Hydroxyapatite coatings in prosthetic joints

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Papers in the literature that discuss HA-coated implants refer to the technical features of this material. Nevertheless, the significance of each of these features for the implant's performance is scarcely known. The results of *in vitro* and *in vivo* studies indicate that HA coatings should have low porosity, good coating-to-surface adhesiveness, medium to high crystallinity and high levels of chemical and phase stability. These characteristics should confer the HA calcium phosphate layer enough chemical stability to permit the gradual fixation of the implant as well as favorable bioactive characteristics.

Key words: *hydroxyapatite, fixation, prosthesis.*

Los recubrimientos de hidroxiapatita en las prótesis articulares

Los artículos publicados sobre implantes recubiertos de hidroxiapatita hacen referencia a las características técnicas de este material. Sin embargo, es poco conocida la importancia de cada una de estas características en el rendimiento del implante. Los resultados de los estudios *in vitro* e *in vivo* indican que los recubrimientos de hidroxiapatita deberían tener una porosidad baja, buena adhesión al sustrato, una cristalinidad de media a alta, y una estabilidad química y de fase altas. Estas características deberían conferir a esta capa fosfocálcica la estabilidad química suficiente para dar tiempo a la fijación del implante y unas características bioactivas favorables.

Palabras clave: *hidroxiapatita, fijación, prótesis.*

Hydroxyapatite (HA) coatings in joint prostheses play a role in accelerating the bone formation process since they are formed by a calcium phosphate material that contains practically the same calcium and phosphorus proportions as human bone. This inorganic material layer accelerates, through the conventional cell signaling processes, the adsorption of extracellular matrix proteins to subsequently promote the adhesion, proliferation and differentiation of osteoblasts around the material.

Apart from a bioactive role, this layer has other secondary effects that improve on the performance of metal in the physiological environment, minimizing or downright preventing ion release and reducing the danger of corrosion.

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These types of HA-coated prostheses are made of metal (stainless steel and titanium or chromium-cobalt alloys) given the mechanical strength and the toughness of this material; the function of the metal is specifically structural. The prostheses also contain a bioactive layer whose function is speeding up biological prosthetic fixation.

Metal HA-coated implants have been in use since the late 1980s and several authors have published studies on them. We can divide these studies between studies dealing with the basic science and clinical studies. In the last few years, a series of parameters and data have been described in the studies devoted to basic science that can aptly be used to provide a scientific typology of the types of materials used. However, this data is often overlooked by clinicians, since very few of them have a clear understanding of the technical characteristics of the implants they use in their practice.

Several studies have looked at the different types of HA-coatings applied to metal, at the different techniques used in their application and at the different classes and proportions of calcium salts employed. The performance of these coatings in relation with living tissue varies greatly. For that reason, when speaking about an HA coating we might ask. «But what kind of HA?

HISTORICAL PERSPECTIVE

The first HA-coated implants were developed to be used in dental implantology. In patients without any teeth where implants could be fixated, the only solution was using metal stems in the maxilla. These implants tended to loosen with time and one of the strategies used to improve fixation to bone was calcium phosphate coating. Subsequently it was found out that these implants also came loose as a result of the septic nature of the oral cavity. But the idea was used in implants placed in such completely sterile areas as joints. There are clinical studies that report preservation of the fixation at nearly 15 years[1].

