〔REVIEW〕

Recent Advances in Functionally Graded Technology in Dental Implants

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Abstract

Functionally graded materials (FGMs) have a functional gradient of compositional change and/or structure from the surface to the interior of the material and have been developed for use in engineering fields including space and nuclear technologies. The potential of FGMs has also attracted attention in both the medical and dental fields. Especially, the application of FGMs to the development of hydroxyapatite (HA)-coated titanium implants has been extensively studied in the dental and orthopedic fields as it would overcome the drawbacks of the plasma- sprayed HA coatings currently in clinical use.

The present paper focuses on recent advances in functionally graded technology in dental implants. The basic concept of FGMs is described and applications of these materials to the development of novel dental implants are summarized. It is suggested that the creation of ideal functionally graded structures for dental implants is a subject for future study.

Key words : Functionally graded material, Dental implant, HA coating, Sunface modification

Introduction

Recently, functionally graded materials (FGMs) have been developed for use in engineering fields including space and nuclear technology. FGMs have a functional gradient of compositional change and/or structure from the surface to the interior of the material[1]. The concept of FGMs offers the potential that one device may possess two different properties. This is an advantage as biomaterials must simultaneously satisfy numerous requirements and possess a wide range of properties such as nontoxicity, corrosion resistance, a thermal expan-

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sion coefficient, thermal conductivity, strength, fatigue durability, and biocompatibility[2]. A single composition with a uniform structure cannot satisfy all these requirements. Therefore, the potential of FGMs has attracted attention in both the medical and dental fields. Particularly, the application of FGMs to the development of hydroxyapatite (HA)-coated titanium implants has been extensively studied in the dental and orthopedic fields to overcome the drawbacks of the plasma-sprayed HA coatings currently in clinical use.

The purpose of the present paper is to review the literature concerning the advantages and problems associated with plasma-sprayed HA coatings and to define the scope of technological approaches in the development of novel dental implants using FGMs.

HA coatings for enhancing bone formation around titanium implants

Titanium is known to be the most biocompatible metallic material for dental and orthopedic implants. Titanium and its alloys, however, do not directly bond with bone, different from some bioactive materials such as calcium phosphate ceramics and bioactive glass. In the past decade, there have been a great many attempts at surface modification of titanium and its alloys with synthetic HA to improve bone bonding or accelerate bone formation in the surrounding tissue. Among the variety of surface modifications proposed, calcium phosphate ceramic and synthetic HA-coatings have been investigated most extensively in an attempt to obtain better stabilization of metallic implants in bone and surrounding tissue.

It is widely accepted that synthetic HA-coatings on titanium implants facilitate rapid bone formation around the implant due to their osteoconductive properties. The advantages of plasma-sprayed HA coatings have been demonstrated in many *in vivo* studies. The HA-coated titanium implant have a significantly higher degree of bone-implant contact than the uncoated titanium implant[3]. Push-out tests[4] and removable torque tests[5] have demonstrated that HA-coating increases the implant attachment strength to the surrounding bone and enhances implant stability. The ultrastructual appearance at the bone-implant interface of the HA-coated implant was found to be different from that of the uncoated titanium implants. There is an intimate, direct bone contact with the HA-coated implant with no intervening fibrous tissue present[6] while there is an amorphous layer of approximately 50 nm between the bone and the uncoated titanium surface[7].

Although it is evident that the HA possesses osteoconductivity, the mechanism of the coated HA to enhance bone formation is not fully understood. *In vitro* studies have demonstrated that increases in the extracellular calcium concentration stimulated osteoblast proliferation[8] and increased the mRNA levels of bone morphogenetic proteins-2 and -4 in normal human bone cells[9]. Further fundamental research is needed to fully understand the bone formation mechanisms around HA-coated implants.

Problems associated with plasma spraying of hydroxyapatite coatings

Bioactive calcium phosphates incorporating plasma spraying have provided the dental and orthopedic hard tissue industry with compounds of great interest for more than 30 years, and this technology is the only commercially available widely used method for coating implant devices with HA. Figure 1 shows X-ray diffraction patterns of two HA plasma-sprayed cylindrical type implants, together with SEM images of their surface. Although the surface morphologies of Products A and B are very similar, the crystallographic characteristics of the two products are entirely different due to different conditions of the plasma spraying. It is recognized that with plasma spraying of HA, numerous variables must be controlled to achieve optimum coatings. These variables include (1) the design and operating conditions of the plasma gun; (2) the composition and flow rate of the carrier gas; (3) the composition and size distribution of the starting powder particles; (4) the method for introduction of the powder particles into the plasma; (5) the distance between the plasma gun and the substrate; (6) the temperature of the substrate during deposition of the coating[10](Fig. 2).

