35

Ceramics in Biology and Medicine

CHAPTER PREVIEW

Bioceramics are ceramics used for the repair and reconstruction of human body parts. As you can imagine, there are many applications for bioceramics; currently, the most important is in implants, such as alumina hip prosthesis. Alumina is classified as an inert bioceramic because it has very low reactivity in the body. On the other hand, bioactive materials have the ability to bond directly with bone. The advantages are:

- Earlier stabilization of the implant
- Longer functional life

However, bioactive ceramics are relatively weak compared with common implant metals and high-strength ceramics such as alumina and zirconia. As a result, they are often used as coatings, relying on the mechanical strength and toughness of the substrate. An important bioactive ceramic is hydroxyapatite (HA). Natural bone is a composite in which an assembly of HA particles is reinforced by organic collagen fibers. HA-reinforced polyethylene composites have been developed in an attempt to replicate the mechanical behavior of bone.

You can appreciate a major problem with this topic when you realize you can't replace bone if you don't understand why bone has such incredible mechanical properties. Therefore, if you work in this field, you must learn about biology.

35.1 WHAT ARE BIOCERAMICS?

A comprehensive definition of a biomaterial was provided at the National Institutes of Health (NIH) Consensus Development Conference on the Clinical Applications of Biomaterials in the United States.

> A biomaterial is any substance, other than a drug, or combination of substances, synthetic or natural in origin, which can be used for any period of time, as a whole or as a part of a system which treats, augments, or replaces any tissue, organ, or function of the body.

This definition was significantly simplified in 1986 at the European Society for Biomaterials Consensus Conference

> Biomaterial—a non-viable material used in a medical device intended to interact with biological systems.

A bioceramic is defined as a ceramic used as a biomaterial (which is great if you know what a ceramic is). The field of bioceramics is relatively new; it didn't exist until the 1970s. However, many bioceramics are not new materials. One of the most important is Al_2O_3, which we first met as a constituent of many traditional ceramic products. Bioceramics are typically classified into subgroups based on their chemical reactivity in the body. The subgroups are listed in Table 35.1, and their relative reactivities are compared in Figure 35.1.

If a nearly inert material is implanted into the body, the body initiates a protective response that leads to encapsulation by a nonadherent fibrous coating about 1 μm thick. Over time this leads to complete isolation of the implant. A similar response occurs when metals and polymers are implanted. In the case of bioactive ceramics, a bond forms across the implant/tissue interface, which mimics the body's natural repair process. Bioactive ceramics such as HA can be used in bulk form but are often used as part of a composite or as a coating. Resorbable bioceramics, such as tricalcium phosphate (TCP), actually dissolve in the body and are replaced by the surrounding tissue. It is an important requirement, of course, that the dissolution products are not toxic. As in the case of HA, TCP is often used as a coating rather than in bulk form. It is also used in powder form (e.g., for filling space in bone).

Figure 35.2 shows a number of clinical uses of bioceramics. They go from head to toe and include repairs

PROSTHESIS
A prosthesis is an artificial replacement for a part of the body.

C.B. Carter and M.G. Norton, *Ceramic Materials: Science and Engineering*,
DOI 10.1007/978-1-4614-3523-5_35,

TABLE 35.1 Classification Scheme for Bioceramics

Nearly inert bioceramics
Examples: Al_2O_3, low temperature isotropic (LTI) carbon; ultra-LTI carbon; vitreous carbon; ZrO_2
Tissue attachment: mechanical
Bioactive ceramics
Examples: HA; bioactive glasses; bioctive glass-ceramics
Tissue attachment: interfacial bonding
Resorbable bioceramics
Examples: tricalcium phosphate (TCP); calcium sulfate; trisodium phosphate
Tissue attachment: replacement
Composites
Examples: HA/autogenous bone; surface-active glass ceramics/PMMA; surface-active glass/metal fibers; polylactic acid (PLA)/carbon fibers; PLA/HA; PLA/calcium/phosphorus-based glass fibers
Tissue attachment: depends on materials

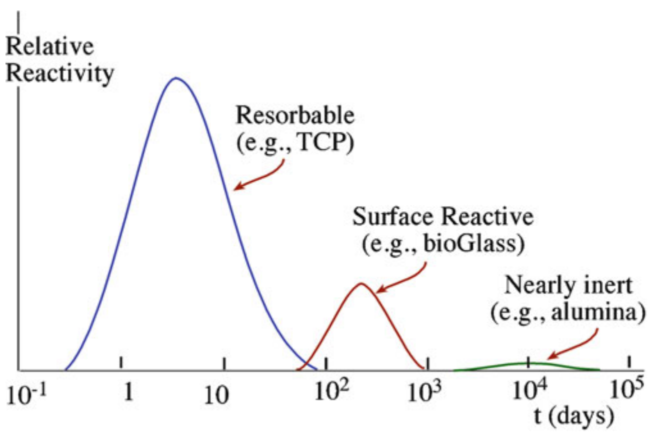

FIGURE 35.1. Relative reactivity of the different classes of bioceramic. TCP tricalcium phosphate.

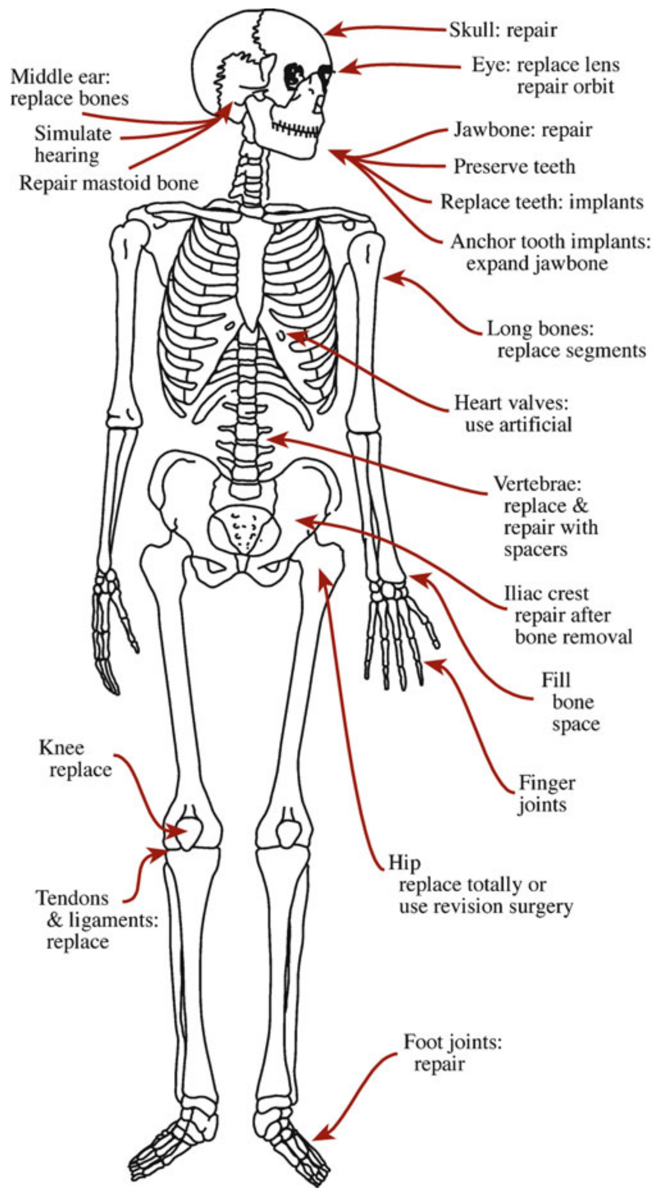

FIGURE 35.2. Illustration of the head-to-toe clinical uses for bioceramics.

to bones, joints, and teeth. These repairs become necessary when the existing part becomes diseased, damaged, or just simply wears out. There are many other applications of bioceramics, including pyrolytic carbon coatings for heart valves and special radioactive glass formulations for the treatment of certain tumors. We describe these two applications toward the end of this chapter. In the next section we look at the advantages and disadvantages of ceramics as biomaterials compared to the use of polymers and metals. We note that nanomaterials show interesting possibilities for such applications but may pose health problems in other situations.

35.2 ADVANTAGES AND DISADVANTAGES OF CERAMICS

In the selection of a material for a particular application we always have a choice. Materials selection is a critical part of any component design process and is especially important for implants and other medical devices.

The three main classes of material that we can select from for a load-bearing application are metals, polymers, and ceramics. Table 35.2 is a comparative list of the significant physical properties of different biomaterials from each of the three classical material classes. Table 35.3 compares the behavior of these different classes relevant to their potential use as implants.

