# Chapter 19 Clinical Outcomes Assessment of Nucleus Pulposus Replacement


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## KEY POINTS

- Nucleus pulposus replacement is a new technology of which there is a paucity of clinical data currently available.
- Both preformed and *in situ* curing polymers have been proposed as nucleus pulposus devices and tested to varying degrees.
- Clinical success, with improved indices on several functional scales, and radiographic success, with maintenance of disc space height and motion, has been reported at follow-up intervals of up to 10 years for the most widely used device, the PDN® prosthetic disc nucleus.
- Some authors have reported an increase in endplate sclerosis and Modic changes associated with nucleus pulposus implants, the significance of which is unknown.
- Longer-term follow-up and randomized controlled trials are needed to fully determine the role of nucleus replacement in the treatment of lumbar degenerative disease.

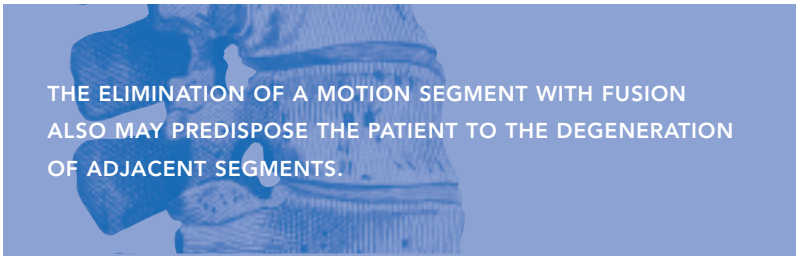
## INTRODUCTION

Lumbar disc degeneration is a natural occurrence of the normal aging process resulting in low back pain and radiculopathy. On occasion, the degenerative process can be a contributing factor associated with symptomatic lumbar stenosis and neurogenic claudication. The annulus fibrosus and the nucleus pulposus of the intervertebral disc work in concert to provide biomechanical stability at each spinal segment, with the nucleus supporting compressive loads and the annulus, together with the facet joints, resisting shear forces.

The nucleus pulposus comprises a sparse cell population that produces an extracellular matrix (ECM) rich in proteoglycans that bind water molecules to provide compressible properties to the nucleus. The ECM of the intervertebral disc naturally undergoes continuous remodeling, but generally maintains a fine homeostasis between ECM production and degradation. A number of factors, including those of genetic, metabolic, and mechanical origin, can alter the homeostatic balance of the ECM, resulting in destruction of proteoglycans and changes in collagen production. As the ECM degrades, loss of water content within the disc results in loss of disc height, altered biomechanics, and eventually advanced degeneration with endplate changes. Disc degeneration can alter the regional biomechanics in the spine placing additional stress on the facet joints or accelerating circumferential degenerative changes. Back pain can result from isolated disc degeneration, secondary to inflammation and irritation of the nerves within the outer annulus, or from circumferential degeneration involving the disc space and posterior facets.[1]

## SURGICAL TREATMENT

Surgical treatment of degenerative disc disease (DDD) has traditionally relied on two techniques, discectomy or fusion, but new technologies like total disc replacement (TDR), nucleus arthroplasty, and posterior motion sparing dynamization are gaining popularity. Discectomy is performed when a portion of the nucleus has herniated into, or through, the annulus and is causing nerve root compression and chemical irritation resulting in radicular pain, numbness, and weakness. In patients that fail to improve with conservative therapies, discectomy is a highly effective procedure for alleviating radicular symptoms but is largely ineffective in treating back pain. Furthermore, discectomy may lead to additional loss of disc height, contributing to hypermobility and biomechanical derangement of the segment. This has the potential to hasten arthritic degeneration and increase low back pain.[2]



THE ELIMINATION OF A MOTION SEGMENT WITH FUSION ALSO MAY PREDISPOSE THE PATIENT TO THE DEGENERATION OF ADJACENT SEGMENTS.