Implant coatings formed by plasma spraying are known to have a complex multiphase structure due to the nonequilibrium nature of the deposition process[11]. In addition to HA, the coatings contain tricalcium phosphate (α- and β-TCP), calcium pyrophosphate (PP), tetracalcium phosphate (TTCP), calcium oxide, and an amorphous or glassy calcium phosphate (ACP). The order of biodegradation of the calcium phosphates is in the following order: ACP > TTCP >> α-TCP > β-TCP >> HA.

The crystallinity of the calcium phosphate also has a significant influence on its biodegradation rate. Figure 3 shows the relationship between the operating conditions of the plasma gun and the amorphicity of the calcium phosphate[11]. The particle size of HA powder introduced into the plasma has the

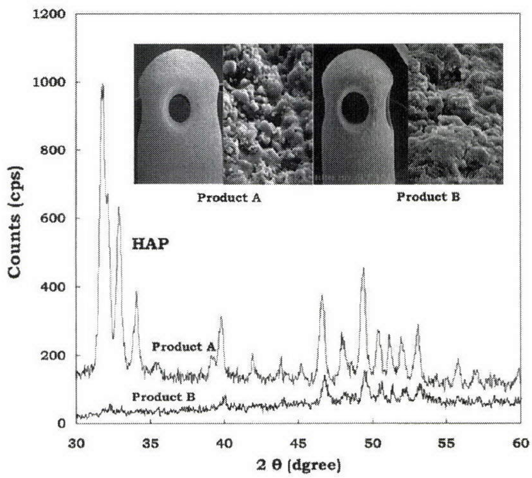

Fig. 1 X-ray diffraction patterns of the two HA plasma-sprayed cylindrical type implants, together with SEM images of their surfaces.

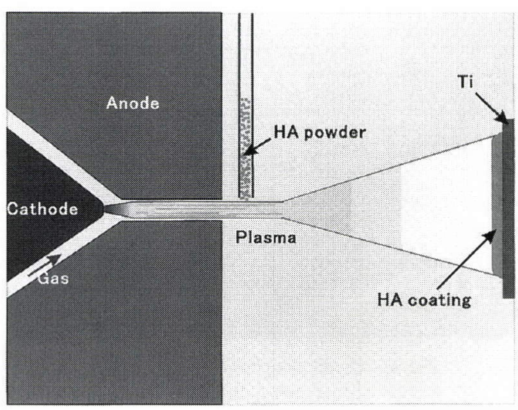

Fig. 2 Apparatus for HA plasma spraying.

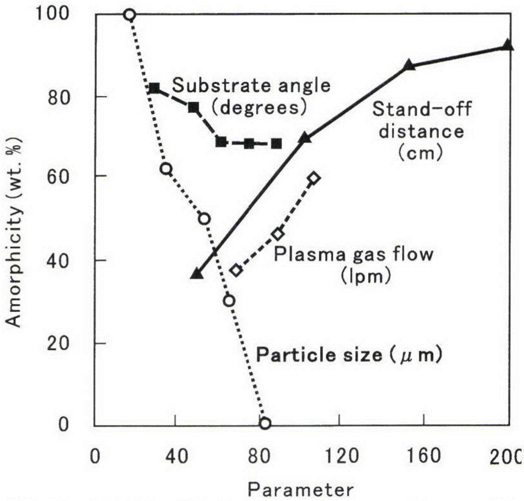

Fig. 3 Relationship between the operating conditions of the plasma gun and the amorphicity of the calcium phosphate.

strongest influence on the amorphicity of the calcium phosphate. For example, using a 30 μm particle size results in an almost amorphous phase while using a 80μm size results in non-amorphous phase. Although the crystallinity and composition of the coatings are believed to affect the biological and mechanical properties of the implants, it is very difficult to control these parameters with the HA plasma spray method. This poses a serious problem in the application of the HA plasma spray method.

Another problem with the HA plasma-sprayed coatings is the presence of cracks in the HA layer and gaps at the interface of the HA coating and the titanium substrate as shown in the SEM images of the cross section of Product A in Fig. 4 (a) and (b). The crack formation will take place with plasma-sprayed HA coatings due to the following reasons. In plasma spraying, the molten particles are rapidly deposited onto the substrate, and as the thermal expansion coefficient of HA (13.3×10^{-6}/°C) is larger than that of Ti and Ti-6Al-4V (8.7×10^{-6}/°C and 9.4×10^{-6}/°C, respectively)[12], tensile stress is induced in the coated layer, resulting in the formation of cracks in the coating because of the brittle character of the calcium phosphate (Fig. 4(c)). These stresses may lead to detachment of the coating when in service in the human body. Failures on dental implants occur after progressive loosening which is preceded by supportive bone loss or fibrous tissue formation.

