

D R A F T

ProDisc™-C Total Disc Replacement

PACKAGE INSERT

Synthes Spine

IMPORTANT INFORMATION ON THE ProDisc™-C Total Disc Replacement

10/07

GPxxxx-X

CAUTION: Federal (USA) law restricts this device to sale by or on the order of a physician (or properly licensed practitioner) that has appropriate training or experience.

Device Description

The ProDisc™-C Total Disc Replacement is made up of three components. The first is the inferior CoCrMo (cobalt chromium molybdenum) alloy plate with a midline keel orientated anterior-posterior that is anchored into the endplate of the inferior vertebral body. The second component is an Ultra High Molecular Weight Polyethylene (UHMWPE) insert that is pre-assembled snap-locked into a tray detail in the inferior CoCrMo alloy plate and provides the inferior convex bearing surface. The third component is a CoCrMo alloy plate with a midline keel that anchors to the superior vertebral body and has a highly polished concave bearing surface that articulates with the convex UHMWPE spherical dome.

The endplate footprints range from 15-19 mm wide (medial-lateral) x 12-18 mm deep (anterior-posterior). Each endplate size is available in three disc heights: 5, 6, and 7 mm. This allows for a wide range of sizing to accommodate individual patient anatomy.

The bone contacting surfaces of the inferior and superior plates as well as both keels are titanium plasma spray coated, which may provide additional fixation through bony ingrowth.

The maximum range of motion allowed by the ProDisc™-C Total Disc Replacement device design is 20° in flexion/extension (17.5° for the 5mm Large, Large Deep, Extra Large, and Extra Large Deep implants), 20° in lateral bending (17.5° for the 5mm Large, Large Deep, Extra Large, and Extra Large Deep implants), and the device is unconstrained in axial rotation as measured through *in vitro* testing.

The device is provided pre-assembled in the following configurations:

Dimensions – Endplates			
Size	A/P (mm)	Lateral (mm)	Disc Heights (mm)
Implant – Medium	12	15	5, 6, 7
Implant – Medium Deep	14	15	5, 6, 7
Implant – Large	14	17	5, 6, 7
Implant – Large Deep	16	17	5, 6, 7
Implant – Extra Large	16	19	5, 6, 7
Implant – Extra Large Deep	18	19	5, 6, 7

Catalog Number	Component Description
09.820.025S	ProDisc-C Implant, medium 5mm, sterile
09.820.026S	ProDisc-C Implant, medium 6mm, sterile
09.820.027S	ProDisc-C Implant, medium 7mm, sterile
09.820.035S	ProDisc-C Implant, medium Deep 5mm, sterile
09.820.036S	ProDisc-C Implant, medium Deep 6mm, sterile
09.820.037S	ProDisc-C Implant, medium Deep 7mm, sterile
09.820.045S	ProDisc-C Implant, large 5mm, sterile
09.820.046S	ProDisc-C Implant, large 6mm, sterile
09.820.047S	ProDisc-C Implant, large 7mm, sterile
09.820.055S	ProDisc-C Implant, large deep 5mm, sterile
09.820.056S	ProDisc-C Implant, large deep 6mm, sterile
09.820.057S	ProDisc-C Implant, large deep 7mm, sterile
09.820.065S	ProDisc-C Implant, extra large 5mm, sterile
09.820.066S	ProDisc-C Implant, extra large 6mm, sterile
09.820.067S	ProDisc-C Implant, extra large 7mm, sterile
09.820.075S	ProDisc-C Implant, extra large Deep 5mm, sterile
09.820.076S	ProDisc-C Implant, extra large Deep 6mm, sterile
09.820.077S	ProDisc-C Implant, extra large Deep 7mm, sterile

Indications for Use

The ProDisc™-C Total Disc Replacement is indicated in skeletally mature patients for reconstruction of the disc from C3-C7 following single-level discectomy for intractable symptomatic cervical disc disease (SCDD). Symptomatic cervical disc disease is defined as neck or arm (radicular) pain and/or a functional/neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI, or X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or loss of disc height. The ProDisc™-C Total Disc Replacement is implanted via an open anterior approach. Patients receiving the ProDisc™-C Total Disc Replacement should have failed at least six weeks of non-operative treatment prior to implantation of the ProDisc™-C Total Disc Replacement.

Contraindications

The ProDisc™-C Total Disc Replacement should not be implanted in patients with the following conditions:

- Active systemic infection or infection localized to the site of implantation
- Osteoporosis defined as DEXA bone density measured T-score \leq -2.5

- Marked cervical instability on neutral resting lateral or flexion/extension radiographs; translation > 3mm and/or > 11° of rotational difference to either adjacent level
- Allergy or sensitivity to the implant materials (cobalt, chromium, molybdenum, polyethylene, titanium)
- Severe spondylosis characterized by bridging osteophytes or a loss of disc height > 50% or an absence of motion (<2°), as this may lead to limited range of motion and may encourage bone formation (e.g., heterotopic ossification, fusion)
- Clinically compromised vertebral bodies at the affected level due to current or past trauma (e.g., by radiographic appearance of fracture callus, malunion, or nonunion)
- Patients with SCDD at more than one level

Warnings

Correct placement of the device is essential to optimal performance. Use of the ProDisc™-C Total Disc Replacement should only be undertaken after the surgeon has become thoroughly knowledgeable about spinal anatomy and biomechanics, has had experience with anterior cervical spinal surgeries, and has had hands-on training in the use of this specific device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, including neurological complications.

The safety and effectiveness of this device has not been studied in the pediatric or adolescent age group (<21 years old).

Due to the proximity of vascular and neurological structures to the implantation site, there are risks of serious or fatal hemorrhage and risks of neurological damage with the use of this device. Care should be taken to identify and protect these structures during surgery.

Precautions

Patient selection is extremely important. In selecting patients for a total disc replacement the following factors can be of importance to the success of the procedure: the patient's occupation or activity level, a condition of senility, mental illness, alcoholism, or drug abuse. In addition, certain degenerative diseases (i.e., degenerative scoliosis or ankylosing spondylitis) may be so advanced at the time of implantation that the expected useful life of the device is substantially decreased.

Furthermore, correct selection of the appropriate implant size is extremely important to assure the placement and function of the device. Please refer to the ProDisc™-C Total Disc Replacement Technique Guide for step by step instructions on the required surgical technique, including determining the correct implant size.

The safety and effectiveness of this device has not been established in patients with the following conditions:

- skeletally immature patients, pediatric or adolescent children (<21 years old), or those over the age of 60
- more than one vertebral level with SCDD

- prior fusion surgery at an adjacent vertebral level
- prior surgery at the level to be treated
- patients with progressive symptoms and signs of spinal cord/nerve root compression with less than six weeks of conservative treatment
- facet joint disease or degeneration at the level to be treated
- neck or arm pain of unknown etiology
- Paget's disease, osteomalacia, or other metabolic bone disease
- pregnancy
- taking medications known to potentially interfere with bone/soft tissue healing (e.g., steroids)
- rheumatoid arthritis or other autoimmune disease
- severe diabetes mellitus requiring daily insulin treatment
- systemic disease including AIDS, HIV, and Hepatitis
- active malignancy

In order to minimize the risk of periprosthetic vertebral fractures, surgeons must consider all co-morbidities, past and present medications, previous treatments, etc. A screening questionnaire for osteopenia or osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation), may be used to screen patients to determine if a DEXA bone mineral density measurement is necessary. If DEXA is performed, the patient should be excluded from receiving the device (per the contraindications listed above) if the DEXA bone density measured T score is ≤ -2.5 , as the patient may be osteoporotic. It may also be advisable to exclude patients with a T score ≤ -1.0 as the patient may be osteopenic.

Use aseptic technique when removing the ProDisc™-C Total Disc Replacement implant from the innermost packaging.

