Bioceramics: The Future of Joint Healing

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Bioceramic implants could one day make revision surgeries obsolete and make joints stronger than they were even before degradation.

The C2a-Taper Acetabular System is a ceramic-on-ceramic hip articulating system. The bearing surfaces consist of ceramic femoral heads and acetabular liners. Both components are made of aluminum oxide. The heads and liners are intended to be used in conjunction with Biomet's titanium acetabular shells, acetabular screws, and titanium alloy femoral stem designs. Image courtesy of Biomet Inc.

Within the next decade, routine total joint replacement may become obsolete, replaced by new orthopedic bioceramics that allow the joint to heal itself. Previously, ceramics had been used only on the articulating surfaces of total joint replacement components, accounting for a small percentage of the overall market. In the last few years, however, manufacturers have developed bioceramics, often made of porous ceramic scaffolds or biodegradable ceramic and polymer composites. As a result, the market for orthopedic ceramics has increased fourfold in a matter of years, with 15% annual growth projected in the future.

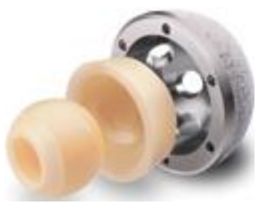
Bioceramics are now being developed to repair defects in bone, cartilage, ligaments, and tendons, which will soon eliminate the need for total joint replacement for a vast number of patients. This article gives a short history of ceramics in orthopedics, discusses current ceramics in use in orthopedics, and reviews the patents and marketplace trends for bioceramics over the next two decades.

History of Ceramics in Orthopedic Applications

Replacing broken and worn out body parts is not a new idea. In fact, the first orthopedic institute was established in 1780 to treat skeletal deformities in children. Nearly 200 years later, in the early 1960s, the first artificial hip joint, a stainless steel stem and cup invented by the English surgeon Sir John Charnley, was implanted. Charnley's design, although simple, was virtually unchanged for three decades, even though surgeons and researchers alike knew there were problems with using metal in the human body. These included corrosion, wear, and loss of bone. Yet, until the 1990s, manufacturers had no alternatives that could match metal's implant lifespan of 10 to 25 years. Then, many orthopedics manufacturers began experimenting with ceramics for implants.

Ceramics are now used extensively in orthopedic implants, particularly hips. Modern bioceramics have even more potential, however. They are both porous and moldable, increasing their applications into other areas of orthopedics. Currently, the focus of this research is on the spine. With more than 300,000 spinal fusion surgeries per year, and an equally large number of restorative spinal procedures, surgeons want lifetime solutions for their patients.

A promising new technology is bone-scaffolding ceramics. These ceramics can be used as slurries to mix with bone for traditional spinal fusion, or they can be inserted into defects in the vertebrae to restore the vertebrae to their normal height and function without the need for spinal fusion. Porous bioceramics allow the body’s own bone to grow within the scaffold, while also creating pathways for nutrients to nourish this new bone. Eventually, the ceramic scaffold is completely incorporated into the patient’s natural bone, restoring the bone to its original condition. Some other applications for these porous ceramics are fixating a hip implant stem within the shaft of the bone and lining the back, mating surfaces of implants. In the future, joint implants will be merely temporary skeletons upon which the body will grow its own new cartilage and bone for a permanent repair.



Zimmer’s Trilogy AB Acetabular System is a ceramic-on-ceramic bearing surface for artificial hips, designed to minimize wear.

Ceramics offer some inherent advantages over metal. They are biologically inert, produce no wear debris, and can be designed to more closely match the material properties of natural bone. For the articulating surfaces on hip, knee, and shoulder implants, two ceramics are most commonly used, alumina and zirconia. These materials are much harder than metal, cannot be scratched, and can be used on both the ball and socket components of an implant, such as the femoral head and the acetabular cup of a hip implant.

