The use of bioabsorbable implants in spine surgery

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The use of bioabsorbable implants in spine surgery is expanding at a rapid pace. These implants are mimicking the roles of traditional metallic devices and are demonstrating similar efficacy in terms of maintaining stability and acting as carriers for grafting substances. Biomechanical studies have demonstrated their ability to stabilize effectively a degenerative cervical and lumbar motion segment. In numerous animal models, researchers have illustrated the ability of bioabsorbable implants to function satisfactorily as an interbody spacer and to achieve satisfactory bone fusion. Investigators have explored various opportunities for these implants to replace their metallic counterparts in clinical studies conducted in humans. The gradual resorption of these implants appears effectively to transfer gradual loads to the grafting substances promoting the biological mechanisms of fusion.

Novel uses of bioabsorbable technology are constantly evolving. Their future as a carrier of biological agents such as bone morphogenetic proteins and bone graft extenders, their radiolucency, and their eventual resorption make them an ideal implant for use in spinal degenerative disease.

**KEY WORDS** • spinal surgery • bioabsorbable implant • polylactic acid • polyglycolic acid

Since the first description of bioabsorbable technology for clinical applications in the mid-1960s, the diversity and potential for widespread applications of these polymers continues to evolve.14 Bioabsorbable implants have been used successfully in craniomaxillofacial, neurological, general surgical, and orthopedic procedures.24 Their use continues to increase in orthopedic subspecialties such as sports medicine, foot and ankle surgery, shoulder surgery, and in the specialty of spine surgery. The evolution of bioabsorbable material has paralleled the development of spinal instrumentation systems, and the merging of the two technologies has expanded the surgical armamentarium of the practicing spine surgeon.

Alpha-polyesters are the bioabsorbable materials used in current clinical applications. The two that have had the most widespread use are polylactide and polyglycolide. The breakdown products of these two materials, glycolic acid and lactic acid, are familiar to the physiological milieu of the body. Polyglycolic acid, which was the first to be widely studied, degrades at a faster rate than polylactic acid.6,11,18,29 As a result, polyglycolide has demonstrated an increased risk of aseptic inflammatory reaction compared with polylactide. Different compositions of bioabsorbable products alter the rates of degradation and strength of the devices. Polylactide has been used in both a pure levo form and in a levodextro copolymer form. A combination of its stereoisomers has decreased the soft-tissue reaction to the implant in animal studies (Fig. 1).

Bioabsorbable technology offers many distinct advantages over conventional metallic devices that are currently being used in spine surgery. First, these implants allow optimal postoperative radiographic evaluation because of their radiolucency and the absence of artifacts associated with similar metallic devices exposed to advanced imaging modalities. Bioabsorbable implants also may offer advantages with respect to fusion healing because of their unique biomechanical properties. With a modulus of elasticity closer to that of bone and with its gradual resorptive properties, bioabsorbable implants gradually decrease the stress shielding seen with rigid metallic implant systems. Flexible and less rigid bioabsorbable implants confer the advantage of stabilizing the motion segments while, over time, allowing a greater transfer of load to the host spine during implant resorption, potentially minimizing junctional degeneration. Although complications such as implant migration, subsidence, and extrusion may still exist with these implants, it obviously becomes less of a problem over time as the devices dissolve into their biochemical environment.

**Biomechanical Studies of Bioabsorbable Implants Used in Spine Surgery**

Numerous studies of bioabsorbable implants have been conducted to determine the unique biomechanical properties of these devices. Ideally these implants are intended to mimic the biomechanical properties of their metallic and tricortical allograft counterparts. These implants should be able to stabilize the spine initially, allowing fusion healing to occur prior to their resorption, while exposing the graft substance they contain to continuous compressive loads in the setting of an interbody implant.
Van Dijk, et al., evaluated the compression strength and mechanical properties of titanium lumbar interbody cages compared with resorbable PLLA cages. The authors postulated that bioabsorable implants had a potential advantage over metallic implants because their modulus of elasticity is closer to that of vertebral bone. Therefore, if the compressive strength of these implants were sufficient, their use would be more beneficial than traditional metallic implants, which have a significantly higher modulus of elasticity and thus a greater potential for implant subsidence. In this investigation, 21 goats underwent a single-level lumbar interbody fusion with either a metallic cage implant or a stiff or flexible PLLA cage. At harvesting, the bioabsorbable cages proved to be mechanically satisfactory for interbody use. Compression strength of the motion segments did not differ between the stiff and flexible PLLA cages. Interestingly, the toothed titanium cages filled with bone graft showed significantly less compression strength compared with the stiff PLLA cages and bone graft. This finding was not observed in the group treated with smooth (nontoothed) titanium cages. The authors concluded that PLLA is an effective polymer for use in lumbar interbody fusion because it stabilizes the motion segment and facilitates an adequate fusion response (Fig. 2).

