



Chapter 23

Nucleus Arthroplasty™ Design and Evaluation Challenges

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KEYPOINTS


- Successful nucleus arthroplasty devices have numerous clinical design challenges including anatomy preservation and restoration of segmental spinal motion.
- There are a number of methods that can be utilized to characterize a nucleus arthroplasty device. It is important to select and perform tests that are appropriate and representative of the physiological conditions for a particular device type.
- In addition to mechanical analyses, functional performance under biological conditions should be studied using *in vivo* experiments.

INTRODUCTION

The science of nucleus arthroplasty represents an exciting multidisciplinary challenge. The successful development of such technologies requires key input from individuals within

many disciplines including biomechanical engineering, design engineering, material sciences, tissue engineering, biology, microbiology, and of course spine surgeons.

**SUCCESSFUL NUCLEUS ARTHROPLASTY DEVICES
HAVE NUMEROUS CLINICAL DESIGN CHALLENGES
INCLUDING ANATOMY PRESERVATION AND
RESTORATION OF SEGMENTAL SPINAL MOTION**



FROM A CLINICAL PERSPECTIVE, THE PRIMARY GOAL OF NUCLEUS ARTHROPLASTY TECHNOLOGIES IS TO REMOVE OR REDUCE DISCOGENIC PAIN, WHILE SEEKING TO PRESERVE AS MANY EXISTING ANATOMICAL STRUCTURES AS POSSIBLE.

Integral to the process is a thorough understanding of the function of the disc, the biomechanics of the spinal segment and the loading of the entire spine. Furthermore, it requires additional knowledge in regard to the corresponding biological responses, biomechanical loads, and resulting deformations at the tissue level.

From a clinical perspective, the primary goal of nucleus arthroplasty technologies is to remove or reduce discogenic pain, while seeking to preserve as many existing anatomical structures as possible. Secondly, it is also desirable to provide segment stabilization and slow the progression of the degenerative cascade.

Thus, in theory, an optimal nucleus replacement should be capable of restoring the function of the spinal segment. This implies that it should re-establish the intact disc height, motion, and the load-sharing behavior between the different structures, thereby restoring the nominal stresses and strains in the collagen fibers of the annulus, remaining nucleus, and endplate.

Currently, there is a wide array of nucleus implants in clinical application or under development.¹ The major design concepts include mechanical, preformed polymer, *in situ* formed polymer, and tissue engineered implants (Volume II, Chapter 8).² However, while each design concept has certain advantages or disadvantages, to date, it is the author's opinion that there is no single device that can be referred to as an optimal nucleus replacement implant.

The following chapter is intended to be multipurpose with Part I focusing on the design challenges associated with nucleus arthroplasty devices. Unfortunately, there is limited data published about the biomechanical or clinical performance of such systems. Thus, in most cases the information that is provided represents the personal opinion and judgment of the author. As such, certain items may not apply to each device type or specific group.

Part II of this chapter provides a review of potential experimental tests and corresponding methods that may be utilized to characterize or benchmark nucleus replacement implants. The testing schemes that are presented are only recommendations; specific tests may not be appropriate for each device type or group.

CLINICAL DESIGN ASPECTS OF NUCLEUS ARTHROPLASTY CONCEPTS

Nucleus replacement implants seek to maintain the anatomical integrity of the disc and restore spinal segment motion. To achieve these goals in design, requires proper consideration of the anatomical and motion preservation characteristics of the native disc.

Anatomical Considerations

From an anatomical perspective, it is important to address and attempt to preserve the structures that compose the healthy spinal segment. Anteriorly, it is important to preserve the anterior longitudinal ligament and annulus, and protect the integrity of the vertebral endplate when performing the nucleotomy. Posteriorly, it is important to maintain the facet joint, capsule, and posterior ligamentous structures. Implant systems that require significant anatomic disruption may place more biomechanical demands on the device, impacting long-term function.

