

Material Fundamentals and Clinical Performance of Plasma-Sprayed Hydroxyapatite Coatings: A Review

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Abstract: The clinical use of plasma-sprayed hydroxyapatite (HA) coatings on metal implants has aroused as many controversies as interests over the last decade. Although faster and stronger fixation and more bone growth have been revealed, the performance of HA-coated implants has been doubted. This article will initially address the fundamentals of the material selection, design, and processing of the HA coating and show how the coating microstructure and properties can be a good predictor of the expected behavior in the body. Further discussion will clarify the major concerns with the clinical use of HA coatings and introduce a comprehensive review concerning the outcomes experienced with respect to clinical practice over the past 5 years. A reflection on the results indicates that HA coatings can promote earlier and stronger fixation but exhibit a durability that can be related to the coating quality. Specific relationships between coating quality and clinical performance are being established as characterization methods disclose more information about the coating. © 2001 John Wiley & Sons, Inc. *J Biomed Mater Res (Appl Biomater)* 58: 570–592, 2001

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INTRODUCTION

Plasma-sprayed hydroxyapatite (HA) coatings have been used as surface coatings on metallic implants in dentistry and orthopedics since the mid 1980s.^{1,2} The advantages that are sought in this application include (i) more rapid fixation and stronger bonding between the host bone and the implant, and (ii) increased uniform bone ingrowth and/or ongrowth at the bone-implant interface.^{3–5} Although little clinical advantage was found in some trials with HA-coated implants,^{6–8} most clinical experience with either weight-bearing or non-weight-bearing models have shown promising results shortly after the implantation and continued fixation for up to 10 years.^{9–13} What is more inspiring is that an HA coating can enhance bone growth across a gap of 1 mm between the bone and the implant in both stable and unstable mechanical conditions, and it is capable of limiting the formation of any fibrous membrane and converting a motion-induced fibrous mem-

brane into a bony anchorage.^{14–16} HA coatings have also suggested to have good sealing effects against the migration of polyethylene particles along the bone-implant interface, which may reduce the incidence of osteolysis and the subsequent implant failure.^{17,1a}

However, there are still many concerns about the use of HA coatings, especially with regard to long-term stability. One important concern is the resorption and degradability of HA coatings in a biological environment, which could lead to disintegration of the coating, resulting in the loss of both the coating-substrate bond strength and the implant fixation. There is also the threat of coating delamination and disintegration with the formation of particulate debris.^{19,20} Another concern is that HA may lead to increased polyethylene wear or third-body wear, and thus result in an increased incidence of osteolysis.^{21–23} Also, hydroxyapatite coatings have been said to occlude the porous implant surface, and this may compromise any advantage in the long term.

The most important concern, however, is the quality of the HA coating, which has been found to affect the major factors for both implant fixation and its long-term stability, such as the coating resorption, bone ingrowth, and mechanical fixation.²⁴ The factors that influence the performance of the HA coating include its compositional, physical, and mechanical

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issues." The implant can be controlled by choosing suitable metals and surface texture, and all other factors can be optimally controlled by varying the processing condition.

This review will relate these material fundamentals of the HA coating with the clinical outcomes of HA-coated implants, with the aim to investigate the optimal HA coating for clinical use and deal with some clinical concerns from material aspects. Most of the clinical performances of HA-coated implants cited in this review have been based on the clinical and radiographic outcome with hip implants obtained within the past five years (1996–2000).

MATERIAL FUNDAMENTALS OF HA COATINGS

Bone consists of three major components: collagen, which is flexible and very tough; bone mineral, which is the reinforcing phase of the composites; and bone matrix or ground substance, which performs various cellular support functions. The mineral phase, which is around 60–70 wt% of the bone,^{26,27} can be described as a calcium phosphate with an apatitic structure and a composition close to hydroxyapatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$, HA, Ca/P = 1.671. About 2 kg of HA is present in an average-sized person and the stoichiometry of the HA varies with its location in the human body. Biological apatites are known to be calcium-deficient ($\text{Ca}_{(10-x)}(\text{HPO}_4)_x(\text{OH})_{2-x}$) with a Ca/P ratio as low as 1.5. Bone apatites contain carbonate, whereas dental enamel contains substantial amounts of fluoride.²⁸ Hydroxyapatite is biocompatible and bioactive in the human body. It is compatible with various tissue types and can adhere directly to osseous, soft, and muscular tissue without an intermediate layer of modified tissue.^{29–32} It also displays an osteoconductivity: a property of a material to encourage bone already being formed, to lie closely to, or adhere to, its surface.³² This is especially useful for an implant where fast healing is required. Despite its excellent properties as a biomaterial, the inherent mechanical properties of HA—specifically, brittleness, poor tensile strength, and poor impact resistance—have restricted its application in many load-bearing situations." Therefore, the concept of applying HA onto metallic implants as a surface coating was developed, and the HA-coated implant combined the good strength and ductility of the metal with the excellent biocompatibility and bioactivity of the HA.^{34,35}

Hydroxyapatite coatings were first introduced in the mid-1980s for improved fixation between bone and the implant.^{36,37} Various methods have been used to deposit HA coatings, such as dip coating–sintering,^{38,39} immersion coating,^{40,41} electrophoretic deposition,^{41,42} hot isostatic pressing (HIP),⁴³ solution deposition,⁴³ ion-beam sputter coating⁴⁴ and dynamic mixing,⁴⁵ thermal spraying techniques such as plasma spraying,^{35,46,47} flame spraying,⁴⁸ and high-velocity oxy-fuel (HVOF) combustion spraying.⁴⁹ Detailed descriptions of these methods have been given by Lacefield³⁸ and Berndt, Haddad, Farmer, and Gross.³⁵ A comparison of these methods has been described by Jaffe and Scott,⁴³ and is summarized in Table I. So far, thermal spraying, especially

the conventional atmospherical plasma-spray method, appears to be the most favorable and, thus, most commonly used for clinical application. This review will concentrate on plasma-sprayed HA coatings; hereafter, the term HA coating refers to a plasma-sprayed HA coating unless specifically stated.

Plasma-sprayed hydroxyapatite coatings are able to bond directly to bone,³ promote earlier and greater fixation,^{50,51} enhance bone ingrowth,⁵² and protect the surrounding bone against metal-ion release from the metallic implant.⁵³ However, plasma spraying involves the acceleration of the feedstock HA powders to a high velocity and temperature (as high as 30,000 K) and a subsequent rapid cooling when the HA adheres to the metallic substrate. The composition and the structure of the HA is significantly modified from the feedstock powders. Therefore, from a materials-science perspective, the physiological response of the coating need not necessarily reflect the exact characteristics of the feedstock. When different spray parameters are employed, such as gas combination and flow rate, spray power, and stand-off distance, this modification will be different, as shown in Figure 1. Even before it is sprayed, the HA powder can be varied in terms of particle morphology, size distribution, microstructure, density, and hydroxyl content, given that fully crystalline HA powders are used. The metallic implant type and surface texture is another variable that influences the formation and performance of the HA coating. Therefore, the overall quality of the HA coating is a combined outcome of feedstock powders, implant metals, and spray parameters.

Critical quality specifications for HA coatings include purity (phase composition), crystallinity, Ca/P ratio, microstructure, porosity, surface roughness, thickness, and implant type and surface texture, which also lead to different mechanical properties, such as cohesive and bond strength, tensile strength, shear strength, Young's modulus, residual stress, and fatigue life.¹⁸ All these variables can lead to different bioactivity and durability of the coating. The different coating designs and especially process methods to achieve these characteristics remain as company intellectual property. It has been suggested that an ideal HA coating for orthopedic implants would be one with low porosity, strong cohesive strength, good adhesion to the substrate, a high degree of crystallinity, and high chemical and phase stability.³⁴ Other documents,^{54,55} however, indicate that an amorphous coating may be more beneficial for early bone ingrowth than a coating with high crystallinity. As well, some properties need to be reconciled with each other because of the nature of the manufacturing process.

Purity and Crystallinity

The typical feedstock for HA coatings is a fully crystalline pure HA powder. It is commonly manufactured by chemical precipitation from a mixture of a calcium-ion-containing so-

"Refers to the sprayable material in the thermal spray industry and includes powders, wires, or liquids.

TABLE I. Comparison of Different Methods for Depositing HA Coatings

Method	Characteristics	Comments/References
Dip coating/sintering	The high-temperature sintering (>1000°) can degrade mechanical properties of metal implants and lead to low bond strength and impurity of HA.	Not applicable to orthopedic implants References 38-42
Electrophoretic deposition	Same problems as dip coatings/sintering, also leads to nonuniform thickness of HA.	
Immersion coating	The high-temperature-process (>1500°) results in a coating of non-HA compound mixture and very poor adherence.	
Hot isostatic pressing	The encapsulating materials react to the HA coating. Difficult to seal borders on implants with complex shapes.	
Solution deposition	A low-temperature precipitation process resulting in a pure, highly crystalline, firmly adherent HA coating. Good for coating evenly for porous and beaded surfaces. Maximum thickness of 20 μm limits its use as a primary mode of fixation.	Marketed in Europe, but not approved in US Reference 43
Sputter coating	Too slow and has a low deposition rate. Ca/P ratio of the coating is higher than that of synthetic HA if RF magnetron sputtering is used.	References 44 and 45
Thermal spraying	High deposition rate. Good chemical and microstructure control, biocorrosion resistance, and substrate fatigue resistance of the coating. Can obtain various coating thickness and be used for complex shapes.	References 35, 46 and 47

lution and a phosphate-containing solution followed by calcination.⁵⁶⁻⁵⁸ After plasma spraying has occurred, both the purity² and the crystallinity³ of the HA decrease because of the decomposition of HA at high temperature and the rapid cooling rate. The new phases that most commonly appear in the HA coating include an amorphous phase, tricalcium phosphate [$\text{Ca}_3(\text{PO}_4)_2$]; i.e., α -TCP and/or β -TCP], tetracalcium phosphate ($\text{Ca}_4\text{P}_2\text{O}_9$); i.e., TTCP and calcium oxide (CaO).^{34,59,60} A solid solution of oxyapatite [$\text{Ca}_{10}(\text{PO}_4)_6\text{O}$, i.e., OAp] in HA, that is, oxyhydroxyapatite [$\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_{-2x}(\text{O})_x(\square)_x$, OHA, where \square represents a vacancy] could also form in the HA coating because of the dehydroxylation of the HA.^{61,62} Hydroxyapatite is very stable in the body fluid, but the dissolution rates of other phases formed during spraying are much higher than HA, which is in the order of $\text{ACP} \gg \text{TTCP} > \alpha\text{-TCP} > \text{OHA} > \beta > \text{-TCP} \gg \text{HA}$.^{61,63} Calcium oxide has no biocompatibility and dissolves significantly faster than TCP,⁶⁴ thus it is a detrimental phase that should be avoided. Table II lists these calcium-phosphate phases, their crystal structure information,^{62,65-68} and their solubility product.⁶⁹ The dissolution of a material is dictated by its free energy and can be evaluated by its solubility product; a lower free energy corresponds to a lower solubility product.

