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# In Vitro Changes of Hydroxyapatite Coatings

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The stability and degradability of hydroxyapatite coatings on dental implants depends on the dissolution of the individual chemical phases. Hydroxyapatite-coated dental implants exhibit a range of amorphous-phase content. Two tests were conducted to observe the course of coating degradation. The first test showed degradation of both crystalline and amorphous coatings by cracking and dissolution after immersion in Ringer's solution. Concomitant saturation of the implants in the solution modified the coated surface with precipitated crystalline apatite. A second test, intended to replicate the conditions of infection by decreasing pH, illustrated preferred dissolution of the amorphous phase, liberating crystalline segments. It is expected that morphologic changes could influence the rate of bone bonding and therefore could alter or control implant-tissue interactions.

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**Key words:** amorphous, crystalline, degradation mechanisms, dissolution, hydroxyapatite coatings, microstructure

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Of the different types of implants that have been used for replacement of the completely or partially edentulous dentition, including subperiosteal, transosteal, and endosseous, the current trend has been to use endosseous implants. These are available in both plate and root forms, the latter being the most popular since long-term studies have shown that such implants maintain osseointegration. The term "osseointegration" was introduced in the literature by Brånemark,<sup>1</sup> who described the intimate contact between a titanium implant surface and the sur-

rounding bone. One accepted definition for osseointegration is "a 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."<sup>2</sup> This phenomenon is essentially what Schroeder et al described as "functional" ankylosis.<sup>3</sup> Osseointegrated implants usually do not have 100% of their surfaces in contact with bone, and are often reported to have between 25% to 85% bone contact.<sup>4</sup>

Another class of implants interacts with bone by a process known as "biointegration." This concept utilizes a bioactive surface to stimulate bone growth, thus encouraging a direct bond between the implant and the surrounding bone. Bioactivity can be defined as a characteristic of an implant material that allows attachment to living tissues, whereas a nonbioactive material would form a loosely adherent layer of fibrous tissue at the implant interface. It has been proposed that covering a titanium implant with a coating made of bioactive glasses, or hydroxyapatite (HA), would promote this "biointegration."<sup>5</sup> Because it has a chemical structure similar to that of bone, hydroxyapatite is biocompatible, nontoxic, and forms a bond with bone. Hydroxyapatite materials have also been used clinically in the augmentation of alveolar ridges and in various spinal-fusion applications.<sup>6</sup> It has been shown to be an osteoconductive, as opposed to an osteoinductive, material, and it is this osteocon-

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ductivity that is believed to be responsible for its ability to promote bone growth toward the implant surface.<sup>7</sup> Gaps of up to 1 mm between HA coating and the bone are bridged by the healing process, leading to a surgical fit or "primary fixation."<sup>8-16</sup>

Clinical evidence indicates that bone bonds directly to sintered HA,<sup>17-19</sup> to HA particles in a polyethylene matrix,<sup>20</sup> and to HA coated on titanium.<sup>21</sup> Unlike biointegrated implants, which have no transition layer between the bone and the HA, on the scale of atomic resolution osseointegrated implants are separated by a 20-nm layer adjacent to the titanium surface.<sup>22</sup> Apatite crystals grow epitaxially from the crystalline HA surface and meet with randomly oriented mineralized collagen fibers.<sup>23</sup> Thomas et al showed that attachment to bone was achieved for HA-coated implants in half the time (ie, 3 weeks) required for noncoated implants, but that this difference diminished over the next 10 weeks.<sup>6</sup> While increased bond strength associated with bone attachment may be short term, it may be very important clinically. Inasmuch as the success of implants has been linked to their primary fixation and initial stability, HA-coated implants may provide earlier take and fixation, which could then increase the success rates in areas where the quality or quantity of existing bone make traditional uncoated dental implants less feasible. However, controversies exist regarding long-term effects of the possible dissolution of HA coatings in conjunction with pen-implant disease, which could lead to loss of osseointegration and to implant failure.

Coating properties depend on the manufacturing process used to make them. Thermal-spray processing can be set to produce a coating with a high amorphous-phase content or a crystalline coating. In the present study, three coatings were examined: a coating with a high amorphous-phase content, a crystalline coating produced by heat treatment of the amorphous phase, and a coating with an intermediate amorphous content. The purpose of this paper is to provide evidence that the presence and proportion of the amorphous phase plays an important role in the dissolution behavior of the coating on dental implants.

## Methods

**Coating Production.** Hydroxyapatite powder was both synthesized<sup>24</sup> and supplied by Osteonics (Allendale, NJ). Coatings for in vitro testing were produced using the synthesized powder (55 to 85 p ~ ), but the coatings for accelerated-aging experiments used powder (sieved to 10 to 40 pm) supplied by Osteonics. The smaller particle size was necessary to produce a coating with a higher amorphous content.

An SG100B gun (Miller Thermal, Appleton, WI) with a plasma gas mixture of argon and helium was used to apply approximately 100- $\mu$ m-thick HA coatings onto grit-blasted stainless-steel substrates (316 grade) of 17  $\times$  17 mm geometry for the in vitro study. Since a long spray distance favors the formation of the amorphous phase, a spray distance of 20 cm was chosen to produce coatings consisting of the amorphous phase. Compressed air was used to aid rapid solidification of the deposited lamellae and to reduce residual stress development. Crystallinity for the in vitro specimens was controlled by heat treating the as-received coating at 800°C in a flowing nitrogen gas to yield a crystalline coating.<sup>25</sup> This process of crystallization was chosen so that the lamellae or splat morphology that is controlled by the spraying operation would be identical, and thus changes in the performance of the coating could be related solely to differences in crystallinity. Coatings with an intermediate amorphous-phase content were produced on titanium substrates with argon and nitrogen plasma gases in a Metco 3MB gun (Sulzer Metco, Westbury, NY) in the usual fashion by adjusting spray parameters.

