Nucleus Implant Parameters Significantly Change the Compressive Stiffness of the Human Lumbar Intervertebral Disc

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Nucleus replacement by a synthetic material is a recent trend for treatment of lower back pain. Hydrogel nucleus implants were prepared with variations in implant modulus, height, and diameter. Human lumbar intervertebral discs (IVDs) were tested in compression for intact, denucleated, and implanted condition. Implantation of nucleus implants with different material and geometric parameters into a denucleated IVD significantly altered the IVD compressive stiffness. Variations in the nucleus implant parameters significantly change the compressive stiffness of the human lumbar IVD. Implant geometrical variations were more effective than those of implant modulus variations in the range examined. [DOI: 10.1115/1.1894369]

Keywords: Lumbar Spine, Intervertebral Disc, Nucleus Pulposus, Hydrogel Nucleus Implant, Compressive Stiffness, Lower Back Pain

Introduction

Nucleus replacement has been investigated as a treatment for lower back pain since Nachemson first described the concept in 1962 [1]. The exploration of this concept is mainly motivated by the limited success of the current treatments such as spinal fusion and discectomy [2–6]. Nucleus replacement by a synthetic material or a tissue engineered structure may help to preserve the annulus fibrosus (AF) and be amenable to minimally invasive surgical techniques, which could be offered to the patient who presents with persistent pain, but not significant degeneration of the annulus fibrosus.

In our earlier studies, we assessed the effect of hydrogel nucleus replacement on the compressive stiffness of the lumbar intervertebral disc [7]. In that work, we demonstrated the feasibility of replacing the nucleus pulposus (NP) with the hydrogel implant. The hydrogel implant restored 88% of the compressive stiffness of the denucleated intervertebral disc (IVD) when implanted in the created nuclear defect. This restored stiffness was a result of synergistic interaction between the hydrogel implant and the intact AF.

The objective of the current study is to systematically assess the effect of variation in the nucleus implant parameters (material modulus and geometric parameters of height/diameter) on the compressive stiffness of the lumbar IVD. It is hypothesized that by altering these nucleus implant parameters, the synergistic interaction (which is responsible for the stiffness restoration) between the nucleus implant and the intact AF can be modulated, thereby achieving the complete restoration of the compressive spinal biomechanics.

Materials and Methods

Nucleus Implant Preparation. A polymer blend containing 95-wt % poly (vinyl alcohol) (PVA) (molecular weight, 138,400 g/mol–146,500 g/mol) and 5-wt % poly (vinyl pyrrolidone) (PVP) (molecular weight, 10,000 g/mol) was prepared. 10% polymer solutions (by weight) of PVA and PVP were prepared by dissolving a mixture of the two polymers in deionized water at 90 °C overnight. The solution was then cast into the custom made molds of three different diameters (D_1=15 mm, D_2=16 mm, and D_3=17 mm) to achieve variation in the hydrogel implant diameter. The filled molds were gelled by six repeated cycles of freezing for 21 h at −19 °C and thawing for 3 h at 25 °C. Variation in the implant height was based on the measured average height (H_2) of an IVD of the test specimen and achieved by cutting the implants, as either undersize (H_1=H_2−1 mm) or oversize (H_3=H_2+1 mm). Variation in the implant modulus (E_1=50 kPa at 15% strain, E_2=150 kPa at 15% strain) was achieved by varying the number of freeze-thaw cycles (two cycles for lower and six cycles for higher modulus) during the preparation [8]. A third higher modulus implant (E_3=1500 kPa at 15% strain) was made from Silastic T2, a commercially available polymer mixture (Dow Corning, MI). Thus, implants with three different moduli, three different heights, and three different diameters were used for assessment of change in the compressive stiffness of the lumbar IVD.

Specimen Preparation. Functional spinal units (FSU) were harvested from four cadavers (one male and three female) with an average age of 63 years, within 72 h of death. Intervertebral motion segments or anterior column units (ACUs) were prepared from the FSUs by removing the facet joints, posterior elements, and other soft tissues. Parallel cuts in the transverse plane were made through the vertebrae to ensure alignment of the axial compression load. Thus, the ACU specimen consisted of an intervertebral disc in between adjacent anterior vertebral bodies.