Annulus Preservation

One of the big advantages of nucleus arthroplasty devices is that the annulus can be preserved to a greater extent than artificial disc prostheses. The degree of annular preservation is largely dependent on the surgical technique, corresponding implant design (preformed, *in situ*, other), and insertion technique. To assist in healing and reduce the potential for implant mobility, it may be of benefit to close the annular opening after implantation.

Endplate Integrity

The importance of maintaining endplate integrity was noted in early studies with the Fernstrom³ ball. The relationship between implant stiffness or compliance, implant shape, and contact area, has a direct impact on the potential for implant subsidence that cannot be overlooked.

Ligaments and Facets

Anatomically, the spinal ligaments and facets play a vital role in nucleus arthroplasty in regard to segment stability. From a design system perspective, damage to these structures during surgical approach or device placement may significantly alter the segment motion and impact both short and long-term effectiveness of the surgical treatment. For example, insertion of implants using a postero-lateral approach may require a hemi-facetectomy, potentially leading to instability. Such concerns will be discussed in more detail in the next section.

Motion Preservation

One of the primary goals of nucleus replacement is to restore or maintain disc height which can assist in improving function and corresponding disc kinematics. The kinematic characteristics of the spinal segment are very complex. The three-dimensional motion is dictated by each of the spinal structures: the annulus, nucleus, ligaments, and facet joints. It also differs from segment to segment and is influenced by the spinal level, the disc height, the degeneration state, and the facet joint orientation. These characteristics determine the coupled and individual motion patterns, based on an applied load or prescribed motion.

The motion patterns produce pathways of the center of rotation when projected into the principle motion planes, or other orientations and axis configurations of interest. These so-called “helical axes” are very sensitive parameters, which are difficult to precisely determine.⁴ While the exact kinematics of the spinal segment are not completely understood, restoration after implantation of a motion preservation device may be critical for long-term clinical benefit.

Some motion preservation technologies represent a compromise in kinematics as the motion pattern is not perfectly re-established. Experiments have shown the coupled motions and thus, the helical axes can be re-established in some cases almost ideally.⁵ In other cases, the coupled motions are diminished and the implant acts more like a hinge joint. The ability to re-establish the appropriate

motion patterns may be better achieved with compliant nucleus arthroplasty devices which absorb energy, mimicking the function of the nucleus.

Physiological Loading and ROM

The ability to re-establish the physiological load sharing between the spinal structures is also important. Recreating the physiological condition requires that an implant solution is capable of reproducing the physiological strains in the annulus and endplates that are present in a healthy segment.^{6,7} Proper restoration of the disc height after nucleotomy has been shown to restore the range of motion to near that of the intact disc.^{8,9} However, further increasing the height, or over-distracting the segment, decreases both the range of motion and neutral zone, while stretching the annulus and stiffening the motion segment. In addition, over-distraction can produce a lifting of the facet joints resulting in an increased range of motion in axial rotation.

Damping Characteristics

Although the native disc exhibits a certain damping effect, little is known about this parameter. Until recently, disc replacement technologies were predominantly non-compliant mechanical implants that paid little attention to this particular area. Most nucleus arthroplasty devices have axial compliance and attempt to address damping to some degree.

The elastic preformed, *in situ* formed polymer implants, and tissue engineered implants may address damping as such implants seek to control physiological strain distribution in the remaining annulus, which is partially responsible for damping. Non-polymer-based designs such as a knitted titanium filament nucleus prosthesis may also work since they can undergo a change in density due to the knitting technique used.¹⁰

Biological Considerations

Whether nucleus arthroplasty technology is able to support a certain degree of biological regeneration is very speculative. As mentioned above, nucleus implants may be an optimal method to restore physiological conditions in the spine, hence potentially slowing down the degeneration process. However, biological regeneration requires a physiologic environment that allows the endplates to provide adequate nutrition combined with viable and healthy cells.^{11,12} However, even if the conditions are perfect, it is questionable whether the true origins of disc degeneration,

which are often genetically predetermined, can be corrected using such an approach.

The future success of this challenging design space will be dependent on our ability to develop and evaluate implants that meet the specific clinical design aspects and physiological conditions.