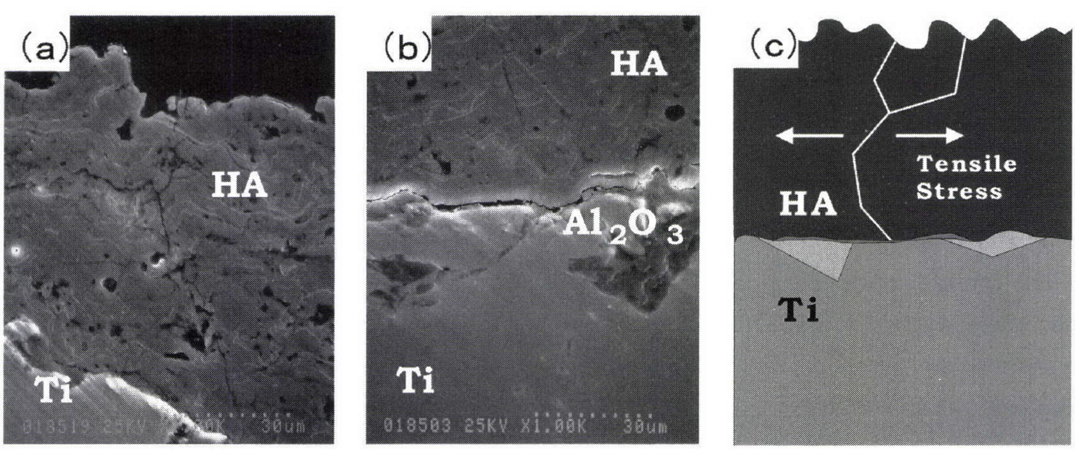

Fig. 4 Cross-sections of Product A in Fig. 1. (a) and (b) : Secondary electron images, (c) : Illustration showing the crack formation ; the values of the thermal expansion coefficients of HA and titanium are 13.3 x 10^{-6} and 9.4 x 10^{-6}/°C.

The thermal stress induced in the coating increases with increases in the thickness of the coating layer. The average thickness of plasma-sprayed HA coatings are approximately 50 μm, and this thickness is presumed to offer a compromise between the more rapid *in vivo* loss of thinner coatings due to resorption and the lower adhesive/cohesive strength of thicker coatings[10].

Functionally graded technologies for overcoming the drawbacks of plasma-sprayed HA coatings

Abrupt transitions in material compositions and properties within a component, as shown in the plasma-sprayed HA on titanium substrate inFig. 5 (a), often result in sharp local concentrations of stress. These stress concentrations are greatly reduced if the transition from one material to the other is made gradually as shown in Fig. 5 (b). If a graded composition of the interface between the HA layer and the titanium substrate is created, the thermal expansion coefficient can be gradually changed, resulting in reductions in the thermal stress at the interface. This presents one solution for decreasing cracks, and is the idea behind functionally graded materials (FGMs).

Many FGMs have been considered in industrial fields, including continuous and discontinuous gradient compositions (Fig. 5 (b) and (c))[1] and both at interfaces and at surface. Details of the structure and other parameters of FGMs reported in the literature are summarized in Table 1. The functionally graded areas investigated so far may be divided into four size scales: atomic level, microscopic level, mesoscopic level, and macroscopic level; Gradients may be continuous or stepwise; The gradient materials are ceramics, metals, or polymers; Gradations is materials, concentration, and/or structure; and the expected functions are biological, biochemical, physical, and/or mechanical.

