Bioactivity of Calcium Phosphate Ceramic Coatings on Metallic Implants

Cheol-Sang Kim and P. Ducheyne*

-Abstract-

Calcium phosphate ceramics have been applied intensively to orthopaedic and dental implants by virtue of their osteoconductive nature. In an attempt to enhance the bone implant intergrity and stability, these ceramics are deposited onto the porous surface of metallic implants. The coating procedure and the ensuing phase transformations of the ceramic alter the mechanical properties and surface chemistry of the ceramic layers as well as those of the substrate. These structural and compositional differences are directly related to the interaction mechanisms at the surface-active ceramic-bone interface. Material and processing induced influences on dissolution, electrokinetic behavior, ceramic-metallic substrate interface and bone growth enhancement are presented.

1. Introduction

Long-term stability of surgical implants has been approached in various ways. Bioactive ceramics, specifically calcium phosphate ceramics(CPC), have been studied as a hard tissue sudstitute because of their similarity to the mineral phase of bone. Calcified tissue growth can be enhanced by these surface active ceramics, which are described as being osteoconductive in nature. These materials have found a wide range of clinical applications including middle ear protheses and tooth root replacements. In the realm of orthopaedics, CPC's are used as a thin lining on porous metallic devices. The number of hip and knee prostheses implanted has been increasing steadily. According to estimates 500,000 joint protheses will be used annually by 1990.[1] The CPC coated porous impalnts are being inserted without the use of bone cement, especially in younger and more active patients.

Various porous surfaces such as bead, regular or irregular wire mesh have been developed as a method of cementless fixation. The metallic core of the implant serves as the load carrying member, whereas the porous or grooved surface interloks with surrounding tissue by bone ingrowth into its pores. Both cemented implants and porous-coated, non-cemented implants have demostrated good shot-term fixation. However, degradation of bone cement has been cited as a contributing factor in many failed protheses. Furthermore, the porous structure causes the great metal ion release due to the increased surface area.

서울대학교 의과대학 의공학연구소
*미국 펜실바니아대학 의공학과
Instifute of Biomedical Eng., Seoul Natl. Univ.
*Dept. of Bioengineering University of Pennsyvania, Philadelphia, PA 19104, USA

Because of the limited mechanical properties of the ceramics, various CPC coating techniques such as plasma spraying, electrophoretic deposition, sputter coating, ion implantation and dip coating have been developed. Quicker bony igrowth, allowing an earlier return to normal patient activity, can be achieved by the CPC layers within the porous metallic implants. Specifically focusing on CPC layers on the porous implants, it has been shown that the interfacial decohesion shear strength for CPC coated porous Ti alloy is enhanced in the immediate period after implantation.[2~4] Parametric variations of the physical and chemical characteristics of the CPC were analyzed, and it was shown that among several CPC coating types there was a statistically significant enhancement of the tissue-implants bonding.[5~7]

Efforts to elucidate the origin of the CPC osteoconductivity have focused on the direct imaging of the CPC surface and surrounding tissues by transmission electron microscopy.[3,8] These observations, however, do not necessarily lead to a description of the atomic and molecular events causing the osteoconductive behavior. As a result, there is still no definitive explanation of the physical, chemical and/or cellular mechanisms leading either to direct bone tissue attachment or enhanced bone formation. It is hypothesized that the beneficial effect of the CPC layers is due to : 1) the surface phenomena of dissolution and precipitation of the bone mineral phase constituent ions from the coating or to CPC induced effects on cellular activity, 2) the electrokinetic properties at the CPC-bone fluid interface, and 3) the shielding or the reduction of the calcification inhibitory metal ion release from the substrate.

A wide variety of CPC differing in structure and composition have been recognized. Hydroxyapatite and tricalciumphosphate have been extensively studied. The coating procedure can alter the surface chemistry of the CPC layers as well as that of the substrate. A vacuum sintering leads to several phase transformations. Hydroxyapatite is transformed to a tetracalciumphosphate because underlying titanium affects the CPC composition.[9] The phase transformation provoke a considerable increase of the in-vitro dissolution of calcium and phosphate. The least dissolution is found with the very stable pure hydroxyapatite. These structual and compositional differences are directly related to the interaction mechanisms at the CPC-damaged bone interface.[7]

Therefore, careful characterization of these materials is essential to understanding of the interaction mechanisms at the interface. This presentation focuses on material induced influences on dissolution of bone mineral phase constituent ions, metal ion release, the zeta potential of calcium phosphate ceramics, the composition of the CPC-metal interface and bone growth enhancement. This study provides fundermental new data to prove or reject the mechanism of minimization of prothesis derived calcification inhibitors and examines the origin of bone growth enhancement. Eventually, the basis for optimizing bioactive ceramic coatings will be provided.

