

EVALUATION OF BIOCERAMIC MATERIALS IN BIOLOGY AND MEDICINE

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The aim of this study was to evaluate the properties of bioceramic materials. Therefore, the use of cell technology and tissue engineering requires excellent biomaterials to retain and cultivate cells and tissues both *in vitro* and *in vivo*. Indeed, polymers and bioceramics have been developed for biomedical applications, and bioceramics have been implanted for a longer time and proved to be safe for humans. Composites of bioceramics with polymers are also recent advances in fabrication technology of bioceramics. It is lastly stressed that very few materials have been developed since the discovery of the above conventional bioceramics such as calcium phosphates, stabilized zirconia, alumina and bioactive glasses. It is necessary to create new bioceramics for a lasting development in the future. Because of the excellent biocompatibility, matching shade, good anticorrosion ability, bioceramics are ever more widely being used in the biomedical field. Most of these bioceramic appliances need to bear forces during their lives. As result of this investigation, bioceramics are expected to be further developed for such newly proposed aims of regenerative medicine.

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1. Introduction

Bone is a composite of mineral, collagen, non-collagenous proteins, other organics and water. It is one of a set of vertebrate mineralised tissues that uses some version of calcium phosphate as their mineral. First there are the tissues that have as their principal organic component type I collagen. These are bone itself, dentine and enameloid. Enameloid is a structure covering the teeth of many fish, and seems (usually!) to be a very highly mineralised collagen-based tissue, rather like the petrodentine of the lungfish *Lepidosiren*. Next there is calcified cartilage. This occurs in two main places. One is a temporary calcification of type II collagen-based cartilage [1-7]. This occurs in the metaphyses of growing long bones, and is soon eroded and replaced by bone. The other, which is much more interesting from the mechanical point of view, is in the permanent skeletal structures of well-mineralised type II collagen-based artilage structures found almost entirely in the chondrichthyan fishes, the sharks, rays and so on. All these different types of mineralised collagens are an embarrassment to people who like neat classifications, but biology is like that. Lastly there is enamel. This is very highly mineralised, and its distinguishing feature is that the organic component, such as it is, is not collagen at all. Bone's organic material is about 90% by mass collagen type I. The other organics are various non-collagenous proteins and glycoproteins. The function of these other organics is the subject of intense research. Some of them have 'biological' functions; for instance, bone sialoprotein and bone morphogenetic protein have roles in the initiation and control of mineralisation and it has been suggested that a glycoprotein is necessary for the determination of apatite nucleation sites. The bone mineral is the version of calcium phosphate called hydroxyapatite, whose unit cell contains $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$. The crystals are impure. In particular about 4–6% of carbonate replaces the phosphate, making the mineral more truly a carbonate apatite (dahlite). The shape of the

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crystal is to some extent in dispute, and partially this is because it is different in different tissues. It is certainly true that in one direction the crystals are small, of the order of 5 nm. They are about 40 nm wide, but sometimes they are hardly wider than 5 nm. What is less clear is the size of the crystals in their long direction (which is the *c*-axis of the crystal). They can be at least 50 nm long, and it is quite possible that they can join, or grow, until they are several hundreds of nanometres long. This small size in one direction may have, as we shall see, profound mechanical implications. One of the reasons that the habit and size of mineral crystal in bone are still not determined fully is that the crystals come in very small lumps, so small in fact that, as has frequently been pointed out, much of the unit cell is actually sitting on the surface of the crystal. As a result preparation for examination is in danger of altering the size and chemical composition of the crystals. One of the key problems of bone structure is how the mineral relates topographically to the collagen. This is, surprisingly, still a matter of considerable dispute. Some mineral crystals lie within the fi brils, somewhat disrupting them as they grow, and some lie between the crystals. The crystals lying within the fi brils are oriented with their long (*c*) axes along the same axis as that of the collagen fibril. Those lying between the fi brils are not constrained in this way. It seems that the mineral lying within the fibrils first nucleates in the 'Hodge-Petruska' gaps, particularly the 'e' band. It then coalesces and extends along the long axis of the collagen fi brils, disrupting them to some extent [3-18]. Bone is a classic hierarchical structure, with different relationships between structures becoming important at different levels. These levels can be briefly characterised as: mineral + collagen, fi brils, fi bres, lamellar vs. woven bone, fibrolamellar vs. Haversian bone, compact vs. cancellous bone, whole bones. These levels are partially shown in Table 1, along with some other structures (such as osteocyte lacunae). I should mention that human bone is rather unusual among the whole set of bone materials that exist. First, most species of vertebrates do not have any bone cells lying within the hard tissue at all. Most species of vertebrates are bony fish, and the great majority of these have acellular bone. Coming to more familiar animals, such as birds and mammals, humans are unusual in having such extensive Haversian (secondary) remodelling of the tissue. This is partially because humans live on average a long time, so there is time for remodelling to occur, but also it seems to be a function of our rather large size, and also other innate characteristics. One often sees in the literature statements to the effect that the 'The secondary osteone (Haversian system) is the primary unit of bone.' This is not true at all of mouse-sized birds and mammals, which have no remodelling, and not even true of mammals in general. Even in humans, because of bone's hierarchical construction, it is not true, because there is no level at which it is correct to talk about the 'primary unit' [1-20].