The main advantage of ceramics over other implant materials is their biocompatibility: some are inert in the physiological environment, whereas others have a controlled reaction in the body. The main disadvantages of most bioceramics are:

- Low toughness (which can affect reliability)
- High E (which can lead to stress shielding; see Section 35.3)

One of the main ways of increasing the toughness of ceramics is to form a composite. The ceramic may be the reinforcement phase, the matrix, or both. An example of a

TABLE 35.2 Significant Physical Properties of Different Biomaterials

Material	*Density (g/cm^3)*	*UTS (MPa)*	*Compressive strength (MPa)*	*$\mathcal{E}$ (GPa)*	*K_{1c} (MPa. $m^{1/2}$)*	*Hardness (Knoop)*	*α (ppm/°C)*	*Fracture surface energy (J/m^2)*	*Poisson's ratio*	*k ($Wm^{-1}K^{-1}$)*
HA	3.1	40–300	300–900	80–120	0.6–1.0	400–4,500	11	2.3–20	0.28	
TCP	3.14	40–120	450–650	90–120	1.20		14–15	6.3–8.1		
Bioglasses	1.8–2.9	20–350	800–1,200	40–140	~2	4,000–5,000	0–14	14–50	0.21–0.24	1.5–3.6
A-W glass ceramic	3.07	215	1,080	118	2					
SiO_2 glass	2.2	70–120		~70	0.7–0.8	7,000–7,500	0.6	3.5–4.6	0.17	1.5
Al_2O_3	3.85–3.99	270–500	3,000–5,000	380–410	3–6	15,000–20,000	6–9	7.6–30	0.27	30
PSZ	5.6–5.89	500–650	1,850	195–210	5–8	~17,000	9.8	160–350	0.27	4.11
Si_3N_4	3.18	600–850	500–2,500	300–320	3.5–8.0	~22,000	3.2	20–100	0.27	10–25
SiC	3.10–3.21	250–600	~650	350–450	3–6	~27,000	4.3–5.5	22–40	0.24	100–150
Graphite	1.5–2.25	5.6–25	35–80	3.5–12	1.9–3.5		1–3	~500	0.3	120–180
LTI-ULTI	1.5–2.2	200–700	330–360	25–40			1–10		0.3	2.5–420
Carbon fiber	1.5–1.8	400–5,000	330–360	200–700						
Glassy carbon	1.4–1.6	150–250	~690	25–40		8,200	2.2–3.2			
PE	0.9–1.0	0.5–65		0.1–1.0	0.4–4.0	170	11–22	500–8,000	0.4	0.3–0.5
PMMA	1.2	60–70	~80	3.5	1.5	160	5–8.1	300–400		0.20
Ti	4.52	345	250–600	117	60	1,800–2,600	8.7–10.1	~15,000	0.31	
Ti/Al/V alloys	4.4	780–1,050	450–1,850	110	40–70	3,200–3,600	8.7–9.8	~10,000	0.34	
Ti/Al/Nb/Ta alloys	4.4–4.8	840–1,010		105	50–80			~17,000	0.32	
Vitallium-stellite alloys (Co-Cr-Mn)	7.8–8.2	400–1,030	480–600	230	120–160	3,000	15.6–17.0	~5,000	0.30	
Low C steel Fe-Cr-Ni alloys	7.8–8.2	540–4,000	1,000–4,000	200	55–95	1,200–9,000	16.0–19.0	~50,000	0.20–0.33	46

TABLE 35.3 General Comparison of Materials for Implants

Material class	*Advantages*	*Disadvantages*
Polymers	Resiliant	Weak
	Tough	Low $\mathcal{E}$
	Easy to fabricate	Not usually bioactive
	Low density	Not resorbable
Metals	Strong	Can corrode in physiological environment
	Wear resistant	High $\mathcal{E}$
	Tough	High density
	Easy to fabricate	Not usually bioactive
		Not resorbable
Ceramics	Biocompatible	Low tensile strength
	Wear resistant	Difficult to fabricate
	Certain compositions lightweight	Low toughness
		Not resiliant

polymer-matrix composite (PMC) reinforced with a bioceramic is polyethylene (PE) reinforced with HA particles. The toughness of the composite is greater than that of HA; and, as we see in Section 35.6, $\mathcal{E}$ is more closely matched to that of bone. Bioceramics are also used as coatings on metal substrates. An example is bioactive-glass coating on stainless steel, which utilizes the strength and toughness of steel and the surface-active properties of the glass.

35.3 CERAMIC IMPLANTS AND THE STRUCTURE OF BONE

The requirements for a ceramic implant depend on what role it is to play in the body. For example, the requirements for a total hip prosthesis (THP) are different from those for a middle ear implant. However, there are two basic criteria.

The ceramic should be compatible with the physiological environment.
Its mechanical properties should match those of the tissue being replaced.

Most bioceramic implants are in contact with bone. Bone is a living material composed of cells and a blood supply encased in a strong composite structure. The composite consists of collagen, which is flexible and very tough, and crystals of an apatite of calcium and phosphate, resembling calcium HA; we proceed here as if it is HA. It is the HA component that gives bone its hardness. The acicular apatite crystals are 20–40 nm in length and 1.5–3.0 nm wide in the collagen fiber matrix. Two of the various types of bone that are of most concern in the use of bioceramics are:

Cancellous (spongy bone)
Cortical (compact bone)

Cancellous bone is less dense than *cortical* bone. Every bone of the skeleton has a dense outer layer of compact bone covering the spongy bone, which is in the form of a honeycomb of small needle-like or flat pieces called trabeculae. Figure 35.3 shows a longitudinal section of a long bone. The open spaces between the trabeculae are filled with red or yellow bone marrow in living bone. Because of its lower density, cancellous bone has a lower $\mathcal{E}$ and higher strain-to-failure than cortical bone, as shown in Table 35.4. Both types of bone have higher $\mathcal{E}$ than soft connective tissues, such as tendons and ligaments. The difference in $\mathcal{E}$ between the various types of connective tissues ensures a smooth gradient in mechanical stress across a bone, between bones, and between muscles and bones.

STRESS SHIELDING

This occurs when a high-$\mathcal{E}$ implant material carries nearly all the applied load.

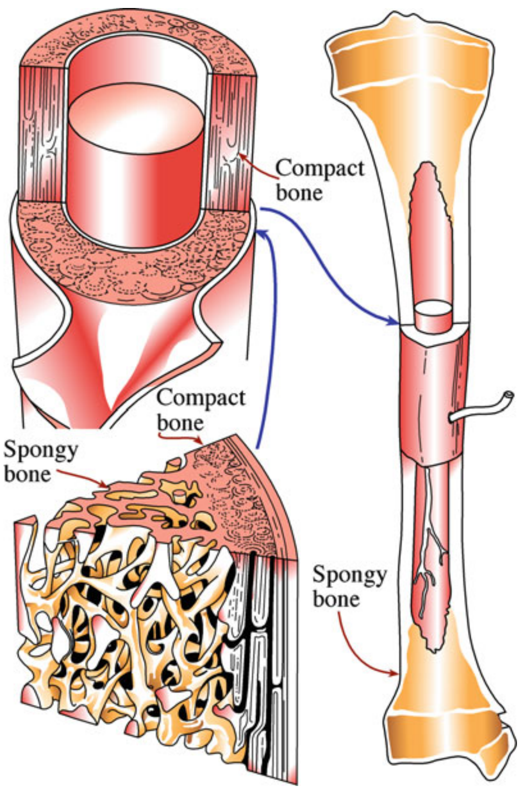

FIGURE 35.3. Longitudinal section showing the structure of long bone.

The mechanical properties of the implant are clearly very important. Figure 35.4 compares $\mathcal{E}$ of various implant materials to those of cortical and cancellous bone.

- $\mathcal{E}$ of cortical bone is 10–50 times less than that of Al_2O_3.
- $\mathcal{E}$ of cancellous bone is several hundred times less than that of Al_2O_3.

If the implant has a much higher $\mathcal{E}$ than the bone it is replacing, then a problem called *stress shielding* can occur. Stress shielding weakens bone in the region where the applied load is lowest or is in compression. (Bone must be loaded in tension to remain healthy). Bone that is unloaded or is loaded in compression undergoes a biological change that leads to resorption. Eliminating stress shielding by reducing $\mathcal{E}$ is one of the primary motivations for the development of bioceramic composites.

TABLE 35.4 Mechanical Properties of Skeletal Tissues

Property	*Cortical bone*	*Cancellous bone*	*Articular cartilage*	*Tendon*
Compressive strength (MPa)	100–230	2–12		
Flexural strength (MPa)	50–150	10–20	10–40	80–120
Strain to failure (%)	1–3	5–7	15–50	10
$\mathcal{E}$ (GPa)	7–30	0.5–0.05	0.001–0.01	1
K_{1c} (MPa m$^{1/2}$)	2–12			
Compressive stiffness (N/mm)			20–60	
Compressive creep modulus (MPa)			4–15	
Tensile stiffness (MPa)			50–225	

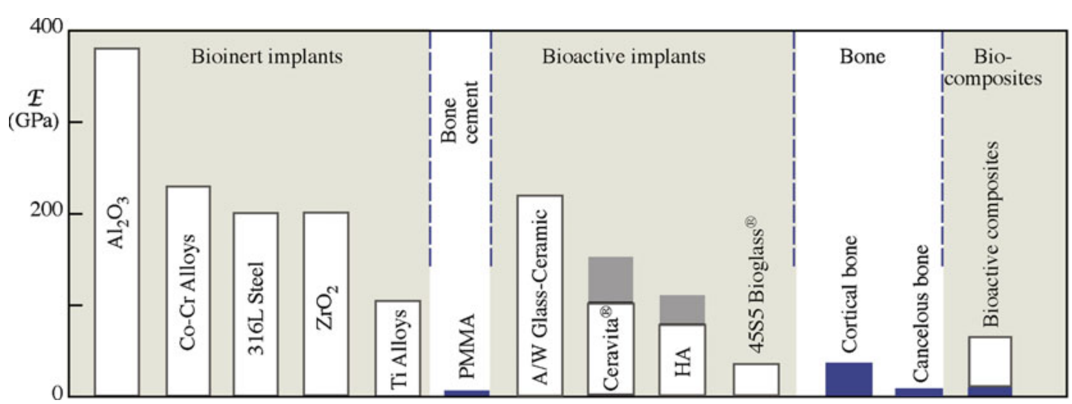

FIGURE 35.4. Young's modulus ($\mathcal{E}$) for various implants compared with bone.

35.4 ALUMINA AND ZIRCONIA

Al_2O_3 and ZrO_2 are two nearly inert bioceramics. They undergo little or no chemical change during long-term exposure to body fluids. High-density, high-purity (>99.5%) alumina is used in a number of implants, particularly as load-bearing hip prosthesis and dental implants. More than one million hip prosthesis were projected to have been performed using an alumina ball for the femoral-head component. Figure 35.5 shows three femoral components of total hip prostheses (THPs) with alumina balls. The U.S. Food and Drug Administration (FDA) approved the use of alumina in this type of application in 1982.

