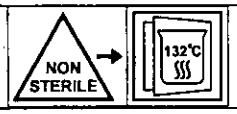
USA:
NuVasive, Inc.
7475 Lusk Blvd.
San Diego, CA 92121

NUVASIVE®
"Speed of Innovation"

PCM®
THE CERVICAL DISC SYSTEM

INSTRUCTIONS FOR USE

Rx Only

GRAPHICAL SYMBOLS	
	Read Instructions Before Use
	Single Use Only
	Catalog Number
	Lot Number
	Sterile by Irradiation
	Non-Sterile, Sterilize by Steam before Use
	Manufacturer
	Use By

HOW SUPPLIED
PCM Cervical Disc Implants – Sterile
Surgical Instruments – Non-sterile (unless otherwise noted on the package label)

DEVICE DESCRIPTION

The PCM Cervical Disc is an artificial cervical disc that is designed to provide an alternative to fusion. The PCM is a two-piece, articulating device that is inserted into the intervertebral disc space at a single cervical level using a standard anterior cervical approach, known as the Smith-Robinson anterior approach.

The PCM Cervical Disc is comprised of two cobalt chromium molybdenum (CoCrMo) alloy metal endplates, one cephalad and one caudal, and an ultra-high molecular weight polyethylene (UHMWPE) spacer fixed to the caudal endplate. The articulation consists of a superior concave metallic surface and the inferior polyethylene convex surface. The plates are available in three sizes (small, medium, and large). The dimensions of the endplates are 14 x 17 mm (small), 16 x 17 mm (medium), and 17 x 20 mm (large). The bone-contacting surface of each of the endplates has a coating that is comprised of two layers of titanium covered by an electrochemically applied layer of calcium phosphate (TiCaP®). This surface has transverse ridges designed to enhance postoperative bone fixation.

The PCM Cervical Disc comes in overall thicknesses of 6.5, 7.2, and 8.0 mm. The contact between the UHMWPE spacer and the cephalad component is a ball-and-socket articulation.

The PCM Cervical Disc implant materials consist of the following:

- CoCrMo Alloy; according to ISO 5832-12
- UHMWPE, according to ISO 5834-1, ISO 5834-2 / ASTM F648
- Unalloyed Titanium, according to ISO 5832-2/ ASTM F67
- Titanium plasma spray (TPS) and calcium phosphate (CaP) coatings

Table 1: PCM Cervical Disc Configurations

Part Number	Description
7680265	PCM-V Disc, S 6.5
7680272	PCM-V Disc, S 7.2
7680280	PCM-V Disc, S 8.0
7680365	PCM-V Disc, M 6.5
7680372	PCM-V Disc, M 7.2
7680380	PCM-V Disc, M 8.0
7680465	PCM-V Disc, L 6.5
7680472	PCM-V Disc, L 7.2
7680480	PCM-V Disc, L 8.0

INDICATIONS FOR USE

The PCM Cervical Disc is indicated for use in skeletally mature patients for reconstruction of a degenerated cervical disc at one level from C3-C4 to C6-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit), with or without neck pain, or myelopathy due to a single-level abnormality localized to the disc space, and manifested by at least one of the following conditions confirmed by radiographic imaging (CT, MRI, X-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. The PCM Cervical Disc is implanted using an anterior approach. Patients should have failed at least 6 weeks of conservative treatment prior to implantation of the PCM Cervical Disc.

CONTRAINDICATIONS

The PCM Cervical Disc should not be implanted in patients with the following conditions:

- Acute or chronic infections, local or systemic
- Osteoporosis (defined as DEXA bone density measured T-Score $\leq$ -2.5) or osteopenia (defined as DEXA bone density measured T-Score $\leq$ -1.0)
- Congenital stenosis
- Allergy or sensitivity to *any* of the implant materials (cobalt, chromium, molybdenum, titanium, or polyethylene).

WARNINGS

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

- Marked cervical instability on neutral resting lateral or flexion/extension radiographs; translation >3.5mm and/or >11° rotational difference from that of either adjacent level;
- Severe spondylosis at the level to be treated, characterized by bridging osteophytes, loss of disc height >50%, an absence of motion (<2°) as this may lead to a limited range of motion and may encourage bone formation (e.g. heterotopic ossification, fusion)
- Severe facet joint arthropathy or pathology
- Significant cervical anatomical deformity or 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) or disease (e.g., ankylosing spondylitis, rheumatoid arthritis)

- The PCM Cervical Disc System should only be used by surgeons who are experienced with anterior cervical spinal procedures and are familiar with the implant components, instruments, procedure, clinical applications, biomechanics, adverse events, and risks associated with the PCM device. A lack of adequate experience and/or training may lead to a higher incidence of adverse events, including neurological complications.
- Correct selection of the appropriate implant size and correct placement of the device are essential to ensure optimal performance and function of the device. Please refer to the PCM Surgical Technique manual for step-by-step instructions on the required surgical technique, including determining the correct implant size.

- 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.
- Heterotopic Ossification (HO) is a potential complication associated with cervical total disc replacement devices, which could result in reduced motion. It is recommended that surgeons take appropriate steps to reduce the chance of developing HO (such as the use of bone wax following the removal of osteophytes and the short-term post-operative use of non-steroidal anti-inflammatory drugs (NSAIDs).

PRECAUTIONS

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

- Intractable radiculopathy or myelopathy due to pathology at more than one level and/or pathology not localized to the disc space;
- Under the age of 21 or over the age of 65;
- Prior cervical spine surgery at the level to be treated, except laminoforaminotomy
- More than one immobile vertebral level between C1-T1 from any cause including but not limited to congenital abnormalities, osteoarthritic "spontaneous fusions", and prior cervical fusions
- Symptoms attributed to more than one vertebral level;
- Neck pain alone;
- Neck or arm pain of unknown etiology;
- Neuromuscular disorders such as muscular dystrophy, spinal muscular atrophy, amyotrophic lateral sclerosis;
- Systemic disease including AIDS, HIV, and Hepatitis;
- Paget's disease, osteomalacia, or other metabolic bone disease;
- Active malignancy including spinal metastases, except non-melanoma skin cancer;
- Taking medications known to potentially interfere with bone/soft tissue healing (e.g. steroids);
- Severe diabetes mellitus requiring daily insulin treatment;
- Autoimmune disorders that impact the musculoskeletal system (e.g., lupus, rheumatoid arthritis; ankylosing spondylitis);
- Morbid obesity, defined as body mass index > 40 or more than 100 lbs. over ideal body weight;
- Acute episode of mental illness and substance abuse;
- Pregnancy;
- Prior fusion at an adjacent vertebral level; similar to the experience in ACDF control group, the use of the PCM Cervical Disc at a spinal level adjacent to a previous fusion may lead to clinical outcomes inferior to those observed for patients without a prior adjacent level fusion. For the PCM Cervical Disc, these include, but are not limited to, possible implant migration and a higher incidence of subsequent device removal.

Before selection of the implant, the surgeon must:

- Ensure that a possible allergy of the patient to a component of the implant material is excluded prior to selecting the implant.
- Assure highly aseptic surgical conditions.
- Ensure that, in accordance with the preoperative planning, all necessary device components are available.
- Ensure that all NuVasive instruments necessary for implantation are available in intact and/or sterile condition.

Before selection of the implant, it is also important to note:

- The presence of anatomical abnormalities and/or deformities may reduce the possibility of the surgeon to ensure proper placement of the implant.
- In some instances, there may be interferences that prevent implantation. In these instances, it may be necessary to perform a fusion procedure.
- The target disc level should be confirmed radiographically to ensure proper placement of the implant and during the whole procedure, e.g., for sizing and safe placement of the implant.
- Thorough decompression is necessary for proper alignment of the implant.
- Failure to remove all anterior osteophytes may result in misalignment of the implant.

Pre-operative:

Patient selection is extremely important. Proper patient selection, including the adherence to the device's indications and contraindications, assessment of co-morbidities and medication use, consideration of the patient's occupation and activity level, mental health, and evaluation of all preoperative imaging studies, is critical to assuring optimum performance of the

device. The patient should be mentally prepared and able to comprehend the importance of precautionary measures and to adhere to them.

A screening questionnaire for osteoporosis should be administered to determine if a DEXA Bone mineral density is necessary. A patient should not receive the PCM Cervical Disc if the DEXA measured T score is ≤ -2.5 as the patient may be osteoporotic.

All alternatives for non-surgical and surgical treatment of the degenerated cervical disc should be discussed. The patient should be informed that the PCM Cervical Disc does not function exactly the same as the natural joint, and only an indication-dependent improvement of the preoperative symptoms can be expected.

The patient should be informed of the potential adverse effects (risks/complications) (see POTENTIAL ADVERSE EFFECTS ON HEALTH section of this package insert).

The presence of anatomical abnormalities and/or deformities that may interfere with the surgeon's ability to place the PCM Cervical Disc should be identified. If these abnormalities prevent implantation, the surgeon should be prepared to perform an alternate procedure.

Pre-operative planning should be used to estimate the required implant size, and to assure that the appropriate range of sizes is available. The procedure should not take place if the appropriate range of sizes is not available.

Ensure that all the NuVasive instruments necessary for implantation are available in intact and/or sterile condition.

Preoperative instructions to the patient are essential. The patient should be made aware of the limitations of the implant and potential risks of the surgery. The patient should be instructed to limit postoperative activity, as this will reduce the risk of bent, broken or loose implant components. The patient must be made aware that implant components may bend, break or loosen even though restrictions in activity are followed. The patient should be provided a copy of the PCM Cervical Disc Patient Information brochure.

Intra-operative:
The PCM Cervical Disc should not be used with components or instruments of spinal systems from other manufacturers. Refer to the PCM Cervical Disc System surgical technique manual for step-by-step instructions.

Care should be used in the handling and storage of the PCM Cervical Disc. Assure highly aseptic surgical conditions, and use aseptic technique when removing the PCM Cervical Disc from its packaging. Inspect the implant and packaging for signs of damage, including scratched or damaged devices or damage to the sterile barrier. Do not use the PCM Cervical Disc if there is any evidence of damage.

Care should be used during surgical procedures to prevent damage to the device(s) and injury to the patient.

The target disc level should be confirmed radiographically to ensure proper placement of the implant and during the whole procedure, e.g., for sizing and safe placement of the implant.

Excessive burring or removal of the endplates, especially at the anterior rim of the caudal vertebral body, may lead to inaccurate placement or insufficient bony support of the implant, which may ultimately result in device migration or subsidence. The implant is primarily fixed in a press fit manner. Patients with certain features of spinal anatomy which may only be discerned intraoperatively, such as sclerotic bone or irregular vertebral endplate surfaces, may not be appropriate candidates for the PCM Cervical Disc, and should be treated with arthrodesis instead.

When preparing the disc, perform a thorough decompression by full discectomy and removal of posterior osteophytes as needed, taking care to minimize bone removal. Correct positioning of the device is critical to avoid early failure of the device.

The use of bone wax following the removal of osteophytes is recommended to reduce the chance of developing heterotopic ossification (HO).

The PCM Cervical Disc should never be re-used or re-implanted.

Any kind of modification of the prosthesis is not permitted. Components (cranial & caudal) packaged together are specially paired and must not be mixed with components obtained from another package.

Post-operative:
Patients should be instructed in post-operative procedures and the importance of adherence to these procedures. Post-operative care includes, neck support, activity modification for a period of time after surgery and formal rehabilitation. The duration of these procedures is determined by the treating physician, taking into consideration the individual patients condition and the stability and functioning of the implant. A course of non-steroidal anti-inflammatories (NSAIDs) may be given to potentially reduce the risk of heterotopic ossification.

Magnetic Resonance (MR) Safety: The PCM Cervical Disc has not been evaluated for safety and compatibility in the MR environment. The PCM Cervical Disc has not been tested for heating or migration in the MR environment.

Important Note To Operating Surgeon: The following are to be taken into account in the indication of a cervical disc implant with consideration of the patient's overall condition.

- That all alternatives for non-surgical and surgical treatment of the joint disease have been included in the deliberations.
- That the cervical disc implant is basically inferior to the function of the natural joint, and only an indication-dependent improvement of the preoperative situation can be aimed for.
- That the patient is mentally prepared to comprehend the importance of precautionary measures and to adhere to them.
- That the patient agreed to the surgery and accepts the associated risks.
- That if foreign body sensitivity is suspected, the selected implant materials have been determined to be compatible by suitable tests.
- In general, the mechanical failure/breaking of joint replacement prosthesis is the rare exception, but this cannot be ruled out with absolute certainty. The reason for this can be, for example, an abnormal prosthesis load, e.g. during a fall. The bone in the area of the prosthesis anchoring/ support can change later owing to absorption such that a normal prosthesis load is no longer assured and a partial overload zone on the prosthesis results.

Spinal fixation should only be undertaken after the surgeon has had hands on training in this method of spinal fixation and has become thoroughly knowledgeable about spinal anatomy and biomechanics. A surgical technique is available for instructions on the important aspects of this surgical procedure.

The patient should be made aware of the limitations of the implant and potential adverse effects of the surgery. The patient should be instructed to limit postoperative activity, as this will reduce the risk of bent, broken, or loose implant components.

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

POTENTIAL ADVERSE EFFECTS ON HEALTH
Potential risks associated with the use of the PCM Cervical Disc 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 PCM Cervical Disc. 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 are therefore reported in the Clinical Study section below.

- 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;

- 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, or pharyngeal perforation; airway obstruction; external chylorrhea; warmth or tingling in the

extremities; damage to the spinal cord, 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; seromas or tissue swelling; and headache;

- Risks associated with implants in the spine, including the PCM Cervical Disc 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; cord or nerve root injury; loss of bowel and/or bladder control; and interference with radiographic imaging because of the presence of the implant;
- Wound, local and/or systemic infections;
- Surgical instrument bending or breakage, as well as the possibility of a fragment of a broken instrument remaining in the patient;
- Inability to resume activities of normal daily living;
- Death.

CLINICAL STUDY

The clinical investigation of the PCM Cervical Disc was a pivotal multicenter, randomized, controlled, unmasked, non-inferiority clinical trial conducted under an approved IDE (G040081), and it evaluated the safety and effectiveness of the PCM Cervical Disc compared to conventional anterior cervical fusion ("ACDF"), using anterior cervical plating with allograft bone, for reconstruction of the cervical disc at one level following discectomy for neurological symptoms associated with degenerative changes of the disc at that level in patients with cervical disc degeneration and neurological symptoms at one level between C3-C4 and C7-T1.

A total of 494 patients were enrolled in the study (302 PCM Disc, 192 Control) at 23 clinical sites in the United States. Of those enrolled, 479 patients were treated (289 with PCM Disc, 190 Control with ACDF) (***Table 2***).

Patients were enrolled in the clinical study according to the following inclusion/exclusion criteria:

Inclusion Criteria

- Age 18-65 years;
- Diagnosis of radiculopathy or myelopathy of the cervical spine, with either radiculopathy symptoms – pain, paresthesias, or paralysis in a specific nerve root distribution C4, C5, C6, C7, or C8, including at least one of the following: arm/shoulder pain (at least 30 mm on 100 mm VAS scale); decreased muscle strength of at least one level on the 0-5 scale described below; abnormal sensation, including hyperesthesia or hypoesthesia; and/or abnormal reflexes; or myelopathy symptoms including positive Romberg evaluation, abnormal heel/toe walk, pathologic hyperreflexia or clonus in lower extremity, positive Babinski, or positive Hoffman's;
- Symptomatic at only one level from C3-C4 to C7-T1;
- Radiographically determined pathology at level to be treated correlating to primary symptoms, including at least one of the following:
    - Decreased disc height compared to adjacent levels on radiographic film, CT, or MRI;
    - Degenerative spondylosis on CT or MRI;
    - Disc herniation on CT or MRI.
- Neck Disability Index score ≥30% (15/50);
- Unresponsive to non-operative treatment for six weeks, or has the presence of progressive symptoms or signs of nerve root/spinal cord compression in the face of conservative treatment;
- Appropriate for treatment using an anterior surgical approach, including having no more than one previous anterior surgical approach to the cervical spine;
- Ability and willingness to comply with follow-up regimen; and

- Written informed consent given by patient or patient's legally authorized representative.