**In Vitro Testing.** Ringer's solution was prepared by adding 8.0 g sodium chloride, 0.37 g potassium chloride, 0.2 g magnesium chloride hexahydrate, 0.16 g sodium monohydrogen orthophosphate, 0.29 g calcium chloride, and 2.0 g sodium bicarbonate to double-distilled water to make up 1 L of solution. Carbogen gas (95% oxygen and 5% carbon dioxide) regulated the pH to 7.35 and replicated the dissolved gases found in the body. An immersion heater kept the temperature of the 20-L bath to 36.6°C while the stirrer was constantly circulating the solution.

The reference substrates (not grit-blasted), as-sprayed coatings, and heat-treated HA coatings were immersed for periods of 1, 2, and 4 days and 1, 2, 4, 8, and 12 weeks. Coatings and reference samples were removed, treated in an ultrasonic bath for 1 minute to remove any loose debris from the coating surface, and then dried in an oven at 180°C. The coating surface was inspected by scanning electron microscopy (SEM), and composition and amorphicity were determined by x-ray Iffraction (a Cu K <sub>$\alpha$ 1</sub> radiation source was used for x-ray diffraction).

**Accelerated Degradation.** Citric acid was prepared to a 0.5 wt% concentration. A coating with an intermediate amorphous-phase content (~ 50 wt%) was ground and polished to a flat smooth surface, planar to the substrate. This enabled identification of the crystalline regions, which appeared as light areas in the light microscope. The coating was then immersed in the citric acid for periods of 2 and 5 minutes and then observed with light microscopy and analyzed by x-ray diffraction.

## Results

**Weight Measurements.** Both the crystalline- and amorphous-coated samples exhibited a distinct trend in weight change. The as-sprayed coating, representing the amorphous calcium phosphate, showed a weight loss with time (Fig 1) that approached a steady state after 4 weeks. The thickness axis has been calculated from the HA density and specimen geometry. It has been presented to indicate the overall response of the samples; however, it should be cautioned that localized regions of the specimen might have accelerated responses. The total weight loss after immersion for 12 weeks corresponds to a 30 wt% coating loss.

Heat-treated coatings, representing the crystalline phase, exhibited a weight increase that amounted to 9% of the coating weight. Most of the weight increase occurred in the first 8 weeks. The results indicate that crystalline coatings are more stable, at least under the conditions of these *in vitro* tests, and will have a longer life.

### Structure and Composition Measurements.

The x-ray diffraction pattern of the as-sprayed coating revealed a diffuse peak, typical for amorphous materials. The amorphous-phase content was about 90 wt%. Heat treatment of this amorphous phase produced a crystalline material, verified by the diffraction peaks in the spectra. Characterization studies of the amorphous phase have shown that it can be hydroxyl deficient,<sup>26</sup> and so heat treatment in the absence of moisture will produce an oxyhydroxyapatite, ie, a hydroxyl-deficient hydroxyapatite. The x-ray diffraction pattern of oxyhydroxyapatite will have the same peak positions as HA, with slight broadening because of a marginal change in lattice parameters. Upon exposure to moisture, a weight increase corresponding to the uptake of hydroxyl ions takes place, and HA forms.

The coating consisting primarily of an amorphous phase contained small amounts of tricalcium phosphate, tetracalcium phosphate, calcium oxide, and HA. According to the x-ray diffraction pattern (Fig 2), these lower solubility phases were still detected on the surface at a slightly higher concentration after 1 week dissolution of the amorphous phase. Furthermore, the calcium oxide has reacted with water to produce calcium hydroxide. After 4 weeks of immersion, x-ray diffraction recorded a noticeable increase in hydroxyapatite content, which continued to rise with immersion time (Fig 3). The x-ray diffraction pattern of crystalline HA did not show discernible changes after immersion.

**Surface Morphology Examination. Amorphous Coatings.** The appearance of the coating displayed changes after immersion in Ringer's solution.

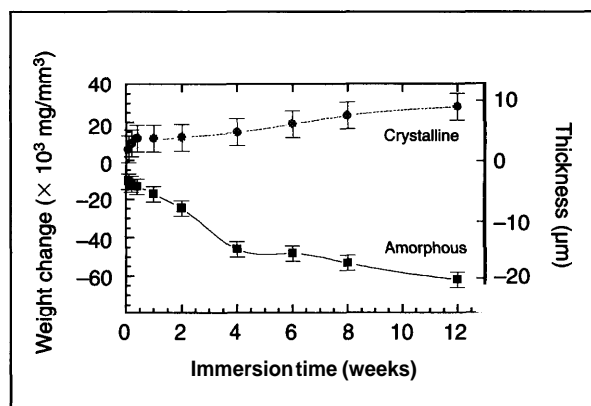


Fig 1 Weight change for amorphous and crystalline samples aged in Ringer's solution. The degradation of the coating is also assessed in terms of thickness.