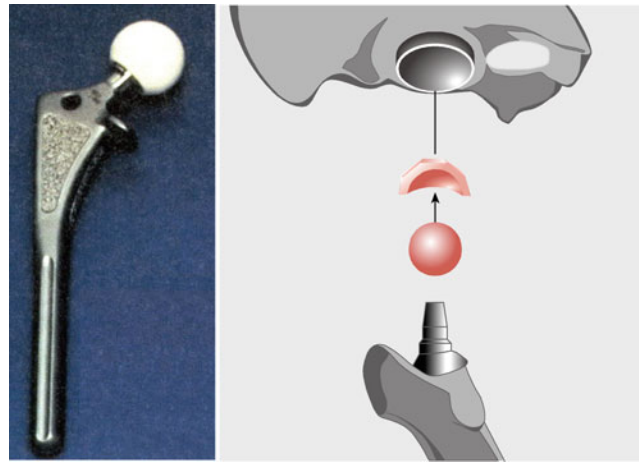

FIGURE 35.5. Medical-grade alumina used as femoral balls in total hip prostheses. The schematic shows how the femoral ball fits into the socket.

Although some alumina dental implants are made from single crystals, most alumina implants are very fine-grained polycrystalline Al_2O_3. These are usually made by pressing followed by sintering at temperatures in the range 1,600–1,800°C. A small amount of MgO (<0.5%) is added, which acts, as we've seen already, as a grain growth inhibitor and allows a high-density product to be achieved by sintering without pressure. Table 35.5 lists the physical characteristics of Al_2O_3 bioceramics. The International Standards Organization (ISO) requirements are also given. The most current ISO standard relating to alumina for implants is ISO 6474: 1994, Implants for Surgery—Ceramic Materials Based on High Purity Alumina. The ISO is the international agency specializing in standards at the highest level. Individual countries also have their own standards organizations.

BIOMEDICAL APPLICATIONS OF Al_2O_3

There are many other applications of alumina as an implant material including knee prostheses, ankle joints, elbows, shoulders, wrists, and fingers.

A MOIETY

A moiety is a group of atoms that forms a distinct part of a large molecule.

An important requirement for any implant material is that it should outlast the patient. Because of the probabilistic nature of failure in ceramics, it is not possible to provide specific and definite lifetime predictions for each individual implant. This was the approach that we discussed in Section 16.14. [See the discussion of Figure 16.27, a diagram showing applied stress versus probability of time to failure (SPT) for medical-grade alumina.] It shows, as you might expect, that increased loads and longer times increase the probability of failure. Results from aging and fatigue studies show that it is essential that Al_2O_3 implants be produced with the highest possible standards of quality assurance, especially if they are to be used in orthopedic prostheses in young patients.

TABLE 35.5 Physical Characteristics of Al_2O_3 Bioceramics

Property	*Commercially available high alumina ceramic implants*	*ISO standard 6474*
Alumina content (wt%)	>99.7	≥99.51
$SiO_2 + Na_2O$ (wt%)	<0.02	<0.01
Density (g/cm^3)	3.98	≥3.94
Average grain size (μm)	3.6	<4.5
Hardness (Vickers, HV)	2,400	>2,000
Bending strength (MPa, after testing in Ringer's solution)	595	>450

Although alumina ceramics combine excellent biocompatibility and outstanding wear resistance, they have only moderate flexural strength and low toughness. This limits the diameter of most alumina femoral head prostheses to 32 mm. Zirconia ceramics have higher fracture toughness, higher flexural strength, and lower $\mathcal{E}$ than alumina ceramics, as shown in Table 35.2. However, there are some concerns with ZrO_2.

There is a slight decrease in flexural strength and toughness of zirconia ceramics exposed to bodily fluids. The reason is associated with the martensitic transformation from the tetragonal to the monoclinic phase. A similar transformation has been observed to occur in aqueous environments.

The wear resistance of zirconia is inferior to those of alumina. In ceramic/ceramic combinations, the wear rate of zirconia can be significantly higher than that of alumina. In combination with UHMWPE (ultra-high-molecular-weight polyethylene) excessive wear of the polymer occurs.

Zirconia may contain low concentrations of long half-life radioactive elements, such as Th and U, which are difficult and expensive to separate out. The main concern is that they emit α-particles (He nuclei) that can destroy both soft and hard tissue. Although the activity is small, there are questions concerning the long-term effect of α radiation emission from zirconia ceramics.

35.5 BIOACTIVE GLASSES

Bioactive materials form an interfacial bond with surrounding tissue. Hench and Andersson gave the following definition.

> A bioactive material is one that elicits a specific biological response at the interface of the material, which results in the formation of a bond between tissues and the material.

The first and most thoroughly studied bioactive glass is known as Bioglass® 45S5 and was developed at the University of Florida. Bioglass® 45S5 is a multicomponent oxide glass with the composition (in wt%): 45% SiO_2, 24.5% Na_2O, 24.4% CaO, and 6% P_2O_5.

The majority of bioactive glasses are based on the same four components, and all current bioactive glasses are silicates. However, the structure of Bioglass® 45S5 is different from that of the silicate glasses we described in Chapter 7. Bioactive glasses have a random, two-dimensional sheet-like structure with low density. This is a result of the relatively low SiO_2 content. (You can compare the bioglass composition with that of other silicates given in Table 21.6). Bioglass is mechanically weak and has low fracture toughness. Both these properties are related to the glass structure.

Bioactive glasses can readily be made using the processes developed for other silicate glasses. The constituent oxides, or compounds that can be decomposed to oxides, are mixed in the right proportions and melted at high temperatures to produce a homogeneous melt. On cooling, a glass is produced. Because bioactive glasses are going to be used inside the body, it is necessary to use high-purity starting materials; and often the melting is performed in Pt or Pt alloy crucibles to minimize contamination.

Bioactive glasses have certain properties that are relevant to their application in the body.

Advantages:

There is a relatively rapid surface reaction that leads to fast tissue bonding. There are five reaction stages on the glass side of the interface. The reaction rates and mechanisms at each of the five stages have been determined by Fourier transform infrared (FTIR) spectroscopy. Bonding to tissue requires a further series of reactions that are, at present, not as well defined. The bonding process starts when biological moieties are adsorbed onto the SiO_2-hydroxycarboapatite layer.

$\mathcal{E}$ is in the range 30–35 GPa, close to that of cortical bone (see Figure 35.4)

Disadvantages:

They are mechanically weak. Tensile bending strengths are typically 40–60 MPa.

The fracture toughness is low.

As a result of this combination of properties bioactive glasses are not found in load-bearing applications; rather, they are used as coatings on metals, in low-loaded or compressively loaded devices, in the form of powders,

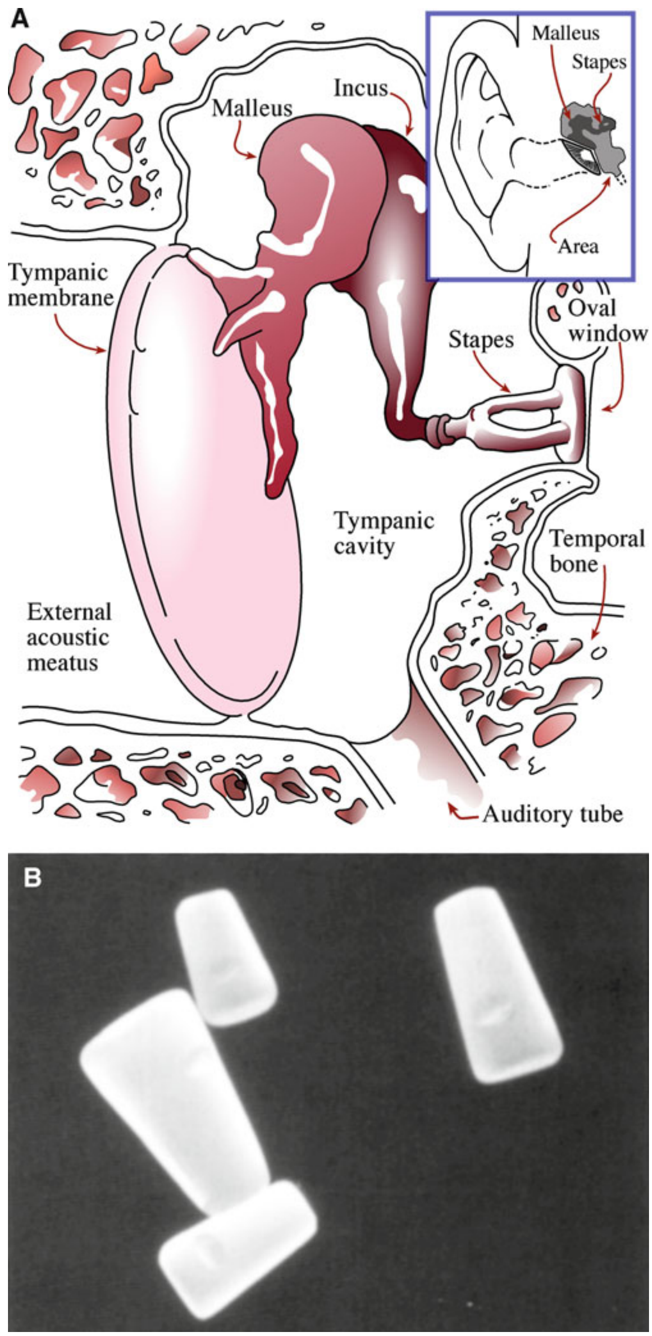

FIGURE 35.6. (A) Middle ear cavity and the auditory ossicles. (B) Ear implants.

and in composites. The first successful use of Bioglass® 45S5 was as a replacement for the ossicles (tiny bones) in the middle ear. The position of these bones is illustrated in Figure 35.6.