Exclusion Criteria

- Infection at the site of surgery;
- History of, or anticipated treatment for, active systemic infection, including HIV infection or hepatitis C;
- Prior attempted or completed cervical spine surgery, except (1) laminoforaminotomy, which includes removal of disc material necessary to perform a nerve root decompression, with less than one-third facetectomy at any level, or (2) a successful single-level anterior cervical fusion;
- More than one immobile vertebral level between C1-T1 from any cause, including but not limited to congenital abnormalities, osteoarthritic "spontaneous" fusions, and prior cervical spinal fusions;
- Previous trauma to the C3-T1 levels resulting in significant bony or disco-ligamentous cervical spine injury;
- Axial neck pain in the absence of other symptoms of radiculopathy or myelopathy justifying the need for surgical intervention;
- Radiographic confirmation of severe facet joint disease or degeneration.
- Osteoporosis: A screening questionnaire for osteoporosis, SCORE (Simple Calculated Osteoporosis Risk Estimation), will be used to screen patients to determine those 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);
- Paget's disease, osteomalacia, or any other metabolic bone disease (excluding osteoporosis which is addressed above);
- Severe diabetes mellitus requiring daily insulin management;
- Active malignancy: a history of any invasive malignancy (except non-melanoma skin cancer), unless the patient has been treated with curative intent and there have been no clinical signs or symptoms of the malignancy for at least 5 years;
- Tumor as source of symptoms;
- Symptomatic DDD or significant cervical spondylosis at two or more levels;
- Marked cervical instability on resting lateral or flexion/extension radiographs demonstrated by:
    - Translation > 3.5 mm and/or
    - > 11° angular difference to that of either adjacent level;
- Known or suspected allergy to cobalt, chromium, molybdenum, titanium, or polyethylene;
- Severe myelopathy to the extent that the patient is wheelchair bound;
- Congenital canal stenosis resulting in a canal diameter of < 10 mm, as measured by CT or MRI;
- Kyphotic segmental angulation of greater than 11 degrees at treatment or adjacent levels;
- Arachnoiditis;
- Pregnant (verified in patients of childbearing potential by a negative urine pregnancy test when preadmission testing is obtained), or interested in becoming pregnant during the duration of the study;
- Autoimmune disorders that impact the musculoskeletal system (e.g., lupus, rheumatoid arthritis; ankylosing spondylitis);
- Congenital bony and/or spinal cord abnormalities that affect spinal stability;
- Spinal axis disease (thoracic or lumbar) to the extent that surgical consideration is likely anticipated within 6 months after the cervical randomized procedure;
- Other degenerative joint disease (e.g. shoulder, hip, knee) to the extent that surgical consideration is likely anticipated within 6 months after the cervical randomized procedure;
- Previous spine surgery within the 6 months preceding the cervical randomized procedure;
- Diseases or conditions that would preclude accurate clinical evaluation (e.g. neuromuscular disorders);
- Medications that could interfere with fusion or other bone/soft tissue healing (e.g. anticipated continued use of systemic steroid medication postoperatively);
- Currently experiencing acute episode of major mental illness (psychosis, major affective disorder, or schizophrenia), or manifesting physical symptoms without a diagnosable medical condition to account for the symptoms, which may indicate symptoms of psychological rather than physical origin;
- Current or recent history of substance abuse (drug or alcohol);
- Morbid obesity, defined as body mass index ("BMI") > 40 or more than 100 lbs. over ideal body weight;
- Currently using, or planning to use, bone growth stimulators in the cervical spine;
- Use of any other investigational drug or medical device within the last 30 days prior to surgery
- Currently a prisoner; or

- Currently pursuing personal litigation (defined as litigation that will likely influence the patient's ability or willingness to accurately report their treatment outcomes) related to the neck or cervical spine injury; however, involvement in worker's compensation related litigation is not a required exclusion.

Study Follow-Up and Evaluations

The protocol required each patient to remain in the study for 24 months post treatment. Study evaluations were completed pre-operatively and post-operatively, at 6 weeks, and at 3, 6, 12, and 24 months. In addition, all patients were required to return for annual follow-up visits until the last enrolled patient reached the 24-month follow-up.

All adverse events, (device-related or not) were monitored over the course of the study and were independently adjudicated by a Clinical Events Committee.

All radiographic endpoints were evaluated independently at a core laboratory, by a board certified independent radiologist. Range of motion was measured segmentally, only at the operative level, by the core lab, using a protocol to determine this measurement incorporating validated computerized techniques to ensure reproducibility.

Please refer to ***Table 2*** below for the Evaluation Summary and Visit Schedule.

Table 2: Evaluation Summary and Visit Schedule

Evaluations	Preoperative (within 30 days prior to surgery)	Follow-Up Visit Windows					
		Post-Operative (7-21 days)	6 Weeks (± 2 wks)	3 Months (± 2 wks)	6 Months (± 2 wks)	12 Months (± 2 wks)	24 Months and Other Annual (± 2 wks)
Eligibility	x						
Demographics	x						
Medical History	x						
Medications	x	x	x	x	x	x	x
Neurological Assessment	x	x	x	x	x	x	x
Radiographic Evaluation	x	x	x	x	x	x	x
Neck Disability Index	x		x	x	x	x	x
Pain VAS	x		x	x	x	x	x
Dysphagia VAS	x		x	x	x	x	x
Bazaz Dysphagia	x		x	x	x	x	x
Nurick's Assessment	x		x	x	x	x	x
Odom's Criteria	x		x	x	x	x	x
SF-36	x		x	x	x	x	x
Employment Status	x		x	x	x	x	x
Patient Satisfaction						x	x
Adverse Events/ Surgical Intervention	x	x	x	x	x	x	x

Clinical Endpoints

The primary endpoint of the study was a composite of several safety and effectiveness endpoints:

- Improvement of at least 20% in the Neck Disability Index (NDI) at 24 months compared to baseline
- No device failures requiring revision, reoperation or removal
- Absence of major complications

The safety of the PCM was assessed by comparing the occurrence of all adverse events, serious adverse events, surgery-related adverse events, implant-related adverse events, unanticipated adverse device effects, neurological assessments, Bazaz dysphagia score, and subsequent secondary surgical interventions. The effectiveness of the PCM Cervical Disc was assessed by evaluating the following secondary endpoints: NDI (success ≥20% improvement), Neck Pain Visual Analog Scale (VAS) (success ≥20mm improvement), Arm Pain VAS (success ≥20mm improvement), SF-36 Quality of Life Questionnaire (success ≥15% improvement), Nurick's Index (success = Maintained or Improved), Odom's criteria (rated as Excellent, Good, Fair or Poor) and Patient Satisfaction VAS evaluation (0-100mm scale). Several additional radiographic endpoints were considered in evaluating both safety and effectiveness, including assessments of range of motion of the spinal motion segment (measured in degrees), disc height (normal ≥80% of superior level), disc height maintenance (success ≥80% of postoperative), displacement or migration of device or graft (graded as Absent, Present or

Explusion), heterotopic ossification (graded on a 5-point scale), radiolucency (>50% length of the prosthesis or graft), dynamic canal stenosis (success if ≥12 mm), and fusion status (PCM success is the absence of evidence of continuous bridging bone, and > 2.0° total angular motion).

The primary analysis dataset was the "per protocol" population, which consisted of randomized study patients who a) met the eligibility criteria, b) had no major protocol violations; and c) completed the 24-month follow-up visit.

Accountability of the PMA Cohort

The patient accountability data are summarized in ***Table 3***, where training cases are referred to as the Training (TRN) group, the randomized investigational patients are referred to as the PCM group, and the randomized ACDF control patients are referred to as the ACDF group.

The follow-up rates are calculated from a maximum Per Protocol population of 75 Training, 211 PCM, and 184 ACDF patients. The patients evaluable for the primary composite overall success endpoint at 24 Months were 74.7%, 89.6% and 82.1% for the Training group, PCM group, and ACDF group, respectively.

Table 3: Patient Accountability

	12 Months (±2 Months)			24 Months (-3 Months, +6 Months)			36 Months (±6 Months)		
	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN	PCM	ACDF
Enrolled/ITT	78	224	192	78	224	192	78	224	192
Not Treated	2	6	7	2	6	7	2	6	7
Treated (MITT)	76	218	185	76	218	185	76	218	185
Treated (Safety)	75	214	190	75	214	190	75	214	190
Deaths	0	1	0	0	1	0	0	1	0
Eligible Deviations	1	6	1	1	6	1	1	6	1
Not Yet Overdue	0	0	0	0	0	0	0	0	0
Per Protocol (Maximum)	75	211	184	75	211	184	75	211	184
Per Protocol (In Window)	66	202	162	56	189	153	46	180	141
Primary Endpoint (Protocol Defined)*	65	198	156	56	189	151	51	182	136
% Follow-up, Primary Endpoint (Protocol Defined)#	86.7%	93.8%	84.8%	74.7%	89.6%	82.1%	68.0%	86.3%	73.9%

ITT = Intent-to-Treat; MITT = Modified Intent-to-Treat.

* Number of patients evaluable for the primary composite overall success endpoint as defined in the protocol.

% Follow-up, Primary Endpoint = Primary Endpoint (Protocol Defined) / Per Protocol (Maximum).

The following flow diagram in ***Figure 1*** illustrates the origins of the analysis populations: Enrolled, Intent-to-Treat (ITT), Modified Intent-to-Treat (MITT), Per Protocol, Per Protocol In Window, and Safety.

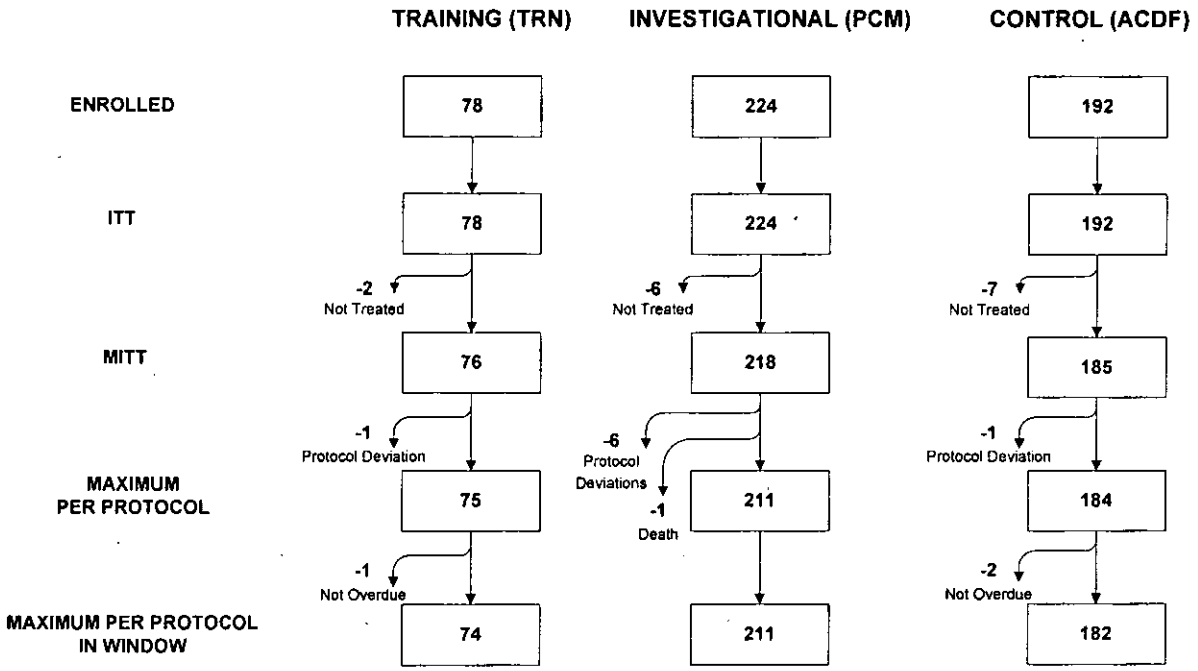
The analysis populations are defined as follows:

- Enrolled population includes any patient who gave Informed Consent and was enrolled. Analysis by group the patient was enrolled to.
- Intent-to-Treat (ITT) population includes any patient who was enrolled (Training) or randomized (PCM, ACDF). Analysis by group the patient was enrolled (Training) or randomized (PCM, ACDF) to.
- Modified Intent-to-Treat (MITT) population includes any patient who was treated. Analysis by group the patient was enrolled (Training) or randomized (PCM, ACDF) to.
- Per Protocol population includes any patient who was treated with the device they were randomized to, met the eligibility criteria, and had no major protocol violations. Analysis by group the patient was enrolled (Training) or randomized (PCM, ACDF) to.
- Per Protocol In Window population includes any patients who was treated with the device they were enrolled/randomized to, met the eligibility criteria, had no major protocol violations, and had a 24 Months visit within the visit window (i.e., 21 to 30 months). Analysis by group the patient was enrolled (Training) or randomized (PCM, ACDF) to.

- Safety population includes any patient who was treated. Analysis by group the patient was actually treated with (i.e., as-treated). The Safety population is the basis of the safety analyses.

Patient Demographics, Baseline Characteristics, and Surgical Characteristics were analyzed using both the MITT and Per Protocol In Window population.

Figure 1: Patient Accountability Flowchart



Patient Data Accounting

The data accounting for the protocol-required 24 Months clinical and radiographic assessments are tabulated in ***Table 4***.

Table 4: Patient Data Accounting at 24 Months

	Training	PCM	ACDF
Enrolled/ITT	78	224	192
Treated (MITT)	76	218	185
Treated (Safety; As-Treated)	75	214	190
Eligible Deviations	1	6	1
Deaths	0	1	0
Per Protocol (Maximum)	75	211	184
Per Protocol (In Window)	56	189	153
Clinical Assessments, n (%)*			
Neck Disability Index (NDI)	55 (73.3%)	187 (88.6%)	151 (82.1%)
VAS Neck and Arm Pain	55 (73.3%)	187 (88.6%)	150 (81.5%)
SF-36	54 (72.0%)	187 (88.6%)	151 (82.1%)
Patient Satisfaction	53 (70.7%)	182 (86.3%)	146 (79.3%)
Dysphagia	52 (69.3%)	187 (88.6%)	149 (81.0%)
Neurological Exam	54 (72.0%)	188 (89.1%)	153 (83.2%)
Radiographic Assessments, n (%)*			
Normal Disc Height	51 (68.0%)	182 (86.3%)	140 (76.1%)
Maintenance of Disc Height	50 (66.7%)	177 (83.9%)	135 (73.4%)
Radiolucency	51 (68.0%)	182 (86.3%)	152 (82.6%)
Migration	51 (68.0%)	182 (86.3%)	152 (82.6%)
ROM	53 (70.7%)	182 (86.3%)	151 (82.1%)
Dynamic Canal Stenosis	51 (68.0%)	182 (86.3%)	144 (78.3%)
Spine Stability	53 (70.7%)	182 (86.3%)	149 (81.0%)
Hypermobility	52 (69.3%)	181 (85.8%)	149 (81.0%)
Heterotopic Ossification	51 (68.0%)	182 (86.3%)	NA
Adjacent Segment Degeneration	41 (54.7%)	147 (69.7%)	119 (64.7%)

ITT = Intent-to-Treat.; MITT = Modified Intent-to-Treat.

* Percentages are based on the Per Protocol (Maximum) patient population.

Patient Demographics and Baseline Parameters

Table 5 summarizes the patient demographics and baseline characteristics.