The phase composition of HA coatings depends on the selection of production parameters and is a deciding factor for the dissolution of HA coatings in the physiological environment. The faster dissolution produces a supersaturated environment, which allows physiologically produced HA to precipitate on the coating and enhance the bone ingrowth, but it also leads to the resorption or degradation of the coating.⁶⁹⁻⁷² Therefore, to obtain HA coatings with predictable properties, both the purity and the crystallinity of the HA should be effectively designed. To achieve this, both the spray parameters and the quality of the original feedstock HA powders should be strictly controlled.

Currently, there is a general agreement that the chemical purity of HA should be as high as possible ($\geq 90\%$) with a Ca/P ratio of 1.67.⁷³ This is followed by most manufacturers to ensure predictable implant performance. However, there is no agreement on the crystallinity, which can be varied from 50% to 90% (usually around 70%). The crystalline HA phase may include both the unmolten core of a particle and the new, recrystallized HA phase. The measurement of the crystallinity has been mainly performed with x-ray diffraction and supplemented with infrared spectroscopy, where both the lower crystal perfection caused by cooling from high temperatures and an amorphous phase are considered. Some standard have been suggested for this measurement, but none have been generally approved. It has been found that the amorphous phase has a higher tendency to form at the coat-

² Refers to the percentage of HA in terms of phase composition.

³ Generally refers to the percentage of crystalline HA with regard to a total of crystalline HA and amorphous phase.

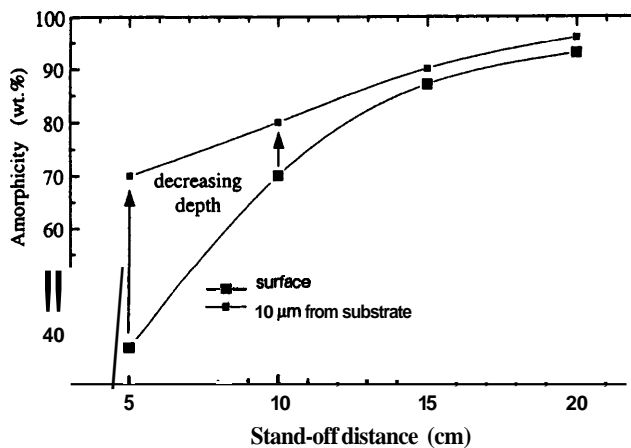
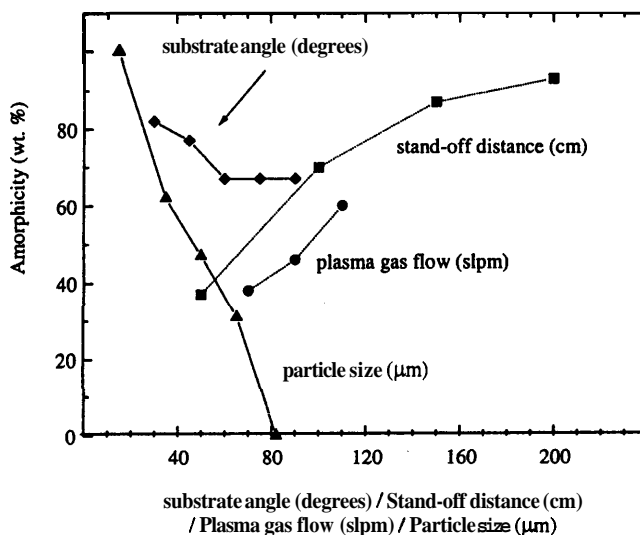


Figure 1. Phase formation and distribution in plasma-sprayed HA coatings.⁷⁴

ing-metal interface than in the coating, as shown in Figure 1, but little information is available on the size of the crystalline areas and their distribution throughout the coating.

Bone growth occurs at a faster rate when the coating has a higher content of amorphous phase because of more rapid initial dissolution. Bone grows toward the implant, and collagen incorporates the HA crystals in the body to produce a strong interface. Faster fixation is especially favorable in hip-implant recipients where the hip is partially weight bearing within approximately a week from the operation. However, the fast resorption of the HA coating may lead to the loss of the fixation and coating bonding (i.e., implant loosening) as well as the production of particle debris in the long term. The trend, therefore, to produce crystalline coatings was supported because of the above concern. It was found that the early biological fixation could also be achieved with a high-crystalline, high-purity HA coating, which is probably because of the existence of residual stress, pores, and the small crystal size of the thermal spray coating. Nonetheless, HA coatings with high crystallinity usually contain more unmelted or partially melted particles, which could also lead to lower bonding and cohesive strength as well as particle debris. Although the crystallinity could be increased by post-heat treatment, such a process is generally accompanied by cracking, and thus is not advised.

Microstructure, Porosity, and Roughness

Microstructure and porosity is another important coating characteristic that influences its performance. The porosity of a commercially available HA coating may vary from 1% to 10%,^{6,13,142,182} and sometimes up to 50%;¹³⁶ but generally, little information is provided by the manufacturer regarding the microstructure. When different feedstock powders and spray parameters are employed, the original particles can become well-flattened splats, accumulated splats, spheroidized particles, partially melted particles, or remain unmelted, as shown in Figure 2. These microstructural features lead to different forms of porosity in the coating. In extreme situations, for example, in cases of fine feedstock powders and very high spray power level, microcracks are more likely to appear in the splats. The nature of the porosity is very

TABLE II. Calcium Phosphate Phases in HA Coatings

Phase	Chemical Formula	Abbreviation	Solubility Constant Ks at 25°C ⁶⁹	Crystal Structure/References	JCPDS No.
Hydroxyapatite	Ca ₁₀ (PO ₄) ₆ (OH) ₂	HA	6.62 × 10 ⁻¹²⁶	Hexagonal P6 ₃ /65	9-432
Amorphous phase	N/A	ACP	N/A	Irregular	N/A
Alpha tricalcium phosphate	α-Ca ₃ (PO ₄) ₂	α-TCP	8.46 × 10 ⁻³²	Monoclinic P2 ₁ /a/66	9-348
Beta tricalcium phosphate	β-Ca ₃ (PO ₄) ₂	β-TCP	2.07 × 10 ⁻³³	Rhombohedral R3c/67	9-169
Tetracalcium phosphate	Ca ₄ P ₂ O ₉	TTCP	N/A	Monoclinic P2 ₁ /68	25-1137
Oxyhydroxyapatite	Ca ₁₀ (PO ₄) ₆ (OH) _{2-2x} (O) _x (□) _x	OHA	~10 ⁻⁶⁹ (oxyapatite)	Hexagonal/62 P6 ₃ /62	9-432

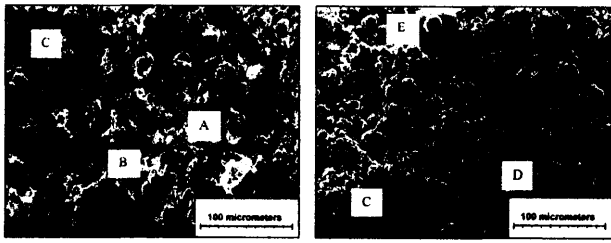


Figure 2. Surface morphology of plasma-sprayed HA coatings. (a) partially melted large particle, (b) partially melted fine particle, (c) flattened splat, (d) accumulated splats, (e) spheroidized particle.

important, because this controls the specific area in contact with the physiological medium and, therefore, influences physiochemical interactions at the implant–host interface.³⁴

Hydroxyapatite coatings may fail by delamination^{75–77} or release of coating segments.⁷⁸ The possibility is increased for coatings of high crystallinity, because, as has been stated before, there are more unmelted or partially melted particles and higher porosity in such coatings, which leads to poor cohesive and bonding strength. If the coating segments or particle debris remain in the vicinity of the implant and are too large, the body is not able to dissolve them by phagocytosis^{19,79} and lowers the local physiological pH in an attempt to dissolve the particle. This lower pH could lead to coating destruction and could modify the bone-formation process around the implant. If coating segments are removed from the coating and are mobile, they may then be transported to another site, such as the bearing surface of the hip joint and, thereafter, produce third body wear and increase the incidence of osteolysis.

Surface roughness of the HA coating also affects its dissolution and the bone apposition on the coating or bone ingrowth, because the coating surface, once implanted, is directly in contact with the bone and body fluid. High surface roughness will increase the coating and body-fluid interface, and thus increase the dissolution rate and apatite precipitation. Roughness can also be controlled by using different feedstock powders and spray parameters.^{34,80}

Thickness

The thickness of the HA coating affects both its resorption and mechanical properties. Thicker coatings usually exhibit poorer mechanical properties. De Groot and co-workers^{81,82} determined that an optimum thickness of 50 μm would avoid fatigue failure, which commonly occurred in coatings thicker than 100 μm , but still provide reasonable coating bioresorption and consistent bone growth.

Wang, Lee, Chang, and Yang have evaluated the effects of the coating thickness on the shear strength at the bone–implant interface and failure mode of HA coatings using both a transcortical implant model⁸³ and an intramedullary implant model.⁸⁴ It was found that in both cases, a 50 μm coating exhibits significantly higher shear strength than a 200 μm coating. In addition, although it has similar histological be-

havior, the 50 μm coating only fractured at the implant–bone interface, whereas the 200 μm coating also fractured within the coating in a cohesive manner or at the coating–implant interface in an adhesive mode. These different failure locations indicated that the residual stress in the thick coating is possibly responsible for a decrease in the mechanical properties of the coating.

A thickness of 50–75 μm has been followed by most manufacturers for commercially used orthopedic implants. The value, however, is completely dependent upon the location of implantation, cellular environment, cleanliness of implant, and coating characteristics; for example, the thickness of the HA coating for dental implants can be several hundred micrometers.

Mechanical Properties

Mechanical properties are important for the long-term performance of the HA-coated implants and is related to the characteristics of the HA coating that have been discussed above. A comparison of the tensile strength and Young's modulus of the main current implant materials with those of bone is shown in Table III.^{85,86} According to the proposed standards, the shear strength should be 22–29 MPa, and the minimum tensile strength should be 51 MPa for the HA coating.^{87,88} No criterion has been suggested on the Young's modulus. The HA coating was found to commonly fail at the coating and substrate interface rather than within the coating during the tensile adhesion testing (TAT), which is the standard adhesion testing technique for thermal spray coatings.^{**} Other researchers^{90,91} also showed that failure mainly occurs at this interface in their *in vivo* studies, and the failure probability at this interface increased with the period of implantation, because the strength of the coating–bone interface tends to increase with time during the initial postoperative recovery. The bond strength of the HA coating is, in addition to the coating characteristics, also related to the thickness of the coating as well as the type and design of the implant, as will be discussed below.

The understanding of other important mechanical properties, such as Young's modulus, thermal stress, fracture tough-

TABLE III. Comparison of Mechanical Properties between Implant Materials and Bone^{85,86}

Material	Young's Modulus (GPa)	Tensile Strength (MPa)
Alumina	365	6–55
Sintered HA	70–90	50–110
HA coating	0.5–5.3 ³⁴	>51 ^{87,88}
316L stainless steel	193	540
Co-Cr alloys	230	900–1540
Ti-6Al-4V, wt %	106	900
PMMA bone cement	3.5	70
HDPE	1	30
Cortical bone	7–30	50–150
Cancellous bone	0.1–1	1.5–3

ness, and fatigue life, is still incomplete. An appropriate Young's modulus for the implant is crucial in order to avoid stress shielding and bone resorption, and it also determines the fatigue behavior of the coating under cyclic loading. It is well known that the Young's modulus of a plasma-sprayed coating is usually much lower than its bulk counterpart. Eberhardt, Zhou, and Rigney⁹² indicated that only a Young's modulus with a value of -5.5 GPa would enable a reasonable prediction of the residual stresses for HA coatings. Tsui, Doyle, and Clyne³⁴ agreed with this prediction and obtained some values of ~ 0.5 – 5.3 GPa using a cantilever-beam test. Using this Young's modulus, together with an *in situ* curvature monitoring technique and a numerical model, they also predicted that residual stresses in the air-plasma-sprayed HA coatings on a Ti-6Al-4V substrate are also relatively low (-20 – 40 MPa) and should always be tensile unless the substrate is held below room temperature during spraying. Brown, Turner, and Reiter,⁹³ however, reported a much higher residual stress level of greater than 200 MPa for air-plasma-sprayed HA.