In other cases, however, the surgeon wants to match the material properties of bone. Because metal has such high stiffness, the bone surrounding an implant no longer bears the load; the implant carries the entire load. As bone is a living tissue, it begins to resorb when it ceases to carry the load, allowing the implant to loosen and eventually require replacement. Ceramics can now be formulated to allow bone to grow within their porous structures, or scaffolds. They can completely incorporate the scaffold with natural bone within five to seven months.

Despite recent progress, current therapy and treatment methods for regenerative medicine, such as bone grafts and bone void fillers, have many flaws and limitations in bone repair and reconstruction. Existing bone substitutes, such as polymethylmethacrylate (PMMA), commonly known as bone cement, do not always meet market demands for large bone defects or injuries. PMMA is a polymer putty that hardens when mixed with an activator. When used around an implant to fix it into position, it creates a solid barrier between the bone and the metal implant. Nutrients cannot nourish this plastic material, and bone cells cannot grow into it either. This represents a big challenge for orthopedic reconstructive surgeons across the world. Porous ceramics could provide them with an exciting alternative.

Historically, ceramics have been major components in a growing number of devices used in total hip replacement, knee replacement, and other joint replacement surgeries. Alumina-based ceramics were not as advanced when they were first introduced in the 1970s, but the technology has since gotten much better. For example, the grain size used to be up to 40 µm. Now, alumina ceramics are engineered to have grains that are between 1 and 4 µm. This finer grain size provides almost zero surface roughness, preventing scratching, corrosion, or wear of the articulating surfaces of implants. Furthermore, the current manufacturing techniques employ isostatic pressing processes that help to close the pores and ultimately minimize brittleness usually associated with ceramics.

Many different materials are actually classified as bioceramics. Calcium phosphate ceramics include hydroxyapatite, tricalcium phosphate, and tetracalcium phosphate. Other bioceramics include materials such as alumina, zirconia, silica-based glass, and pyrolitic carbon. These materials range from inert to bioactive based on their biological activity, as they can remain unchanged, dissolve, or actively take part in physiological processes to enhance bone tissue formation.

Perfection regained: The perfect fit of the Sandia ceramic scaffolding in the model jaw also recreates the upper line of the original jawbone. The scaffold layering, which cross each other like a child's Lincoln Logs, are approximately 500 µm apart to expedite passage of new bone and blood vessels. Photo by Randy Montoya

In the past, ceramics were generally brittle and not suitable for load-bearing applications in orthopedic implants. In the 1990s, manufacturers started creating durable ceramics for areas under a compressive load, such as the femoral head or acetabular cup socket in a hip implant. But places where the loading was in tension, bending—or torsion—still required a metal implant. Orthopedics manufacturers tried to overcome the limitations by making the surfaces of these metal implants rough, or porous, allowing some bone cells to interlock with the metal surface for fixation. Unfortunately, this is only a fragile membrane of new bone that can fracture and loosen as the surrounding bone resorbs and weakens. Bioceramics overcome this limitation by allowing new bone cells to completely penetrate the implant, creating a reinforced bone region that will strengthen over time.

Numerous studies show that polymer-ceramic composites can indeed improve the mechanical properties of an orthopedic implant to better match the natural load-bearing tissues.[1,2] Bioactive ceramic materials like tricalcium phosphates, hydroxyapatite, and bioglass have gained significant importance as scaffolds for bone tissue engineering. These scaffolds can either induce the formation of bone from the surrounding tissue or can act as carriers or guides for enhanced bone regeneration by cell migration, proliferation, and differentiation. It is worth noting that bioceramics have been used as synthetic bone graft substitutes for more than 30 years but typically have had insufficient elastic stiffness and compressive strength as compared to natural human bone tissues. New polymer-ceramic composites and nanoceramic-based scaffolds that biodegrade after implantation are considered alternatives destined to overcome such limitations.

