Applications of a Resorbable Interbody Spacer via a Posterior Lumbar Interbody Fusion Technique

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Abstract

Polyhydroxyacids are a promising class of bioreabsorbable materials with potential applications in spinal surgery. One such polymer, MacroPore (MacroPore Biosurgery Inc, San Diego, Calif), offers a balance of strength, predictable degradation, lack of stimulus of foreign body reaction, and biocompatibility with neural tissue. MacroPore can be formed into an array of shapes and can be manufactured, sterilized, and stored with conventional techniques. Limited clinical experience has been gained with bioreabsorbable implants that are used as load-sharing devices in a posterior lumbar interbody fusion construct.

Implants placed during spinal fusion surgery have several functions. Pedicle screw rod or plate systems utilized in conjunction with a posterior intertransverse bone graft maintain spinal alignment and provide immediate structural stability, therefore allowing early mobilization of the patient while promoting arthrodesis. The bone graft is not under compression and there is significant stress on the hardware, particularly in the presence of deficient anterior column support.1 Both of these factors may contribute to some of the failures seen after spinal fusion surgeries. On the other hand, a bone graft or spacer device placed in the anterior column can function both in a direct load-sharing manner and to provide temporary segmental stability through distraction of a disk space with the resulting tensioning of the annulus fibrosus.1 Such an interbody spacer can be placed through anterior, lateral, posterior, or transforminal surgical approaches, utilizing both open and endoscopic techniques. Although stand-alone procedures are still performed, interbody constructs are generally supplemented by posterior instrumentation, a “360° procedure,” and high rates of fusion have been reported with these techniques. Regardless of the manner of insertion, the spacer must function until the formation of a solid bone bridge through the former disk space is complete.2,3

A variety of materials have been explored for use in filling the defect that results after preparation of the disk space for interbody grafting. The “gold-standard” has been autologous iliac crest graft, which has osteoconductive and osteoinductive properties in addition to its structural function. In many cases, there may be inadequate bone remaining because of previous graft harvest. Iliac crest may not be strong enough for the planned construct (especially in the elderly or osteoporotic patient) and the harvest of an adequate sized graft may not be possible. In addition, there has been appreciable morbidity and long-term pain associated with iliac crest harvest.4 Allograft bone has been used for this purpose, but concerns of infection and graft strength remain (depending on the methods of harvest and processing). Also, problems of inadequate supply in some countries and cultural prohibitions against allograft in other countries make this option less desirable.

Both titanium alloy and stainless steel have been shaped into a variety of spinal implants. Although both of these metals have performed well in primary function, there are drawbacks such as stress-shielding due to the excessive rigidity and permanence of the constructs that can in turn lead to bone resorption and osteopenia.5,6 Corrosion, wear debris, and rare allergic reactions
used in orthopedic trauma surgery, craniomaxillofacial reconstruction, and drug delivery systems.\textsuperscript{2,9} Biodegradable materials must not induce significant inflammatory reactions, must not be carcinogenic, mutagenic, or teratogenic, and must not cause allergic or toxic responses.\textsuperscript{3,9} Fashioned into an implant, the material must maintain adequate biomechanical properties for a length of time suitable to its function in the construct.\textsuperscript{2} The material should degrade at a rate that allows for the metabolism and clearance of the byproducts. Ideally, the material should be able to be shaped, stored, and sterilized using common techniques.\textsuperscript{5}

Polyhydroxyacids are polymers that are the best known and most studied resorbable materials for implantation. The mechanical and physical properties of polyhydroxyacids depend on the constituents of the polymer.\textsuperscript{5} The primary degradation is caused by the mechanism of random, bulk hydrolysis of the ester bonds between the molecules of the chain. The monomeric acids that result from this process are subsequently metabolized via the Krebs cycle to carbon dioxide and water (Figure 1).\textsuperscript{3,5} As degradation proceeds, the implant will begin to fragment, with the expected loss of strength. Once the polymer has been reduced to fragments of low molecular weight, there can also be a variable contribution of phagocytosis and enzymatic activity in the final degradation of the material.\textsuperscript{10}

The most common polyhydroxyacids are composed of polyactic acid (PLA), polyglycolic acid (PGA), or a mixture of both, although there are many other closely related compounds that have similar characteristics.\textsuperscript{5} No significant toxicity, carcinogenicity, teratogenicity, or mutagenesis has been associated with either PLA or PGA.\textsuperscript{3,9}

The implant resorption time is most affected by the chemical composition of the polymer, but there are many additional variables in this process.\textsuperscript{2,9} Gogolewski\textsuperscript{5} has identified the physical structure and mass, polymeric molecular weight, chain orientation, and presence of additives of the implant as factors influencing the rate of degradation, along with the stress on the implant and the characteristics of the implantation site. For example, an implant placed under significant load in a highly vascularized site will likely degrade at an accelerated rate.\textsuperscript{5} Generally, PGA polymers degrade more rapidly than PLA polymers, with copolymers being intermediate.\textsuperscript{9} The specific requirements of the implant depend on which polymer is preferable.\textsuperscript{5}