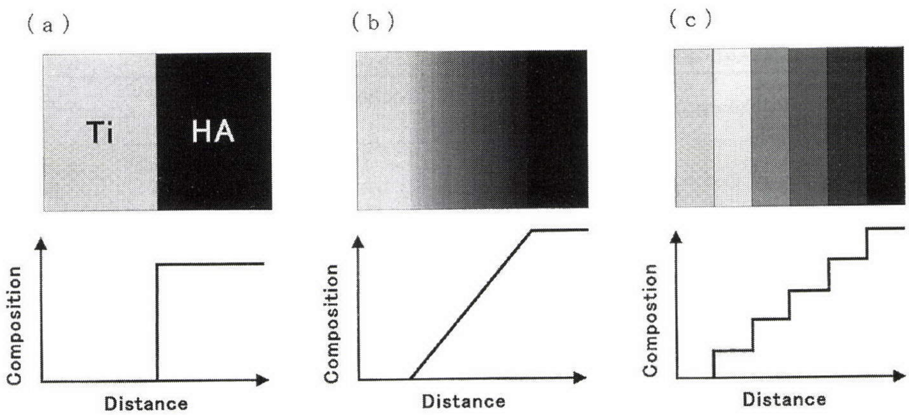

Fig. 5 Schematic illustrations showing the cross-sections of three materials.
(a) : plasma-sprayed HA on titanium, (b) : functionally graded material (continuous),
(c) : functionally graded materials (discontinuous).

Functionally graded materials for dental implants

Functionally graded technology has been applied in HA-coated titanium implants to overcome the drawbacks of plasma-sprayed HA-coatings. The fabrication technologies employed in reported functionally graded HA-coated implants can be divided into the three processes: (1) Physical vapor deposition (PVD, dry process), (2) Wet processes, and (3) Sintering.

(1) Physical Vapor Deposition (PVD)

Table 2 shows technologies employed in the fabrication of functionally graded HA-coated implants by PVD. To improve the brittleness of the HA coated on the titanium alloy, a thin ceramic layer (1-5μm) was formed by ion-plating[13),14)]. The ion beam dynamic-mixing method was introduced as suitable for fabricating thin and adherent ceramic layers. This method is a combination of ion implantation and another PVD[17)]. The amorphous coatings produced by the dry process are not acceptable for biomedical applications due to their high dissolution rates. However, the solubility of the coatings is significantly reduced by crystalline formation in the coatings after heat treatment[18),19)]. A review on the subject of dry-process surface modification for titanium dental implants has been published by Yoshinari et al.[20)].

Figure 6 shows a schematic representation of the process of ion implantation[13)]. The ion implantation modifies only the properties of a thin surface layer, while the mechanical prop-

Table 1 Structural details of the functionally graded materials.

Size scale	Atomic(<100nm), Microscopic(100nm-100μm), Mesoscopic(100μm-1.0mm), Macroscopic(>1.0mm)
Gradient	Continuous, Stepwise
Material	Ceramics, Metal, Polymer
Gradation	Materials, Concentration, Structure
Function	Biological, Biochemical, Physical, Mechanical

Table 2 Physical vapor deposition (PVD) fabrication technologies of functionally graded materials.

PVD	Researcher
Ion implantation	Hanawa et al.[13)], Miyayama et al.[14)]
Ion beam mixing	Wang et al.[15)]
Ion beam dynamic Mixing	Ishikawa[16)],Yoshinari et al.[17),18)]

erties of the bulk substrate usually remains unchanged. In addition, the boundary between the surface-modified layer formed by the ion implantation and the bulk substrate is fuzzy, there are few or no fractures at the interface between the surface-modified layer and the substrate, unlike at the interface between calcium phosphate coated by plasma spraying and substrate.

(2) Wet processes

Table 3 lists wet process technologies employed in the fabrication of functionally graded HA-coated implants. These methods are particularly attractive for coating of irregularly shaped substrates, which are difficult to coat with dry processes.

Ishizawa et al.[21] have developed a new method in wet process: An anodic titanium oxide film containing Ca and P (AOFCP) was formed on commercially pure titanium which was anodized at 350 V in an electrolytic solution of dissolved β-glycerophosphate and calcium acetate. HA crystals were precipitated by hydrothermally heating the AOFCP at 300°C, and 1-2 μm thick HA layer were formed on the surface (Fig. 7). Figure 8 shows SEM of the surface anodized

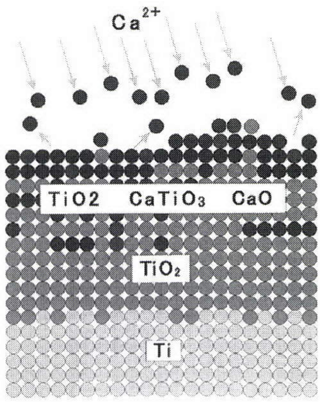

Fig. 6 Schematic illustration of ion implantation and the functionally graded structure of titanium produced by ion implantation.