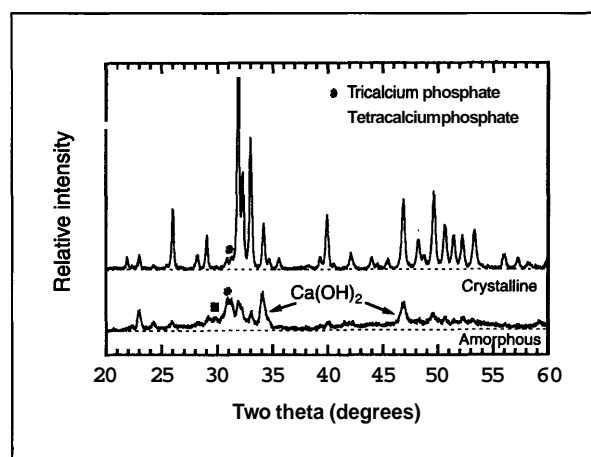


Fig 2 Crystallinity and composition for as-sprayed (amorphous) and heat-treated (crystalline) coatings after 1 week's immersion in Ringer's solution. The amorphous phase has dissolved, revealing the tricalcium phosphate, tetracalcium phosphate, and calcium hydroxide. The calcium hydroxide has formed from the reaction of the calcium oxide with the water.

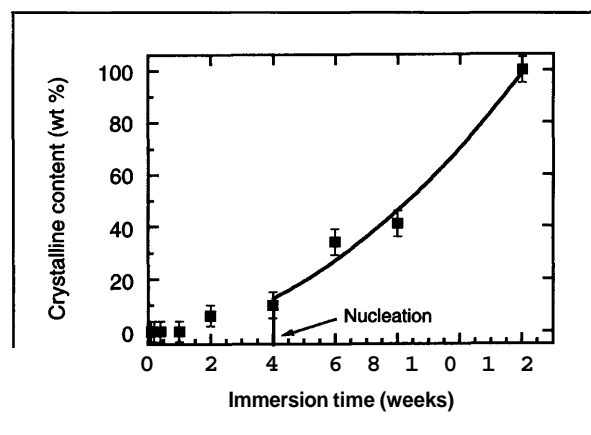
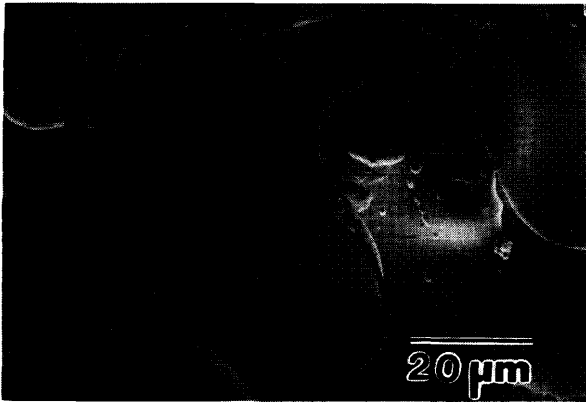
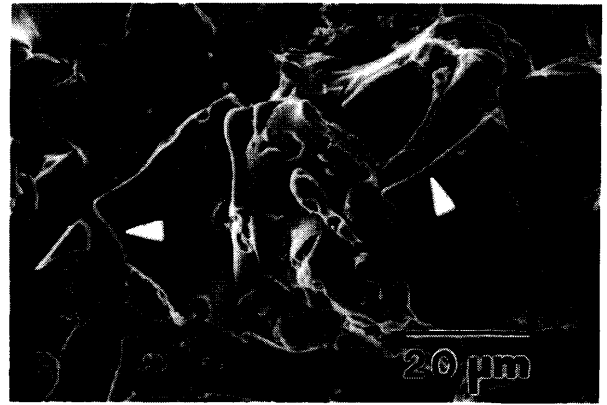


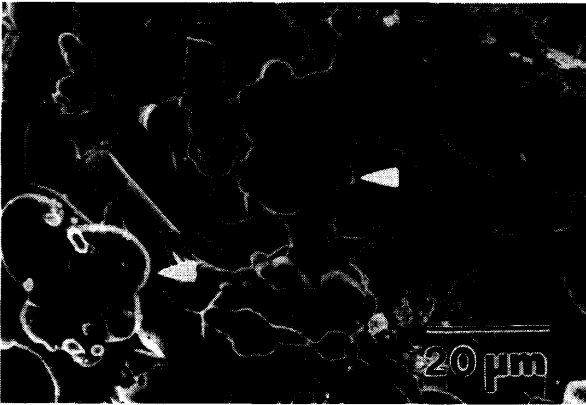
Fig 3 Increase in the coating's hydroxyapatite content with immersion time in Ringer's solution.



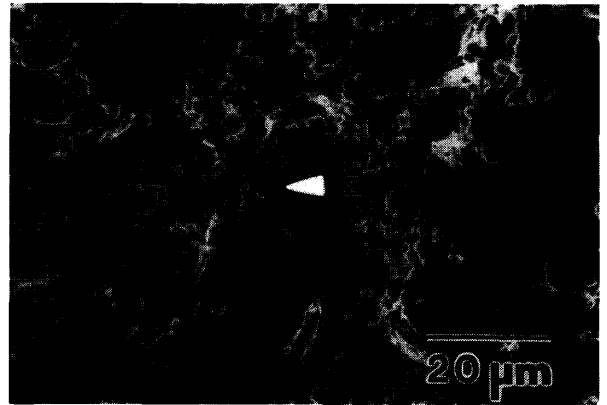
**Fig 4a** Surface morphology of an as-sprayed hydroxyapatite coating.



**Fig 4b** The surface topography exhibits cracking after 1 day in Ringer's solution. **Arrows** indicate fractured lamellae.



**Fig 4c** After 4 weeks in Ringer's solution, the coating begins to show signs of dissolution. **Arrows** indicate rounded lamellae.



**Fig 4d** After 8 weeks in Ringer's solution, precipitation of apatite can be observed. **Arrows** indicate spherical precipitate.