Use care when handling the ProDisc™-C Total Disc Replacement implant to ensure that it does not come in contact with objects that could damage the implant. Exercise care to ensure that implantation instruments do not contact the highly polished articulating surfaces of the endplates. Damaged implants are no longer functionally reliable.

To prevent unnecessary damage to the bearing surfaces, ensure that blood or other debris is not trapped within the device.

ProDisc™-C Total Disc Replacement implant should not be used with components or instruments of spinal systems from other manufacturers. See the surgical technique manual for step by step instructions.

Surgical implants must never be re-used or re-implanted. Even though the device appears undamaged, it may have small defects and internal stress patterns that may lead to early breakage.

Patients should be instructed in postoperative care procedures and should be advised of the importance of adhering to these procedures for successful treatment with the device including the avoidance of heavy lifting, repetitive bending, and prolonged or strenuous

activity initially and for a period of weeks to months depending on the individual patient's progress and the stability and functioning of the implant.

Adverse Events

The ProDisc™-C Total Disc Replacement was implanted in 103 investigational subjects and compared to 106 control subjects who received an anterior cervical discectomy and fusion (ACDF) in a multi-center, prospective, randomized, non-inferiority clinical trial. The number of patients who experienced one or more adverse event was not statistically different (p = 1.0000).

The following adverse events were reported during the clinical study comparing ProDisc™-C Total Disc Replacement to ACDF.

Table 1: All Adverse Events

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2 - 42 days)		Short Term (>42-210 days)		Long Term (>210 days)		ACDF (N=106)		ProDisc-C (N=103)	
	ACDF	PRC	ACDF	PRC	ACDF	PRC	ACDF	PRC	Patients (%)	Events (E/Pt)	Patients (%)	Events (E/Pt)
ALL ADVERSE EVENTS									86 (81.1%)	254 (2.40)	84 (81.6%)	237 (2.30)
Adjacent Level DDD or DJD	0	0	0	0	1	0	3	0	4 (3.8%)	4 (0.04)	0 (0.0%)	0 (0.00)
Burning or Dysesthetic Pain	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Cancer	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Cardiovascular	2	2	0	1	3	1	2	1	7 (6.6%)	7 (0.07)	5 (4.9%)	5 (0.05)
DDD Progression, Non-Cervical	0	0	0	0	1	0	0	1	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Dermatological	0	0	1	0	0	0	0	1	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Dizziness	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Dural Tear	0	1	0	0	0	0	0	1	1 (0.9%)	1 (0.01)	6 (5.8%)	6 (0.06)
Dysphagia	3	2	5	3	0	0	0	0	9 (8.5%)	9 (0.08)	0 (0.0%)	0 (0.00)
Dysphonia	1	0	0	0	0	0	0	0	1 (0.9%)	1 (0.01)	2 (1.9%)	2 (0.02)
Edema	1	2	0	0	0	0	0	0	1 (0.9%)	0 (0.00)	1 (1.0%)	1 (0.01)
Fatigue	0	1	0	0	0	0	0	0	0 (0.0%)	0 (0.00)	0 (0.0%)	0 (0.00)
Fracture - Vertebral	0	0	0	0	0	0	1	0	1 (0.9%)	1 (0.01)	0 (0.0%)	0 (0.00)
Gastrointestinal	11	15	1	1	-2	1	2	2	15 (14.2%)	16 (0.15)	16 (15.5%)	19 (0.18)
Genitourinary	2	4	0	1	0	0	1	0	3 (2.8%)	3 (0.03)	5 (4.9%)	5 (0.05)
Headache	1	3	2	4	3	4	8	9	12 (11.3%)	14 (0.13)	18 (17.5%)	20 (0.19)
Infection - Non-Wound	0	1	0	0	2	2	4	0	6 (5.7%)	6 (0.06)	2 (1.9%)	3 (0.03)
Infection - Superficial Wound	0	0	1	0	0	0	0	0	1 (0.9%)	1 (0.01)	0 (0.0%)	0 (0.00)
Insomnia	3	4	0	1	0	0	0	1	3 (2.8%)	3 (0.03)	6 (5.8%)	6 (0.06)
Musculoskeletal	0	1	4	3	2	10	15	7	16 (15.1%)	21 (0.20)	18 (17.5%)	21 (0.20)
Musculoskeletal (Spasms - Back)	0	0	1	0	0	0	0	1	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Musculoskeletal (Spasms - Neck)	1	0	2	0	1	2	1	1	5 (4.7%)	5 (0.05)	3 (2.9%)	3 (0.03)
Musculoskeletal (Spasms - Non-Specific)	2	2	0	0	2	0	0	1	4 (3.8%)	4 (0.04)	3 (2.9%)	3 (0.03)
Narcotics Use	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Neurological	0	1	0	0	0	1	1	2	1 (0.9%)	1 (0.01)	4 (3.9%)	4 (0.04)
Numbness Index Level	0	0	0	0	0	0	2	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Numbness Non-Index Level	0	2	0	1	3	2	4	8	7 (6.6%)	7 (0.07)	11 (10.7%)	13 (0.13)
Ossification	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Other	1	1	0	2	2	1	4	1	6 (5.7%)	7 (0.07)	4 (3.9%)	5 (0.05)
Pain - Back	0	0	1	2	4	3	3	6	8 (7.5%)	8 (0.08)	11 (10.7%)	11 (0.11)
Pain - Back and Lower Extremities	0	0	0	1	0	1	2	3	2 (1.9%)	2 (0.02)	4 (3.9%)	5 (0.05)
Pain - Incision Site	0	1	0	0	0	0	1	0	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Pain - Neck	2	1	2	2	10	7	11	6	22 (20.8%)	25 (0.25)	16 (15.5%)	16 (0.16)
Pain - Neck and Other	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Pain - Neck and Shoulder	0	2	0	1	2	1	4	4	6 (5.7%)	6 (0.06)	7 (6.8%)	8 (0.08)
Pain - Neck and Upper Extremities	0	0	0	0	1	2	6	1	6 (5.7%)	7 (0.07)	3 (2.9%)	3 (0.03)
Pain - Neck and Upper Ext. with Numbness	0	0	0	1	5	2	2	3	6 (5.7%)	7 (0.07)	6 (5.8%)	6 (0.06)
Pain - Other	6	0	0	0	0	0	3	5	7 (6.6%)	9 (0.09)	5 (4.9%)	5 (0.05)
Pain - Shoulder	0	0	1	1	2	4	6	5	9 (8.5%)	9 (0.08)	9 (8.7%)	10 (0.10)
Pain - Upper Extremities	0	2	0	0	2	3	3	4	5 (4.7%)	5 (0.05)	8 (7.8%)	9 (0.09)
Pain - Upper Extremities with Numbness	0	0	1	0	1	1	3	3	5 (4.7%)	5 (0.05)	4 (3.9%)	4 (0.04)
Pseudoarthrosis	0	0	0	0	0	0	2	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Psychological	3	3	0	0	0	0	2	1	5 (4.7%)	5 (0.05)	4 (3.9%)	4 (0.04)
Pulmonary Infection	0	0	0	0	0	1	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Furitis	1	0	1	0	0	0	0	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Reflex Change	0	0	0	1	0	0	0	0	0 (0.0%)	0 (0.00)	1 (1.0%)	1 (0.01)
Respiratory	0	2	0	1	2	0	1	1	3 (2.8%)	3 (0.03)	4 (3.9%)	4 (0.04)
Seizures	1	0	0	0	1	0	0	0	2 (1.9%)	2 (0.02)	0 (0.0%)	0 (0.00)
Sore Throat	0	1	0	0	1	0	0	0	1 (0.9%)	1 (0.01)	1 (1.0%)	1 (0.01)
Surgery - Index Level	1	0	1	0	2	1	6	1	10 (9.4%)	10 (0.09)	2 (1.9%)	2 (0.02)
Surgery - Other	0	0	3	3	7	1	17	12	21 (19.8%)	27 (0.25)	12 (11.7%)	16 (0.16)
Wound Issues, Other	0	3	1	1	1	0	0	0	2 (1.9%)	2 (0.02)	3 (2.9%)	4 (0.04)

Patients experiencing adverse events in more than one category are represented in each category in which they experienced an adverse event.