Table 5: Patient Demographics and Baseline Characteristics (Modified Intent-to-Treat Population)

	Training (N=76)	PCM (N=218)	ACDF (N=185)	P-Value*
Age, mean (SD) years	42.2 (8.2)	45.3 (9.0)	43.7 (8.3)	0.059 (b)
Female, no. (%)	29 (38.2%)	105 (48.2%)	89 (48.1%)	0.991 (a)
Race, no. (%)				
Caucasian	70 (92.1%)	202 (92.7%)	170 (91.9%)	0.145 (a)
Black	2 (2.6%)	10 (4.6%)	7 (3.8%)	
Asian	0 (0.0%)	0 (0.0%)	5 (2.7%)	
Hispanic	3 (3.9%)	3 (1.4%)	2 (1.1%)	
Other	1 (1.3%)	3 (1.4%)	1 (0.5%)	
Height, mean (SD) inches	68.3 (4.4)	67.4 (4.2)	67.3 (3.8)	0.737 (b)
Weight, mean (SD) pounds	186.0 (40.2)	182.9 (39.9)	177.1 (38.8)	0.143 (b)
BMI, mean (SD) kg/m^2	28.0 (4.9)	28.2 (4.6)	27.3 (4.8)	0.079 (b)
Current Tobacco Use, no. (%)	39 (51.3%)	113 (51.8%)	90 (48.6%)	0.524 (a)
History Nonoperative Care, no. (%)				
Medication Used	73 (96.1%)	210 (96.3%)	181 (97.8%)	0.558 (c)
Injections	34 (44.7%)	117 (53.7%)	80 (43.2%)	0.045 (c)
Physical Therapy	54 (71.1%)	157 (72.0%)	126 (68.1%)	0.444 (c)
Brace	5 (6.6%)	24 (11.0%)	25 (13.5%)	0.449 (c)
Chiropractic	24 (31.6%)	66 (30.3%)	75 (40.5%)	0.036 (c)
Other	20 (26.3%)	33 (15.1%)	39 (21.1%)	0.151 (c)
History Prior Surgery, no. (%)				
Lamino-foraminotomy without Facetectomy	2 (2.6%)	1 (0.5%)	3 (1.6%)	0.337 (c)
Lamino-foraminotomy with Facetectomy	0 (0.0%)	1 (0.5%)	4 (2.2%)	0.184 (c)
Fusion	14 (18.4%)	29 (13.3%)	20 (10.8%)	0.541 (c)
Neurological Symptoms, no. (%)				
Radiculopathy and Myelopathy	11 (14.5%)	33 (15.1%)	45 (24.3%)	0.023 (c)
Radiculopathy Only	65 (85.5%)	184 (84.4%)	140 (75.7%)	
Myelopathy Only	0 (0.0%)	1 (0.4%)	0 (0.0%)	
Radiographic Findings, no. (%)				
Herniated Nucleus Pulposus	66 (86.8%)	176 (80.7%)	155 (83.8%)	0.437 (c)
Spondylosis	11 (14.5%)	41 (18.8%)	28 (15.1%)	0.355 (c)
Loss of Disc Height	16 (21.1%)	39 (17.9%)	53 (28.6%)	0.012 (c)

Note: Percentages are based on total number of patients for each treatment group.

* Comparing PCM and ACDF (two-sided): (a) Chi-squared test; (b) t-test; (c) Fisher's exact test. P-values are not adjusted for multiplicity. They are included to help clinical interpretation, without defining statistical significance.

Preoperative clinical and radiographic endpoints, including Neck Disability Index (NDI) scores, Visual Analog Scale (VAS) Neck Pain, VAS Arm Pain (left, right, worst arm), SF-36 (Physical Component Score [PCS] and Mental Component Score [MCS]), neurological status, and index level range of motion (ROM) and translation, are shown in ***Table 6***.

Based on the baseline evaluations, it was concluded that the randomization was successful and the PCM and ACDF groups were similar and well balanced.

Table 6: Baseline Evaluation of Clinical Endpoints
(Per Protocol 24 Months In Window Population)

Endpoint	Training (N=56)	PCM (N=189)	ACDF (N=153)	P-Value
Neck Disability Index (NDI)	51.2 (13.8)	55.8 (14.5)	54.7 (14.0)	0.470 (a)
VAS Neck Pain, mm	66.8 (24.5)	68.4 (22.3)	73.5 (18.6)	0.076 (a)
VAS Right Arm Pain, mm	49.3 (34.3)	47.9 (33.7)	50.6 (33.4)	0.625 (a)
VAS Left Arm Pain, mm	43.0 (36.7)	51.2 (33.9)	50.0 (32.6)	0.679 (a)
VAS Worst Arm Pain, mm	74.9 (17.3)	73.4 (19.4)	74.4 (18.2)	0.791 (a)
SF-36 PCS	36.3 (6.3)	34.4 (6.8)	34.6 (6.3)	0.681 (b)
SF-36 MCS	43.0 (12.7)	43.3 (12.3)	41.9 (11.4)	0.303 (b)
Neurological Status, no. (%)				
Motor (normal)	18 (32.1%)	63 (33.3%)	57 (37.3%)	0.495 (c)
Sensory (normal)	24 (42.9%)	87 (46.0%)	68 (44.4%)	0.827 (c)
Reflexes (normal)	49 (87.5%)	167 (88.4%)	124 (81.0%)	0.068 (c)
Range of Motion, degrees	7.9 (4.5)	7.9 (4.7)	7.8 (4.4)	0.910 (b)
Translation, mm	0.8 (0.5)	0.9 (0.6)	0.9 (0.7)	0.470 (b)

Note: Continuous variables are reported as means and standard deviations.
* Comparing PCM and ACDF (two-sided): (a) Mann-Whitney-Wilcoxon rank sum test; (b) t-test; (c) Fisher's exact test. P-values are not adjusted for multiplicity. They are included to help clinical interpretation, without defining statistical significance.

Surgical and Hospitalization Parameters

Typical operative characteristics, including the distribution of the spinal levels treated, surgical time, blood loss, and length of hospital stay, are reported in ***Table 7***.

Table 7: Surgical Data
(Modified Intent-to-Treat Population)

	Training (N=76)	PCM (N=218)	ACDF (N=185)
Treated Level, no. (%)			
C3-C4	1 (1.3%)	0 (0.0)%	8 (4.3%)
C4-C5	5 (6.6%)	31 (14.2%)	17 (9.2%)
C5-C6	33 (43.4%)	109 (50.0%)	98 (53.0%)
C6-C7	35 (46.1%)	76 (34.9%)	62 (33.5%)
C7-T1	2 (2.6%)	2 (0.9%)	0 (0.0%)
Surgery Time, mean (SD) min.	126.7 (45.6)	100.8 (42.0)	85.7 (40.5)
Blood Loss, mean (SD) mls.	82.5 (58.5)	65.6 (48.3)	58.6 (46.1)
Hospitalization, mean (SD) days	1.3 (0.6)	1.2 (0.6)	1.4 (0.7)

Safety and Effectiveness Results

Primary Endpoint and Subcomponents

Table 8 presents the primary endpoint and subcomponents success at 24 Months based on the Per Protocol population. The PCM group had an overall success rate of 75.1% (142/189) compared to 64.9% (98/151) in the ACDF group. Therefore, based on the FDA-requested non-inferiority delta of 10.0%, non-inferiority was demonstrated.

Table 8: Primary Endpoint and Subcomponent Success at 24 Months (Per Protocol Population with a Primary Endpoint)

Component	Training (N=56)	PCM (N=189)	ACDF (N=151)
NDI (≥20% Improvement)	45/54 (83.3%) [71.0% - 91.2%]	154/186 (82.8%) [76.7% - 87.6%]	121/149 (81.2%) [74.1% - 86.7%]
Neurological Success	48/53 (90.6%) [79.3% - 96.3%]	177/187 (94.7%) [90.3% - 97.2%]	134/150 (89.3%) [83.3% - 93.4%]
SSSI Success§	49/56 (87.5%) [76.1% - 94.1%]	178/189 (94.2%) [89.8% - 96.8%]	141/151 (93.4%) [88.1% - 96.5%]
Radiographic Success	50/51 (98.0%) [88.7% - 100.0%]	178/180 (98.9%) [95.8% - 100.0%]	138/150 (92.0%) [86.4% - 95.5%]
Overall Success	38/56 (67.9%) [54.8% - 78.6%]	142/189 (75.1%) [68.5% - 80.8%]	98/151 (64.9%) [57.0% - 72.1%]

§ Absence of SSSI (Subsequent Secondary Surgical Intervention) includes revisions, reoperations, removals, and supplemental fixation, although only reoperations and removals were observed.

Confidence intervals provided under the rates were determined using the Adjusted Wald by Agresti-Coull method.

In addition to the protocol-defined overall success criteria, FDA established an alternate definition of overall success to include improvement in NDI of ≥15-points rather than ≥20% from baseline. Analysis using the alternate-defined endpoint is provided in ***Table 8***. As shown in ***Table 9***, the PCM group had an overall success rate of 72.0% (136/189) compared to 60.9% (92/151) in the ACDF group. The corresponding 90% confidence interval for the difference in success rates is 2.6% to 19.5%. Therefore, based on the FDA-requested non-inferiority delta of 10.0%, non-inferiority was demonstrated.

Table 9: Alternate Primary Endpoint and Subcomponent Success at 24 Months (Per Protocol Population with a Primary Endpoint)

Component	Training (N=56)	PCM (N=189)	ACDF (N=151)
NDI (≥15-Point Improvement)	42/54 (77.8%) [64.9% - 87.0%]	147/186 (79.0%) [72.6% - 84.3%]	112/149 (75.2%) [67.6% - 81.4%]
Neurological Success	48/53 (90.6%) [79.3% - 96.3%]	177/187 (94.7%) [90.3% - 97.2%]	134/150 (89.3%) [83.3% - 93.4%]
SSSI Success§	49/56 (87.5%) [76.1% - 94.1%]	178/189 (94.2%) [89.8% - 96.8%]	141/151 (93.4%) [88.1% - 96.5%]
Radiographic Success	50/51 (98.0%) [88.7% - 100.0%]	178/180 (98.9%) [95.8% - 100.0%]	138/150 (92.0%) [86.4% - 95.5%]
Overall Success	37/56 (66.1%) [53.0% - 77.1%]	136/189 (72.0%) [65.1% - 77.9%]	92/151 (60.9%) [53.0% - 68.3%]

§ Absence of SSSI (Subsequent Secondary Surgical Intervention) includes revisions, reoperations, removals, and supplemental fixation, although only reoperations and removals were observed.

Confidence intervals provided under the rates were determined using the Adjusted Wald by Agresti-Coull method.

Safety Results

Adverse Events

Table 10: Definitions for Adverse Event Categories

Category	Definition
Implant Related Events - Related or possibly related to the implant	
Adjacent Level Disease	Onset of degeneration or spinal disease at a level adjacent to the implant.
Implant Displacement/Loosening	Migration or loosening of the implant.
Malpositioned Implant	Improper placement of the implant.
Neck/Arm Pain	Pain in the neck and/or arm.
Non-union	Failure of the vertebral bodies to fuse at the treated level.
Other	Other events not defined, includes implant related headaches and implant noise.
Radiolucency	Transparency of the bony structures surrounding the implant.
Spinal Event	Degeneration or disease of the spine, including bone growth and stenosis.
Subsidence	Events associated with implant subsidence into the vertebral bone.
Trauma	Damage inflicted on the body as the direct or indirect result of an external force.
Surgery Related Events - Related or possibly related to the surgical procedure	
Dysphagia/Dysphonia	Difficulty swallowing or speaking.
Gastrointestinal	Ailments relating to or affecting the stomach or intestines.
Incision Site	Events associated with the surgical incision site.
Infection	Ailments associated with an infectious agent.
Neck/Arm Pain	Events primarily associated with reports of neck and/or arm pain.
Neurologic	Conditions related to or potentially related to the neurological system.
Other	Events or unknown etiology or that cannot be readily classified into other criteria
Respiratory	Ailments or symptoms associated with respiration or the respiratory system.
Spinal Event	Events or conditions associated with the spine.
Urogenital	Conditions relating to or affecting the organs or functions of excretion and reproduction.
Vertebral Fracture	Fractures of the vertebra.
Systemic Events - Unrelated to the device or surgical procedure	
Cardiac Events	Any condition primarily associated with the heart and/or vascular system.
Dysphagia/Dysphonia	Difficulty swallowing or speaking.
Gastrointestinal	Ailments relating to or affecting the stomach or intestines.
Infection	Ailments associated with an infectious agent.
Mental Disorder	Ailments or disorders of a psychiatric nature or origin.
Musculoskeletal Trauma	Conditions pertaining to the muscles and skeleton, such as fracture, ligament tear, arthritis of any kind, and degenerative conditions, excluding muscle spasms and events related to spinal degenerative conditions
Musculoskeletal/Adjacent Level Disease	Conditions pertaining to the muscles and skeleton associated with Adjacent Level Disease of the spine
Musculoskeletal/Back/Leg Pain	Conditions pertaining to the muscles and skeleton primarily associated with reports of back and/or leg pain.
Musculoskeletal/Neck/Arm Pain	Conditions pertaining to the muscles and skeleton primarily associated with reports of neck and/or arm pain.
Musculoskeletal/Other	Conditions pertaining to the muscles and skeleton of unknown etiology or that cannot be readily be classified in another category.
Musculoskeletal/Spinal Event	Conditions pertaining to the muscles and skeleton primarily associated with the spine.
Neurologic	Conditions related to or potentially related to the neurological system.
Other	Events or unknown etiology or that cannot be readily classified into other criteria.
Other Trauma	Traumatic events associated with symptoms not identified in any other category.
Respiratory	Ailments or symptoms associated with respiration or the respiratory system.
Urogenital	Conditions relating to or affecting the organs or functions of excretion and reproduction.

A summary of all adverse events is shown in ***Table 11***. There were a total of 226 AEs in the Training group, 507 AEs in the PCM group, and 484 AEs in the ACDF group.

Table 11: Summary of Adverse Events
(Safety Population)

Category	Counts	Training (N=75)	PCM (N=214)	ACDF (N=190)	P-Value*
All Adverse Events (AEs)	Patients (%)	59 (79%)	180 (84%)	163 (86%)	0.678
	Events (E/pt)	226 (3.0)	507 (2.4)	484 (2.6)	
Implant-Related AEs	Patients (%)	26 (35%)	29 (14%)	44 (23%)	0.014
	Events (E/pt)	35 (0.5)	33 (0.2)	54 (0.3)	
Surgery-Related AEs	Patients (%)	23 (31%)	59 (28%)	67 (35%)	0.107
	Events (E/pt)	35 (0.5)	79 (0.4)	97 (0.5)	
Serious Adverse Events (SAEs)	Patients (%)	23 (31%)	68 (32%)	57 (30%)	0.747
	Events (E/pt)	51 (0.7)	95 (0.4)	86 (0.5)	
AEs within 48 Hours of Surgery	Patients (%)	12 (16%)	31 (14%)	26 (14%)	0.887
	Events	15 (0.2)	32 (0.2)	35 (0.2)	
Device Failures (Revision, Reoperation, Removal, or Supplemental Fixation)	Patients (%)	9 (12%)	16 (7%)	14 (7%)	1.000
	Events (E/pt)	11 (0.1)	16 (0.1)	14 (0.1)	

Note: 1. Adverse Events (AEs) based on cumulative AE database as of September 2011.
2. Percentages and events/patients are based on total number of patients for each treatment group.
* Comparing PCM and ACDF based on Fisher's exact test (two-sided). P-values are not adjusted for multiplicity. They are included to help clinical interpretation, without defining statistical significance.

Adverse Events Listing

Table 12 lists the adverse events by category for the All PCM group (Training and PCM) and the ACDF group.

Adverse events that occurred in greater than 5% of the patients in the PCM group included Implant-Related Spinal Event (5.1%), Surgery-Related Dysphagia/Dysphonia (6.5%), Surgery-Related Incision Site (5.6%), Surgery-Related Neck/Arm Pain (9.8%), Surgery-Related Neurologic (5.6%), Systemic Gastrointestinal (5.6%), Systemic Infection (7.0%), Musculoskeletal Trauma (19.6%), Musculoskeletal Back/Leg Pain (16.8%), Musculoskeletal Other (13.6%), Musculoskeletal Spinal Event (15.0%), Musculoskeletal Neurologic (5.6%), and Systemic Other (19.6%).

Adverse events that occurred in greater than 5% of the patients in the ACDF group included Implant-Related Adjacent Level Disease (14.2%), Implant-Related Non-Union (5.8%), Surgery-Related Dysphagia/Dysphonia (12.1%), Surgery-Related Neck Arm Pain (16.8%), Surgery-Related Neurologic (5.3%), Systemic Infection (6.3%), Musculoskeletal Trauma (16.8%), Musculoskeletal Back/Leg Pain (17.4%), Musculoskeletal Neck/Arm Pain (35.8%), Musculoskeletal Other (8.9%), Musculoskeletal Spinal Event (11.6%), Musculoskeletal Neurologic (14.2%), and Systemic Other (13.7%).