CHARACTERIZATION OF THE NUCLEUS ARTHROPLASTY DESIGN CONCEPTS

As noted above, there are significant challenges associated with the design of a nucleus arthroplasty implant. To improve the odds for success, each proposed design concept must be properly evaluated or characterized using preclinical experiments. Initially, the implant can be tested using several different methods to ensure that it can withstand the expected physiological load environment. In addition to isolated implant testing, cadaveric studies must be performed with the implant to determine the impact of the surgical approach and procedure. Finally, functional performance under biological conditions should be studied using *in vivo* experiments. The following paragraphs provide an overview and describe a battery of tests that may be applicable in evaluating an implant design.

Mechanical Characterization

Mechanical test standards (i.e. ISO, ASTM) for evaluating nucleus replacement devices do not exist. Using FDA guidance documents, test methods may be developed to adequately characterize the device performance. Mechanical characterization involves both static and dynamic tests. The test methods and the justifications of the test parameters (i.e. loading mode, frequency of testing, failure loads, test environment) need to be defined prior to initiation.

Static Characterization

Static testing needs to be carried out to sufficiently characterize the performance properties of the individual components and the finished device in simulated physiologic conditions. Strength testing should evaluate the robustness of the device construct and/or device under extreme loads. Testing should be conducted on both the device components (if applicable) and finished device to a representative worst-case physiologic load or to

failure, whichever occurs first. At a minimum, static characterization should address the following: single cycle strength testing, compression characterization testing, creep recovery testing, subsidence testing and hydration/polymerization rate testing.

Test Rate, Temperature and Constraint Analysis

Most of the nucleus arthroplasty devices on the market are manufactured from materials that have viscoelastic, or rate dependent, properties. Therefore, the test rate utilized in a characterization test is critical. Based on the various designs, one rate may not be appropriate. Testing needs to be performed on the individual device to identify the appropriate test rate as this could bias the test results.

The effect of temperature needs to be addressed when conducting tests on polymeric devices or tissue-based implants as device properties may vary at body temperature compared to room temperature.

For devices with unconstrained deformation that depend or expect contact with the annulus during *in vivo* use, the various tests identified below should be performed in unconstrained and confined constraints using special test setups (Figures 1 & 2). Based on implant design and intended function, the bulk properties of the implant may be greatly impacted by test constraints.

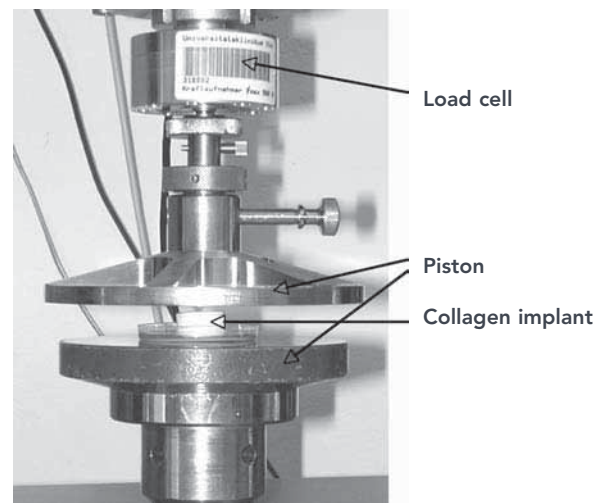


Figure 1: Unconfined testing of a tissue engineered nucleus implant in a material testing machine.