Sergo, Sbaizero, and Clarke⁹⁴ determined with Raman piezospectroscopy that the residual stresses of HA coatings were tensile (-100 MPa) when deposited in air and compressive (-60 MPa) when deposited in a vacuum. They concluded that the existence of residual stress in HA coatings can alter the concentration of supernatant species in solution, tensile stresses enhancing dissolution, and compressive stresses impeding dissolution. The great variability among the residual stresses obtained by different authors probably arises from different coating characteristics as well as different measurement techniques.

The interfacial fracture toughness of the HA/Ti-6Al-4V system obtained from two types of Mode I tests has been reported. Filliaggi, Coombs, and Pilar⁹⁵ used a short bar chevron notch test and obtained values of K_{Ic} equal to 0.60 – 1.41 MPa/m^{1/2}. Gross⁹⁶ and Tsui et al.³⁴ obtained some similar values of K_{Ic} of -0.28 – 1.1 MPa/m^{1/2} using a single-edge, notch-bend test. However, the interfacial fracture toughness of the system under mixed-mode conditions still needs to be investigated, because this is most relevant to its in-service condition.

Metallic Implants

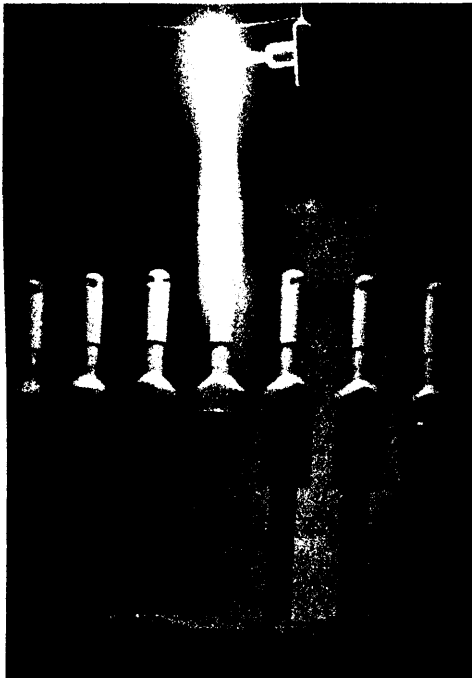
The metallic materials commonly used as implants are cobalt–chromium (Co-Cr) alloy and titanium (Ti) and its alloy, Ti-6Al-4V, as these provide good corrosion resistance and reasonable fatigue life. These alloys are much stiffer than cortical bone, as shown in Table III, whereas the titanium alloys result in less potential proximal stress shielding and bone resorption because of the lower Young's modulus.^{97,98} Titanium alloy also demonstrated a 33% percent increase in bonding strength to the HA coating *in vitro* compared to Co-Cr alloy. It was suggested that this increase arose because of the formation of a chemical bond between Ti and HA in addition to the expected mechanical locking.^{3,99–101} This interfacial diffusion or reaction, however, was not observed

in all work,¹⁰² which is probably because of the different plasma spray parameters, used such as the nature of the secondary gas employed.

The coefficient of thermal expansion is another important factor to consider, and again, there is more of an agreement between titanium (9 – 10×10^{-6} /°C) and HA (12×10^{-6} /°C) as opposed to Co-Cr alloy (16×10^{-6} /°C) and HA. A smaller difference in thermal expansion is important to minimize the residual stresses within the coating. The added advantage of a Ti alloy is the low density and good bone bonding capacity.'''

Before plasma spraying takes place, the surface of the metallic implant can be textured into microstructured, macrostructured, or porous morphologies.⁴³ The microstructuring can be grit blasting or beading. Grit blasting is a surface-preparation method used prior to the application of plasma-sprayed coatings; it alters the smoothness of the metal surface to produce a roughness of around several micrometers ($R_a \approx 3$ – 6 μ m). This method has proved successful for implant fixation and is currently the major method for implants in clinical use. Macrostructuring can be in the form of grooves, threads, meshes, or a deposited metal coating. Improved fixation has been demonstrated with grooved-surface implants *in vivo* both in the initial period and 1 year after implantation.¹⁰⁴ The purpose of macrostructuring is to increase the shear strength between the substrate and the coating, and this could result in improved long-term fixation between the implant and the bone if biodegradation of the coating occurs.^{105–107}

The use of porous coatings is another method for implant surface treatment, and such structures have been shown to be of more benefit than a grit-blasted surface.¹⁰⁸ The porous coating itself can promote biological fixation between the implant and the bone, but many clinical retrieval studies of porous implants have revealed fibrous fixation rather than bone ingrowth.^{109,110} Some strict operative techniques (such as the use of autogeneous-graft bone chips at the time of operation) and implant design could promote consistent bone growth into a porous-coated implant. However, a layer of fibrous tissue still could be seen in the regions where the gaps were not filled with autogeneous-graft bone chips. Also, the amount of bone that can grow into the porous coating is determined by and can be no more than the amount of host bone, which may not be sufficient for bone-implant fixation at some anatomical sites.¹¹ The fibrous membrane is a sign of incomplete osseointegration of the implant; but with HA this condition could be changed. Although grit blasting and the HA coating could occlude some pores and decrease the surface roughness of the porous coating, the addition of the HA coating improved the osseointegration of the implant. The presence of HA was found to limit the formation of fibrous membranes and induce their conversion to bone, and even to be capable of overcoming a 1-mm gap between the implant and the bone.^{14,15,112,113} This osteoconductive effect is not limited to immobilized implants, but has been reported to be prolonged under loaded conditions, so that the move-



(a) dental implant being sprayed



(b) HA-coated hip implant



(c) knee implant

Figure 3. Typical (a) dental, (b) hip, and (c) knee implants (www.sulzermetco.com and www.osteonics.com).

ment-induced fibrocartilagenous tissue is replaced by bone when it is immobilized.¹⁶

The osteoconductiveness is important when preparing the bone bed for insertion of the implant. An uncoated titanium prosthesis cannot tolerate a gap with the bone and will not undergo successful integration if the gap separation is larger than 0.1 mm. Hydroxyapatite has been employed as a coating because its presence can lead to bone formation and successful fixation at a gap distance of 1 mm.¹¹³ The bone density will initially be lower as a result of more rapid ingrowth in spaces, but is modified by further bone remodeling as a response to the load environment.^{16,104}

CLINICAL PERFORMANCE OF HA COATINGS

The first reported clinical trials of HA coatings were with femoral stems by Furlong and Osborn¹ in 1985 and by Geesink² in 1986. Since then, hydroxyapatite coatings have been extensively used in both dental and orthopedic prostheses, such as hip and knee implants, and in screws and pins used in bone plates for fixing bone fractures; here the coating is in close contact with bone. Most of these clinical practices and studies, however, are still with femoral stems of hip

implants, therefore this is the focus of this review. Hydroxyapatite coatings have been found to promote fast fixation and enhance fixation strength, but the long-term stability of the fixation is still in controversy. Another main controversy in this clinical application is the possibility that HA coatings increase polyethylene wear or third-body wear and osteolysis.

Dental and Orthopedic Implants

Dental implants include subperiosteal, transosteal, and endosseous implants. It is the endosseous form that is most commonly used. Endosseous implants can take the form of plate or root, with the majority of implants in the root form. A root form implant consists of a post, an abutment and a crown. Hydroxyapatite is usually coated to the surface of dental posts [Figure 3(a)]. Tooth implants that fit closely to the bone can enable bone attachment. After careful preparation of the implant site, the post is placed into the maxilla or mandible. The gingiva covers the implant and a 3-month healing phase enables new bone to form close to the immobile implant. The implant site is then opened, and the crown is mounted with an abutment so that the post can be exposed to masticatory forces. For the next 18 months, the newly formed bone

remodels according to the magnitude, direction, and frequency of the applied force.

Orthopedic prostheses include both temporary devices such as bone plates, screws, pins, and **intramedullary** nails, and permanent devices such as hip, knee, elbow, and ankle implants. Hydroxyapatite has been coated to bone screws and pins, and hip and knee implants for faster and stronger fixation. Bone screws and pins, although not the prime application, are important because, unlike the permanent prostheses, they require fast initial fixation and have an implantation time of 3 months.¹⁴ The removal torque of HA-coated screws was significantly greater than uncoated titanium screws,¹¹⁵ and the adhesion between the coating and the screw remained unaffected.

The replacement of a hip or knee is usually conducted because of osteoarthritis, osteoporosis, or some form of injury. Chances of successful fixation are reduced in the former two cases. Orthopedic implants have a more complex geometry than dental implants and have accordingly, more sophisticated tooling to prepare the bone bed. Primary fixation depends on the prosthesis geometry and this is supplemented by a secondary mechanism—tissue bonding to HA. However, there is inevitably a space between the implant and surrounding bone in some locations. This will affect the bone growth and, hence, attachment to the implant. The orthopedic implant can bear partial weight 1 week after surgery; that is, there is no resting stage for the bone regeneration as with dental implants; therefore the requirements for good bonding are more stringent.

A hip prosthesis [so-called total hip arthroplasty (THA), Figure 3(b)] consists of an acetabular cup implanted into the hip and a femoral stem placed into the femur. Acetabular reconstruction is used for relief of pain, the restoration of joint function, the preservation of bone stock, and the maintenance of implant stability. Various designs exist with geometries that maximize the stress transfer from the femoral stem to the surrounding bone. Otherwise, bone will resorb and the implant will become loose, causing aseptic loosening and pain, which are indications for revision surgery. Hydroxyapatite is usually coated to the surface of the femoral stem, and the outer face of the acetabular cup. The application of a HA coating can be over the entire stem (or cup) or proximally, whereas the interface stress transfer is more **uniform** in the latter proximally coated stem. In case of infection a partly coated stem (or cup) is easier to remove than a fully coated stem (or cup). The mechanical and biological environments for hip implants are also more complex compared to dental implants, and vary with the implantation site. For example, the femoral stem placed laterally into the bone is in contact with the cortical bone in the proximal region and the trabecular bone at the distal end of the stem. A coating on a femoral stem and a acetabular cup will experience shear stresses as well as normal direct stresses (tension or compression). The magnitude of each stress component, however, depends on the particular loading characteristics, the shape of the component, the surrounding structures such as trabecular and cortical bone, **the elastic** properties of implant materials,

and the bonding characteristics of the interface, which may be fully coated or proximally coated.^{116,117}

A knee prosthesis [so-called total knee arthroplasty (TKA), Figure 3(c)] consists of a femoral component and a tibial component. Hydroxyapatite coatings have been applied to the tibial component to enhance its fixation because loosening of the tibial component is far more common than loosening of the femoral components in knee prostheses.¹¹⁸ The tibial component is subject to great torque and shear forces, which is different from the load condition on hip prostheses. In a similar fashion to the development of the total knee prostheses, which was started many years later **than** the total hip prostheses, the application of HA coatings for knee implants is relatively **recent**.^{8,119,120} Therefore, the benefits of HA coatings on the fixation of the tibial component are still not well documented in the open literature.