Adverse event categories identified as Musculoskeletal are further defined as:

- Musculoskeletal (spasms – back): any event involving muscular spasms in the lumbar spine region

- Musculoskeletal (spasms – neck): any event involving muscular spasms in the cervical spine region
- Musculoskeletal (spasms – non-specific): any event involving general complaints of muscular spasms not related to the lumbar or cervical spine
- Musculoskeletal: classifies all events related to muscles, tendons, ligaments, cartilage, bones, joints and surrounding tissues that do not fall into one of the categories above.

Adverse event category “Neurological” broadly includes AEs related to the nervous system. Any specific episodes of numbness or reflex changes are further classified in the following categories: Numbness Index Level, Numbness Non-Index Level, and Reflex Change.

*Other – the following 5 adverse events in 4 ProDisc™-C patients: Keratitis, diagnosed with Dry Eye Syndrome, IV Infiltrated, Left leg weakness and heavy, and Horner’s Syndrome as well as the following 7 adverse events in 6 ACDF patients: diagnosed with early Diabetes, Radiographic films show no evidence of a solid fusion, worsening of Diabetes, Wegener’s disease, Polycythemia, Ringing bilateral ears, and Ringing ears.

The table below shows all adverse events that were considered implant related and the time-course of their occurrence:

Table 2: Implant Related Adverse Events

Adverse Event	Intra-Op (0-2 days)		Peri-Op (>2 - 42 days)		Short Term (>42-210 days)		Long Term (>210 days)		Total	
	ACDF	PRC	ACDF	PRC	ACDF	PRC	ACDF	PRC	ACDF	PRC
Dysphagia	0	0	1	0	0	0	0	0	1	0
Infection - Superficial Wound	0	0	1	0	0	0	0	0	1	0
Musculoskeletal	0	0	1	0	0	0	0	0	1	0
Pain - Neck	0	0	1	0	0	0	0	0	1	0
Surgery - Index Level	1	0	1	0	2	0	1	2	5	2

There were nine (9) implant related AEs in seven (7) ACDF patients and two (2) implant related AEs in two (2) ProDisc-C patients. All “Surgery – Index Level” AEs were considered severe or life threatening as well as the “Infection – Superficial Wound” AE in the ACDF group. The relationship of an adverse event to the implant was determined by the treating physician.

The following secondary surgical procedures at the index level were reported during the study:

Table 3: Secondary Surgical Procedures – Index Level

Tx Group	Cause	Action	Days Post-op
ACDF	Worsening Cervical Radiculopathy	Plate Removal - (C5-6), ACDF (C6-7)	1079
ACDF	MVA	Supplemental Fixation C6-7 and L4-5 PSF	420
ACDF	Adjacent Level Disease	Plate Removal - (C5-6), ACDF (C6-7)	732
ACDF	C5-6 Pseudoarthrosis;	C5-6 Supplemental Fixation	377
ACDF	Allograft Subsidence At C6-7	Revision C6-7 ACDF	296
ACDF	Dysphagia	Revision C6-7 ACDF	14
ACDF	Neck Pain	Revision C6-7 ACDF	425
ACDF	Adjacent Level Disease	Plate Removal - (C5-6), ACDF (C6-7)	826
ACDF	Neck Pain	Revision C4-5 ACDF	644
ACDF	Non Union C6-7	Supplemental Fixation C6-7	637
ACDF	Stenosis C6-7, Subsidence C6-7	Re-operation C6-7, Bone Fortification	300
PRC	Pt Had Worsening Pain	Removal of TDR with Fusion	499
PRC	Neck Pain	Removal of TDR with Fusion	492

One ACDF patient underwent a second revision surgery at the index level at 917 days post-op in response to ongoing pain and weakness.

Table 4: Secondary Surgical Procedures – Index Level – Time Course (Randomized)

	Prior to Discharge		6 wks		3 mo		6 mo		12 mo		18 mo		24 mo		>24 mo		Total		
	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	ACDF	ProDisc-C	
	Removals	0	0	0	0	0	0	0	0	1	0	0	2	0	0	0	0	1	0
Reoperations	0	0	0	0	0	0	0	0	1	0	1	0	1	0	3	0	8	0	0
Revisions	0	0	1	0	0	0	1	0	1	0	1	0	1	0	3	0	8	0	0
Supplemental Fixation	0	0	0	0	0	0	0	0	1	0	1	0	1	0	0	0	3	0	0

There were no statistically significant differences between the ProDisc™-C and ACDF treatment groups for the percentage of patients experiencing at least one adverse event in the following categories:

- All Adverse Events (p=1.0000)
- Device-related Adverse Events (p=0.1706)
- Surgery-related Adverse Events (p=0.4113)

A statistically significant difference in favor of ProDisc™-C was detected for the percentage of patients experiencing at least one severe or life-threatening adverse event (p=0.0137).

Unintended fusion (i.e., heterotopic ossification resulting in bridging trabecular bone and a loss of motion (<2°)), occurred in three ProDisc-C patients in the randomized clinical trial.

Potential Risks

Potential risks associated with the use of ProDisc-C™ Total Disc Replacement include: 1) those commonly associated with any surgery; 2) those specifically associated with cervical spinal surgery using an anterior approach; and 3) those associated with a spinal implant, as well as those pertaining to the ProDisc-C™ Total Disc Replacement. However, the causality of these adverse events is not exclusive to these categories. There is also the risk that this surgical procedure will not be effective, and may not relieve or may cause worsening of preoperative symptoms. Some of these effects were observed in the clinical study and therefore have been previously reported in the adverse events table.

1. Risks associated with any surgical procedure are those such as: abscess; cellulitis; wound dehiscence; wound necrosis; edema; hematoma; heart and vascular complications; hypertension; thrombosis; ischemia; embolism; thromboembolism; hemorrhage; thrombophlebitis; adverse reactions to anesthesia; pulmonary complications; organ, nerve or muscular damage; gastrointestinal compromise; seizure, convulsion, or changes to mental status; and complications of pregnancy including miscarriage and fetal birth defects;
2. Risks associated with anterior interbody surgery of the cervical spine include: dysphagia; dysphasia; dysphonia; hoarseness; vocal cord paralysis; laryngeal palsy; sore throat; recurring aspirations; nerve deficits or damage; tracheal, esophageal; and pharyngeal perforation; airway obstruction; external chylorrhea; warmth or tingling in the extremities; deficit or damage to the spinal chord, nerve roots, or

- nerves possibly resulting in paralysis or pain; dural tears or leaking; cerebrospinal fistula; discitis, arachnoiditis, and/or other types of inflammation; loss of disc height; loss of proper curvature, correction, height or reduction of the spine; vertebral slipping; scarring, herniation or degeneration of adjacent discs; surrounding soft tissue damage, spinal stenosis; spondylolysis; otitis media; fistula; vascular damage and/or rupture; and headache;
3. Risks associated with implants in the spine, including the ProDisc-C™ Total Disc Replacement device, are: early or late loosening of the components; disassembly; bending or breakage of any or all of the components; implant migration; malpositioning of the implant; loss of purchase; sizing issues with components; anatomical or technical difficulties; implant fracture; bone fracture; skin penetration; irritation, pain, bursitis resulting from pressure on the skin from component parts in patients with inadequate tissue coverage; foreign body reaction to the implants including possible tumor formation, autoimmune disease, metallosis, and/or scarring; possible tissue reaction; bone resorption; bone formation that may reduce spinal motion or result in a fusion, either at the treated level or at adjacent levels; development of new radiculopathy; myelopathy or pain; tissue or nerve damage caused by improper positioning and placement of implants or instruments; loss of neurological function; decreased strength of extremities; decreased reflexes; appearance of cord or nerve root injury; loss of bowel and/or bladder control; and interference with radiographic imaging because of the presence of the implant;
 4. Wound, local and/or systemic infections;
 5. Inability to resume activities of normal daily living;
 6. Death

NOTE: Additional surgery may be necessary to correct some of the adverse effects.

