



A review of plasma-assisted methods for calcium phosphate-based coatings fabrication [☆]

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ABSTRACT

The review is focused on the latest achievements in the field of plasma-assisted fabrication of biocompatible CaP-based coatings for medical implants with the emphasis on the coatings composition, structure, mechanical and biological performance. The discussed properties of biocompatible CaP coatings have been recently prepared using the most frequently applied plasma-assisted techniques such as plasma spraying (PS), radio-frequency (RF) magnetron sputtering, pulsed laser deposition (PLD), and ion beam-assisted deposition (IBAD). The review shows that plasma-assisted fabrication allows us to prepare dense, homogeneous, pore-free and high adherent biocompatible coatings able to prevent the leaching of toxic ions from metal to the surrounding tissues or rough and porous coatings capable of stimulating osteogenesis of a new bone. The main advantages and limitations of the described techniques of CaP-based coatings fabrication are presented as well as the most important challenges and critical issues are highlighted.

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[☆] Dedicated to the blessed memory of Dr. Vladimir Pavlovich Yanovskiy.

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1. Introduction

Metallic biomaterials like stainless steel (SS), cobalt-based alloy, titanium (Ti) and its alloys are widely used as artificial hip joints, bone plates and dental implants due to their excellent mechanical properties and endurance [1]. However, there are some problems associated with the metallic implants including corrosion and wear in biological environments resulting in ions release and accumulation of wear debris, poor implant fixation owing to the lack of osteoconductivity and osteoinductivity, and infections due to bacterial adhesion and colonization at the implantation site. Because of poor osteoconductivity, metallic implants often get encapsulated by fibrous tissue prolonging the healing time [2]. To overcome these surface-related problems, a variety of surface modification techniques have been used on metallic implants, including chemical treatment, physical and biological methods [3,4]. Over the last decade, biomaterials research has been focused on the improvement of implant design features in an attempt to accelerate bone healing at early implantation times. Considering that the implant surface is the first part of the implant that interacts with the host, surface modification has been essential in enhancing biocompatible and osseointegrative properties of the implant [4,5]. Hydroxyapatite (HA, $\text{Ca}_{10}(\text{PO}_4)_6(\text{OH})_2$) is the main chemical constituent of bone tissue (~70%) and has been widely employed in non-load-bearing applications, as a bioactive material with desirable bone response [6–9]. However, due to the very brittle nature of bulk HA ceramics, it cannot be used in orthopedic devices that must withstand substantial forces during their expected lifetimes. Still, as a coating HA allows the significant improvement of the metallic implants osteoconductivity as it is chemically very similar to inorganic bone matrix [10–15].

It is established that the HA coating must meet the minimal requirements as described by the U.S. Food and Drug Administration (FDA) and the International Organization for Standardization (ISO) [16–19]. A variety of plasma-assisted techniques have been employed to obtain CaP-based, most frequently HA, coatings with desirable features including powder as well as suspension or liquid plasma spraying (PS) [20–41], radio-frequency (RF) magnetron sputtering [42–64] or direct current (DC) magnetron sputtering [65,66], pulsed laser deposition (PLD) [67–81] or combination of different techniques [82]. Furthermore, there are various ion beam techniques, including ion implantation [83–85], ion beam sputtering [86,87], ion beam dynamic mixing (IBDM) [84,88], and ion beam-assisted deposition (IBAD) [89–104]. Though the IBAD technique could not utilize a plasma source to generate an ion beam, this technique is included here since the basic principles of CaP thin film deposition using IBAD and their characteristics can be compared to those of plasma-based techniques [105]. Currently several types of biocompatible CaP-based coatings are prepared: pure HA [10,20,57,58,106–111], Si-containing HA (Si-HA) [13,27,108,112–119], Sr-doped HA [120–123], Mg-substituted HA [114], alendronate HA [122,124], carbonated HA [14,75,114], fluorinated HA [45,106,125,126] and antibacterial Ag-containing HA (Ag-HA) [3,98,100,127–130]. Plasma processes allow adjusting surface properties of solids with negligible effect on their bulk [131]. In addition, it has recently been shown that plasma-based technology is very promising as it can modify the surface properties, even creating a nano-sized surface topography [111,132]. Additional information on the methodologies for CaP ceramic coatings preparation and their performance can be found elsewhere [13,133].