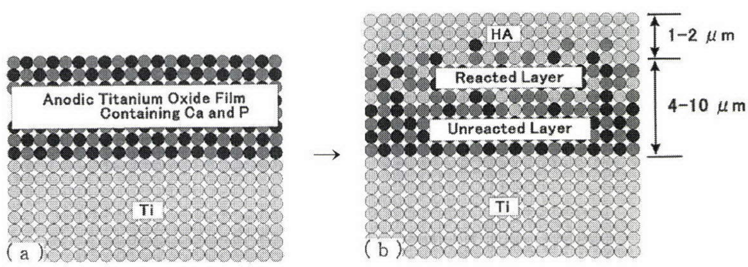

Fig. 7 Schematic illustration of the functionally graded structure of titanium produced by anodic oxidation (a) and subsequent hydrothermal treatment (b).

Table 3 Wet process fabrication technologies of functionally graded materials.

Wet process	Researcher
Anodic oxidation+ hydrothermal treatment	Ishizawa et al.[21], Kajimura et al.[22]
Alkali treatment + heat treatment	Kim et al.[23),24]
Gradient fluoride-carbonate supply method	Okazaki et al.[26)27]
Anodic-cathodic discharge method	Shibata et al.[28]

at 350 V before and after the hydrothermal treatment. There is a porous surface after the anodic oxidation and fine needle-like HA crystals are tightly precipitated on the porous TiO_2 matrix. With Ishizawa's method, the adhesive strength of the film was about 40 MPa, which was higher than that of plasma-sprayed HA coatings on titanium, which is about 10-20 MPa. The push-out shear strength was 20 MPa after 8 weeks of implantation in rabbit femurs. With the Ishikawa method, Kajimura et al.[22] have reported early bone formation around implants inserted into the mandible of beagles.

Kim et al.[23),24] have reported an attempt to induce bioactivity of titanium metal by forming a thin titanium hydrogel layer on the titanium surface with a chemical treatment (Fig. 9). With this method, the pure titanium was treated with NaOH or KOH aqueous solution at 60 °C to form an alkali titanate amorphous layer up to 1 μm thick on the surface, and then subjected to heat treatment at 600°C to improve the adhesion of the amorphous layer to the substrate. The thus-treated titanium formed a dense and uniform bone-like apatite layer on its surface when it was soaked in simulated body fluid[23](Fig. 9 (c)). Figure 10 shows SEM micrographs of the surface after the NaOH treatment and after immersion in the simulated body fluid. The

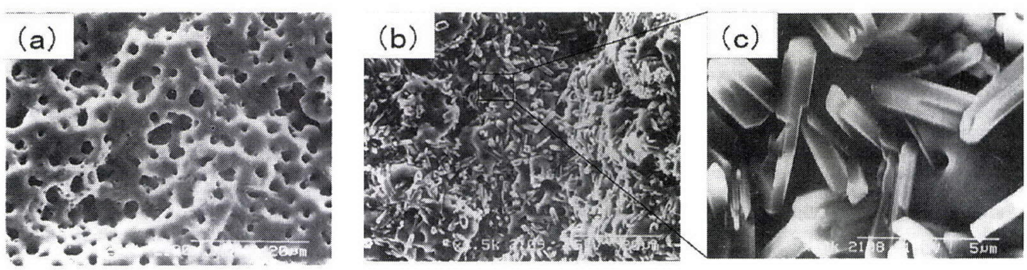

Fig. 8 Scanning electron micrographs of titanium surfaces after anodic oxidation (a) and subsequent hydrothermal treatment (b), magnified (c). (Courtesy of K. Ishibashi)

