

The future of spinal arthroplasty: a biomaterial perspective

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Both total hip and knee arthroplasty have demonstrated outstanding clinical results. The functional spinal unit composed of the intervertebral disc and facet joints is at least as complex. The intricacies of the coupled motions of the functional spinal unit have made development of an artificial disc a challenge. There have been several failed attempts to create a disc replacement that recapitulates normal motion while providing significant longevity and a low incidence of complications.

Better understanding of the biomechanics of the intervertebral disc complex and improvements in implant material have made successful intervertebral disc replacement a likely reality, now that several artificial discs have completed Food and Drug Administration clinical trials. In this manuscript the authors detail the biomaterials used in disc arthroplasty and discuss joint wear and the host response to wear debris.

**KEY WORDS • cervical vertebra • degenerative disc disease • herniated disc •
intervertebral disc • joint prosthesis • spinal fusion • spinal arthroplasty**

The concept of disc reconstruction with a prosthetic device that maintains motion and alignment is not new; attempts at disc replacement date back to the 1960s. As a result of both a process of trial and error and an analysis of biomechanics, disc replacement will soon be clinically available. The use of arthroplasty eliminates the need for fusion and theoretically prevents abnormal stress at adjacent levels. If adjacent-segment degeneration could be reduced, spinal arthroplasty would have a distinct advantage over arthrodesis. The purpose of this paper is to review the design of disc prostheses, the materials used for their manufacture, and technical concerns that remain regarding their in vivo degradation and the potential immunological response.

OVERVIEW

Theory of Spinal Arthroplasty

The belief that spinal fusion leads to accelerated degeneration of adjacent disc levels is widely held. A new direction in treating degenerative disc disease surgically is the development of a functional disc prosthesis that offers the same benefits as fusion while providing motion and protecting adjacent-level discs.^{34,40} Keeping in mind that any new device or arthroplasty in the future should provide relief from objective neurological symptoms and signs, provide stability, withstand biomechanical forces, reduce pain by excision of the nucleus pulposus, and still provide

normal range of motion, we have reviewed the available devices and those awaiting imminent approval.

To date, disc replacement design technology has produced two types of prostheses, the unconstrained and the constrained. The unconstrained model has a core bearing that permits rotation and some degree of translation in all three anatomical axes (x, y, and z). In contrast, constrained devices have a fixed axis of rotation such that both the x- (anteroposterior) and y-axis (medial to lateral) translations are limited, but there are no restrictions in rotational motion. The constrained design concept is thought to minimize x-axis (anteroposterior) movement at the treated facet level, potentially reducing stresses on these structures.

Theoretically, the use of a prosthetic disc preserves the normal range of motion in the interspace and protects against adjacent-level degeneration. It should be understood, however, that accelerated degeneration caused by increased stress at adjacent disc levels after fusion has only been postulated; it has not been documented or proven experimentally. Whether this theory is accurate or whether adjacent-level disease reflects the natural disease process is unclear at this time.

Normal Disc Anatomy, Physiology, and Degeneration

The intervertebral disc is a structure consisting of a peripheral collagenous band (anulus fibrosus) uniting adjacent vertebral endplates. In the center lies the nucleus pulposus, composed of a mucopolysaccharide gel and

proteoglycans. Peripherally the annulus is a collagenous band composed of 15 to 20 concentric layers of alternating oblique fibers. The highly complex structure of the disc allows small movements along the x, y, and z anatomical axes. The alternating arrangements of collagen fibers in the annulus fibrosus make an efficient system to control motion, especially rotation, while still providing stability.

Degenerative disc disease has some similarity to degenerative joint disease such as arthritis of the hip, but it also has unique features. In its early stages the hydrophilic properties of the nucleus are diminished. The annulus also develops tears and loses ability to contain the nucleus. Later the bone endplates become sclerotic and irregular and eventually resemble the end stage in any diarthrodial joint degeneration. The origin of pain in the degenerative spine is complex and less understood than in peripheral joints that have degenerated. It is believed that both the annulus fibrosus and nucleus pulposus contribute to the generation of spinal pain; removal or surgery extensive enough to alter these structures significantly is thought to relieve pain.

Biomaterials Used in Joint Replacement

Disc arthroplasty designs have been heavily influenced by orthopedic joint arthroplasty, with the majority of recent designs using a combination of polymers and metals.^{1,3,4,8,12,13,16,44,45} Polymers provide a low-friction surface for articulation as well as some degree of “shock absorption.”⁶⁷ Metals provide a base of support for the polymer surfaces as well as a surface for fixation to bone to be done. Currently in orthopedics, there are three principal metal alloys used in joint replacement technology: titanium, cobalt, and stainless steel. These all have desirable mechanical properties such as high tensile strength and corrosion resistance, and some have been used for disc arthroplasty.