2. The most frequently used plasma-assisted techniques to prepare a CaP coating

An overview of the most-frequently applied plasma-assisted techniques to deposit CaP-based coatings is given in Table 1. Typically prior to the coatings deposition the substrates are cleaned ultrasonically in an acetone and ethanol bath to remove dirt, oil and other

contaminants adhering to the surface [105,134,135]. They can be chemically pre-treated [101,136–141], and sand- or grit-blasted [101,137,138,142–144]. Laser surface treatment methods can also be used [145,146]. The CaP- or HA-based coatings are usually prepared on the surface of Ti6Al4V [11,29,54,78,81,102,108,110,117,126,129,147–155], Ti [2,14,28,33,38,39,49,57,71,75,102,116,156–163], stainless steel 316L SS [26,164–168] or 304 SS [169], Ti–24Nb–4Zr–7.9Sn alloy [24], Ti–35Ta–15Zr [47], Ti5Al2.5Fe [170–172], NiTi [44,57,58,73,173,174], nanotubular Ti–35Nb–xHf alloys ($x=0, 3, 7, 15$ wt.%) [175], Al_2O_3 [95,157], Mg alloy AZ31 [176], ultra-high-molecular-weight polyethylene (UHMWPE) [177], polyether ether ketone (PEEK) [178], and polymethylmetacrylate (PMMA) [179].

2.1. Radio-frequency (RF) magnetron sputtering

For the first time RF magnetron sputtering was used to prepare HA coating by the research group of Yamashita [180], Jansen, Wolke et al. [55,59,61,62]. Sputtering is a process whereby atoms or molecules of some materials are ejected in a vacuum chamber by bombardment with high-energy ions [13,105,135,181]. The typical setup for the preparation of CaP-based thin films (Fig. 1) includes vacuum chamber, RF generator, matching network, magnetron, and cooling system. Typically, RF magnetron sputtering employs a sinusoidal wave generator operating at 13.56 MHz [43,112,150,182,183], 5.28 MHz [57,58,111] or 1.78 MHz [170,184]. The use of a matching network and a controller allows the RF supply to match the generator output impedance to the impedance of the cathode and anode. The parameters that directly affect the quality and integrity of CaP coating include discharge power, gas flow rate, working pressure, substrate temperature, deposition time, post-heat treatment or negative substrate bias [10,43,105,111,134,135,156,157,161,165,183,185]. The substrate can be kept at a constant temperature during the deposition process (e.g. 100 °C) [134,165], or be subjected to plasma irradiation without any additional external heating [57,58,111,179]. Different types of CaP-based coatings are deposited, such as pure HA [10,53,57,58,111], Si-HA [115,119], carbonated HA [14], and Zn, Mg, and Al-doped CaPs [49].

2.2. Plasma spraying (PS)

During the 1980s and 1990s, pioneering experiments with PS to prepare biocompatible HA films were undertaken by Newesley and Osborn [186], de Groot, Geesink and Klein [36,187,188], Soballe et al. [189], Geesink and Manley [190], Zyman et al. [191–193], Cook, Thomas and Jarcho [194,195], and others [196–198]. There are many thermal spray processes, e.g. PS (atmospheric plasma spraying (APS), vacuum plasma spraying (VPS), suspension plasma spraying (SPS), liquid plasma spraying (LPS), etc.), high-velocity suspension flame spraying (HVSFS), high velocity oxy-fuel (HVOF), gas tunnel type plasma spraying (GTPS), detonation gun spraying etc., which are elaborated to fabricate a bioactive CaP-based coating [41,86,199–212]. A novel cold spraying method for the formation of HA coatings has been proposed [213]. However, powder plasma spraying (PPS) is currently the most frequently applied technique to prepare biocompatible CaP coating [2,3,13,63,110,126,181,210,214,215]. PS can be used as a so-called thermal printing to prepare separate deposits of CaP for studying mechanical compatibility between a coating and a substrate [216,217].