Table 12: All Adverse Events (Safety Population)

Adverse Event	Intraop (0 - 2 Days)		Periop (>2 Days -6 Wks.)		Short Term (>6 Wks. - 12 Mon.)		Long Term (>12 - 24 Mon.)		Longer Term (>24 Mon.)		All PCM (N=289)		ACDF (N=190)	
	All PCM	ACDF	All PCM	ACDF	All PCM	ACDF	All PCM	ACDF	All PCM	ACDF	Pts (%)	Events (E/Pt)	Pts (%)	Events (E/Pt)
All Adverse Events	**47**	**35**	**78**	**40**	**182**	**120**	**179**	**138**	**247**	**151**	**239 (82.7%)**	**733 (2.54)**	**163 (85.8%)**	**484 (2.55)**
Implant Related - Adjacent Level Disease	0	0	0	0	4	5	2	17	3	7	9 (3.1%)	9 (0.03)	27 (14.2%)	29 (0.15)
Implant Related - Implant Displacement/Loosening	0	0	2	0	8	1	6	0	6	0	22 (7.6%)	22 (0.08)	1 (0.5%)	1 (0.01)
Implant Related - Malpositioned Implant	0	0	0	0	0	0	1	0	0	0	1 (0.3%)	1 (<0.01)	0 (0.0%)	0 (0.00)
Implant Related - Neck/Arm Pain	0	0	0	0	0	0	0	0	0	1	0 (0.0%)	0 (0.00)	1 (0.5%)	1 (0.01)
Implant Related - Non-union	0	0	0	0	0	2	0	8	0	2	0 (0.0%)	0 (0.00)	11 (5.8%)	12 (0.06)
Implant Related - Other	0	0	0	0	0	1	0	0	1	0	1 (0.3%)	1 (<0.01)	1 (0.5%)	1 (0.01)
Implant Related - Radiolucency	0	0	0	0	5	0	4	2	0	1	9 (3.1%)	9 (0.03)	3 (1.6%)	3 (0.02)
Implant Related - Spinal Event	1	0	1	0	3	0	9	2	7	2	20 (6.9%)	21 (0.07)	4 (2.1%)	4 (0.02)
Implant Related - Subsidence	0	0	1	1	1	1	0	0	1	0	3 (1.0%)	3 (0.01)	2 (1.1%)	2 (0.01)
Implant Related - Trauma	0	0	0	0	0	1	1	0	1	0	2 (0.7%)	2 (0.01)	1 (0.5%)	1 (0.01)
Surgery Related - Dysphagia/Dysphonia	5	10	8	1	5	8	3	3	3	6	22 (7.6%)	24 (0.08)	23 (12.1%)	28 (0.15)
Surgery Related - Gastrointestinal	2	2	1	0	0	0	0	0	0	0	3 (1.0%)	3 (0.01)	2 (1.1%)	2 (0.01)
Surgery Related - Incision Site	4	0	7	3	3	0	1	1	0	0	14 (4.8%)	15 (0.05)	4 (2.1%)	4 (0.02)
Surgery Related - Infection	0	0	1	1	0	0	0	0	0	0	1 (0.3%)	1 (<0.01)	1 (0.5%)	1 (0.01)
Surgery Related - Neck/Arm Pain	5	4	11	5	18	14	8	9	5	3	37 (12.8%)	47 (0.16)	32 (16.8%)	35 (0.18)
Surgery Related - Neurologic	2	3	2	2	2	1	6	3	3	1	14 (4.8%)	15 (0.05)	10 (5.3%)	10 (0.05)
Surgery Related - Other	5	3	0	2	0	2	0	0	0	0	5 (1.7%)	5 (0.02)	7 (3.7%)	7 (0.04)
Surgery Related - Respiratory	1	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (<0.01)	0 (0.0%)	0 (0.00)

Adverse Event	Intraop (0 - 2 Days)		Periop (>2 Days -6 Wks.)		Short Term (>6 Wks. - 12 Mon.)		Long Term (>12 - 24 Mon.)		Longer Term (>24 Mon.)		All PCM (N=289)		ACDF (N=190)	
	All PCM	ACDF	All PCM	ACDF	All PCM	ACDF	All PCM	ACDF	All PCM	ACDF	Pts (%)	Events (E/Pt)	Pts (%)	Events (E/Pt)
Surgery Related - Spinal Event	0	1	0	0	1	1	0	4	1	2	2 (0.7%)	2 (0.01)	8 (4.2%)	8 (0.04)
Surgery Related - Urogenital	0	1	0	1	0	0	0	0	0	0	0 (0.0%)	0 (0.00)	2 (1.1%)	2 (0.01)
Surgery Related - Vertebral Fracture	1	0	0	0	0	0	0	0	0	0	1 (0.3%)	1 (<0.01)	0 (0.0%)	0 (0.00)
Systemic - Cardiac Events	3	2	1	1	2	1	3	2	4	0	12 (4.2%)	13 (0.04)	6 (3.2%)	6 (0.03)
Systemic - Dysphagia/Dysphonia	0	0	0	0	2	0	1	4	1	0	3 (1.0%)	4 (0.01)	4 (2.1%)	4 (0.02)
Systemic - Gastrointestinal	2	0	2	1	6	2	5	1	3	2	14 (4.8%)	18 (0.06)	6 (3.2%)	6 (0.03)
Systemic - Infection	0	2	2	2	1	0	4	2	15	8	19 (6.6%)	22 (0.08)	12 (6.3%)	14 (0.07)
Systemic - Mental Disorder	0	1	0	0	1	0	1	2	2	1	4 (1.4%)	4 (0.01)	4 (2.1%)	4 (0.02)
Systemic - Musculoskeletal Trauma	1	0	4	2	15	16	20	12	35	16	59 (20.4%)	75 (0.26)	32 (16.8%)	46 (0.24)
Systemic - Musculoskeletal/Adjacent Level Disease	0	1	0	0	1	0	0	0	1	0	2 (0.7%)	2 (0.01)	1 (0.5%)	1 (0.01)
Systemic - Musculoskeletal/Back/Leg Pain	0	0	1	1	20	7	16	10	25	16	47 (16.3%)	62 (0.21)	33 (17.4%)	34 (0.18)
Systemic - Musculoskeletal/Neck/Arm Pain	1	0	13	9	54	36	35	15	41	36	114 (39.4%)	144 (0.50)	68 (35.8%)	96 (0.51)
Systemic - Musculoskeletal/Other	1	1	4	0	6	4	15	5	23	8	37 (12.8%)	49 (0.17)	17 (8.9%)	18 (0.09)
Systemic - Musculoskeletal/Spinal Event	0	0	1	1	3	4	12	6	21	14	36 (12.5%)	37 (0.13)	22 (11.6%)	25 (0.13)
Systemic - Neurologic	2	0	4	2	6	9	6	11	7	9	23 (8.0%)	25 (0.09)	27 (14.2%)	31 (0.16)
Systemic – Other	7	3	5	4	14	3	15	13	31	12	57 (19.7%)	72 (0.25)	26 (13.7%)	35 (0.18)
Systemic - Other Trauma	3	0	3	1	1	0	1	1	1	0	9 (3.1%)	9 (0.03)	2 (1.1%)	2 (0.01)
Systemic - Respiratory	0	0	2	0	0	0	3	1	1	1	4 (1.4%)	6 (0.02)	2 (1.1%)	2 (0.01)
Systemic - Urogenital	1	1	2	0	0	1	1	4	5	3	7 (2.4%)	9 (0.03)	8 (4.2%)	9 (0.05)

Note: Adverse Events (AEs) based on cumulative AE database as of September 2011.

The cumulative number and incidence rates for each adverse event category were compared between the PCM and ACDF groups in ***Table 13*** which also reports unadjusted p-values (two-sided). As a result of multiplicity, caution should be used when making statistical inferences regarding difference in incidence rates.

Adverse events that occurred in greater than 5% of the patients in the PCM group included Implant-Related Spinal Event (5.1%), Surgery-Related Dysphagia/Dysphonia (6.5%), Surgery-Related Incision Site (5.6%), Surgery-Related Neck/Arm Pain (9.8%), Surgery-Related Neurologic (5.6%), Systemic Gastrointestinal (5.6%), Systemic Infection (7.0%), Musculoskeletal Trauma (19.6%), Musculoskeletal Back/Leg Pain (16.8%), Musculoskeletal Other (13.6%), Musculoskeletal Spinal Event (15.0%), Musculoskeletal Neurologic (5.6%), and Systemic Other (19.6%).

Adverse events that occurred in greater than 5% of the patients in the ACDF group included Implant-Related Adjacent Level Disease (14.2%), Implant-Related Non-Union (5.8%), Surgery-Related Dysphagia/Dysphonia (12.1%), Surgery-Related Neck Arm Pain (16.8%), Surgery-Related Neurologic (5.3%), Systemic Infection (6.3%), Musculoskeletal Trauma (16.8%), Musculoskeletal Back/Leg Pain (17.4%), Musculoskeletal Neck/Arm Pain (35.8%), Musculoskeletal Other (8.9%), Musculoskeletal Spinal Event (11.6%), Musculoskeletal Neurologic (14.2%), and Systemic Other (13.7%).

Table 13: Comparison of Adverse Events (Safety Population)

Adverse Event	Patients Experiencing Adverse Events (%)		P-Value*
	PCM (N=214)	ACDF (N=190)	
All Adverse Event	**180 (84.1%)**	**163 (85.8%)**	**0.678**
Implant Related - Adjacent Level Disease	5 (2.3%)	27 (14.2%)	< 0.001
Implant Related - Implant Displacement/Loosening	10 (4.7%)	1 (0.5%)	0.012
Implant Related - Neck/Arm Pain	0 (0.0%)	1 (0.5%)	0.470
Implant Related - Non-union	0 (0.0%)	11 (5.8%)	< 0.001
Implant Related - Other	1 (0.5%)	1 (0.5%)	1.000
Implant Related - Radiolucency	3 (1.4%)	3 (1.6%)	1.000
Implant Related - Spinal Event	11 (5.1%)	4 (2.1%)	0.121
Implant Related - Subsidence	1 (0.5%)	2 (1.1%)	0.603
Implant Related - Trauma	1 (0.5%)	1 (0.5%)	1.000
Surgery Related - Dysphagia/Dysphonia	14 (6.5%)	23 (12.1%)	0.059
Surgery Related - Gastrointestinal	2 (0.9%)	2 (1.1%)	1.000
Surgery Related - Incision Site	12 (5.6%)	4 (2.1%)	0.079
Surgery Related - Infection	1 (0.5%)	1 (0.5%)	1.000
Surgery Related - Neck/Arm Pain	21 (9.8%)	32 (16.8%)	0.040
Surgery Related - Neurologic	12 (5.6%)	10 (5.3%)	1.000
Surgery Related - Other	4 (1.9%)	7 (3.7%)	0.361
Surgery Related - Respiratory	1 (0.5%)	0 (0.0%)	1.000
Surgery Related - Spinal Event	2 (0.9%)	8 (4.2%)	0.511
Surgery Related - Urogenital	0 (0.0%)	2 (1.1%)	0.221
Surgery Related - Vertebral Fracture	1 (0.5%)	0 (0.0%)	1.000
Systemic - Cardiac Events	7 (3.3%)	6 (3.2%)	1.000
Systemic - Dysphagia/Dysphonia	2 (0.9%)	4 (2.1%)	0.426
Systemic - Gastrointestinal	12 (5.6%)	6 (3.2%)	0.334
Systemic - Infection	15 (7.0%)	12 (6.3%)	0.844
Systemic - Mental Disorder	2 (0.9%)	4 (2.1%)	0.426
Systemic - Musculoskeletal Trauma	42 (19.6%)	32 (16.8%)	0.520
Systemic - Musculoskeletal/Adjacent Level Disease	2 (0.9%)	1 (0.5%)	1.000
Systemic - Musculoskeletal/Back/Leg Pain	36 (16.8%)	33 (17.4%)	0.895
Systemic - Musculoskeletal/Neck/Arm Pain	87 (40.7%)	68 (35.8%)	0.356
Systemic - Musculoskeletal/Other	29 (13.6%)	17 (8.9%)	0.160
Systemic - Musculoskeletal/Spinal Event	32 (15.0%)	22 (11.6%)	0.380
Systemic - Neurologic	12 (5.6%)	27 (14.2%)	0.004
Systemic – Other	42 (19.6%)	26 (13.7%)	0.143
Systemic - Other Trauma	6 (2.8%)	2 (1.1%)	0.291
Systemic - Respiratory	3 (1.4%)	2 (1.1%)	1.000
Systemic - Urogenital	2 (0.9%)	8 (4.2%)	0.051

Note: Adverse Events (AEs) based on cumulative AE database as of September 2011.

* Comparing PCM and ACDF based on Fisher's exact test (two-sided). P-values are not adjusted for multiplicity. They are included to help clinical interpretation, without defining statistical significance.

Implant Related AEs

Implant-related adverse events are shown in ***Table 14***. Implant-related AEs with an incidence rate greater than 5% were spinal events (5.1%) in the PCM group, and adjacent level disease (14.2%) and non-union (5.8%) in the ACDF group. In addition, implant displacement/loosening occurred at a rate of 4.7% in the PCM group.

Table 14: Implant-Related Adverse Events
(Safety Population)

Adverse Event	Intraop (0 - 2 Days)		Periop (>2 Days - 6 Wks.)		Short Term (>6 Wks. - 12 Mon.)		Long Term (>12 - 24Mon.)		Longer Term (>24 Mon.)		PCM (N=214)	ACDF (N=190)
	PCM	ACDF	PCM	ACDF	PCM	ACDF	PCM	ACDF	PCM	ACDF	Patients (%)	Patients (%)
Implant Related - Adjacent Level Disease	0	0	0	0	2	5	2	17	1	7	5 (2.3%)	27 (14.2%)
Implant Related - Implant Displacement/Loosening	0	0	1	0	3	1	1	0	5	0	10 (4.7%)	1 (0.5%)
Implant Related - Neck/Arm Pain	0	0	0	0	0	0	0	0	0	1	0 (0.0%)	1 (0.5%)
Implant Related - Non-union	0	0	0	0	0	2	0	8	0	2	0 (0.0%)	11 (5.8%)
Implant Related - Other	0	0	0	0	0	1	0	0	1	0	1 (0.5%)	1 (0.5%)
Implant Related - Radiolucency	0	0	0	0	3	0	0	2	0	1	3 (1.4%)	3 (1.6%)
Implant Related - Spinal Event	1	0	0	0	0	0	6	2	5	2	11 (5.1%)	4 (2.1%)
Implant Related - Subsidence	0	0	1	1	0	1	0	0	0	0	1 (0.5%)	2 (1.1%)
Implant Related - Trauma	0	0	0	0	0	1	0	0	1	0	1 (0.5%)	1 (0.5%)

Note: Adverse Events (AEs) based on cumulative AE database as of September 2011.

The cumulative totals of adverse events related to pain are tabulated in ***Table 15***. Over 62% of patients reported at least one AE related to pain in patients with more than one pain AE and in the total number of pain AEs. There were no significant differences between groups except for the "Other" category which included fibromyalgia, myofascial pain syndrome, jaw pain, kidney stones, corneal abrasion, and other miscellaneous non-spine related reports of pain.

Table 15: Summary of Pain Adverse Events
(Safety Population)

Category	TRN (N=75)	PCM (N=214)	ACDF (N=190)	P-Value*
Patients with ≥1 Pain AE	47 (62.7%)	132 (61.7%)	120 (63.2%)	0.837 (a)
Total Number of Pain AEs (AEs/Patient)	104 (1.39)	264 (1.23)	232 (1.22)	0.909 (b)
Pain AEs by Location (AEs/Patient)				
Neck Only	26 (0.35)	64 (0.30)	56 (0.29)	0.937 (b)
Arm Only	29 (0.39)	64 (0.30)	68 (0.36)	0.303 (b)
Neck and Arm	14 (0.19)	35 (0.16)	42 (0.22)	0.188 (b)
Headache	5 (0.07)	12 (0.06)	9 (0.05)	0.702 (b)
Back and/or Lower Extremity	21 (0.28)	69 (0.32)	52 (0.27)	0.372 (b)
Other	9 (0.12)	20 (0.09)	5 (0.03)	0.011 (b)

Note: Adverse Events (AEs) based on cumulative AE database as of September 2011.
* Comparing PCM and ACDF (two-sided): (a) Fisher's exact test; (b) Chi-squared test (rate ratio). P-values are not adjusted for multiplicity. They are included to help clinical interpretation, without defining statistical significance.

The number and relative frequency of adverse events by treatment level is presented in ***Table 16***. These reflect the number of patients who experienced an AE relative to the number of patients treated at that level within each group. There are no statistical differences in the incidence of adverse events between the PCM and ACDF groups at the treated levels.