Fixation Mechanisms

A prerequisite for any orthopedic arthroplasty or dental implant is permanent fixation to the surrounding environment with no intervening soft tissue. A successful fixation should be fast and strong initially and exhibit lifelong stability. Fixation takes place by osseointegration, which was first described by Brånemark¹²¹ as the intimate contact between a titanium implant surface and the surrounding bone. The currently accepted definition for osseointegration is "contact established between normal and remodeled bone and an implant surface without the interposition of non-bone or connective tissue, at the light microscopic level."¹²²

Prostheses have been implanted into the human body by either cemented or cementless fixation methods. Although the traditional cemented fixation using polymethylmethacrylate (PMMA) can obtain immediate fixation between the implant and bone, this type of prosthesis is not suitable for young (< 50 years) active patients where more stable fixation and bone growth are needed. Problems of cell necrosis from the exothermic reaction, cement failure, or monomer release and loss of endosteal bone are still a concern with the cement fixation **method**.^{123,124} Thus, cementless fixation, primarily by biological means whereby press-fit insertion is followed by bone growth into a porous surface, has been developed. However, there is little histological evidence of sufficient bone **ingrowth** in retrieved uncemented porous-coated prostheses^{125,126} and it has been shown that bone must be within 50 μm of the porous coating for **ingrowth** to occur.¹²⁷ Meanwhile, fibrous rather than bony **ingrowth** into porous surfaces has been found, and the loss of endosteal bone still exists. Although consistent bone growth into the porous coating has been reported to be possible if strict operative techniques (such as the use of autogenous-graft bone chips at the time of operation) and implant design are used, a layer of fibrous tissue still could be seen in the regions where the gaps were not filled with autogenous-graft bone chips.¹¹¹

Bioactive materials such as HA and bioactive glass can stimulate a direct bond to form between the implant and the surrounding bone and improve osseointegration. This **bone-**

implant bonding is one of the most important factors for implant fixation and function. HA coatings have been shown to achieve a very strong bond with living bone, in a relatively short period, even under loaded conditions and with the presence of a gap.^{14–16}

The process has been suggested to be initiated with the dissolution of the coating soon after the implantation and can be described as follows: (a) partial dissolution of HA coating where calcium and phosphate ions are released from the coating, which will cause a rise of the calcium and phosphate ion concentration in the local environment around the coating; (b) precipitation of crystals on HA coating and ion exchange with surrounding tissues; (c) formation of a carbonated calcium phosphate layer of microcrystals and macrocrystals with the incorporation of a collagenous matrix and bone growth toward the implant; (d) bone remodeling in area of stress transfer: osteoclasts resorb normal bone by actively secreting hydrogen ions into the extracellular space, creating a local pH of approximately 4.8, and leading to fast resorption of both carbonated HA in bone mineral and the HA coating; and (v) the bone-implant interface is subjected to further bone ingrowth and remodeling, and a biological fixation can be achieved through the bidirectional growth of a bonding layer. A diagram that schematically models this process is shown in Figure 4.

Mechanical loading is usually found to accelerate coating resorption, bone remodeling, and growth processes. Faster dissolution/resorption is likely to result in faster and stronger fixation in the initial period of implantation, but could also lead to disintegration of the coating, with rapid loss of the bonding strength and mechanical fixation, delamination, and the production of particles, which has been cited as a potential complication. By contrast, slow controlled resorption may allow the surrounding bone the opportunity to replace resorbed coating and maintain long-term stability. The actual establishment of bonding, however, is complex and involves many factors, including implant-related factors, such as material, shape, topography and surface chemistry, mechanical loading, surgical technique and procedure, and bone bed preparation, and patient variables, such as bone quality and quantity.¹²⁸

Clinical Performance

After more than a decade's clinical practice with HA-coated prostheses, there is general agreement that the originally pursued benefits of HA coatings, that is, earlier fixation and stability with more bone ingrowth or ongrowth, can be achieved. Most components became stabilized within 3 months with bone apposition. It was suggested that migration of the femoral component within the first 2 years is related to the final outcome.^{129,130} A large group of clinical trials with HA coatings have also shown continued fixation for longer periods (2–10 years), but doubts still exist concerning the durability of the fixation. A main concern is the degradability of the HA coating and the disintegrated HA granules, which are claimed to accelerate the polyethylene wear or cause

third-body wear. Any HA degradation will lead to increased osteolysis, and there is the potential that the degradation products will enter the joint space and damage the articulating surfaces.¹³¹

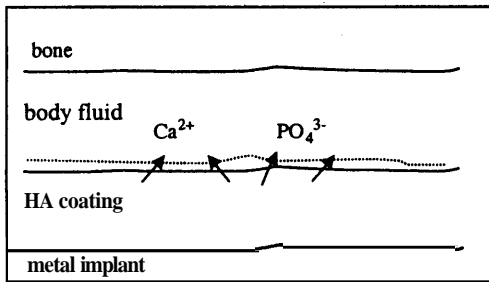
In summary, the following section will review the clinical performance of various HA-coated implants, femoral stems, acetabular cups, knees, pins, and teeth, with respect to their initial fixation and stability and long-term performance. It will then address two major concerns with their clinical use: resorption and wear.

Fixation and Durability

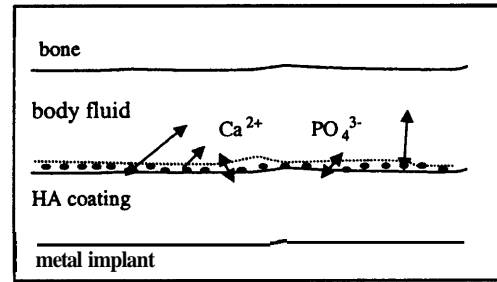
(I) Application in Femoral Stem Most clinical practice with HA coatings has been with total hip arthroplasty, mainly on the femoral component. Fixation of a hip prosthesis can be assessed by two ways: by failure rate^{11,132} or by radiographic features,^{132,133} as shown in Table IV, with the latter used most often. Bone remodeling is generally characterized by calcar resorption, distal cortical hypertrophy, and cancellous condensation. This progressive bone remodeling and new bone formation phenomenon occurred around the implant. It is different from normal bone remodeling, which happens in bones all the time through a balanced two-phase process—resorption and formation, without net loss of bone. Cancellous condensation and cortical hypertrophy occurs around the stem in the femur as a result of the adaptation of bone to the stresses that act upon it. The insertion of an endoprosthesis into a femur changes the stress distribution within the femur, which is a combination of axial, bending, and torsional stresses,^{116,117} and this causes the bone to remodel according to the stress transfer from the stem. Cancellous condensation is defined as new bone formation between the implant and endosteal surface of the femur, as indicated by so-called spot welding.⁷ Many studies have described the radiographic features of bone remodeling and osseointegration around HA-coated femoral stems and/or estimated their failure rate, which showed a promising outcome with the use of HA coatings. Information on the corresponding HA-coating specification is shown in Table V. However, the clinical performance of HA-coated implants can not be easily related to the coating specification since many variables are involved in the whole implant system and during implantation.

D'Lima, Walker, and Colwell¹³⁴ followed up an Omnit-HA titanium alloy stem with a proximal third circumferential HA coating in 60 THAs in 56 patients for 2–5 years. Both the clinical and radiographic outcome were excellent, with absence of nonprogressive subsidence after 1 year and stable bony ingrowth around the proximal third (HA-coated portion) of the stem as well as absence of distal endosteal lysis.

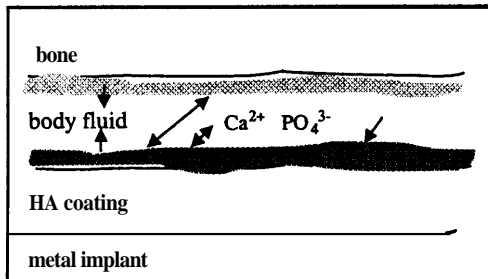
In a multicenter study of 316 hips (282 patients, average age of 50 years) with a proximally HA-coated titanium stem and either a HA- or porous-coated pure titanium cup (all manufactured by Osteonics, Allendale, NJ), Capello, Antonio, Manley, and Feinberg¹³⁵ confirmed that HA-coated hip components do enhance ingrowth or ongrowth with no dete-



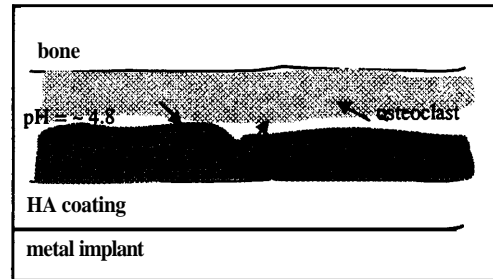
(i) Partial dissolution of HA coating causing an increase of Ca^{2+} and PO_4^{3-} ion concentrations in the local area around the coating



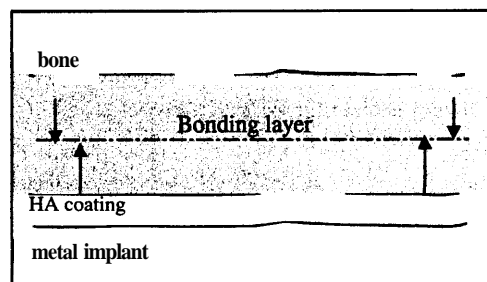
(ii) Precipitation of crystals on HA coating and ion change with surrounding tissues



(iii) Formation of a carbonated calcium phosphate layer with the incorporation of a collagenous matrix and bone growth toward the implant



(vi) Bone remodeling – osteoclasts resorb normal bone, creating a local pH of -4.8 , leading to faster resorption of both carbonated HA in bone and the HA coating



(v) Bidirectional growth and formation of a bonding layer between bone and HA coating through further bone remodeling

Figure 4. Schematic diagram of the establishment of bone-implant bonding. (a) Partial dissolution of HA coating causing an increase of Ca^{2+} and PO_4^{3-} ion concentrations in the local area around the coating. (b) Precipitation of crystals on HA coating and ion change with surrounding tissues. (c) Formation of a carbonated calcium phosphate layer with the incorporation of a collagenous matrix and bone growth toward the implant. (d) Bone remodeling—osteoclasts resorb normal bone, creating a local pH of -4.8 , leading to faster resorption of both carbonated HA in bone and the HA coating. (e) Bidirectional growth and formation of a bonding layer between bone and HA coating through further bone remodeling.

rioration of femoral component fixation for an average of 8.1 years. Radiographic analysis of the HA-coated stems suggests enhanced bone **ongrowth** as shown by progressive modeling (cancellous condensation and cortical hypertrophy) of the femur around the middle and distal portions of the stem.

Røkkum et al.¹³⁶ followed 100 consecutive entirely HA-coated Ti-6Al-4V hip arthroplasties for 7–9 years. The HA coating was applied over the whole stem and has a mean thickness of $155 \pm 3.5 \mu\text{m}$. The clinical results were excellent, and bony incorporation was extensive in all components.