A schematic setup and an example of actual experimental conditions during the gas plasma spray of HA powders is shown in Fig. 2. During PS, usually at atmospheric pressure (APS) [26,40,218–220] or in the vacuum (VPS or low-pressure plasma spraying (LPPS)) [31,108,116,129,221], the precursor material to be deposited (feedstock) – typically as powder (PPS) [33,110,168], sometimes as either a liquid (LPS) [40,41,114,222] or a suspension (SPS) [21,32,37,222–224] is introduced into the plasma jet, emanating from a plasma torch [13,31]. The APS coatings are relatively thick (about 200–300 μm) and porous. The composition of plasma gas (mostly Ar/He/ H_2 / N_2), gas flow rate, plasma gun input power, spray

Table 1

The most frequently applied plasma-assisted techniques to deposit CaP-based coatings and their characteristics. * – variations are possible due to different deposition control parameters.

Method	Thickness*, μm	Main advantages	Main limitations	References
PPS	~30–300	High deposition rates; low cost; regarded as the most efficient and economical technique; coatings usually have micro-rough surface and porosity to enhance the adhesion of osteoblast cells and their subsequent proliferation; in most cases tensile adhesion strength above 15 MPa	Line-of-sight technique; expensive, high temperatures induce decomposition; rapid cooling produces cracks in coatings; poor control of chemical and physical coating parameters; lack of uniformity of the coating thickness; poor control of biodegradation	[2,3,6,10,13,37,39,110,153,210,215,237,263,295]
LPS and SPS	~5–50	High deposition rates; pure (only HA phase), crystalline, both nearly fully dense and highly porous coatings can be obtained; excellent control on the coating microstructure (including OH^- groups); tensile adhesion strength ~17–20 MPa	Line-of-sight technique; expensive; high temperatures induce decomposition; lack of uniformity of the coating thickness	[30–32,37,40,41,207,210,223,224]
RF magnetron sputtering	~0.04–3.5	Uniform coating thickness; dense pore-free coating; ability to coat heat-sensitive substrates; high-purity films; ability to control the coating structure (amorphous or crystalline) and the Ca/P ratio; bonding strength of the coating exceeds 30 MPa	Line-of-sight technique; expensive; time consuming due to low deposition rate; in most cases Ca/P ratio of the coating is higher than that of synthetic HA due to P_2O_5 evaporation and coating resputtering effect	[3,6,10,13,53,57,58,111,134,161,165,277,278,440]
Laser ablation (or PLD)	~0.05–10.00	Coatings by crystalline and amorphous phases; dense and porous with controlled phases and Ca/P ratios; MAPLE further increases the variety of molecules and macromolecules, in particular heat-labile compounds which can be co-deposited with CaPs	Line-of-sight technique; expensive; high substrate temperature (usually 350–750 °C) is necessary to prepare a crystalline HA coating	[3,6,10,11,13,74,75,77,78,122,125,159,179,245]
IBAD	~0.03–4	Uniform coating thickness; high reproducibility and controllability over microstructure and chemical composition; dense pore-free coating; bond strengths of the coatings are enhanced by atomic bonding at the interface (85–89 MPa); tensile bond strength ~70 MPa	Line-of-sight technique; expensive; as-deposited CaP coating is amorphous, which leads to high dissolution rate in biological fluids; difficult to obtain crystalline as-deposited HA film	[3,5,98–102,138,149,215,252–254,260]