2. Immersion induced changes and metal ion release

The surface and the interface of CPC coating, electrophoretically deposited with Ca-deficient HA and vacuum sintered(925℃, 2 hours, 10^{-6}-10^{-7} torr), on titanium and its alloy were determined by scanning Auger electron spectroscopy(SAES), prior to and post immersion in Hank's balanced salt solution(HBSS) with 1.5mM DS-EDTA. Titanium, aluminum and vanadium release rate were determined by electrothermal atomic absorption spectrometry in the solution for the specimen types : CPC

coated Ti orderly oriented wire mesh(OOWM) on Ti-6Al-4V substrate, noncoated OOWM and control sample.

In the CPC coating-metal interfaces, the phosphorous was diffused beyond the titanium oxide layer, leading to compositional change in the CPC layer near the CPC coating-metal interface. The phosphorous concentration in the interface followed a Gaussian distibution for both unalloyed and alloyed titanium. Upon immersion, the thick and uniform titanium-phosphide layers were observed on the interfaces of the both metal substrates(Fig. 1). Whereas the reference solutions show a Ti release increasing as a function of immersion time, the solutions that had the CPC coated specimens contain no measurable amount titanium. In contrast, the aluminum in solution from the CPC coated specimens was significantly larger than the concentration around non-coated specimens(Fig. 2).

Electrophoretic deposition followed by sintering has been choosen by virtue of the uniform coating into porous implants and of enhanced adherence in the CPC-metal interface. It is suggested that the uniform and stable Ti-P compound on the CPC-Ti interface may conduct an important enhancement of biological fixation in virtue of this bioactive ionic interaction between this implant and hard tissue. It was shown that, for the non coated porous Ti, the cathodic layer obtained by the passivation could not block the titanium dissolution in the physiological environment. However the thick Ti-phosphide interface incorporated beyond the oxide layer has a strong reduction effect on titanium ion release.[10]

Furthermore, upon immersion phosphorous having great affinity with Ti might be stuffed continuously by substantial or intersticial diffusion to the equilibrium defects. New calcium phosphate layer can be precipitated from body fluids on the CPC coating and that it elicits cellular formation

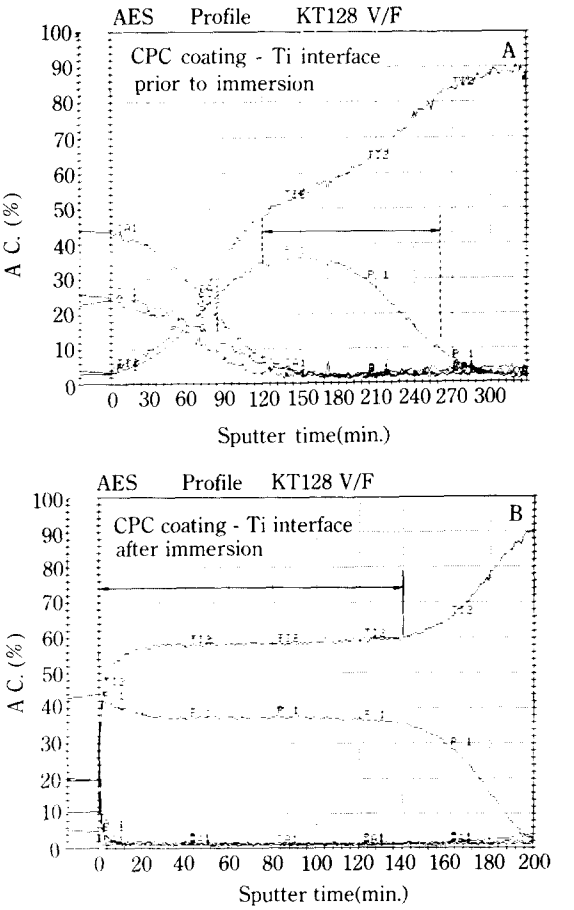

Fig. 1 SAES depth profiles on :
A) the sintered CPC-Ti interface
B) the interface after 4 weeks immersion in HBSS with 1.5mM EDTA

and mineralization of osteoid at the implant.[11]

