# Materials Science of Crystalline Bioceramics: A Review of Basic Properties and Applications

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## I. INTRODUCTION

***Socio-economic consequences.*** The number of patients requiring and receiving biomedical implants to correct skeletal defects and heal diseases are constantly increasing. Worldwide, large demand exists for load-bearing hip, knee and dental endoprosthetic implants, but also for bone replacement parts in the maxillar-mandibular area, the ossicular chain of the inner ear, and alveolar ridge and iliac crest augmentation. To date, in the United States and in Europe, more than 800,000 hip and knee arthroplasties are being performed annually, with increasing tendency.

The properties and function of biomaterials, in particular bioceramics are frequently being discussed in the context of hip endoprosthetic implants. Hence this review will deal with most commonly utilized bioceramic materials such as alumina, stabilized zirconia (Y-TZP, Y-stabilized **T**etragonal **Z**irconia **P**olycrystal), and calcium phosphates, in particular hydroxyapatite.

The increasing demand for endoprostheses is the result of the wear and tear the hip and knee joints are subjected to during a human lifetime. Consider this: an average person walks about 1 million steps per year with a frequency of about 1 Hz. Using a conservative width of stride of 1.5 m, this amounts in an average lifespan of 75 years to $10^8$ load changes during walking a distance of 100,000 km or 2.5 times the circumference of the earth. The load on the joints is roughly one time the body mass during rest, 2 to 3 times the body mass during normal walking, up to 5 times while jogging, and up to 8 times during jumping. Beyond that threshold the risk of damage to the joints increases dramatically. Since people generally live longer and get increasingly overweight due to overeating and lack of exercise eventually the protective tissue lining of the acetabular cup wears away, friction increases, and inflammation, pain and finally immobilization will result. At this point a THR (total hip replacement) is the only reasonable option to maintain mobility, freedom from pain and hence a rewarding life in old age. However, with increasing frequency younger people require such an operation because their lifestyle including damaging sports activities promotes premature wear on their joints. Here a problem arises since the younger patient will generally outlive the average lifetime of todays implants so that a remediation operation is required with substantial additional cost to the healthcare system of the country involved. Moreover, the early onset of pain and associated mental stress on the patient adds another dimension to the problem of the incompatibility of the lifespan of both the patient and the implant.

An additional serious problem exists: osteoporosis. Increasingly, loss of bone substance occurs in elderly people leading to embrittlement with the associated risk of fracture. This is caused by lack of calcium possibly related to nutrition too rich in meat, wheat and dairy products that produce an acidic environment in the body. Hence calcium ions are being used by the body to keep the pH of the blood serum within acceptable limits. The cost of this is substantial: in Germany about 150,000 osteoporotic fractures of the neck of the femur occur annually, 40 times the number of, for example, Thailand. It is thus not suprising that in 2002 the World Health Organization (WHO) has put osteoporosis on the list of the ten most frequent diseases worldwide.

***Design of endoprosthetic implants.*** While the stems and femoral balls of hip implants can be fashioned from austenitic surgical stainless steel or cobalt chromium molybdenum alloy, state-of-the art for hip endoprosthetic implants is a shaft manufactured from bioinert Ti6Al4V alloy and equipped with an alumina or Y-stabilized zirconia femoral ball that articulates against an acetabular cup anchored in the hip bone (Fig.1). This cup is made from cp-Ti or Ti alloy and lined with either ultrahigh molecular weight polyethylene (PE-UHWM) or, in recent developments, alumina to assure a low coefficient of friction when articulating against a femoral ball also made from alumina. This is desired since the natural highly viscous synovial fluid based on hyaluronic acid and acting as an efficient lubricant is absent in the implant system.

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The technology of total hip replacement (THR) has been clinically solidly established. Many engineering solutions exist to vary the form, length and surface details of the metallic stems as well as the diameter, neck length and type of inside taper of the ceramic femoral balls, made from either alumina or Y-stabilized zirconia. In addition, there is frequently a thin stable bioactive hydroxyapatite coating applied to the metallic stem that will elicit a specific biological response at the interface of the implant material by control of its surface chemistry through adsorption of non-collageneous proteins. This will result in a strong and lasting osseoconductive bond between living tissue and biomaterial. More detailed aspects of the function and performance requirements of hydroxyapatite coatings will be discussed below.

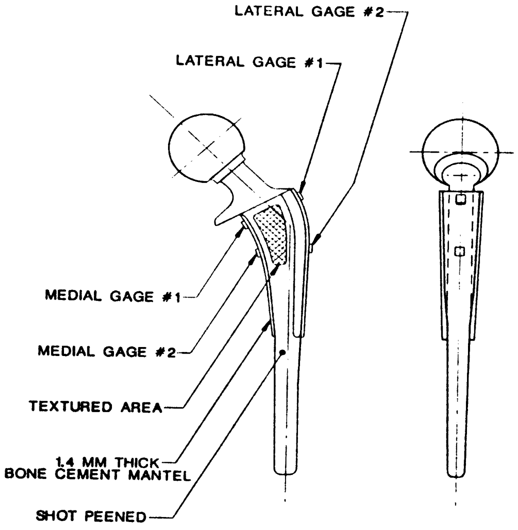

Figure 1. Schematic representation of a hip endoprosthetic implant (Bushelow et al., 1994).

In this review discussion will be limited to three typical bioceramic materials - alumina, Y-stabilized zirconia and hydroxyapatite - applied as components of hip endoprostheses to restore the mobility and the well-being of an increasing number of patients. As discussed in the introductory paragraph there is a tendency the first-time recipients of such an implant to become generally younger so that increasing demand exists for the long-term *in vivo* stability of the individual components of the implant system. This includes the fatigue strength and corrosion resistance of the bioinert metallic stem but also the bending and shear strengths as well as the surface friction properties of the monolithic ceramics parts and the polymeric liners of the acetabular cups, as well as the cohesive and adhesive strengths, and resorption resistance of the bioactive hydroxyapatite coatings. However, as mentioned above we are faced with the fact that an increasing proportion of patients will outlive the expected lifetime of presently 15 to 20 years of their hip endoprostheses. Consequently, research is ongoing worldwide to provide improved biomaterials with increased mechanical, chemical, biological and friction properties that will be sustained for a long time in the body environment.

## II. CONCEPT AND DEFINITION OF BIOCOMPATIBILITY

Any material incorporated into a human organism has to abide by certain properties that will assure that there are no negative interactions with living tissue. Biomaterials by definition are inorganic compounds that are designed to replace a part or a function of the human body in a safe, reliable, economic, and physiologically and aesthetically acceptable manner (Hench and Ethridge, 1982). Since biomaterials are inorganic structures they do not include renewable materials obtained from natural sources such as wood, plant fibres, hides, sinew, bone, ivory and others[1].

One of the important properties of biomaterials is their so-called *biocompatibility*. However, this is not an individual property *per se* but relates to the various interactions on the cell and tissue levels the material is subjected to. Hence a systems approach is required (Williams, 1985). According to this modern view, biocompatibility refers to the ability of a material to perform with an appropriate host response, in a specific application. Hence biocompatibility is neither a single event nor a single phenomenon but is meant to be a collection of processes involving different but interdependent interaction mechanisms between material and living tissue (for further details on definition of biocompatibility, see Williams, 1990).

In increasing order of biocompatibility the interaction of biomaterials with living tissue can be defined as follows (Wintermantel and Ha, 1996).

