Disc nucleus fortification for lumbar degenerative disc disease: a biomechanical study

Derrick A. Dupré, MD, Daniel J. Cook, MS, J. Brad Bellotte, MD, Michael Y. Oh, MD, Donald Whiting, MD, and Boyle C. Cheng, PhD

Department of Neurosurgery, Allegheny General Hospital, Pittsburgh, Pennsylvania

OBJECTIVE Spinal stability is attributed in part to osteoligamentous structures, including the vertebral body, facets, intervertebral discs, and posterior elements. The materials in this study provide an opportunity to augment the degenerated nucleus without removing native disc material, a procedure introduced here as “fortification.” The objective of this study was to determine the effect of nucleus fortification on lumbar disc biomechanics.

METHODS The authors performed in vitro analysis of human cadaveric functional spinal units (FSUs), along with characterization and quantification of movement of the units using biomechanical data in intact, disc-only, and fortified specimens. The units underwent removal of all posterior elements and annulus and were fortified by injecting a biogel into the nucleus pulposus. Each specimen was subjected to load testing, range of motion (ROM) quantification, and disc bulge measurements. Optoelectric tracking was used to quantify disc bulge. These criteria were assessed in the intact, disc-only, and fortified treatments.

RESULTS Disc-only FSUs resulted in increased ROM when compared with intact and fortified conditions. Fortification of the FSU resulted in partial restoration of normal ROM in the treatment groups. Analysis of hysteresis loops showed more linear response in the fortified groups when compared with the intact and disc-only groups.

CONCLUSIONS Disc nucleus fortification increases linearity and decreases ROM.

http://thejns.org/doi/abs/10.3171/2015.8.SPINE141043

KEY WORDS fortification; hysteresis; nonlinearity; range of motion; nucleus pulposus; discectomy; augmentation; biogel; lumbar; degenerative

Back pain is a global phenomenon affecting millions of people and is a source of immense financial burden to society, amounting to total health care expenditures in the US of nearly 100 billion dollars by the end of the last century.14 Back pain is often attributed to intervertebral disc disease (IDD), which itself has long-standing management guidelines.2,4,10 The majority of patients with newly diagnosed IDD are managed expectantly. In some cases, a strict regimen of physical therapy, pain control, and steroids is successful. The current school of thought is that surgery, routinely involving partial or total disc removal, should be offered after the failure of conservative management. It is the type and timing of surgical intervention that is of great controversy and has blighted the health care community for decades.

The type and timing of interventions for IDD are highly variable. Sources range in recommendation from 1 month to up to 1 year before proceeding with operative management.1,16,17 While there is an abundance of literature on the operative management of IDD, much of it is inconsistent with regard to timing of intervention-specific treatments, and is variable between spinal segments.

Operations are typically recommended for appropriate candidates, and selection criteria include, but are not limited to, the following: uncontrollable pain, pronounced neurological deficits, or failed long-term conservative management. In the setting of a disease that is self-limiting in many cases, these criteria provide a justification for such an invasive procedure with potential complications. As such, alternatives to the traditional musculoskeletal dissection involved in removing a herniated disc have long been anticipated.
Disc nucleus removal, as well as removal in combination with replacement by synthetic materials, has been used in the treatment of degenerative disc disease for decades. In the more than 40 years since the discectomy was introduced, many novel procedures, techniques, and implants have surfaced while outcomes have plateaued. Starting in the mid–twentieth century, investigators began using injectable material, pegs, spheres, silicone rubber, and metal ball bearings in the disc space after discectomy. Numerous prostheses have been designed and are in various stages of commercialization, including hydrogel cores wrapped in polyethylene jackets, elastic memory-coiling spirals, hydrogel polyvinyls, ceramic, and metal implants that have been devised to occupy the space once taken up by the intervertebral disc.

Augmentation, as referred to in the current literature, refers to the replacement of disc material or annulus, or both, by synthetic materials after diseased tissue has been removed. Fortification, defined here as reinforcement of the native intervertebral disc via injection of synthetic biomaterial, is the concept addressed at present. The authors suspect that leaving the native diseased disc material while making it more robust may yield greater benefits than the previously studied augmentation methods where discectomy and anuclecmy occur. There have been no studies to characterize the effects of fortification on the human intervertebral disc.

Multiple techniques and implants related to disc augmentation have been proposed, yet there are currently no approved methods for use in clinical practice that do not involve an incision. While potentially a great resource for spine surgeons and patients alike, current models show promise but are unable to aptly address all issues at hand. One of the most appealing aspects of fortification procedures would be the lack of invasiveness, although currently there are no FDA-approved bioinjectable disc fortification implants. In this study, the biomechanical characteristics of one nucleus fortification device are described by quantifying the stability of fortified functional spinal units (FSUs). The purpose of this study was to characterize the mechanical changes in fortified FSUs.

