CHAPTER **48**

HYDROXYAPATITE AS A BONE SUBSTITUTE

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BONE AND BONE GRAFTS

The incorporation and structure of coralline hydroxyapatite involves many characteristics similar to normal bone.[1] Bone is a highly vascular, living, constantly changing mineralized connective tissue. It is remarkable for its hardness, resilience and regenerative capacity, as well as its characteristic growth mechanisms.[2] The unique mechanical properties of bone are a result of its components. Bone consists of cells (primarily osteocytes in mature bone) and intercellular matrix. The inorganic or mineral component is made of hydroxyapatite which gives bone its hardness and rigidity. The organic component is primarily collagen and glycosaminoglycans which gives elasticity and resiliency to the bone to resist fracture when mechanically loaded.[2]

Almost all of the adult osseous skeleton is made up of lamellar bone. Lamellar bone consists of mineralized matrix with collagen fibers arranged in layers, in which osteocytes are embedded.[2] The arrangement of the lamella defines bone as being cortical or cancellous. Cortical bone is dense and compact. It is composed of haversian systems, called secondary osteons, which are formed by internal remodeling of pre-existing bone. The system is cylindrical in shape with its long axis parallel to the long axis of the bone. Cancellous or trabecular bone consists of a lattice-work of trabeculae enclosing large marrow spaces. The trabeculae are oriented with the adjacent bone surface.

Types of bone grafts include autografts, allografts, and xenografts. An autograft is taken from the same individual, an allograft is taken from the same species, and a xenograft is a taken from a different species. Coralline hydroxyapatite is a xenograft.[1]

It is generally accepted that autogenous bone is the ideal material for bone grafting procedures. Autogenous grafting provides three primary elements for bone healing. There is the passive function of osteoconduction (providing a scaffold for vascular and bony ingrowth), an active function of osteoinduction (stimulation of new bone formation by the conversion of mesenchymal cells into osteoprogenitor cells), and osteogenesis (bone production due to the transfer of viable osteoprogenitor cells).[3] However, there are also disadvantages to autogenous bone grafting. A study by Younger and Chapman, in 1989, documented the morbidity of harvesting an autogenous bone graft.[4] In some cases, this morbidity may outweigh the benefits. Harvesting the graft requires a second surgery which increases the chance of infection and operating room time. Compromise of the graft site (usually the iliac crest) may result in fatigue fracture, pelvic instability, delayed ambulation, stress risers, and increased pain.[3,5] Pain and blood loss are significant with iliac crest graft procurement procedures. Major complications have been reported to occur in 5% to 10% of these grafts, and minor complications in 10% to 20%.[4]

Allografts are relatively easy to handle, and have the advantage of not requiring a second procedure. However, the risk of rejection, due to antigenicity, and the possible transfer of disease are factors, which although rare, should be considered when using allogenic grafts.[1]

The need for bone substitutes is clear, and there has been an increase in research in this area. Coralline hydroxyapatite is an example of a xenograft. For over twenty years researchers have been experimenting with certain types of sea coral which may be processed for use as a bone substitute.

SEA CORAL AS A BONE SUBSTITUTE

The search for a suitable bone replacement material is not a new concept. In 1920, F. H. Albee injected triple calcium phosphate solutions into bone defects. The search continues even today.[6] However, considerable interest has been focused on a porous hydroxyapatite substratum that is obtained after hydrothermal conversion of the

calcium carbonate exoskeletal microstructure of the scleration reef-building corals: *Porites and Goniopora*.[1,7-10] This hydrothermal exchange subjects the coral to high temperatures and pressures as it converts the carbonate exoskeleton into pure hydroxyapatite.[1]

These types of coral were chosen because their pore size and pattern are similar to human bone. The difficulty in controlling pore size, and more importantly, the size of the adjacent interconnecting pores has been a major limitation in the production of porous ceramics.[11] The genus *Porites* has a pore size of its parallel channels of 230 μm in diameter and interconnecting fenestrations between channels of 190 μm in diameter.[2] The potential for this material was recognized by Holmes who proposed that coralline hydroxyapatite *Porites* appeared to be similar to the osteon evacuated bone with parallel channels.[7] The genus *Goniopra* has a pore structure analogous to that of cancellous bone with pore sizes of 500 μm.[2] These products are prepared commercially and are available in block form, which may be contoured to the desired shape, or in granules, to fill voids and interconnect to form a continuous matrix.[1] Blocks come in various sizes from 5 x 12 x 40 mm up to 12 x 30 x 30 mm (Interpore Orthopedics, Inc., Irvine, California) (Fig. 1).