In a biomechanical study in which human cadaveric specimens were used, DiAngelo, et al., evaluated the use of a bioabsorbable anterior lumbar plate combined with a traditional metallic cage in anterior lumbar interbody fusions. The goal of their study was to determine if the addition of an anterior bioabsorable plate improved the biomechanical stability of the fusion construct. The addition of a bioabsorbable plate was found to decrease interspace motion in extension, flexion, and right lateral bending over the intact nonfused (no cage) specimens. The specimens with anterior plates demonstrated significantly decreased extension motion compared with nonplate-treated specimens stabilized with cage implantation. The investigators suggested that the increased stability afforded by the addition of an anterior absorbable plate should increase the fusion rate over nonplate-treated cage fusions. Also, with the recreation of the anterior tension band (the anterior longitudinal ligament is largely sacrificed with this approach), the need to augment this surgery with posterior instrumentation may be diminished in certain clinical situations. Additionally, the use of a bioabsorbable plate at the L5–S1 anterior interspace, in proximity to the great vessels, may lessen the risk for vessel erosion caused by late implant migration.12

**Evaluation of Bioabsorbable Implants in Animal Trials**

Many of the biomechanical and fusion studies of bioabsorbable implants have been conducted in animal models. In particular, sheep and goats have been most widely used as test subjects for bioabsorable products in trials to discern their effectiveness and safety (Fig. 3). Studies have shown that the biomechanical environment of axial loading of the sheep and goat spine is comparable to that of the human spine.8,20,32,33

**Cervical Spine Studies.** Bioabsorbable implants have been developed to mimic the roles of traditional cervical spine implants such as anterior cervical plates and interbody cages (Fig. 4). Cahill, et al., evaluated the efficacy of a bioabsorbable anterior cervical cage compared with ABG for anterior cervical fusion in an animal model. Twelve goats underwent a two-level anterior cervical disectomy and fusion. Of the 12, eight underwent fusion with an 85:15 polylactide/polyglycolide bioabsorbable cage packed with ABG, and the remaining four underwent...
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Fig. 4. Plain x-ray film showing a bioabsorbable anterior cervical graft containment mesh implant covering the anterior cervical interspace in a goat.

Fusions with autologous bone grafting alone. The goats were evaluated 12 weeks postoperatively. Stable interbody fusions were obtained in only three (19%) of 16 in the group treated with the bioabsorbable device and in one (14%) of seven in the group treated with ABG. Although the group treated with bioabsorbable cages had a higher fusion success rate than the animals that received ABG, the authors cited three potential reasons for such low fusion rates in both groups. The first problem posited was that the time period of 12 weeks might not have been enough time to judge if a union is stable in a goat model. The second, as has been seen in retrospective analysis of human applications of interbody cages, is that multilevel stand-alone constructs often have an unacceptably high failure rate in the absence of adjunctive anterior plate fixation, especially in animals that are impossible to immobilize postoperatively. The third is that resorbable polymers containing polyglycolides typically have a much faster resorption time; because of this, the implants may not have had sufficient mechanical strength during the critical healing period in the cervical spine.

Histological analysis of the fusion sites demonstrated a primary fibrous union in the group treated with bioabsorbable devices, along with a 50% foreign body granuloma reaction to the 85:15 polylactide/polyglycolide polymer. These researchers postulated that the granulomatous response may be a factor of the time course of degradation of the implant and not of properties of the material itself. It was asserted that a longer degradation halftime (changing the stereoisomer ratio) may provide increased biomechanical stability and decrease the histologically observed granulomatous response.

Lumbar Spine Studies. Poynton, et al.,19 assessed the efficacy of a bioresorbable graft containment device in protecting and enhancing a posterolateral fusion mass. Twenty rabbits underwent a one-level posterolateral lumbar spinal fusion with either ABG alone, ABG covered with an MP (MacroPore Biosurgery, Inc, San Diego, CA) containment device (ABG + MP), DBM alone, or DBM covered with an MP containment device (DBM + MP). The animals were assessed 6 weeks postsurgery with volumetric helical computerized tomography scans and Faxitron high-resolution radiographs. Fusion mass scores were significantly increased in both the ABG + MP and the DBM + MP groups compared with the ABG or DBM groups treated without the containment device. Interestingly, the rates of fusion, as judged from radiographic findings, were not significantly different among the groups.