TABLE IV. Methods of Assessing Fixation of Hip Implants

Method 1—By Failure Rate ^{11,132}	Method 2—By Radiographic Features ^{132,133}
<ul style="list-style-type: none"> Mechanical failure rate: due to aseptic loosening or radiographic loosening Clinical failure rate: due to osteolysis or pain or activity-limited pain with well-fixed stems Combined failure rate: the sum of the former two 	<ul style="list-style-type: none"> Presence of radiolucent lines Level of migration or subsidence Appearance of bone Degree of cancellous condensation and cortical hypertrophy Incidence of endosteal lysis Level of pain

No stem loosened or subsided, which is more satisfactory compared to other cementless fixation.

D'Antonio, Capello, Manley, and Franklin¹³² specifically addressed the remodeling of bone around HA-coated femoral stems and presented a detailed description about the progressive remodeling process. They followed 224 THAs with a proximally HA-coated femoral component in 201 patients for a mean duration of 71 months. Of the 224 THAs, 208 (93%, 190 patients) yielded a good or excellent clinical result, 4 patients (2%) reported mild-to-moderate activity-related pain in the thigh, and 2 (1%) experienced aseptic loosening. The radiographs showed progressive new-bone formation (cortical hypertrophy and cancellous condensation) throughout the zones adjacent to the middle and distal portions of the stem.

Bone remodeling began early, with extensive proximal fixation of the implant. The distal stress transfer through the implant was predictable and progressed through the follow-up period, as shown in Figure 5. Cortical hypertrophy about the middle and distal portions of the stem occurred predominantly in the mediolateral plane (47% compared with 6% in the anteroposterior plane), and it was more common in patients who had poorer bone quality preoperatively. **Intramedullary** osteolysis was present in one femur (0.4%) at 5 years, and the osteolytic area was less than 5 mm in its largest dimension and had not progressed at the time of the 6-year follow-up evaluation.

Capello, D'Antonio, Feinberg, and Manley¹¹ also found excellent clinical and radiographic results with HA-coated total hip femoral components in patients younger than 50 after 5–8 years of follow-up of 152 hips in 143 patients (16–49 years old, average 39). Radiographic changes consistent with bone remodeling (cancellous condensation and cortical hypertrophy) typically were seen around the **midpart** of the shaft of the prostheses, and all stems were radiographically osseointegrated. A review of serial radiographs (Figure 6) showed mechanically stable implants with osseous ingrowth, evidence of stress transfer at the middle part of the stem, and minimum endosteal osteolysis. This promising result in young patients is important because cemented stems do not exceed the life expectancy of young patients, and because of some other inherent problems with cemented fixation, such as cell necrosis and loss of **endosteal bone**.¹²³

TABLE V. Specifications of HA Coatings in Some Clinical Studies With Femoral Stems

Author	Thickness (T)/Porosity (P)/Density (D)	Crystallinity (C)/Purity (P)	Tensile Bond Strength (T)/Shear Strength (S)/Fatigue Life (F)	Others
Capello and co-workers ^{11,135}	T = 50 μm	N/A	N/A	N/A
D'Antonio et al. ¹³²	T = 50 μm	P > 90 wt %	N/A	N/A
D'Lima et al. ¹³⁴	T = 50 μm Dense	C = 70% P = 95 wt %	T > 65 MPa F > 107 cycles at 8.3 MPa	Implanted with a 4% press fit Ra = 6–16 μm
Donnelly et al. ¹³⁸	T = 50–90 μm	C > 70–90% P = 97–98 wt %	S > 25 MPa	
Dorr et al. ¹⁴²	T = 55 \pm 5 μm D = 3.02 g/cm ³	C > 72% P > 94 wt %	S = 34–38 MPa T = 45–48 MPa	Porous Ti alloy stem (pore size = 750 μm and 490 \pm 30 μm before/after HA coating; Ca/P = 1.75)
Onsten et al. ¹³⁷	T = 50 μm	N/A	N/A	N/A
Røkkum et al. ¹³⁶	T = 155 \pm 3.5 μm D = 1.2–1.6 g/cm ³	C = 50–70% P > 98 wt %	T = 20–30 MPa	Thick coating; Ra = 10 μm
Rothman et al. ⁶	T = 50–70 μm D = 3.135 g/cm ³	C > 62% P > 95 wt %	N/A	Porous Ti stem
Tonino et al. ¹⁸²	P < 10%	C > 75% P > 90 wt %	T = 62–65 MPa	Vacuum sprayed, with a Ti bond coat; Ca/P = 1.67
Yee et al. ¹⁴⁰	T = 50–70 μm D = 3.135 g/cm ³	C > 62% P > 95 wt %	N/A	N/A

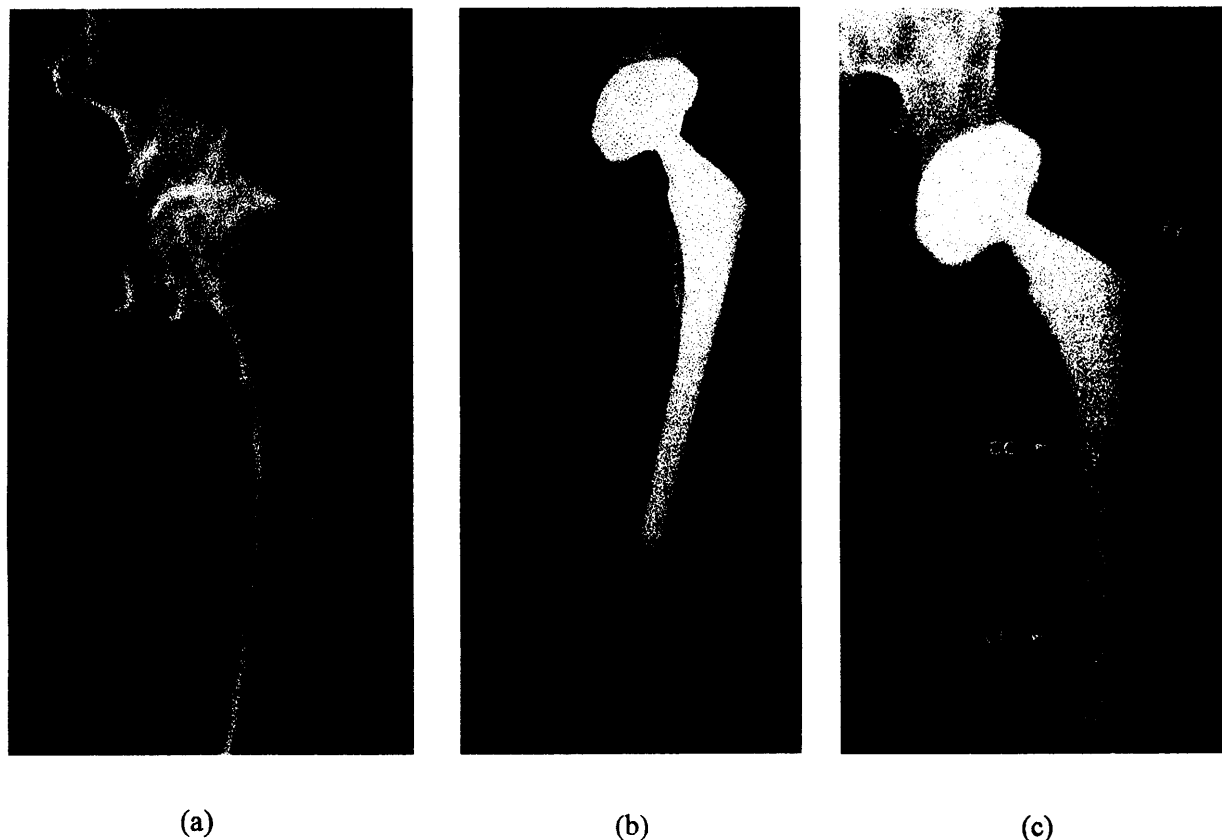


Figure 5. Radiographs of a 54-year-old woman who had osteoarthrosis and type-C bone. (Courtesy of D'Antonio et al.¹⁴⁵) (a) Preoperative radiograph. The joint space is obliterated, with partial collapse of the femoral head and periarticular osteophyte formation. (b) Anteroposterior radiograph made 6 weeks postoperatively. (c) Anteroposterior radiograph made 6 years postoperatively, showing the full extent of the cancellous condensation adjacent to the middle and distal portions, and cortical hypertrophy in Zones 2, 3, and 5.

HA-Coated vs. Cemented Fixation Some authors specifically compared the fixation of the HA-coated stem with that of the cemented stem and found comparable and even preferable results with the use of the HA-coated stem. Onsten, Carlsson, Sanzen, and Besjakov¹³⁷ followed up a consecutive series of 30 total hip replacements with proximally HA-coated stems for 2 years. It was found that the micromotion of these prostheses were comparable to that of the cemented Charnley prostheses, which have been used as controls, with respect to migration and wear.

Donnelly et al.¹³⁸ compared the radiological results and survival of four types of fixation of femoral stems with one design, including (a) a press-fit, shot-blasted, smooth Ti-Al-V stem; (b) a press-fit, shot-blasted, proximally ridged stem; (c) a proximally HA-coated stem, and (d) a cemented stem. They followed up 538 replaced hips for 5–10 years. Survival analysis at 5–6 years showed better results for HA-coated and cemented stems (100% survival rate) and a lower mean rate of migration. More radiolucent lines and osteolytic lesions were observed in the press-fit groups, with a trend for a lower incidence in the HA compared with the cemented group. Proximal osteopenia increased in the press-fit and cemented prosthesis with time, but did not occur in the HA group.

There was also a higher incidence of femoral neck resorption with time in the cemented group than the other three.

The results with the HA-coated stems in this study is particularly surprising, because the stems were used in the more demanding younger group (< 60 years). This compares to the slightly less satisfactory survival rates and increased incidence of radiolucent lines and lytic lesions in cemented prostheses used in the older patients (> 60 years). The apparent absence of proximal osteopenia in the HA group seems to be a further advantage in the longer term, which is presumably because only this group of prostheses secured reliable proximal, but not distal, fixation. Therefore, although HA and cemented interfaces both provide secure fixation, there is a trend in favor of HA in terms of fewer radiolucent lines, fewer lytic lesions, and less proximal osteopenia, and longer survival.