The use of surgical fusion has been advocated for the treatment of discogenic back pain, but the clinical success of this procedure is highly variable and often dependent on complex psychosocial factors. In addition to involving a much more difficult patient selection, fusion entails a greater surgical risk because of complications related to the more complex surgical approach, hardware failure, autograft donor-site morbidity, and potential for nonunion. The elimination of a motion segment with fusion also may predispose the patient to the degeneration of adjacent segments.

Total disc replacement, in which a mechanical artificial joint device is placed within the intervertebral disc space after total removal of the nucleus and some of the annulus, is being studied extensively. The hope is that TDR will remove the pain generator, while maintaining motion, to reduce the risk of adjacent-segment degeneration. TDR has been used in Europe for more than a decade, but use within the United States has been limited to clinical studies and a low usership during the last few years. Early clinical studies have shown that TDR has at least equivalent outcomes to fusion procedures, but its use is still controversial and further study is needed to establish long-term safety and efficacy. Other concerns about TDR include the cost and longevity of the artificial joint devices and the complexity of revision procedures due to the proximity of the greater vessels.

Nucleus Arthroplasty™ technology is receiving interest in the treatment of lumbar disc disease as a means of restoring normal biomechanical function to the degenerative spine. The goal of such technologies is to preserve motion at the index level by simulating the biomechanical properties of the native nucleus and, in theory, maintaining or restoring disc height. By replacing only the nucleus, these devices largely preserve the annulus and cartilaginous endplates, while re-establishing annular and ligamentous tension, and subsequent biomechanical function.[3] Additionally, by restoring disc height and near normal motion, nucleus replacement may delay or prevent facet degeneration after discectomy, and adjacent segment degeneration after fusion. Advantages of nucleus replacement in comparison with TDR include the possibility for less and/or minimally invasive placement, less complex revision, and more natural biomechanics with preservation of most of the annulus.

A broad array of nucleus replacement devices have been created and tested biomechanically and *in vivo* using animal models. There are basically two main types of devices: preformed implants, which are implanted into the nucleus space, and *in situ* formed implants, which are injected into the nucleus space. Preformed implants have the advantage of providing more uniform implant material characteristics and superior biocompatibility. *In situ* polymers, on the other hand, are designed to be injected through a smaller annular window and cured within the nuclear cavity to improve implant conformity and stress distribution, while decreasing the incidence of dislodgement. Only a few implants in either group, however, have been tested in humans. This chapter will review the currently available clinical results regarding nucleus pulposus implantation.

## CLINICAL EVALUATION OF NUCLEUS REPLACEMENT

As the new generation of nucleus replacement devices is developed, the rigorous assessment of clinical outcomes will be paramount in proving superiority to existing technology. Widely accepted standards, including the Oswestry Disability Index (ODI), Prolo Scale, Visual Analog Scale (VAS), and SF-12 or SF-36 (Table 1), have been used to assess outcomes and provide a basis from which to compare the results of these procedures to the results of other treatment strategies. The real clinical utility of these devices will be answered in long-term studies evaluating motion preservation and the prevalence of adjacent and same-segment disc disease. In the near term, however, surrogates of these endpoints can be assessed with imaging, specifically by the examination of the maintenance of disc space height, range of motion, and facet and endplate integrity.

## EXISTING CLINICAL DATA

### *PDN®—Prosthetic Disc Nucleus (Raymedica, LLC, Minneapolis, MN)*

The PDN prosthetic disc nucleus has the most clinical data reported to date. The PDN implant consists of a hydrogel core encased in a polyethylene jacket. The hydrogel core can absorb up to 80% of its weight in water, which allows the device to expand and maintain or restore disc space height. The implant jacket prevents overexpansion and subsequent overdistraction of the disc space that could cause endplate fracture.

The PDN device has traditionally been placed through a posterior approach following an annulotomy. Early versions of the design were used in a paired configuration, while later versions used a single PDN (PDN-SOLO®), with the long axis of the implant oriented in the coronal plane (Figure 1).