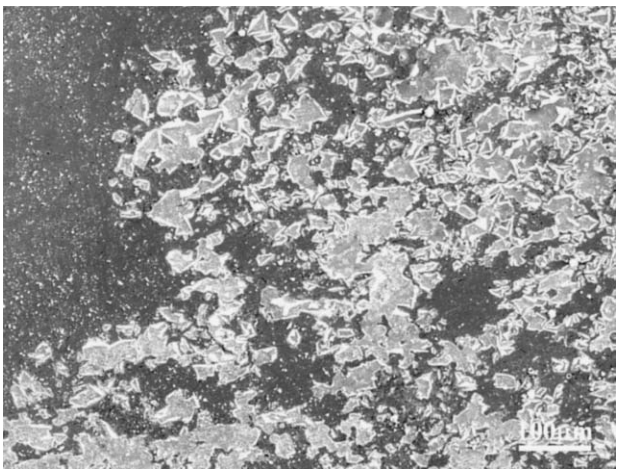


Figure 1. *Corrosive materials in a prosthesis coated with a bioactive film. Corrosion caused by 316L stainless steel covered by a calcium phosphate layer with silicon. Silicon-chromium compounds were formed which were intolerable to the human body and thus disturbed the biological performance of the prosthesis.*

BASIC CONCEPTS ON HYDROXYAPATITE IMPLANTS

The characteristics of HA coatings most commonly cited in the literature are their roughness, thickness, high proportion of calcium salts, purity, porosity, crystallinity as well as the way in which the coating is applied. Also features related to the implant design are mentioned such as the location of the HA coating, the metal alloy onto which it is applied and the nature of the substrate surface (smooth, fiber-mesh, microparticulate, etc.).

The bioactive layer that is applied must meet a series of requirements:

Chemical stability

The coating should not disintegrate in the physiological environment in the short term or react with the substrate metal. Reaction with the metal could have catastrophic results since reaction by-products are in general cytotoxic and the metal's mechanical properties may decrease to the extent that its very mechanical integrity may be put at stake (fig. 1). The coating should not alter the chemical composition of the substrate, which should remain homogeneous throughout its structure[2].

Mechanical stability

The coating should exhibit good adherence to the substrate so that the structural integrity of the bioactive layer is not affected when the surgeon introduces the prosthesis. Furthermore, the layer must not contain any cracks that may embrittle it[3-5].

Several methods have been used to coat the substrate: the plasma-*spray* method, laser ablation, sol-gel, hot isostatic compaction, high speed thermal spray coating, ion beam coating, etc., with the first two ones being the most frequently used at present.

The most usual calcium phosphate coating method is plasma *spray,* which is based on producing calcium phosphate plasma by means of powerful energy sources and projecting the plasma (at temperatures above 9.000°C) onto the metal substrate (fig. 2). This process can be carried out in air or in vacuum. Calcium phosphate is applied onto the metal without covalent or ionic bonding, which would produce maximum levels of adhesion, but rather through interaction forces and by mechanical anchors. As this bond is not very strong, one some occasions the calcium phosphate layer might flake off under shear stress.