Methods

Human cadaveric lumbar specimens were used in this study. A total of 16 fresh-frozen specimens were processed and stripped of soft tissue outside the osteoligamentous structures. The specimens were then sectioned, with each spine randomized to 1 of 2 patterns. FSUs L1–2, L3–4, and L5–S1 comprised the first pattern group, while L2–3 and L4–5 comprised the second. Each specimen was CT scanned and graded for degenerative classification independently by 2 neurosurgeons. The anterior and posterior columns of each FSU were graded as either none, mild, moderate, or severe based on the presence of endplate sclerosis, disc height loss, osteophyte formation, or facet hypertrophy. Specimens that were graded as severe in either the anterior or posterior columns by either surgeon were disqualified. This provided 25 FSUs from the qualifying lumbar spines, which were then set within a potting compound (Bondo, 3M) and prepared for testing. Table 1 demonstrates limited demographic data of specimens.

<table>
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<tr>
<th>Specimen No.</th>
<th>Sex</th>
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Once the FSUs were prepared and separated, they underwent flexibility testing with a SmartTest spine tester (Bose) with 6 degrees of freedom. This initial load control test consisted of 3 cycles (2 preconditioning cycles followed by the third cycle used for analysis) of axial compression (250 Nm), flexion-extension (5 Nm), lateral bending (5 Nm), and axial torsion (5 Nm). To visualize the posterior aspect of the intervertebral disc surface and isolate the biomechanical properties of the disc, the units were stripped of posterior elemental structures, including laminae, spinous processes, facet complexes, posterior ligaments, and pedicles. Infrared light-emitting diodes were then affixed to the posterior, lateral, and posterolateral portions of the intervertebral disc to evaluate disc bulge by a previously described method. They subsequently underwent repeated flexibility testing by the same protocol. The kinematic response of each specimen was monitored and recorded by an optoelectronic system (Optotrak Certus, Northern Digital).

After the disc-only units were tested, the FSUs underwent nucleus fortification with volumes ranging from 0.5–2.3 ml of an injectable in situ–cured hydrogel (BCNP, BioCure Inc.) under fluoroscopy. The specimens were tested again under the same protocol following nucleus fortification. To maintain physiological conditions required for proper curing of the hydrogel, all specimens were heated to a temperature of 37°C before testing and were frequently hydrated with an isotonic solution to prevent dehydration.

Biomechanical Measures

For each treatment, including the intact condition, ROM was analyzed. Maximum disc bulge at the posterior, posterior lateral, and lateral positions was measured for the disc-only and fortified treatment conditions. Cubic splines were fit to the displacement-load data for each treatment condition from peak flexion to peak extension using ro-
bust regression in MATLAB (version 7.12, MathWorks). The spline fits were analytically differentiated to calculate the slope of the displacement-load curve throughout the ROM. This measurement corresponds to the laxity of the joint at each load value. The nonlinearity of the displacement-load curve was calculated by dividing the maximum by the mean slope of the curve between $-4$ and $4 \text{ Nm}$. The range of this calculation was constrained to avoid discontinuity in the slope that occurs near the end of the ROM.

**Statistical Analysis**

The means of each treatment group were subjected to repeated-measures ANOVA difference testing (SPSS, version 18, IBM). A Bonferroni post hoc analysis was then conducted if statistical significance was detected. This was used to determine specific differences between treatments.

**Results**

**Range of Motion**

For each test, the ROM of the FSU was taken from the third cycle of loading. The change in the angular (flexion-extension [FE] bending, lateral bending [LB], axial torsion [AT]) or translational motion (axial compression [AC]) was calculated for each specimen. For each treatment, the mean from all specimens was calculated and is reported along with the standard deviation in Table 2.

With regard to FE bending, there was a statistically significant difference between the disc-only and the intact FSU ($p < 0.001$). When comparing the intact to the disc-only FSU, the disc-only to the fortified, and the intact to the fortified in AT, all displayed statistical significance ($p < 0.001$, $p = 0.001$, and $p = 0.022$, respectively). In the LB and AC modes, there was no statistical significance detected between the different treatments.

**Nonlinearity**

Implantation of the nucleus fortification device produced a marked increase in the linearity of the displacement-load behavior of the specimens tested. This is exemplified in Fig. 1, which shows the hysteresis loop for a representative specimen under each treatment condition, and in Fig. 2, which shows the slope of the hysteresis loop for the same specimen for $4 \text{ Nm}$ flexion to $4 \text{ Nm}$ extension under each treatment condition. The nonlinearity of the fortified condition was significantly less than the intact ($p = 0.002$) and disc-only ($p < 0.001$) treatment conditions (Fig. 3).