2. Bioceramic materials in biology and medicine

The term 'bioceramics' refers to biocompatible ceramic materials, applicable for biomedical or clinical uses. Bioceramics can be produced in crystalline and amorphous forms, and they are generally classified from their chemical compositions into two groups; calcium phosphates (CP) and others, including yttria (Y₂O₃)-stabilized tetragonal zirconia (ZrO₂) (YTZP), alumina (Al₂O₃) and some silicate and phosphate families of glasses and crystallized glasses (glass-ceramics). Table 1 summarizes the bioceramic products in terms of compositions and shapes. The most clinically used ceramics of the CP group are hydroxyapatite (Ca₅(PO₄)₃OH, HA: Calcium hydroxyapatite) and β-tricalcium phosphate (Ca₃(PO₄)₂, β-TCP), for they are analogous to the inorganic constituents of hard tissues of vertebrates. Use of Y-TZP and alumina is attributable to their excellent mechanical strength and toughness. The glasses and crystallized glasses in the SiO₂-P₂O₅-CaO-Na₂O system are classified as bioactive glasses and bioactive glass-ceramics. They have also been recognized as bioactive and resolvable ceramics; in particular so-called A-W glass-ceramics have been synthesized using a scientific design of strength and biocompatibility. Clinical applications require various shapes of bioceramics from thin films and nano-sized powders to porous or dense bodies. Bone substitutes use massive porous HA, β-TCP (Tricalcium phosphate (Ca₃(PO₄)₂) and their mixture: defective bones which are not always exposed to high stress can be replaced by porous HA or β-TCP. Commercial porous products of HA with a porosity of 70–80% are already distributed to clinics and hospitals. Highly dense ceramics of Y-TZP and alumina are applied to hip joint balls and cups, while thin films of HA are coated on hard metals for artificial teeth and hip joints. In order to satisfy these demands, an appropriate fabrication method and process must be chosen for each clinical device. For fine fabrication of tough Y-TZP cups and balls, fine-grained ceramics of Y-TZP must be sintered with

pure and fine powders under a controlled sintering program. In general, tough and strong ceramics consist of fine-grained microstructure, whose average grain diameter is less than 1 μm . It is important to eliminate impurities from bioceramics; even minor impurities bring harm to a body, or provoke critical defect in the mechanical properties of bioceramics during long implantation *in vivo*. To undertake advantageous sintering, it is essential to control chemical and ceramic powder processing. The preparation of pure, fine powders enables the microstructure of bioceramics to be controlled (Table 1-4, Figures 1-4) [1-26].

Table 1. Table showing the main morphological features of bone Woven bone.

Woven bone	Parallel-fibred bone	Lamellar bone	
Fibrils 0.1–0.3 μm wide, arranged in a felt	Intermediate	Fibrils 2–3 μm wide in sheets (lamellae) 2–10 μm thick (Fig. 1.1)	
Bone cells (osteocytes) Roughly isodiametric ca 20 μm in diameter		Oblate spheroids 5:1 greatest to least axes. Major axis about 20 μm long	
Connected to each other and, indirectly, to blood channels by cell processes in tubes (canaliculi) 0.2–0.3 μm wide. About 50–100 canaliculi per cell			
Four types of bone microscopically			
Lamellar	Woven	Fibrolamellar	Secondary osteones
In large lumps in reptiles In circumferential lamellae in mammals and birds	In large lumps in young animals and in fracture calluses	Alternating sheets of lamellar and woven bone, with 2-dimensional sheets of blood vessels. About 200 μm between repeats	(Haversian systems) Cylinders of lamellar bone. Solid save central tube for blood vessels. About 200 μm in diameter
<i>Primary and secondary</i> (Figs 1.1 and 1.2)	<i>Primary</i>	<i>Primary</i> (Fig. 1.2)	<i>Secondary</i> (Fig. 1.3)
Two types of bone macroscopically			
Compact bone		Cancellous (trabecular) bone	
Solid, only porosity for canaliculi, osteocyte lacunae, blood channels and erosion cavities		Porosity visible to the naked eye. Rods and plates of lamellar bone. Multiply connected, never forming closed cells (Fig. 1.4)	