Table 16: Adverse Events by Level Treated (Patient Counts)
(Safety Population)

Level Treated	Training (N=75)	PCM (N=214)	ACDF (N=190)	P-Value*
C3-4	1 (100%)	0 (0%)	8 (100%)	NA
C4-5	5 (100%)	27 (90%)	16 (89%)	1.000
C5-6	26 (79%)	93 (87%)	84 (84%)	0.561
C6-7	26 (76%)	59 (79%)	55 (86%)	0.376
C7-T1	1 (50%)	1 (50%)	0 (0%)	NA
Total	59 (79%)	180 (84%)	163 (86%)	0.678

Note: 1. Adverse Events (AEs) based on cumulative AE database as of September 2011.
2. Percentages are based on total number of patients treated at the reported level for each treatment group.
* Comparing PCM and ACDF based on Fisher's exact test (two-sided). P-values are not adjusted for multiplicity. They are included to help clinical interpretation, without defining statistical significance.

Secondary Surgical Procedures

As shown in ***Table 17***, there were 11 SSSI events in the Training group, 16 in the PCM group, and 14 in the ACDF group. No significant difference in SSSI rates were observed between the groups. There were 27 secondary surgical procedures performed in the Training and PCM groups. There were 22 device removals (4 with two-level fusions), 4 foraminotomy procedures, and 1 laminoplasty procedure. For the device removal procedures, 13 were removed for pain adverse events (5 for pain alone, 6 for pain associated with device migration, loosening, or subsidence, and 2 for adjacent level disease), 5 for dysphagia associated with migration adverse events, 2 for migration alone, and 2 for unknown causes. The foraminotomy procedures were performed for neck and/or arm pain or adjacent level disease. The laminoplasty procedure was performed for unresolved pain and multi-level spinal stenosis. Two removals for dysphagia occurred early (42 and 44 days postoperatively), and 3 were performed at later timepoints (202, 1,134, and 1,486 days postoperatively).

Table 17: Secondary Surgical Interventions at the Index Level
(Safety Population)

	Intraop (0 - 2 Days)			Periop (>2 Days - 6 Wks.)			Short Term (>6 Wks. - 12 Mon.)			Long Term (>12 - 24 Mon.)			Longer Term (>24 Mon.)			Patients (%)		
	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN (N=75)	PCM (N=214)	ACDF (N=190)
Revision	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 (0%)	0 (0%)	0 (0%)
Removal	0	0	0	1	0	1	2	6	1	2†	2	5	4	5	7	9 (12.0%)	13 (6.1%)	14 (7.4%)
Reoperation	0	0	0	0	0	0	2	1	0	0	2	0	0	0	0	2 (2.7%)	3 (1.4%)	0 (0%)
Supplemental Fixation	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0	0 (0%)	0 (0%)	0 (0%)
Total (Patients)	0	0	0	1	0	1	4	7	1	2†	4	5	4	5	7	9 (12.0%)	16 (7.5%)	14 (7.4%)
Total (Events)	0	0	0	1	0	1	4	7	1	2	4	5	4	5	7	11	16	14

Note: Adverse Events (AEs) based on cumulative AE database as of September 2011.
† The two Training (TRN) patients who had reoperations during the Short Term period had removals during the Long Term period.

Table 18: Secondary Surgical Procedure Details
(Safety Population)

Group	Level	Cause/Adverse Event	Action	Days
PCM Training Group				
TRN	C6-7	Dysphagia, device migration	Removal with ACDF	42
TRN	C5-6	Unresolved pain followed by trauma	Removal with ACDF	152
TRN	C5-6	Dysphagia, device migration	Removal with ACDF	202
TRN	C6-7	Arm and Shoulder Pain	Posterior Foraminotomy	245
TRN	C5-6	Pain/Radiculopathy due to osteophytes	C6 Left Foraminotomy	364
TRN	C6-7	Increased pain, adjacent segment disease, implant loosening	Removal with 2 level ACDF (C5-6)	569
TRN	C5-6	Unresolved pain	Removal with ACDF	696
TRN	C5-6	Trauma followed by pain and migration	Removal with ACDF	801
TRN	C6-7	Unresolved pain, device migration	Removal with ACDF	981
TRN	C6-7	Increased arm pain, adjacent disease	Removal with 2 level fusion (C7-T1), osteophytectomy (C4-5)	876
TRN	C6-7	Unknown	Removal	1092
PCM Investigational Group				
PCM	C6-7	Dysphagia, device migration	Removal with ACDF	44
PCM	C5-6	Migration	Removal with ACDF	56
PCM	C4-5	Neck pain and subsidence	Removal with ACDF	137
PCM	C4-5	Unresolved pain, multi-level stenosis	C3-7 Laminoplasty	147
PCM	C5-6	Neck and shoulder pain	Removal with ACDF	181
PCM	C5-6	Pain, adjacent segment disease, trauma and device migration	Removal with ACDF	225
PCM	C5-6	Increased neck and arm pain	Removal with ACDF	328
PCM	C5-6	Increased neck pain, multi-level stenosis	2 Level Bilateral Neuroforaminotomy & Hemilaminotomy (C6-7)	410
PCM	C6-7	Increased neck pain, adjacent level pseudoarthrosis	2 level Removal with ACDF and Foraminotomy (C5-6)	581
PCM	C5-6	Unknown	Removal	631
PCM	C4-5	Increased neck pain, adjacent disease	Foraminotomy, adjacent TDR (C3-4)	640
PCM	C5-6	Trauma followed by pain and adjacent disease	Removal with 2 level ACDF (C4-5)	938
PCM	C5-6	Trauma followed by pain and migration	Removal with ACDF	1083
PCM	C6-7	Trauma followed by migration and dysphagia	Removal and implant of Prodisc	1134
PCM	C6-7	Device migration	Removal with ACDF	1281
PCM	C5-6	Dysphagia, migration	Removal with ACDF	1486

Note: Adverse Events (AEs) based on cumulative AE database as of September 2011.

Neurological evaluations that consisted of motor strength, sensory, and reflex, were routinely performed as a part of the study's safety assessments. ***Table 19*** presents a summary of neurological status. Patient neurological status was compared to their preoperative status at the 3 Months, 6 Months, 12 Months, and 24 Months, postoperative time points and categorized as neurologically stable or improved. At 24 Months, 90.7% of the patients in the Training group, 94.7% of the patients in the PCM group were determined to be neurological stable or improved compared to 89.5% of the patients in the ACDF group.

Table 19: Neurological Status
(Per Protocol In Window Population)

Month	Status	Training	PCM	ACDF
3	Stable or Improved	47/52 (90.4%)	171/182 (94.0%)	135/150 (90.0%)
6	Stable or Improved	45/52 (86.5%)	175/184 (95.1%)	134/146 (91.8%)
12	Stable or Improved	50/53 (94.3%)	174/185 (94.1%)	131/147 (89.1%)
24	Stable or Improved	49/54 (90.7%)	178/188 (94.7%)	137/153 (89.5%)

Effectiveness Results

Timecourse of Overall Success

The rates of protocol-defined overall success at 6 Months, 12 Months, 24 Months, 36 Months, and 48 Months for the Training, PCM, and ACDF groups are presented in ***Table 20***. For the PCM group, the Overall Success rates ranged from 72.5% to 83.5%. For the ACDF group, the Overall Success rates ranged from 33.1% to 64.9%. Using the FDA's alternate overall success definition, the overall success rates for the PCM group ranged from 70.3% to 78.5%, and for the ACDF group ranged from 31.3% to 60.9%.

Table 20: Time Course of Primary Overall Success Endpoint
(Per Protocol Population)

Overall Success	Group	Months				
		6	12	24	36	48*
Protocol Definition (NDI; ≥20% Improvement)	TRN (N=75)	48/67 (71.6%)	47/65 (72.3%)	38/56 (67.9%)	34/51 (66.7%)	28/46 (60.9%)
	PCM (N=211)	167/200 (83.5%)	155/198 (78.3%)	142/189 (75.1%)	132/182 (72.5%)	114/155 (73.5%)
	ACDF (N=184)	54/163 (33.1%)	84/156 (53.8%)	98/151 (64.9%)	85/136 (62.5%)	71/117 (60.7%)
Alternate Definition (NDI; ≥15-Point Improvement)	TRN (N=75)	47/67 (70.1%)	46/65 (70.8%)	37/56 (66.1%)	33/51 (64.7%)	28/46 (60.9%)
	PCM (N=211)	157/200 (78.5%)	146/198 (73.7%)	136/189 (72.0%)	128/182 (70.3%)	109/155 (70.3%)
	ACDF (N=184)	51/163 (31.3%)	82/156 (52.6%)	92/151 (60.9%)	80/136 (58.8%)	67/117 (57.3%)

* Not all patients completed 48 Months follow-up as of September 2011.

The PCM group had an overall success rate of 75.1% (142/189) compared to 64.9% (98/151) in the ACDF group. The corresponding 90% confidence interval for the difference in success rates is 2.0% to 18.5%. Therefore, at the protocol-specified 12.5% non-inferiority delta, non-inferiority is demonstrated ($p<0.0001$). At the FDA-requested non-inferiority delta of 10.0%, non-inferiority was also demonstrated ($p<0.0001$). All p-values are one-sided.

In addition to the protocol-defined overall success criteria, FDA established an alternate definition of overall success to include improvement in NDI of ≥15-points rather than ≥20% from baseline. Analysis using the alternate-defined endpoint, the PCM group had an overall success rate of 72.0% (136/189) compared to 60.9% (92/151) in the ACDF group. The corresponding 90% confidence interval for the difference in success rates is 2.6% to 19.5%. Therefore, at the protocol-defined 12.5% non-inferiority delta, non-inferiority is demonstrated ($p<0.0001$). At the FDA-requested non-inferiority delta of 10.0%, non-inferiority was also demonstrated ($p<0.0001$). All p-values are one-sided.

The overall success rates by treatment level are provided in ***Table 21***.

Table 21: Primary Overall Success Endpoint at 24 Months by Level Treated (Per Protocol Population with a Primary Endpoint)

Overall Success	Training (N=56)	PCM (N=189)	ACDF (N=151)
Protocol Definition (NDI; ≥20% Improvement)			
C3-4	1/1 (100.0%) [16.8% - 100.0%]	0/0 (0.0%) [NA]	4/6 (66.7%) [29.6% - 90.8%]
C4-5	2/3 (66.7%) [20.2% - 94.4%]	23/30 (76.7%) [58.8% - 88.5%]	8/11 (72.7%) [42.9% - 90.8%]
C5-6	19/27 (70.4%) [51.3% - 84.3%]	67/95 (70.5%) [60.7% - 78.8%]	51/81 (63.0%) [52.1% - 72.7%]
C6-7	16/24 (66.7%) [46.6% - 82.2%]	51/62 (82.2%) [70.8% - 90.0%]	35/53 (66.0%) [52.5% - 77.4%]
C7-T1	0/1 (0.0%) [0.0% - 83.2%]	1/2 (50.0%) [9.4% - 90.5%]	0/0 [NA]
Alternate Definition (NDI; ≥15-Point Improvement)			
C3-C4	1/1 (100.0%) [16.8% - 100.0%]	0/0 (0.0%) [NA]	4/6 (66.7%) [29.6% - 90.8%]
C4-C5	2/3 (66.7%) [20.2% - 94.4%]	21/30 (70%) [52.0% - 83.5%]	8/11 (72.7%) [42.9% - 90.8%]
C5-C6	19/27 (70.4%) [51.3% - 84.3%]	65/95 (68.4%) [58.5% - 76.9%]	48/81 (59.3%) [48.4% - 69.3%]
C6-C7	15/24 (62.5%) [42.6% - 78.9%]	49/62 (79.0%) [67.2% - 87.5%]	32/53 (60.4%) [46.9% - 72.4%]
C7-T1	0/1 (0.0%) [0.0% - 83.2%]	1/2 (50.0%) [9.4% - 90.5%]	0/0 (0.0%) [NA]

Confidence intervals provided under the rates were determined using the Adjusted Wald by Agresti-Coull method.

Radiographic evaluations of motion measurements, angulation and translation (during flexion and extension), at the treated level at the preoperative, 12 Month and 24 Month time points are shown in ***Table 22***.

Table 22: Radiographic Range of Motion for PCM (Per Protocol 24 Months In Window Population)

	Preoperative			12 Months			24 Months		
	TRN (N=56)	PCM (N=189)	ACDF (N=153)	TRN (N=56)	PCM (N=189)	ACDF (N=153)	TRN (N=56)	PCM (N=189)	ACDF (N=153)
n	50	178	142	50	175	138	53	182	151
Range of Motion, mean (SD) degrees	7.9 (4.5)	7.9 (4.7)	7.8 (4.4)	7.2 (4.2)	5.8 (3.9)	0.9 (0.9)	6.6 (4.0)	5.7 (3.9)	0.8 (0.8)
n	49	176	135	48	173	131	51	180	144
Translation, mean (SD) mm	0.8 (0.5)	0.9 (0.6)	0.9 (0.7)	1.3 (1.1)	1.0 (0.7)	0.1 (0.1)	1.2 (1.0)	1.0 (0.8)	0.1 (0.1)

Note: Includes patients who have a valid 24 Month range of motion or translation result.

The average angulation range of motion (flexion-extension arc) for the PCM and ACDF groups at the preoperative, 3 Months, 6 Months, 12 Months and 24 Months visits are illustrated in ***Figure 2***. The mean postoperative ROM for the PCM patients was 5.9° at 12 Months and 5.7° at 24 Months, and the mean ROM for the ACDF patients remained at less than 1°at those time points. With the exception of the preoperative visit, regarding ROM there is a statistical difference between PCM and ACDF at each postoperative visit.

Figure 2: Mean Range of Motion
(Per Protocol 24 Months In Window Population)

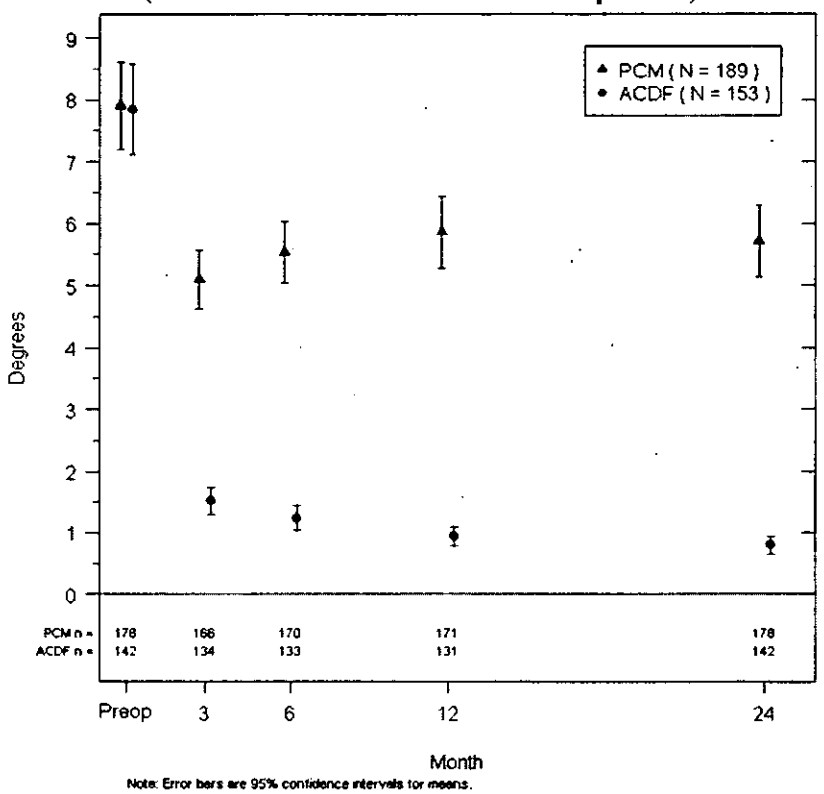
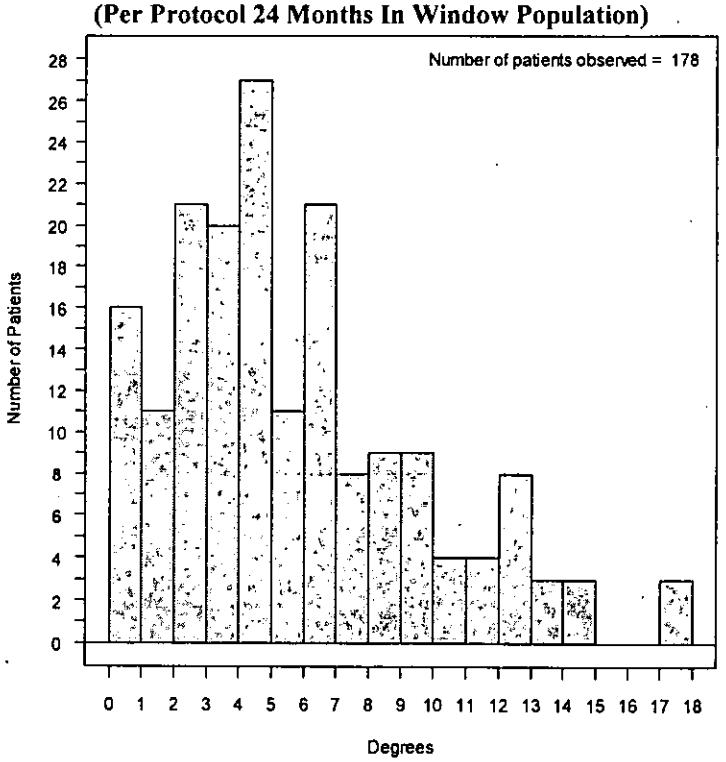


Figure 3: Histogram of Range of Motion at 24 Months for Randomized PCM
(Per Protocol 24 Months In Window Population)



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Radiographic evaluation of disc height of the treated level at the preoperative, 6 Months, 12 Months, and 24 Months time points are shown in ***Table 24*** for all patients. A disc height equal to 80% or more of the height of the adjacent cephalad disc was regarded as "normal." At 24 Months, 96.7% of PCM patients had normal disc height compared to 85.0% of ACDF patients.