The mechanical properties of the implant are determined by the conditions of the synthesis and processing of the polymer, along with the other factors that have already been discussed.\textsuperscript{2,5} Implants with better mechanical properties such as bending strength or elastic modulus tend to take longer to resorb.\textsuperscript{5} The ideal polymer or implant depends on the demands of the particular application for which it is designed. Local tissue reaction to polyhydroxyacid implants is governed by the chemical nature of the polymer, the physical characteristics of the implant, and its degradation rate. Towards the latter part of the degradation process, the implant may lose structural integrity, and the production rate of polymeric debris may exceed the tissue tolerance and transport potential of the implantation site.\textsuperscript{3,9} In turn, this can stimulate a “nonspecific foreign body reaction” rather than a true inflammatory response.\textsuperscript{1,2} Therefore, a large implant made of a fast-degrading polymer is likely to produce a more pronounced inflammation than a small implant composed of a slow-degrading polymer. Polyglycolic acid polymers have been associated with a higher rate of tissue reaction,\textsuperscript{5,22} including the formation of fibrous capsules, sterile cysts, and sinuses. On the other hand, pure PLA polymers have a low or nonexistent rate of tissue reaction, whereas copolymers are intermediate.\textsuperscript{3}

Polyactic acid polymers and PLA-PGA copolymers are biocompatible
with the dura. Polyactic acid biocompatibility has also been specifically tested in reference to neural tissue, including brain and spinal cord tissue as well as peripheral nerves. No effect on neuronal cells, nonneuronal cells, or axonal growth has been noted.

**PLA Polymers and HydroSorb**

Polyactic acid is found in two distinct forms, poly(L-lactide) (PLLA) and poly(D,L-lactide). The PLLA form is characterized by a high crystalline content, high strength, and a prolonged resorption time, while the D,L-lactide form has lower strength and more rapid degradation. Variations in the ratio of these forms in a single copolymer will significantly influence the strength and degradation characteristics of the resulting material. HydroSorb (Medtronic Sofamor Danek, Memphis, Tenn) is a noncrystalline copolymer with a 70/30 ratio of poly(L-lactide) to poly(D,L-lactide).

HydroSorb is characterized by a degradation time of 18-36 months. The loss of strength during degradation has been well characterized and is predictable (Table 1). However, the strength and degradation characteristics of any specific HydroSorb implant will be influenced by the manufacturing processes, implant size and geometry, and characteristics of the implantation site, among other factors. HydroSorb can be formed into a variety of shapes, and it can be stored and sterilized using conventional techniques. HydroSorb can be heated and shaped for conformation to the actual site of implantation, and it will hold the desired shape once cooled without loss of structural integrity.

HydroSorb devices cannot be readily visualized on routine radiographic studies, although the devices can be seen distinctly on computed tomography scans prior to significant degradation. Polyactic acid implants do not degrade magnetic resonance images (MRI), and MRI scanning has been used to evaluate the tissue response of PLA implants. Polyactic acid implants are visible on MRI images as areas of homogeneous low-signal intensity, which can be distinguished from the high-signal intensity of the adjacent bone.

**EARLY CLINICAL EXPERIENCE WITH BIORESORBABLE IMPLANTS**

HydroSorb sheets have been used to reconstruct iliac crest donor site defects. Iliac crest reconstruction may diminish pain, prevent bowel herniation through large defects, improve cosmesis, and improve donor site regeneration. The benefits of a protected healing space have been recognized in promoting optimal bone healing. Specifically, if soft tissue is prevented from prolapsing into a bone defect, the regrowth of bone may be better than with graft materials alone. In terms of the iliac crest, once the bone is harvested, the donor site is backfilled with allograft or bone matrix material if desired. A Macropore sheet is then heated to 70°C, contoured to the defect site, and allowed to cool. It is then secured with screws or tacks. This is an example of the potential use of Macropore as a barrier type of implant.

Limited experience has been gained in the use of HydroSorb as a load-sharing device in spinal fusion constructs. The authors have previously reported the off-label use of HydroSorb cement limiters in an instrumented PLIF construct in 15 patients. All patients had symptomatic, one-level lumbar spondylosis or grade I spondylolisthesis, had failed conservative treatment, and were deemed to be candidates for a fusion procedure. Cement limiters are plugs that are placed in the medullary cavity of a bone adjacent to an arthroplasty to block unwanted spread and allow pressurization of polymethylmethacrylate cement, and improve the performance of the implantation of the intramedullary device. Cement limiters have been manufactured in a variety of materials and are available in a range of shapes and sizes. Recently, experience has been obtained with the use of biodegradable cement limiters in the femur during hip arthroplasty, which seem to perform as well as those made of nonresorbable materials.