Mechanical Testing Method. The IVD specimens were constrained in a custom made test fixture with the help of screws, which connected the distal vertebrae to the test fixture. A commercially available potting mixture (Cargroom®, U.S. Chemical and Plastics, OH) was used for the potting of specimens in the custom made fixture. Only the inferior vertebra was potted, with care to ensure that the potted material was not touching the IVD. The superior vertebra was compressed against the flat compression

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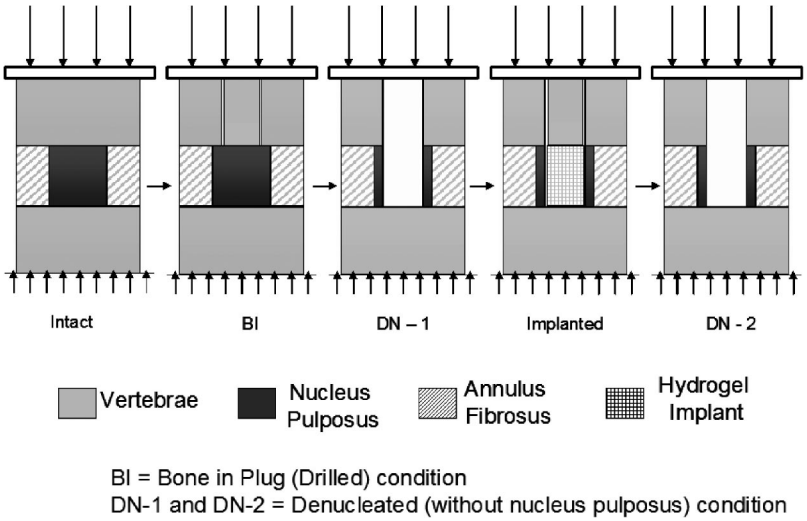

Fig. 1 Schematic of implantation method of a human lumbar intervertebral disc

plate attached to the load cell. In order to keep the specimen moist, a solution of protease inhibitor was sprayed on the specimen, throughout the test protocol.

Compression Testing Protocol. An Instron (Canton, MA) mechanical testing hydraulic machine (Model 1331) was used for the testing using displacement control mode. The specimens were preconditioned for 50 cycles at 3% strain (based on the average IVD height). The observed load range corresponding to this preconditioning was 40 N–140 N. Specimens were then axially compressed to 15% strain based on the measured average disc height. The testing was performed with a triangular wave form and a loading rate of 15% strain/s for five loading cycles, for each tested condition.

Implantation Sequence. For each specimen, implant modulus was varied ($E_1/E_2/E_3$) with a constant implant height (H_2) and diameter (D_2). Similarly, implant height was varied ($H_1/H_2/H_3$) with a constant implant modulus (E_2) and diameter (D_2). Finally, implant diameter was varied ($D_1/D_2/D_3$) with a constant implant modulus (E_2) and height (H_2). For each specimen, the order of the implants inserted was chosen randomly to minimize any effect of implant parameters on the test specimen.

IVD Implantation and Test Protocol. A series of axial compressive tests were completed on each specimen, as shown in Fig. 1. First, the intact specimen was tested using the compression testing protocol (intact condition—IC). Then, a 16 mm diameter Cloward core drill bit was used to drill perpendicular to the cut surface of superior vertebra through the bone to the IVD level and a cylindrical bone plug (height equal to that of superior vertebra) above the disc was removed. For the second test condition, the cylindrical bone plug was reinserted and the test protocol was repeated (Bone plug Inserted condition—BI). Then, the bone plug was removed from the upper vertebra and the nucleus was incised in line with the core drill. The central portion of the nucleus in line with the core drill (equal to 16 mm diameter, wet weight 2.5–3.0 g) was removed using standard surgical instruments, keeping the residual NP and the AF intact. The testing protocol was then run on the denucleated specimen without the bone plug (first denucleated condition, DN–1). The nucleus implants were inserted in the nuclear defect, in a random fashion. For all the nine implanted conditions, the bone plug was placed in its original position over the nucleus implant and testing protocol was repeated (implanted conditions—$E_1,E_2,E_3,H_1,H_2,H_3,D_1,D_2,D_3$). Finally, the nucleus implant and bone plug were removed and the specimen was tested again (second denucleated condition, DN–2) to determine if there was any damage to the specimen during testing.

Data Analysis. Data for the fifth loading cycle were taken for analysis and instantaneous compressive stiffness values (N/mm) were calculated at representative strain levels of 5%, 10%, and 15%, for each condition, for each specimen. A two-way, repeated measures analysis of variance (ANOVA) was performed for compressive stiffness with two subject factors; implant parameter variable (modulus, height, or diameter) and strain level (5%, 10%, and 15%). Follow up paired *t* tests were conducted to assess the individual effects of modulus variation, effect of height variation, effect of diameter variation, restoration ability of the nucleus implant (BI versus all nine implanted conditions) and crosscheck (DN-1 and DN-2). The acceptable rate for a type-I error was chosen as 5% for all tests.