Cone-shaped plugs of bioactive glasses have been used in oral surgery to fill the defect in the jaw created when a tooth is removed. Bioactive glass implants have also been used to repair the bone that supports the eye (the orbital socket).

In powder form, bioactive glasses have been used in the treatment of periodontal disease and for the treatment of patients with paralysis of one of the vocal cords. When mixed with autologous bone they have been used in maxillofacial reconstruction (i.e., mixed with natural bone to rebuild a jaw).

35.6 BIOACTIVE GLASS-CERAMICS

We know that glass-ceramics are produced by ceramming a glass (see Chapter 26), converting it to a largely crystalline form by heat treatment. Several glass-ceramic compositions are bioactive. Their behavior in the body is very similar to that of the bioactive glasses; that is, they form a strong interfacial bond with tissue.

Cerabone® A-W is a glass-ceramic containing oxyfluoroapatite (A) and wollastonite (W).
Ceravital® is primarily now used in middle ear operations.
Bioverit I® is a class of bioactive machinable glass.

Cerabone® A-W is a glass-ceramic produced by crystallization of a glass of composition (in wt%), 4.6 MgO, 44.7 CaO, 34.0 SiO_2, 6.2 P_2O_5, 0.5 CaF_2. The crystalline phases are oxyfluoroapatite [$Ca_{10}(PO_4)_6(O,F)_2$] (the A phase) and β-wollastonite ($CaO.SiO_2$), the W phase. These phases precipitate out at 870°C and 900°C, respectively. The composition of the residual glassy phase is (in wt%) 16.6 MgO, 24.2 CaO, and 59.2 SiO_2. The properties of A-W glass ceramic are shown in Table 35.2. The applications include vertebral prostheses, vertebral spacers, and iliac crest prostheses.

Ceravital® refers to a number of different compositions of glasses and glass-ceramics that were developed in the 1970s in Germany for biomedical applications. The only field in which Ceravital® glass-ceramics are clinically used is replacement of the ossicular chain in the middle ear. In this application, the mechanical properties of the material are sufficient to support the minimal applied loads.

Bioverit I® consists of two crystalline phases in a glass matrix. The key crystalline component that makes this glass-ceramic machinable is mica. We have already described the idea behind machinable glass-ceramics in Section 18.10. For bioactivity, the other crystalline phase is apatite. The type and amounts of each phase depends on the initial glass composition. Table 35.6 shows the typical composition range of Bioverit I® glass-ceramics. Composition 1 produces fluorophlogopite mica and apatite. Composition 2 produces tetrasilicic mica and apatite. There are several clinical applications of bioactive machinable glass-ceramics, such as spacers in orthopedic surgery and middle ear implants.

TABLE 35.6 Composition Range (wt%) of Bioverit® Glass Ceramics

Constituent	*Composition range*	*Composition 1*	*Composition 2*
SiO_2	29.5–50.0	30.5	38.7
MgO	6–28	14.8	27.7
CaO	13–28	14.4	10.4
Na_2O/K_2O	5.5–9.5	2.3/5.8	0/6.8
Al_2O_3	0–19.5	15.9	1.4
F	2.5–7.0	4.9	4.9
P_2O_5	8–18	11.4	8.2
TiO_2	Additions	—	1.9

35.7 HYDROXYAPATITE

The apatite family of minerals has the general formula $A_{10}(BO_4)_6X_2$. In HA, or more specifically calcium hydroxyapatite, A = Ca, B = P, and X = OH. The mineral part of teeth and bones is made of an apatite of calcium and phosphorus similar to HA crystals. Natural bone is ~70% HA by weight and 50% HA by volume.

Hydroxyapatite is hexagonal (space group is $P6_3/m$) with $a = 0.9432$ nm and $c = 0.6881$ nm. The hydroxyl ions lie on the corners of the projected basal plane and occur at equidistant intervals [one half of the cell (0.344 nm)] along columns perpendicular to the basal plane and parallel to the c axis. Six of the ten Ca^{2+} ions in the unit cell are associated with the hydroxyls in these particular columns. One group of three Ca^{2+} ions describing a triangle, surrounding the OH group, is located at $z = 0.25$; the other set of three is at $z = 0.75$. The six phosphate $(PO_4)^{3-}$ tetrahedra are in a helical arrangement from levels $z = 0.25$ to $z = 0.75$. A network of $(PO_4)^{3-}$ groups provides the skeletal framework that gives the apatite structure its stability. (Complicated but certainly crystalline and very natural!)

Substitutions in the HA structure are possible. Substitutions for Ca, PO_4, and OH groups result in changes in the lattice parameter as well as in some of the properties of the crystal such as solubility. If the OH^- groups in HA are replaced by F^-, the anions are closer to the neighboring Ca^{2+} ions. This substitution helps to further stabilize the structure and is proposed as one of the reasons that fluoridation helps reduce tooth decay, as shown by the study of the incorporation of F into HA and its effect on solubility. Biological apatites, which are the mineral phases of bone, enamel, and dentin, are usually referred to as HA. Actually, they differ from pure HA in stoichiometry,

TABLE 35.7 Comparative Composition, Crystallographic, and Mechanical Properties of Human Enamel, Bone, and HA Ceramic

	Enamel	*Cortical bone*	*HA*
Constituents (wt%)			
Calcium, Ca^{2+}	36.0	24.5	39.6
Phosphorus, P	17.7	11.5	18.5
(Ca/P) molar	1.62	1.65	1.67
Sodium, Na^{+}	0.5	0.7	Trace
Potassium, K^{+}	0.08	0.03	Trace
Magnesium, Mg^{2+}	0.44	0.55	Trace
Carbonate, CO_3^{2+}	3.2	5.8	—
Fluoride, F^{-}	0.01	0.02	—
Chloride, Cl^{-}	0.30	0.10	—
Total inorganic	97.0	65.0	100
Total organic	1.0	25.0	—
Absorbed H_2O*	1.5	9.7	—
Crystallographic properties			
Lattice parameters (± 0.03 nm)			
a	0.9441	0.9419	0.422
c	0.6882	0.6880	0.6880
Crystallinity index	70–75	33–37	100
Crystallite size, nm	130 × 30	25 × 2.5–5.0	
Products after sintering			
>800°C	HA + TCP	HA + CaO	HA
Mechanical properties			
E (GPa)	14	20	10
Tensile strength (MPa)	70	150*	100

composition, crystallinity, and other physical and mechanical properties, as shown in Table 35.7. Biological apatites are usually Ca-deficient and are always carbonate-substituted: $(CO_3)^{2-}$ for $(PO_4)^{3-}$. For this reason you sometimes see biological apatites referred to as carbonate apatite and not as hydroxyapatite or HA.

For use in biomedical applications, HA is prepared in one of two forms: dense or porous. We now discuss how these two forms are produced and some of the applications for each.

DENSE HA

Porosity <5 vol%
Pore size <1 μm diameter
Grain size >0.2 μm

RESORPTION

Resorption is the process of reabsorbing biological material.

The methods used to produce *dense HA* are ones that we've already encountered in Chapter 23. The simplest is to dry-press HA powder. Mold pressures are typically 60–80 MPa. The powder may also be mixed with a small amount of a binder. Suitable binders are 1 wt% cornstarch and water, steric acid in alcohol, or low-molecular-weight hydrocarbons. After pressing, the green ceramic is sintered in air. Sintering temperatures are up to 1,300°C, with dwell times at peak temperature of several hours.

TABLE 35.8 Applications for Dense HA Ceramics

Application	*Form*
Augmentation of alveolar ridge for better denture fit	Blocks
Orthopedic surgery	Blocks
Target materials for ion-sputtered coatings	Blocks
Filler in bony defects (dental and orthopedic surgery)	Particles
Plasma-sprayed coatings on metal implants	Particles
Filler in composites and cements	Particles

By using hot-pressing techniques, we can achieve densification at much lower temperatures (900°C vs. 1,300°C). The use of lower sintering temperatures not only saves on energy costs but prevents the formation of other calcium phosphate phases (e.g., TCP), which usually form when HA is sintered at temperatures >900°C.

Hot isostatic pressing (HIPing) has also been used to form HA ceramics. HIPing results in products with more uniform densities than those obtained by uniaxial pressing and higher compressive strength.

The disadvantage of both hot pressing and HIPing is the equipment costs.

There are many applications for dense HA in both block form and as particles, as listed in Table 35.8. One important application is replacements for tooth roots following extraction. The implants help minimize alveolar ridge resorption and maintain ridge shape following tooth loss, which affects millions of people.

The particular advantage of *porous HA* is that it permits ingrowth of tissue into the pores, providing biological fixation of the implant. The minimum pore size necessary is ~100 μm. When used as a bone graft substitute, porous HA should mimic the framework (or stromal component) of the bone. The ideal microstructure for regeneration of cortical bone is an interconnected porosity of 65%, with pore sizes ranging from 190 to 230 μm. The ideal graft substitute for cancellous bone would consist of a thin framework of large (500–600 μm) interconnected pores.

Several methods have been used to produce porous HA ceramics. Remember that historically much of ceramic processing was concerned with trying to produce components that are fully dense. Therefore, to produce porous components, particularly where we need to control pore size. Often requires ingenuity and a rethink. We discussed porous ceramics in Section 23.15, so here we just point out special features for producing porous HA ceramics.