- ***Incompatible materials*** are materials that release to the body substances in toxic concentrations and/or trigger the formation of antigenes that may cause immune reactions ranging from simple allergies to inflammation to septic rejection with the associated severe health consequences.

- ***Biocompatible materials***, in contrast, are those that also release substances but in non-toxic concentrations that may lead to only benign tissue reactions such as formation of a fibrous connective tissue capsule or weak immune reactions that cause formation of giant cells or phagocyts. These materials are often called ***biotolerant*** and include austenitic stainless steels or bone cement consisting of polymethylmethacrylate (PMMA), see Table 1.

- ***Bioinert materials*** do not release any toxic constituents but also do not show positive interaction with living tissue. As a response of the body to these materials usually a non-adherent capsule of connective tissue is formed around the bioinert material that in the case of bone remodelling manifests itself by a shape-mediated *contact osteogenesis*. Through the bone-materials interface only compressive forces will be transmitted ("bony on-growth"). Typical bioinert materials are titanium and its alloys, ceramics such as alumina, zirconia and titania, and some polymers, as well as carbon, see Table 1.

- ***Bioactive materials*** show a positive interaction with living tissue that includes also differentiation of immature cells towards bone cells. In contrast to bioinert materials there is chemical bonding to the bone along the interface, thought to be triggered by the adsorption of bone growth-mediating proteins at the biomaterials surface. Hence there will be a biochemically-mediated strong *bonding osteogenesis*. In addition to compressive forces, to some degree tensile and shear forces can also be transmitted through the interface ("bony in-growth"). Typical bioactive materials are calcium phosphates and bioglasses,

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[1] However, in the case of alloplastic bone replacement of diseased bone this clear definition becomes blurred

see Table 1. It is believed that bioactivity of calcium phosphates is associated with the formation of carbonate hydroxyapatite (CHAp), similar to bone-like apatite (LeGeros and LeGeros, 1997).

Table 1. Examples of biomaterials and their applications (Willmann, 1999).

| **Material** | **Application** | **Biological behaviour** |
|---|---|---|
| Stainless (austenitic) steel | Osteosynthesis (bone screws) | biotolerant |
| Bone cement (PMMA) | Fixation of implants | biotolerant |
| cp-titanium | Acetabular cups | bioinert |
| Ti6Al4V alloy | Shafts for hip implants, tibia | bioinert |
| CoCrMo alloy | Femoral balls and shafts, knee implants | bioinert (?) |
| Alumina | Femoral balls, inserts of acetabular cups | bioinert |
| Zirconia (Y-TZP) | Femoral balls | bioinert |
| HD-polyethylene | Articulation components | bioinert |
| Carbon (graphite) | Heart valve components | bioinert |
| CFRP | Inserts of acetabular cups | bioinert |
| Hydroxyapatite | Bone cavity fillings, coatings, ear implants, vertebrae replacement | bioactive |
| Tricalcium phosphate | Bone replacement | bioactive |
| Tetracalcium phosphate | Dental cement | bioactive |
| Bioglass | Bone replacement | bioactive |

## III. INTERACTION OF IMPLANT MATERIAL AND LIVING TISSUE: A BASIC APPROACH

Fixation of an implant in the human body is a dynamic process that remodels the interface zone between the implant and living tissue at all dimensional levels from the molecular up to the cell and tissue morphology level and at all time scales from the first second up to several years after implantation (Kasemo and Lausmaa, 1991). This is represented in Fig. 2 in which the logarithmic length and time scales indicate this complex dynamic process. While immediately following the implantation a space filled with biofluid exists next to the implant surface, with time proteins will be adsorbed at the oxide surface of only several nanometers thickness covering the titanium alloy surface that will give rise to osteoinduction by proliferation of cells and their differentiation towards bone cells, revascularisation and eventual gap closing. Ideally, a strong bond will be formed between implant and tissue. However, sometimes connective tissue is being formed at the interface resulting in a fibrous tissue capsule that prevents osteointegration (see inset) and will cause implant loosening.

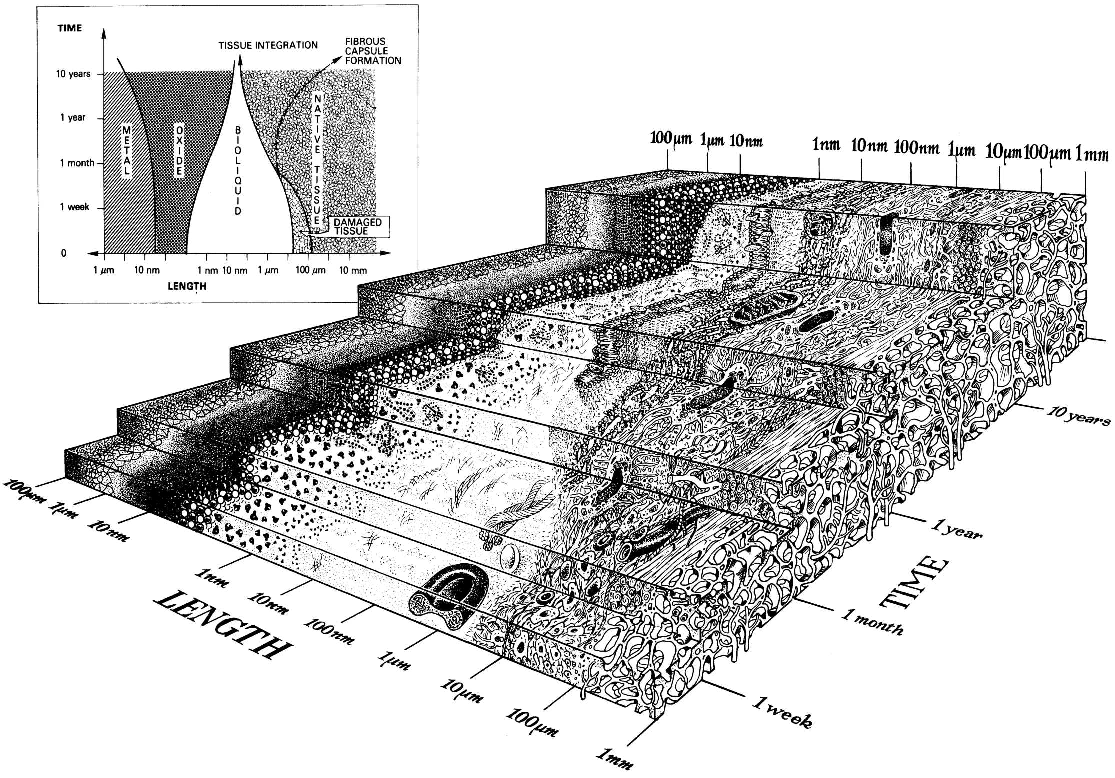

Figure 2 Dynamic behaviour of the interface between implant (left) and bony tissue (right) (Kasemo and Lausmaa, 1991).

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The composition of the bioliquid changes with time in response to chemical adsorption processes of molecules that mediate bone formation and also to transport reactions by outward diffusion of titanium atoms or ions through the thin oxide layer and concomittant inward diffusion of oxygen to the metal-oxide interface. This diffusion process is aided by lattice defects such as grain boundaries, isolated vacancies or vacancy clusters, and interstitial atoms. Several other reactions may occur, for example corrosion and partial dissolution/resorption of the oxide layer. This process appears to be a limiting factor for some implants even though the resorption rate is slow owing to the high chemical stability of titanium oxide.

