it uses all relevant information.

## RESULTS

A total of 209 patients were randomized such that 103 received ProDisc-C and 106 receive an ACDF. Patient demographics and pre-operative characteristics have been described previously.<sup>1</sup> Five-year follow-up rates were 72.7% (72/99) for the ProDisc-C group and 63.5% (61/96) for the ACDF group. Patients were excluded from the analysis due to death not related to study treatment (2 ProDisc-C and 3 ACDF) and withdrawal from the long term follow-up (2 ProDisc-C and 7 ACDF).

At 5 years, the ProDisc-C patients had a statistically significantly higher probability of no secondary surgery at the index and adjacent levels compared to the ACDF patients (97.1% and 85.5% respectively with p-value = 0.0079), See Figure 2. No reoperations in ProDisc-C patients were performed for device breakage or failure.

A total of 12 ACDF patients had reoperations with three of the 12 having more than one secondary procedure, totaling 16 reoperations. As displayed in Table 1, of the 16 procedures, eight involved the index level and nine included an adjacent level. Six of the eight index level procedures were performed due to pseudarthrosis, one to address foraminal stenosis, and one to correct a plate shift causing dysphagia. All adjacent level procedures were in response to symptomatic adjacent level degeneration. Four of the 16

procedures included posterior fixation, while all others involved additional ACDF procedures. Figures 3a-3b illustrate an ACDF patient with a reoperation.

As shown in Table 2, three ProDisc-C patients had reoperations. One involved the index level only to treat persistent pain, and two incorporated the index and adjacent levels for persistent pain and adjacent level degeneration. The ProDisc-C was removed in two patients and the levels converted to anterior fusions. One ProDisc-C was left intact with a posterior foraminotomy and fusion with stabilization. Figures 4a-4b illustrate a ProDisc-C patient with a reoperation.

## **DISCUSSION**

At the inception of the ProDisc-C IDE study, safety and efficacy of the TDR technology compared to the gold standard of an ACDF were the main study goals. However, most surgeons were aware of the rates of adjacent level disease following single level ACDF, and hoped that longer term follow-up of these patients might demonstrate a sparing effect on adjacent level degeneration (radiographic) and adjacent level disease (clinical). Reoperations at both index and adjacent levels are a clinically significant indicator of this phenomenon. This is one of the first reports specifically addressing the issue of differential reoperation rates.

Eck et al.<sup>8</sup> showed a 2-fold increase in adjacent level disc pressure in the fusion constructs in a cadaver model comparing TDR with fusion. Dmitriev et al.<sup>9</sup> studied adjacent level intradiscal pressure and segmental kinematics in 10 human cadaver spines and reported significantly increased intradiscal pressure under flexion/extension testing in the fusion constructs compared to TDR. Laxer et al.<sup>10</sup> utilizing miniature intradiscal



strain-gauge-based transducers, reported that adjacent level cervical discs experience substantial lower pressure after TDR when compared to fusion.

Over the past decade, many clinical studies comparing cervical TDR with fusion have reported increased range of motion or increased degeneration at the adjacent levels in the fusion cohorts. Park et al.<sup>21</sup> compared 272 TDR patients with 182 ACDF patients and reported that the fusion patients had increased angular motion at the superior adjacent level. Wigfield et al.<sup>11</sup> reported that at 12 months fusion resulted in increased motion at adjacent levels when compared to TDR. In a review of 187 patients, Auerbach et al.<sup>14</sup> showed increased ROM in adjacent levels below fusions not seen in TDR patients. Shin et al.<sup>18</sup> reported increased ROM at 2-year follow-up at the levels adjacent to fusion with normal adjacent level motion in TDR. Adjacent level degeneration was reported by Kim et al.<sup>19</sup> to be 3.5 times higher in 54 cervical fusion patients when compared to 51 TDR cohorts. Coric et al.<sup>16</sup> also compared 57 cervical TDR patients with 41 fusion patients and reported less adjacent level degeneration in those with TDR.