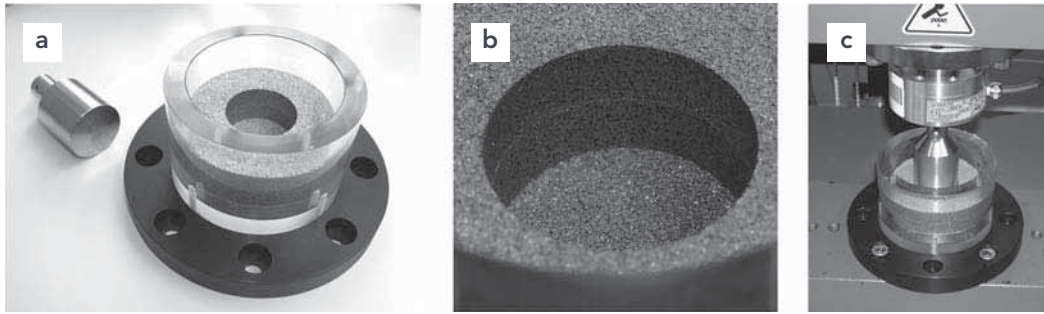


Figure 2: Confined testing of a tissue engineered nucleus implant using a porous stainless steel chamber (a, b) in a material testing machine (c).

Single Cycle Device Burst Testing

A nucleus replacement device may be subjected to extreme *in vivo* compressive loads. *In vivo* studies performed in our lab showed that the maximum load when bending over to lift a load of 20 kg with straight legs was about 4000 N.¹³ Published literature reports peak compressive loads during lifting of heavy objects to be as large as 7000 N through a vertebral segment, with approximately 15% of the load carried through the facet joints in an upright position.^{14,15} Therefore, peak loads through the anterior column are estimated at 6000 N maximum; similar vertebral fracture loads are defined in the literature.¹⁶

In the anterior column, load is distributed nearly equally between the nucleus and the annulus.^{17,18} However, based on implant design, a portion of, or all of the anterior column load may pass through the device. Therefore, depending on the load-sharing characteristics of the implant, a maximum device load between 3000 N and 6000 N is representative of a single cycle worst-case physiologic load. Upon completion of testing, the data should identify where and how device failure initiated.

Load Deflection Testing

Loads passing through the spinal column are cyclic in nature. Therefore, a nucleus arthroplasty device should ideally be able to absorb loads representative of daily living and recover upon load removal. In order to estimate how the device will function clinically, compressive load deflection testing should be performed to characterize the acute performance of the device. Relevant loads may be determined based on a review of the literature. *In vivo* research estimates a load of 200 N to represent supine disc loads, 800 N to represent relaxed standing, 2000 N to replicate standing

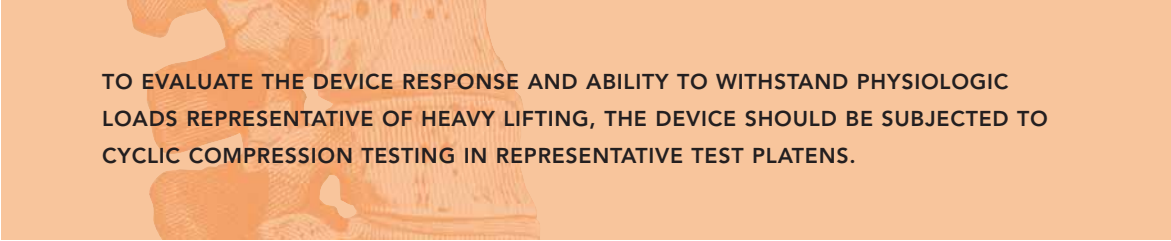
with flexion and up to 4000 N representing standing with flexion while lifting 20 kg.¹³ Based on implant design and accounting for load sharing between the facet joints and annulus, load-deflection implant characterization should be conducted to maximum load between 1700 N-4000 N to be representative of physiologic loading.

Contact Footprint and Pressure Testing

Loads applied to the vertebral bodies are transferred through a nucleus replacement device. This load transfer also occurs through the endplate-implant interface. To understand the conformability and endplate stress associated with a nucleus arthroplasty device, contact stresses should be analyzed. For characterization purposes, concave steel load platens are recommended to isolate device performance and minimize variation in cadaveric tissue. Calibrated Tekscan pressure film, or equivalent, provides a good measure of contact footprint, contact stress and conformity for characterization testing. As above, to represent a physiologic condition, testing should be conducted to 1700 N-4000 N.