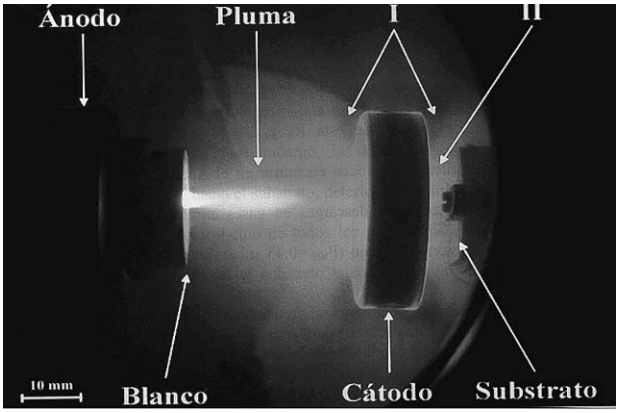
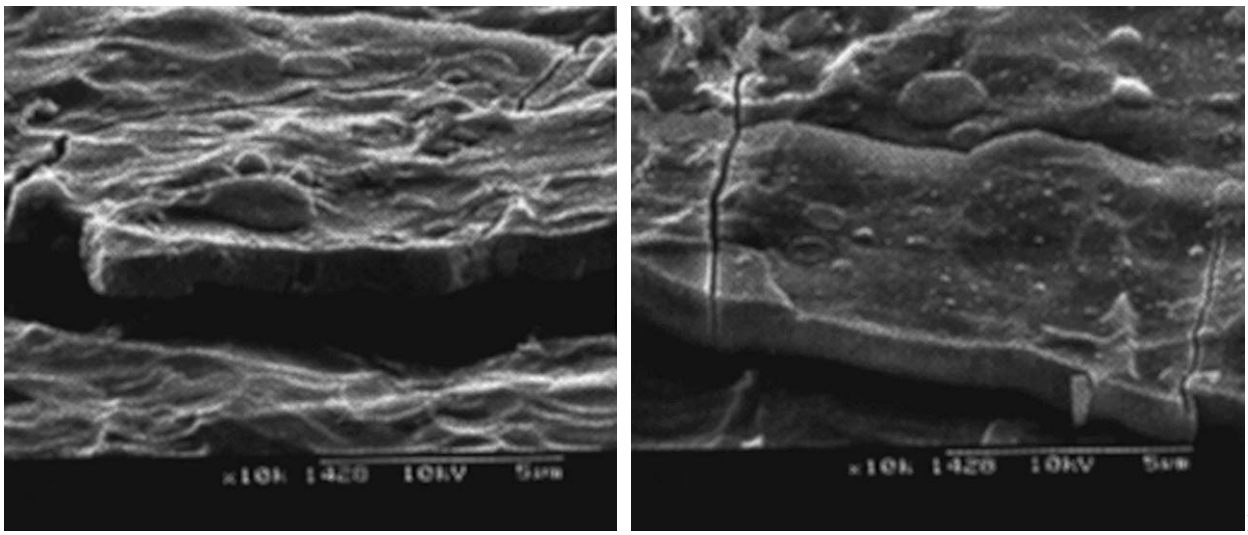


Figure 2. *Plasma spray. An electric field projects calcium phosphate particles at great speed onto the implant's metal surface.*

In general, implants are sand blasted with abrasive particles, which confer them with a level of surface roughness that will be fundamental for the mechanical fixation of the bone. Afterwards, the calcium phosphate is applied, which covers the rough implant providing the biological fixation needed.

The coating material is not crystallized hydroxyapatite, since the cooling off process from very high temperatures to



A B

Figure 3. *The image shows that no bond exists between the calcium phosphate and the substrate (A) y (B). Cracks can be observed on the calcium phosphate surface.*

room temperature occurs is a short period of time, which is insufficient to form an orderly structure on the whole of the sophisticated crystallographic structure of the HA coating. Therefore a significant part of the coating will contain an amorphous kind of calcium phosphate with no crystalline organization. It must not be forgotten that this amorphous material is more soluble than HA and will have different properties from those of the crystalline phase.

Furthermore, it must be taken into account that the rapidity with which the calcium phosphate coating is formed produces cracks in the coating given the poor thermal shock resistance of ceramic materials (fig. 3). As we know, ceramic materials are brittle and incapable of absorbing energy in their structure. For this reason, the changes in volume and the internal stresses that occur in the solidification of calcium phosphate cannot be absorbed, leading to the formation of cracks on the surface of the material. This increases the brittleness of the coating.

It should also be stated that, in the absence of a chemical bond, there are vacuum areas between the metal and the coating. These areas are prone to bacterial colonization, which can propagate throughout the voids that exist between the metal and the coating (figs. 3 and 4). This fact is important for dental implant, but not so much for joint prostheses.

The process whereby the HA binds to the metal implant, in particular the cooling off rate, will determine the proportion of amorphous salts to crystalline HA as well as crystallinity.

Other techniques for applying HA to a surface, such as laser ablation, are technically more complicated and costly but could allow a better control of the characteristics of the HA coating.