3. Bioactivity and electrokinetic behavior of CPC

It has been suggested that surface structure and composition of these ceramics influence their cito-compatibility and affect the sequence of steps leading to bone bonding.[12~14] The variation of the structure and composition of the implant surface in contact with the surrounding fluids gives rise to

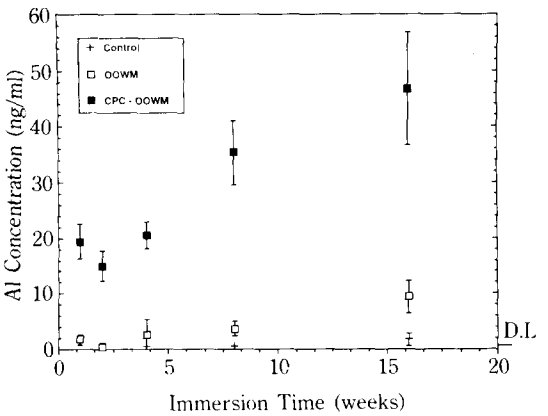

Fig. 2 Concentration of aluminum in solution(HBSS with 1.5mM EDTA) at various periods of immersion for the control, the reference(OOWM) and CPC coated specimen(OOWM-CPC)

electrical charge distributions and a unique property characterizing these variations, i.e. the zeta potential. Thus we arrive at the hypothesis that the zeta potential of the CPC, which is the value of the electrical potential of the double layer at the slip plane between the CPC and surrounding fluids, affects bone formation and attachment. It is implied that the change of the zeta potential as a function of time reflects the gradual change of the CPC surface during ion exchange with the solution, dissolution into solution, or precipitation from solution. This would allow the incorporation of the CPC into developing bone tissue. It is also possible that, in analogy to the effect of surface charge in bone,[15,16] fluid flow along the charged surfaces produces an electrokinetic potential resulting in bone growth.

First step was the determination of the zeta potential of stoichiometric and calcium-deficient hydroxyapatite(HA) during immersion in various aqueous solutions with a constant isoelectric point. We achieve this by the addition of HNO_3-KOH, since KNO_3 does not affect the isoelectric point.[17] We measured in several solutions with varying initial pH values to determine the role of proton and hydroxide ions on the zeta potential, and we followed the time dependent variation of the zeta potential.

The major change of the zeta potential which occured in this experiment and the considerable time it takes to reach steady state are significant observations possibly related to the mechanisms of bioactivity of these materials. Clearly the surface of both HA materials undergoes changes. Whether this is due to ion exchange with, dissolution with or precipitation from solution has not been established. It is known, though, that the main potential determining ions for this ceramic are H, OH, P, Ca and the ions formed by their reaction.[18] Thus, negatively charged ions such as OH and $HxPO_4$ determine the net negative charge in the beginning of the immersion of Ca-deficient HA, when most zeta potential values are negative. As shown as an example in Fig. 3, the net change of the point of zero zeta potential(or point of zero charge, PZC) was observed in Ca-dificient HA with time. The PZC of Ca-deficient HA was initially(after about 3 minutes after adding the powder) around 6 of pH (m) and continously shifted towards a higher pH value until steady state. A value of around pH7 of PZC was obtained after immersion for 1 week, and after steady state no PZC was observed throughout the pH range of our study. On the other hand, for the pure HA, there was no systematic changes in the PZC.