Death, a potential adverse event, did not occur during the randomized clinical trial. There was one death reported in the continued access cohort of the study that was due to a methadone overdose approximately one and a half weeks postoperatively and was not considered to be associated with the implant or the implantation procedure.

Clinical Study

Clinical data were collected to evaluate the safety and effectiveness of the ProDisc™-C Total Disc Replacement as compared to the control device, an anterior cervical discectomy and fusion (ACDF) surgery with the use of allograft bone (cortical ring) and an anteriorly applied plating system in patients undergoing single-level discectomy for intractable SCDD. The purpose of the study was to determine whether the ProDisc™-C Total Disc Replacement was non-inferior to ACDF. A total of 209 subjects were enrolled, randomized and treated (103 patients in the investigational ProDisc™-C treatment group and 106 patients in the control group). To qualify for enrollment in the study, patients met all the inclusion criteria and none of the exclusion criteria listed in the following table:

Inclusion	Exclusion
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1. Symptomatic cervical disc disease (SCDD) in only one vertebral level between C3-C7 defined as:
 - Neck or arm (radicular) pain; and/or a functional / neurological deficit with at least one of the following conditions confirmed by imaging (CT, MRI or X-rays)
 - Herniated nucleus pulposus;
 - Spondylosis (defined by the presence of osteophytes); and/or
 - Loss of disc height
 2. Age between 18 and 60 years.
 3. Unresponsive to non-operative treatment for approximately six weeks or has the presence of progressive symptoms or signs of nerve root/spinal cord compression in the face of conservative treatment.
 4. NDI score greater than or equal to 15/50 (30%) (Considered moderate disability).
 5. Psychosocially, mentally and physically able to fully comply with this protocol including adhering to follow-up schedule and requirements and filling out forms.
 6. Signed informed consent.
1. More than one vertebral level requiring treatment.
 2. Marked cervical instability on resting lateral or flexion/extension radiographs:
 - a. translation greater than 3 mm and/or
 - b. greater than 11 degrees of rotational difference to that of either adjacent level .
 3. Has a fused level adjacent to the level to be treated.
 4. Radiographic confirmation of severe facet joint disease or degeneration.
 5. Known allergy to cobalt, chromium, molybdenum, titanium or polyethylene.
 6. Clinically compromised vertebral bodies at the affected level(s) due to current or past trauma, e.g., by the radiographic appearance of fracture callus, malunion or nonunion.
 7. Prior surgery at the level to be treated.
 8. Severe spondylosis at the level to be treated as characterized by any of the following:
 - a. Bridging osteophytes;
 - b. A loss of disc height greater than 50%; or
 - c. Absence of motion (<2°).
 9. Neck or arm pain of unknown etiology.
 10. Osteoporosis: A screening questionnaire for osteoporosis, SCORE¹ (Simple Calculated Osteoporosis Risk Estimation), will be used to screen patients who require a DEXA bone mineral density measurement. If DEXA is required, exclusion will be defined as a DEXA bone density measured T score ≤ -2.5 (The World Health Organization definition of osteoporosis.²)
 11. Paget's disease, osteomalacia or any other metabolic bone disease (excluding osteoporosis which is addressed above).
 12. Severe diabetes mellitus requiring daily insulin management
 13. Pregnant or interested in becoming pregnant in the next 3 years.

¹ Lydick E, Cook K, Turpin J, et al. Development and validation of a simple questionnaire to facilitate identification of women likely to have low bone density. Am J Man Care 1998; 4:37-48.

² The WHO Study Group: Assessment of fracture risk and its application to screening for postmenopausal osteoporosis. Geneva, World Health Organization, 1994.

14. Active infection - systemic or local.
15. Taking medications or any drug known to potentially interfere with bone/soft tissue healing (e.g., steroids).
16. Rheumatoid arthritis or other autoimmune disease.
17. Systemic disease including AIDS, HIV, hepatitis.
18. Active malignancy: A patient with a history of any invasive malignancy (except non-melanoma skin cancer), unless he/she has been treated with curative intent and there have been no clinical signs or symptoms of the malignancy for at least 5 years.

Following surgery, investigators were advised to prescribe the appropriate rehabilitation program and manage patient progress on an individual basis. They were given certain guidelines to follow irrespective of the subject's treatment group. The guidelines included a hard or soft collar at the surgeon's discretion. Direction was given to the patient regarding standard wound care procedures. Limitations were placed on patients in regard to prolonged or strenuous activity initially and for a period of weeks to months depending on the individual patient's progress. The patients were instructed not to resume heavy physical activity until the surgeon had reviewed postoperative radiographs and was confident that the implant was stable and functioning. In addition, patients were instructed to immediately report any change in their pain or neurologic status to their doctor.

Patients were not treated with NSAIDs postoperatively in either treatment group despite some reports in the literature that short-term postoperative use of NSAIDs may reduce the incidence of heterotopic ossification in total disc replacement patients.

Subjects were evaluated pre-operatively, intra-operatively, and immediately post-operatively followed by evaluations at 6 weeks, 3 months, 6 months, 12 months, 18 months and 24 months. Complications and adverse events, device-related or not, were evaluated over the course of the clinical trial. At each evaluation time-point, the primary and secondary clinical and radiographic outcome parameters were evaluated.

Safety and effectiveness was assessed in all randomized subjects.

The safety of the ProDisc™-C Total Disc Replacement was assessed by monitoring intra-operative and post-operative adverse events. Radiographs were used to monitor the occurrence of some of the adverse events, including device subsidence, migration, and breakage as well as heterotopic ossification and unintended fusion in the investigational group.

All radiographic endpoints were evaluated independently by a core laboratory (Medical Metrics, Inc., Houston, TX) and reviewed by an independent radiologist.

The overall success analysis using the composite primary endpoint, as described in the IDE, is presented. FDA requested that in addition to the IDE overall success criteria (presented herein as Overall Success), analysis of Overall Success be presented using an improvement in NDI of ≥ 15 points relative to the pre-operative baseline (presented herein as Additional Analysis). FDA also requested that a non-inferiority delta of 10% be applied to the analyses. Sensitivity analyses for both definitions used a non-inferiority delta of 10%.

Table 5: Overall Success Definitions

Overall Success	Additional Analysis
The patient's NDI score improves by at least 20% over baseline value	The patient's NDI score improves by at least 15 points over baseline value
The patient's neurologic parameters, i.e. motor sensory, and reflexes are maintained or improved	The patient's neurologic parameters, i.e. motor sensory, and reflexes are maintained or improved
No removals, revisions, re-operations or additional fixation were required to modify any implant	No removals, revisions, re-operations or additional fixation were required to modify any implant
No adverse events occur which are related to the treatment, ProDisc-C or its implantation or ACDF surgery or its associated implants or graft material	No adverse events occur which are related to the treatment, ProDisc-C or its implantation or ACDF surgery or its associated implants or graft material

The secondary endpoints assessed were quality of life measured with the SF-36 questionnaire, improvement on a Visual Analog Scale (VAS) for neck and arm pain intensity and frequency, and several radiographic assessments (device migration, subsidence, disc height, range of motion, heterotopic ossification, fusion status). Other outcomes measured included VAS subject satisfaction, willingness to have the same surgery again, employment status, and medication use.