Results

Table 1 shows the details of each specimen level, disc height, and corresponding peak force observed for the intact condition at 15% strain. Each of these is within the previously described range of loads [9]. Figure 2 shows the stiffness of different testing conditions (BI, denucleated, and implanted) at representative strain levels of 5%, 10%, and 15% for implant parameters of modulus, height and diameter. A two-way, repeated measures ANOVA for IVD compressive stiffness with two subject factors; implant parameter variable (modulus, height, or diameter) and strain level (5%, 10%, and 15%) showed significant interaction between the two factors ($p<0.05$).

Using paired *t* test for comparison of the compressive stiffness of the denucleated conditions (DN-1 and DN$-2\cong$DN) for all specimens at all strain levels (5%, 10%, 15%), no significant differences were observed ($p>0.60$). This suggests that the specimen returned to its original denucleated condition after implant removal without any damage.

Denucleating the IVD (DN) significantly reduced the compressive stiffness (52%) in comparison to the BI condition at all strain levels ($p<0.001$). The compressive stiffness of all implanted intervertebral segments was significantly greater than that of the denucleated IVD (DN-1) at each strain level ($p<0.001$). Moreover, with the exception of the H_1 and D_1 conditions at 10% and 15% strain, all implanted conditions were not statistically different than the corresponding BI condition ($p>0.05$). Thus, for all im-

Table 1 Intervertebral disc heights (mm) and peak forces (N) observed

Specimen	Disc level	Intact disc height (mm)	Intact peak force (N) at 15% strain level
1	L2-L3	7.65	577
2	L3-L4	9.50	1397
3	L3-L4	11.00	1366
4	L1-L2	9.00	1559
5	L2-L3	10.00	670
6	L1-L2	11.00	1407
7	L4-L5	12.50	1347
8	L2-L3	11.00	1953
9	L4-L5	12.00	2058

plants (except the undersized H_1 and D_1 implants), the implanted IVD had a compressive stiffness that was comparable to the BI condition and was significantly greater than the denucleated condition. Hence, implantation of the IVD restored the IVD compressive stiffness after denucleation to that of BI condition.

Discussion

This work examined the effect of nucleus implant parameters on the compressive behavior of the human lumbar IVD. To our knowledge, no human cadaver studies have reported the effect of nucleus implant parameters on the compressive behavior of the IVD. Meakin et al. used sheep discs to assess the effect of nucleus implant modulus on bulging direction of the AF fibers, in pure compression [10]. They showed that inward annular bulging can be prevented by inserting the nucleus implant with suitable material properties. The synergistic interaction between the NP implant and the AF is central to the IVD mechanics; however, in most of the studies reported in the literature [10–15], the nucleotomy and implantation was facilitated by making an incision through the AF. The denucleation approach through the endplate used in the present study is not feasible for clinical in vivo implantation. However, it does allow more precise control of nucleus removal and thus monitoring the fit-fill of the nucleus cavity (nucleus implant and the intact annulus). The current surgical acute transannular approach does not allow a delineation of the relative contributions of the AF injury, the NP depressurization, and the NP resection to the observed alteration of IVD mechanical behavior with NP removal. Moreover, while an acute transannular discectomy approach in vitro mimics the acute in vivo surgical discectomy procedure, it does not reflect on the mechanical condition of the disc with an intact AF or after healing of the annulotomy as the annulus is compromised in such an in vitro approach. Finally,