**Disc Bulge**

A significant reduction in posterior disc bulge was observed during LB for the fortified treatment compared with disc-only ($p = 0.008$). A significant reduction in posterolateral disc bulge was observed for the fortified treatment in LB and AC ($p = 0.012$ and $p = 0.011$, respectively). A significant reduction in lateral disc bulge was observed for the fortified treatment in LB and AC ($p = 0.017$ and $0.014$). Figure 4 illustrates the mean and standard deviation disc bulge for each location in each mode of loading.

**Discussion**

The flexibility (characterized via ROM) and stability
Nucleus fortification

(quantified by nonlinearity and disc bulge) of the FSUs were demonstrated in vitro in the study of 25 FSUs. The appeal behind nucleus fortification devices lies in the potential to restore or maintain functionality (or both) without significant manipulation of tissues and would theoretically maintain normal biomechanical characteristics with the appropriate device. Perhaps the greatest challenge would be to determine who would be a candidate for early intervention. Radiological findings lend themselves to support back pain as being discogenic. For example, Modic changes, especially Modic Type 1, are strongly associated with low-back pain and early degeneration. Postsurgical reherniation potential exists in 9%–48% of cases, oftentimes necessitating a reoperation; therefore, the notion of disc fortification takes on yet another appealing role. Functional performance of the intervertebral disc was assessed with and without the implanted device.

Intervertebral joint laxity has long been associated with spine degeneration and pain. A variety of techniques have been used to evaluate the range of joint laxity, commonly referred to as the neutral zone or lax zone. The authors have developed an objective description of joint laxity based on a spline-fitting technique applied to the displacement-load curve of the FSU. The nonlinearity parameter developed as part of this analysis represents the magnitude of change in joint stiffness throughout the ROM of the FSU. Several significant differences were observed between the treatment groups. When comparing the intact FSU to the treatment group during FE bending after removal of the posterior elements, the mean angular sagittal ROM was larger compared with the intact condition. As one would expect, removal of the posterior elements increased ROM. Compared with the disc-only group, fortification reduced only the AT ROM. While ROM has been quantified in the lumbar spine, one objective of the study was to characterize a measure more specific to the stiffness behavior of the FSU; hence, of greater interest was the finding that there was an alteration in the displacement-load behavior of the FSU with hydrogel injection. A statistically significant decrease in nonlinearity of the hysteresis loop was shown for the FSU after injection with the nucleus fortification material compared with both the intact and disc-only treatment conditions in FE.

Adequate treatment of discogenic back pain should include preservation or “fortification” of existing structures, which would consist of early identification and treatment in an attempt to strengthen the compromised framework. Fortification may prevent the cascade of water and proteoglycan loss from the matrix of the nucleus, which leads to increased vascularity of a thinned endplate, the development of fissures throughout the nucleus, sclerosis of subchondral bone, and apoptosis. The goal of injecting a biomaterial into the nucleus is to restore the native normal (to endplate) forces, which are lost over time through de-

Fig. 2. Slope of the displacement-load curve over the range (−4 Nm to 4 Nm) under each treatment condition. Figure is available in color online only.

Fig. 3. Bar graph showing FE nonlinearity. Asterisk indicates statistically significant difference compared with the fortified condition.
hydration and degeneration, leading to nociceptive fibers leaking through the disrupted annulus. In such instances where the degenerated discs lose their height, adjacent structures, such as ligamentum flavum, facet joints, and neural foramina, are disrupted. Moreover, the device should reduce any joint laxity associated with degeneration while allowing for adequate ROM.

Most fixation devices to date have used ROM as a sole metric. With the development of more sensitive tools and more specific biomechanical metrics, it has become possible to characterize the more subtle effects of nonfusion devices. The authors were able to combine traditional metrics such as ROM with disc bulge and hysteresis nonlinearity to better characterize the biomechanics of the intervertebral discs. As new technologies such as motion preservation devices are introduced, it is important to consider additional metrics to ROM to best characterize the biomechanical performance of such technologies and to determine the impact on a patient's FSU.

The clinical effects of fortification remain unknown. Without performing the procedure in vivo, the authors would be speculating on whether this procedure would incite or aggravate discogenic pain. While there are at present no clinical criteria to objectively determine whether pain is due solely to increased mobility, practitioners routinely use dynamic imaging studies to confirm increased mobility at a joint of interest for surgical decision making. Therefore, the theoretical potential to reduce this type of pain through such an approach (reduction of hypermobility-associated discogenic pain) should be considered if it has any potential to benefit society.