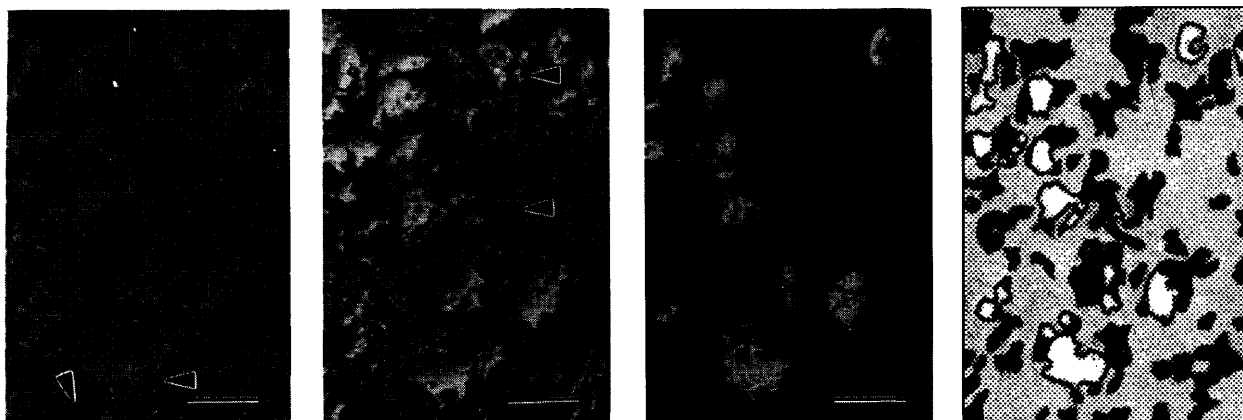
Initially, the surface was covered with well-molten splats and fine cracks (Fig 4a). The surface topography, after 1 day in Ringer's solution, displayed cracking of the lamellae. Cracking progressed with time, imparting a rougher appearance to the surface (Fig 4b). An increase in crack size and population has also been reported by Klein et al.<sup>27</sup> Fractured splats then become more rounded with time, suggesting a dissolution process (Fig 4c).

After a period of 4 weeks, small spheres containing calcium and phosphorus (as ascertained by energy-dispersive x-ray analysis) appear on lamellae boundaries, where a higher nucleation rate is expected. These small 2 to 5 μm spheres appear with a higher frequency after 6 weeks (Fig 4d) and form a dense blanket after 8 weeks, thus nearly masking the visual-coating morphology.

**Crystalline Coatings.** The crystalline coatings exhibited wide cracks, about 0.8 μm wide, as a result

of heat treatment, which occasionally penetrated the coating thickness to the substrate. Otherwise the surface morphology appeared identical to the as-sprayed coatings. Upon immersion, cracks open up further and eventually lead to delamination of some particles; however, the frequency of this event was low. The appearance of the crystalline coating resembles Fig 4b except that the dislodged particles may be larger as a result of the more extensive crack network.

In the same fashion as the amorphous coatings, the spheres appeared on sites requiring a lower activation energy for nucleation. Since the detection of apatite spheres occurred only a little later on crystalline coatings, it appears that nucleation of apatite is initially dependent on the saturation level of the surrounding liquid and only then on the type of calcium phosphate. Therefore, a coating with both amorphous and crystalline regions should be covered with hydroxyapatite spheres at similar times.

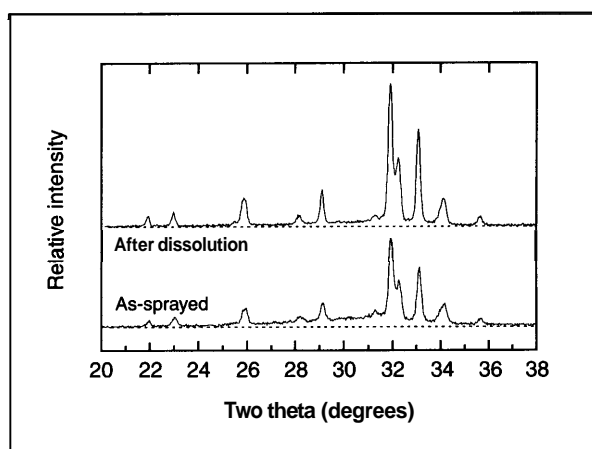


**Figs 5a to 5d** A hydroxyapatite coating viewed with a light microscope (a) after polishing, showing the crystalline phase, and (b) after accelerated dissolution with 0.5 wt% citric acid for 2 minutes, and (c) after accelerated dissolution with 0.5 wt% citric acid for 5 minutes. The arrows in (a) and (b) show crystalline regions that have detached from the coating. A map of all crystalline areas is shown in (d); detached crystalline segments are colored black. (Bar = 20  $\mu\text{m}$ .)

**Accelerated Degradation.** The crystalline regions that appear within the coating were randomly distributed in the amorphous phase. The black regions in the amorphous calcium phosphate represent either (1) crystalline areas that were removed during the polishing process or (2) porosity, when located within a splat. This porosity was present in the powder used to prepare the coating and hence directly transferred to the coating (Fig 5a). The arrows show small crystalline regions that are removed after immersion in 0.5 wt% citric acid (Figs 5a and 5b). After 3 minutes, only those crystalline regions that are largest in size remain anchored in the coating (Fig 5c). A map of all crystalline areas is shown in Fig 5d; the black areas represent a cavity left by detached crystalline segments as a result of degradation. An x-ray diffraction pattern of the coating before and after 5 minutes' immersion indicates that the amorphous phase was preferentially removed, revealing the underlying crystalline material (Fig 6).