Chemical adsorption of biomolecules such as chondroitin sulfate at the oxide surface provides a template for adhesion of collagene strands that precede the osseointegration.

## IV. MECHANICAL PROPERTIES OF ADVANCED BIOCERAMICS

It is mandatory that any material introduced into the human body with the intent to remain there for a long time be tolerated by the organism. In particular, biocompatibility has to be achieved which is defined as shown above. On the other hand, there are extremely strong quantitative differences of the mechanical properties between natural bone and bioinert ceramics as shown in Table 2. These differences lead to strong gradients of the modulus of elasticity (Young´s modulus) that give rise to so-called "stress shielding", meaning that load put on the implant during movement will not be transmitted by the bone but through the stiff ceramic femoral ball into the likewise very stiff titanium alloy stem. Since regular tensile loads are required for living bone to stay healthy their absence will eventually lead to atrophic loss of cortical bone matter.

While alumina is stiffer and has higher compressive strength compared to Y-TZP the latter performs mechanically better in terms of tensile and flexural strengths and, in particular, fracture toughness. This is related to delay of the well-known martensitic phase transformation from the tetragonal high temperature to the monoclinic low temperature modification of zirconia by stabilization with other oxides, most often yttria, but also calcia and magnesia. The resulting so-called transformation toughening accounts for dissipation of crack energy by delayed transformation of metastable tetragonal grains to thermodynamically stable monoclinic grains with lower density. Hence the transformation to a phase with lower density will exert compressive stresses onto the surrounding ceramic matrix that slows down and eventually arrests crack movement thus leading, for a ceramic material, to exceptionally large fracture toughness values. It should be noticed, however, that fracture toughness of cortical bone exceeds even that of stabilized zirconia confirming impressively nature´s ingenuity to design strong and tough structures.

Table 2. Comparison of mechanical properties of alumina, zirconia (Y-TZP) and bone (Kohn 1992; Hulbert 1993; Rieger, 1993).

| **Properties** | **Aluminia** | **Y-TZP** | **Bone**[1] |
|---|---|---|---|
| Density [g/cm$^3$] | 3.98 | 6.08 | 1.7-2.0 |
| E-modulus [GPa] | 380-420 | 210 | 3-30 |
| Compressive strength [MPa] | 4000-5000 | 2000 | 130-180 |
| Tensile strength [MPa] | 350 | 650 | 60-160 |
| Flexural strength [MPa] | 400-560 | 900 | 100 |
| Fracture toughness [MNm$^{-3/2}$] | 4-6 | >9 | 2-12 |

[1] The lower values refer to trabecular (spongy) bone, the higher values to cortical (dense) bone.

Attempts have been made to reduce the stiffness differences between implant and bone by so-called "isoelastic" implants. In this approach a sheath of polymer surrounds the metallic shaft of a hip endosprosthetic implant that is designed to provide a smooth gradient of the modulus of elasticity. However, degradation of the polymer in the harsh body environment has hampered these activities so far.

## V. BIOINERT OXIDE CERAMICS

***Alumina.*** The properties and required purity of alumina used in biomedical applications are summarized in Table 3 in which empirical values provided by Müller and Greener (1970) are contrasted to the existing ISO 6474 norm and a new ISO norm under development (Hulbert, 1993). The new ISO norm deviates from the existing norm in that a much lower average grain size is specified with a concurrent increase in the flexural strength to beyond 450 MPa. This can be achieved by grain boundary engineering based on the suppression of grain growth at the high sintering temperature required by addition of minor amounts of magnesium oxide in the range of a few tenth of a percent. Accumulation of magnesium oxide along the grain boundaries of alumina will result in a thin surface layer consisting of spinel ($MgAl_2O_4$) that acts as a barrier towards the grain boundary movement required for the process of recrystallization. Hence the formation of large grains by recrystallization will be effectively suppressed

Table 3. Properties of clinically utilized alumina ceramics (Müller and Greener, 1970; Hulbert 1993).

| **Properties** | **Aluminia** | **Aluminia ISO 6474** | **Aluminia new Iso norm** |
|---|---|---|---|
| Density [g/cm$^3$] | 3.98 | >3.90 | >3.94 |
| $Al_2O_3$ [%] | >99.7 | >99.5 | |
| $SiO_2$+$Na_2O$ [%] | <0.02 | <0.1 | |
| $SiO_2$+$Na_2O$+CaO [%] | | | <0.1 |
| Average grain size [µm] | 3.6 | <7 | <4.5 |
| Vickers hardness [HV0.1] | 2400 | >2000 | |
| E modulus [GPa] | 380-420 | . | . |
| Compressive strength [GPa] | 4-5 | | |
| Tensile strength [MPa] | 350 | | |
| Flexural strength [MPa] | 400-560 | >400 | >450 |
| Fracture toughness [MN m$^{-3/2}$] | 4-6 | | |

***Y-stabilized zirconia.*** As zirconia is produced from naturally occurring zirconium silicate (zircon, $ZrSiO_4$) or baddeleyite (monoclinic m-$ZrO_2$) trace amounts of uranium and thorium replacing the isovalent zirconium ion in the crystal lattice may remain in the processed material making it slightly radioactive. This indeed was a major concern that in the past had hampered the development of otherwise mechanically superior zirconia ceramics for biomedical applications. Novel processing routes, however, have decreased the content of potentially dangerous radioactivity down to virtually zero (Cales and Stefani, 1995). Table 4 shows selected properties of commercially available Y-TZP (Hulbert, 1993; Rieger, 1993; Stevens, 1986).

The Y-stabilized TZP contains vacancies in its oxygen sub-lattice that facilitate ionic conductivity at high temperature. However, these vacancies are also the source of colour centres that will be activated by irradiation with high energy radiation such as X-rays or $\gamma$-rays and hence cause the slightly ivory-coloured as-sintered ceramic to attain a greyish-purple shade (Dietrich et al., 1998; Heimann and Willmann, 1999). Since hip endoprostheses will be sterilized with $\gamma$-irradiation by the manufacturer before shipping to the hospital such a colour change may suggest to the operating surgeon an intolerable degree of contamination with impurities while the actual cause of the reversible discolouration is on an electronic level and does neither compromise the mechanical nor the biomedical performance of the device.

Table 4. Mechanical properties of commercially available zirconia.

| **Property** | **Range of values** |
|---|---|
| Density [g/cm³] | 6.05 – 6.09 |
| Zirconia content [%] | 95 – 97 |
| Yttria content [%] | 3 – 5 |
| Average grain size [µm] | 0.2 – 0.4 |
| Vickers hardness [HV0.1] | 1200 – 1300 |
| E modulus [GPa] | 150 – 210 |
| Compressive strength [MPa] | > 2000 |
| Tensile strength [MPa] | > 650 |
| Flexural strength [MPa] | 900 – 1300 |
| Fracture toughness [MN $m^{-3/2}$] | 7 – 9 |

## VI. PERFORMANCE REQUIRREMENT AND QUALITY CONTROL OF CERAMIC FEMORAL BALL HEADS

Femoral ball heads of hip endoprostheses made from bioinert ceramics such as alumina or zirconia have to sustain high mechanical stresses, resorption/corrosion by aggressive body fluid, and abrasive wear over the lifetime of the implant in the human body of 15 to 20 years. Some important properties of ceramic femoral ball heads are listed in Table 5 (Willmann, 1995).