Subsidence Testing

In addition to the contact footprint and pressure testing, subsidence testing in accordance with ASTM F2267-04 should be performed to determine the relative resistance of the device to subsidence in simulated cancellous bone foam. To better establish clinical relevance of the values calculated from the ASTM test, it is recommended to utilize a control device with documented clinical experience.



TO EVALUATE THE DEVICE RESPONSE AND ABILITY TO WITHSTAND PHYSIOLOGIC LOADS REPRESENTATIVE OF HEAVY LIFTING, THE DEVICE SHOULD BE SUBJECTED TO CYCLIC COMPRESSION TESTING IN REPRESENTATIVE TEST PLATENS.

Creep Recovery

Nucleus arthroplasty devices may be subjected to sustained loads; therefore, characterizing the creep recovery response is important. This test may be designed to generally comply with ASTM D2990-01 “Standard Test Methods for Tensile, Compressive, and Flexural Creep and Creep-Rupture of Plastics.” The devices should be subjected to various load ranges, load rates, and recovery times.

Dynamic Characterization

As with single cycle test rate analysis, for dynamic testing, test rate analysis should be performed prior to dynamic characterization. The dynamic testing may include load deflection hysteresis testing, compression-shear fatigue testing, and cyclic wear testing. The test methods and rationale will be somewhat dictated by device design.

Load Deflection Hysteresis

To evaluate the device response and ability to withstand physiologic loads representative of heavy lifting, the device should be subjected to cyclic compression testing in representative test platens.

Load sharing through a vertebral segment varies during activities involving flexion, extension, and lateral bending. Compressive loads during relaxed standing are reported to be 800 N and, during lifting of 20 kg objects, can be as large as 4000 N through the vertebral segment.¹³ A worst-case scenario can be established by assuming that the majority of the loads may pass directly through the device. Excluding the reported 15% compressive load sharing of the facet joints and accounting for annulus load sharing, the physiologic spinal segment compressive cyclic testing scheme representative of standing and heavy lifting is 400 N to 2000 N.¹³ Estimating that heavy lifting is performed twice a week for 20 years, each device should be subjected to 2000 peak load cycles during the course of evaluation.

Compression Shear Fatigue

Due to the small amount of torsion in the lumbar spine, it is believed that the potential failure modes in dynamic compression-shear testing exemplify the worst-case loading condition seen by a nucleus arthroplasty device.

Testing conducted at our laboratory, recorded compressive loads experienced by the disc during typical daily activities (i.e. resting, standing, sitting, walking, stair climbing) ranges from 200 N to 1250 N.¹³ During walking, we measured a compressive load of approximately 1150 N. Others have reported lumbar compression and shear loads during walking to be as high as 1850 N and 560 N, respectively.¹⁹ Shear loads in the literature are reported to be up to 1200 N at L5/S1 with more strenuous activities.²⁰ Therefore, selecting loads measured during walking as representative of physiologic cyclic loads and accounting for load distribution across the segment, a simultaneous axial compression of 925 N and 280 N shear is recommended. It is generally recommended to evaluate a minimum of six devices to a minimum of 10 million cycles.

Cyclic Wear Testing

Cyclic wear properties can vary with implant design and material choice. Limited data is currently available for such tests as they are often performed in-house during development with the results used for regulatory purposes and not publication. Local and systemic reaction from wear particulate is a risk with any implantable device. Particle size, morphology, and quantity have been demonstrated to be key factors in the body’s response to wear debris. Therefore, testing should be conducted to determine the wear debris generated over a representative device lifetime. The compression shear fatigue loading described above may be utilized to assess the durability and potential wear debris generation of nucleus arthroplasty devices. All devices should be tested in Ringer’s solution to simulate the *in vivo* environment. The Ringer’s solution should be analyzed after 5 million and 10 million cycles to characterize any wear particulate.

Cadaveric Studies

The nucleus arthroplasty device interactions with soft tissue structures (i.e. annulus, ligamentous structures, facet joints) are difficult to predict and replicate in bench tests. Therefore, upon completion of the characterization bench tests, various cadaveric studies should be performed to help bridge the characterization test results to expected clinical performance.