## Discussion

**Quantitative Analysis.** The weight-change response exhibits three main regimens: (1) initial cracking and de-adhesion of lamellae on immersion; (2) dissolution of lamellae; and (3) nucleation and growth of apatite spheres. The first two mechanisms produce a weight loss, but the latter leads to a weight gain. The inflection point at 4 weeks and the general shape of the curve have also been observed by Klein et al<sup>28</sup> by measuring an increase of calcium and phosphorus ion concentration in a simulated body fluid. This point will be moved to a shorter time period for a smaller



**Fig 6** An x-ray diffraction pattern of the as-sprayed polished coating and after immersion in 0.5 wt% citric acid. The decrease in the diffuse background as indicated by the dashed line and the increase in peak height after dissolution suggest that the amorphous phase was preferentially dissolved.

volume of solution that can be saturated more quickly. A decrease of 10  $\text{mg}/\text{mm}^3$  can be interpreted as the removal of one lamella layer from the surface of the coating, taking one lamella to be 5  $\mu\text{m}$  thick.<sup>29</sup> The weight loss can then be thought of in terms of the number of splats that are removed from the coating (see Fig 1).

An overall 5.3 wt% increase for the heat-treated coatings can be attributed to different phenomena. The apparent rise in weight that took place in the first couple of days could be attributed to the uptake

of hydroxyl ions into the lattice, the adsorption of moisture into the cracks and pores of the coating,<sup>30</sup> and the reaction of calcium oxide to form calcium hydroxide. The water adsorbed in pores cannot be removed by heat treatment at 180°C, so the large crack population could represent the initial weight gain. The weight gain that occurred after 4 weeks could be attributed to corrosion of the heat-treated stainless steel in the grit-blasted areas located in the root of cracks passing through the coating to the substrate.

**Degradation Mechanisms.** The initial coating has both interlamellar (ie, between) and intralamellar (ie, within) cracks. Upon immersion, the crack density increases, producing jagged lamellae segments (Fig 4b), which de-adhere from the surface. This cracking, arising from the release of residual stresses, has also been documented with rat bone marrow cells<sup>31</sup> and simulated body fluid.<sup>32</sup> The cracks form randomly and give rise to the initial weight loss.

The second mechanism of weight loss occurs by dissolution. Other workers<sup>28,33,34</sup> measured dissolution by following the calcium and phosphate concentration in the solution and found an initial rapid rise followed by a plateau. The same tendency was also observed in the present study (Fig 1). Cracked coating areas and delaminated segments add to the available surface area for dissolution. Furthermore, amorphous coatings dissolve more readily than do crystalline coatings, creating rounded lamellae from the jagged morphologies. The presence of other calcium phosphate phases (eg, B-tricalcium phosphate and oxyapatite) also have a high resorbability and could aid in the fragmentation of lamellae.

In the case of a coating with an intermediate amorphous-phase content, the degradation is dictated by the more rapidly dissolving amorphous phase. The amorphous phase may be located adjacent to the substrate or interspersed throughout the coating. Small crystalline regions will be released as the amorphous phase is dissolved from the coating, but the removal of larger crystalline areas will occur after a longer time. The accelerated degradation indicates that in an infected site, where the pH is lowered, the implant can be rendered nonfunctional by preferentially resorbing the coating and hence compromising any established bone-coating contact.

**Apatite Precipitation.** A thin layer of crystalline apatite microspheres, as evidenced by x-ray diffraction, appear on the surface of the coating. This is a general feature observed on calcium phosphate coating in sintered HA,<sup>36</sup> tricalcium phosphate,<sup>37</sup> calcium carbonate,<sup>38</sup> calcium phosphate-based glass ceramics,<sup>39</sup> apatite-wollastonite-containing glass ceramics,<sup>40</sup> Bioglass (Gainesville, FL),<sup>41,42</sup> and bioac-

tive glasses.<sup>43</sup> In vitro results in this study indicate an increase in crystalline content after 4 weeks; this is shown in Fig 3 as the nucleation time. The induction time before apatite deposition is dependent on the presence of certain ionic species in the solution,<sup>44-46</sup> material purity, composition, specific coating surface area (ie, porosity and roughness), residual stresses within the coating, and the implant site. The apatite spheres will appear earlier for the amorphous coatings, which dissolve more readily to create the required calcium and phosphorus concentration for nucleation. This suggests that bone attachment will occur more rapidly with amorphous coatings.<sup>36</sup> Animal studies have indicated that carbonate is included in the precipitating apatite to form carbonapatite crystals.<sup>47,48</sup> This modified apatite has a higher solubility than HA and facilitates faster bone remodeling.

**Microstructural Considerations.** It has been shown that coating degradation occurs initially by cracking and dissolution. Dissolution is more dominant for amorphous coatings. Features such as cracks, pores, unmolten or respheroidized molten droplets, which are transferred to the coating, are sites where dissolution can begin to dislodge pieces of the coating into the solution. Lamellae can have isolated areas of no contact with the underlying material. These micropores, together with microcracks that may occur at the lamellae boundaries, explain the delamination of single lamellae. The lamellae size, which is related to initial particle size, is also an important parameter. Small splats confer a lower coating roughness and a larger interlamellae boundary area, which increases the number of sites for dissolution. The delamination of smaller coating fragments thus prolongs the life expectancy of the coating by creating a larger effective surface area, which assists in saturating the coating environment.

Most coatings are a combination of the amorphous and crystalline phases. Present research is directed at identifying the distribution of the amorphous phase, the size of crystalline areas within the coating, and the variation of the amorphous phase with coating thickness and at various locations on the implants.