These factors must be taken into account when it comes

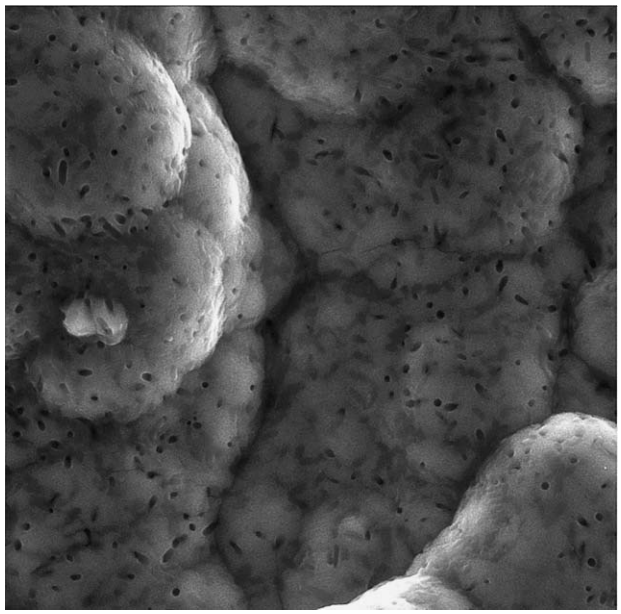


Figure 4. *Bacterial colonization on the calcium phosphate layer.*

to clinical applications. Manufacturers keep making improvements to their coatings and new technologies are now available to enhance their biological and mechanical performance.

HOW DOES IT ACT?

Implantation into bone of extraneous load-transferring elements requires very strong bonding of the material to avoid loosening. The weak link in load transmission is the implant/bone interface. HA coatings make it possible for

the bone to bind to the implant as if the latter was a graft.

HA is biocompatible, osteoconductive[6,7], bioactive and bioresorbable. These properties stimulate the interaction between implant and bone to accelerate and induce prosthetic incorporation. The mechanism at work is not clear, but it appears to be related to the binding of cells to the HA layer. These cells differentiate into osteoblasts and start creating bone matrix. The latter will grow from the surface of the implant to the host bone. Once this gap has been filled, the bone matrix will mature into lamellar bone, creating an implant/host bone bond without fibrous tissue interposition[8].

DISCUSSION

In a study with dogs, Bragdon[9] demonstrated that ingrowth in HA-coated hip prostheses 20% higher than the same prosthetic model with porous coating after 3 weeks. But after 6 weeks, there was no difference between noth groups of animals. The study does not mention any of the characteristics of the HA used, except that they used the plasma *spray* method.

A post-mortem study of 58 hip prostheses comparing a single stem model with three different coatings showed greater osteointegration in the group where HA was used[10].

Amorphous calcium salts are reabsorbed faster than crystalline HA[11]. The coating of a metal rich in these salts will react rapidly with its osseous environment, but possibly at a faster rate than that at which it can incorporate the implant. An excessively rapid disintegration of the HA coating could result in a fibrous implant/bone apposition. Calcium triphosphate dissolves faster in a neutral pH medium than crystalline HA, with more amorphous types of HA increasing the material's dissolution rate. A coating rich in crystalline HA will take longer to reabsorb and, therefore, the incorporation of such an implant will also be slower. This means that an appropriate balance between amorphous calcium salts and HA is necessary to allow rapid and lasting implant incorporation[12].

It is generally agreed that HA purity should be as high as possible (above 90%), with a calcium/phosphorous ratio of 1.67. However, no consensus has been reached as to its degree of crystallinity, which ranges from 50 to 90% in the different kinds of implants available on the market.

A modification of the plasma *spray* technique would allow the creation of a structure gradient. This means that the outermost layer of the coating sould be rich in fast-dissolving amorphous salts, whereas inside there would be a higher proportion of crystalline HA to facilitate osteointegration. Thus, the most superficial layer would produce rapid bone apposition whereas the deepest one would provide a solid and long-lasting bond[13].