The authors realize the utility of including an experimental arm in which partial discectomy is compared. Such a category would afford insight into the biomechanics observed in the clinical setting as it compares to the cohorts at hand. Additionally, the tissue adhesion coefficients were not analyzed by the authors, as the focus was on the attainability of gross biomechanical alterations attributable to such a minimally invasive maneuver. Several variables remain that would potentially alter the clinical applicability of such a procedure; however, the scope of the current study was to explore the potential of this material to reduce motion in a unit with an intact disc space, as the clinical translation would pertain to those intervertebral discs that have not yet undergone surgical intervention. More rigorous investigation into various physical and chemical properties of potential fortifying agents is warranted, as is the determination of whether such materials would be suitable for the treatments of discs with an intact annulus in addition to those with disrupted annular rings.

FIG. 4. Comparison of posterior (A), posterolateral (B), and lateral (C) disc bulge. Lines connecting 2 bars indicate significant differences between treatment conditions.
Features that account for the attractiveness of a potential fortifying agent include cure time, extrusion potential, bioreactivity (potential for inflammatory reactions, osteoinductive/osteocative conductive, and tumefactive capacity), elasticity, adhesion/cohesion coefficients, expansile/osmotic properties, brittleness, and viscosity, to name a few. These qualities were not assessed in the current study, although they should be thoroughly investigated in future analyses of experiments of a similar nature. Admittedly, the aims of the current pilot study were limited from the inception of the experiments to the analysis of any gross biomechanical changes that might have been encountered due to the reluctance of the authors to believe that such a method would actually produce significant changes. Furthermore, the role of fortification when compared with nucleus replacement or total disc replacement has yet to be elucidated. While the material used in the current study appeared to be appropriate in consistency and cure time, it is still unknown whether there is a more suitable or physiological substance.

The data presented provide evidence for the need to advance in vitro studies to include animal models and ultimately human trials with the understanding that the potential benefits in humans are many. Fortification may prove to be a great advancement in the management of discogenic back pain, and the benefits of such procedures have not been discussed in the current literature. To maintain the biosynthetic pathways of the disc, maintain disc height, and preserve the load-bearing column all through a needle is an attractive concept that warrants further development. Many nucleus replacement devices have failed, largely because of disruption of adjacent-level endplates and extrusion into the canal or foramina, causing significant pain, or neurological deficits, or both. The goal of fortification would be to restore height and function to the FSU while at the same time avoiding significant tissue manipulation and further pain potentially caused by a foreign body. Native nucleus material is integral to the normal physiological functions of the spine. By using radiological findings such as Modic changes, in addition to clinical circumstances, investigators may soon be able to determine which patients would benefit most from fortification procedures.

The authors’ intent is not to promote a particular technique or material, but rather to incite interest and thought in a field in which the development of consistently efficacious treatments has eluded practitioners, especially in comparison with the rest of medicine and other surgical subspecialties. Ideally, future investigations would focus on elucidating which material properties of an injectable would be best suited for the concept at hand, including viscosity, adhesion properties, inflammatory and reactivity profiles, and extrusion potentials. At present, the concept of fortification remains in its infancy and a great deal of information remains to be elucidated prior to advancement into further stages of investigation.

**Key Points**

- The disc nucleus is essential to the normal function and stability of the spine. All efforts to preserve native disc material should be made prior to removal.
- ROM is critical to the functionality of the human spine. Removal of posterior elements destabilizes the spine, while fortification increases stability. Disc height contributes to the functionality of the FSU, and restoration of disc height should be attainable without removal of the intervertebral disc.
- By injecting a biogel into the disc space, linearity of hysteresis is increased and ROM is reduced.

**Acknowledgments**

This study was funded in part by Medtronic.

**References**


Disclosures

The authors report no conflict of interest concerning the materials or methods used in this study or the findings specified in this paper.

Author Contributions

Conception and design: Cheng. Acquisition of data: Cook, Belotte, Oh, Whiting. Analysis and interpretation of data: Cook. Drafting the article: Dupre. Critically revising the article: Dupre. Reviewed submitted version of manuscript: Dupre. Statistical analysis: Cook. Administrative/technical/material support: Cheng, Oh, Whiting. Study supervision: Cheng.

Correspondence

Boyle C. Cheng, Department of Neurosurgery, Allegheny General Hospital, 420 E. North Ave., Ste. 302, Pittsburgh, PA 15212. email: bcheng@wpahs.org.