In this PLIF application, the devices are placed bilaterally in a manner similar to impacted allograft bone, following appropriate bony decompression, complete disectomy, and disk space distraction. Marselized allograft bone is packed both within and around the devices. Preliminary results show equivalent clinical outcomes at 6 months to those obtained with a historical cohort of patients with allograft bone spacers, and ongoing follow-up of these patients has now reached 1 year with the same conclusion (unpublished data). The devices produce no artifact on postoperative imaging, allowing better visualization of the maturing bone fusion. Serial radiographs demonstrate maintenance of the disk space height during the early phase of bone healing, consistent with the known rate of degradation of this material.

**DISCUSSION**

Ralph Cloward, MD, was one of the first surgeons to both recognize and apply the advantages of interbody fusion in the treatment of lumbar degenerative disease, beginning in the 1940s. He was able to achieve successful fusion rates using either autograft or allograft placed via a PLIF technique. Although his results have been confirmed by other surgeons, the "carpentry" involved in his
technique was demanding and it was never widely adopted within the spine surgery community. With the introduction of posterior instrumentation systems, this technique was abandoned. In the 1990s, better understanding of the biomechanics of the spine, growing dissatisfaction with both clinical and radiological outcomes of posterior intertransverse fusions in the treatment of degenerative spondylosis,
and and the regulatory status of the pedicle screw led to a renewed interest in the interbody fusion.

Difficulties with obtaining adequate autograft or allograft and with the need for considerable time-consuming, precise shape and insertion of the grafts in the traditional technique spurred a search for more reproducible alternatives. Successful outcomes obtained in preclinical studies with the use of stand-alone, titanium cylindrical cages placed via a PLIF technique led to rapid Food and Drug Administration (FDA) clearance and widespread adoption of this procedure.

In some cases, strict patient selection criteria and careful adherence to recommended insertion protocols were not followed, which led to an unexpectedly high construct failure and revision rate. The titanium nature of these devices made revision and removal challenging, as well as hampered the assessment of the progression of fusion.

In response to these complications, the traditional technique of allograft PLIF has been modified. Preformed cortical allograft bone grafts have been developed, along with specialized instrumentation systems that facilitate safe and precise insertion. Similar to the allograft anterior lumbar interbody fusion procedure, these grafts are supplemented with autograft and segmental fixation devices, and high rates of fusion have been reported.

Fusion assessment is easier without the metallic artifact in the disk space. A critical shortage of suitable allograft bone continues to hamper the spread of this technique in the United States. Worldwide, cultural and supply-related problems exist with the use of allograft. For these reasons, a search continues for synthetic materials with the necessary characteristics.

Extensive experience has been gained with polyhydroxyacid implants in Europe, particularly in orthopedic trauma applications. In spinal applications, bioresorbable materials can serve as interbody spacers and fixation devices. In both applications, once the support or tension-band functions have been fulfilled and the fusion has matured, the "hardware" has no further function and hinders imaging studies by the creation of artifact. The biomechanical demands on an interbody spacer are considerably less than that of a fixation screw-plate construct. The gradual degradation of an interbody graft may promote arthrodesis by exposing the maturing interbody bone to increased load sharing. This is opposed to the stress riser at a screw-rod junction, which may significantly alter the expected local degradation rate of the biopolymer and lead to sudden "catastrophic" failure of this type of implant.

**SUMMARY**

The versatile nature of bioresorbable material allows it to be formed into cages, dowels, and interbody spacer shapes. In addition, its desirable strength and degradation characteristics, lack of artifact on imaging, low potential for foreign body reaction, and the biocompatibility with the dura and nervous tissue make it a promising material for this application. Although the challenges are greater, it is likely that resorbable polymers can be developed into other spine fixation systems. Because such implants may have to be bulky to meet biomechanical needs, there may be problems with the possibility of foreign body type reactions in the terminal degradation phase. Early potential applications in the spine might be screws for C1-C2 transarticular, lumbar trans-facet, or odontoid fixation, as well as interference screws for anterior interbody grafts. Small, nonconstrained plating systems intended to provide a cervical tension-band effect can also be envisioned.

**REFERENCES**

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EDITORIAL COMMENT
ORTHOPEDICS: Intuitively, the optimum interbody spacer would be a device that provides immediate rigidity, maintains foraminal distraction, and allows osteointegration either along its border (macrointegration) or throughout the spacer. Bioresorbable implants theoretically possess many of these requirements but also offer the ability to resorb completely through normal biologic processes. This obviates the potential complications of long-term implant migration, issues of image degradation, and many of the technical difficulties of revision surgery. Issues regarding biocompatibility, implant resorption time parameters, and biomechanical strength parameters are being investigated. It is important that the reader understand that the science of resorbable implants in spinal surgery is in its infancy. Currently in the United States, the authors have used bioabsorbable technology in an off-label or investigational manner when they use it as an interbody spacer. The product used by Dr. Alexander and colleagues is cleared by the FDA for use as a cement restrictor in orthopedic surgeries of the femur and tibia in hip and knee replacements.