Clinical Patient Population

Thirteen (13) sites treated patients in the pivotal study with a total of two hundred and nine (209) subjects enrolled, randomized, and treated; 103 subjects in the investigational treatment arm (ProDisc™-C Total Disc Replacement) and 106 subjects in the control arm (ACDF) were treated.

Subject Demographics

The table below shows select demographics and baseline characteristics of the investigational and control groups.

Table 6: Demographic and Baseline Characteristics

	ProDisc-C (N Trtd=103)	ACDF (N Trtd=106)	Two-Sided p-value
Implant Level			0.4764
C3-C4	3 (2.9%)	1 (0.9%)	
C4-C5	10 (9.7%)	6 (5.7%)	
C5-C6	58 (56.3%)	61 (57.5%)	
C6-C7	32 (31.1%)	38 (35.8%)	
Age at Surgery (years)			0.2025
Mean	42.1	43.5	
STD	8.42	7.15	
Age Group [N (%)]			0.5810
<=42 years	52 (50.5%)	49 (46.2%)	
>42 years	51 (49.5%)	57 (53.8%)	
Gender [N (%)]			0.8897
Female	57 (55.3%)	57 (53.8%)	
Male	46 (44.7%)	49 (46.2%)	
Race [N (%)]			0.1000
Caucasian	88 (85.4%)	97 (91.5%)	
African-American	4 (3.9%)	1 (0.9%)	
Hispanic	3 (2.9%)	5 (4.7%)	
Asian American	5 (4.9%)	0 (0.0%)	
Other	3 (2.9%)	3 (2.8%)	
Smoking Status			0.9159
Never	51 (49.5%)	49 (46.2%)	
Former	18 (17.5%)	20 (18.9%)	
Current	34 (33.0%)	37 (34.9%)	
Height (in)			0.2839
Mean	67.23	67.77	
STD	3.703	4.106	
Weight (lbs)			0.0943
Mean	171.04	180.27	
STD	41.797	47.331	
Body Mass Index (kg/m²)			0.0896
Mean	26.44	27.34	
STD	5.319	5.54	
NDI Score (%)			0.4560
Mean	53.93	52.28	
STD	15.096	14.544	
Duration of Neck/Arm Pain			0.9645
<6 weeks	3 (2.9%)	3 (2.8%)	
6 weeks to a year	44 (42.7%)	44 (41.5%)	
>1 year	56 (54.4%)	59 (55.7%)	

Surgical and Hospitalization Information

The mean intra-operative time in the ProDisc™-C Total Disc Replacement group was 107.2 minutes whereas it was 98.7 minutes in the ACDF group (p<0.0078). The mean estimated blood loss (EBL) in the ProDisc™-C Total Disc Replacement group was 83.5cc whereas it was 63.5cc in the ACDF group (p<0.0094). The length of hospital stay was analogous in both groups; 1.4 days ProDisc™-C and 1.3 days ACDF, p<0.7882. While the differences in the means for estimated blood loss and operative time were statistically significant, in each case the ranges were similar so the statistical significance may not be clinically significant.

The table below describes the implant sizes used in the ProDisc-C patients:

Table 7: Implant Sizes Used

Inlay	Medium	Medium Deep	Large	Large Deep	Extra Large	Extra Large Deep
5 mm	23 (22.3%)	16 (15.5%)	25 (24.3%)	6 (5.8%)	1 (1.0%)	0 (0.0%)
6 mm	7 (6.8%)	6 (5.8%)	14 (13.6%)	4 (3.9%)	0 (0.0%)	0 (0.0%)
7 mm	0 (0.0%)	0 (0.0%)	0 (0.0%)	1 (1.0%)	0 (0.0%)	0 (0.0%)

Clinical Effectiveness Evaluation

The primary effectiveness endpoint of this study was the difference in proportion of Overall Success between the two treatment groups at 24 months post-operatively. The success status of subjects was summarized by treatment group.

The population which was used to assess these endpoints consisted of all randomized subjects in the pivotal study who completed all evaluations at the 24-month time point, regardless of when the 24-month measurements occurred.

Table 8: Components of Overall Success

Component of Overall Success	ProDisc-C	ACDF	Fisher's Exact Test p-value (One Sided)
NDI Success (IDE)* (≥20% Improvement from Baseline)	84/ 99 (84.9%)	79/ 92 (85.9%)	0.6561
NDI Success (FDA)* (≥15 Point Improvement from Baseline)	79/ 99 (79.8%)	72/ 92 (78.3%)	0.4665
Neurological Success* (Maintenance or Improvement from Baseline)	90/ 99 (90.9%)	81/ 92 (88.0%)	0.3407
Absence of Revisions, Removals, Re-operations or Supplemental Fixation at the Index Level	101/103 (98.1%)	97/106 (91.5%)	0.0327
Absence of Adverse Events Related to the Implant or Implantation	100/103 (97.1%)	99/106 (93.4%)	0.1779
Analysis	ProDisc-C	ACDF	
Overall Success (IDE) (20% NDI)	78/101 (77.2%)	75/101 (74.3%)	0.3715
Additional Analysis (FDA) (15 point NDI)	73/101 (72.3%)	69/101 (68.3%)	0.3222

* Denominators for NDI and Neurological Success (92 ACDF, 99 ProDisc™-C) reflect only patients that completed the study. Denominators for Re-operations and Adverse Events (106 ACDF, 103 ProDisc™-C) include all patients treated in the study. Denominators for Overall Success reflect all patients with known outcomes at month 24. The relationship of adverse events to the implant or its implantation was determined by the treating physician.

The results of both overall success analyses indicate that the ProDisc™-C Total Disc Replacement is statistically non-inferior to the ACDF control group. As stated in the IDE protocol, “The test of the sole, primary hypothesis that ProDisc™-C Total Disc Replacement is non-inferior to ACDF is based on an exact 95% one-sided, upper confidence bound for the difference in success probabilities, PA-PB, where A denotes the

fusion (ACDF) arm and B denotes the ProDisc™-C Total Disc Replacement arm. If the upper bound is $\delta = 0.15$ or less, then ProDisc™-C Total Disc Replacement is considered non-inferior to ACDF.” The Overall Success upper bound of the exact 95% one-sided confidence interval was 7.10%. This result is below the 15% delta needed to establish non-inferiority under the IDE protocol and below the 10% delta needed to establish non-inferiority under the FDA’s requested analysis. Using the Additional Analysis criteria for overall success, the upper bound of the exact 95% one-sided confidence interval was 7.0%. This result is below the 10% delta needed to establish non-inferiority. To assess the impact on the conclusion of non-inferiority of patients with unknown outcomes at Month 24 (5 ACDF, 2 ProDisc™-C) a number of sensitivity analyses were conducted. The following conditions were applied for all patients with unknown outcomes at Month 24 for both Overall Success and the Additional Analysis:

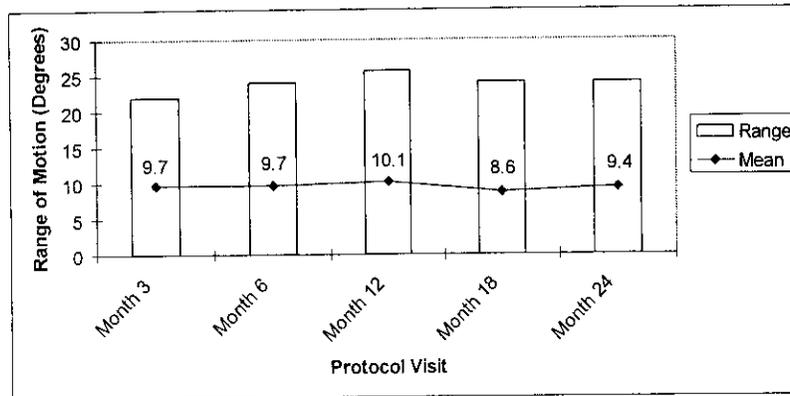
- All Failures (all designated as failure regardless of treatment group)
- All Success (all designated as success regardless of treatment group)
- Last observation carried forward (LOCF), if there were no outcomes for a patient for any post-operative time-point the patient was removed from analysis
- Modified LOCF using only Month 12 or Month 18 results, if a patients had no known outcomes at Month 12 or beyond they were designated as success if ACDF and failure if ProDisc™-C Total Disc Replacement
- Worst Case (all ACDF designated as success, all ProDisc™-C Total Disc Replacement designated as failure)

Under all sensitivity analyses the ProDisc™-C Total Disc Replacement remained non-inferior, with the upper bound of the exact 95% one-sided confidence intervals under worst case analysis falling below the 15% non-inferiority delta for Overall Success and below the 10% non-inferiority delta for FDA’s requested Additional Analysis.