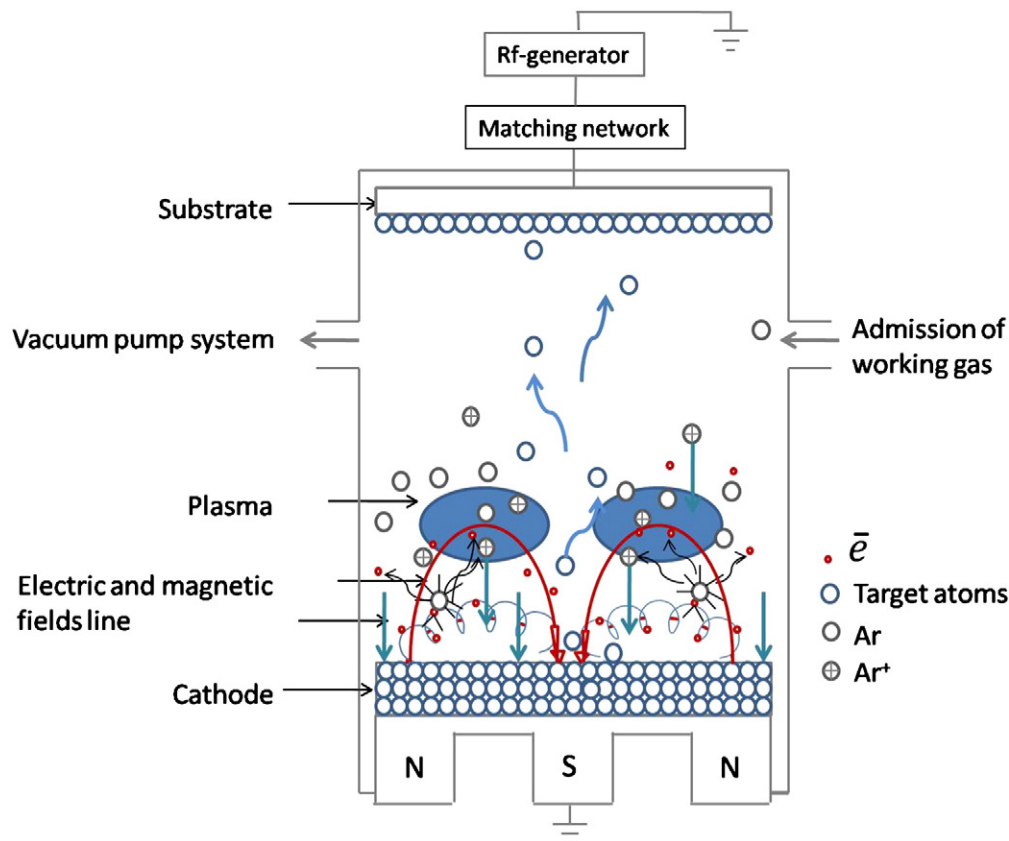


Fig. 1. Schematic diagram of the typical RF magnetron sputtering facility.

stand-off distance, powder feeding rate and the characteristics of feed materials are commonly varied [13,29,108,116,126,168,178,220,225,226]. Influence of deposition parameters on thermally sprayed HA coatings properties is described elsewhere [210,222]. In the jet, where the temperature is of the order of 10,000 K [2,41,227], 12,000 K [140] or as high as 30,000 K [13,126], the material is melted and propelled towards a substrate [193,221,228]. Due to high temperature in the plasma jet, the absence of the OH⁻ bands in the coatings was observed, which indicates dehydroxylation of HA [2,191]. In contrast, coatings prepared using a supersonic nozzle retained the crystallinity and phase purity of HA due to a relatively short exposure time of HA particles in the plasma [2].

The SPS or LPS technology is based on injection of fine nanometric or submicronic powder particles suspension (or liquid) into high-temperature plasma [21,30,41,114]. SPS was pioneered by Bouyer et al. and allows obtaining relatively thin coatings of 5–50 μm being a few times thinner than those obtained by dry powder processing with

the use of powder particles having the diameters ranging from a few submicrometers to a few micrometers [32,207,208,224,229]. This adds an important advantage to PS deposition, *i.e.*, a reduction in the coatings thickness. Another option to PS is a method of microplasma spraying (MIPS) to deposit CaP ceramic coatings [158,230–235]. Due to the low heat input of the microplasma jet, overheating of the powder particles, as well as excessive local overheating of the substrate is reduced [233,235,236].

HA [20,40,108,163,178,223,224,237,238], Si-HA [108,116], and antibacterial Ag-containing HA coatings [129,130,162,239] were plasma sprayed. Titania-HA functionally-graded (FG) coatings were deposited on Ti alloy substrates by APS [151,240]. FG Ti/HA films were prepared using a well-controlled DC-plasma jet [241]. Using laser engineering net shaping (LENSTM) processing and PS, the preparation of compositionally graded HA/tricalcium phosphate (TCP, Ca₃(PO₄)₂) coatings on Ti has been successfully demonstrated [82]. To improve the bioactivity of Ti6Al4V alloy, an innovative cladding method has been developed to bond a Ti/FA composite onto the alloy for load-bearing applications [155].