Factors determining disc arthroplasty survivability are similar to those for joint replacement technology, and include prosthetic wear, formation of wear debris, and tissue reaction to the wear debris. Particulate debris generated by wear stimulates the formation of an inflammatory reaction, which promotes a host-tissue response that has the ability to invade the bone-implant interface.^{2-23,27-31,48,50-64,66} This commonly results in progressive local bone loss that threatens the fixation of implanted devices. Despite their high resistance to corrosion, all metal alloy implants corrode in vivo. When this degradative process is severe enough it can damage the structural integrity of the implant, and corrosion products are potentially toxic.^{1,5-7,9,14,16,18,24,33,37,46,49,50,56,57,59-64,70} Disc replacement designs incorporate cobalt-chromium-molybdenum alloy endplates that are externally coated with titanium for bone ingrowth. The metallic endplates are fixed to polymeric cores and motion takes place between articulating polymer surfaces.

Corrosion resistance is important in selecting metals for disc arthroplasty. Alloys are protected from the progressive degradation of corrosion by the formation of a protective surface oxidative film.^{1,4} The Laplace law, a discussion of which is beyond the scope of this article, can be used to predict the behavior of the metallic surfaces in an in vivo fluid environment.¹ Nevertheless, based on data from the Laplace law and other complex physical, chemical, and material science computations, many joint arthro-

plasties are performed with a cobalt-chromium-molybdenum alloy.

Surface Coatings

Several surface coatings have been designed to improve bone ingrowth. These include titanium, porous cobalt-chromium or titanium beads, titanium wire mesh, plasma-sprayed titanium, and newer bioactive nonmetallic materials such as hydroxyapatite or other calcium phosphate compositions that have been developed to create a tighter interdigitation between implant and bone. This minimizes motion at the implant-bone junction as well as corrosion.

Wear Analysis

Based on studies of failed devices used in orthopedic joint replacement surgery, it has been determined that prosthetic debris is the leading factor causing prosthetic loosening and requiring revision surgery. Wear debris is formed over time with any prosthesis. All wear debris causes a foreign-body reaction that induces an inflammatory response, which results in progressive local bone loss (osteolysis) and possible prosthetic loosening and failure.^{2-23,27-31}

The mechanism of debris generation involves the loss of particles from the prosthesis as a consequence of friction between moving surfaces. Any articulating materials, if placed under a sufficient load, will generate debris. The wear rate can be calculated using the following formula: $V = KFx$, where V is volumetric wear (mm^3/year), K is a material constant of the material couple, F is the contact force, and x the distance of travel (in millimeters).³² The harder the material the less it will wear, and if different materials are articulated, the harder of the bearing materials will wear less rapidly. In a metal-on-polymer pair, the polymer wears almost exclusively, whereas in a metal-on-ceramic pair, the metal wears to a greater extent. Volumetric wear can be directly related to the number of particles released in vivo.

Clinical wear rates have been seen to increase in patients with hip replacements, based on the patient's weight, the geometry and size of implants, and the mechanical properties of implant materials. There is limited information regarding pure metal wear in spinal arthroplasty. Nevertheless, in a recent study reported by Hellier, et al.,⁴⁰ the authors showed that the best metal for minimizing wear was the cobalt-chromium-molybdenum alloy. This alloy provided for the smallest amount of wear debris, with a mean wear volume rate of 0.09 to 0.126 $\text{mm}^3/\text{million cycles}$ in wear simulation with lumbar disc replacement. If one assumes that 1 million simulator cycles is representative of 1 year of clinical use, the rate of wear per year is estimated to be 0.96 mm^3/year . This compares very favorably (two orders of magnitude less) to wear observed in orthopedic joint arthroplasty. For example, numerous clinical studies have shown wear rates ranging from 50 to 100 mm^3/year in hip arthroplasties.² From these studies it appears that wear degradation in disc arthroplasty will not be as big a problem as it is in hip replacement. It is a concern, however, that wear debris and any resultant inflammatory reaction would occur in close proximity to neural structures.

The Charité artificial disc (Depuy Spine, Inc., Rayn-

ham, MA) was originally developed at the Charité Clinic in Berlin, Germany. In 1982, through cooperation between leading orthopedic spine specialists and the staff at Waldemar Link GmbH, a European medical device manufacturer based in Hamburg, Germany, the first artificial lumbar disc was implanted. The Charité consists of two endplates made with a cobalt-chromium alloy enclosing an ultra-high molecular weight polyethylene core.

Recently, Anderson and colleagues² performed an in vitro wear test of the Bryan Cervical Disc prosthesis (manufactured by Spinal Dynamics Corp., Seattle, WA [a division of Medtronic, Inc., Minneapolis, MN]) in a cervical spine simulator. Biological response to wear was assessed in chimpanzee and goat animal models. These researchers showed that particulate wear generation took place at the rate of 1.2 mg/106 cycles, with the loss of prosthetic height occurring at 0.02 mm/106 cycles in vitro. This compared favorably with orthopedic joint replacement in vitro data. Wear debris was present in the periprosthetic and epidural spaces in some animals. More importantly, there was no significant inflammatory response observed and no wear material was found distant from the implant in draining lymph tissue, the liver, or the spleen. As a result, the investigators were able to conclude that the Bryan disc has satisfactory wear characteristics and does not produce a significant inflammatory response.