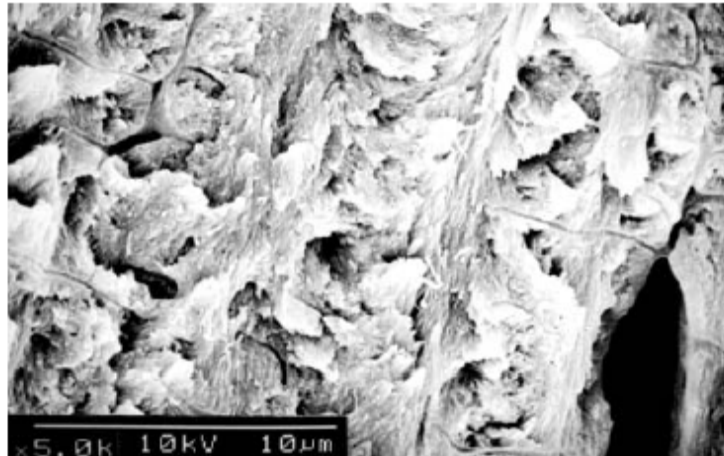


Fig. 1. Scanning electron micrograph of fracture surface of lamellar bone.

The lamellae are in rotating sheets that repeat their orientation about every 8 μm . The large cavity (lacuna) would contain an osteocyte in life. Note the thin half-tubes running WNW to ESE. These are fractured 'canaliculi', the tubes that allow the osteocytes to communicate with each other. There are about 50–100 canaliculi per lacuna. The fact that the fracture surface has run long several of them suggests that they are brittle, possibly by having hypermineralised sheaths, like dentinal tubules.

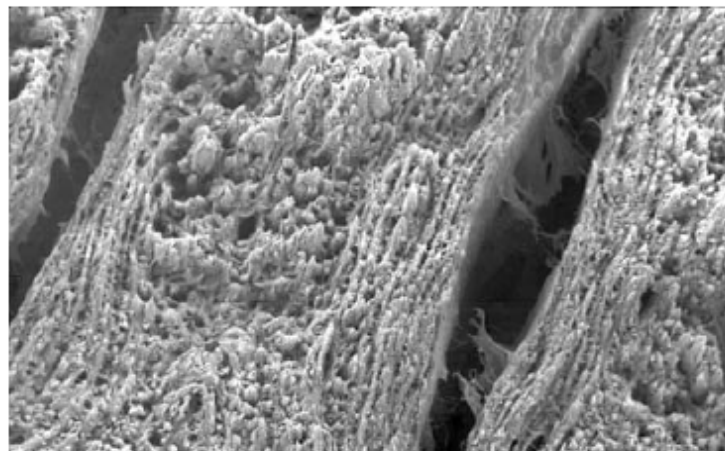


Fig. 2. Scanning electron micrograph of fracture surface of fibrolamellar bone.

The fracture surface is normal to the long axis of the whole bone. The repeat distance is about 200 μm . The large cavities are spaces for blood vessel networks. Each blood vessel network is flanked by lamellar bone, which in turn has more randomly arranged woven bone between it and the next lamellar bone.



Fig. 3. Scanning electron micrograph of Haversian (secondarily remodelled) bone.

The bone was infiltrated with resin before being polished and the bone etched away a little. The resin was not etched, allowing one to see the osteocyte lacunae and their connecting canaliculi. Note how different layers of the lamellar bone etch differentially. Width of field of view about 200 μm .