Secondary Efficacy Analysis

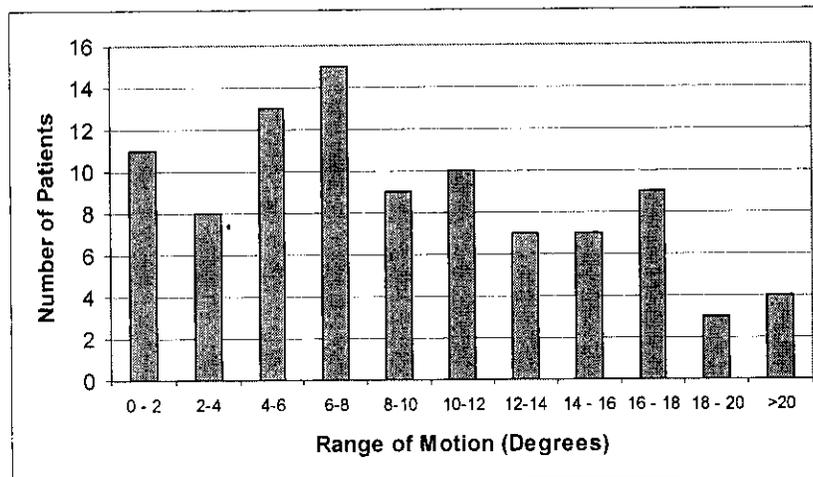
Flexion/extension range of motion (ROM) in degrees at the operative level, determined as the difference in Cobb measurements between dynamic flexion/extension lateral radiographs, was determined at pre-op, 3, 6, 12, 18 and 24 months for ProDisc™-C Total Disc Replacement.

Figure 1: ProDisc™-C Total Disc Replacement Time Course of Mean Flexion/Extension Range of Motion



A histogram is provided showing the range of ROM values recorded for all ProDisc™-C Total Disc Replacement subjects at 24 months. This histogram used values obtained by rounding recorded range of motion for each subject to the nearest integer.

Figure 2: Histogram of ProDisc™-C Total Disc Replacement Flexion/Extension ROM at 24 Months (N=96 subjects)



Analysis of the range of motion data versus overall success for the ProDisc™-C subjects with available range of motion data at 24 months was also performed. The overall success rates at month 24 of subjects with $\geq 4^\circ$ of motion were compared to subjects with $< 4^\circ$ of motion using both the IDE Overall Success analysis as well as the Additional Analysis (FDA) success criteria. Neither success criteria demonstrated a statistically significant difference ($p=0.7439$, $p=0.7587$ respectively) between the groups.

How Supplied

The ProDisc™-C Total Disc Replacement implants are supplied pre-packaged and sterile. The integrity of the packaging should be checked to ensure that the sterility of the contents is not compromised. Remove the implants from the packaging using aseptic technique, only after the correct size has been determined.

Instrument Cleaning

Cleaning instruments by hand, when properly performed, causes less damage than mechanical cleaning. When cleaning instruments by hand, the following should be observed:

1. Clear any corners or recesses of all debris. (Note: extra care should be taken to clean out any cannulated areas by using an appropriate cleaning stylet and rinsing immediately.)
2. Remove all traces of blood and other such residues immediately. Do not allow these to dry.
3. The instruments should be submerged (if applicable) and cleaned with a commercially available manual cleaner. (i.e. Instraclean from Calgon or Medline High Suds Detergent) prepared according to the manufacturer's recommendation.
4. A soft nylon bristled brush is then used to manually clean the devices while immersed in the cleaning solution. Never use steel brushes or abrasive pads, as these rupture the passive layer of the instrument surface which can lead to corrosion.
5. The instruments should be thoroughly rinsed after cleaning. Distilled water should be used.
6. Dry instruments immediately after cleaning.

Conformance to Standards

The ProDisc™-C Total Disc Replacement endplates are manufactured from CoCrMo conforming to ISO 5832-12 (1996) "Implants for surgery – Metallic materials – Part 12: Wrought cobalt-chromium-molybdenum alloy. The surfaces of both inferior and superior plates that abut against the bone are plasma sprayed with CPTI conforming ISO/DIS 5832-2 (1999) "Implants for surgery – Metallic materials– Part 2: Unalloyed titanium". The inlays are manufactured from ultra-high molecular weight polyethylene (UHMWPE) conforming to ISO 5834-2 and ASTM 648.

Device Retrieval

Should it be necessary to remove a ProDisc™-C Total Disc Replacement, please contact Synthes Spine to receive instructions regarding the data collection, including histopathological, mechanical, and adverse event information. Please refer to the ProDisc™-C Total Disc Replacement Technique Guide for step by step instructions on the required surgical technique for device retrieval and instructions for returning the explanted device to Synthes Spine. All explanted devices must be returned to Synthes Spine for analysis.

Please note that the disc replacement device should be removed as carefully as possible in order to keep the implant and surrounding tissue intact. Also, please provide descriptive information about the gross appearance of the device in situ, as well as descriptions of the removal methods, i.e., intact or in pieces.

Note: All implant removals must be reported immediately to Synthes Spine.

Limited warranty and disclaimer: Synthes Spine products are sold with a limited warranty to the original purchaser against defects in workmanship and materials. Any other express or implied warranties, including warranties of merchantability or fitness, are hereby disclaimed.

"See Directions for Use at <http://products.synthes.com> or call 1-800-523-0322"

Synthes Spine
1302 Wrights Lane East
West Chester, PA 19380

ProDisc™-C Total Disc Replacement

Patient Information

Why Have I Been Given This Information Brochure?

After reviewing your medical history and x-rays, and taking into account the results of other diagnostic studies, your doctor has decided that you may benefit from spine surgery. This patient information brochure is provided to assist you in making a decision about the treatment of your arm and/or neck pain with the ProDisc™-C Total Disc Replacement made by Synthes Spine.

What Is Important For Me To Understand About My Spine?

Your spine is the structure that supports and stabilizes your body and allows motion. It gives you the ability to perform activities such as walking, bending and sitting. It also provides protection for your spinal cord and nerve roots.

Your spine is made up of bones called vertebrae that are stacked on top of each other to form a column. Each vertebra has a hole in the center through which the spinal cord passes. The spinal cord contains nerves that carry signals from your brain to the rest of the body. The vertebrae are separated by soft, cushioning intervertebral discs which maintain an appropriate space to support motion and allow nerves to pass through your spine to many different parts of your body.

Your spine is divided into four regions:

- The cervical region (commonly called the neck) - contains the seven upper-most vertebrae in your neck.
- The thoracic region (commonly known as the rib section) - contains the twelve vertebrae in your mid-back.
- The lumbar region (commonly known as the lower back) - contains the five vertebrae in your lower back.
- The sacrum and coccyx region (commonly called the tail bone) – contains the bones in the base of the spine.