The Prestige disc (Medtronic, Inc.) is not made from the metal-on-polymer articulation that other designs use and instead features metal-on-metal articulation, in which endplates and articulating surfaces are constructed of stainless steel or titanium. The design of metal-on-metal was used to eliminate polyethylene wear debris, which generates a more aggressive inflammatory response. A downside to this type of articulation is that the amount of metallic debris generated is several orders of magnitude higher than a metal-on-polymer articulation produces. Patients with metal-on-metal hip replacements have been reported to have nine times the level of chromium in the serum, a 35-fold increase in levels of chromium in the urine, and three times the level of cobalt in the serum.⁴⁶

Corrosion, Metallic Wear, and the Host Immune System

All metals implanted into a biological system corrode and release metal ions.⁶²⁻⁷³ The more motion there is in a prosthesis-bone interface, the higher the rate of corrosion due to continual degradation and reformation of new oxide layers that have no protective coating against degradation. Metal-on-metal articulating surfaces are also a major source of released metal ions. As a result, the immune system can be activated and microscopic implant particles released by corrosion also become embedded in local tissue and are recognized by the host immune system.⁶¹⁻⁷³ These particles are bound by proteins and are eventually transported to immune tissue. Although most implant alloys are chemically inert elements, in vivo they can become toxic through biochemical conversion. They can be converted through a series of immunological interactions to form metallic moieties forming haptens, which can elicit an immunological reaction.^{58-69,71-73}

Stainless steel alloys corrode the most of all alloys used in arthroplasty.^{8,11-13,34} In recent studies investigators have found that there is an eightfold increase in the incidence of

corrosion when dissimilar metal junctions are used, compared with only 7% of cases studied in which similar metal junctions were implanted.²⁶ The results of these studies indicate that the actual material can play an important role in corrosion and that we need to evaluate carefully the effects of different metal alloys and the impact they have on the host immune system.

Nickel, cobalt, and chromium are essential trace elements that are required for normal homeostasis. In larger amounts than has ever been documented to be associated with surgical arthroplasty, nickel leads to dermatitis and is carcinogenic.^{37,38,46,49} Cobalt is known to cause polycythemia, thyroid dysfunction, cardiomyopathy, and is carcinogenic.^{56,59} Chromium and vanadium can cause both cardiac and renal dysfunction as well as psychosis. The nonessential metallic alloys can also be toxic. Titanium can induce pulmonary disease in people with inhalational exposure as well as platelet dysfunction.^{56,59,61,62} Aluminum produces bone marrow suppression, renal failure, and neurological dysfunction, possibly including Alzheimer disease. These toxicities result from extremely high circulating concentrations of the elements or their inhalation, and it is unlikely that such levels would result from prosthetic implant degradation.^{37,38,46,49,56,57,61,62} There is no study to date that demonstrates a cause and effect relationship between arthroplasty devices and toxic levels of metal release, but these data should not be forgotten.

There are several cell types, including macrophages, osteoblasts, osteoclasts, fibroblasts, and endothelial cells as well as immune cells that are stimulated by the corrosion particles.^{15,31,58} In recent studies investigators have evaluated the effect of spinal hardware debris on local tissue and its effect on fusion.¹⁵ Early case reports of aseptic inflammation associated with posterolateral fusion surgery in which stainless steel hardware was used were initially thought to be late infections.¹⁰ Nevertheless, histological studies proved otherwise, with findings of granuloma formation and a Type IV delayed hypersensitivity response. The inflammation around spinal implants eventually leads to formation of an inflammatory zone adjacent to the implant that contains a number of mediators and cell types that can effect bone turnover and cause osteolysis.⁵⁸

There are a few in vivo investigations in which the effect of metal debris from spinal implant fixation has been measured.^{25,34-36,39,41-43} The concept of an inflammatory zone that surrounds spinal instrumentation undergoing wear or corrosion has been demonstrated clinically and by laboratory investigation as well.³¹ In animal studies it has been shown that local inflammatory mediators like tumor necrosis factor- α are upregulated.⁵⁵ This factor acts as a chemokine to recruit neutrophils and monocytes to the site of release and to stimulate macrophage release of inflammatory cytokines in the spine.^{65,66}

Finally, normal bone homeostasis is an intricate balance between bone formation and resorption mediated by osteoblasts and osteoclasts.^{68,69} Fibroblasts exposed to wear debris can disrupt this balance by resorbing bone and causing osteolysis. In recent studies researchers have shown that particulate debris may also suppress osteoblast function.^{47,72,73} In osteoblasts exposed to titanium debris, there is diminished expression of collagen Type I and III precursors.⁷²

CONCLUSIONS

With the emerging technology of spinal arthroplasty, a variety of new clinical problems may arise in the very near future. The purpose of this paper was to review the design of disc prostheses, the materials used for their manufacture, and technical and theoretical concerns that remain regarding their use in vivo. We have focused on the effects of particulate and ionic debris associated with spinal implants. Meticulous clinical follow-up evaluation of these patients will be necessary to identify not only gross mechanical failure but also less obvious loosening associated with a debris-induced immune response. In addition, we will have to continue to monitor potential systemic effects resulting from disc arthroplasty vigilantly, as is currently done for similar orthopedically implanted materials.

Disclaimer

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