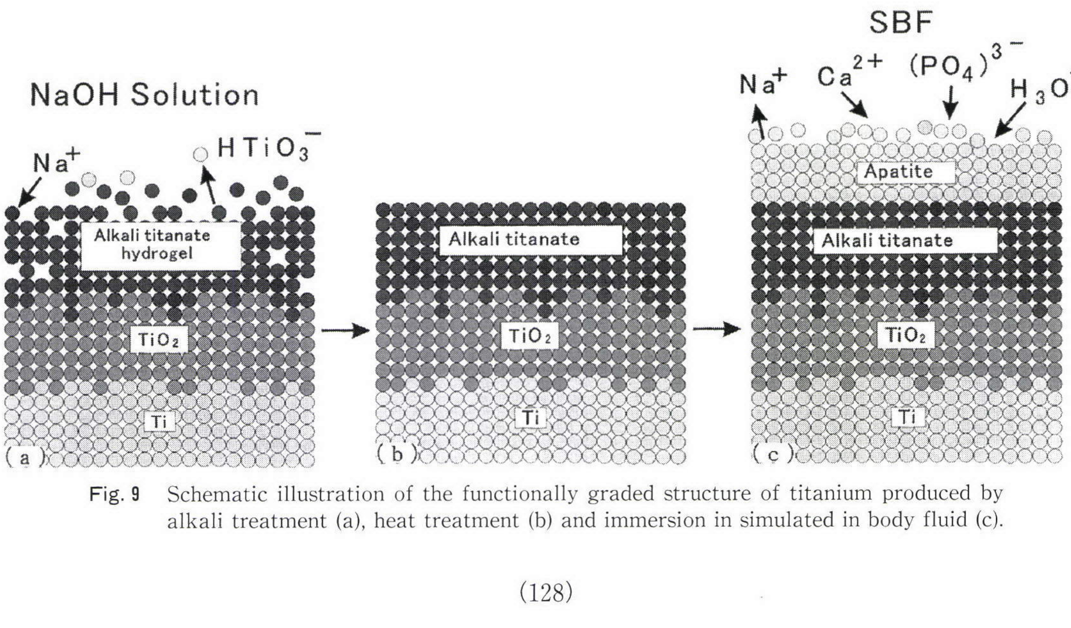

Fig. 9 Schematic illustration of the functionally graded structure of titanium produced by alkali treatment (a), heat treatment (b) and immersion in simulated in body fluid (c).

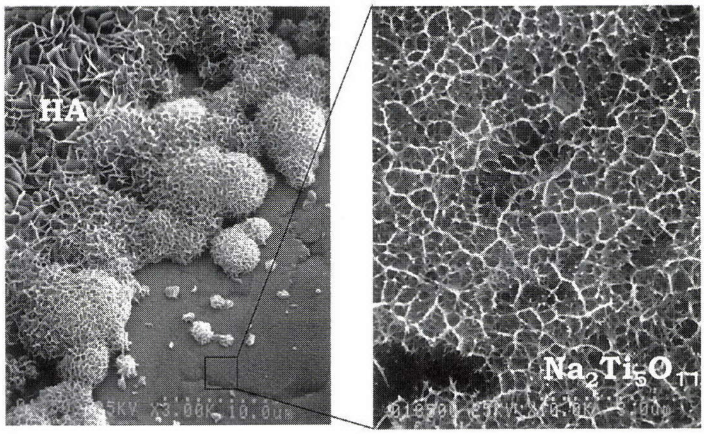

Fig.10 Scanning electron micrographs of HA precipitated HA on alkali-treated titanium surface.

result is a network of the alkali titanate and HA crystals on the alkali titanate surface. With this method, Yan et al.[25] have reported that after implantation in animals the treated implants showed significantly higher failure loads than with the untreated implants.

Okazaki et al.[26] synthesized graded carbonate-containing apatite (CO_3 apatite) with a solubility gradient in its crystal structure. They also synthesized graded fluoridated apatite that had higher acid resistance than homogeneous HA and two-layer fluoridated apatite (Fig. 11).

(3) Sintering

The sintering process can also be used to form FGMs. Those FGMs are created by blending and packing different kinds of powders using different mixing ratios.

Ban et al.[29] have developed a composite material consisting of titanium coated with a glass-hydroxyapatite ceramic layer. The ceramic layer incorporates a gradient in the coating with an increase in the HA concentration from the innermost sublayer towards the outermost sublayer (Fig. 12). The titanium substrate contributes to the mechanical strength of the composite, whereas exposed HA particles have a bioactive role. The compressive strength and Vickers hardness decrease with the increase in HA content in the glass.

Watari et al.[2] have studied a sintering method for composites comprised of titanium and HA. The composite is composed of more titanium in the upper part where occlusal forces are directly applied and more apatite in the lower part that is implanted inside the jaw bone (Fig. 13). Powders with different ratios of Ti and HA were packed into molds, producing a gradient in the concentration from one end to the other. The specimens were compressed at 400 MPa using cold isostatic pressing, and sintered in argon gas by high frequency induction heating at around 1300°C. The average flexural strength of the FGM implant was about 150 MPa, which is comparable to the strength of human living bone. Implantation tests to evaluate the biocompatibility of the implants were performed in rats.

Kon et al.[30] developed a functional gradient bioceramic consisting of HA and the more biodegradable α-TCP. This FGM is covered with α-TCP and the composition changes gradually to HA with increasing depth from the surface as shown in Fig. 14. Upon implantation of this material, its surface is in contact with interstitial fluid and the α-TCP will dissolve to supply calcium and phosphate. After the dissolution of α-TCP from the surface of the FGM, fresh HA appears very close to the highly concentrated calcium phosphate solution.