Biomaterials in Orthopedic Applications

Among various biomaterials used in orthopedic applications, ceramics (especially alumina) have been used historically in total hip replacement, knee replacement, and other joint replacement surgeries. Porous ceramics are used for bone bonding (e.g. hydroxyapatite), bone spacing (e.g. porous alumina), and small orthopedic joints such as fingers and spinal inserts.

The key to manufacturing a successful porous ceramic scaffold is to either use a bioactive, conductive ceramic material or to coat the scaffold with a bioactive material. These new materials, often called bioceramics, are the subject of extensive research. Hydroxyapatite (HA) is a naturally occurring bone ceramic that manufacturers have used to coat metal implants for many years. Now, this HA bioceramic is being seeded or coated onto a porous scaffold, allowing bone cells to grow into the scaffold as if it were regular bone. Seeding is a process from the semiconductor industry that grows an entire ceramic wafer or scaffold from a single grain of the desired ceramic.

Bioinert alumina ceramic is another popular choice for scaffolds, as it can be easily processed to achieve the desired porosity and material properties for the application. Also, various natural tissues, such as HA and bone marrow stromal cells, will readily adhere to an alumina scaffold.

The third most popular ceramic scaffold is the family of calcium phosphate ceramics. Biophasic calcium phosphate has good mimetic properties in terms of porosity and surface area that promote cell attachment and ingrowth. Plus, the struts' orientation in the scaffold improves strength and provides good biomechanical compatibility with bone. Tricalcium phosphate is osteoconductive like HA and induces neither an immune nor an inflammatory response when implanted in the body.

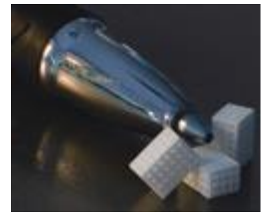
Market studies show that the spinal market was the largest orthopedic segment in 2006, surpassing the knee market for the first time. With the advent of bioceramics in spinal fusion, we can expect this market segment to continue to grow at a rapid pace. While these orthobiologics are increasingly used in spinal, joint, trauma, and soft tissue surgeries, synthetic bone graft substitutes and resorbable products are beginning to replace traditional autografts and allografts (bone bank grafts), which account for more than 75% of today's bone graft procedures, according to Espicom Business Intelligence. This market is fueled by various factors such as aging population, better treatment options for younger patients, improved materials and treatment methods, and generally higher patient demands. Autografts are invasive and donor allografts are in short supply, so tissue-engineered solutions are in demand as suitable alternatives.

The global orthopedic biomaterials market grew from $4.2 billion in 2005 to about $5.4 billion in 2007, according to Healthpoint Capital. Tissue engineering techniques using biomaterial cell-scaffold hybrids have been emerging as alternative and valid approaches to the current therapies for bone regeneration/substitution. In contrast to a classic biomaterial approach, tissue engineering is based on the understanding of tissue formation and regeneration, and aims to induce new functional tissues, rather than just to implant new spare parts. We can expect to see the use of biomaterials increase in orthopedics, leading to new, integrated implants that enhance the function of the joint or tissue rather than simply repair.

Technology Trends

A review of the literature in porous bioceramic scaffolds shows that many clinical studies are in progress to evaluate the efficacy of these products in various tissue engineering applications, both in bone regeneration and bone growth. Different studies are underway to assess micro- and macro-architecture of bioceramic scaffolds and how they impact tissue proliferation and tissue growth. The key is to use scaffolds that can support adequate cell migration into and around the scaffold, and provide short-term support of these cells following implantation with an adequate supply of oxygen and nutrients. A review of the patent activity confirms the direction of these technological trends. Some of the patents describe how scaffolds are designed and how the biomechanical and biochemical properties of these scaffolds are crucial in tissue remodeling and growth. Some important trends are scaffolds that degrade over time, creating pores for bone cells and nutrients to grow into; porous bone grafting materials for filling voids in bone; and composite ceramic scaffold polymer materials for mimicking bone structural properties.