One of the inherent properties of all bioabsorbable implants is their gradual degradation in the human body when exposed to body fluids. To elucidate the degradation process of PLLA spinal interbody fusion cages, van Dijk, et al.,23 studied the in vitro degradation processes in a goat model. In the in vitro condition, PLLA cages were placed in a phosphate-buffered saline solution. In the in vivo assessment, 18 goats underwent a single-level lumbar fusion with either stiff or flexible PLLA cages, both containing autologous bone graft. The animals were killed at 3, 6, or 12 months.

No radiographic differences or alterations in cage configuration were seen between the stiff and the flexible cages at the 3-, 6-, and 12-month time points. After 6 months, both sets of cages were still intact and maintained their original 10-mm height. Mechanical strength of the cages was not maintained at 12 months in both settings. Radiographic studies confirmed a successful fusion at 6 months in four of six of the animals killed at that time. No differences existed between the stiff and flexible cages with regard to fusion. Overall, at the 1-year follow-up review, fusion was present in four of the six specimens in the presence of the degraded interbody cages. Comparison of the in vivo and in vitro groups demonstrated an increased degradation rate in the in vivo group. The authors concluded that compressive cyclic loads acting on the in vivo cages are most likely responsible for the increased rate of degradation. This trend has also been seen in other studies.3,10,12

Toth, et al.,23 evaluated the combination of 70% L-lactide and 30% D.L-lactide copolymer (brand name HYDROSORB) as an interbody fusion cage in a sheep model. In a short-term follow-up period of 3 months, fusion was present in one (25%) of four sheep treated with the HYDROSORB cages. In histological analyses performed at 6 months, fusion was noted in 50% of the sheep.

Stiffness increased and radiographically and histologically confirmed fusion was progressive from the 3- to 24-month time points. In particular, at the 24-month time point, significant implant degradation was observed, accompanied by bone replacement of the space formerly occupied by the polymer and normal staining (trichrome stain) of the bone mineralization immediately adjacent to the remnants of the polymer device. A mild-to-moderate chronic inflammatory response was noted at planned death in all animals; however, no adverse clinical events were noted and no osteolysis was found in perimplant tissues. These authors suggested that the HYDROSORB polymer combination may be a viable alternative to metallic implants.

Bioabsorbable interbody cages composed of PLLA and metallic cages were studied by Wuisman, et al.,34 in a goat model. The PLLA cages (two types: stiff and flexible) as well as titanium cages were placed in a retroperitoneal fashion at a single interbody level. The goats were followed up for 3 to 30 months. At 6 months, four (80%) of
five in the PLLA group demonstrated radiographic evidence of interbody fusion. The rate of bone formation was decreased in the titanium compared with the PLLA group, a finding the authors believed was the result of metallic stress shielding. Considering all specimens, the rate of fusion was significantly higher in the PLLA group than in the titanium group. Bone remodeling was found to be complete in the group treated with bioabsorbable cages at the 2-year follow-up evaluation. At the 3-year follow up, the degradation of the PLLA cages was found to be almost complete. During the absorption of PLLA, a mild inflammatory reaction was noted.

The histological characteristics of fusion maturation in the setting of a bioabsorbable containment device were assessed by Smit, et al.,22 in a goat model. Using specimens from another study, these investigators compared the histological characteristics of the fusion mass in goats that received PLLA cages with those treated with titanium cages. The PLLA cages consisted of more “mature” bone, characterized as coarser and more homogeneous than the bone sampled in the titanium cages. The authors believed the decreased stiffness of the PLLA cages was responsible for such superior bone formation.

**Long-Term Animal Studies**

Van Dijk, et al.,27 reported on the long-term results of the use of PLLA cages for lumbar interbody fusion in a goat model. A total of 36 goats underwent an inter-body fusion at L3-4; 30 goats received PLLA cages and six received titanium cages. Similar to the previously cited studies, interbody fusion occurred at approximately 6 months in the PLLA group, whereas fusion was comparatively delayed in the titanium group. At 36-month follow up, the PLLA cage fusion rate was 86% (19 of 22) compared with 33% (two of six) in the goats that underwent fusion with titanium cages. By 12 months postoperatively, the PLLA cages were demonstrating progressive degradation, and 50% of them were completely absorbed at 36 months.

The authors then assessed the flexibility of the bioabsorbable cages in terms of their effect on bone healing biology and biomechanics. The stiff and flexible cages yielded similar results with respect to fusion, local tissue response, bone volume, activity of bone formation, and motion segment subsidence. The flexible cages increased the amount of lamellar bone formation, however, when compared with stiff cages.