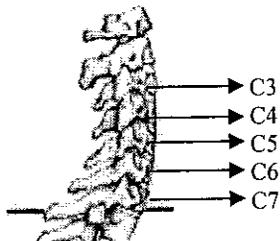
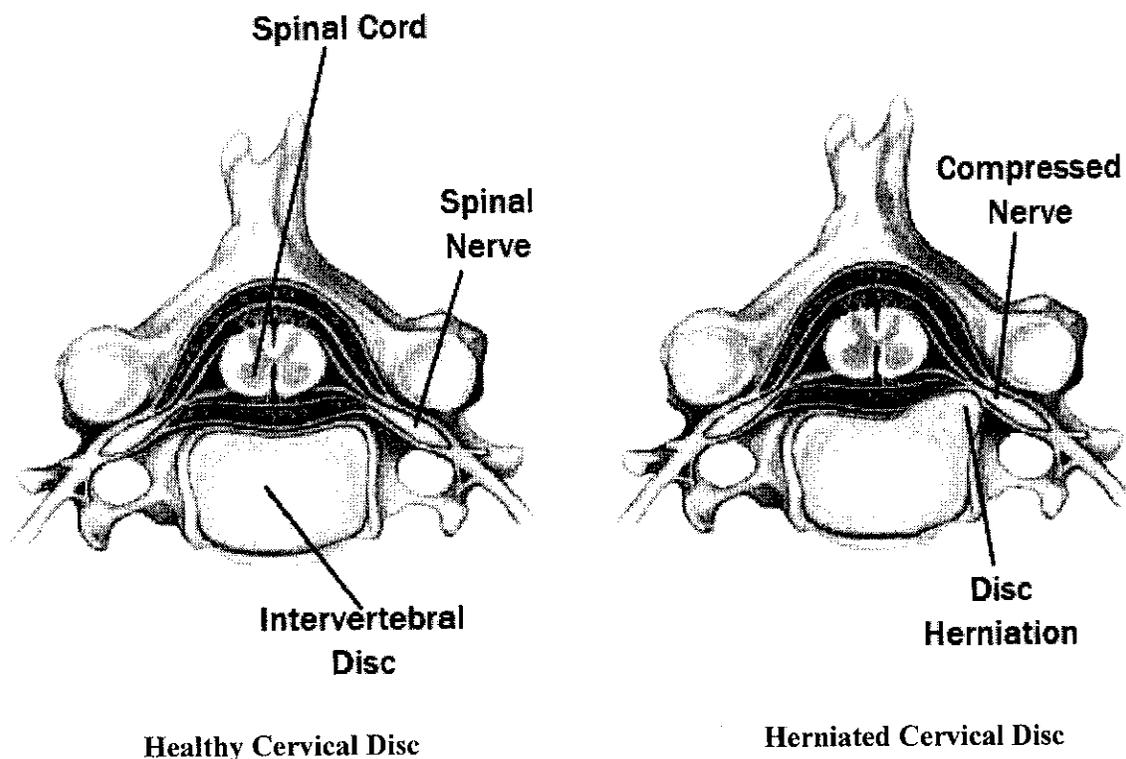


Image caption: The ProDisc™-C Total Disc Replacement is used to treat the lower cervical spine. Your doctor may refer to the involved cervical areas as C3, C4, C5, C6, or C7.

Why May I Need Surgery?

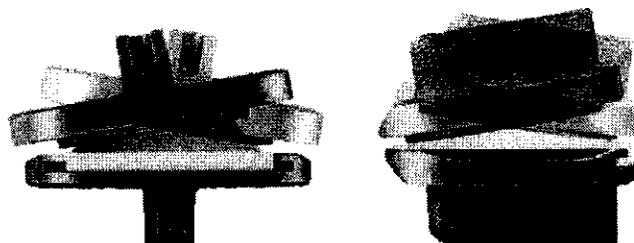
Your doctor has diagnosed you with **Symptomatic Cervical Disc Disease (SCDD)**. Your doctor may call your condition a **herniated disc**, **spondylosis** or **radiculopathy**. Normally, the intervertebral disc between each pair of vertebrae provides the cushioning space that keeps the bones separated. Symptomatic Cervical Disc Disease (SCDD) can occur when the discs no longer work normally because of wear or from being injured. This can cause the vertebral bodies to compress or lose height, and they may press on the nerves or the spinal cord. This can cause pain and/or numbness in the arms and neck and limit your ability to perform daily activities.

If you have been diagnosed with SCDD and your pain has failed to improve after at least six weeks of conservative (non-surgical) treatment such as physical therapy or medication, you may get relief by having surgery. One type of surgery is total disc replacement surgery. A Computed Tomography (CT) scan, Magnetic Resonance Imaging (MRI) and/or X-rays may be required to confirm the source of your pain and to help your doctor determine if you are a suitable candidate for surgery, including total disc replacement.



What is the ProDisc-C Total Disc Replacement?

The ProDisc™-C Total Disc Replacement implant is composed of top and bottom metal (cobalt chromium molybdenum) endplates and a plastic inlay (ultra-high molecular weight polyethylene) that forms a ball and socket joint. The ProDisc™-C Total Disc Replacement implant provides the possibility for motion by allowing the top endplate to move over the plastic ball attached to the bottom endplate. The materials used in the ProDisc™-C Total Disc Replacement implant have been used in spinal disc replacement for over 20 years in Europe and are the most commonly used materials in knee and hip replacements worldwide.



How Is Surgery With the ProDisc-C Different From Other Surgical Choices?

ProDisc™-C Total Disc Replacement surgery is an alternative to Anterior Cervical Discectomy and Fusion (ACDF), which is the surgery that is most commonly done for your condition. In both the

ACDF and the ProDisc™-C Total Disc Replacement procedures, the unhealthy disc is removed and the height at that level of your spine is restored to relieve pressure on the nerves and/or spinal cord. In an ACDF procedure, after the unhealthy disc is removed, the bones are fixed in position with implants and bone graft. In some ACDF procedures, the bone graft may come from your hip in a separate incision. After surgery, the two bones are supposed to grow together, creating one solid piece of bone and eliminating motion at that level of your spine. In the ProDisc™-C Total Disc Replacement procedure, the device is inserted into the disc space to restore the height at that level of your spine, while potentially allowing some motion. The ProDisc™-C Total Disc Replacement procedure does not require a bone graft.

Who Should Receive the ProDisc™-C and What is it Designed to Do?

The ProDisc™-C Total Disc Replacement is used to replace one unhealthy (diseased and/or degenerated) disc of the cervical spine after the unhealthy disc is removed. The ProDisc™-C Total Disc Replacement is designed to reduce pain by removing the unhealthy disc while potentially allowing your neck to move after surgery. The ProDisc™-C Total Disc Replacement should only be used in patients who are at least 21 years of age, have only one unhealthy disc, and have had neck or arm pain for at least six (6) weeks that did not respond to non-operative care (physical therapy, medication, etc.).

Who Should Not Receive the ProDisc™-C?

You should not receive the ProDisc™-C Total Disc Replacement if you have any of the following:

- Any type of infection, especially infection in the spine and/or surrounding area
- Poor quality bone (osteoporosis or osteopenia)
- An unstable or overly weak neck
- Allergies or sensitivity to metals (cobalt, chromium, molybdenum, and/or titanium) or plastic (polyethylene)
- Stiffening of the neck or severe degeneration
- Weakened bones at the treatment level due to past or present injury
- More than one unhealthy disc in your neck

In addition, in order to receive this device you must be old enough so that the bones in your body are mature and are no longer growing.

What Warnings and Precautions Should I Pay Attention To?