Table 5. Important mechanical and functional properties of ceramic femoral ball heads (Willmann, 1995).

| **Materials property** | **Prerequisite for** |
|---|---|
| High hardness<br>No plastic deformation under load<br>No elastic deformation under load<br>No creep | Wear resistance over many years |
| Finely grained microstructure<br>Dense (no porosity) | Excellent surface finish, low coefficient of friction |
| High bending strength | Load bearing capability |
| High compression strength | High fracture strength |
| Good fatigue resistance | Reliable product |
| Extreme corrosion resistance | Biocompatibility |
| High purity | Bioinertness |
| No radioactive impurities[1] | |
| Electrical insulator | No galvanic reactions, *i.e.* no fretting Corrosion |

[1] in case of zirconia

Table 6. Wear data of combinations used in femoral ball/acetabular cup liner wear pairs (Heimann and Willmann, 1999).

| **Materials combination** | **Linear wear [μm/year]** |
|---|---|
| Metal/PE-UHMW[1] | 200 |
| Alumina/PE-UHMW | <100 |
| Alumina/CFRP[2] | <4 |
| Y-TZP[3]/PE-UHMW | <100 |
| Biolox™/Biolox™ [4] | <5 |
| Biolox forte™/Biolox forte™ | <1 |
| Y-TZP/Y-TZP | disastrous |

[1] PE-UHMW = Polyethylene-ultrahigh molecular weight

[2] CFRP = carbon fibre-reinforced polymer

[3] Y-TZP = yttria-stabilized tetragonal zirconia polycrystal

[4] Biolox, Biolox forte = tradenames of medical alumina ceramics produced by CeramTec AG, Plochingen, Germany

The wear performance of the sliding couple ceramic femoral ball/acetabular cup liner is of crucial importance since the lubricating synovial fluid present in natural hip joints is absent in the artificial system. Hence the coefficient of friction must be as low as possible. Some data of linear wear of clinically established wear couples as well as data obtained during wear screening tests (Fig. 5) are shown in Table 6 (Heimann and Willmann, 1999).

Figure 3 shows a schematic representation of the manufacturing process of ceramic femoral balls (Clarke and Willmann, 1994). Starting from high purity alumina or Y-stabilized zirconia powders (A) a cylindrical precursor shape is formed by cold uniaxial pressing (B) that subsequently is being turned on a CNC-lathe to shape the inside taper and outside spherical surface (C). A laser-etched engraving for identification is provided (D) before firing at up to 1,600°C to densify the ceramic green body by sintering (E). Finishing is being done by grinding with diamond tools the internal bore and the spherical surface to a very low roughness value to achieve a low coefficient of friction (F,G). Final inspection (H) will assure an extremely high degree of reliability that is required for long-term survival of the ball in a hostile and aggressive body environment.

Figure 4 shows three standard diameter sizes (22, 28, and 32 mm) of zirconia femoral balls with laser markings to unequivocally identify the individual part. For example, the top ball carries the identification code 32-12/14 M 96 @ Z 8179 that refers to a diameter of 32 mm, an inside taper of 12/14 mm, a medium neck length M, the year of manufacture (1996), the type of ceramics Z for zirconia, as well as the production number 8179. With this complete identification it is possible to establish a quality test protocol and trace the history of this part that may be very important in any court procedure associated with litigation cases against the producer, the hospital, and the surgeon who has performed the operation. It also provides a unique means of identification in case other identification traits have been obliterated as for example of a body charred in a fiery accident.

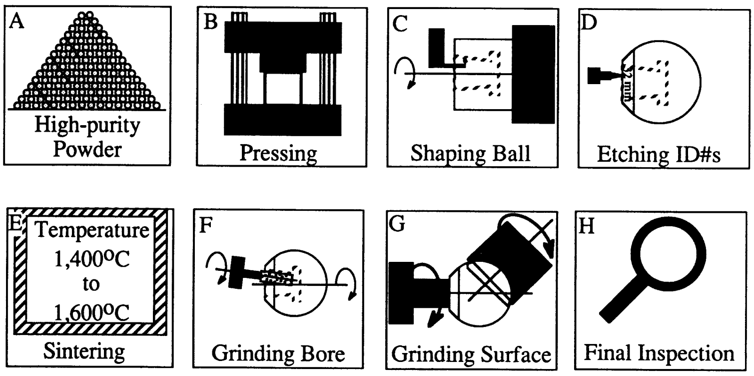


Figure 3. Schematic of the manufacturing process of ceramic femoral balls (Clarke and Willmann, 1994).

Figure 4. Laser markings of zirconia femoral ball heads (Heimann and Willmann, 1999).

Since stringent quality control measures during production of femoral ball heads are of the utmost importance wear screening and corrosion tests are being performed on simplified specimen geometries (cylindrical pins, annulus) in the presence of lubricating simulated body fluids (Ringer´s solution, Hank´s Balanced Salt Solution etc.) or protein-containing solutions such as foetal bovine serum and human serum albumin solutions under physiological conditions. Figure 5 shows several wear screening tests applied to bioinert ceramic materials according to ASTM F 603 (pin-on-flat test) and ISO 6474 (annulus-on-flat test) designations as well as in a more sophisticated hip joint simulator (Clarke and Willmann, 1994). Some of these tests are carried on for up to 2 million cycles that correspond to a time of 2 years considering the average number of load changes during walking for one year.

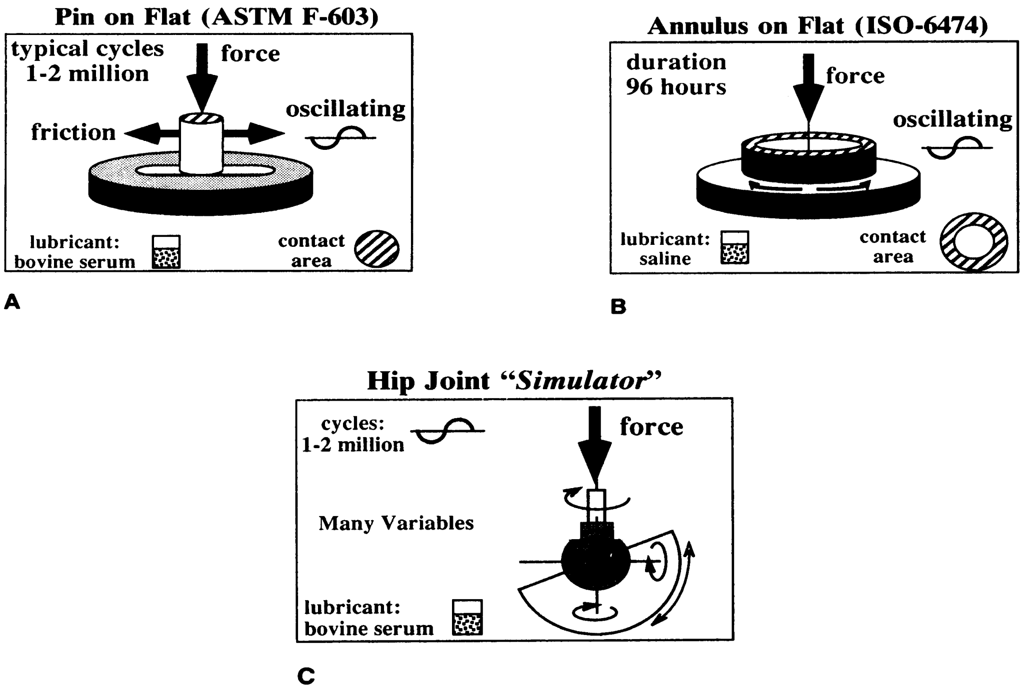


Figure 5. Wear screening tests of simplified specimen geometries (Clarke and Willmann, 1994).