Creation of ideal functionally graded structure for dental implants

The arrangement of components in the internal architecture is also an important consideration in the fabrication of functional structures for dental implants. The arrangement of two components (gold and iron) as shown in Fig. 15 in parallel (a) and serially (b) shows different mechanical features under tensile loads even when the materials in both arrangements are the

Fig.11 Schematic model of functionally graded carbonate-containing and fluoridated apatite crystal.

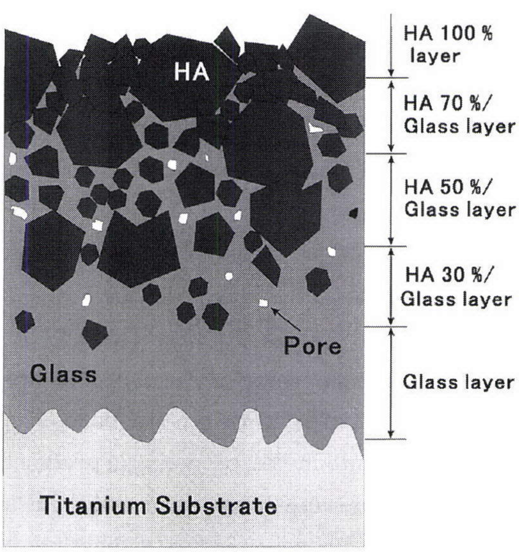

Fig.12 Schematic illustration of a cross-section of the HA-glass-titanium functionally graded structure.

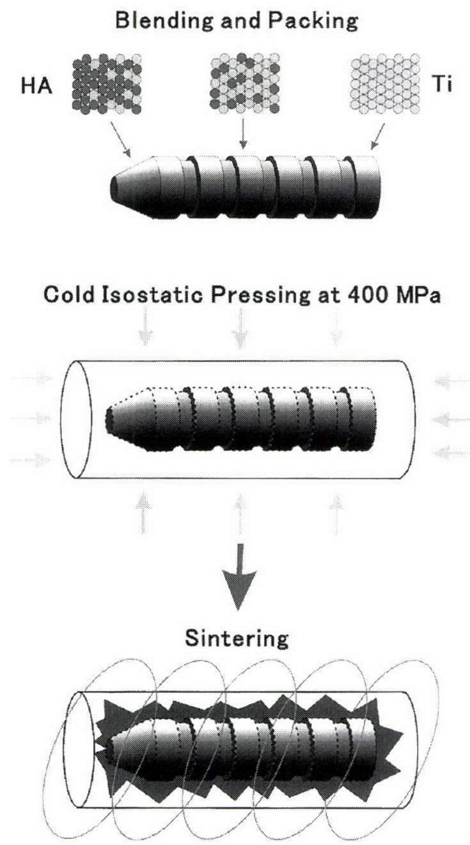

Fig.13 Manufacturing process of the functionally graded implant by spark plasma sintering.

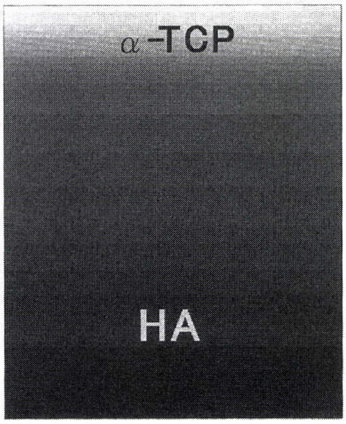

Fig.14 Schematic illustration of ceramic calcium phosphate with controlled compositional gradient. α-TCP : tri-calcium phosphate.

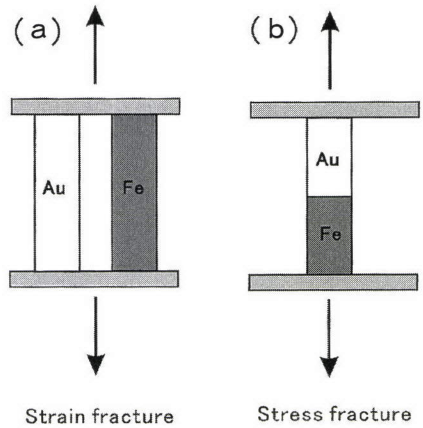

Fig.15 Strain fracturing (a) and stress fracturing (b) with the same components. Arrows show the direction of the applied forces.

same. Type (a) breaks in the iron component (strain fracture) and type (b) breaks in the gold (stress fracture), showing that a change in the structure results in a change of the mechanical functionality[31].