**Clinical Implications.** Hydroxyapatite coatings on endosseous implants are subjected to chemical and cellular activity, physical stresses during function, and the risk of infection. All of these clinical factors affect the coating and modify the in vitro response, which will either lead to degradation of the coating-bone interface or to good fixation. The rough nature and lower crystallinity of HA coatings will enhance osteoblast attachment<sup>49-51</sup> but promote osteoclastic resorption during infection,<sup>52-54</sup> leading to coating resorption.<sup>55</sup> The more rapid changes at the surface

of coatings with a lower crystalline content is accompanied by higher rates of bone remodeling,<sup>56</sup> which leads to faster fixation. The effect of higher bone remodeling rates on bone quality remains to be determined.

Any study of the behavior of HA coatings must include *in vitro* tests. By evaluating the characteristics of amorphous and crystalline coatings, an HA coating can be designed that will accomplish a specific purpose in the body. There is much controversy concerning the long-term stability of the HA coating to the titanium substrate. It has been suggested that this interface may be the "weak link" of the coated implant and eventually will be the failure site of the HA-coated implant years after apparent "osseointegration." The amount of amorphous-phase content should be reduced to increase the longevity of the coating, but equally important is the location and distribution of the amorphous phase within the coatings.

It has been shown that the amorphous phase can encompass crystalline regions. The degradation of such a coating will occur by dissolution of the amorphous phase, followed by detachment of crystalline segments from the coating into the area around the implant. Small crystalline regions are more likely to prevent a foreign-body response and maintain sufficient attachment of the bone to the implant for stabilization. Based on this finding, an advantageous coating design will utilize the amorphous phase as the outer layer of the coating to promote faster bone attachment and ensure that crystalline material is adjacent to the substrate for good coating attachment. Removal of the amorphous phase could then be rapid to aid fixation, and further resorption of the crystalline layer will occur slowly under conditions of bone remodeling.

The performance of hydroxyapatite-coated hip appliances will undergo a similar course of resorption, being modified by the different biologic moieties, stress environment, bone type, and metabolism rate in that implant site. A cavity prepared for placement of a femoral stem is more intricate in geometry, and thus the surgical fit will be more difficult to produce. Any gap between the prosthesis and the bone can transport dislodged hydroxyapatite particles, resulting in third-body wear<sup>57</sup> between the femoral head and polyethylene inserts of acetabular cups. Reports of third-body wear suggest that HA-coated devices are no more a problem than the porous or cemented prosthesis.<sup>58</sup> A good hydroxyapatite coating will decrease the likelihood of third-body wear, prevent particle migration<sup>56-60</sup> by establishing bone attachment in a well-prepared cavity,<sup>61</sup> and provide less pain for the recipient by minimizing downward migration of the prosthesis.<sup>62</sup>

## Conclusions

The *in vitro* behavior of HA coating depends on its chemical phase and lamellae structures. Crystalline coatings are more stable than amorphous coatings. They show no signs of degradation except cracking, which is attributable to the release of residual stresses. Amorphous coatings undergo a weight loss, which has been shown to occur by de-adhesion of cracked lamellae and dissolution of lamellae on the coating surface. Crystalline apatite nucleates and grows in the form of spheres on both amorphous and crystalline coatings. The formation of apatite spheres appears first for the amorphous structure. The different mechanisms of degradation operating on amorphous and crystalline HA coatings may play an important role in the successful osseointegration with bone and the long-term maintenance of the coated implant.

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## References

1. Brånemark P-I. Osseointegration and its experimental background. *J Prosthet Dent* 1983;50:399-410.
2. Oral Implantology Glossary of Terms. American Academy of Implant Dentistry. *Implant Dent* 1986;12:284.
3. Schroeder A, Pohler O, Sutter F. Gewebereaktion auf ein Titan-Hohlzylinderimplantat mit Titan-Spritzschichtoberfläche. *Schweiz Mantszeitschr Zahnheil* 1976;86:713-727.
4. Meffert R. Implant therapy. In: Proceedings of the World Workshop in Clinical Periodontics. Chicago: The American Academy of Periodontology 1989;8-10.
5. Hench LL. Bioactive ceramics. In: Ducheyne P, Lemons J (eds). *Bioceramics: Material Characteristics Versus In-Vivo Behavior*. Boca Raton, FL: Annals of New York Academy of Science 1988;54.
6. Thomas K, Kay J, Cook S, Jarcho M. The effect of surface macrotexture and hydroxylapatite coating on the mechanical strengths and histologic profiles of titanium. *J Biomed Mater Res* 1987;21:1395-1414.
7. Parson J, Ricci J, Alexander H. Osteoconductive composite grouts for orthopedic use. In: Ducheyne P, Lemons J (eds). *Bioceramics: Material Characteristics Versus In-Vivo Behavior*. Boca Raton, FL: Annals of New York Academy of Science 1988;191.
8. Carlsson L, Rostlund T, Albrektsson B, Albrektsson T. Implant fixation improved by close fit. Cylindrical implant-bone interface studied in rabbits. *Acta Orthop Scand* 1988;59:272-275.
9. Soballe K, Hansen H, Rasmussen H, Pedersen M, Bunger C. Hydroxyapatite coating enhances fixation of porous coated implants. *Acta Orthop Scand* 1990;61:299-306.