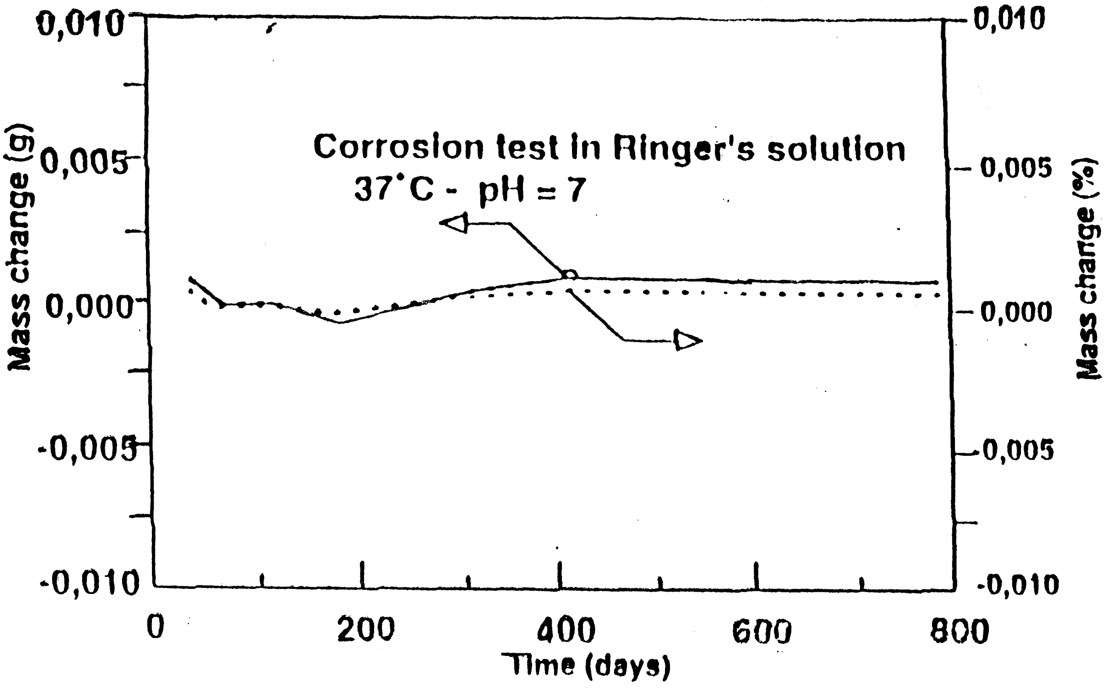


Figure 6. Mass changes of Y-TZP samples during immersion in Ringer´s solution under physiological conditions (37 °C, pH = 7) (PROZYR$^{TM}$, Ceramiques Techniques Desmarquest, Saint-Gobain Ceramiques Industrielles).

The aging behaviour of Y-TZP (Prozyr™, Ceramiques Techniques Desmarquest, Saint-Gobain Ceramiques Industrielles, France) in Ringer´s solution is shown in Fig. 6, confirming the extraordinary corrosion stability of this material for periods exceeding 2 years. On PE-UHMW-liners of acetabular cups articulating against femoral balls made from alumina, zirconia and CoCr alloy, combined wear and corrosion („corrabrasion") tests were performed in foetal bovine serum + 20 mmol EDTA corresponding to an exposure time of 5 years (Fig. 7). According to this data zirconia outperforms both alumina and metal femoral heads in terms of protection against the synergistic action on PE-UHMW of mechanical wear and chemical corrosion.

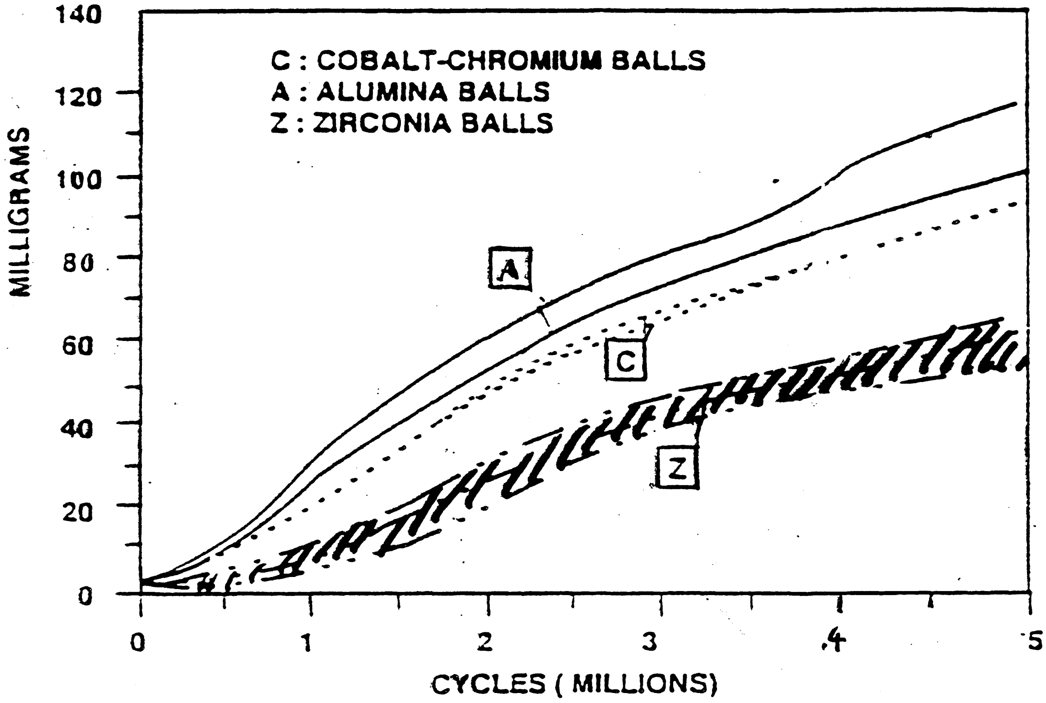


Figure 7. Wear of PE-UHMW-lined acetabular cups in contact with femoral balls made from alumina, zirconia and CoCr alloy in foetal bovine serum + 20 mmol EDTA solutions (PROZYR™, Ceramiques Techniques Desmarquest, Saint-Gobain Ceramiques Industrielles).

## VII. BIOACTIVE HYDROXYAPATITE CERAMICS

The bond formed between a metallic titanium alloy implant and the bone tissue is mediated by a so-called contact osteogenesis. Bone tissue is one-directionally growing towards to interface and "bony on-growth" occurs that is able to transmit compressive loads. However, the actual loads the interface is subjected to during movement of the patient contain also strong tensile and shear components that have to be taken care of. In the clinical practise in many cases a bioactive hydroxyapatite layer is provided that will allow a bonding osteogeneses that through "bony in-growth" will be able to transmit these tensile and shear forces. Here two ossification fronts develop, one growing from the bone towards the implant and another growing from the implant towards the bone (Soballe, 1993). Evidence is mounting that a 150 µm long-term stable bioactive hydroxyapatite coating will elicit a specific biological response at the interface of the implant material by control of its surface chemistry through adsorption of non-collageneous proteins such as osteocalcin, osteonectin, silylated glycoproteins and proteoglycanes. This will result of the eventual establishment of a strong and lasting osseoconductive bond between living tissue and biomaterial. The advantages of bioactive coatings include (i) the prevention of a fibrous capsule of connective tissue surrounding the implant, (ii) fast bone apposition rates through preferential adsorption of proteins, (iii) bonding osteogenesis providing a continuous and strong interface between implant and tissue that is able to transmit not only compressive but also tensile and shear loads, (iv) accelerated healing compared to implants without a bioactive coating, as well as (v) reduced release of titanium ions to the surrounding tissue thus minimizing the perceived risk of a cytotoxic response.