Table 23: Radiographic Disc Height
(Per Protocol 24 Months In Window Population)

	Preoperative			6 Months			12 Months			24 Months		
	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN	PCM	ACDF	TRN	PCM	ACDF
Normal Disc Height (≥80% of Superior Level)	65/65 (100%)	190/193 (98.4%)	151/157 (96.2%)	60/60 (100%)	185/188 (98.4%)	129/151 (85.4%)	58/58 (100%)	178/186 (95.7%)	121/144 (84.0%)	49/51 (96.1%)	176/182 (96.7%)	119/140 (85.0%)
No Change in Disc Height (≥80% of Postoperative)	NA	NA	NA	58/59 (98.3%)	178/182 (97.8%)	121/145 (83.4%)	53/57 (93.0%)	168/180 (93.3%)	114/138 (82.6%)	43/50 (86.0%)	160/177 (90.4%)	112/135 (83.0%)

NA = not applicable.

Available radiographs for all treated PCM patients at the 6 Months, 12 Months, 24 Months and later time points were assessed by independent radiographic evaluators for heterotopic ossification (HO) grade, based on the modified McAfee scale (Mehren classification system[13]). Results are shown in ***Table 25***. At 24 Months, 95.7% (223/233) PCM patients had Grades 0, Grade I or Grade II HO, and 4.3% (10/233) PCM patients had Grade III or Grade IV HO.

Table 24: Heterotopic Ossification for PCM
(Per Protocol 24 Months In Window Population)

Month	Grade*	Training (N=56)	PCM (N=189)	All PCM (N=245)
6	n (Observed)	49	175	224
	Grade 0	41 (83.7%)	163 (93.1%)	204 (91.1%)
	Grade I	1 (2.0%)	5 (2.9%)	6 (2.7%)
	Grade II	7 (14.3%)	6 (3.4%)	13 (5.8%)
	Grade III	0 (0.0%)	1 (0.6%)	1 (0.4%)
	Grade IV	0 (0.0%)	0 (0.0%)	0 (0.0%)
12	n (Observed)	50	175	225
	Grade 0	30 (60.0%)	132 (75.4%)	162 (72.0%)
	Grade I	7 (14.0%)	26 (14.9%)	33 (14.7%)
	Grade II	13 (26.0%)	14 (8.0%)	27 (12.0%)
	Grade III	0 (0.0%)	2 (1.1%)	2 (0.9%)
	Grade IV	0 (0.0%)	1 (0.6%)	1 (0.4%)
24	n (Observed)	51	182	233
	Grade 0	28 (54.9%)	113 (62.1%)	141 (60.5%)
	Grade I	5 (9.8%)	29 (15.9%)	34 (14.6%)
	Grade II	16 (31.4%)	32 (17.6%)	48 (20.6%)
	Grade III	1 (2.0%)	6 (3.3%)	7 (3.0%)
	Grade IV	1 (2.0%)	2 (1.1%)	3 (1.3%)

* McAfee *et al., Journal of Spinal Disorders*, 2003.[14]

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Secondary Effectiveness Endpoints
In addition to the components of the primary endpoint presented above, secondary effectiveness variables are provided in ***Table 25***.

Table 25: Secondary Effectiveness Endpoints at 24 Months (Per Protocol 24 Months In Window Population)

Component	PCM (N=189)	ACDF (N=153)
Clinical Endpoints		
Neck Disability Index (≥20% Improvement)	156/187 (83.4%)	123/151 (81.5%)
Neck Disability Index (≥15-Point Improvement)	149/187 (79.7%)	114/151 (75.5%)
VAS Neck Pain (≥20mm Improvement)	139/187 (74.3%)	113/150 (73.3%)
VAS Left Arm Pain (≥20mm Improvement)	107/187 (57.2%)	79/150 (52.7%)
VAS Right Arm Pain (≥20mm Improvement)	89/187 (47.6%)	80/150 (53.3%)
VAS Worst Arm Pain (≥20mm Improvement)	148/187 (79.1%)	113/150 (75.3%)
SF-36 PCS (≥15% Improvement)	133/187 (71.1%)	98/151 (64.9%)
SF-36 MCS (≥15% Improvement)	87/187 (46.5%)	75/151 (49.7%)
Myelopathy (Nuricks; Maintained or Improved)	185/185 (100.0%)	148/153 (96.7%)
Dysphagia Bazaz Score (Maintained or Improved)	164/187 (87.7%)	123/149 (82.6%)
Dysphagia VAS Hoarseness, mean (SD) mm	7.3 (14.3)	10.1 (18.5)
Dysphagia VAS Swallowing, mean (SD) mm	8.8 (16.3)	12.1 (20.1)
Patient Satisfaction VAS, mean (SD) mm	82.8 (27.1)	81.4 (25.7)
Satisfaction (Odom's Criteria)		
Excellent	129/188 (68.6%)	82/153 (53.6%)
Good	43/188 (22.9%)	50/153 (32.7%)
Fair	15/188 (8.0%)	15/153 (9.8%)
Poor	1/188 (0.5%)	6/153 (3.9%)
Radiographic Endpoints		
Range of Motion, mean (SD) degrees	5.7 (3.9)	0.8 (0.8)
Hypermobility†	179/181 (98.9%)	149/149 (100.0%)
Normal Disc Height (≥80% of Superior Level)	176/182 (96.7%)	119/140 (85.0%)
Disc Height Maintenance (≥80% of Postoperative)	160/177 (90.4%)	112/135 (83.0%)
Radiolucency (>50% Length of the Prosthesis or Graft)		
Superior Level	14/182 (7.7%)	0/152 (0.0%)
Inferior Level	0/182 (0.0%)	0/152 (0.0%)
Dynamic Canal Stenosis‡	1/182 (0.5%)	4/144 (2.8%)
Adjacent Level Degeneration§		
Superior	30/175 (17.1%)	35/137 (25.6%)
Inferior	34/147 (23.1%)	35/119 (29.4%)
Either level	59/151 (39.1%)	60/122 (49.2%)

† Reitman *et al.*, *Spine*, 2004.
‡ Baba *et al.*, *Spine*, 1993.
§ Walraevens *et al.*, *European Spine Journal*, 2009.

Conclusions Drawn from the Study Data
The clinical data support the reasonable assurance of safety and effectiveness of the PCM Cervical Disc when used in accordance with the indications for use. The clinical study demonstrated that the PCM was non-inferior to the control treatment. Based on these results, it is reasonable to conclude that the clinical benefits of the use of the PCM Cervical Disc outweigh the potential risks associated with the device and procedure for implantation when used in the indicated population in accordance with the directions for use.

HANDLING OF THE IMPLANT

- Before removing the implants from the package, make sure that the protective packaging is unopened and undamaged. If the packaging is damaged, the implants have to be considered as NON-STERILE and may not be used.
- Upon removal from the package, compare the descriptions on the label with the package contents (product number and size)
- Note the STERILE expiry date. Implants with elapsed STERILE expiry dates have to be considered as non-sterile!
- Take particular care that aseptic integrity is assured during removal of the implant from the inner packaging.
- Open the pouches carefully, beginning from the triangular corner. Take suitable measures to ensure that the implant does not come into contact with objects that could damage its surfaces. Use only the recommended instruments for implantation of the PCM. Damaged implants must not be used.

HOW SUPPLIED

The PCM 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 device from the packaging using aseptic technique, only after the correct size has been determined.

Packages for each of the components should be intact upon receipt. All implant and instrument sets should be carefully examined for completeness, and for lack of damage, prior to use. Damaged packages or products should not be used, and should be returned to NuVasive.

INSTRUMENT CLEANING AND DECONTAMINATION

All instruments must first be thoroughly cleaned using the validated methods described below before sterilization and introduction into a sterile surgical field. Contaminated devices should be wiped clean of visible soil at the point of use, prior to transfer to a central processing unit for cleaning and sterilization. Cleaning instructions for the PCM Cervical Disc System instruments are as follows:

1. Prior to soaking the instruments, rinse the instruments under running tap water and wipe off all visible residual soil or debris. Ensure to flush out any lumens, cracks or crevices while rinsing.
2. Prepare an enzymatic cleaning solution, such as Enzol®, per manufacturer's recommendations. Place the instruments in the solution in the open position (as appropriate for the specific instrument) and allow to soak for a minimum of 5 minutes. While soaking, actuate the instruments through a full range of motion (as appropriate for the specific instrument) to allow complete penetration of the cleaning solution.
3. After the 5 minute soak time, remove the instruments and wipe all visible soil or debris. Then, place the instruments into a fresh batch of an enzymatic cleaning solution, and using a soft bristled brush, brush the entire instrument. As appropriate for the specific instrument, actuate the instruments while brushing to ensure hard to reach areas are reached. Use a syringe and lumen brush to clean hard to reach areas.
4. Remove the instruments from the detergent and rinse by agitating and actuating in RO/DI water for a minimum of 30 seconds. Flush all hard to reach areas with a sterile syringe.
5. Prepare a detergent solution, such as Renu-Klenz®, per manufacturer's recommendations (1oz/gal) in a sonication unit. Allow the devices to sonicate for 10 minutes.
6. Remove the devices from the detergent and rinse by agitating in RO/DI water for a minimum of 30 seconds. Actuate through a full range of motion while rinsing and flush hard to reach areas.
7. Transfer the instruments into the washer for processing. Below is the validated and recommended cycle:

Phase	Recirculation Time	Water Temperature	Detergent Type & Concentration *(if applicable)*
Pre-wash	1 minute	Cold Tap Water	N/A
Enzyme Wash	1 minute	Hot Tap Water	EnzyCare2®, ¼ oz/gallon
Wash	2 minutes	65.5°C (set point)	Renu-Klenz®, ¼ oz/gallon
Rinse	1 minute	RO/DI Water	N/A
Drying	7 minutes	115°C	N/A

8. Using a clean soft towel, dry the instruments.

Note: Certain cleaning solutions such as those containing bleach or formalin may damage some devices and must not be used. Visually inspect the instruments following performance of the cleaning instructions prescribed above. Ensure there is no visual contamination of the instruments prior to proceeding with sterilization. If possible contamination is present at visual inspection, repeat the cleaning steps above. Otherwise, contact your NuVasive representative – contaminated instruments should not be used, and should be returned to NuVasive.

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INSTRUMENT STERILIZATION

All instruments are provided non-sterile and must be sterilized prior to use. All components of the instruments are sterilizable by steam autoclave using standard hospital practices. Devices are to be packaged in a FDA-cleared sterilization wrap prior to placement in an autoclave. In a properly functioning and calibrated steam sterilizer, effective sterilization may be achieved using the following parameters:

Method:	Steam
Cycle:	Prevacuum
Temperature:	270°F (132°C)
Exposure Time:	4 minutes
Dry Time:	30 minutes

Always sterilize the devices in the disassembled, open, unlocked position, and avoid sudden cooling of the components.

Ensure that all functions are unimpaired before use. In addition, periodically inspect the instruments for wear and tear, such as corrosion or discoloration. For instruments that are no longer functional, or exhibit excessive wear and tear, please return instruments to NuVasive.

PATIENT INFORMATION

The surgeon should advise the patient of the following:

- Use a soft collar at the discretion of the surgeon. The neck may be moved through a comfortable range of motion when the patient is fully awake.
- Should pre-operative symptoms fail to improve or worsen or new symptoms develop the surgeon should be promptly notified.
- Placement of the implant does not prevent future surgical arthrodesis at the treated level should it become necessary.
- To identify complications as early as possible, the condition of the cervical disc is to be checked periodically by suitable measures.

CONFORMANCE TO STANDARDS

The materials used to construct the PCM Disc are manufactured in conformance to international standards. Specifically, the CoCrMo Alloy is manufactured according to ISO 5832-4 / ASTM F-75 or ISO 5832-12; the UHMWPE is manufactured according to ISO 5834-2 / ASTM F648; the Calcium phosphate is manufactured according to ASTM F1609; and the Unalloyed Titanium is manufactured according to ISO 5832-2/ ASTM F67.

PRODUCT COMPLAINTS

Complaints of any nature may be reported to NuVasive at 800- 475-9131 or to customerservice@nuvasive.com. When reporting the complaint, please provide the component names or catalog number, with lot or serial number, and your name and contact address. A brief description of the complaint should be provided.

DEVICE RETRIEVAL EFFORTS

Should it be necessary to remove a PCM Cervical Disc, please call NuVasive prior to the scheduled surgery for product/tissue retrieval information. Also refer to the Surgical Technique Manual for instructions on removal. All explanted PCM Discs must be returned to NuVasive for analysis.

INFORMATION

To obtain a Surgical Technique Manual or should any information regarding the products or their uses be required, please contact your local representative or NuVasive directly at 800-475-9131. You may also email: customerservice@nuvasive.com.