10. Stephenson PK, Freeman MAR, Revell PA, Germain J, Tuke M, Pirie CJ. The effect of hydroxyapatite coating on ingrowth of bone into cavities in an implant. *J Arthroplasty* 1991;6:51-58.
11. Jansen JA, van der Waerden JPCM, Wolke JGC. A histological evaluation of the effect of hydroxyapatite coating on interfacial response. *J Mater Sci Mater Med* 1993;4:466-470.
12. Kay JF. Hydroxylapatite-coatings for non-precision implant placements. In: Horowitz E, Parr J (eds). *Characterization and Performance of Calcium Phosphate Coatings for Implants*, ASTM STP 1196. Philadelphia: American Society for Testing and Materials 194:149-162.
13. Klein CPAT, Wolke JGC, Vriesde RC, de Blicke-Hogervorst JMA. Cortical bone ingrowth in grooved implants with calcium phosphate coatings: A gap model study. *J Mater Sci Mater Med* 1994;5:569-574.
14. Maxian SH, Zawadsky JP, Dunn MG. Effect of Ca/P coating resorption and surgical fit on the bone/implant interface. *J Biomed Mater Res* 1994;28:1311-1319.
15. Clemens JAM, Klein CPAT, Dhert WJA, Rozing PM, de Groot K. Bone apposition on apatite coatings inhibited by large gaps. In: Andersson OH, Happonen R-P, Yli-Urpo A (eds). *Bioceramics 7*. London: Butterworth-Heinemann, 1994:201-205.
16. Dalton JE, Cook SD, Thomas KA, Kay JF. The effect of operative fit and hydroxyapatite coating on the mechanical and biological response to porous implants. *J Bone Joint Surg [Am]* 1995;77:97-110.
17. Tracy BM, Doremus RH. Direct electron microscopy studies of the bone-hydroxyapatite interface. *J Biomed Mater Res* 1984;18:719-726.
18. Sautier JM, Nefussi JR, Forest N. Ultrastructural study of bone formation on synthetic hydroxyapatite in osteoblast cultures. *Cells and Materials* 1991;1:209-217.
19. Bagambisa FB, Joos U, Schilli W. Mechanisms and structure of the bond between bone and hydroxyapatite ceramics. *J Biomed Mater Res* 1993;27:1047-1055.
20. Bonfield W, Luklinska ZB. High-resolution electron microscopy of a bone implant interface. In: Davies JE (ed). *Bone-Biomaterial Interface*. Toronto: Toronto University Press, 1991:88-93.
21. Garcia R, Doremus RH. Electron microscopy of the bone-hydroxyapatite interface from a human dental implant. *J Mater Sci Mater Med* 1992;3:154-156.
22. Listgarten MA, Lang NP, Schroeder HE, Schroeder A. Periodontal tissues and their counterparts around endosseous implants. *Clin Oral Implants Res* 1991;2:1-19.
23. Kay JF. Bone-hydroxylapatite bonding revealed at the ultrastructural level. *Orth Trans* 1994;18:796.
24. Gross KA. *Surface Modification of Prostheses* [thesis]. Australia: Monash University, 1990.
25. Gross KA, Berndt CC. Optimization of spraying parameters for hydroxyapatite. In: Blum-Sandmeier S, Eschnauer H, Huber P, Nicoll AR (eds). *2nd Plasma Technik Symposium*, vol 3. Lucerne: Plasma Technik, 1991:159-170.
26. Gross KA, Gross V, Berndt CC. Thermal analysis of the amorphous phase in hydroxyapatite coatings. *J Am Cer Soc* 1997 (in press).
27. Klein CPAT, Wolke JGC, de Blicke-Hogervorst JMA, de Groot K. Features of calcium phosphate plasma-sprayed coatings: An in vitro study. *J Biomed Mater Res* 1994;28:961-967.
28. Klein CPAT, de Blicke-Hogervorst JMA, Wolke JGC, de Groot K. Solubility of hydroxylapatite, tricalcium phosphate and tetracalcium phosphate coatings on titanium in vitro. In: Heimke G, Soltesz U, Lee AJC (eds). *Clinical Implant Materials, Advances in Biomaterials*, vol 9. Amsterdam: Elsevier Science Publishers B.V., 1990:277-282.
29. Bianchi L, Grimaud A, Blein F, Lucchese P, Fauchais F. Comparison of plasma-sprayed alumina coatings by RF and DC plasma spraying. *J Thermal Spray Technol* 1995;4:59-66.
30. Furedi-Milhofer H, Hlady V, Baker F, Beele R, Wikholm N, Kittelberger J. Temperature programmed dehydration of hydroxyapatite. *J Colloid Interface Sci* 1979;70:1-9.
31. de Bruijn JD, Klein CPAT, de Groot K, van Blitterswijk CA. The ultrastructure of the bone-hydroxyapatite interface in vitro. *J Biomed Mater Res* 1992;26:1365-1382.
32. Liu DM, Chou HM, Wu JD. Plasma sprayed hydroxyapatite coating: Effect of different calcium phosphate ceramics. *J Mater Sci Mater Med* 1994;5:147-154.
33. Wolke JGC, Klein CPAT, de Groot K. Plasma-sprayed hydroxylapatite coatings for biomedical applications. In: Bernecki TF (ed). *Thermal Spray Research and Applications*. Materials Park, OH: ASM International, 1990:413-417.
34. Whitehead RY, Lucas LC, Lacefield WR. The effect of dissolution on plasma sprayed hydroxylapatite coatings on titanium. *Clin Mater* 1993;12:31-39.
35. Radin SR, Ducheyne P. The effect of calcium phosphate ceramic composition and structure on in vitro behavior. II. Precipitation. *J Biomed Mater Res* 1993;27:35-46.
36. Hyakuna K, Yamamuro T, Kotoura Y, Oka M, Nakamura T, Kitsugi T, et al. Surface reactions of calcium phosphate ceramics to various solutions. *J Biomed Mater Res* 1990;24:471-488.
37. Adam P, Nebelung A, Vogt M. Verhalten von mit Tricalciumphosphatbeschichteten Titan implantaten bei der Behandlung mit Wasser von 80°C. *Sprechsaal* 1988;121:941-944.
38. Damien CJ, Ricci JL, Christel P, Alexander H, Patat J-L. Formation of a calcium phosphate-rich layer on absorbable calcium carbonate bone graft substitutes. *Calcif Tissue Int* 1994;55:151-158.
39. Blumenthal NC, Posner AS, Cosma V, Gross U. The effect of glass-ceramic bone implant materials on the in vitro formation of hydroxyapatite. *J Biomed Mater Res* 1988;22:1033-1041.
40. Neo M, Kotani S, Fujita Y, Nakamura T, Yamamuro T, Bando Y, et al. Differences in ceramic-bone interface between surface-active ceramics and resorbable ceramics. A study by scanning and transmission electron microscopy. *J Biomed Mater Res* 1992;26:255-267.
41. Hench LL, Paschall HA. Histochemical responses at a biomaterials interface. *J Biomed Mater Res* 1974;8:49-64.
42. Rehman I, Hench LL, Bonfield W. Comparison of hydroxycarbonate apatite layers on bioactive glasses with human bone. In: Ducheyne P, Christiansen D (eds). *Bioceramics 6*. London: Butterworth-Heinemann, 1993:123-128.
43. Andersson OH, Kangasniemi I. Calcium phosphate formation at the surface of bioactive glass in vitro. *J Biomed Mater Res* 1991;25:1019-1030.
44. Blumenthal N, Cosma V. Inhibition of apatite formation by titanium and vanadium ions. *J Biomed Mater Res* 1989;23:13-22.
45. Chander S, Fuerstenau DW. Interfacial properties and equilibria in the apatite-aqueous solution system. *J Colloid Interface Sci* 1979;70:506-516.
46. Okamoto Y, Hidaka S. Studies on calcium phosphate precipitation: Effects of metal ions used in dental materials. *J Biomed Mater Res* 1994;28:1403-1410.