Details and recommendations for a standardized *in vitro* stability test, as well as information about handling of specimens, can be found in another publication.²¹

Functional *In Vitro* Flexibility Tests

In contrast to the pure mechanical tests, flexibility tests are designed with the goal of evaluating the *in situ* performance. Ideally, such evaluations incorporate the use of cadaveric specimens mounted on mechanical testing machines that produce loads that simulate the expected physiological motion (Figure 3).²²

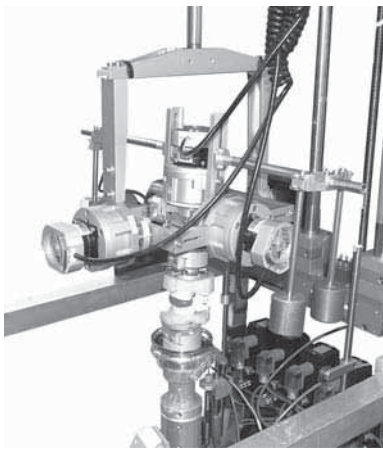


Figure 3: Custom-built spine loading apparatus to determine the functional flexibility of a cadaveric spinal segment—the simulator consists of three axes with integrated motors, gears, and clutches, which allow application of pure moments.

Testing should be carried out in flexion/extension, lateral bending, and axial rotation. After completing the basic tests, additional studies using shear loading, compression, muscle forces, and other representative *in vivo* loads may also be considered.

To assess device performance and account for potential variation in cadaveric specimens, it is recommended that such *in vitro* studies be performed for the intact, nucleotomized/degenerated, and implanted states. It is also recommended for standardization purposes that evaluations be performed under pure moments without preload.²¹

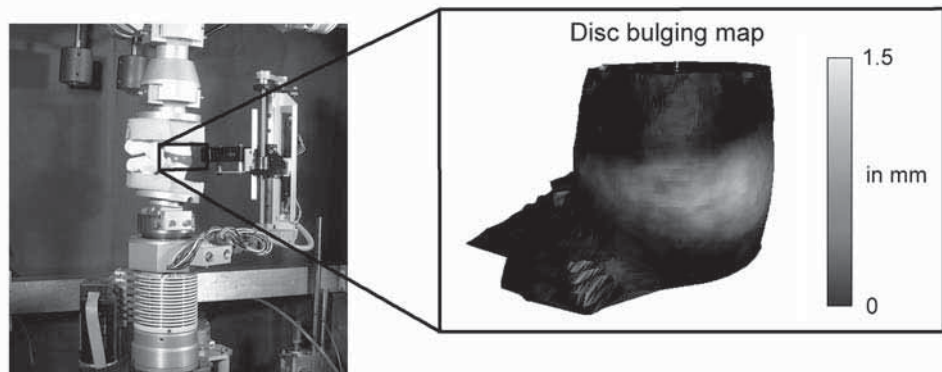
The parameters of interest are the range of motion, the neutral zone in the different motion planes, the shear translations, and the corresponding changes in height. Additionally, information such as the centers of rotation, helical axes, and load-sharing capabilities of the different spinal structures, help to provide a complete kinematic picture (Figure 4).

Test methods and corresponding results are included in Volume II of the publication series. Details and recommendations for a standardized *in vitro* stability test, as well as information about handling of specimens, can be found in another publication.²¹

Expulsion Testing

Depending on the type of device, expulsion or subsidence of the implant may be a serious problem. In order to evaluate this type of biomechanical failure, the specimens should be subjected to complex cyclic loading regime, as during daily activities, the spine is not only loaded axially, but rather eccentrically.

Figure 4: Disc bulging can be measured with a three-dimensional laser scanning device fixed in the spine loading apparatus.



TO SIMULATE THIS COMPLEX LOADING, OUR LAB HAS DEVELOPED A TEST SETUP SUCH THAT DURING CYCLIC LOADING THE SPECIMEN REVOLVES CLOCKWISE AROUND AN AXIS LOCATED IN THE CENTER OF THE VERTEBRAL BODY AT A RATE OF 360°/MIN.