The thickness of the HA layer will affect incorporation in a similar way as its composition. An overly thin layer will reabsorb faster without allowing sufficient bone ongrowth around it. On the other hand, an overly thick layer could prove more brittle and therefore might flake off during surgical implantation. 25-100 Ìm coatings provide good stability, whereas those equal too r thicker than 150 Ìm are more brittle[14]. The HA coating of most implants on the market has a thickness of 50-70 Ìm.

The microstructure of HA coatings depends on the technique used in their manufacturing process. In this process, HA particles are applied at high speed and temperature. When impacting on the implant, they can adopt a more-or-less flattened spheroidal shape depending on the technique used. These shapes will determine the porosity of the HA-coating. Porosity entails the presence of small holes through which osteoblasts may proliferate in order to bind the fixate to the bone[15].

The surface characteristics of the metal will determine the contact surface between implant and bone; the greater the irregularity, both macroscopic and microscopic, the larger the contact area between the implant and the surrounding bone, and the firmer its long-term fixation. The microscopic surface irregularity is defined by its roughness. In *in vitro* titanium and HA-coated implants, medium and high roughness levels cause a higher cell reaction, whereas extra high roughness causes a lower proliferation[16]. Roughness determines whether the surrounding bone grows faster or slower towards the implant in order to incorporate it.

The presence of more or less voids between the coating and the implant will determine the HA-coating's proneness to delamination; this phenomenon can occur notable during surgical implantation since significant shear stresses are created when a prosthetic component impacts on a bone surface. The different implant coating techniques provide for a stronger or weaker bonding between the substrate metal and the HA layer. Crystallinity is also a key factor. After implantation and prosthetic incorporation, one of the factors that could cause delamination in well-integrated prostheses could be differences between the bone and the metal in terms of their elasticity patterns; these could lead to micromotion on weight-bearing. Under these circumstances, the HA layer should stay bound to the newly formed bone and leave a gap between HA and metal[17]. Subsequently, remodeled bone could take up this space again making the prosthesis stable[6]. In an animal lamb model, this remodeling process was completed at 200 days, although the prostheses became stably incorporated at 90 days[18]. Nevertheless, in areas in direct apposition with the joint cavity, polyethylene and metals particles could accumulate, which seem to favor or accelerate HA cell degradation HA[19] without affecting the clinical performance of the implant. New techniques are being developed to decrease the delamination phenomenon, for eg. by interposing a layer of titanium oxide[20].

Further to the surgical implantation of a HA-coated prosthesis a process of incorporation into the host bone be-

gins, similar to what happens in the case of a fracture, where bone trabeculae appear between the margins. In the prosthetic context, the trabeculae become visible between host bone and the HA coating, and afterwards the whole of the tissue is remodeled over time. This creates a bone envelope that is in close apposition to the metal implant and stabilizes it[6,7,10,21]. If the implant has irregularities on the surface, its stability will increase, whereas if it is completely smooth, loosening may occur within the «envelope», which will gradually destroy the trabecular microstructure in contact with the implant, giving rise to a situation comparable to a pseudoarthrosis. This would be an aseptic loosening of a prosthetic component which had initially achieved firm bone ingrowth[22,23].

The appearance of a fibrous membrane between implant and bone seems to be more closely related to micromotion[9] than with the type of bond (HA or porous coating).

The weak link in HA-coated prostheses could be the mechanical bond that exists between the metal and the HA layer. It seems that the plasma *spray* technique, performed at high temperature and with rapid cooling off, is apt to alter both the chemical composition and the crystalline structure of HA, resulting in an amorphous and more soluble calcium phosphate component. In addition, the degree of surface roughness of the implant influences the implant/HA mechanical bond on the one hand, and the HA/bone apposition on the other[24]. Manufacturers are trying to improve these characteristics by looking into new ways to apply the bioactive components of the plasma *spray*[20,25] and trying to come up with new coating methods such as precipitation techniques, which could provide a more crystalline HA layer applied at room temperature[26], and laser surface alloying[27]. Another line of research is based on the incorporation of bioactive substances to HA coatings in order to increase cell adhesion and bone ingrowth in the surrounding area[28].