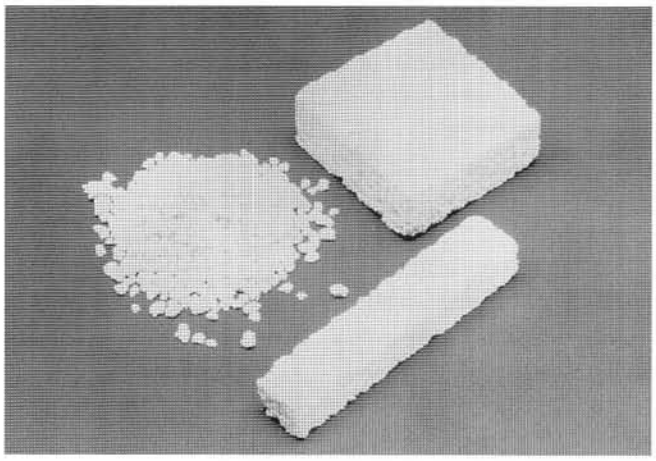

Figure 1. Various forms of Pro Osteon, including block and granular forms.

ADVANTAGES

Virtually all the animal and human studies show no evidence of adverse reaction or rejection of the implant. The material is nontoxic, nonallergenic, possesses high compressive strength, and has adequate pore size for fibrovascular ingrowth and osteon formation.[1] Bucholz et al. stated that hydroxyapatite satisfies most of the requirements of a filling agent for defects in bone.[12] Filling agents should be readily available in adequate volume and should be easily contoured to the dimensions of the defect. The material should have sufficient mechanical strength and should permit rapid bone ingrowth. Holmes et al. observed that the genus *Goniopora* exhibited anisotropic behavior because of its structural geometry, as does cancellous bone.[7] This provides different structural properties along different planar orientations to allow for elastic deformation and load distribution.[1] Several of the early studies surrounding coralline hydroxyapatite focused on its osteoconductive nature, in that it acts as a scaffold for new bone formation.[1,5,8,9,12] Over time, complete bony ingrowth into the material was a consistent finding.

DISADVANTAGES

The principle limitations of calcium phosphate implant materials are its mechanical properties. The material is brittle, has low impact resistance, and relatively low tensile strength.[13] The initial mechanical weakness of the material prevents its use in a setting where it must bear a structural load alone. Mechanical stresses must be defended and minimized by internal fixation and/or bony architecture.[7] Initial studies have shown that once incorporated, the material has greater strength than cancellous bone at six months post-implantation.[1] However, more recent studies indicate that hydroxyapatite has strength limitations, and its use in orthopedics should be limited to low load applications.[14]

Cooke stated that ceramics have not achieved wide acceptance because of their tendency for unpredictable catastrophic failure in load-bearing applications.[14] Upon cooling of the material during processing, micro cracks are induced, thus lowering the expected strength of the material. When subjected to load, the local stresses around the crack tips are much greater than at other locations. After cyclic loading, the cracks grow locally. If the load is great enough and the crack large enough, the crack will propagate rapidly, almost instantaneously, and complete fracture will occur with no permanent or plastic distortion. This is brittle failure.[14]

One of the earliest concerns about coralline hydroxyapatite was its degradation-resistant character.[1,5,8,12,15] Louise et al. noted only a slight biomaterial remodeling after thirty-six months in a clinical trial.[16] Others observed a lack of biodegradation, and indicated an absence of osteoclastic resorption over the same time frame.[17,18] It is well known that changes in the environment, or forces applied to bone and joints result in adaptation.[19] This adaptation is explained by Wolffe's Law, which states "Modifications in the form and function of a bone are followed by changes in its internal architecture and secondary alterations in its external configuration in accordance with mathematical laws."[20] If these hydroxyapatite blocks are not being replaced by normal bone, they may be a mechanical weak point.[17]

Hydroxyapatite implants do not exhibit properties of osteoinduction.[1,5,7,8] There is no evidence that coralline grafts provide osteogenic stimulus beyond their function as an architectural framework.[8] Implant placement must, therefore, be in direct contact with bone in order to conduct osseous cells through the implant.[1]

CLINICAL FINDINGS

The senior author has used the Interpore 500 material in approximately thirty cases, mostly as a packing material for the donor site of calcaneal bone grafts (Fig. 2). There have been no cases of infection, inflammation, or rejection. Extruded material caused by the brittleness of the implant resulted in two cases of bone formation with prominence. Neither was particularly symptomatic, and they were both left untreated. The senior author now routinely inspects the wound carefully for any loose pieces and performs a thorough lavage of the wound. The implant provides good hemostasis at the donor site.