Sinter HA powders
Make a cement
Use a natural template

Sinter HA powders, or a mixture of suitable reactant powders, with naphthalene particles that volatilize during heating to create an interconnected porous network. Similar approaches have been used to produce foam glass (see Section 26.9) and in the fugitive electrode method of producing multilayer chip capacitors (MLCCs) (see Section 31.7).

By mixing water-setting HA *cements* with sucrose granules, porosity can be created when the sucrose is dissolved prior to the cement setting. One example of an HA cement is that obtained by the following reaction is an aqueous environment.

$$Ca_4(PO_4)_2 + CaHPO_4 \rightarrow Ca_5(PO_4)_3OH \tag{35.1}$$

The *natural-template method* was developed in 1974. It can produce porous HA powders. A suitable template was found to be the calcium carbonate ($CaCO_3$) skeleton of reef-building corals, such as those found in the South Pacific. The reaction to produce HA involves a hydrothermal exchange reaction of carbonate groups with phosphate groups, which can occur via the following chemical reaction.

$$\begin{aligned} &10\ CaCO_3 + 6(NH_4)_2HPO_4 + 2H_2O \\ &\quad \rightarrow Ca_{10}(PO_4)_6(OH)_2 + 6(NH_2)CO_3 \\ &\quad + 4H_2CO_3 \end{aligned} \tag{35.2}$$

The HA structure produced by this exchange reaction replicates the porous marine skeleton, including its interconnected porosity. HA grown on *Porites* and *Goniopora* coral skeleton templates can be used to mimic the stroma of cortical bone and cancellous bone, respectively.

AISI 316L
$\alpha = 20.0 \times 10^{-6}\ °C^{-1}$ (to 200°C)
$\alpha = 21.8 \times 10^{-6}°C-1$ (to 400°C)

BIOGLASS® 45S5
$\alpha = 18.0 \times 10^{-6}\ °C^{-1}$ (to 450°C)

35.8 BIOCERAMICS IN COMPOSITES

The main reason for forming composites is to improve the mechanical properties, most often toughness, above that of the stand-alone ceramic. For bioceramic composites, we often are trying to increase K_{IC} and decrease $\mathcal{E}$.

The first bioceramic composite was a stainless steel fiber/bioactive glass composite made of Bioglass® 45S5 and AISI 316L stainless steel. The composite was made by first forming a preform of the discontinuous metal fibers, then impregnating it with molten glass, and finally heat-treating the composite to develop the desired mechanical properties.

For effective stress transfer between the glass matrix and the reinforcing metal fibers when the composite is under load, there must be a strong glass–metal bond. This requires that the glass wet the metal surface during processing. Wetting is achieved by oxidizing the metal fibers before they are immersed in the glass. Chemical analysis across the glass/metal interface showed that there is Fe diffusion from the oxide into the glass and Si diffusion from the glass into the oxide. The composition gradient across the interface indicates chemical interaction between the two phases, which leads to improved adhesion.

Assuming that the fibers are aligned in the direction of the applied load, and that there is good adhesion with the matrix such that the elastic strains are equal in both components, we can write:

$$\sigma_c = \sigma_f V_f + \sigma_m V_m \tag{35.3}$$

where the subscripts c, f, and m refer to the composite, fiber, and matrix, respectively; and V is the volume fraction of each phase. If we assume 45 vol% of steel fibers, that $\sigma_f = 530$ MPa, and that $\sigma_m = 42$ MPa, then $\sigma_c = 262$ MPa. This value, which is close to experimentally measured values, represents significant strengthening above that of the glass alone.

One of the potential problems associated with forming composites is that of mismatch in α between the two components, which is significant for glass and steel. For reinforcing fibers where the difference in α with the glass phase is even greater than that with steel (e.g., Ti), it is necessary to change the composition of the glass to lower its α.

Other current bioceramic composites of interest are:

Ti-fiber-reinforced bioactive glass
ZrO_2-reinforced A-W glass
TCP-reinforced PE
HA-reinforced PE

Hydroxyapatite-reinforced PE is a good illustration of where a composite can have properties that are not available in a single material. These composites were developed as bone replacement that would have a matched modulus, be ductile, and be bioactive. Figure 35.7 shows how, by increasing the volume fraction of HA to 0.5, a composite can be achieved with $\mathcal{E}$ in the range of that of cortical bone. When the volume fraction of HA in the composite is increased above about 0.45, the fracture mode changes from ductile to brittle. For clinical applications, a volume fraction of 0.4 has been found to be optimum. The

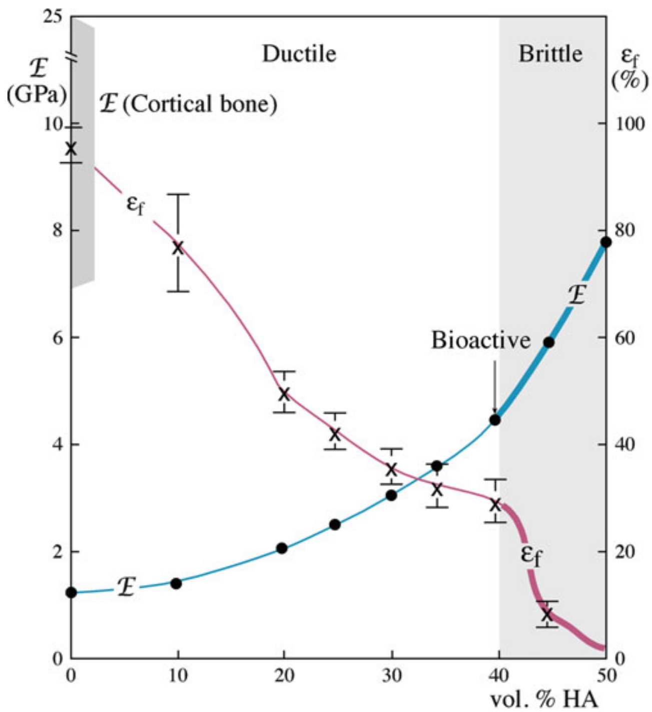

FIGURE 35.7. Effect of the volume fraction of HA on $\mathcal{E}$ and strain to failure of HA-reinforced polyethylene composites in comparison to cortical bone.

HA-reinforced PE composite is designated commercially as HAPEX™, and several thousand patients have received middle ear implants made from this material. The technology was granted regulatory approval by the FDA in the United States in 1995.

35.9 BIOCERAMIC COATINGS

Applying a glass or ceramic coating onto the surface of a substrate allows us to have the best of both worlds. We have the bulk properties of the substrate and the surface properties of the coating. The three main reasons for applying a coating are:

1. Protect the substrate against corrosion
2. Make the implant biocompatible
3. Turn a nonbioactive surface into a bioactive one

We can list four substrate-coating combinations:

1. Ceramic on ceramic
2. Glass on ceramic
3. Ceramic on metal
4. Glass on metal

Bioceramic coatings are often used on metallic substrates, where the fracture toughness of the metal is combined with the ability of the coating to present a bioactive surface to the surrounding tissue. The use of a bioceramic coating on a metal implant can lead to earlier stabilization of the implant in the surrounding bone and extend the functional life of the prosthesis. Under the proper conditions, a cementless prosthesis should remain functional longer than a cemented device, in which stability is threatened by fracture of the bone cement.

The important ceramic coatings are HA and TCP. We described the structure and properties of HA, a bioactive ceramic, in some detail in Section 35.6. TCP is a resorbable bioceramic. It occurs in two polymorphs: α-whitlockite and β-whitlockite. The β form is the more stable. When TCP is implanted into the body it eventually dissolves and is replaced by tissue. The role of resorbable bioceramics is to serve as scaffolding, permitting tissue infiltration and eventual replacement. Essentially, this is the same function as bone grafts. TCP has been clinically applied in many areas of dentistry and orthopedics. Bulk material, available in dense and porous forms, is used for alveolar ridge augmentation, immediate tooth root replacement, and maxillofacial reconstruction. However, because bulk TCP is mechanically weak, it cannot be used in load-bearing applications. Therefore, TCP is often used as a coating on metal substrates.

The most widely used method for applying coatings of HA and TCP is plasma spraying. We already described this technique in Section 27.5; it is one of the methods used to produce thermal barrier layers. Plasma spraying uses a plasma, an ionized gas, that partially melts the HA particles and carries them to the surface of the substrate. For HA coatings, the starting material is pure 100% crystalline HA particles in the 20–40-μm range. One of the advantages of plasma spraying is that the substrate remains at a relatively low temperature (generally <300°C; the plasma temperature may exceed 10,000°C!) so the mechanical properties of the metal are not compromised. The coating thickness typically averages 40–60 μm with a residual porosity <2%. HA coatings prepared by plasma spraying typically contain considerable amounts of amorphous calcium phosphate and small amounts of other crystalline phases. Heat-treating the coating can increase crystallinity and improve the adhesion to the substrate. However, this process is not usually done because of economic factors and concerns about the adverse effects it might have on the mechanical properties of the substrate.

In addition to plasma spraying, other methods have been used to apply HA coatings.

- Electrophoretic deposition when line-of-site deposition is not possible
- Sputtering when very thin coatings are needed
- HIPing when we need a very dense material

Electrophoretic deposition (see Section 27.6 for a description of the technique) can be used to coat porous surfaces that cannot be completely coated by line-of-sight techniques such as plasma spraying. However, the adhesion of the HA particles to the substrate and each other is weak, and high-temperature sintering after deposition is usually necessary.

Sputtering has been used to produce thin (1 μm) HA coatings. The deposited films are amorphous because the sputtered components don't possess enough kinetic energy to recombine in a crystalline form. Heat treatment at 500°C is enough to crystallize the amorphous film. Durability of thin sputtered films in the body has not yet been demonstrated.