**Figure 1**
Dehydrated PDN-SOLO®

A Phase I clinical feasibility trial using the PDN paired design was initiated in 1996. Two-year results were reported by Schönmayr, et al,[4] in 1999. In this study, 11 patients were treated with an early, rectangular-shaped implant. Improvement was noted in mean Prolo and Oswestry scores, and eight of ten patients were considered to have an "excellent" result. One patient required reoperation

**TABLE 1: OUTCOME MEASURES USED IN THE TREATMENT OF LUMBAR SPINAL DISORDERS.**

| Outcome Measure | Description | Scale |
|---|---|---|
| Oswestry Disability Questionnaire | Widely used back-specific questionnaire considered the "gold standard," the questionnaire assesses functional ability in ten categories including pain, sitting, standing, and walking tolerance, and social and sex life | Ability rated on a 100 point scale, with 100 being the best |
| Prolo Scale | Ten-point scale consisting of only two questions evaluating the functional and economic status of the patient | Scores of 9 and 10 are excellent while score of <4 is poor |
| Visual Analog Scale | Simple ten-point rating scale for pain | 0=no pain; 10=worst imaginable pain |
| SF-12/SF-36 | Validated survey assessing eight components of general health including psychological, physical, and social function | Each category rated on a 100-point scale with higher scores being better |

for a migrated implant and another had early reoperation with fusion for recurrent pain associated with marked facet degeneration. Two other patients whose outcomes were nonetheless "excellent" were noted to have some migration of the implant on imaging that did not require reoperation.

Ten-year follow-up on this initial patient group was reported at the 6th Annual Spine Arthroplasty Society Meeting, Montréal, QC, Canada in May 2006. All ten patients were able to work, three had sporadic minor low back pain, and only one was taking occasional analgesics. Radiographic evaluation demonstrated a mean range of motion of 5.2° at the operated level, but there was a slight decrease in disc space height from 10.4mm postoperatively to 8.3mm at the latest follow-up. Nine of the patients expressed satisfaction with their results stating that they "definitely would" undergo the procedure again.

Additional studies performed with the PDN paired design had rather mixed results. In a Phase II trial (1997), 17 patients were treated with a reported success rate of 62%; failures were largely due to device migration. Modifications to the implant shape, instrumentation, surgical technique and post operative care showed continued improvements. A Phase III trial (1998) performed with 26 patients showed an improved success rate of 79%. In a subsequent Phase IV trial (1999), 51 patients were implanted with a success rate of 91%. Again, failures in this group were largely due to device migration with patients requiring additional surgery within three months.[5]

Klara, et al,[5] reviewed the outcomes of 423 patients in whom a PDN paired design was implanted between 1996 and 2002 and reported an explant rate of 10%. Analysis of the explant data indicated that patients that were overweight or had smaller disc spaces were more likely to have problems with device migration. These findings prompted modifications to the clinical treatment protocol to lessen the incidence of failure. In addition, the PDN device design was revamped to utilize a single implant approach, the PDN-SOLO.

Clinical studies with the PDN-SOLO, such as that by Shim, et al,[6] have demonstrated encouraging results. This group reported on 46 patients with follow-up greater than six months. Mean VAS scores improved from 8.5 to 3.1, mean ODI scores decreased from 58.9% to 18%, and mean Prolo scores increased from 5.2 to 7.2 at one year. However, roughly 11% of patients experienced a major complication, including device migration, requiring reoperation (4 patients). Additionally, there was a high incidence of endplate sclerosis and vertebral body Modic changes (68.9% and 82.2%, respectively) on follow-up imaging. While the clinical relevance of Modic changes is unknown at this time, such radiographic findings certainly warrant further investigation as they may be associated with back pain and ongoing degeneration in some patients.[7]

Shim and Lee presented interim data on their 20 patient cohort of a 75 patient multi-center international clinical evaluation of the PDN-SOLO at the 6th Annual Spine Arthroplasty Society Meeting, Montréal, QC, Canada in May 2006. The primary indication was discogenic back pain, with or without leg pain. Nine of the 20 patients had reached the 24 month time point. Mean ODI improved from 51.7 to 12 at 24 months, VAS decreased from 8.2 to 3. Mean ODI and VAS showed continued improvement as the follow-up interval lengthened and segmental motion was maintained. Two patients had persistent postoperative pain, one for a concomitant condition not discovered preoperatively. There were no reoperations reported; the surgical success rate was 90%.