47. Daculsi G, LeGeros RZ, Heughebaert M, Barbieux I. Formation of carbonate-apatite crystals after implantation of calcium phosphate ceramics. *Calcif Tissue Int* 1990;46:20–27.
48. LeGeros R. Biodegradation and bioresorption of calcium phosphate ceramics. *Clin Mater* 1993;14:65–88.
49. Bowers KT, Keller JC, Randolph BA, Wick DG, Michaels CM. Optimization of surface micromorphology for enhanced osteoblast responses in vitro. *Int J Oral Maxillofac Implants* 1992;7:302–310.
50. Keller JC, Zaharias R, Chang YL, Hurson S. Osteoblast responses to hydroxyapatite coatings of varying crystallinity [abstract 83]. *J Dent Res* 1995;22.
51. Maxian SH, Melican MC, Gross KA, Berndt CC, Zawadsky JP. Effect of hydroxyapatite crystallinity on coating dissolution and bone cell behavior [abstract]. 21st Annual Meeting of Society for Biomaterials. Minneapolis: Society for Biomaterials 1995:200.
52. de Bruijn JN, Bovell YP, Davies JE, van Blitterswijk CA. Osteoclastic resorption of calcium phosphates is potentiated in postosteogenesis culture conditions. *J Biomed Mater Res* 1994;28:105–112.
53. Basle MF, Chappard D, Grizon F, Filmon R, Delecrin J, Daculsi G, et al. Osteoclastic resorption of Ca-P biomaterials in rabbit bone. *Calcif Tissue Int* 1993;53:348–356.
54. Kieswetter K, Merritt K, Myers R. Effect of crystallinity of plasma sprayed hydroxyapatite coatings on microbial induced degradation In: Ducheyne P, Christiansen D (eds). *Bioceramics 6*. London: Butterworth-Heinemann, 1993:443–447.
55. Verheyen CCPM, Dhert WJA, Petit PLC, Rozing PM, de Groot K. In vitro study on the integrity of a hydroxyapatite coating when challenged with staphylococci. *J Biomed Mater Res* 1993;27:775–782.
56. Klein CPAT, Wolke JGC, de Blicke-Hogervorst JMA, de Groot K. Calcium phosphate plasma-sprayed coatings and their stability. An in vivo study. *J Biomed Mater Res* 1994;28:909–918.
57. Bloebaum RD, Dupont JA. Osteolysis from a press-fit hydroxyapatite-coated implant. A case study. *J Arthroplasty* 1993;8:195–202.
58. Bauer TW, Taylor SK, Jiang M, Medendorp SV. An indirect comparison of third-body wear in retrieved hydroxyapatite-coated, porous, and cemented femoral components. *Clin Orthop* 1994;298:11–18.
59. Rahbek O, Overgaard S, Soballe S, Bunger C. Hydroxyapatite coating might prevent pen-implant particle migration: A pilot study in dogs. *Acta Orthop Scand* 1996;67(suppl 267):58–59.
60. Onsten I, Carlsson AS, Sanzen L, Besjakov J. Migration and wear of a hydroxyapatite-coated hip prosthesis: A controlled roentgen stereophotogrammetric study. *J Bone Joint Surg [Br]* 1996;78:85–91.
61. Geesink RGT, Hoefnagels NHM. Six-year results of hydroxyapatite-coated total hip replacement. *J Bone Joint Surg [Br]* 1995;77:534–547.
62. Soballe K, Toksvig-Larsen S, Gelineck J, Fruensgaard S, Hansen ES, Ryd L, et al. Migration of hydroxyapatite coated femoral prosthesis. *J Bone Joint Surg [Br]* 1993;75:681–687.