HIPing is a technique we met earlier but not in the context of forming films. If a metal implant is coated with HA particles, then HIPing can be used to form a dense adherent coating. To achieve a uniform application of pressure on the HA particles, an encapsulation material (e.g., a noble metal foil) is necessary. As we mentioned earlier, HIPing allows the use of lower sintering temperatures than pressureless techniques; as a result, there is less chance of altering the microstructure or mechanical properties of the metal substrate.

There are several requirements for HA coatings used for prosthetic devices.

- Correct crystalline phase
- Stable composition
- Dense
- Good adhesion to the substrate
- High purity
- No change to the substrate

Plasma-sprayed coatings often contain a mixture of crystalline and amorphous phases, which may be undesirable. The adhesion of plasma-sprayed HA coatings to metal substrates is principally mechanical, and so surface roughness of the substrate plays an important role.

Bioactive glass coatings are also important for implant devices. These are usually applied by one of the following techniques.

- Enameling
- Flame spraying
- Dip coating

Flame spraying is similar to plasma spraying except that the carrier gases are not ionized, and the temperatures are considerably lower than in plasma spraying. In dip coating, the metal implant is preoxidized to provide a suitable surface for wetting the molten glass. The heated metal is then dipped into the molten glass.

Enameling is a traditional method of applying glass coatings and uses a particulate form of the glass called a frit, which is formed when molten glass is quenched in water. The resulting coarse particles of the frit are ground to a fine powder, which is applied to the metal substrate by painting, spraying, or dipping. The coated article is then heated to soften the glass and form a uniform coating. In traditional enameling, the adhesion between the glass and metal is improved by using what enamelers call a "ground coat." This is a mixture of metal oxides that react chemically with both the metal and the glass, enabling formation of a chemical bond. However, this approach has not proved to be successful with bioactive glasses, and alternative approaches are being used.

35.10 RADIOTHERAPY GLASSES

Radioactive yttrium aluminosilicate (YAS) glasses have been used to provide in situ irradiation of malignant tumors in the liver. Although primary liver tumors are relatively rare in the United States (about 3,000–4,000 deaths per year; 1.2 million worldwide), they are almost always lethal. Most of these tumors are inoperable due to various medical complications. Irradiating the tumors inside the body allows the use of large (>10,000 rad) localized doses of radiation directly to the tumor while minimizing damage to surrounding healthy tissue. This procedure represents an important tool in treating this disease.

YAS glasses are particularly suitable because they are:

- Not toxic
- Easily made radioactive
- Chemically insoluble while the glass is radioactive

The sol–gel process has been used to produce high-purity YAS glass spheres, shown in Figure 35.8. The radioactive isotope produced when the YAS glass spheres are irradiated is ^{90}Y, a β-emitter with a half-life of 64.1 h. The average penetration of β-particles (electrons) in human tissue is 2.5 mm (maximum penetration ~10 mm). For the radioactive material to reach the site of the tumors, between 1 and 15 million microspheres are injected into the hepatic artery, which is the primary blood supply for

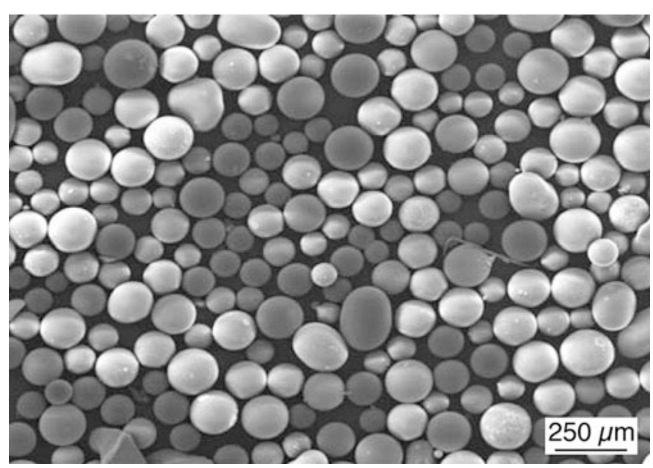

FIGURE 35.8. Lithium calcium borate glass microspheres produced by passing through a flame at 1,400°C.

the target tumors. Treatment time is 2–4 h. The microspheres are 15–35 μm in diameter, and this allows the blood to carry them into the liver, but they are too large to pass completely through the liver and enter the circulatory system. The microspheres concentrate in the tumor because it has a greater than normal blood supply. There they irradiate it with β-particles. Because the half-life of ^{90}Y is 64.1 h, the radioactivity decays to a negligible level in about 3 weeks.

Although the use of radiotherapeutic glass spheres in treating liver cancer is still at a relatively early stage, the results appear promising. The commercially available product, called TheraSphere™, made by MDS Nordion, is approved in the United States and Canada for treating patients with inoperable liver cancer. Other medical applications for these glass spheres have been considered, such as the treatment of cancers of the kidney and brain.

35.11 PYROLYTIC CARBON HEART VALVES

Carbon is an important bioceramic. It combines outstanding biocompatibility and chemical inertness. Carbon exists in many forms, and we've already met some of these forms in earlier chapters. The most important form of carbon for biomedical applications is a type of pyrolytic graphite known as the low-temperature isotropic form (LTI carbon).

The LTI is an example of what are referred to as turbostratic carbons. These have a disordered structure based on graphite (and thus are also called turbostratic graphite). In turbostratic carbon, the ABABA stacking sequence is disrupted through random rotations or displacement of the layers relative to each other. The individual LTI carbon crystallites are only ~10 nm in size and are arranged randomly in the bulk material. This microstructure leads to the material having isotropic mechanical and physical properties, unlike graphite where the properties are highly anisotropic. The density and mechanical properties of LTI are influenced by the number of carbon vacancies in each of the layers and distortions within each plane. The densities range from 1,400 kg/m^3 up to a theoretical maximum of 2,200 kg/m^3.

LTI
Low T refers to the forming $T < 1500°C$. For ceramics 1500°C is not a high T.

High-density LTI carbons are the strongest bulk form of turbostratic carbon; we can increase their strengths further by adding Si. The material then consists of discrete submicrometer β-SiC particles randomly dispersed in a matrix of roughly spherical micrometer-size subgrains of pyrolytic carbon; the carbon itself has a "subcrystalline" turbostratic structure, with a crystallite size typically <10 nm. This is analogous to the microstructure produced during precipitation hardening of metals.

FIGURE 35.9. LTI pyrolytic carbon-coated heart valves.

A chemical vapor deposition (CVD) process (see Section 28.4) involving the co-deposition of carbon and SiC is typically used to produce the LTI-Si alloys. Two possible reactions are:

Decomposition of propane:

$$C_3H_8 \rightarrow 3C + 4H_2 \tag{35.4}$$

Decomposition of methyltrichlorosilane

$$CH_3Cl_3Si \rightarrow SiC + 3HCl \tag{35.5}$$

The articles to be coated are suspended within a fluidized bed of granular particles, usually ZrO_2. The reactions take place in the range 1,000–1,500°C, and the products coat the components as well as the ZrO_2 particles.

One of the major applications for LTI carbon is in making prosthetic heart valves, as shown in Figure 35.9. This is one of the most demanding applications for biomaterials. The first use of LTI carbon in humans as a prosthetic heart valve was in 1969. The majority of artificial heart valves currently use Si-alloyed LTI pyrolytic carbon.

35.12 NANOBIOCERAMICS

There are many books on the uses of nanoparticles, and there are hundreds of research papers on this topic. There are also many papers discussing the toxicity of these materials. The asbestos fibers linked to respiratory illness have widths <250 nm; amphibole (red or blue asbestos)

FIGURE 35.10. Microbarcodes from Corning. The cylindrical bars are typically 100 μm long and 20 μm in diameter.

fibers are ~75 to ~240 nm wide, thus definitely counting as nanoparticles.

Examples of a microbarcode made by Corning are shown in Figure 35.10. The information is coded into the small glass bars so that they fluoresce. The pattern can then be read by illuminating the glass with ultraviolet (UV) radiation; otherwise, it is not only too small to see but the information would not be detected.

The magnetite crystals we discussed in Chapter 33 are used by nature in ways we don't fully understand, but they appear to allow certain species to detect the earth's magnetic field and use it to navigate.

Functionalized magnetic nanoparticles can be used as drug carriers to target specific abnormalities in the body, such as tumor cells. The particles can be directed using an externally applied magnetic field. In hyperthermia treatment, a ferrite or other magnetic material produces localized heating in the presence of an alternating magnetic field. The implanted nanomaterial and the surrounding area heat up, and this kills the targeted cancerous cells. A clinical study in Germany using prostate cancer patients showed that localized temperatures as high as 48.5°C could be obtained with a magnetic field strength of 4 kA/m. Cell death usually begins around 41°C, and necrosis (rapid death) occurs above 50°C (a healthy body temperature is 37°C).

TiO_2 nanoparticles are used in sunscreen to protect the skin from UV radiation. The particles used for this application are typically 10–100 nm in diameter and block both UVA (320–400 nm) and UVB (290–320 nm) irradiation. There is some concern that these nanoparticles (and those of ZnO) are so active that they might catalyze the breakdown of DNA, but they do not appear to penetrate the outer layers of the skin. The positive aspect of this is the potential for using these same TiO_2 nanoparticles for photo-killing malignant cells—known as photodynamic therapy. TiO_2 and ZnO particles are actually being coated with silica so the particle surface is more inert (a use for core-shell nanoparticles).