HA-Coated vs. Porous Fixation Before the adoption of HA coatings, the femoral stem with a porous surface was once the most preferred in cementless fixation, with the aim being to increase bone growth into the pore structure of the implant. However, some clinical retrieval studies have exhibited fibrous, rather than bony, ingrowth into porous surfaces,¹⁰⁹ so the addition of HA may improve osseointegration. Animal

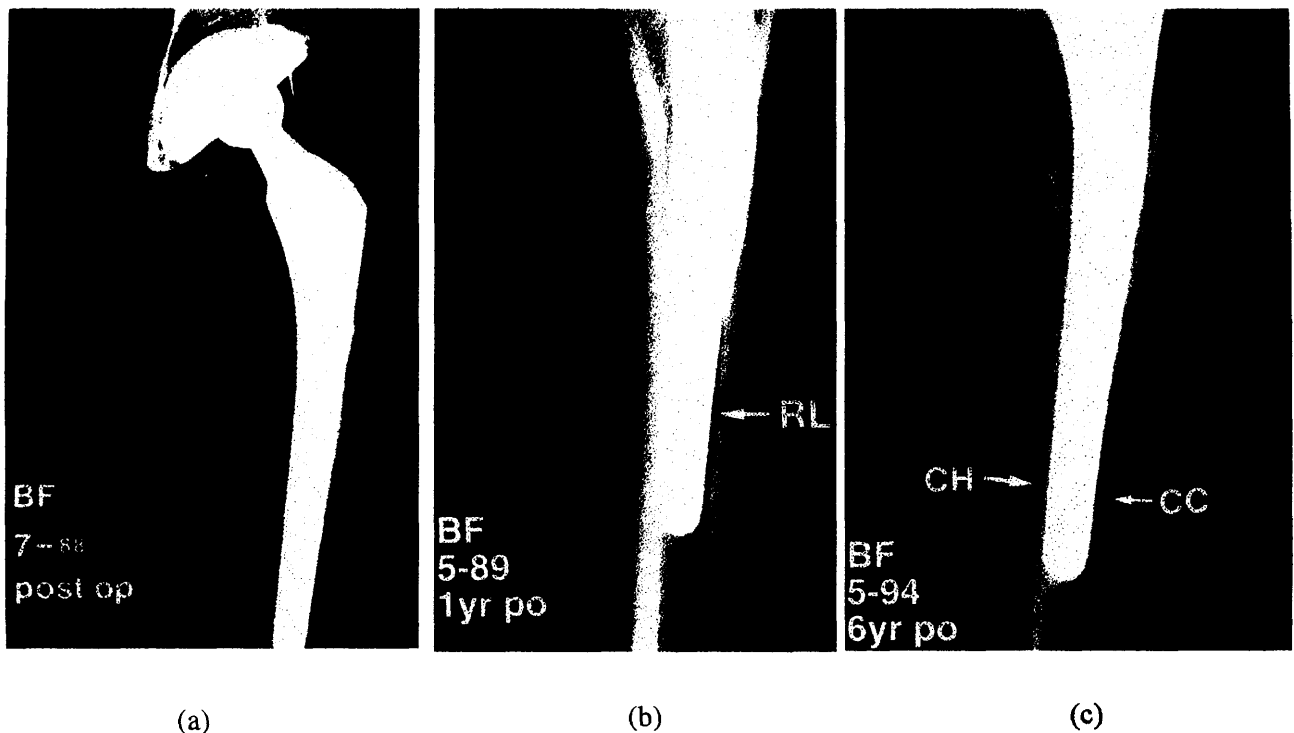


Figure 6. Radiographs of a 25-year-old man who had avascular necrosis of the left hip. (Courtesy of Capello et al.¹¹) (a) Early postoperative anteroposterior radiograph. (b) Close-up radiograph, made 1 year postoperatively, showing evidence of a radiolucent line around the distal part. (c) Close-up radiograph, made 6 years postoperatively, showing areas of cancellous condensation and cortical hypertrophy, but no evidence of radiolucent line around the distal part.

models have supported the belief that, unlike uncoated porous titanium implants, HA-coated ones may limit the extent of the fibrous membrane formed and can even overcome a 1-mm gap between the implant and bone.^{14,15,139}

Many clinical trials have compared the clinical performance of these two types of fixation. Rothman, Hozack, Ranawat, and Moriarty⁶ found no clinical or radiographic advantage with the use of HA in primary total hip arthroplasties. This was a retrospective, matched-pair analysis after following up for an average of 2.2 years, where a HA-coated porous titanium femoral stem and its non-coated counterpart were implanted in 52 pairs of patients. McPherson, Dorr, Gruen, and Saberi⁷ found better bone remodeling but no clinical differences in a 3-year, matched-pair comparison of porous-coated stems with proximally sprayed HA and porous-coated stems. In a prospective, randomized trial, 62 total hip arthroplasties with either HA-coated or non-coated femoral prostheses were implanted by one surgeon in 55 patients. The dual tapered femoral stem, with a Ti-6Al-4V porous coating at the proximal third of the stem (some prostheses also included an HA coating); a roughened, grit-blasted textured surface on the middle third of the prostheses; and a smooth surface at the distal third. No femoral prostheses failed, and migration or subsidence was not observed after an average of 4.6 years. Although the Harris hip score¹⁴¹ and femoral stem survivorship in this study do not indicate a significant clinical advantage with the use of HA-coated

femoral prostheses, the HA-coated stems showed trends toward increased distal stem related cortical hypertrophy, increased cancellous condensation and less endosteal cavitation.

Dorr, Wan, Song, and Ranawat¹⁴² suggested that the use of HA coating did provide improved fixation and the possibility of improved durability. They followed up 15 patients who have bilateral hip replacement with the same porous titanium alloy stem design where only one of the stems incorporated an HA coating, for an average of 6.5 years. Despite the small number of patients, compared to the above two comparative methods, this method allowed the complete control of bone type and metabolism, immunology, activity, weight, age and emotional response of the patients. The radiographic measurements revealed fewer radiolucent lines ($P = 0.013$) in the fixation with HA-coated stems and improved bone modeling as measured by proximal cancellous hypertrophy, and this was prolonged to the final follow-up. In addition, the occlusion of pores with the HA coating in this study did not change the improved radiographic fixation.

(2) *Application in Acetabular Component* Despite the encouraging clinical results in femoral prostheses, the use of the HA coating on the acetabular component does not seem as successful as in femoral components. Moilanen et al.¹⁴³ compared the HA-coated (71 same size) and noncoated (40 Sample size) press-fit Co-Cr alloy acetabular cups in total hip replacements after 2–3 years of implantation. It was found

that HA coatings enhanced the stability of acetabular components, with a reduced rate of proximal migration and a significant reduction in rotational migration and the number of radiolucent lines.

Manley et al.¹⁴⁴ evaluated 377 patients (428 hips) with a porous-coated, press-fit acetabular cup, an HA-coated threaded screw-in cup, or one of two similar designs of HA-coated press-fit cups after an average of 7.9 years of follow-up. All cups were made of commercial pure titanium and the same Osteonics femoral components were used in all cases. Radiographic evaluation of the 383 acetabular cups that were in *situ* at the time of the most recent follow-up showed that (a) 123 (99%) of the 124 HA-coated threaded cups, (b) 101 (98%) of the 103 porous-coated cups, and (c) 139 (89%) of the 156 HA-coated press-fit cups were stable with osseous ingrowth, as indicated by the absence of radiolucent line at the interface and the absence of migration within the acetabulum. The probability of revision due to aseptic loosening was significantly greater for the HA-coated press-fit cups than for the HA-coated threaded cups or the porous-coated, press-fit cups ($p < .001$ for both comparisons.) The HA-coated threaded cups and the porous-coated press-fit cups continued to perform well more than 5 years after the operation. In the multicenter study by Capello et al.,¹³⁵ the HA-coated femoral stem showed enhanced bone ingrowth and fixation for as many as 10 years with only one (0.3%) stem exhibiting aseptic loosening. However, 3 (2.7%) porous-coated cups, 24 (14%) HA-coated press fit cups, and one (2.6%) HA-coated threaded cup were revised for aseptic loosening.

The unsatisfactory results on the acetabular component suggest that in the specific biomechanical environment of the acetabulum, physical interlocking between the cup and the supporting bone beneath it may be a prerequisite for long-term stability; thus cup design is very critical for its performance. Therefore, despite the good short term (2–3 years) results with the HA-coated cups, fatigue failure between the metal surface and the HA coating, arising in response to prolonged distraction stress medially imposed by the patients' activity, was thought to be responsible for the separation of the socket from the bone in the case of press-fit cups in the long term.¹³⁶

Similarly, the HA-coated femoral stem in the Røkkum et al. study¹³⁶ also demonstrated excellent clinical results with no stem loosening or subsidence. However, five cups (5%) in this study were revised because of loosening after having functioned painlessly for 3.8–5.5 years with radiological ingrowth exhibited, and this is higher compared to other studies.^{145,146} This late occurrence of acetabular loosening contrasts with the porous-coated cups, for which a high incidence of early lucent lines suggesting poorer bonding has been reported.^{147,148} In addition to the inherent problems with the acetabular cups described above, the loosening of cups may be attributed to the use of thick coatings ($155 \pm 3.5 \mu\text{m}$) in this study (the commonly used HA coatings are $50 \mu\text{m}$ thick^{81,82}), because thicker coatings may have poor mechanical properties, and the HA-to-metal interface is thought to be

the weak point.^{83,131,149} This difference may also explain the fact that loose cups in this study had almost completely lost their HA coating.

(3) *Application in Knee Prostheses* New methods are constantly being developed to improve the fixation of tibial components, especially for young active patients. Since the development of the knee arthroplasty and the promising clinical results with noncoated cementless fixation are relatively recent, studies on the use of HA coatings for knee prostheses are rare. Nilsson, Cajander, and Karrholm⁸ have described subsidence as much as 1 cm and delamination of the coating in one type of knee prosthesis with a thick coating. Nelissen, Valstar, and Rozing¹¹⁹ performed a prospective, randomized, double-blind study to evaluate three different means of fixing tibial components, 11 cemented, 11 HA-coated, and 10 noncoated. After 2 years of follow-up, it was found that micromotion of the HA-coated components was similar to that of the cemented components. Both HA-coated prostheses exhibited far less micromotion along the longitudinal axis (subsidence) and less translation along the transverse axis and sagittal axis throughout the follow-up period than the noncoated components. This result indicates that the HA coating may be used as a biological mediator, which is necessary for adequate fixation of tibial components when cement is not used. In the randomized studies of Toksvig-Larsen, Jorn, Ryd, and Linderstrand¹²⁰ on 62 tibial prosthetic fixations, the HA coating was found to have a strong positive effect on the tibial component fixation after a 1–2 year follow-up. The HA-coated groups had far less micromotion compared to the porous-coated groups and no prosthesis in this group showed continuous migration.

(4) *Application in Pin/Screw Components* The bone-to-pin/screw interface is the site of major complications in external fixations: bone-pin loosening and pin-track infection.^{150–152} Due to excellent advantages exhibited in hip prostheses, HA coatings were also proposed for use in external fixation with the aim to improve the pin osseointegration and fixation stability.^{153,154} Moroni and co-workers^{155,156} showed enhancement of bone-to-pin osseointegration and interfacial strength in HA-coated pins compared with uncoated or titanium coated pins in two animal studies under loaded conditions. They further proved this in their clinical studies with three groups of seven patients, who had external fixation of mid-diaphyseal tibial fractures using, respectively, uncoated pins, uncoated bicylindrical pins, and HA-coated bicylindrical pins.¹⁵⁷ They found that both types of uncoated stainless-steel pins showed a lower extraction torque than insertion torque in all cases, whereas the mean extraction torque of the HA-coated pins was unchanged. Seven of the 14 patients receiving uncoated pins revealed pin-track infection, compared with none of the patients with HA-coated pins. Thus, HA-coated external pins did increase stability and, thereby, reduce the risk for pin-track infection and mechanical failure of fracture fixation. The authors¹⁵⁷ also indicated that although pin removal was more painful with HA-coated pin extraction than with the uncoated pins, the pain was of

short duration and should not be the reason for not placing such pins into clinical use.