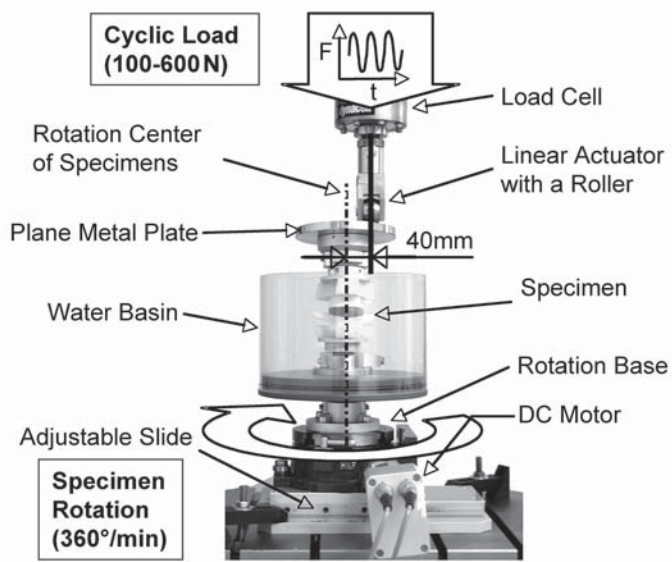


Figure 5: Setup in a dynamic material testing machine to load the cadaveric specimens cyclically with an eccentric preload (100 N-600 N, x 40 mm lever arm with 5 Hz) while the specimen is rotated around its own axis at 360°/minute.

To simulate this complex loading, our lab has developed a test setup such that during cyclic loading the specimen revolves clockwise around an axis located in the center of the vertebral body at a rate of 360°/min (Figure 5).²³ This setup provides complex motion as during testing the specimen experiences loading in flexion, left lateral bending, extension, and right lateral bending in a continual manner.

A total of 100,000 cycles at 5 Hz with an eccentric load (lever arm of 40 mm) and an amplitude between 100 N-600 N should be applied.²³ Depending on the type of implant, testing should be performed in a Ringer's solution; however, degradation of the cadaveric tissue may influence the ability to perform long-term tests (Figure 6).

Cyclic loading may also provoke subsidence or a loss in implant height which can be quantified by measuring the overall height. Measurements should be taken pre and post-loading and after every 20,000 cycles in the material testing machine (Figure 7). In order to obtain reproducible measurements, the upper plane of the PMMA block should be leveled horizontally with the specimen loaded using a standardized preload, for example 100 N axial preload. Following the cyclic test, secondary flexibility and height measurement evaluations should also be performed.

Please note that the results obtained with the suggested test setup may not correlate directly to clinical rates of device extrusion, but should serve as a basis for comparison of the relative risk profile.

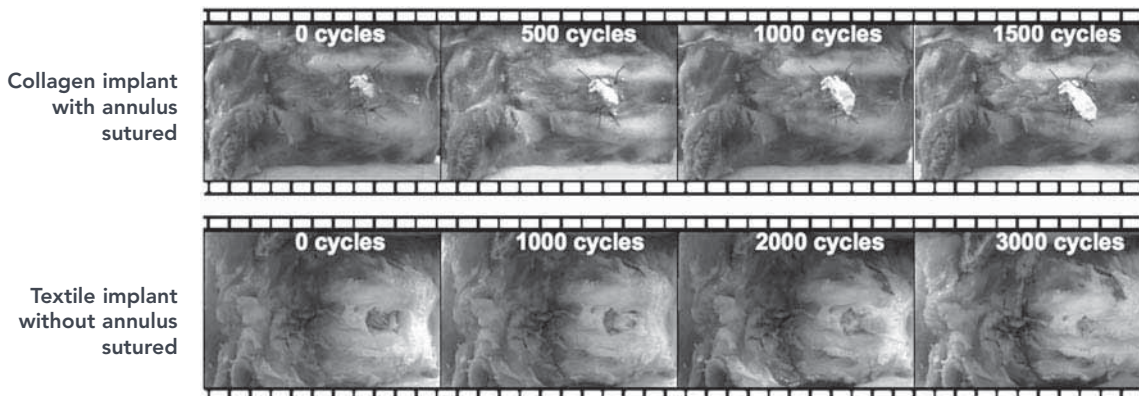


Figure 6: Examples for the process of nucleus implant extrusion (<300 cycles).