Prospective, randomized FDA IDE trials have been conducted in the United States for three cervical TDR devices compared to ACDF and all three devices were subsequently approved by FDA.<sup>2, 3, 4</sup> All three studies have shown an increased reoperation rate in the ACDF control cohort. At a minimum 2 year follow-up, Murrey et al.<sup>2</sup> reported a reoperation rate of 8.5% in the fusion group and 1.9% in the ProDisc-C group. Anderson et al.<sup>20</sup> reported significantly more reoperations in the fusion group compared to the Bryan TDR cohort. Burkus et al.<sup>5</sup> reported the results of the Prestige TDR and showed significantly less reoperations in the TDR group. Zhang et al.<sup>13</sup>

reported on a randomized trial comparing 60 fusion patients to 60 Bryan TDR patients and reported a 4 times increased reoperation rate in the fusion group.

In the longer-term follow-up of the two patient groups in the prospective randomized IDE study comparing ProDisc-C to ACDF, the reoperation rates differed significantly between the fusion control and TDR patient cohorts. The ACDF patients were observed to have a 5 times higher rate of reoperations. The most common reason for reoperation at the index level in the fusion cohort was pseudarthrosis, and in one patient a lift off of the plate causing swallowing difficulties which required revision surgery. Half of the reoperations in the ACDF patients were performed for adjacent level degeneration. Among the ProDisc-C patients, no reoperations were performed for implant breakages or device failures. All reoperations in this group were for recurring pain, at either index or adjacent levels.

## **CONCLUSION**

The results of this 5-year follow-up analysis are consistent with the published biomechanical and clinical studies comparing cervical TDR with ACDF demonstrating a significant sparing effect of TDR on the adjacent level. These patient cohorts will be followed for an additional two years, so that additional data will be generated with even longer term follow-up.

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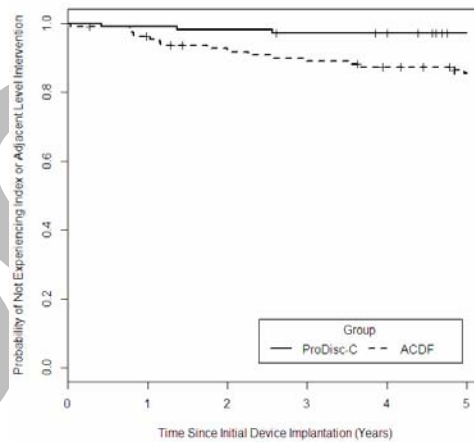
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**Figure Titles:**



**Figure 1.** ProDisc™-C (Synthes Spine USA Products, LLC, West Chester, PA)



**Figure 2.** Probability of Not Experiencing a Secondary Surgical Intervention by Group (Andersen-Gill model with p-value Wald Ch-Square: at 5-years ProDisc-C 97.1% and ACDF 85.5% with p=0.0079).



**Figure 3A.** ACDF at C5-C6 level. Approximately 3 years after this index surgery, patient developed neck and radiating arm pain with triceps' weakness. One year later, patient underwent C5-C6 plate removal and C6-C7 ACDF for the adjacent level disease.



**Figure 3B.** One year following the reoperation for adjacent level disease (5 years following the original surgery).



**Figure 4A.** Index TDR C4-C5. After 6 months, patient began developing increasing neck pain. After failing conservative care, including epidural and facet injections, patient underwent removal of the TDR and fusion of the level. Note the small TDR footprint and the anterior placement.