DENTAL RESTORATIONS

- Feldspathic veneers
- Porcelain jacket crowns (PJCs)
- Metal-ceramic crowns
- Inlays and onlays
- Implants

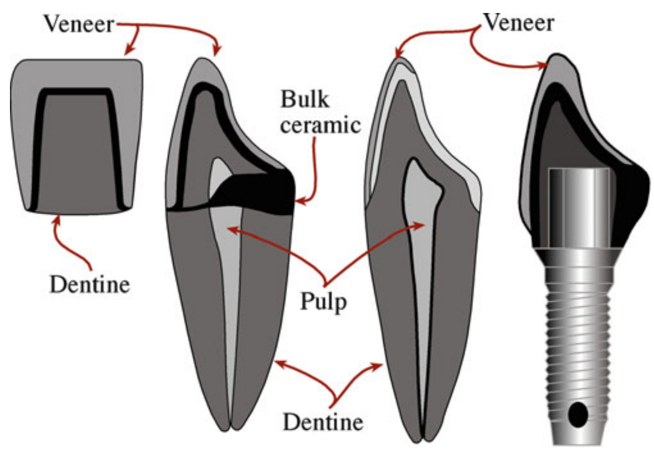

FIGURE 35.11. Tooth restoration.

35.13 DENTAL CERAMICS

The felspathic porcelains (porcelain based on feldspar) are used as the veneer to "cap" the front of a tooth for cosmetic reasons; these veneers are ~500 μm thick. Today, this material is mainly replaced by glass, although the name may not have changed. Leucite is added to modify the thermal expansion coefficient. Dicor is the glass-ceramic developed by Corning for constructing replacement teeth. The tooth is cast as a glass using a lost-was mold and then cerammed. Alumina has also been used to form the tooth although porosity causes failure during "use." One way to improve this is to infiltrate the alumina with a lanthanum-containing glass (known commercially as In-Ceram). The different restorations are shown in Figure 35.11.

35.14 BIOMIMETICS

The topic of biomimetics was actually mentioned earlier but not using the new name. The principle underlying the development of biomimetics is "learning from nature." Biomimetics can potentially lead to an enormous subset of ceramics. Not only are the materials important, their topology and microstructure are also special. The aim is to mimic natural materials that have special behaviors but to do it with "better" (i.e., ceramic) materials.

Shells (especially the abalone shell). Biological materials deposit inorganic layers. The abalone shell consists of layers of aragonite with ~5 wt% organic material (e.g., protein) between the layers to toughen it. A schematic cross section and a scanning electron microscopy (SEM) image of the aragonite layers are shown in Figure 35.12.

Coral. Used in the manufacture of bone grafts "as harvested" or after processing. It is a natural porous ceramic and can be converted to porous HA (see Section 35.7). Surgeons in the United States perform ~500,000 bone grafts each year.

Petrified wood. A natural material is infiltrated by a ceramic.

Petrified wood provides a good illustration of the surprising potential of biomimetics in a way that is analogous to the conversion of coral. Wood can be intentionally converted into biomorphic, microcellular SiC-based ceramics using a reactive melt-infiltration process or, more specifically, liquid-Si infiltration (LSI). The images in Figure 35.13 illustrate the possibility: the microstructure of the resulting composite depends on the nature of the wood used. Beech, pine, and rattan produce very different microstructures; and they are, of course, different in cross section and longitude. In this example, the infiltrating liquid was a molten Si-M alloy (Mo, Ta, Ti, and Fe were explored as the metal, M). For Mo, this produces a $MoSi_2$/Si composite. The LSI technique has been used previously to produce SiC and Si_3N_4; the special feature here is the biomimetic structure produced by the wood.

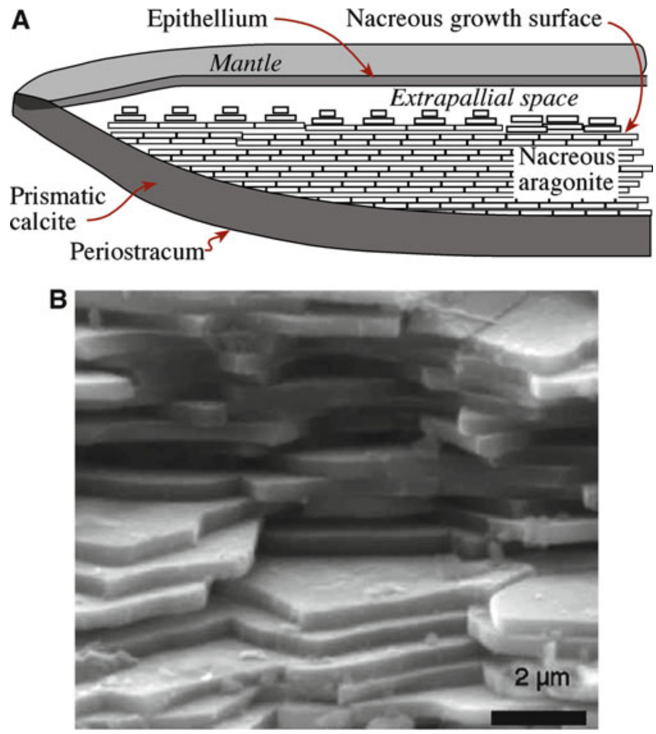

FIGURE 35.12. (A) Schematic of the abalone shell. (B) Abalone slabs.

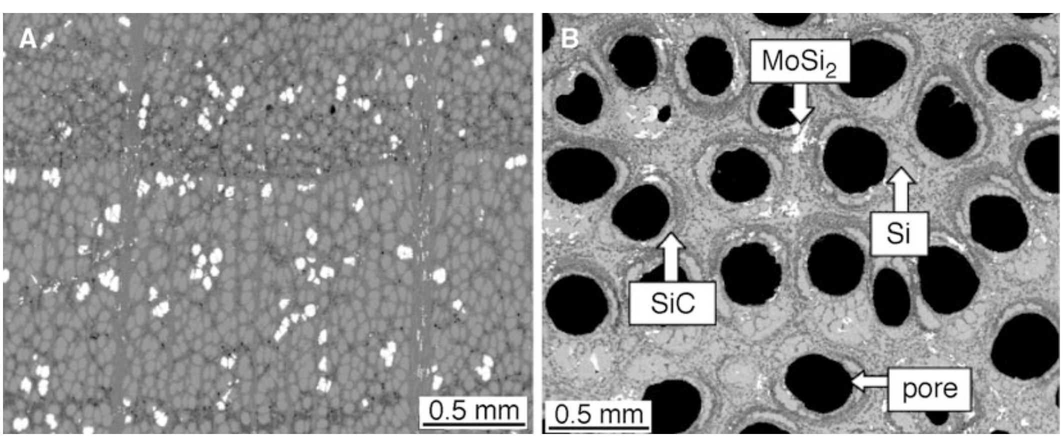

FIGURE 35.13. Wood converted into ceramics by a reactive melt-infiltration process.

CHAPTER SUMMARY

Bioceramics is a relatively new field and an increasingly important one. Bioceramics are implanted into the human body to replace existing parts that have become diseased, damaged, or worn out. More than one million hip prostheses using alumina components have been implanted. Alumina is a very important bioceramic because it is biocompatible—it doesn't produce any adverse reactions in the body. One of the disadvantages of alumina is that it is also an example of what is termed a nearly inert bioceramic: it doesn't allow interfacial bonding with tissue. When bioactive ceramics and glasses are implanted into the body, they undergo chemical reactions on their surface, leading to strong bond formation. The most important bioactive ceramic is HA, which is very similar to the mineral part of teeth and bones. HA is brittle and mechanically weak; but if it is combined with a polymer, we can produce a composite that is ductile and has $\mathcal{E}$ close to that of bone. HA and other bioactive ceramics and glasses are often used as coatings on metal supports. This allows the excellent mechanical properties of the metal to be combined with the biocompatibility of ceramics. Another ceramic material that is used in the form of a coating is pyrolytic carbon. The application here is artificial heart values, which is a very demanding materials application: reliability is critical. We concluded the chapter with a brief discussion of biomimetics (which is related to bionics, etc). and emphasized that this will become a large field in itself, but you must understand the materials to take full advantage of this potential.

PEOPLE AND HISTORY

Duchateau, Alexis (1714–1792) was the pharmacist in Paris who made the first porcelain dentures in ~1770.

Dubois de Chémant, Nicolas (1753–1824) wrote a dissertation on artificial teeth describing the advantages using mineral paste to make replacement teeth. He escaped to England from the French Revolution and later obtained porcelain paste from Wedgwood.

Gluck, Themistocles (1853–1942) is generally regarded as the inventor of artificial biomaterials (ivory was a favorite).

Hench, Larry (born 1938) developed Bioglass® in 1969. He is Emeritus Professor of Materials at Imperial College, London.

Hippocrates (460–370 BCE). One of his aphorisms can be translated as: those diseases which medicines do not cure, iron cures; those which iron cannot cure, fire cures; and those which fire cannot cure, are to be reckoned wholly incurable. Modern hyperthermia treatment uses ferrite nanoparticles to locally generate heat.

EXERCISES

35.1 Briefly compare and contrast the suitability of metals, ceramics, and polymers for use in biomedical applications. In your answer, consider the following factors: biocompatibility, mechanical properties, and ease of processing.

35.2 Alumina (Al_2O_3) ceramic implants are required to have a small grain size (<4.5 μm). (a) Why do you think a small grain size is important? (b) How does the addition of MgO to the powder mixture help to keep the grain size small? (c) Are there any other ways that could be used to limit the extent of grain growth?

35.3 Explain why tetragonal zirconia polycrystal (TZP) and Mg-partially stabilized zirconia (PSZ) ceramics have higher toughness than alumina ceramics.

35.4 The Weibull modulus of an alumina bioceramic is given as 8.4. (a) What does a value of $m = 8.4$ imply? (b) For an implant made out of a metal, the value of $m \sim 100$. What implications would this have for lifetime predictions for the metal component compared to the alumina component? (c) How does the value of m affect the design of a component for a load-bearing application?