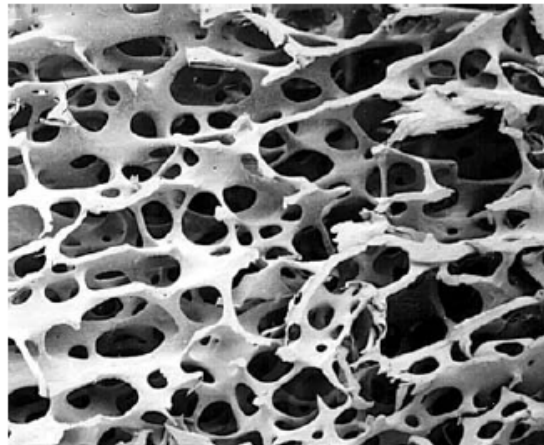


Fig. 4. Cancellous bone. Both the bone and the spaces (filled in life with marrow fat) are interconnected.

Table 2. Some values of mechanical properties of bone.

Property	Modal value ^a	Upper limit ^b	Lower limit ^c	Comments
Young's modulus of elasticity (E)	15 GPa	45 GPa <i>densirostris</i> rostrum	6 GPa Deer antler	Probably same in tension, compression and bending
Tensile yield Stress	120 MPa		10 MPa Ear bones, <i>densirostris</i>	Higher in compression
Tensile strength	150 MPa	300 MPa Some deer antler	15 MPa Ear bones, <i>densirostris</i>	
Ultimate tensile strain	0.03	0.12 Deer antler	0.002 Ear bones	
Compressive strength	250 MPa			
Bending strength	250 MPa		30 MPa Ear bone	
Fatigue life at 0–100 MPa tension	1000		200 Antler	Cycles for a 10% reduction in modulus

This is for orientation purposes only, and original work should be consulted for definitive values.

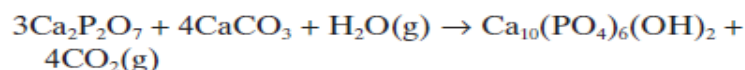
- This is the value near which most 'ordinary' bone would lie.
 - 'Upper limit' Approximately the largest value for the property that has been recorded.
 - 'Lower limit' approximately the lowest value for the property that has been reported.
- All values (except fatigue) are for quasi-static tests, that is at low strain rates.

Conventional processing of bioceramics

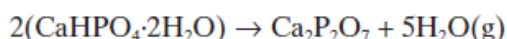
Crystalline bioceramic products are generally prepared through sintering moulded powders at high temperatures. As introduced above, tough and strong ceramic products must consist of pure, fine and homogeneous microstructures. To attain this, pure powders with small average size and high surface area must be used as the starting sources. The sintering procedure is carried out according to a controlled temperature program of furnaces in adjusted ambience of air with necessary additional gasses. Bioactive glasses are conventionally prepared by melting the starting powders with adjusted compositions and pouring them into a mould, then annealing to release induced stresses at a designated temperature in a furnace for a sufficient time. Bioactive glass-ceramics are obtained by crystallizing bioactive glasses at appropriate high temperatures. First, starting powders must be prepared [1,5,23,24,25,26].

Powder processing

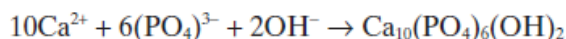
Powders are synthesized according to dry and wet chemical routes: dry chemical process uses the high-temperature chemical reactions among solid-state sources. High-temperature treatment is necessary for enhancement of diffusion process of ions. A desired bioceramic product (AB) is generally made from the sources A and B via a solid-state reaction expressed as $A(s) + B(s) \rightarrow AB(s)$. An example for HA is shown in eq., where A and B are $Ca_2P_2O_7$ (pyrocalcium phosphate) and $CaCO_3$ powder. As HA includes hydroxide ions, the reaction must be done under controlled water vapour supply :



On the other hand, thermal decomposition of compounds ($A \rightarrow B + C$) can be used for preparation of powders; $CaHPO_4 \cdot 2H_2O$ or $CaHPO_4$ is thermally decomposed to various pyrocalcium phosphates from amorphous to α -, β - and γ -forms. Which polymorph is formed depends on the heating temperature, as eq. :



The powders thus prepared are generally coarse owing to agglomeration of particles during a solid-state reaction at high temperature. Inhomogeneity of products is also a problem in dry routes, because source elements must diffuse through the initially formed layers at powder interfaces to continue further chemical reactions. Ball-milling is effective for crushing and grinding reacted powders; thereafter high-temperature treatment is repeatedly required for the ball-milled powders. Wet-chemical methods use solutions as starting sources. The wet chemical process is widely used to synthesize crystalline bioceramics, because high compositional homogeneity can be easily achieved at low temperature. The advantage arises from the use of a liquid state precursor, in which the source elements are thoroughly mixed at the atomic level. For several bioceramics, the wet-chemical process is regarded as the best synthesis method; commercialized HA powders are generally obtained from mixed solutions of calcium and phosphate salts via the precipitation method, the hydrothermal method, the spray or gel pyrolysis method, etc. Here, $Ca(NO_3)_2$, $Ca(OH)_2$ or $CaCl_2$ and $(NH_4)_2HPO_4$ or H_3PO_4 are preferably used as calcium and phosphorus sources, respectively. For instance, aqueous solutions of calcium and phosphorus are homogeneously mixed and solidified in aqueous solutions to form HA precursors. The obtained HA precursors then undergo Ostwald ripening to be changed to HA crystallites:



In this process, the pH of solutions must be kept over 10 to precipitate HA particles. To perform this, CO₂ must be purged from the ambient gas in reaction vessels. The hydrothermal method is also a popular technique. It is a kind of wet-chemical process promoted under high-pressured water above 100 °C. Although the condition under the pressure of several tens of MPa below 300 °C is commonly selected for this method, conditions up to 400 MPa and 800 °C are permitted by using high-pressure apparatus. The hydrothermal method is particularly effective in the crystallization of poorly soluble compounds: it enables the synthesis of HA whiskers and small-sized single crystals which are hardly obtained both via dry-chemical and wet-chemical processes under ordinary pressure and temperature. CaHPO₄ (monetite), CaHPO₄·2H₂O (brushite) and ACP (amorphous calcium phosphate) are used as a starting compound for the synthesis of HA whiskers. Organic acid with an ability to mask a particular crystal plane of HA is added into the reaction system with the aim of the control of the growth direction. Citric acid, oxalic acid and ethylenediamine tetraacetic acid (EDTA) are the representative additives for this purpose. Drying is the necessary treatment in the wet-chemical process. The process sometimes determines the secondary particle structure of the crystalline powders, because the agglomeration of crystalline easily occurs with the dissolution. Drying is mainly divided into heating and non-heating processes. In addition to the usual convective, conductive and radiation drying by external heat sources, internal heat drying induced by electromagnetic wave is also classified into the heating process. Freeze-drying proceeds through the freezing process of wet precipitated powders and the following evacuation of air under freezing. The solidified solvent is then changed directly into vapor by supplying latent heat of sublimation and removed from the drying object (**Fig. 5**). This technique provides fine powders with large surface areas. The dried powders are subjected to a forming process to produce the shapes desired before sintering [12,15,17,18,19,23,25,26].

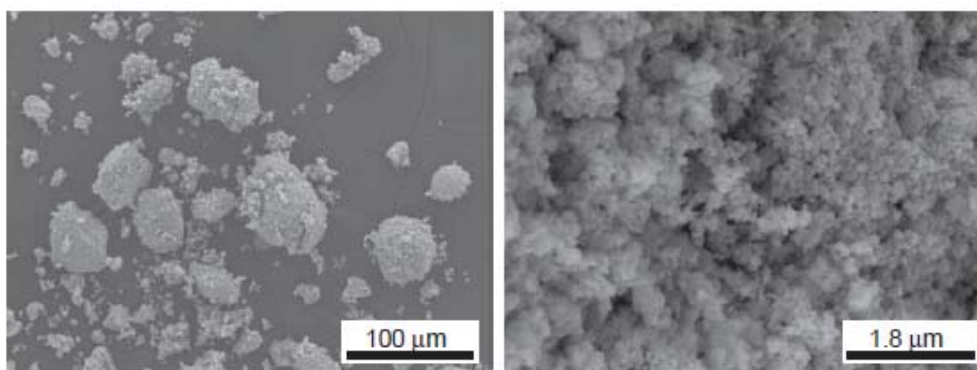


Fig. 5. SEM photographs of HA powders obtained via freeze-drying.

In most drying processes, a wet body goes through a condition that the surface is partially soaked by the solvent and is partially exposed to the ambient gas-phase. Under this condition, the drying object is subject to the interface tension between the solvent and the ambient gas.

Forming of green body

Forming is one of the important processes in making bioceramic products. Forming is carried out through various techniques using either dried powders with additives or wet powders with viscous fluid. Defl oculants (glues) are usually inorganic chemicals of sodium carbonates and sodium silicates, and organic polymers of polyacryl acid. Organic additives of polyvinyl

alcohol (PVA), methyl cellulose and paraffi n are used for forming, strengthening and making green bodies plastic (**Table 3**). The simple forming of green bodies is uniaxial compaction of powders mixed with appropriate organic binders and defl oculants of a few wt% in a desirably shaped mold. To avoid locally remained stress or increase green density (up to 60% of theoretical values), cold isostatic pressing (CIP) is sometimes employed, which enables uniform pressing in a soft rubber mold. The method is done according to Archimedes principle using Ar gas or water as the medium of equiaxial pressure [1,2,4,19,12,15].