It was suggested that the continuous zeta potential changes could be due to simply to pH changes or dissolution. However, the gradual pH changes without zeta potential changes obtained on pure HA and zeta potential increase without considerable change of Ca and phosphorous dissolution do not support such an argument. This results show that instability or reactivity of these materials are related to not only dissolution rate or strongly re-

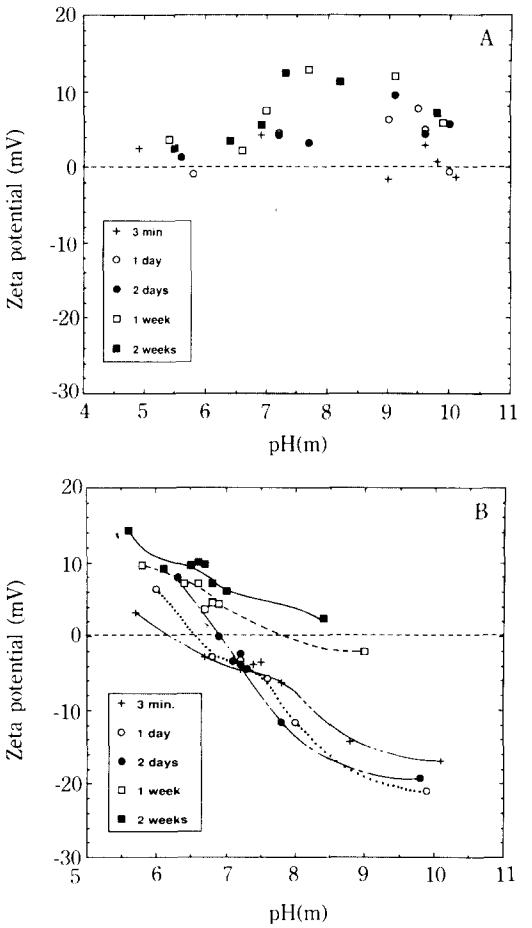

Fig. 3 Variation of zeta potential of pure HA(A) and Cadeficient HA(B) as a function of pH(m), the net shift towards higher pH value of the point of zero zeta potential(PZC) is shown in Ca-deficient HA with immersion time

lated to the pH chanegs but also the different surface charge of the solid or the potential changes in double layer by an adsorption of specific ions.

If the observations could be confirmed in physiological solutions, the different behavior of the two HA's support the hypotheses in a dual way. First, the absolute values of the zeta potential of the more unstable HA are significantly greater than for the stoichiometric HA. Such values are related to electrokinetic potentials with a possively greater effect on the cellular activities of bone tissue formation. Futhermore, the considerable change of the zeta potential of the same Ca-deficient HA, evidences gradual changes of the surface composition. The magnitude and duration of these changes may be related to a net precipitation of new crystalline material thereby bridging the ceramic surface with the surrounding developing tissue.

4. Discussion

The electrophoretic deposition and sintering technique used to coat CPC on porous titanium has the potential of changing the titanium surface by interdiffusion of Ti, Ca, P and O. The interdifusion of Ti and P changes the metal composition, and therefore it may alter the passive dissolution mechanisms and kinetics of the substrate. To date, in spite of the wide use of Ti and Ti alloys, the effect on bony ingrowth or on Ti-tissue interaction are in conflicting. Anyway it has been reported that Ti is not inert in aggressive physiological medium, and releases corrosion products into the surrounding tissues and fluids.[19] It was hypothesized that the phenomenon of metal ion release and oxygen counter diffusion are related to electrochemical mechanisms of interaction.[20] In addition, an inhibitory effect of titanium or vanadium on HA formation was documented by direct precipitation and the growth of HA seed crystal tests.[21] The possible adverse effect of aluminum is well reported.[22] Considering that the calcium phosphate coating produced an important increase of biological fixation, yet a greater aluminum was released from the CPC coated Ti alloy implant. More systematic research is required to determine the origin of the higher Al release and to understand the effect of metal ions on calcification mechanisms.

The coating procedure influences the structure and composition of the coating and CPC-metal interface, and these changes affected the bone-impant bonding strength or tissue reaction. A required composition and structure of the coating could be controlled by the sintering temperature, sintering time governing the phosphorous diffusion coefficient or the coating thickness. It is proposed that the favorable biologic response of this CPC coating is due to first its instability such as high dissolution rate, high surface charge or high zeta potential, and to the active phosphorous interaction in the interface with great reduction of titanium ion release by the stable Ti-phosphide layer. The bone growth enhancement may be due to a combination of any of the above factors. Thus, the higher instability of the Ca-deficient HA would lead to a higher rate of osteoconduction since bioactive processes are nonequilibrium process,[22,25] and during equilibrium the mineral does not have a constant surface property. This suggestion parallels the results of an implantation study that showed a rate of bony ingrowth enhancement increasing with ceramic instability.[7]

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