35.5 The composition of Bioglass® 45S5 is 45% SiO_2, 24.5% Na_2O, 24.4% CaO, and 6% P_2O_5. (a) Classify each of the oxide constituents of 45S5 as either network formers, modifiers, or intermediates. (b) What would the composition of Bioglass® 45S5 be in mol%? (c) Explain briefly how the structure of 45S5 differs from the silicate glasses described in Chapter 7 and what implications this difference has on the properties of 45S5.

35.6 The substitution of ions in the hydroxyapatite (HA) structure can change the lattice parameters of the unit cell. Explain how you think the substitution of Ca^{2+} for the following ions would change both the a and c lattice parameters: Sr^{2+}, Ba^{2+}, Pb^{2+}, Mg^{2+}, Mn^{2+}, and Cd^{2+}.

35.7 According to ASTM Standards [American Society for Testing and Materials (1990) Annual Book of ASTM Standards, Section 13, F 1185–1188], the acceptable composition for commercial HA is a minimum of 95% HA, as established by X-ray diffraction (XRD) analysis. Describe how XRD can be used to determine phase proportions in a mixture.

35.8 We mentioned that in steel fibers/bioactive glass composites it was important that there was chemical interaction between the two components to ensure stress transfer during loading. We have just formed a bioceramics company and want to hire you as a consultant. We want you to determine whether such interactions have occurred in a composite we have just made. What analytical technique or techniques would you use for your evaluation? Explain the reasoning behind your answer and some of the pros and cons of the technique or techniques you chose.

35.9 One of the advantages of plasma spraying for producing HA coatings on metallic implants is that the substrate temperature can be kept relatively low. What possible mechanisms can lead to a loss in the mechanical strength of a metal if it is exposed to high temperatures? (You can limit your discussion to the cases of Ti alloys and stainless steel).

35.10 Explain why the mechanical properties of turbostratic carbons such as LTI are different from those of graphite. Both are forms of carbon and are chemically identical.

35.11 We can use several definitions of a biomaterial. Discuss at least three that have been proposed and explain why you prefer the one given here.

35.12 Explain why HA and TCP behave differently in the body.

35.13 Name the two main types of bone. Say where they are found in the body and why.

35.14 Why is stress shielding a problem for prostheses?

35.15 Why is alumina used as the femoral ball, and why is so much work aimed at improving this device?

35.16 What is a bioactive ceramic, and why has Bioglass been so successful?

35.17 Discuss the composition and structure of Cerabone and explain why it was so designed.

35.18 Write down the general formula for HA and state its percentage in bone by weight and volume. How does its structure relate to its properties?

35.19 Discuss why thermal spraying is the preferred method for producing HA and TCP coatings.

35.20 Summarize and justify five uses for nanobioceramics.

GENERAL REFERENCES

Hench LL (1991) Bioceramics: from concept to clinic. J Am Ceram Soc 74(7):1487–1510 (1,844 cites by 2011)

Hench LL, Wilson JK (eds) (1993) An introduction to bioceramics. World Scientific, Singapore, A collection of chapters on different aspects of bioceramics written by expects in the field. This is an excellent but aging resource

LeGeros RZ, LeGeros JP (eds) (1998) In: Bioceramics, Volume 11, Proceedings of the 11th international symposium on ceramics in medicine. World Scientific, Singapore. The most recently published proceedings in this annual conference series. Covers the latest developments in all aspects of the field of bioceramics

Marieb EN (2008) Human anatomy and physiology, 8th edn. Benjamin Cummings, Menlo Park, Reference for a more detailed description of bone

Park JB, Lakes RS (2010) Biomaterials science and engineering. Reprint of 3 E (2007) Springer, New York. A textbook covering all aspects of biomaterials. The section covering ceramic implant materials is quite brief but there is information about polymers and metals and a general background about the field

Ravaglioli A, Krajewski A (1992) Bioceramics: materials, properties, and application. Chapman and Hall, London, Covers history of bioceramics, scientific background to the field, and state-of-the-art as of 1991

Ratner BD, Hoffman AS, Schoen FJ, Lemons JE (2004) Biomaterials science, 2nd edn. Elsevier, Amsterdam, Used in our courses

Williams DF (1999) The Williams dictionary of biomaterials. Liverpool University Press, Liverpool, The latest collection of definitions used in the field of biomaterials

Yamamuro T, Hench LL, Wilson-Hench J (eds) (1990) Handbook of bioactive ceramics, vol I: bioactive glasses and glass ceramics, vol II: calcium phosphate and hydroxylapatite ceramics. CRC Press, Boca Raton, A collection of articles on bioactive and resorbable bioceramics

Journals and Conference Proceedings

The following journals and conference proceedings are the main places where reports of advances in bioceramics are reported

Acta Biomaterialia

Bioceramics. This is the title of the proceedings of the international symposium on ceramics in Medicine. The symposium has been held annually since 1988

Biomedical Materials and Engineering. Covers all aspects of biomaterials and includes details of clinical studies. Usually found in with medical journals rather than physical science or engineering publications

Journal of Materials Science Materials in Medicine. Spun off from *Journal of Materials Science*, this is another growing journal

Journal of the American Ceramic Society. Covers the entire ceramics field including bioceramics

Nature. A journal with a wide readership. Publishes important news articles having a significant impact on the field

SPECIFIC REFERENCES

Annual Book of ASTM Standards, 13.01, *Medical Implants*, ASTM, Philadelphia. The American Society for Testing and Materials (ASTM) has developed several standards related to bioceramics for surgical implants: the *Annual Book of ASTM Standards*

Bokros JC, LaGrange LD, Fadali AM, Vos KD, Ramos MD (1969) J Biomed Mater Res 3:497–528, First use of carbon heart valves in humans

Bonfield W, Grynpas MD, Tully AE, Bowman J, Abram J (1981) Hydroxyapatite reinforced polyethylene: a mechanically compatible implant. Biomaterials 2:185

Brömer H, Pfeil E, Käs HH (1973) German Patent 2,326,100. Patent for Ceravital

Chakrabarti O, Weisensel L, Sieber H (2005) Reactive melt infiltration processing of biomorphic Si–Mo–C ceramics from wood. J Am Ceram Soc 88(7):1792–1798

Cherukuri P, Glazer ES, Curley SA (2010) Targeted hyperthermia using metal nanoparticles. Adv Drug Deliv Rev 62:339, A recent review that covers not only oxides, but also other nanoparticles such as Au

Ducheyne P, Hench LL (1982) The processing and static mechanical properties of metal fibre reinforced bioglass®. J Mater Sci 17:595, Diffusion across a bioglass-metal interface

Galletti PM, Boretos JW (1983) Report on the consensus development conference on clinical applications of biomaterials. J Biomed Mater Res 17:539, Defined "biomaterial"

Hench LL (1991) Bioceramics: from concept to clinic. J Am Ceram Soc 74:1487, An excellent review on this topic

Hench LL, Andersson O (1993) Bioactive glasses. In: Hench LL, Wilson JK (eds) An introduction to bioceramics. World Scientific, Singapore, pp 41–62

Johannsen M, Gneveckow U, Eckelt L, Feussner A, Waldöfner N, Scholz R, Deger S, Wust P, Loening SA, Jordan A (2005) Clinical hyperthermia of prostate cancer using magnetic nanoparticles: presentation of a new interstitial technique. Int J Hyperthermia 21:673–647, A clinical trial on prostrate cancer patients

Klawitter JJ, Hulbert SF (1971) Application of porous ceramics for the attachment of load bearing orthopedic applications. J Biomed Mater Res 2:161, Determined that a minimum pore size of 100 μm is necessary for bone ingrowth

Lübbe AS, Bergemann C, Huhnt W, Fricke T, Riess H, Brock JW, Huhn D (1996) Preclinical experiences with magnetic drug targeting: tolerance and efficacy. Cancer Res 56:4694, The ferrofluid contained 50–150nm diameter Fe_3O_4 particles and a 0.5T magnetic field was used

Mehmel M (1930) Z Kristallogr 75:323, One of two original determinations of the structure of hydroxyapatite. The structure was originally taken to be the same as that of fluorapatite, $Ca_{10}(PO_4)_6F_2$, which had been already resolved

Merwin GE, Wilson J, Hench LL (1984) In: Grote JJ (ed) Biomaterials in otology. Nijhoff, The Hague, pp 220–229, Description of bioglass

Náray-Szabó S (1930) The structure of apatite (CaF) $Ca_4(PO_4)_3$. Z Kristallogr 75:387, The other early paper on the structure of hydroxyapatite

Posner AS, Perloff A, Diorio AF (1958) Refinement of the hydroxyapatite structure. Acta Crystallogr 11:308–309, Determined atom positions, bond lengths, and lattice parameters for the HA crystal structure

Roy DM, Linnehan SK (1974) Hydroxyapatite formed from coral skeletal carbonate by hydrothermal exchange. Nature 247:220, Developed the natural-template method for making porous HA

Sarakiya M (1994) An introduction to biomimetics: a structural viewpoint. Microsc Res Techn 27:360, A very useful introduction

Sato T, Shimada M (1985) Transformation of yttria-doped tetragonal ZrO_2 polycrystals by annealing in water. J Am Ceram Soc 68:356, Described the martensitic transformation in ZrO_2 in aqueous environments

Wang Q, Huang W, Wang D, Darvell BW, Day DE, Rahaman MN (2006) Preparation of hollow hydroxyapatite microspheres. J Mater Sci Mater Med 17:641
Williams DF (ed) (1987) DiB: definitions in biomaterials. Elsevier, Amsterdam, pp 6–7, Includes a discussion of biocompatibility

WWW

Journal of Biomedical Materials Research: A and B. Now past volume 100. Find the Society for Biomaterials at http://www.biomaterials.org
www.mds.nordion.com/therasphere/. The TheraSphere® website