**IN COMPARISON WITH THE EARLIER PDN DESIGNS, THE HYDRAFLEX™ TECHNOLOGY HAS A MORE ANATOMICALLY CONTOURED SHAPE, A SOFTER CORE, A LARGER FOOTPRINT, AND FASTER HYDRATION CHARACTERISTICS.**

Raymedica has recently made further revisions to the PDN technology with the development of the HydraFlex™ Nucleus Arthroplasty System™ (NAS). In comparison with the earlier PDN designs, this device has a more anatomically contoured shape, a softer core, a larger footprint, and faster hydration characteristics (Figure 2). The system also incorporates a new instrumention system that is designed to place the implant through an anterolateral retroperitoneal approach (ARPA). An Investigational Device Exemption clinical trial approved by the U.S. Food and Drug Administration is currently underway in the United States.

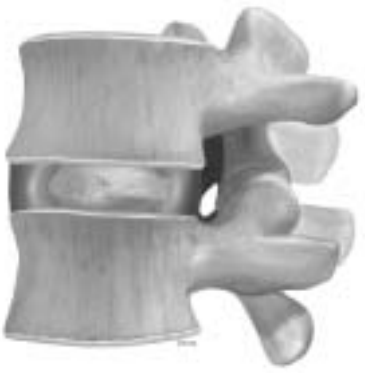


**Figure 2**
HydraFlex device

AS THE NEW GENERATION OF NUCLEUS REPLACEMENT DEVICES IS DEVELOPED, THE RIGOROUS ASSESSMENT OF CLINICAL OUTCOMES WILL BE PARAMOUNT IN PROVING SUPERIORITY TO EXISTING TECHNOLOGY.

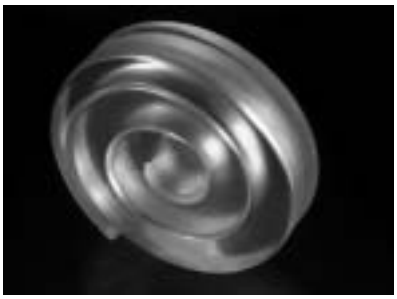


**Figure 3**
NewCleus

### *Newcleus (Zimmer, Inc., Warsaw, IN)*

The Newcleus implant is composed of polycarbonate urethane (PCU) and has a unique spiral shape derived from memory coiling (Figure 3), which enables it to be implanted through a very small annular incision and recoil into its original shape. The unique shape also eliminates any fixed axis of the device, which allows for easy positioning, as rotation or movement within the disc space is not an issue. Clinical results on five patients with an average follow-up of 23.6 months (range 6–64 months) have been reported.[9] Results of this very limited study were promising, with all patients experiencing an improvement in Oswestry score and all being satisfied with their outcome. There were no device dislodgements, neurologic deficit creations, or reoperations reported. Disc height was maintained during follow-up examinations and flexion/extension radiographs demonstrated retained motion over the operated segments. Rotational CT scanning demonstrated normal function of the facets without arthropathy. All patients demonstrated vertebral body signal changes (Modic changes) on magnetic resonance imaging, a finding of questionable significance. An international multicenter study is currently underway to assess the long-term efficacy of this implant.