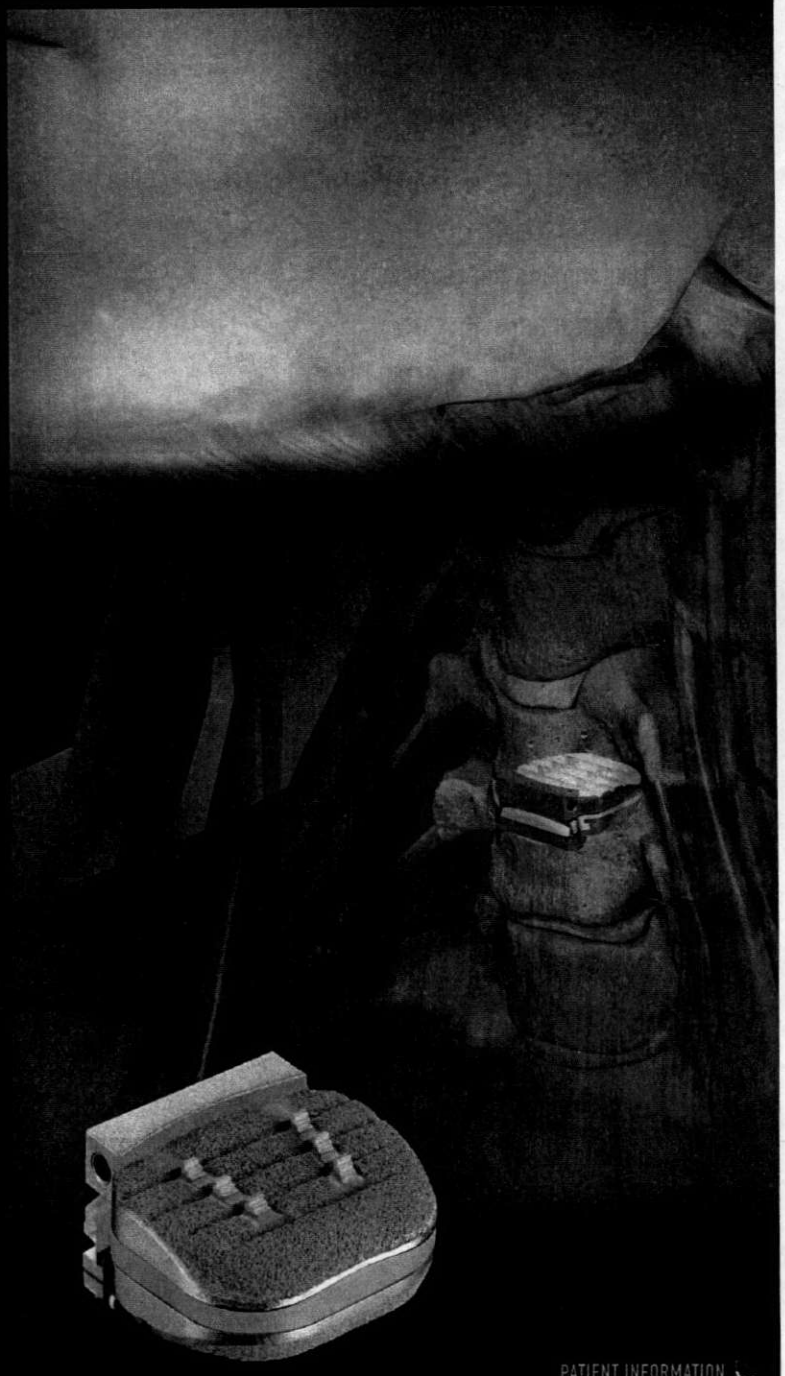
PCM

THE CERVICAL DISC SYSTEM

NUVASIVE

Speed of Innovation

Motion Preservation for the Cervical Spine



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PATIENT INFORMATION

PCM
THE CERVICAL DISC SYSTEM

Table of Contents

Please refer to glossary in the front of this brochure for important key terms

Glossary

Abscess: a localized collection of pus surrounded by inflamed tissue.

Ankylosing spondylitis: rheumatoid arthritis of the spine.

Anterior: situated toward the front of the body.

Anterior cervical discectomy and fusion (ACDF): surgery from the front of the neck that often successfully addresses spinal symptoms; consists of removing the damaged disc and then growing bone between the vertebrae above and below; may be performed either with or without the use of a device, such as a plate, to serve as an internal brace on the front of the spine until fusion occurs.

Arachnoiditis: an inflammation of the arachnoid membrane (thin membrane of the brain and spinal cord).

Arthritis: a form of joint disorder that involves inflammation of one or more joints.

Autoimmune disease: a condition when your immune system attacks healthy cells in your body by mistake.

Bone resorption: loss of bone.

Bursitis: inflammation of a bursa (a small fluid sac between a tendon and a bone).

Cellulitis: a diffuse and especially subcutaneous (under the skin) inflammation of connective tissue.

Cerebrospinal fistula: an abnormal passage that leads from the spinal canal to another area of the body allowing for cerebrospinal fluid to leak out.

Congenital: existing at or dating from birth.

Diabetes mellitus: a condition in which the pancreas no longer produces enough insulin or cells stop responding to the insulin that is produced, so that glucose in the blood cannot be absorbed into the cells of the body.

Disc herniation: a protrusion of the disc's internal material (nucleus pulposus) through the outer membrane (annulus fibrosis).

Discectomy: the surgical removal of an intervertebral disk.

Discitis: an infection in the intervertebral disc space.

Dural tear: damage to the dura mater, which is the tough fibrous membrane that envelops the spinal cord.

Dysphagia: difficulty in swallowing.

Dysphonia: defective use of the voice.

Edema: an abnormal excess accumulation of fluid in connective tissue.

Embolism: the sudden obstruction of a blood vessel by an abnormal particle (e.g., air bubble) circulating in the blood.

Esophageal: of or pertaining to the esophagus (muscular membranous tube for passage of food and liquid from your mouth to the stomach).

Facet joint: a small stabilizing joint located between and behind adjacent vertebrae.

Fistula: abnormal connection between an artery and a vein.

Hematoma: a mass of usually clotted blood that forms in a tissue, organ, or body space as a result of a broken blood vessel.

Hemorrhage: a copious discharge of blood from the blood vessels.

Heterotopic ossification: bone formation at an abnormal anatomical site.

Hypertension: higher than normal blood pressure.

Ischemia: a deficient supply of blood to a body part (e.g., heart or brain) that is due to obstruction of the inflow of arterial blood (as by the narrowing of arteries by spasm or disease).

Laminoforaminotomy: a posterior approach to removing bone or disc material causing stenosis.

Laryngeal palsy: an uncontrollable tremor or quivering of the larynx, which is the upper part of the respiratory passage.

Lupus: a chronic inflammatory disease that is caused by autoimmunity.

Malignancy: a tumor that is malignant (cancerous), that can invade and destroy nearby tissue, and that may spread to other parts of the body.

Metabolic bone disease: abnormalities of bones caused by a broad spectrum of disorders.

Metallosis: an infectious and often inflammatory disease of bone that occurs around metal implants as a result of corrosion or hypersensitivity reaction.

Migration: movement of an implant from its original position.

Morbid obesity: the condition of weighing two or more times the ideal weight, so called because it is associated with many serious and life-threatening disorders.

Myelopathy: a disease or disorder of the spinal cord.

Osteopenia: a condition characterized by a decrease in bone mass with decreased density that may develop into osteoporosis.

Osteoporosis: a condition characterized by a greater decrease in bone mass with decreased density and enlargement of bone spaces producing porosity and brittleness.

Paget's disease: a chronic disease of bones characterized by their great enlargement and rarefaction with bowing of the long bones and deformation of the flat bones–also called osteitis deformans or osteodystrophia deformans.

Paralysis: loss of voluntary movement as a result of damage to nerve or muscle function.

Pathology: a diseased condition.

Pharyngeal: relating to the throat.

Radicular symptoms or pain: relating to or involving a nerve root.

Radiculopathy: any pathological condition of the nerve roots.

Introduction

Rheumatoid arthritis: a usually chronic disease that is considered an autoimmune disease and is characterized by pain, stiffness, inflammation, swelling, and sometimes destruction of joints.

Spinal (or intervertebral) disc: a tough elastic disc that is interposed between adjoining vertebrae and that consist of an outer annulus fibrosus enclosing an inner nucleus pulposus.

Spinal fusion: the surgical immobilization of a joint so that the bones grow solidly together.

Spinal stenosis: a narrowing or constriction of the spinal canal causing myelopathic or radicular symptoms.

Spondylolysis: the disintegration or dissolution of a vertebra.

Thromboembolism: the blocking of a blood vessel by a particle that has broken away from a blood clot at its site of formation.

Thrombophlebitis: the inflammation of a vein with formation of a thrombus (blood clot).

Thrombosis: the formation or presence of a blood clot within a blood vessel.

Trachea: a thin-walled, cartilaginous tube descending from the larynx (vocal cords) to the lungs. Also called windpipe.

Vertebrae (or vertebral body): one of the square-shaped bones that make up the spinal column, separated one from another by the intervertebral discs; there are seven cervical vertebrae (C1-C7), twelve thoracic vertebrae (T1-T12), and five lumbar vertebrae (L1-L5).

Your doctor has recommended that you consider surgery to address your arm pain, weakness, or discomfort using the PCM® Cervical Disc. This patient information brochure is intended to help you understand your treatment options for your neck pain and related problems. This brochure will also provide background about cervical spine (neck) surgery and the PCM Cervical Disc in general. This brochure is not intended to replace professional medical care or provide medical advice.

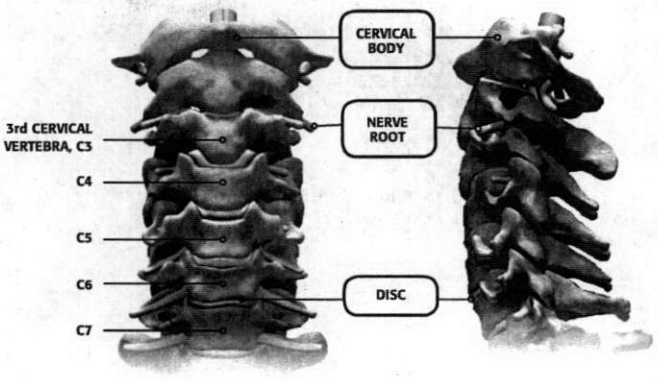
You should always explore all options and ask questions in order to make an informed decision if this surgery is right for you. Please consult your doctor who is the only one qualified to diagnose and treat your spinal condition. As with any surgical procedure, you should find a doctor who is experienced in performing the specific surgery you are considering.

PCM
THE CERVICAL DISC SYSTEM

About the Cervical Spine and Cervical Disc Degeneration

THE CERVICAL SPINE

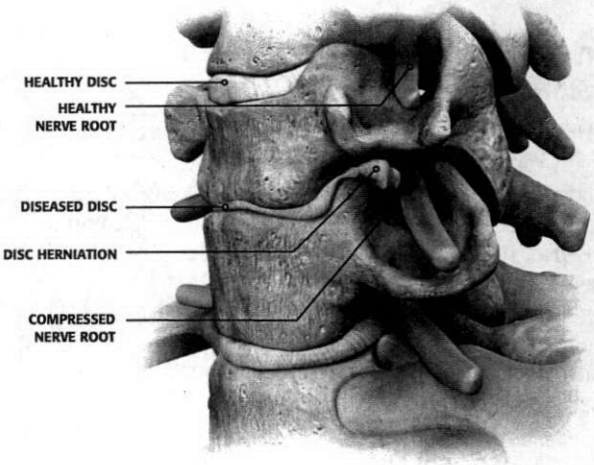
The cervical spine is the section of your spine located in your neck. The cervical spine is composed of seven bones, called vertebrae, which are stacked up to create a column. Each of these vertebrae is numbered C1 to C7. There is a disc between each vertebra that acts as a shock absorber. The disc has a thick outer layer and a soft gel-like center. There are also two smaller joints on each side connecting these vertebrae called facet joints. Motion naturally happens between the vertebrae and involves movement between each bone, compression of the disc, and sliding of the facet joints. The normal motion of the cervical spine is: flexion-extension (bending the head backward and forward), lateral bending (bending the head from side to side) and rotation (turning your neck). The cervical spine also contains a pathway for the spinal cord which contains nerves that carry signals from your brain to your body. These nerves pass from the spinal cord out to the body through holes in the side of the spinal column.



FRONT AND SIDE VIEWS OF THE CERVICAL SPINE

DEGENERATION OF THE CERVICAL DISC

Degeneration of the cervical disc occurs as we age. Injury, daily wear and tear, and genetics can also contribute to this process. Degeneration consists of damage to the cervical disc, which may then become narrowed or may herniate. This causes the symptoms of pain, numbness, tingling, and/or weakness in the arms or shoulders, and may also cause neck pain. The available treatments are directed at these symptoms and do not represent a cure for the degenerative process.



ALTERNATIVE NON-OPERATIVE TREATMENT OPTIONS

You have been assessed for treatment of pain and other symptoms of cervical disc degeneration or disc herniation. Some of the non-operative options to treat your symptoms are rest, heat, electrotherapy, physical therapy, injections, bracing, pain management modalities, and pain medicine. You should talk to your doctor about your options. Because your symptoms did not improve with other methods, your doctor has suggested spinal surgery.

CERVICAL SPINE SURGERY

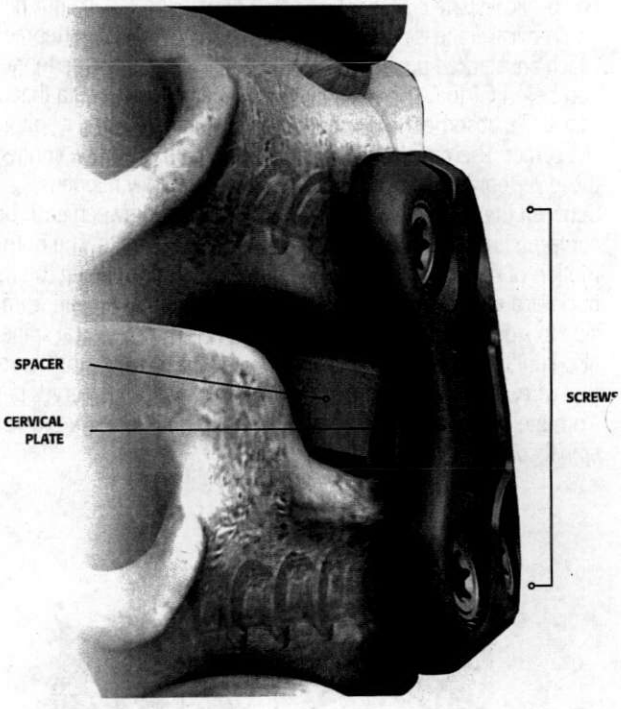
Cervical spine surgery for pain and other symptoms of cervical disc degeneration or herniation begins by making an incision in the neck, once anesthesia has been administered. During surgery, the surgeon will access the cervical spine from the front of your neck, and will remove the damaged disc and any tissue that is compressing the spinal cord and/or nerves. After removing the disc, the surgeon will implant a device to help stabilize the joint. Anterior cervical discectomy and fusion (ACDF) and cervical disc replacement procedures are comparable in their surgical approach and length of surgery time.

ANTERIOR CERVICAL DISCECTOMY AND FUSION (ACDF) SURGERY

ACDF is the current standard of care for cervical disc disease. Fusion surgery consists of removing the damaged disc. After the disc is removed, bone graft (bone taken from another area) or a synthetic spacer is placed into the disc space and a cervical plate with screws is used for stabilization. The goal of this procedure is to permanently fuse two or more vertebrae together so they do not move except as a single unit. This procedure may alleviate the pain and other symptoms of cervical disc disease. While an ACDF usually relieves pain and other symptoms, it does result in loss of motion in the fused joints.

CERVICAL DISC REPLACEMENT SURGERY

An alternative procedure to an ACDF is a cervical disc replacement surgery, which aims to stabilize the spine while still allowing motion to occur at the joint instead of fusing the vertebrae together. For that reason, artificial cervical disc replacement devices such as the PCM Cervical Disc have been developed.



TRADITIONAL CERVICAL SPINE FUSION PROCEDURE AT ONE LEVEL WITH STABILIZING PLATE

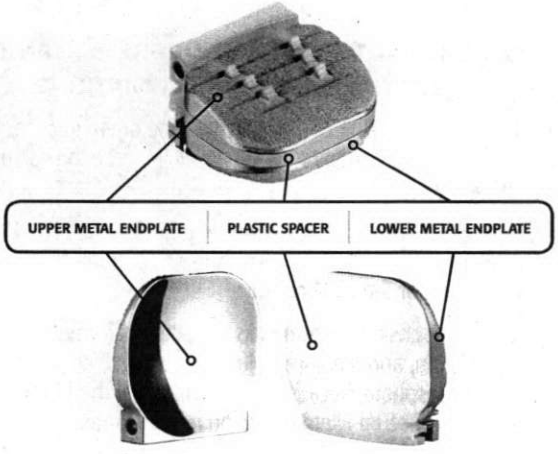
PCM
THE CERVICAL DISC SYSTEM

PCM® Cervical Disc System

THE PCM® CERVICAL DISC

PRODUCT INFORMATION

The PCM Cervical Disc is designed to replace the diseased disc, providing support for the vertebrae while allowing for movement of the joint. The PCM Cervical Disc consists of the following parts: an upper metal (cobalt chromium molybdenum alloy) endplate, and a lower metal endplate to which a plastic (polyethylene) spacer is attached. These materials are the same as the ones used for most spinal and orthopedic devices. Several device sizes are available to best fit the disc space.