Nowadays, the most commonly used technology used to apply HA-coatings is plasma spraying. It seems that other technologies could improve the binding characteristics of this calcium phosphate layer until a certain degree of chemical binding is achieved through several apposition layers (technique described by de T. Kokubo)[29]. However, these techniques must be perfected and made more affordable. Plasma spray can be applied in air or in vacuum. The vacuum technique offers the possibility of altering the roughness and the porosity of the implant. This will make it possible to obtain implants with coating that features a stronger bond to the implant as well as a degree of bone ongrowth that rapidly binds the implant to the bone.

A review of the specifications of the HA on several implants used in some clinical studies shows that there exist differences between them and, especially, that many of these papers do not refer to these characteristics (table 1). All the studies listed on the table refer to HA-coated implants where the plasma *spray* method was used, although the majority do dot specify if application was in air or in vacuum. Differences between implants regarding their HA specifications are difficult to relate to their clinical results since many factors are involved. The literature on hip implants contains more studies than that on knee or ankle implants as well as follow-up periods of up to 10 years (tables 2 and 3).

Most clinical studies are optimistic about the long-term performance of HA-coated prostheses. However, differences have been found between cemented and uncemented prostheses[56]. These discrepancies can probably be attributed to differences in the characteristics of the HA coating, in the patient populations studied or in the designs of the prostheses analyzed.

Clinical studies on HA-coated hip prostheses show longer survivorship rates for femoral ítems than for acetabular cups[32-47]. The reported survivorship of the former is 99-100% at 10 years and goes down to 92% in flawed designed models[35]. Reported cup survivorship is 80-100% at 10 years. This fact is attributed to the different load-sharing pattern of both components.

The use of HA coatings is also extending to total knee prostheses, with good results as in the hip, although there is scarce published literature on the subject.

The use of HA coatings is also becoming a common occurrence in ankle prostheses. In this anatomical location, clinical studies show a longer survivorship for these implants as compared with those using other techniques for bone fixation[54].

Unlike cemented prostheses, the use of coated, implants forces the surgeon to achieve a perfect match in the bone bed in order to permit primary stability and early incorporation. That is the reason why the cutting material must be accurate.

The design of joint prostheses determines their performance further to osteointegration. That is why incorporation and long-term stability should not be entrusted solely to HA coatings, although it must be admitted that the latter help overcome small technical errors with respect to the adaptation of implants to the bone bed[57]. HA coatings have shown themselves effective to compensate for any design deficiencies in the implant's design[5].

CONCLUSIONS

An HA coating can disappear from a prosthesis as a result of osteoclast resorption during the bone remodeling process, chemical dissolution, delamination resulting from weaker mechanical adhesion to the metal and mechanical abrasion due to a lack of primary stability[6]. Nevertheless, this does not imply that the implant will come loose, but rather that it becomes involved in the physiological bone remodeling process.

Table 1. Hydrohyapatite (HA) specifications in several clinical studies on hip prostheses