In another clinical study by Magyar, Toksvig-Larsen, and Moroni,¹³ the HA coating was also found to increase threaded pin fixation. The torque forces for the extraction of the standard screws were much lower than that for the HA-coated pins. All 18 of the metaphyseal standard screws were loose at extraction, but only one of the HA-coated screws in the metaphysis was loose. The standard screws in the distal tibia lost around 40% of their fixation compared to the HA-coated screws, which retained full fixation strength. No adverse effect has been found in using the HA-coated screw in this study.

(5) **Application in Dentistry** As in hip implants, HA coatings have been used clinically in root-form endosseous implants for over a decade. The short-term survival rates of HA-coated implants have been found comparable to those of titanium implants.¹⁵⁸⁻¹⁶⁰ The main concern with the clinical use of HA-coated dental implants is their long-term survival, with the longest-running studies of 6 or 7 years compared to the good survival rate of titanium implants for over a 25-year period.¹⁶¹ Biesbrock and Edgerton¹⁶¹ have reviewed clinical use of HA-coated dental implants and concluded that HA-coated implants are as predictable as titanium implants in short-term periods. They also suggested that HA-coated implants may be useful treatment modalities in a variety of clinical situations, such as in type-IV bone (cancellous bone), in shorter implants (implant size less than or equal to 10 mm), in fresh extraction sites (immediate implants), and in graft-augmented maxillary and nasal sinuses.

Another concern with the use of HA-coated dental implants is the increased incidence of infection. In vitro studies by Wolinsky, deCamargo, Erard, and Newman¹⁶² have demonstrated that specific bacteria (e.g., *Streptococcus sanguis* and *Actinomyces viscosus*) can more easily adhere to HA powder and/or beads than titanium powder and/or beads. Johnson¹⁶³ suggested that HA coatings are more susceptible to bacterial colonization than titanium implants or natural teeth because of the surface roughness and hydrophilicity of HA. He even proposed that putative periodontal pathogens, such as *Fusobacterium* species and *Peptostreptococcus prevotii*, might preferentially adhere to HA surfaces, predisposing peri-implantitis. However, many clinical microbiologic studies do not seem to support this concern. Gatewood, Cobb, and Killoy¹⁶⁴ examined the maturation of subgingival dental plaque on titanium, HA, and cementum surfaces and found the sequence and composition of microbial morphotypes in the maturation process were similar regardless of the surface. Rams et al.¹⁶⁵ compared the microbial colonization of 30 HA-coated implants and 10 titanium implants in a 10-month clinical study and found no significant difference in the development of microflora.

In a prospective study, Roynedal, Ambjornsen, Stovne, and Haanas¹⁶⁶ investigated the clinical outcome and marginal bone resorption of three different endosseous implants placed in the anterior mandibles of 15 elderly patients. The results of 3-year follow-up indicated that, compared to titanium plas-

ma-sprayed cylinder implants, the titanium screw-shaped and the HA-coated cylinder implants were significantly better in terms of bone resorption. They also concluded that an overdenture in the mandible supported by a few implants with ball attachments is a predictable, simple, and economic treatment method that can be used in most patients with expected favorable prognoses. The long-term stability of HA-coated implants has been questioned by the possibility of the existence of HA detachment and resorption.

Piattelli, Scarano, Alberti, and Piattelli¹⁶⁷ retrieved two HA-coated implants after 12 months of loading because of an abutment fracture and found close contact between the bone and the coating with no gap or connective tissue capsule at the interface under light microscopy, as shown in Figure 7(a). A reduction in the coating thickness was also found, just in one area, along with the presence of some detached HA particles embedded in the newly formed bone [Figures 7(b) and 7(c)]. This suggests that the resorption or the detached HA particles would not cause any adverse problem for the long-term survival of the implant.

Coating Resorption and Bone Growth. In HA-coated implants, one of the most important events occurring at the bone-implant interface is the resorption of the HA coating, also called degradation or coating loss, sometimes with the presence of HA particles. Although it is essential for the establishment of bone-implant bonding, this has been one of the main concerns for the durability of the HA-coated implants. Some studies have shown resorption of HA coatings up to 2 years after implantation,¹⁶⁸⁻¹⁷⁰ and a complete loss of a 60- μm -thick HA coating after 4 years.¹⁷¹ Based on the observation of animal studies and human retrievals, Bauer¹⁷² hypothesized and described four mechanisms whereby HA coating can be lost from the implant surface: (a) dissolution at neutral pH, (b) osteoclastic resorption of the coating as part of normal bone remodeling, (c) delamination due to bond failure, and (d) abrasion from lack of primary fixation. This has been supplemented by Gross, Ray, and Røkkum¹⁷³ with two more mechanisms: (e) lamellae cracking from the release of residual stress on the coating surface; and (f) preferential amorphous phase dissolution producing free crystalline debris.

The HA particles can be resorbed by macrophages if their size is sufficiently small compared to the macrophages (approximately 30 μm).^{174,175} HA particles in the macrophage will persist as a cellular irritant. When a macrophage phagocytizes the particles, the cells release cytokines, prostaglandins, and collagenases almost immediately. It has been reported that release of these factors begins immediately after HA ingestion and that maximal release occurs between 12 and 24 h.¹⁷⁶ If the particles do not dissolve within the lifespan of the macrophage, more macrophages will accumulate at the site in response to the release of cytokines to digest the dead macrophages and undissolved HA particulates. As well, particles larger than a macrophage (> 30 μm) will not be digested by macrophages and will probably become engulfed by a giant cell. The excessive cellular reaction to HA particulates and the stimulation of a foreign-body response could

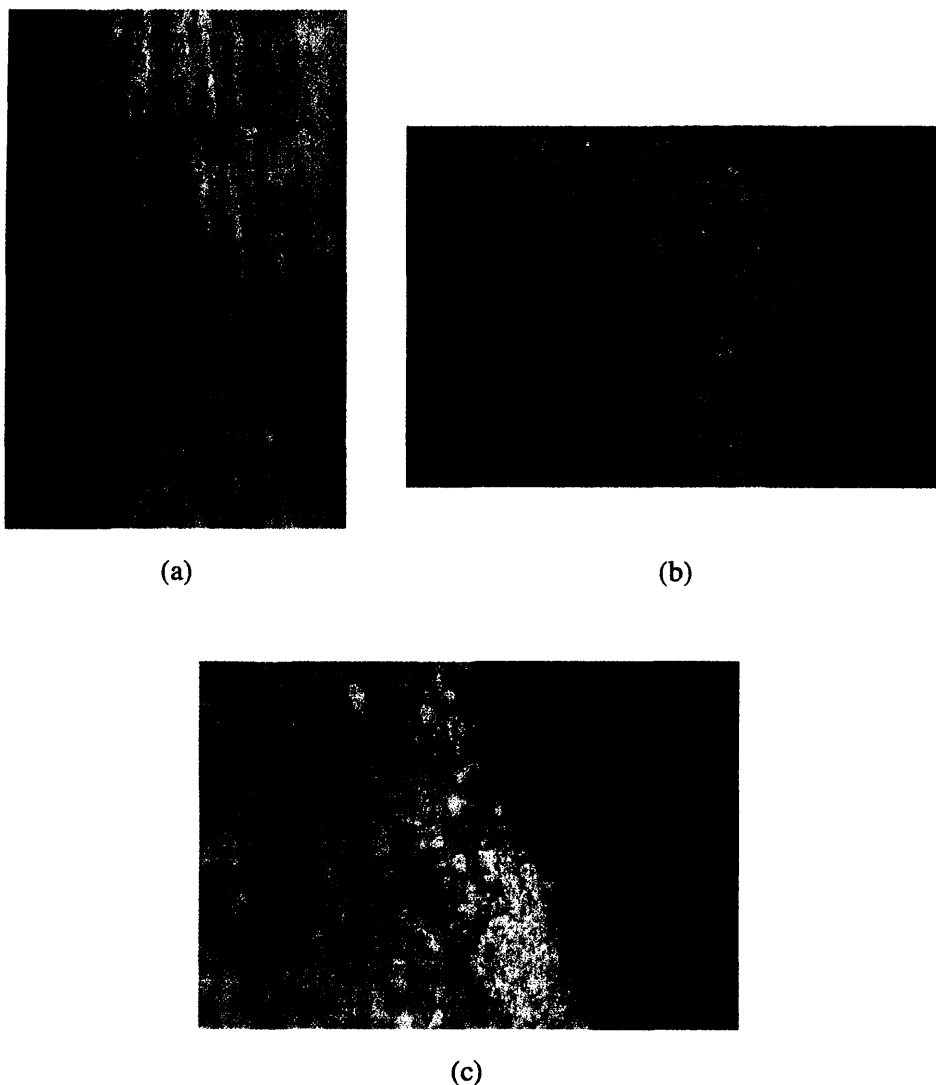


Figure 7. Interface between a HA-coated dental implant and bone. (a) Implant in intimate contact with mature lamellar bone. (b) Resorption of the HA coating in some portions of the interface, with some detached HA embedded in the newly formed bone (arrow) and biological material inside the coating. (c) A reduction of coating thickness in some portions of the interface (basic fuchsin and toluidine blue, original magnification $\times 400$). [From Piattelli et al., *Int J Oral Maxillofac Implants*, 14, 233–238, 1998, Quintessence Publishing Co., Inc, reproduced with permission.]

lead to a decrease in local pH, which disrupts the bone remodeling process, causing the resorption of both HA and bone. Additional problems could arise if particulate debris travels to the hip bearing surface, producing third-body wear and component **loosening**.¹⁷⁷ Although described as a significant theoretical problem, coating delamination has only been identified in some animal studies, probably because of the small thickness and low crystallinity of the HA coating in clinical **use**.¹⁷⁸ Delaminated HA particles, if present, were found to act more like a bone graft substitute; that is, they were commonly surrounded by bone and not associated with a foreign-body giant cell reaction, histiocytic proliferation, fibrosis or osteolysis, so they cannot be a significant cause of bone resorption or implant **abrasion**.¹⁷² The HA-coating abrasion is more of a theoretical problem. The latter two mech-

anisms (e) and (f) still need further investigation. So generally there is only concern for the former two (a) and (b) resorption mechanisms.

Partial dissolution of the HA coating is essential to trigger bone growth. Less crystalline coatings usually promote earlier bone growth and stronger fixation, as was discussed in Section 3.1. Meanwhile, bone remodeling proceeds; that is, osteoclasts resorb normal bone by actively secreting hydrogen ions into the extracellular space, creating a local pH of approximately 4.8. Although the highly crystalline HA coating may be very stable at neutral pH, it is more soluble at these acidic local environments, and the low-crystallinity coating shows even more rapid dissolution. So both the low-crystalline carbonated HA in bone mineral and the HA coating can be focally dissolved by osteoclasts at pH 4.8. This

resorption of the coating as part of normal bone remodeling is probably the main coating loss mechanism in the long run and has been shown in many time-related studies on histological specimens.^{179–181} The coating can disappear with time as a response to this bone remodeling process, but the absence of coating was usually replaced with the presence of new bone, especially in some areas with load transfer, suggesting the acceleration of coating resorption and bone remodeling with mechanical loading.^{19,168}

Tonino, Therin, and Doyle¹⁸² retrieved five total hip arthroplasties with vacuum plasma sprayed HA-coated Ti-6Al-4V stems after 3.3–6.2 years of implantation. They proved that the resorption of the HA coating is cell-mediated and dependent on bone-remodeling processes. This conclusion was based on the fact that most HA resorption takes place at the most proximal level of the metaphysis with less at the more distal sections. All the stems were fixed in the femur and showed osseointegration of both the proximal (HA-coated) and distal (uncoated) parts, as evidenced by the radiological extension of new endosteal or periosteal bone apposition. The appearance of the coating was nonuniform, as shown in Figure 8. In areas covered by bone it was thick and regular, but in those covered by bone marrow it was thin and fully absorbed or irregular; an intermediate stage (50% of HA loss or 50% of the original thickness) was seldom observed. Bone marrow was observed directly in contact with the metal or coating surface without any fibrous interface, illustrating the quality of the osseointegration and the absence of micro-movement. In areas where bone resorption was focally increased, the resorption of HA was also increased, and some osteoclasts were observed. When bone marrow was adjacent to the stem, HA granules were sometimes seen with active signs of phagocytosis. The almost complete loss of HA, as seen in one case, did not seem to jeopardize fixation or osseointegration, and the amount of bone-implant contact in this case did not change substantially in the proximal-stem region and was similar to the other osseointegration. There is no coating delamination, which, according to the authors,¹⁸² may be attributed to the excellent homogeneity and bonding strength of the coating obtained by vacuum plasma spraying.