Future applications in orthopedics for porous ceramics are promising. Currently, a hip implant may last only 15 to 25 years, and a knee only 10 to 15 years. As knee patients are often only in their 50s, avoiding revision surgery in their advanced age would be a major breakthrough. By using porous ceramics on the anchoring portions of these implants and hard, sintered ceramic on the articulating surfaces, the lifespan of an implant could exceed the lifespan of the patient. In most cases, revision surgery would become obsolete, and the replacement implant would become an improved part of the patient's body.


Reference scaffolds made by Porogen BV. Material is ß-TCP (beta-tricalcium phosphate). These scaffolds are intended to support various research activities in stem cells, regenerative medicine/tissue engineering, and tissue models.

Nanosized bioceramics have been used increasingly in various research activities, and new products are being developed for producing composite materials that can mimic other joint structures and ultimately achieve equivalent material properties. Orthomimetics Inc. (Cambridge, UK) is one company with products using nanosized bioceramic particles in biodegradable polymer scaffolds as biomimetic materials resembling cartilage, ligament, and tendon. Thus, patients can now receive treatment for soft tissue injuries long before a total joint replacement is required, effectively delaying or even preventing the need for such a joint replacement. Considering the vast majority of joint replacements are for worn or missing cartilage, developing a nanobioceramic particle that could effectively regrow cartilage within the natural joint would be revolutionary.

Composite materials containing bioceramics have been developed and used successfully as prosthetic materials in various orthopedic and nonorthopedic applications. For example, Hapex, developed by Gyrus ENT LLC (Bartlett, TN), combines HA with high-density polyethylene, and has been used successfully for middle ear implants. The material provides the increased stiffness and bioactivity of HA with the toughness of polyethylene. While many composite materials have been developed and used for bone repair, it appears that the ones that incorporate mineralized collagen are particularly promising.

The market for spinal fusion will also continue to show rapid growth. With an estimated market value of more than $3.3 billion in spine fusion in just the United States, many companies are increasingly developing products and technologies that can improve patient outcomes and achieve better long-term results. For instance, Nuvasive Inc. (San Diego) produces Fomograft, which can be used as a physical scaffold upon which bone will grow and can be easily hydrated with bone marrow during spine surgery. Fomograft, which received FDA 510(k) clearance in May 2005, is a combination of highly purified type I collagen, HA, and tricalcium phosphate. This composite material promises an ideal matrix to deliver robust bone growth and can improve fusion results in both lumbar and cervical spinal fusion procedures, effectively restoring the spine to its original performance.

Another trend in the orthopedic market appears to be the collaboration and codevelopment between different orthopedics companies, which has been successful in many cases. For instance, Orthovita Inc.'s (Malvern, PA) synthetic ceramic-collagen matrices (Vitoss) and Aastrom Biosciences Inc.'s (Ann Arbor, MI) proprietary bone marrow-derived cells, tissue repair cells (TRCs), appear to be ideal products to address a broad range of orthopedic indications. Vitoss scaffolds are marketed specifically to provide nonload-bearing geometric support during new tissue growth. On the other hand, TRCs are a mixture of stem, stromal, and progenitor cells produced from the patient's own bone marrow to encourage the regeneration of bone and blood vessels.

Conclusion

Orthopedic research in bioceramics continues to advance at a rapid pace as new techniques and materials are applied to repair damaged musculoskeletal tissues, bone defects, and worn out body parts. Thus, new biomaterials and better scaffolds to target major diseases such as fracture healing, soft tissue repair, osteoporosis, and osteoarthritis continue to be an important research focus. Some of the most exciting new materials, porous ceramic scaffolds for bone repair and bony ingrowth, are now on the market and will soon be common in the orthopedic arena, improving the expected lifespan of implants and other surgical procedures to last for the life of the patient. Eventually, we can expect routine total joint replacement to become a procedure of the past, as tissue engineering and products such as bioceramic scaffolds become commonplace.

References

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