Figure 8. shows how a plasma-sprayed hydroxyapatite coating on a porous titanium layer covering the titanium alloy surface (solid bars) dependent on the implantation time will improve the interfacial bond strength compared to uncoated porous titanium (light bars) (Hench, 1991).

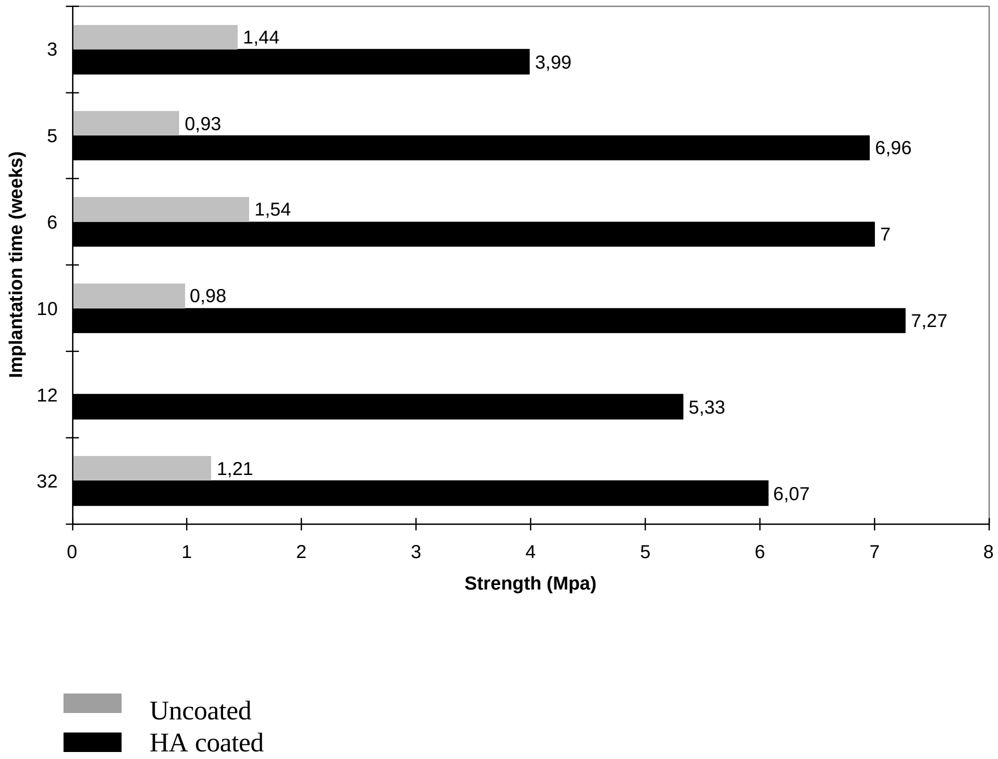


Figure 8. Comparison of interfacial bond strength of porous titanium with (solid bars) and without (light bars) a plasma-sprayed hydroxyapatite coating (Hench, 1991).

***Biomimetic films.*** Nucleation of ´bone-like´ hydroxyapatite occurs readily on contact of materials with functional groups such as Si-OH, Ti-OH, Zr-OH, Ta-OH or Nb-OH with simulated body fluid (SBF) (Kokubo et al., 2000). This is somewhat different from earlier assumptions that the presence of $PO_4$ in the substrate is required to nucleate apatite (Ohura et al., 1991). Slow formation of films of < 5 µm thickness was achieved by biomimetic control during reactive immersion of calcium silicate substrates in simulated phosphorus-containing body fluid (Kokubo, 1991). Obviously the functional groups mentioned above catalytically mediate the formation of apatite nuclei in acellular simulated body fluid with ion concentrations resembling those of human blood plasma. In particular, silicon may be associated with calcium ions in an early stage of bone calcification (Carlisle, 1970) and hydrated soluble silica has been shown to enhance proliferation of bone cells (osteoblasts) and active cellular production of transforming growth factors (Hench, 1996). The apatite nuclei formed grow spontaneously by consuming the calcium and phosphate ions from the surrounding fluid since the SBF (and the blood serum) are already highly supersaturated with respect to hydroxyapatite. Incorporation of carbonate ions creates an environment that is conducive to in-growth of bone by preferential proliferation and differentiation of osteoblasts on this biomimetically formed bone-like apatite layer (Loty et al., 2000). It is worth mentioning that the presence of an alkali titanate hydrogel layer at the surface of titanium activated by NaOH modifies the biological response of the metal towards bioactivity (Kokubo, 1997).

***Thin films by surface modification.*** In the past many attempts have been made to deposit, by various surface modification techniques, thin and well-adhering films of hydroxyapatite onto titanium implant surfaces to mediate bone apposition and improved anchoring of the implant within the cavity of the femur. Some of them have been reviewed by Heimann et al., (1997). Ducheyne (1990) deposited by electrophoretic techniques hydroxyapatite from a calcium phosphate solution and densified the film by sintering. The composition of the film was found to be mixture of hydroxyapatite and tetracalcium phosphate, the latter being presumably the product of thermal decomposition during sintering. From a calcium phosphate glass target Yamashita (1994) produced by r.f. sputtering thin stoichiometric hydroxyapatite as well as defect apatite films whose composition depended on both the $CaO/P_2O_5$ ratio and the partial pressure of water. Amorphous calcium phosphate films of $< 1$ µm thickness were deposited by dynamic ion beam mixing that on annealing for 1 hour at $600^oC$ crystallized, forming hydroxyapatite with apparent self-repair function through Ca-P-Ti-OH complexes (Ohtsuka, 1994).

***Thick coatings by plasma spraying***. It is well known that thin hydroxyapatite coatings below about 50 µm will be rather quickly resorbed *in vivo*. Hence if long-term stable coatings are desired thicker coating of 100-150 µm are called for that have been produced by several techniques including deposition of hydroxyapatite powder or suspensions on the implant and subsequent sintering below $1200^oC$ with or without a bond coat (Toriyama, 1990,1991; Kawamoto, 1991), and bonding of hydroxyapatite granules with an organic glue, e.g. PMMA to the implant surface. The latter technique is thought to provide improved load transmission to the bone through a graded structure with quasi-elastic properties. However, state-of-the-art to deposit thick, rather well-adhering and resorption resistant coatings is by atmospheric plasma spraying (APS), high velocity oxyfuel spraying (HVOF) or low pressure plasma spraying (LPPS) (Heimann and Vu, 1997). The principles of these techniques have been discussed elsewhere (Heimann, 1996).