### *NuCore (Spine Wave, Inc., Shelton, CT)*

The NuCore injectable nucleus is an *in situ* curing polymer composed of a recombinant protein hydrogel (Figure 4). Early results on 12 patients have recently been reported. Four of these have been followed for a year and five have achieved 6-month follow-up. Thus far, all have experienced good pain relief and maintenance of disc height. There have been no device extrusion or device-related complications.[10]

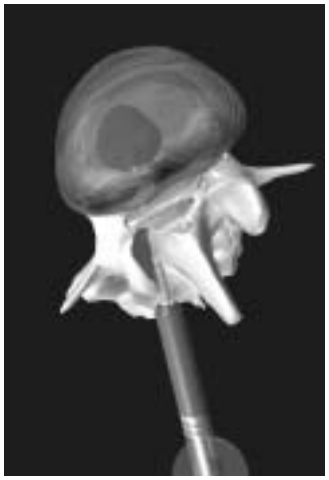


**Figure 4**
NuCore

### *BioDisc (CryoLife, Inc., Kennesaw, GA)*

BioDisc is a protein hydrogel composed of a mix of bovine albumin and glutaraldehyde (Figure 5). Nine patients with radiculopathy have been enrolled in a clinical trial of this device and early results are encouraging, with patients demonstrating significant improvements in Oswestry score (mean 50.6 to 9.1), VAS score (mean 5.9 to 1.6), and SF-36 physical component (mean 28.5 to 48.1) after three months of follow-up.[11] No surgical complications were noted and magnetic resonance imaging at follow-up examinations demonstrated no migration of implants. Although these early results are encouraging, it is unclear from the data reported how many of these patients were treated for only radicular symptoms and thus might have enjoyed similar improvement for the discectomy portion of the procedure alone.

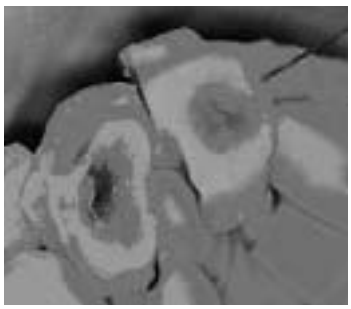


**Figure 5**
BioDisc

### *DASCOR (Disc Dynamics, Inc., Eden Prairie, MN)*

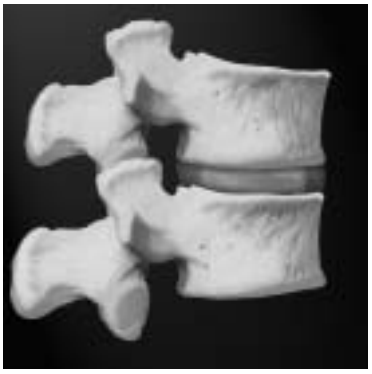


**Figure 6**
DASCOR

The DASCOR device consists of an injectable polyurethane that polymerizes minutes after being injected into a balloon inserted into the disc space (Figure 6). European and U.S. trials are currently underway. Data from the first 16 patients enrolled has been presented as promising.[1]

### *Nubac (Pioneer Surgical Technology, Marquette, MI)*

The Nubac device is an articulating PEEK-on-PEEK nucleus replacement implant (Figure 7). Nubac received the CE mark approval in 2005 and a U.S. FDA conditional approval for clinical trials was granted in 2006.

**Figure 7**
NuBac

### *Regain (EBI Biomet, Warsaw, IN)*

The Regain nucleus replacement is a one-piece pyrocarbon device (Figure 8). Pyrolytic carbon has a significant use history in long-term implantable devices thus biocompatibility is not considered and issue. The Regain is in clinical trials in Europe; it is not commercially available in the United States.

**Figure 8**
Regain

## CONCLUSION

Nucleus arthroplasty in the lumbar spine is a promising technology that may prove to be effective in treating back pain and preventing same and adjacent-level degeneration. Clinical experience with these devices is limited, and a large experience has only been reported with one, the PDN device. Thus far, results have been promising, with improvements in numerous functional indices and maintenance of segmental motion and disc space height being reported in most studies. Of concern is the frequency of device migration and the increases in vertebral Modic changes and endplate sclerosis. Longer-term follow-up and randomized controlled trials will be needed to conclusively determine whether this technology is more beneficial than simple discectomy or fusion procedures.

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