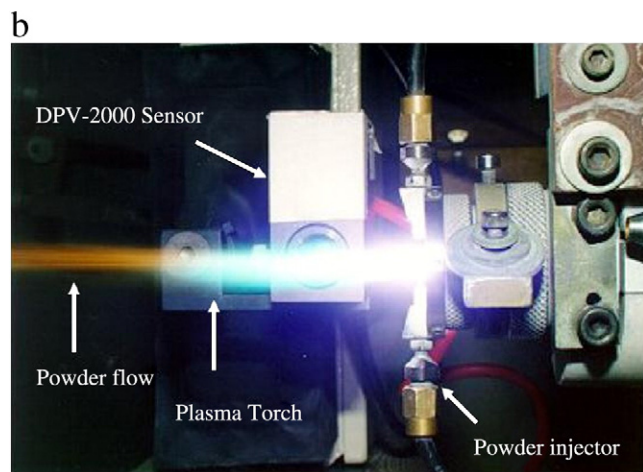
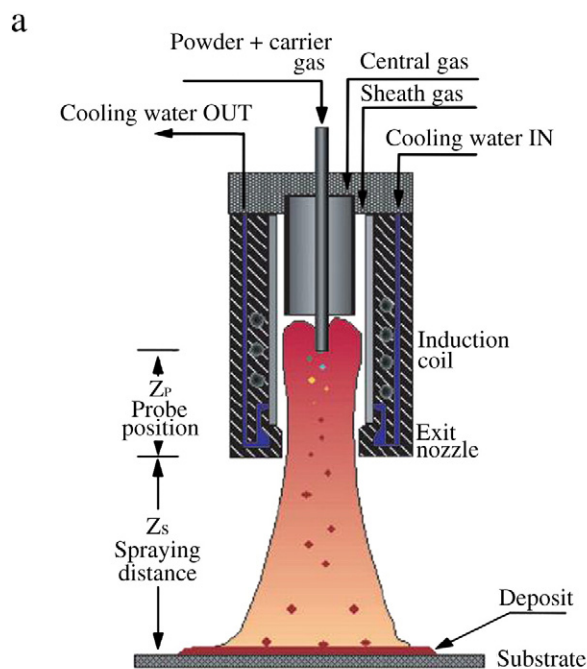


Fig. 2. Schematic diagram of an RF plasma torch (a) and an example of the actual experimental conditions during the gas plasma spray of HA powder (b). Here, a high temperature sensing system DPV2000 (Tecnar) was employed to monitor the temperature and velocity profiles of the HA powder from the feeding torch. Reprinted from [439] and [178] with authorization of IOP Publishing Ltd and Elsevier, respectively.

2.3. Pulsed laser deposition (PLD)

PLD is a physical vapor deposition technique to deposit thin films of materials of technological interest [67,70,72,79,122,148,242]. The deposition of CaP thin films by PLD was first described by Cotell [243,244]. The PLD system is shown schematically in Fig. 3 [10]. The major components typically include a KrF excimer laser source, an ultrahigh vacuum deposition chamber equipped with a rotating target and a fixed substrate holder plus pumping systems. Mostly, the substrates are attached to the surface parallel to the target surface at a target-to-substrate distance of 2–10 cm. PLD technology is based on the irradiation of a solid target by a focused pulsed laser beam resulting in a gaseous cloud. The laser-target interaction produces molecules due to HA decomposition such as Ca₂P₂O₉, Ca₃(PO₄)₂, CaO, P₂O₅, and H₂O [11]. This plasma cloud, composed of electrons, atoms, ions, molecules, molecular clusters and, in some cases, droplets and target fragments, expands, either in vacuum or in a gaseous environment, and deposits on a substrate, producing a film [158]. When PLD is used to prepare biocompatible CaP thin films, depositions are mostly performed using a UV KrF excimer laser (λ = 248 nm) [11,13,68,72,74,77,80,81,124,125,159,172,179,245,246], Nd:YAG (λ = 355 nm) [78], or ArF excimer laser (λ = 193 nm) [70,247]. The thorough investigation of plasma plume expansion process during an ArF laser ablation of HA is well-described elsewhere [70].

The substrate temperature during thin films deposition by PLD is typically in the range of 350–600 °C thus ensuring the formation of a highly crystalline and phase pure coating on implant materials [78,81,125]. PLD allows preparing films with a composition close to that of the initial target material by variation of the substrate temperature in the range of 500–600 °C and laser fluence of 2 J cm⁻² [125]. Moreover, lower or higher substrate temperature could be chosen to provide films with different fine texture and roughness, depending on the coatings application. It is also reported that post-deposition annealing at 300 °C has the potential to produce pure, adherent, crystalline HA coatings that show no dissolution in SBF [11]. Antibacterial Ag-HA coatings [72,80], HA [69,147,159,174,179,242,248–250], and fluorinated HA [125] coatings were prepared.