Author	Year	Model	Cases	Purity	Crystallinity	Porosity	Thickness (mm)	HA roughness (mm)	Metal roughness (mm)	Metal	Tensile bond strength (MPa)
Crawford[30]	2004	Restoration	59	NA	NA	NA	NA	NA	NA	NA	NA
Gosens[31]	2003	Mallory-Head	63	NA	62%	NA	55	NA	21	Ti-6Al-4V	NA
McNally[32]	2000	Furlong	100	NA	NA	NA	NA	NA	NA	NA	NA
Moilanen[33]	1996	SLF cup	69	> 98%	> 75%	NA	80-120	NA	NA	CoCr	20-40
Oosterbos[34]	2004	ABG	100	NA	> 75%	< 10%	60 ± 20	3-4	NA	pure Ti	62-65
Palm[35]	2002	LS	12	98%	70%	NA	200	NA	NA	Ti-6Al-4V	40
Park[36]	2003	SROM	20	NA	NA	NA	50	NA	NA	NA	NA
Rasquinha[37]	2002	Ranawat-Burstein	92	95%	62%	99%	50-75	NA	NA	Co-Cr + Ti layer	NA
Reikeras[38]	2003	Corail femur	291	> 97%	> 50%	< 10%	155-35	7.5-9.5	4-6	NA	>10
Reikeras[39]	2002	Corail cup	191	> 97%	> 50%	< 10%	155-35	7.5-9.	4-6	NA	>10
Rohrl[40]	2004	Reflection cup	22	96%	66%	NA	30-50	NA	NA	NA	44.6-73.8
Rokkum[41]	2003	Corail	10	> 98%	50-70%	NA	155 ± 35	10	NA	NA	20-30
Skinner[42]	2003	Freeman (2 versiones)	NA	NA	NA	NA	80-120	NA	3	CoCr & Ti	NA
Soballe[43]	1993	Biometric	15	NA	NA	NA	NA	NA	NA	NA	NA
Tonino[44]	2001	ABG	6 > 90%	> 75% < 10	60 ± 30	5 ± 1	NA	Ti-6Al-4V	62-65		
Won[45]	2004	APR	17	98%	NA	NA	55	NA	4.8-8.4	Ti6-Al4-V	NA

NA: not available.

Table 2. Hydroxyapatite (HA) specifications in several clinical studies on knee prostheses

Author	Year	Model	Cases	Purity	Crystallinity	Porosity	Thickness (mm)	Roughness (mm)	Metal femur	Metal tibia	Tensile bond strength (MPa)	Density
Gejo[46]	2002	NexGen	96	70%	NA	NA	70	NA	CoCr	Ti-6Al-4V	NA	NA
Murty[47]	2003	Freeman-Samuelson	36	> 98%	> 75%	NA	80-120	NA	NA	NA	20-40	NA
Nelissen[48]	1998	Interax	10	> 90%	> 90%	NA	60 ± 30	NA	NA	NA	NA	90 ± 2%
Onsten[49]	1998	PFC	50	95%	62-72%	40% (tibia)	55	425-710 (tibia)	NA	Ti-6Al-4V	NA	NA
Petersen[50]	2005	Interax	8	NA	NA	NA	NA	NA	NA	NA	NA	NA
Regner[51]	2000	FS	25	> 98%	88%	15-20%	150-250	NA	NA	NA	NA	NA

NA: not available.

Table 3. Hydroxyapatite (HA) specifications in several clinical studies on ankle prostheses

Author	Year	Model	Cases	Purity	Crystallinity	Porosity	Thickness (mm)	Roughness (mm)	Metal talus	Metal tibia	Tensile bond strength (MPa)	Ca/P
Anderson[52]	2003	STAR	51	NA	NA	25-35%	100 + 25	75-200	NA	NA	NA	1:67
Bonnin[53]	2004	Salto	93	NA	NA	NA	200	NA	NA	NA	NA	NA
Kofoed[54]	2004	STAR	25	NA	NA	NA	NA	NA	CrCoMo	CrCoMo	NA	NA
Hintermann[55]	2004	Hintegra	122	NA	NA	20%	Double layer	NA	CoCr	CoCr	NA	NA

NA: not available.

The physical-chemical characteristics of the HA coating on joint prostheses play a role in their incorporation to the bone and need to be taken into consideration when performing a clinical assessment of implants. In the same was as we cannot regard these implants merely as uncemented prostheses, the different HA characteristics should be stated in the published studies on prostheses with this coating.

HA coatings in joint prostheses help accelerate and improve their bonding to bone thanks to their bioactive and osteoconductive properties.

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Conflict of interests

The authors have declared that they have no conflict of interests.