It is important to select a surgeon who has attended a training course sponsored by the company who makes the ProDisc™-C Total Disc Replacement (Synthes Spine, Inc.).

This device is placed close to nerves and blood vessels in the cervical spine. There is a risk of nerve damage or serious and potentially fatal bleeding if damage to these structures occurs during or after surgery.

It is very important that you let your doctor know about any allergies you have, any medications you take on a regular basis, if you are pregnant or if you have any other treated or untreated illnesses, such as rheumatoid arthritis, cancer, cardiac disease, diabetes, hepatitis, osteoporosis, previous surgeries or injuries you may have that may impact whether this device is right for you.

What Are the Potential Risks With the ProDisc™-C?

As with any surgery, there are some possible problems that can occur when you have neck surgery, including surgery with the ProDisc™-C Total Disc Replacement. There is a risk that the surgery may not make you feel better or may cause you to feel worse. If this happens you may need another surgery to help you feel better. Specific possible problems that may occur include:

- Allergic reaction to the anesthesia used during your surgery
- Allergic reaction to the implant materials that may lead to implant loosening or failure
- Change in the curvature of your neck
- Death
- Difficulty or pain when you swallow
- Difficulty with or change in your speech
- The implant may not stay in place or may break, bend, loosen, or move, potentially causing pain, paralysis, or damage to blood vessels, nerves, or the spinal cord
- Pain in your neck, arms, or other parts of your body
- Numbness or tingling in your extremities
- Muscle weakness in your extremities or in general
- Failure of the device/procedure to make you feel better
- Fracture of the bones in your neck
- Seizures
- Infection (of your wound, your spine or an infection in your blood)
- Inability to move your neck at the treated level (unintended fusion)
- Development or progression of disease at other levels in your cervical spine
- Bleeding or a collection of clotted blood (hematoma)
- Blood clots in your extremities, lungs, brain (stroke) or other parts of your body
- Swelling
- Complications of pregnancy including miscarriage and fetal birth defects
- Inability to resume activities of normal daily living;

In a U.S. clinical study of 103 patients who received ProDisc-C, there were six (6) patients who did not get any relief of their symptoms and a number of other patients whose improvement was likely not significant enough for them to notice a difference. There were two (2) patients who needed additional surgery on their neck. Throughout the course of the clinical study patients reported health related problems to their physicians. Some of the most common were pain, headaches, and muscle aches. There may be other risks associated with treatment using the ProDisc-C. Although many of the major risks are listed in this patient information brochure, a more complete list is provided in the physician's package insert, which your doctor has received. Please ask your doctor for more information about any additional risks possibly related to your planned surgery.

What Can I Expect Before the Surgery?

Your doctor will review your condition with you and explain what all of your possible choices are including medications, physical therapy, and other surgeries such as removal of the diseased disc, fusion, etc.

What Can I Expect During the Surgery?

During the total disc replacement surgery, you will be under general anesthesia. The surgeon will make a small incision in the front of your neck to get to your unhealthy disc. Then the surgeon will remove the unhealthy disc. The surgeon will insert the ProDisc™-C Total Disc Replacement implant into the disc space. Finally, the surgeon will close the incision.

What Can I Expect After the Surgery?

Surgery with the ProDisc™-C Total Disc Replacement is considered major surgery. As with any major surgery, you should expect some discomfort as well as a period of rehabilitation. Your doctor may prescribe medicines to help you manage any pain or nausea you may experience. On average, you should expect to stay in the hospital for a day or two.

After you go home

You and your doctor should talk about a plan to steadily bring you back to normal activity while the healing process occurs. It is very important that you follow your doctor's instructions. You can begin moving soon after surgery, but try not to do too much, too soon.

Your doctor may recommend the following instructions:

- A hard or soft collar may be used if your doctor thinks it is necessary
- Avoid prolonged or strenuous activity
- Avoid heavy physical activity until your doctor tells you it is okay
- You will be taught how to clean and care for your wound

After surgery, your doctor may refer you to a physical therapist who will teach you exercises to improve your strength and mobility while protecting your spine.

Contact your doctor immediately if you:

- have a fever,
- notice fluid draining from your wound,
- have trouble swallowing or breathing,
- have trouble urinating
- have new or increased neck pain, arm pain, numbness, or weakness.

Caution: Please be sure to tell any doctors you later see that you had surgery with the ProDisc™-C Total Disc Replacement before you have a magnetic resonance imaging (MRI) taken. The metal in the ProDisc™-C Total Disc Replacement can effect the quality of images taken.

What are the Expected Outcomes of the Surgery?

The U.S. clinical study of the ProDisc™-C Total Disc Replacement showed that ProDisc™-C Total Disc Replacement was just as good as fusion surgery in helping to relieve pain and restore normal function. The rates of complications were about the same between the two groups in the first two years following surgery. The clinical benefit beyond two years has not been measured. Ask your surgeon for more details about the clinical study and its results.

Making the Choice for Surgery

You should discuss both surgical and nonsurgical treatment options with your doctor. If surgery is selected, your occupation, activity level, weight, and the condition of your spine will be considered when determining if you are an appropriate candidate for ProDisc™-C Total Disc Replacement. Only your doctor can decide if you are an appropriate candidate. **Inform your doctor if you have an active infection or allergy to cobalt, chromium, molybdenum, polyethylene or titanium. Also inform your doctor if you have been diagnosed with osteoporosis, osteopenia, or if you have any other health issues.**

Conclusion

You have been diagnosed with Symptomatic Cervical Disc Disease (SCDD) and your doctor believes that surgery is the best treatment option. After considering the alternatives, your doctor may recommend the ProDisc™-C Total Disc Replacement, as a treatment alternative. If you would like additional information or have more questions about total disc replacement surgery, please call or see your doctor.

This patient information brochure is not a replacement for professional medical advice. Only your doctor is qualified to diagnose and treat your neck and/or arm pain.

For information about obtaining insurance reimbursement for the ProDisc™-C Total Disc Replacement procedure, you may contact our Reimbursement Hotline at 1-866-223-0508.

Glossary

Alleviate – To make something less severe or more bearable, especially pain

Degenerated – To fall below a normal or desirable state functionally, to decline in quality, to deteriorate

Incision – During surgery, a cut into a body tissue or organ with a sharp instrument

Intervertebral – Located between the spinal vertebrae

Lordosis – The natural curve of the spine in both the neck (cervical) and lower back (lumbar) regions. The spine's natural curves position the head over the pelvis and work as shock absorbers during movement. An excessive curve of the spine can be painful sometimes affecting movement.

Lymph – A watery fluid derived from body tissues that contains white blood cells. Lymph acts to remove bacteria and certain proteins from the body tissues, transport fat from the small intestine and supply mature lymphocytes to the blood.

Lymphatic vessel – Any of the vascular channels that transport lymph throughout the lymphatic system, which is an interconnected system of spaces and vessels between body tissues and organs.

Osteopenia – mild loss of bone mineral density (BMD), usually seen as a precursor to osteoporosis

Osteoporosis - A disease in which the bones deteriorate and become weakened, fragile, and easily broken. BMD is reduced as minerals, such as calcium, leach out. Any bone can be affected by

osteoporosis, but spinal or vertebral fractures can cause severe back pain and lead to loss of height and spinal deformity.

Rehabilitation – To restore to good health or good condition through therapy and education.

Spinal Stenosis – A condition that occurs when the space that holds the spinal cord and nerves roots becomes narrowed or restricted. Stenosis can squeeze nerves and the spinal cord leading to pain in the lower back and legs, or in the neck, arms, and hands depending on where the narrowing is occurring in the spine.

Ultra-High Molecular Weight Polyethylene – Hard plastic used between the metal endplates

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CAUTION: Federal (United States) law restricts this device to sale by or on the order of a physician (or properly licensed practitioner) who have appropriate training and experience.

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