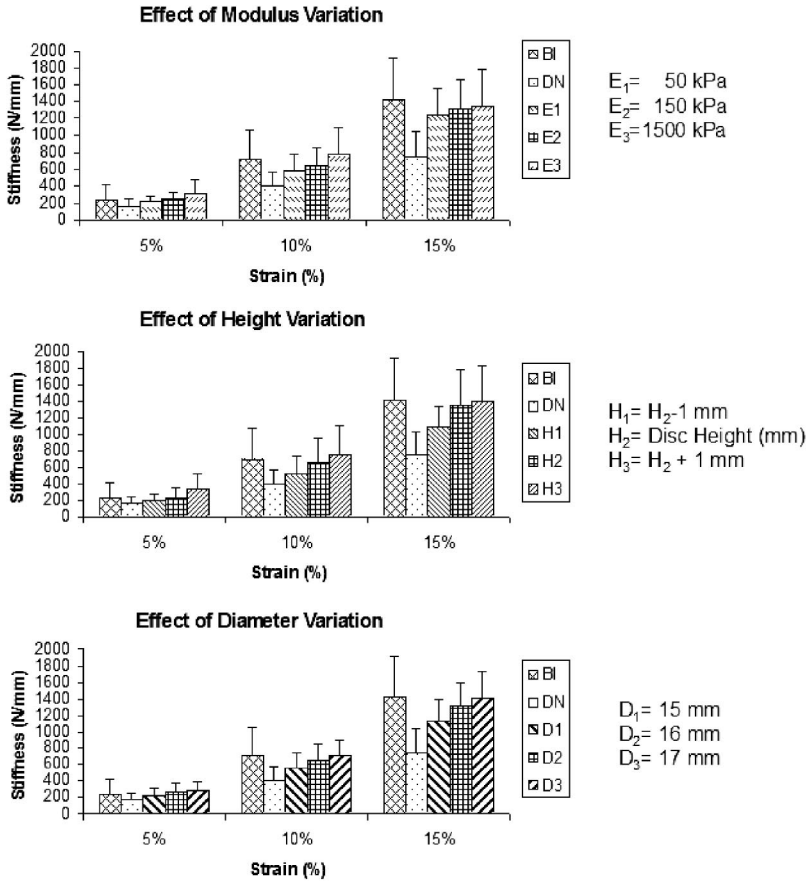

Fig. 2 Effect of nucleus implant parameter variations on the compressive stiffness of the lumbar intervertebral disc

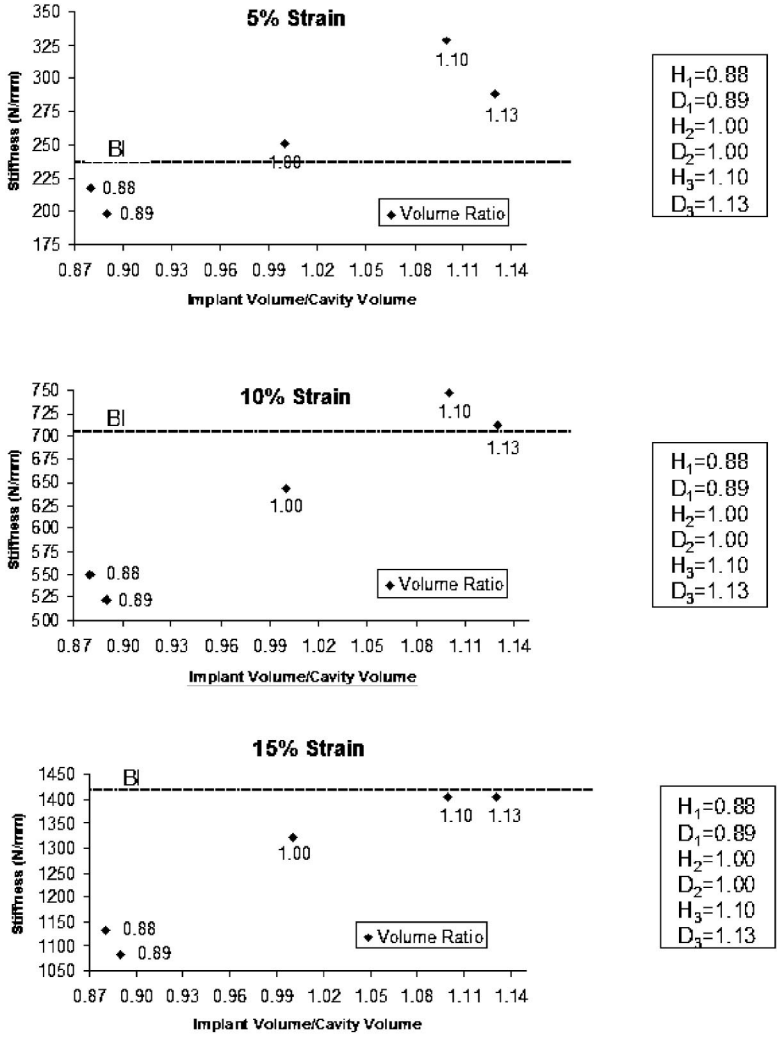

Fig. 3 Stiffness versus implant volume ratio of nucleus implant at different strain levels

precise and repeatable cavity shape and size are not easily if at all accomplished with this technique. Therefore, for a model system, where exploration of implant properties is the goal, the AF approach as is done today, may not serve to best address these fundamental questions.