COMPONENTS OF THE PCM CERVICAL DISC

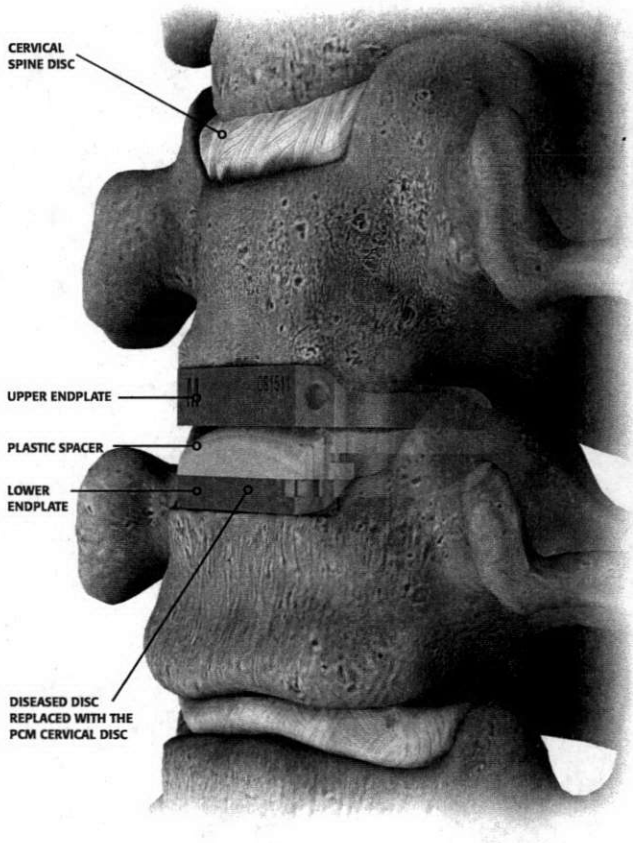
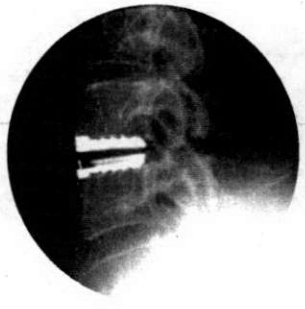


ILLUSTRATION OF THE IMPLANTED PCM CERVICAL DISC

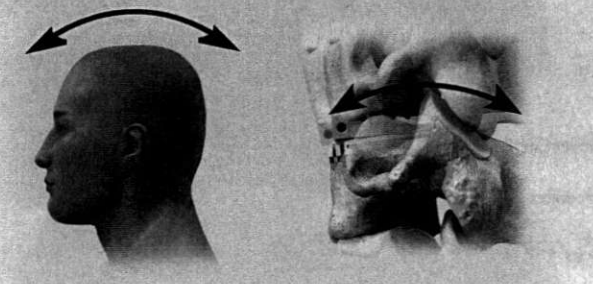


X-RAY IMAGE OF THE IMPLANTED PCM CERVICAL DISC

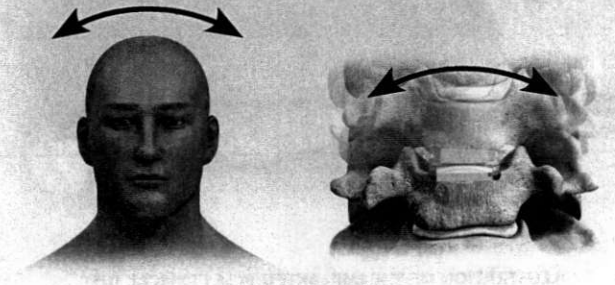
PCM® Cervical Disc System

MOTION WITH THE PCM® CERVICAL DISC

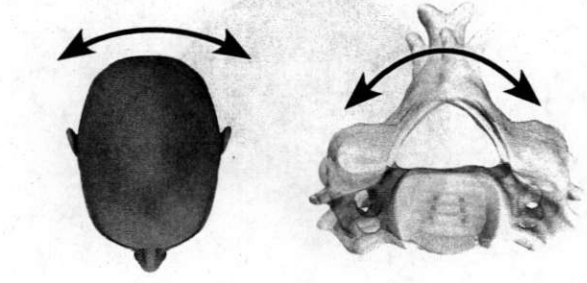
The PCM Cervical Disc may allow patients to preserve all aspects of motion at the level of surgery, including flexion-extension (nodding up or down), lateral bending (side-to-side bending), and axial rotation (turning your neck).



FLEXION-EXTENSION



LATERAL BENDING



AXIAL ROTATION

INDICATIONS:

The PCM® Cervical Disc is indicated for use in skeletally mature patients for reconstruction of a degenerated cervical disc at one level from C3-C4 to C6-C7 following single-level discectomy for intractable radiculopathy (arm pain and/or a neurological deficit), with or without neck pain, or myelopathy due to a single-level abnormality localized to the disc space and manifested by at least one of the following conditions confirmed by radiographic imaging (CT, MRI, x-rays): herniated nucleus pulposus, spondylosis (defined by the presence of osteophytes), and/or visible loss of disc height as compared to adjacent levels. The PCM Cervical Disc is implanted using an anterior approach. Patients should have failed at least 6 weeks of conservative treatment prior to implantation of the PCM Cervical Disc.

THE PCM CERVICAL DISC SHOULD NOT BE IMPLANTED IN PATIENTS WITH THE FOLLOWING CONDITIONS:

- Active infection of the whole body or the operating site, because any pre-existing infection will increase the risk of infecting the PCM Cervical Disc device
- Osteoporosis or osteopenia of the bone, because weak or thinning bone could increase the risk of bone fracture or loosening of the PCM device
- Allergies or sensitivities to metals (cobalt, chromium, molybdenum, and titanium), plastics (polyethylene), or calcium phosphate, because these make up the PCM device and could cause an allergic reaction if implanted
- Congenital stenosis, a condition of narrowing of the spinal canal since birth

It is extremely important that you let your doctor know about any medications you are taking, any allergies you have, if you are pregnant, or if you have any other illnesses or medical conditions that may help your doctor decide if the PCM Cervical Disc is the right choice for you.

PCM® Cervical Disc System

WARNINGS AND PRECAUTIONS

The clinical study was limited to patients that met certain criteria, therefore the safety and effectiveness of the PCM® device has not been established in patients with the following conditions:

- Intractable radiculopathy or myelopathy due to disease at more than one level or disease outside of the disc space;
- Marked cervical instability as determined by your doctor;
- Significant cervical anatomical deformity or clinically compromised vertebral bodies at the affected level due to current or past trauma or disease;
- Those under the age of 21 or over the age of 65;
- More than one immobile vertebral level;
- Severe spondylosis as determined by your doctor;
- Patients whose bones are still growing;
- Previous spine surgery at the level to be treated;
- Symptoms attributed to more than one vertebral level;
- Neck pain alone;
- Neck or arm pain of unknown origin;
- Severe facet joint arthritis of the level of spine for which surgery is planned;
- Paget's disease, osteomalacia, or other metabolic bone disease;
- Cancer;
- Those taking medications known to potentially interfere with bone or soft tissue healing (e.g., steroids);
- Diabetes mellitus;
- Systemic disease including AIDS, HIV, and hepatitis;
- Auto-immune disorders that impact the musculoskeletal system such as lupus, rheumatoid arthritis, or ankylosing spondylitis;
- Neuromuscular disorders such as muscular dystrophy (progressive loss of muscle), spinal muscular atrophy (decreased muscle), amyotrophic lateral sclerosis (Lou Gehrig's disease);
- Morbid obesity;
- Pregnancy;
- Mental illness and substance abuse;
- Prior fusion at an adjacent vertebral level. Similar to the experience in the ACDF control group, the use of the PCM Cervical Disc at a spinal level adjacent to a previous fusion may lead to clinical outcomes inferior to those observed for patients without a prior adjacent level fusion. For the PCM device, these include, but are not limited to, possible implant migration and a higher incidence of subsequent device removal.

MAGNETIC RESONANCE IMAGING (MRI) SAFETY:

The PCM Cervical Disc System has not been evaluated for safety and compatibility in the MRI environment. The PCM Cervical Disc System has not been tested for heating or migration in the MRI environment.

RISKS

As with any surgery, there are some possible serious risks that can occur when receiving the PCM® Cervical Disc. Potential risks associated with the use of the PCM Cervical Disc 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 PCM Cervical Disc. However, the causality of these adverse events is not exclusive to these categories. Some of the following effects were observed in the clinical study.

- **Risks associated with any surgical procedure are those such as:** Abscess (localized collection of pus surrounded by inflamed tissue); cellulitis (a diffuse and especially subcutaneous inflammation of connective tissue); wound dehiscence (wound breaks open along surgical suture); wound necrosis (wound contains dead tissue); edema (abnormal excess accumulation of fluid in connective tissue); hematoma (a mass of usually clotted blood that forms in a tissue, organ, or body space as a result of a broken blood vessel); heart and vascular complications; hypertension (higher than normal blood pressure); thrombosis (formation or presence of blood clot within a blood vessel); ischemia (a deficient supply of blood to a body part due to obstruction of inflow of arterial blood); embolism (sudden obstruction of a blood vessel by abnormal particle (e.g., air bubble) circulating in the blood); thromboembolism (the blocking of a blood vessel by a particle that has broken away from a blood clot at its site of formation); hemorrhage (a copious discharge

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RISKS CONTINUED

of blood from the blood vessels); thrombophlebitis (the inflammation of a vein with formation of a thrombus); adverse reactions to anesthesia; pulmonary complications (pertaining to the lung); organ, nerve or muscular damage; gastrointestinal compromise; seizure, convulsion, or changes to mental status; and complications of pregnancy including miscarriage and fetal birth defects.

- **Risks associated with anterior interbody surgery of the cervical spine include:** Dysphagia (difficulty swallowing); dysphonia (defective use of the voice); hoarseness; vocal cord paralysis; laryngeal palsy (an uncontrollable tremor or quivering of the larynx, which is the upper part of the respiratory passage); sore throat; recurring aspirations; nerve deficits or damage; tracheal, esophageal and pharyngeal perforation; airway obstruction; external chylorrhea (flow or discharge of chyle (fluid consisting of lymph and emulsified fat); warmth or tingling in the extremities; deficit or damage to the spinal cord, nerve roots, or nerves possibly resulting in paralysis or pain; dural (membrane that envelops spinal cord) tears or leaking; cerebrospinal fistula (an abnormal passage that leads from the spinal canal to another area of the body allowing for cerebrospinal fluid to leak out); discitis (an infection in the intervertebral disc space), arachnoiditis (an inflammation of the arachnoid membrane, a thin membrane of the brain and spinal cord), 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 (a narrowing or constriction of the spinal canal causing myelopathic (spinal) or radicular (nerve) symptoms); spondylolysis (the disintegration or dissolution of a vertebra); otitis media (an acute or chronic inflammation of the middle ear); fistula (abnormal connection between an artery and a vein); vascular damage and/or rupture; and headache.
- **Risks associated with implants in the spine, including the PCM Cervical Disc device:** 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 (implant is no longer secured properly to bone); 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 (an infectious and often inflammatory disease of bone that occurs around metal implants as a result of corrosion or hypersensitivity reaction), and/or scarring; possible tissue reaction; bone resorption (loss of bone); bone formation (heterotopic ossification) that may reduce spinal motion or result in a fusion, either at the treated level or at adjacent levels; development of new radiculopathy (any pathological condition of the nerve roots); myelopathy (a disease or disorder of the spinal cord) 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.
- **Wound, local and/or systemic infections**
- **Surgical instrument bending or breakage, as well as the possibility of a fragment of a broken instrument remaining in the patient**
- **Inability to resume activities of normal daily living**
- **Death**

It is also possible that the surgery will not reduce or relieve your symptoms, and that treatment may not result in therapeutic or direct health benefits or may cause worsening of preoperative symptoms. Promptly notify your surgeon if the preoperative symptoms fail to improve or worsen, or new symptoms develop. This cannot be predicted for either the PCM implant or fusion surgery. If the implant does not relieve symptoms or if there is a problem with the device, it is usually possible to have it removed. This would require another surgery.

POTENTIAL ADVERSE EFFECTS

In the U.S. clinical study of 214 patients who received the PCM® Cervical Disc, the most commonly reported device or surgery related adverse events included neck and arm pain 2.3% (5 patients), incision site complications 5.6% (12 patients), dysphagia/dysphonia

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POTENTIAL ADVERSE EFFECTS CONTINUED

5.1% (11 patients), and implant loosening or dislodgement 2.3% (5 patients). In addition, 6.0% (13 patients) required removal of the PCM device and 1.4% (3 patients) required reoperations. There may be other risks associated with using the PCM Cervical Disc. Of the 190 control group patients who underwent ACDF, the most commonly reported device or surgery related adverse events included neck/arm pain 16.8% (32 patients), adjacent level disease 14.2% (27 patients), dysphagia/dysphonia 12.1% (23 patients), nonunion 5.8% (11 patients), and neurologic 5.3% (10 patients). Although many of the major risks are listed in this patient information brochure, more comprehensive safety information is provided in the physician's package insert for the product. Please ask your doctor for more information and an explanation of these risks.

BENEFITS

If the PCM Cervical Disc procedure is a success, it may result in relief of symptoms such as decreased neck/arm pain. In addition, the joint may retain some degree of motion. The PCM Cervical Disc may allow patients to preserve cervical motion at the level of surgery, including axial rotation (turning your neck), lateral bending (side-to-side bending), and flexion-extension (nodding up or down). This may allow you to return to many of your normal activities.

BEFORE SURGERY

Your doctor will review your condition and explain all of your treatment options, including medications, physical therapy, and other surgeries such as removal of the diseased disc, fusion, etc. Your doctor may also speak with you about preparations that you should make at your home, arranging for assistance, and the risks and benefits of this procedure. Please ensure that you have read and that you understand this entire brochure.

DURING SURGERY

During the PCM Cervical Disc surgery, you will be under general anesthesia. The surgeon will access your spine from the front of your neck, and will remove the damaged disc and any tissue or obstructions that are compressing the nerves or spinal cord. After shaping the edges of the vertebrae to ensure a proper fit, the PCM Cervical Disc is inserted. The surgery lasts approximately one-to-two hours and most patients leave the hospital the following day.

AFTER SURGERY

POSTOPERATIVE COURSE

Treatment with the PCM® Cervical Disc is major surgery. As with any major surgery, you should expect some discomfort as well as a period of rehabilitation. Your doctor may prescribe medications to manage any pain or nausea you might experience. On average, you should expect to stay in the hospital for one or two days.

AFTER YOU GO HOME

You and your doctor should discuss your recovery plan while the healing process takes place. It is very important to follow your doctor's instructions. Your doctor may give you 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 gives you permission
- You will be taught how to clean and care for your wound
- Your doctor may refer you to a physical therapist who will teach you exercises to improve your strength and mobility while protecting your spine and also different ways to position your neck to avoid reinjuring your spine.

CONTACT YOUR DOCTOR IMMEDIATELY IF:

- You have a fever
- The wound starts leaking fluids
- You have trouble swallowing or breathing
- You have new or increased neck or arm pain, numbness, or weakness
- You have nausea and/or vomiting

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LIMITATIONS TO POSTOPERATIVE ACTIVITY

Your doctor will instruct you on how to limit postoperative activity to reduce the risk of adverse events. The use of a cervical collar may be prescribed, depending on the doctor's assessment of your activity level and overall condition. Generally, at one day postoperatively, you may start physical therapy but, non-impact exercises are preferred. Generally, at 3 weeks postoperative, you may do Pilates or light weight training with a 40lb weight-lifting restriction. Generally, after the 6 week visit, you may be unrestricted with regard to weight training provided radiographs demonstrate good alignment. Repetitive cervical flexion and extension bending or the extremes of lateral bending and rotation should be avoided for 6 weeks postoperatively. Remember to consult with your doctor before performing any of these activities.

FREQUENTLY ASKED QUESTIONS

CAN I SHOWER AFTER SURGERY?

Depending on your surgical incision, you may have showering restrictions. Ask your doctor for appropriate instructions.

WILL I HAVE A SCAR?

The surgical incision is usually about one inch long and usually heals so that it is barely visible. Ask your doctor for more information as every patient is different.

WHEN CAN I DRIVE?

For a period of time after your surgery, you may be cautioned about activities such as driving. Your doctor will tell you when you may drive again.

CAN I TRAVEL?

The PCM® Cervical Disc may interfere with metal detection devices depending on the sensitivity of the equipment. Because of increased airport security measures, please call your local airport authority before traveling to get information that might help you pass through security more quickly and easily. Ask your surgeon to provide a patient identification card.

If you have any questions about the PCM Cervical Disc or cervical spine surgery, please call or see your doctor, who is the only one qualified to diagnose and treat your spinal condition. This patient information brochure is not a replacement for professional medical advice.

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