An interesting observation in the Røkkum et al. study¹³⁶ is that their histological studies of HA-coated prostheses retrieved from patients have shown no resorption of HA coating up to 9 months after implantation. The crystallinity of the coating used in this study is 50–70%, which would be more soluble even in neutral pH environments. However, the clinical results of their study are still excellent, with extensive bony incorporation in all components. The reasons for this are not clear, but the coating they used is quite thick and it is applied to the entire femoral stem.

Wear and Osteolysis. Another concern about the clinical use of HA coating is that it will lead to increased polyethylene wear or third-body wear, and, thus, result in increased incidence of osteolysis. Harris¹⁸³ stated that osteolysis, but not the fixation method, is the leading issue in contemporary total hip arthroplasty. Osteolysis was described as any focal

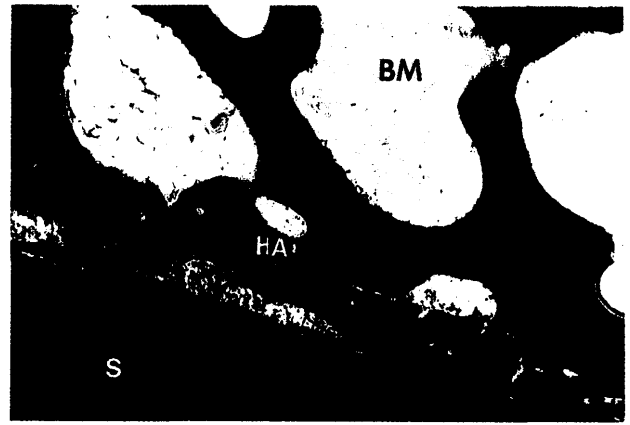


Figure 8. Details of the anterior side of the Gruen zone 1A to 7A of a HA-coated femoral stem (Courtesy of Tonino et al.¹⁸²). HA coating is thicker and more regular in areas covered with trabecular bone (TB) than in areas in contact with bone marrow (BM). The mature TB is spread on the implant (S) surface ($\times 20$).

area of bone loss adjacent to the prosthesis, which is believed to be caused by the biological response to wear debris, mainly polyethylene particles, but also including metallic and HA particles.^{22,184} Osteolysis of the femoral cortex has often been found with both cemented and porous-coated stems,^{185–188} and it most often appeared around cementless acetabular components in hips with abundant polyethylene particles.^{189–191} Metallosis in hips with incomplete polyethylene wear implies third-body wear.

Critics of HA argue that the most probable third bodies are particles of HA that may detach during insertion, especially from the threads of a screw cup, as well as HA evolving from resorption of the coating.^{22,169} Bloebaum and co-workers^{22,184} anticipated that HA would increase wear and osteolysis based on experience with implant retrievals obtained at revisions. Buma and Gardeniers¹⁷¹ expressed similar concerns of fragmentation and loss of HA coating, as observed from a single stem revised for thigh pain. HA lost from surfaces uncovered by bone could more easily enter the joint and damage the articulating surfaces.¹³¹ However, no fragmentation has been observed in some other implant retrievals.^{19,192} D'Antonio, Capello, and Jaffe¹⁴⁵ and Geesink¹⁹³ have not observed osteolysis with the HA Omnifit stem. Thus, HA resorption and, probably, fragmentation most likely do occur but do not seem to promote increased wear and osteolysis in the absence of loose implant.^{11,194} HA particles, if present, would not cause any adverse problems; small particles can be resorbed by macrophages,¹⁷⁴ and the large ones usually act like a bone graft surrounded by new bone.¹⁷²

On the other hand, proponents of HA coating suggest that, because of its biocompatibility and potential circumferential bone apposition, HA coatings may prevent polyethylene and metal debris from migrating along the bone-implant interface and, thus, reduce the incidence of osteolysis and the failure of implants. Moilanen et al.¹⁴³ found no increased wear with the use of HA-coated implants, and their results on the fixation with HA-coated acetabular components revealed few radiolu-

cent lines and migration compared with press-fit acetabular components. In the multicenter study of 316 hip implants by Capello et al.,¹³⁵ there are no cases of distal endosteal femoral osteolysis (intramedullary osteolysis), whereas proximal femoral osteolysis and polyethylene wear was no greater than that seen with other cementless or cemented components. This suggests that a circumferential HA coating may prevent the distal egress of wear debris effectively.

In the Dorr et al. bilateral total hip arthroplasty study,¹⁴² the overall wear in the hips was high, with an average of 0.136 mm linear wear⁴ per year, but the wear and osteolysis were not increased in porous-coated stems hips with HA coatings. The D'Lima et al. study with an Omnifit-HA stem¹³⁴ also showed an absence of distal endosteal lysis, along with correlation of calcar erosion to polyethylene wear, suggesting that early circumferential bony ingrowth afforded by the HA coating prevents distal endosteal access to polyethylene debris at short term follow-up. Donnelly et al.¹³⁸ also found the absence of lytic lesions in their study with 538 HA-coated hips for 5–10 years, implying that an HA coating impedes the access of polyethylene debris to the interface.

Røkkum et al.¹³⁶ specifically addressed the problem of polyethylene wear, osteolysis, and acetabular loosening in their study with 100 consecutive extensively HA-coated hip arthroplasties. The polyethylene wear and osteolysis in their study was worse than general cemented and cementless studies. Eighteen hips with excessive polyethylene wear required surgery and six needed revisions. Osteolysis was found in 66 hips, including all those reoperated on for excessive polyethylene wear. They also found that both calcium phosphate and metal particles were embedded within the polyethylene surface, as has been reported by others.^{22,184} It is unclear whether these particles have arisen from the coating or are simply bone fragments. The poor mechanical properties of these thick coatings may have enhanced HA abrasion and provided a source of HA particles. The largest lesion was in the cancellous bone. The gap often seen lateral to the proximal part of the stem could be a route for the transport of particles into the greater trochanter; whereas the hole in the metal backing could have provided access to the acetabular bone. The complete absence of femoral endosteal cortical osteolysis in spite of the abundance of particles is assuring, which may be explained by the fact that the extensive HA coating of the stem seals the whole interface and blocks the passage of particles.

In the histological and histomorphometric examination of five HA-coated hip implants, Tonino et al.¹⁸² found metal particles with little inflammatory response in nearly all metaphyseal sections; mostly in combination with some HA granules in areas where there was resorption of the HA coating. Hydroxyapatite debris, when present, was only seen adjacent to the metaphyseal part of the stem and never distal to the level of the coating, so did not cause any adverse or

inflammatory reaction. Osteoclasts or macrophages were sometimes seen phagocytosing the HA granules. They also confirmed the absence of polyethylene particles at the interface, because it was closed proximally by circumferential osseointegration.

SUMMARY AND FUTURE DEVELOPMENT

Plasma-sprayed HA coatings have demonstrated advantages in promoting faster and stronger fixation and bone growth both *in vivo* and clinically, and shown promising short-term and medium-term clinical results in femoral stems, knee prostheses, pins/screws, and dental implants. Its application in acetabular components, however, is more dependent on the design of the acetabular cup. HA coatings allow direct bonding to living tissues compared to a loosely adherent layer of fibrous tissue at the implant interface in other cementless fixation, which is especially beneficial for young active patients.

The wear and osteolysis problem did not exhibit any obvious increase in HA-coated implants compared to other cemented and cementless fixation methods. The HA coating even seemed to be able to seal the polyethylene and metal debris from entering the bone–implant interface and reduce wear and osteolysis.

Resorption of the HA coating did occur in most clinical cases, mainly cell-mediated as the result of normal bone remodeling. The initial resorption generally relies on the dissolution rate of the coating, and faster dissolution is preferred to initiate quicker and stronger fixation. The loss of the coating is usually followed by the growth of new bone. Thus, if the resorption rate can be optimally controlled so that the new bone can grow immediately to replace the resorbed coating, the durability of the bone-implant fixation should not be affected. Both the initial dissolution and the resorption for the HA coating are a direct influence of the phase composition, microstructure and coating defects (i.e., cracks, pores), and surface characteristics. Therefore, the feedstock HA powders, coating design, and manufacturing technique are very important. The overall implant performance, however, cannot be well connected with the HA coating, because it depends on a combination of factors such as coating manufacture, implant material and design, bone bed preparation, bone quality and quantity, and surgical technique.

As to future development, the knowledge bases regarding for example, amorphous and impurity phases and their distribution throughout the coating; mechanical properties, residual stress control, and their influences on the resorption and wear of the coating, are still incomplete. These materials-science aspects still need further investigation. Meanwhile, the characterization and testing methods vary from person to person, and standards need to be established to ensure better quality control. Besides these points, some other material-design methods, such as gradient structures, surface treatment, and composite coatings, have also been developed. The concept of gradient structures is to have a very amorphous

⁴ Wear is measured as smallest radius from the center of femoral head to outer border of the acetabular cup.

coating surface with high initial dissolution and gradually increase the crystallinity to a higher level at the coating–implant interface to improve coating durability. This method, however, is not easy to control in manufacturing.

An alternative method is to use a composite of HA with a calcium phosphate with higher solubility, such as β -TCP. The surface layer can be β -TCP, and the HA/ β -TCP ratio increases with the gradient of the coating. The base of the coating should be a pure and highly crystalline HA.³⁴ The concept of surface treatment is to alter a thin surface layer of the crystalline HA coating to become more amorphous for a more rapid initial dissolution rate while still keeping the crystalline structure for the underlying coating. The design of HA/ZrO₂ composite coatings is based on the high strength of ZrO₂ and its special stress-induced transformation toughening or toughening caused by crack–particle interaction to increase the toughness of the coating.^{195–197} A final design concerning the use of HA/polymer coating aims to obtain a composite with a Young's modulus close to, cortical bone, superior toughness, and considerable bioactivity.^{198,199}

In summary, the outlook on using HA coatings on orthopedic appliances, formed by thermal spray methods, as functional bioactive agents to aid the healing process, is favorable. Future developments that revolve around process control in order to predetermine the precise coating chemistry and exact thickness of the HA or HA-composite coating will assure agreeable clinical results.

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