In this long-term study, PLLA cages demonstrated a more rapid and complete rate of bone formation compared with the titanium cages. Investigators attributed this finding to increased stress shielding provided by titanium cages. In vitro histomorphometric testing allowed confirmation of a decrease in bone volume and bone formation rate associated with titanium cages.

**Recent Trials of Bioabsorbable Implants in Humans**

**Cervical Spine.** Vaccaro, et al.,24 demonstrated the effective use of a bioabsorbable anterior cervical graft containment plate (Fig. 5) for the treatment of symptomatic degenerative and traumatic disc herniations (Fig. 6). Nine patients underwent an allograft interbody fusion followed by application of a HYDROSORB anterior cervical plate.
The carrier or cage would function initially as a stabilizing device until the contained biological agent has begun its healing function. The bioabsorbable carrier would then gradually degrade, leaving behind the degradation end products and the effects of the passively delivered carrier, that is, bone healing. Kandziora, et al., specifically evaluated the efficacy of PDLLA-coated titanium cages impregnated with insulin-like growth factor-I and transforming growth factor-β1 to enhance interbody fusion in an animal model. In their study, an anterior cervical disectomy and fusion at C3–4 was performed in 32 sheep. The sheep were divided into four different groups: 1) iliac crest bone graft; 2) titanium cage; 3) titanium cage coated with a PDLLA carrier; and 4) titanium cage coated with a PDLLA carrier, insulin-like growth factor-I, and transforming growth factor-β1. The titanium cage coated with the PDLLA and growth factor combination had, on histological inspection, a significantly higher level of bone mineral content, bony callus volume, and bone mineral density than the other cages. Biomechanically, the PDLLA and bone growth factor group displayed a greater mean stiffness in rotation and bending than the other groups.

### Iliac Crest Harvest Site Reconstruction

Complications relating to bone graft harvesting commonly include pain and cosmetic deformity, the possibility of herniation of abdominal contents through the harvest site, hematoma requiring surgical intervention, and fracture of the anterior or superior iliac spine. Bioabsorbable membranes have demonstrated the ability to act as a barrier to prevent fibrous and scar tissue permeation of grafting agents while allowing access to blood and vital nutrients in the surrounding environment. To facilitate controlled bone regrowth in a defined anatomical location, bioabsorbable sheets have been used successfully to cover the iliac crest after bone graft harvesting.

Cornwall, et al., evaluated the use of resorbable sheets (MacroPore Biosurgery, Inc.) in iliac crest reconstruction after bone graft harvesting. In this study, sheep were divided into a control group with no crest coverage and an experimental group in which polylactic acid sheets were used to cover the iliac crest defect. In the nonprotected control group, 10.7% of the defect was filled with new bone, whereas in the resorbable sheet–protected group, 25.9% of the defect was filled with new bone. Wang, et al., reported that patients whose defects were reconstructed with MP protective sheeting had significantly less pain than control patients in whom no iliac crest reconstruction was performed. In a separate clinical series, Epstein and Hollingsworth found no difference in postoperative pain when comparing patients with reconstructed iliac crests and control patients in whom no reconstruction was performed. Nevertheless, the authors did note that the protected and reconstructed iliac crest yielded new bone growth as assessed on computerized tomography scans.

### Epidural Membrane Scar Barrier

It is a well-known fact that any form of invasive manipulation leads to soft-tissue trauma and scar formation. Resorbable films have been developed that are intended to function as a barrier to epidural scar or fibrous tissue deposition on the neural elements (Fig. 10). Welch, et al., evaluated the effectiveness of a polylactide resorbable film (MacroPore Biosurgery, Inc.) in preventing the formation of fibrosis after...
spine surgery in ovine and canine models. Two different thicknesses (0.02 and 0.2 mm) of bioabsorbable films were compared. When no film was used, a dense posterior scar adhering to the dura mater at the laminotomy window was observed. Both film sizes were found to create a plane for dissection on subsequent surgical exposures and reduced the amount of tissue adherence to the dura.

**Future Research**

Several new experimental bioabsorbable devices are in the process of consideration as spinal implants. These include a myriad of posterior lumbar interbody fusion devices, anterior spinal plates, and a variety of screw and mesh designs (Fig. 11). In more than 16,000 patients in whom more than 300,000 absorbable devices have been implanted clinically, there has only been a 0.07% incidence of sterile sinus formation reported.

**CONCLUSIONS**

As bioabsorbable technology continues to evolve, its application in spine surgery will continue to expand. Future design considerations will include a better understanding of implant stiffness and its effect on bone healing, and optimization of the mechanical characteristics of implant materials in order to expand the range of applications and ultimately to eliminate the need for metal hardware.

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