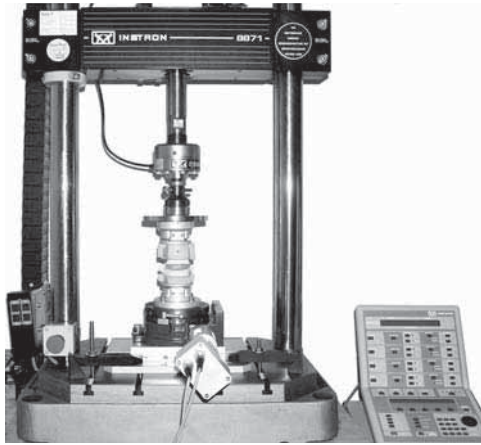


Figure 7: Height measurements should be performed under reproducible conditions, the upper vertebra should be leveled horizontally with the specimen loaded using a standardized preload.

Functional In Vivo Studies

The baboon model is considered a relevant model for the human spine based on the baboon's anatomy, physiology, *in vitro* mechanics, pseudo-bipedal gait and extremely active daily activities.^{24, 25} In addition, the results from Ledet et al.²⁵ suggest the mechanical loads in baboons are equivalent to the human spine. However, the disc space is smaller than the human spine and requires miniaturized devices for implantation. Based on the materials utilized in most nucleus arthroplasty devices, miniature devices may not have equivalent performance characteristics as those utilized for human implants. Thus, the baboon model represents a worst-case *in vivo* evaluation and has been used for numerous nucleus replacement technologies primarily to assess the safety of the device material when exposed to daily movements.²⁴ One of the primary purposes in performing such *in vivo* baboon model testing is to assess device wear generation and the

associated local and systemic histological response to any such wear debris. Other species like the sheep may also be considered, but the limitations of these models have always to be discussed.²⁶

Biocompatibility Testing

Manufacturers should consider performing all relevant tests recommended by ISO 10993-1, FDA's Blue Book Memorandum #G95-1, and possibly a carcinogenicity assay. Tests performed included cytotoxicity; sensitization; irritation/intracutaneous reactivity; acute systemic toxicity; subacute, subchronic, and chronic systemic toxicity (for general systemic and local effects); material-mediated pyrogenicity; and genotoxicity (bacterial, and *in vivo* and *in vitro* mammalian) and hemolysis.

CONCLUSION

Nucleus arthroplasty is an exciting and challenging technology and may be a promising alternative to other non-fusion concepts. While current patient demographics continue to support the need for such innovative ideas, creating a nucleus arthroplasty device requires a multi-discipline approach with respect to the design, development, and testing.

This chapter outlined the design challenges, methods of characterization, and importance of biomechanical testing. Based on the specific biomechanical demands, each type of nucleus arthroplasty device may have a target population in which it works well clinically. The challenge is to balance the biomechanics with the other surgical and pathology factors that are often difficult to identify and control.

Although the described test methods may have limitations, they provide important and useful information during development and may provide relevant findings prior to clinical application. Nevertheless, even if a particular implant performs well in the lab, the ultimate test of the biomechanical data will be the clinical outcomes.



BASED ON THE SPECIFIC BIOMECHANICAL DEMANDS, EACH TYPE OF NUCLEUS ARTHROPLASTY DEVICE MAY HAVE A TARGET POPULATION IN WHICH IT WORKS WELL CLINICALLY. THE CHALLENGE IS TO BALANCE THE BIOMECHANICS WITH THE OTHER SURGICAL AND PATHOLOGY FACTORS THAT ARE OFTEN DIFFICULT TO IDENTIFY AND CONTROL.

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