Radiographically, the implant stays radiodense for a prolonged period of time (Fig. 3). This is one of the factors that makes it a less desirable material to use in fusions (Fig. 4) or for other uses requiring radiographic determination of bone healing.

Bucholz has noted that long term (ten-year) histomorphic studies are needed. In addition, he has noted that use of the material in a situation of cyclic loading is uniformly unsuccessful in the absence of internal fixation.

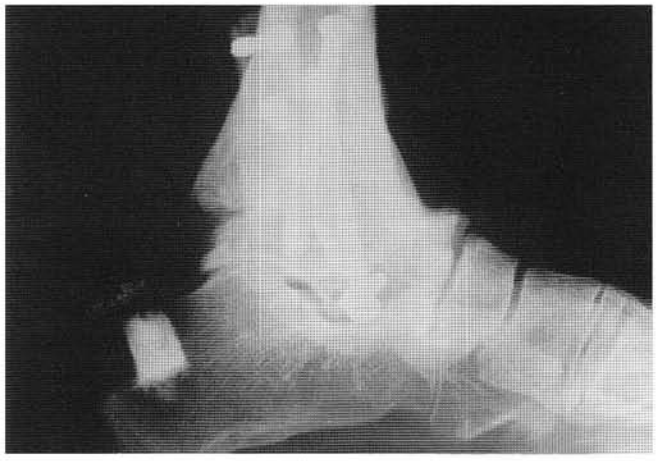

Figure 2. Hydroxyapatite used to pack the donor site of a calcaneal bone graft. The autogenous bone was used successfully as an anterior bone graft in a revisional ankle fusion.

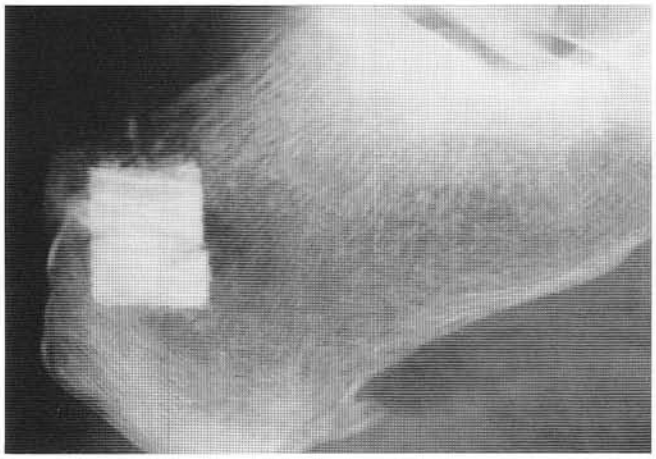

Figure 3. Lateral view of hydroxyapatite graft at 18 months postoperative. Note that there is little change in the implant. A small amount of ectopic bone is noted on the posterior superior margin of the implant.

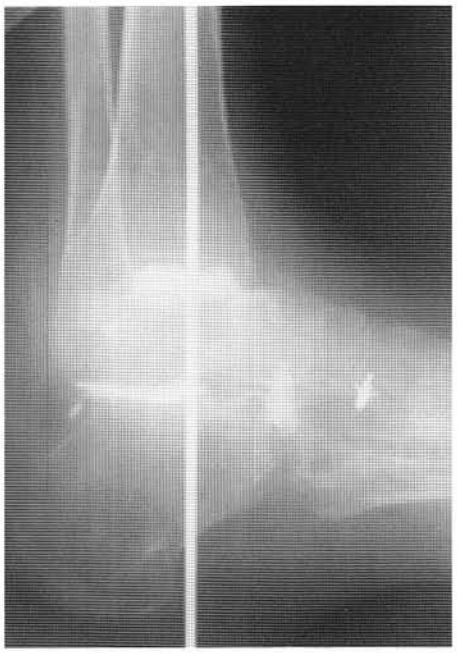

Figure 4. Lateral view of a pantalar fusion, with hydroxyapatite packing. The density of the material makes evaluation of the fusion more difficult.

SUMMARY

Synthetic hydroxyapatitite is a relatively new material in orthopedic surgery. The follow-up times of implanted hydroxyapatitite in vivo have been short in most studies.[16] Bay et al. noted the characterization of the implant alone is only part of the picture.[21] How the host reacts to the implant is equally important. The key factors are the range of implant properties to which the bone can adapt, and the rate at which that adaptation can occur. Further studies are needed to assess these factors in clinical situations.

The most recent literature indicates that the future of coralline hydroxyapatite will involve its combination with osteoinductive proteins,[10,22,23] or as coatings on metal implants where it can induce and/or promote bonding with bone.[14]

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