Table 3. Various techniques of the green body formation with organic additives and solvents.

Methods	Additives	Solvent
Uniaxial compaction	Water-soluble resin (polyvinyl alcohol), gum arabic, etc. 3.0–5.0wt%	Water 0–1.0wt%
Cold isostatic pressing	Water-soluble resin (polyvinyl alcohol), gum arabic, etc. 2.0–5.0wt%	Water 0–1.0wt%
Slip casting	Methylcellulose, sodium alginate, etc. 0.5–3.0wt%	Water 30.0–60.0wt%
Pressure mold forming	Water-soluble resin (polyvinyl alcohol), paraffin, etc. 8.0–15.0wt%	Water 15.0–30.0wt%
Injection mold forming	Thermoplastic resin, paraffin, etc. 10.0–25.0wt% Plasticizer (phthalate ester, etc.) 0.5–5.0wt%	
Doctor blade method	Acrylic ester, polyvinyl butyral, etc. 8.0–15.0wt% Plasticizer (phthalate ester, etc.) 3.0–8.0wt%	Water, alcohol, ketone, etc. –50.0wt%

Table 4. Compositions and shapes of the various bioceramics.

Category	Materials and compositions	Shapes
Calcium phosphate (CP) group	Hydroxyapatite (HAp (or HA)) $\text{Ca}_5(\text{PO}_4)_3\text{OH}$	Sintered body (dense and porous) Powder Coating Composite Fiber
	β -Tricalcium phosphate (β -TCP) $\text{Ca}_3(\text{PO}_4)_2$	Sintered body (dense and porous) Powder
	Others	
	Dicalcium phosphate anhydrate (monetite, DCP or DCPA) CaHPO_4	Powder
	Dicalcium phosphate dihydrate (brushite, DCP2 or DCPD) $\text{CaHPO}_4 \cdot 2\text{H}_2\text{O}$	Powder
	Calcium pyrophosphate (CPP) $\text{Ca}_2\text{P}_2\text{O}_7$	Powder
	α -Tricalcium phosphate (α -TCP) $\text{Ca}_3(\text{PO}_4)_2$	Powder
	Tetracalcium phosphate (TeCP) $\text{Ca}_4(\text{PO}_4)_2\text{O}$	Powder
	Octacalcium phosphate (OCP) $\text{Ca}_8\text{H}_2(\text{PO}_4)_6\text{H}_2\text{O}$	Powder
	Amorphous calcium phosphate (ACP) $\text{Ca}_3(\text{PO}_4)_2 \cdot n\text{H}_2\text{O}$	Powder
Others	Yttria-stabilized tetragonal zirconia (Y-TZP) $\text{Y}_2\text{O}_3\text{-ZrO}_2$	Sintered body (dense)
	Aluminum oxide (alumina) Al_2O_3	Sintered body (dense)
	Titanium oxide (titania) TiO_2	Sintered body (dense)
	Silicon nitride Si_3N_4	Sintered body (dense)
	Silicon carbide SiC	Sintered body (dense)
	Carbon C	Fiber
	Bioactive glasses system	
	$\text{SiO}_2\text{-P}_2\text{O}_5\text{-Na}_2\text{O-CaO}$	Bulk
	$\text{SiO}_2\text{-P}_2\text{O}_5\text{-Na}_2\text{O-K}_2\text{O-CaO-MgO}$	Bulk
	$\text{SiO}_2\text{-P}_2\text{O}_5\text{-CaO-Al}_2\text{O}_3$	Bulk
Bioactive glass-ceramics system		
$\text{SiO}_2\text{-P}_2\text{O}_5\text{-CaO-MgO}$ (A-W)	Bulk	
$\text{SiO}_2\text{-P}_2\text{O}_5\text{-Na}_2\text{O-K}_2\text{O-CaO-MgO}$ (Ceravital)	Fiber	

Recent advances

CAD/CAM technique

CAD/CAM (computer-aided design/computer-aided manufacturing) attracts increasing attention and has already been applied in dentistry to dental restorations with ceramics. CAD/CAM enables the build up of tailormade ceramics with complicated structures. In this method, sintered porous ceramics of α -Al₂O₃ for dental restorations are automatically cut into objective shapes according to the digital data stored in the computer. In general, original data for the shapes are collected by 3-D scanning of target specimens. CAD/CAM-fabricated ceramics are also obtained through the process: firstly, the green body is sliced as x-sectional pieces along the digital data. Second, the objective shapes are built up by combining the sliced pieces, then sintered [3,4,7,9,12,13,14,17,19,20,21].