Important performance criteria of plasma-sprayed hydroxyapatite coatings are (i) adhesion to the Ti6Al4V substrate that depends crucially on microstructural features of the coatings such as porosity, degree of deformation of spray particle splats, and the presence of micro-and macrocracks as well as residual stresses at the coating-substrate interface, and (ii) biochemical resistance against aggressive body fluid that depends on the crystallinity of the hydroxyapatite and the nature and amount of thermal dehydroxylation (oxyapatite; Trombe et Montel 1971) and decomposition (tricalcium phosphate, tetracalcium phosphate, CaO) products (McPherson et al., 1995) as well as the presence of amorphous calcium phosphate (ACP). However, high adhesion strength requires high plasma enthalpy that in turn causes increased thermal decomposition of hydroxyapatite and a low biochemical resistance. To solve this conundrum a compromise is needed. Optimization of coating performance can be achieved principally through three routes: control of plasma spray parameters, microstructural engineering of spray powders prior to deposition, and the application of bioinert bond coats (Heimann, 1999). However, even then thermal decomposition of hydroxyapatite in the extremely hot plasma jet is inevitable owing to its incongruent melting at 1570°C (Fig. 9).

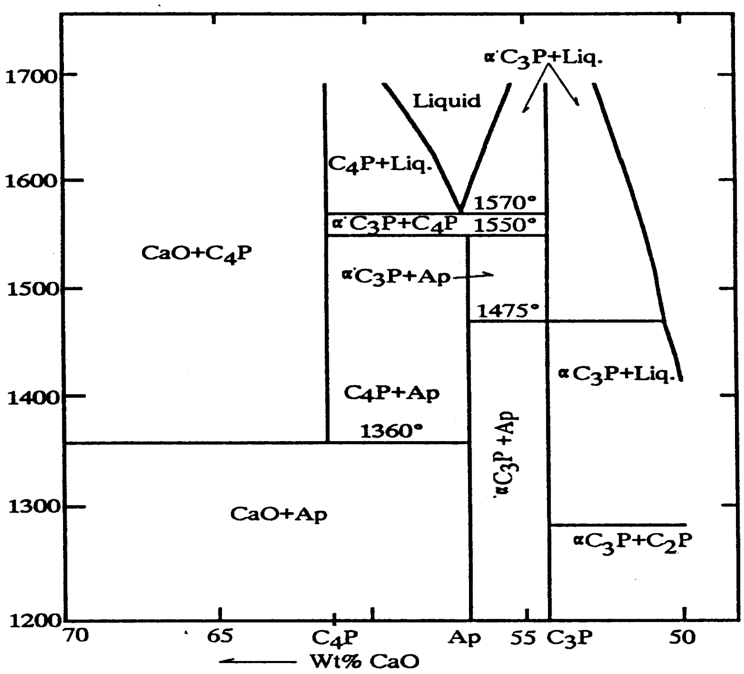


Figure 9. Phase diagram of the quasi-binary system $CaO$-$P_2O_5$-$H_2O$ at a water partial pressure of 65.5 kPa (Riboud, 1973).

The thermal decomposition of hydroxyapatite in the plasma jet occurs in four steps:

Step 1: $Ca_{10}(PO_4)_6(OH)_2 \rightarrow Ca_{10}(PO_4)_6(OH)_{2-2x}O_x\ _x + x\ H_2O$
(hydroxyapatite) (oxyhydroxyapatite)

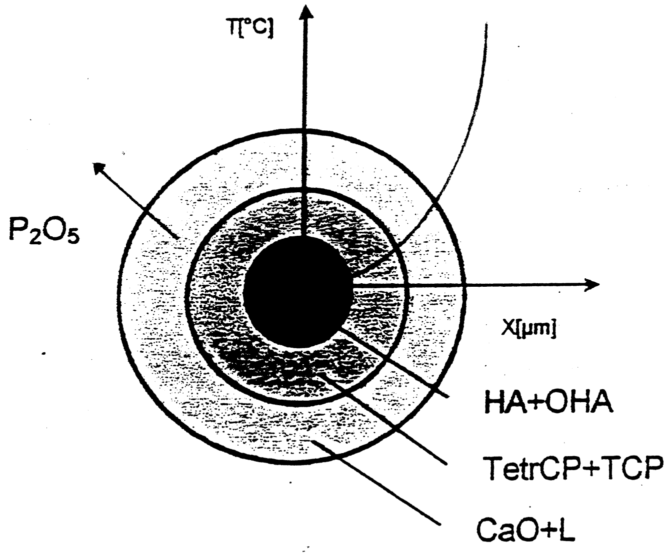
Step 2: $Ca_{10}(PO_4)_6(OH)_{2-2x}O_x\ _x \rightarrow Ca_{10}(PO_4)_6O + (1-x)\ H_2O$
(oxyhydroxyapatite) (oxyapatite)

Step 3: $Ca_{10}(PO_4)_6O \rightarrow 2\ Ca_3(PO_4)_2 + Ca_4(PO_4)_2O$
(oxyapatite) (tricalcium phosphate) (tetracalcium phosphate)

Step 4: $Ca_4(PO_4)_2O \rightarrow 4\ CaO + P_2O_5\uparrow$ or $Ca_3(PO_4)_2 \rightarrow 3\ CaO + P_2O_5\uparrow$

Figure 10 shows a model of thermally induced phase transformation in a spherical hydroxyapatite powder particle considering a parabolic temperature gradient according to Fourier´s Law. During the short residence time of the particle in the plasma jet the innermost core is still at a temperature well below 1550°C owing to the low thermal diffusivity, showing hydroxyapatite (HA) and oxyapatite (OA) as stable phases (steps 1 and 2). The second shell has been heated to a temperature above the incongruent melting point of hydroxyapatite (1570°C), and consists of a mixture of tri- and tetracalcium phosphates (step 3; see also Fig. 9). The outermost spherical shell of the particle consists of CaO + melt (L) since evaporation of $P_2O_5$ shifts the composition along the liquidus towards CaO-richer phases (step 4). The temperature increases to well beyond 1800°C, and the only unmelted composition is CaO. When the particle impinges at the metal implant surface to be coated the clear phase separation will be lost. The result is an inhomogeneous calcium phosphate layer in which HA (hydroxyapatite), OA (oxyapatite), TCP (α´-TCP, β-TCP (whitlockite)), TTCP (hilgardite) and CaO (oldhamite) are interspersed on a microcrystalline scale (Götze et al., 2000). At the immediate interface to the solid substrate a very thin layer of amorphous calcium phosphate (ACP) may exist formed by rapid quenching of the outermost melt layer with heat transfer rates beyond $10^6$ K/s. This thin layer takes on a special significance as its high solubility in body fluid may be one of the leading causes of coating delamination. Hence many research activities are directed towards well-crystallized hydroxyapatite layers with a minium of amorphous component.

Figure 10. Schematic model of the thermal composition of a spherical hydroxyapatite particle subject to high temperature in a plasma jet (Graßmann and Heimann, 2000).



According to the performance requirements of plasma-sprayed coatings discussed above a list of essential properties has been developed that is shown in Table 7 (Wintermantel and Ha, 1996). Materials properties of hydroxyapatite have been compiled by Willmann (1993). However, it should be mentioned that the tendency to apply very thin plasma-sprayed coatings (< 50 µm) or even thinner biomimetic coatings is on the increase, simply because of their higher adhesion strength and lower residual stresses.