It was hypothesized that an undersized implant would have less synergistic interaction with the AF while an oversized implant will have better synergistic interaction with the AF. The results presented in Fig. 2 also support these hypotheses. Nucleus implant parameters have a significant effect on the mechanical behavior of the IVD. Complete restoration of the IVD mechanical behavior can be achieved by generating more synergistic interaction by means of an oversize implant (between the AF and the implant). As noted above, the IVD compressive stiffness increases and decreases with both height and diameter of the implant. This can be visualized graphically in Fig. 3, where the volumetric ratio (defined as the ratio of Implant volume $[V_i]$ to that of drilled cavity volume $[V_c]$) versus the compressive stiffness (N/mm) at different strain levels is plotted. The IVD stiffness was sensitive to the volumetric ratio of the size of the implants investigated. An increase in total volume of the nucleus implant resulted in increased compressive stiffness. At 15% strain level, an increase in implant height produced 15 N/mm change in the compressive stiffness per percent increase while increase in implant diameter produced 21 N/mm change in the compressive stiffness per percent increase, as compared to implant modulus increase, which produced 0.04 N/mm change in the compressive stiffness per percent increase.

Interestingly, the result that a volume ratio of 1 at 10% and 15% strain produces stiffness which is less than that of the BI condition, suggests that the annulus is probably the largest contributor to the disc stiffness at higher strain levels while the nucleus dominates this behavior at lower strain/load levels. As the applied displacement increases, the annulus, by a tensioning of its fibers through interaction with the nucleus implant plays a major role in resisting the deformation. For the undersized implants, it takes higher displacement before the implant and annulus exhibit an interaction, therefore, at lower applied strain levels, the stiffness of the undersized implant is less than that of the line-to-line or overfilled conditions (for both diameter and height).

In a normal disc, the NP contributes in the disc mechanics by transferring any vertical loads acting on the disc in a radial direction by means of hydrostatic pressure (and tension in the fibers) on the annulus. The nucleus implant, while mimicking the function of the natural nucleus pulposus, takes a different path to create tension on the annulus. It generates mechanical stress on the annulus (this stress being equivalent to the hydrostatic pressure experienced by the inner annulus layers) because of the high lateral deformation due to a high Poisson's ratio and thus, achieves the desired function of the load transfer to the annulus. While

implant modulus, regardless of three orders of magnitude difference examined here, each restored the line-to-line implanted condition to the same level (that of the BI condition), there was no statistical difference between the different moduli groups. In this case, the modulus was not a dominant parameter in stiffness restoration. More likely, the Poisson's ratio of the implants is the critical parameter. Because the hydrogel and silicone materials used in this study were all highly elastomeric, the Poisson's ratios for each material were approaching 0.5. This may explain the lack of effect of modulus on the restoration of the compressive disc stiffness.

This study indicated that the resulting IVD compressive stiffness after nucleus implantation is a complex phenomenon. The resulting implanted IVD stiffness is a function of three major factors: the Poisson effect of polymeric implant, synergistic interaction between the nucleus implant/AF (preload and constrained bulk modulus effect), and compressive strain levels. Although compression is the major load acting on the IVD, other loading modes or, combination of loading modes such as flexion extension, axial rotation, and lateral bending are of utmost importance from the physiological point of view. The results presented here are for compression alone and may not necessarily hold true for other complex loading modes. The effect of nucleus implant parameters under the conditions of complex loading needs to be studied, to further understand the interactions between the intact annulus and the nucleus implant. Indeed, in the functional application of the device, the fatigue behavior of the construct would certainly be an important consideration as well. While we have examined the long-term (ten million cycles) compression - compression fatigue of the PVA/PVP implant material (unpublished data), in this work we do not address the effect of repeated loading on the implanted disc mechanics. While many questions remain, this paper serves to begin to systematically address the effect of nucleus implant design on the functional behavior of the lumbar IVD. Although the annuli of the tested specimens were intact and were not compromised functionally, results reported should be interpreted considering the degree of degeneration of the tested specimens, limited sample size, and its relevance with respect to the biomechanics of the normal intervertebral disc.

Conclusions

The effect of nucleus implant modulus and geometric parameters on the compressive stiffness of the IVD was determined in this study. It was observed that variations in geometric parameters of a nucleus implant are more effective in modifying the compressive stiffness of the implanted IVD than those of implant modulus over the ranges examined. The PVA/PVP hydrogel material examined here in both a line-to-line and overfilled geometric conditions did restore the compressive stiffness of the human lumber IVD to that of the BI level. This may have clinical implications in the restoration of disc biomechanics of the degenerated IVD. Future studies of complex loading conditions will help us further elucidate the role of the nucleus implant parameters in the restoration of intervertebral disc mechanics.

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