**Figure 4B.** 5 years following TDR removal and subsequent fusion (6 years following the original surgery).



**Table 1. ACDF Case Summary Secondary Surgical Procedures (in ascending order by time to surgery)**

Patient	Group	Index Surgery Level	Time to Surgery	Reason	Description	Secondary Surgery Affected Level
1	ACDF	C6-C7	0.5 mos	Plate lift-off	-Dysphagia; difficulty swallowing -Radiographs demonstrated plate shifted/elevated off bone 5mm -Plate removed	C6-C7
2	ACDF	C4-C5	9.5 mos	Pseudarthrosis	-Significant increase in neck pain, right-sided weakness -C4-C5 pseudarthrosis identified on radiographs and CT -Revision ACDF	C4-C5
3	ACDF	C6-C7	10 mos	Pseudarthrosis	-Moderate to severe neck pain; radiographs revealed non-union - Graft subsidence after patient hit head in pool -Revision ACDF	C6-C7
4	ACDF	C6-C7	10 mos	Foraminal stenosis	-TMJ symptoms and hand weakness -Foraminal stenosis diagnosed at C6-C7 -Posterior laminectomy/foraminotomy	C6-C7
5	ACDF	C5-C6	12.5 mos	Pseudarthrosis	-Persistent neck/shoulder pain and arm numbness, radiculopathy -Lucency in the inferior screws and pseudarthrosis C5-C6 -Posterior supplemental fixation	C5-C6
6	ACDF	C6-C7	14 mos	Pseudarthrosis	-Following a motor vehicle accident, increased cervical pain -Gross motion C6-C7 in flexion and extension. -Posterior supplemental fixation	C6-C7
7	ACDF	C6-C7	14 mos	Pseudarthrosis	-Persistent neck pain - C6-C7 pseudarthrosis identified on CT -Revision ACDF	C6-C7
8	ACDF	C6-C7	21 mos	Pseudarthrosis	-Persistent neck pain - Non-union and graft resorption at C6-C7 -Posterior supplemental fixation	C6-C7
9	ACDF	C5-C6	24 mos	Adjacent level disease	-Neck/arm pain; radiculopathy -Adjacent level degeneration diagnosed at C6-C7 - Plate removed at C5-C6 and ACDF at C6-C7	C5-C6; C6-C7
10	ACDF	C5-C6	27.5 mos	Adjacent level disease	-Radiculopathy; foraminal stenosis at C6-C7 - Plate removed at C5-C6 and ACDF C6-C7	C5-C6; C6-C7
2	ACDF	C4-C5	31 mos	Adjacent level disease	-Increased neck/upper extremity pain and weakness; adjacent level radiculopathy - Plate removed at C4-C5 and ACDF at C5-C6	C4-C5; C5-C6

**Table 1. ACDF Case Summary Secondary Surgical Procedures (in ascending order by time to surgery)**

Patient	Group	Index Surgery Level	Time to Surgery	Reason	Description	Secondary Surgery Affected Level
11	ACDF	C6-C7	36 mos	Adjacent level disease	-Recurrence of headaches; neck pain and radiculopathy -Disc bulge/protrusion on MRI at C5-C6 -Plate removed at C6-C7 and ACDF at C5-C6	C5-C6; C6-C7
3	ACDF	C6-C7	43 mos	Adjacent level disease	-Neck pain with radiation to arm -Loss of disc height and foraminal stenosis -Plate removed at C6-C7, ACDF at C5-C6 with a plate that spanned C5-C7	C5-C6; C6-C7
12	ACDF	C5-C6	44.5 mos	Adjacent level disease	-Increased neck/upper extremity pain -Plate removal at C5-C6 and ACDF at C6-C7	C5-C6; C6-C7
2	ACDF	C4-C5	48 mos	Adjacent level disease	-Herniation, neck/upper extremity pain -Plate removed at C5-C6 and ACDF at C3-C4	C3-C4; C5-C6
10	ACDF	C5-C6	60 mos	Adjacent level disease	-Neck pain and suboccipital headaches -ACDF at C4-C5	C4-C5

**Table 2. ProDisc-C Case Summary Secondary Surgical Procedures (in ascending order by time to surgery)**

Patient	Group	Index Surgery Level	Time to Surgery	Reason	Description	Secondary Surgery Affected Level
1	ProDisc-C	C4-C5	16.5 mos	Pain	-Increased pain radiating to bilateral shoulders; persistent pain -ProDisc-C removed and converted to ACDF	C4-C5
2	ProDisc	C4-C5	16.5 mos	Pain; adjacent level disease	-Ongoing neck and severe arm pain -Removal ProDisc-C and converted to ACDF C3-C5	C3-C4; C4-C5
3	ProDisc	C6-C7	31 mos	Pain; adjacent level disease	-ProDisc-C subsidence at C6-C7 with increased myofascial cervicothoracic pain -ProDisc-C left intact; foraminotomy and fusion C6-T1 with posterior stabilization	C6-C7; C7-T1