Another example is the architecture of bone. Bone has a functionally graded structure from the surface cortical compact toward inside with the inner cancellous trabeculae. At the proximal end of the femur, cancellous trabeculae appear to be dense along the trajectory of the principal stress calculated mathematically[32]. The cortical and cancellous bones are of the same substances while the structure is different. Figure 16 shows SEM micrographs of a fractured human enamel structure along with a schematic representation of the enamel. The one side view is a simple repetition of the unit structure. The other side, however, is a very complex structure. These structures and substances achieve the tough and stiff characteristics of enamel. The example of this hard tissue suggests that it is necessary to consider both the components in the material and also the structural arrangement. There have been no studies on the functionally graded structures so far and more attention must be directed towards this aspect.

In bone, HA crystals are found within and around collagen fibrils. The fibrous component, the collagen, has a much lower modulus than the HA, and the stiffness of bone is roughly as would be expected from a composite of the bone structure and composition. The mechanical behavior of bone must be considered in relation to the fact that it is a composite material[33]. Biological structures are complicated and nonuniform, materials and components with different strengths incorporated in the same structure result in hybrid systems with properties that may be designated for specific purposes[1].

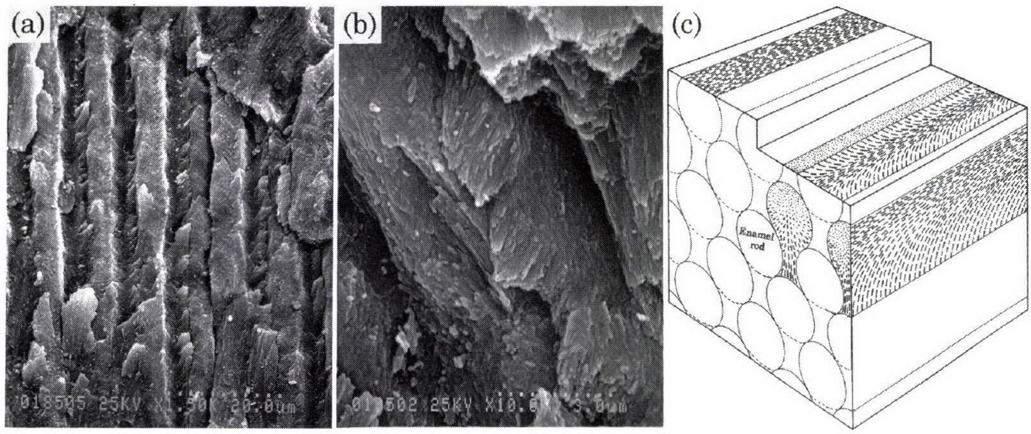

Fig.16 Scanning electron micrographs of the fractured enamel (a), (b) and illustration of the enamel structure.

Future issues

In oral implantology, numerous clinical trials have been performed with development of new materials prior to fundamental research. Further fundamental research is needed with respect to the bone formation mechanism around an implant to develop a biocompatible HA-coated implant with osseoconductivity. Surface modifications of titanium to enhance epithelial and connective tissue attachment to implant necks should be also investigated to enhance the integrity of the biologic seal between implant and soft tissue.

The basic concept of FGMs is an active control of the structure of the materials to ensure the desired properties. The composition profiles, as well as the microstructures of such materials have to be optimized with respect to the intended material function. For this reason the compositional dependence of the material properties is needed to obtain an optimum design. Building from this understanding of skeletal materials, engineering theory can be applied to optimize the shape and distribution of structural elements within organisms and the overall design strategy of complete skeletal systems[33].

Another consideration in producing implants is the production of surfaces that promote desirable responses in the cells and tissue in contact with the implant. Some studies have reported the surface modifications for controlling the adsorption of proteins, bacteria, and cells on biomaterials; including studies on composites of BMP with pure titanium[34] and the immobilization of human plasma fibronectin[35] or bisphosphonates[36] on titanium and its alloys.

Table 4 shows development stages and activity levels in the research and clinical application of biomaterials. Major attention in implant research will focus on replacement by FGMs (Stage III), proceeding from replacement by layered structures (Stage II). The final goal is to realize the production of structures simulating those found in the living body (Stage V) as in the structures of bone and teeth.

Table 4 Developmental stages and research activity levels of biomaterials for dental implants.

Development stage	Description of the activity	Activity level*	
		Research	Clinical application
I	Replacement by single materials (application of Ti or HA)	2	3
II	Replacement by layered structures (HA plasma spraying coatings on Ti)	5	5
III	Replacement by functionally graded materials	2	0
IV	Replacement by functionally graded materials and structures	1	0
V	Replacement by structures simulating those in the living body	0	0

* "5" means most activity
"0" means no activity

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