Table 7. Performance requirements of bioceramic hydroxyapatite coatings (Wintermantel and Ha, 1996)

| **Property** | **Requirement** | **Reason** |
|---|---|---|
| Coating thickness | 50 µm | Coating < 50 µm will be resorbed |
| Coating thickness | 200 µm | Upper limit for maintenance of sufficient strength |
| Porosity/roughness | 100-200 µm | Minimum porosity for ingrowth of bone tissue |
| HAp content | > 95% | Minimum purity for biocompatibility |
| HAp content | > 98% | Chemical stability |
| Crystallinity | > 90% | Increasing resorption with decreasing crystallinity |
| Adhesion strength | > 35 MPa | Prevention of spalling |

## VIII. THE NEED AND ROLE OF BIOINERT BOND COATS

Because of the chemical and structural similarities of the bioactive hydroxyapatite coating and the inorganic constituent of the composite material bone, the bond between HA and living bone is decisively stronger than that between HA and the nanometer-thin oxide layer covering the Ti alloy. Since there exists a strong gradient of the modulus between the metallic implant and the bone, a gap may develop by prolonged shear-loading of the implant. Into this gap acellular connective tissue will invade with consecutive aseptic loosening of the implant (Wolke et al., 1992; Müller and Patsalis, 1997). Depending on the literature source, in up to 10% of all implant failure cases this will require a remediation operation with the associated high mental stress and pain to the patient and high financial burden to society. Hence it is desired to reduce the extent of loosening of the implant by adding a bioinert bond coat to the bioactive HA coating that will be able to withstand the high local tensile and shear stresses during micromovements of the patient that even by fixation of the patient will inevitably occur during the first stages of the healing phase after implantation.

The functions of bioinert bond coats include (i) improvement of the adhesion of the coating to the metal implant, (ii) prevention of a direct contact between metallic Ti and hydroxyapatite that is thought to catalytically activate the thermal decomposition of the latter, (iii) reduction or even prevention of the release of potentially cytotoxic metal ions to the surrounding tissue, (iv) reduction of the thermal gradient at the metal/coating interface and hence suppression of the formation of amorphous calcium phosphate, (v) reduction of the steep gradient of the coefficient of thermal expansion and hence the large interfacial residual coating stresses, and (vi) cushioning of damage initiated by micromotions of the patient during the healing phase that may lead to coating cracking and delamination.

The search for suitable bond coats is still under way (Lamy et al., 1996; Kurzweg et al., 1998; Heimann et al., 1999). Recent *in vivo* experiments in a sheep animal model showed conclusively that the presence of a thin $TiO_2$ bond coat of about 15 µm connecting the hydroxyapatite coating to the metallic implant will retain a strong adhesion of the coatings to the implant (Heimann et al., 2002). Hence formation of a gap will be suppressed. These experiments appear to confirm the assumption obtained from previous *in vitro* experiments that such a suitable bond coat will substantially increase the adhesion strength of the bioactive hydroxyapatite coating to the Ti6Al4V substrate that forms the mechanically stable implant body. The excellent adhesion of the bond coat to the metal can be seen in the fact that the $TiO_2$ layer acts as a structural extension of the already existing thin native oxide layer of only several nanometers thickness. The reason of the good bonding to the hydroxyapatite top layer is still obscure but may be related to the formation of an extremely thin reaction layer consisting of calcium titanates of various stoichiometries (Ji et al., 1992) or the formation of a solid solution of titanium oxide with hydroxyapatite (deGroot et al., 1987). Both mechanisms would serve to augment the mechanical bonding of the coating layers typical for plasma-sprayed coatings by a strong diffusive bonding. In addition, owing to its low heat transfer coefficient the bond coat will act as a thermal barrier slowing down the cooling rate of the plasma-sprayed coating and thus increasing the amount of crystalline hydroxyapatite at the expense of ACP, and also the resorption resistance in contact with body fluid.

## IX. NOVEL DEVELOPMENTS AND OUTLOOK

As already discussed in the Introduction, the development of novel biomaterials with improved lifetime, reliability and bioactive functions is high up on the agenda of worldwide research. The limited stability of hydroxyapatite and its thermal decomposition products in a body environment (Fazan and Marquis, 2000) calls for bioactive materials with increased resorption resistance. Such materials can be based, for example, on the quaternary system $CaO\text{-}P_2O_5\text{-}TiO_2\text{-}ZrO_2$ (Schneider et al., 2000) in which stoichiometric compositions exist with much improved mechanical and chemical stability compared to the calcium phosphates. For example, $CaTiZr_3(PO_4)_6$ shows solubilities in simulated body fluids that are at least one order of magnitude lower than that of hydroxyapatite. Plasma-sprayed coatings of this composition result in good adhesion to Ti6Al4V substrates (> 40 MPa; Lugscheider et al., 1996) even though considerable thermal decomposition has been observed that leads to formation of zirconium pyrophosphate ($ZrP_2O_7$), rutile ($TiO_2$), and baddeleyite (m-$ZrO_2$). There is some evidence, however, that these bioinert products of incongruent melting of the coating material may lead to particle-mediated reinforcement of the coating microstructure. *In vitro* biocompatibility tests with primary rat bone marrow cells showed substantial cell proliferation in the presence of foetal bovine serum. Animal tests proved that 150 µm thick coatings based on $CaTiZr_3(PO_4)_6$ applied to Ti6Al4V rods implanted in the femur of sheep led to neoformation of dense bone at a stable interface implant-bioceramic coating without the coating delamination often observed with hydroxyapatite (Müller, 2001). In addition, $CaTiZr_3(PO_4)_6$ is a member of the so-called NASICON family (**Na**trium **S**uper**i**onic **Con**ductors, Alamo, 1993) with the general formula $AM_2X_3O_{12}$ where A = alkali or alkaline earth metals, M = Ti, Zr, Hf etc. and X = P, Si or S. These materials show ionic conductivity already at room temperature. It is being conjectured that a Ti6Al4V/$TiO_2$/NASICON/(hydroxyapatite) coating system would have an equivalent circuit of a “bio”capacitor that by proper poling could store negative electrical charges close to the interface with the growing bone thus presumably enhancing bone apposition rate and bone density (Yamashita et al., 1996).

A different route in the quest for new promising biomaterials is based on ceramic-polymer composites that are being designed to mimic the mechanical and biological performance of natural bone, for example composites of polylactic acid and hydroxyapatite, polyethylene and hydroxyapatite as well as collagen and hydroxyapatite (see, for example Bonfield et al., 1984). Such novel materials have been designated ´íntelligent´ and are defined as human-friendly materials that can change their characteristics in response to surrounding conditions, for example varying stress fields. The presence of the polymeric component with a low modulus acts as an ´ isoelastic´ medium by reducing considerably the strong gradient of the stiffness between natural bone and metallic implant and thus reduces also stress shielding with its negative consequences (see above). While the composite at present is experimentally applied only under low-loading conditions its use for loaded implants can be implied in future developments.

Ceramic-ceramic composites are presently tested, for example hydroxyapatite with addition of bioglass (Tancred et al. 2001). Adding 5% bioglass of composition 53% $SiO_2$, 26% $Na_2O$, 13% CaO, 5% $P_2O_5$, 0.5% $Al_2O_3$, 3% $B_2O_3$ increases the fracture toughness by a factor of 2 but results in reduced density and hardness.

Lastly, developments are under way to improve the wear resistance of ceramic femoral heads by application of ultrahard coatings, for example diamond-like carbon (DLC) or TiN coatings that not only improve the mechanical abrasion wear resistance of the ceramic when articulating against the PE-UHMW lined acetabular cup but also reduce the coefficient of friction (Affatato et al., 2000).

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