Gel casting method

The gel casting method is also rather new. In this method, slurries mixed with organic monomers and polymeric initiator are firstly poured into a mold and the monomers are polymerized by controlling external conditions. The slurries used in this method are basically the same as those used in the slip casting process, but different from conventional slip casting. Gel casting enables all particles in slurries to be fixed almost at the same time in the mold. This has the advantage of obtaining homogeneous green bodies [11,12,15,17,18,19,20,21,22,23].

Microwave sintering

When green bodies are irradiated with microwaves, internal water absorbs microwaves and the molecular vibration of water is increasingly accompanied by the frictional heat generation. Sintering of green bodies using internal heat generated by microwaves is called microwave sintering. Compared with conductive or radiation heating, microwave heating is superior to usual sintering both in heating time and heat efficiency. Short-term sintering is advantageous in the preparation of homogeneous and dense sintered body with fine-grained microstructure. Moreover, local heating can be performed with this method [7,14,16,17,23,24,25,26]. Mechanical properties of bioceramics are shown in Table 5.

Table 5. List of mechanical properties of some advanced bioceramics.

Bioceramics	Flexural strength (MPa)	Weibull modulus (m)	Elastic modulus (GPa)	Hardness (GPa)	Poisson's ratio	Fracture toughness (MPa m ^{1/2})
Cortical bone	50–150	–	7–30	–	–	2–12
Human tooth enamel	8–35	–	9–90	3.2–4.4	–	0.52–1.3
Human tooth dentin	31–104	–	11–20	0.25–0.8	–	2.8–3.1
Sintered hydroxyapatite	115–120	–	80–110	500 (HV)	–	1.0
Pressable ceramic (IPSEmpress I)	106 (17)	9.0	65 (1.5)	6.5 (0.4)	–	1.2 (0.14)
Pressable ceramic (IPSEmpress II)	303 (49)	8.0	90 (3.7)	5.5 (0.2)	–	3.0 (0.65)
Full sintered zirconia ceramic (Vita Zirkon)	840 (140)	7.5	220 (7.5)	12 (0.2)	0.33	7.4 (0.62)
Glass ceramic (MGC-fine)	–	–	70.5	4.15 (0.07)	–	1.04 (0.04)
Glass-infiltrated zirconia ceramic (Vita In-Ceram Zirconia)	476 (50)	10.5	240 (9)	11 (0.9)	0.26	4.9 (0.36)
Glass-infiltrated alumina ceramic (Vita In-Ceram Alumina)	440 (50)	9.5	265 (10)	11 (1.1)	0.25	3.6 (0.26)
Feldspathic porcelain (Vita D)	95 (20)	5.0	64	–	0.21	0.9
Feldspathic porcelain (Vita Alpha)	95 (15)	5.0	60	–	0.22	0.9
Alumina bioceramic (Al ₂ O ₃ > 99.8%)	595	–	400	2300 (HV)	–	5–6

3. Results and discussion

The ability to bond to bone tissue is a unique property of bioactive ceramics. This has led to their wide clinical use in both orthopedics as well as dentistry. Bioactive ceramics are used as bone substitute materials for bone grafting and as coatings for titanium and its alloy. These coatings have been found to accelerate initial stabilization of implants by enhancing bony ingrowth and stimulating osseous apposition to the implant surface, promoting a rapid fixation of the devices to the skeleton. Most commonly long-term stable calcium-phosphates which exhibit a low biodegradability such as hydroxapatite are used for producing bioactive calcium phosphate coatings. The current gold standard for bone reconstruction in orthopedics and cranio-maxillofacial repair is the use of autogenous bone grafts. Of the more than 1 million fractures that are treated with osteosynthetic materials each year in the USA, approximately 80% of these require adjuvant grafting. Resorption of the alveolar ridge after tooth extraction frequently mandates site development by augmentation before dental implants can be placed. Although autogenous bone grafts are currently the standard of care, bone substitute materials are extensively studied in order to avoid harvesting autogenous bone. In fact, there are several disadvantages associated with using autogenous grafts: the additional surgical site, donor site morbidity exceeding that at the treatment site, often insufficient volume of harvested bone, and, in dentistry, the need for general anesthesia to harvest extraoral bone. Among alternative graft choices, synthetic bone substitute materials benefit from several advantages over freeze-dried human

allografts or bovine deproteinized bone xenografts. Owing to their ability to stimulate bone formation bioactive calcium phosphate ceramics and bioactive glasses are excellent candidate grafting materials for bone augmentation. Among the bioactive ceramics most commonly investigated for use in bone regeneration are β -tricalcium phosphate (β -TCP), hydroxyapatite (HA) and bioactive glass.

All of these materials are biocompatible and osteoconductive. However, they differ considerably in the rate of resorption. HA resorbs very slowly compared with β -TCP, and bioactive glass. Recent improvements in tricalcium phosphate (TCP) ceramics include products with a high phase purity (>99%) and homogeneous solubility characteristics, so as to prevent premature separation of microparticles from the structural compound. In the past, these types of microparticle have been shown to elicit inflammatory tissue responses. Furthermore, the use of TCP particles with increased porosity has been proposed in order to increase the biodegradability. These particles exhibit a material structure with micro-, meso- and macropores, which is designed to enhance the degradation process. This structure allows for a reduced bulk density. The microporosity allows circulation of biological fluids, increases the specific surface area and thus accelerates the degradation process. The interconnectivity of the pores creates a capillary force that actively draws cells and nutrients in the center of the particles. The macroporosity is created to encourage the ingrowth of bone by permitting penetration of cells and vascularization. In modern dentistry, the use of oral implants has become a common treatment to replace missing or lost teeth.¹¹ Furthermore, resorption of the alveolar ridge after tooth extraction frequently mandates site development by augmentation before implants can be placed. Among the various techniques to reconstruct or enlarge a deficient alveolar ridge, the concept of guided bone regeneration (GBR) has become a predictable and well-documented surgical approach for localized lateral ridge augmentation. Furthermore, augmentation of the maxillary sinus floor with autogenous bone grafts has become a well-established pre-implantology procedure for alveolar ridge augmentation of the posterior maxilla. Recently, the use of tricalcium phosphate and bioactive glass 45S5 particles as alloplastic bone graft materials for alveolar ridge augmentation and sinus floor elevation procedures has received increasing attention in implant dentistry. This is due to an overall effort to develop augmentation procedures that involve reduced surgical effort, thereby increasing patient comfort in addition to decreasing treatment cost, while yielding the same clinical success rates as conventional procedures that utilize autogenous bone grafts. As a result, in recent years an increasing number of clinical studies have been published which provide valuable data regarding the biodegradability as well as the bone regenerative capacity of these materials in a clinical setting, since these data were derived from histological studies of human biopsies. As a result considerable efforts have been undertaken to produce rapidly resorbable bone substitute materials, which exhibit good bone bonding behavior by stimulating enhanced bone formation at the interface in combination with a high degradation rate. This has led to the synthesis of a new series of bioactive, rapidly resorbable glassy crystalline calcium alkali orthophosphate materials. These are glassy crystalline calcium-alkali-orthophosphates, which exhibit stable crystalline $\text{Ca}_2\text{KNa}(\text{PO}_4)_2$ phases. These materials have a higher solubility than TCP and therefore they are designed to exhibit a higher degree of biodegradability than TCP. On this basis, they are considered as excellent alloplastic materials for alveolar ridge augmentation.

4. Conclusions

Bioceramics are produced in a variety of forms and phases and provide many different functions in repair of the human body. In many biomedical applications bioceramics are used in the form of bulk or porous materials with a specific shape such as implant, prostheses, or prosthetic devices. In addition, bioceramics are used in powder form to fill defect spaces while the natural repair processes restore function and are used as a coating on a substrate, or a second phase in a composite material to achieve the enhanced mechanical and biological activities such as osteoinduction or osseointegration. Bioceramics are prepared by many different preparation methods and thus result in different phases such as single crystal, polycrystalline, glass, glass-ceramics, or composites. The characterization of the microstructure of bioceramics should be observed from many viewpoints such as chemical composition (stoichiometry or purity),

homogeneity, phase distribution, morphology, grain size/grain shape, grain boundaries, crystallite size, crystallinity, pores, cracks and surface, etc.

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