Matrix assisted pulsed laser evaporation (MAPLE) was developed as an alternative to PLD necessary for delicate and accurate (organic or biologic) material transfer to the thin films (*e.g.* alendronate-doped HA, composite HA silk fibroin, HA and a sodium maleate copolymer) [122,124,140,246,251]. MAPLE provides a more gentle mechanism for transferring different compounds, including large molecular weight species, and it is expected to ensure an improved stoichiometric transfer, a more accurate thickness control and a higher uniformity of the coatings. Additional information and current challenges on PLD deposition of CaP-based coatings can be found elsewhere [69].

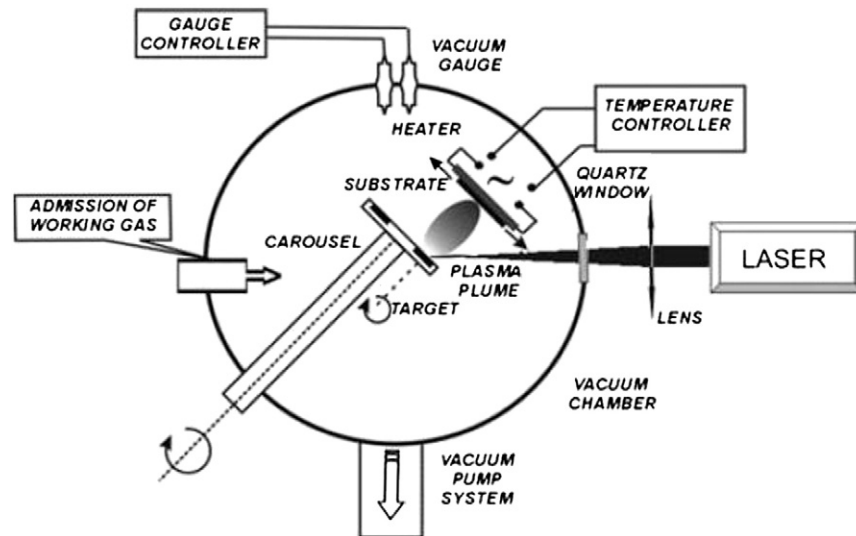


Fig. 3. Schematic diagram of the PLD system used to deposit HA coatings. Reprinted from [67] with authorization of Springer.

2.4. Ion beam-assisted deposition (IBAD)

IBAD is a vacuum deposition technique to prepare thin ceramic coatings on metals [91,93,97,101,105,252–254], polymers [97] or ceramics [95,128]. While ion implantation modifies surface properties by the penetration of the ions into the surface of a substrate, IBAD is a thin film deposition process that adds a layer on the surface of the substrate to form a coating. Due to the low operating pressure of various broad-beam ion sources, it has been possible to combine ion bombardment and sputtering with evaporative deposition. Depending on the configuration, these two techniques can operate independently in the same chamber [255]. A typical IBAD system (Fig. 4) consists of two main parts: electron [13,89,102,176,255,256] or ion [103,257] beam bombarding and vaporizing a HA bulk target to produce an elemental cloud towards the surface of a substrate and a source for simultaneous irradiation of a substrate with highly energetic inert (e.g. Ar^+) or reactive (e.g. O_2^+) gas ions to assist in the deposition of HA. Generally, the source of ions for IBAD is an ion or

plasma gun [105,258]. CaP coatings from a few angstroms to several (2–4 μm) micrometers thick can be prepared [102,158]. The high bond strength associated with the IBAD prepared films is considered a consequence of an atomic intermixing interfacial layer which can be a few μm thick. It is suggested that a chemical bond forms at the HA/Ti interface as a consequence of the energetic ion bombardment process [102]. A series of antibacterial FG HA coatings with different concentrations of Ag [98–100], and CaP coatings [91,94,95,101, 103,138,253,254,257,259,260] were deposited.

3. The main CaP coatings characteristics

3.1. Surface morphology

It is well-established that surface morphology plays a crucial role in the overall success of an implant [261]. Either rough or flat surface morphology of an implant is needed in any particular clinical case. RF magnetron sputtering and IBAD techniques allow us to prepare

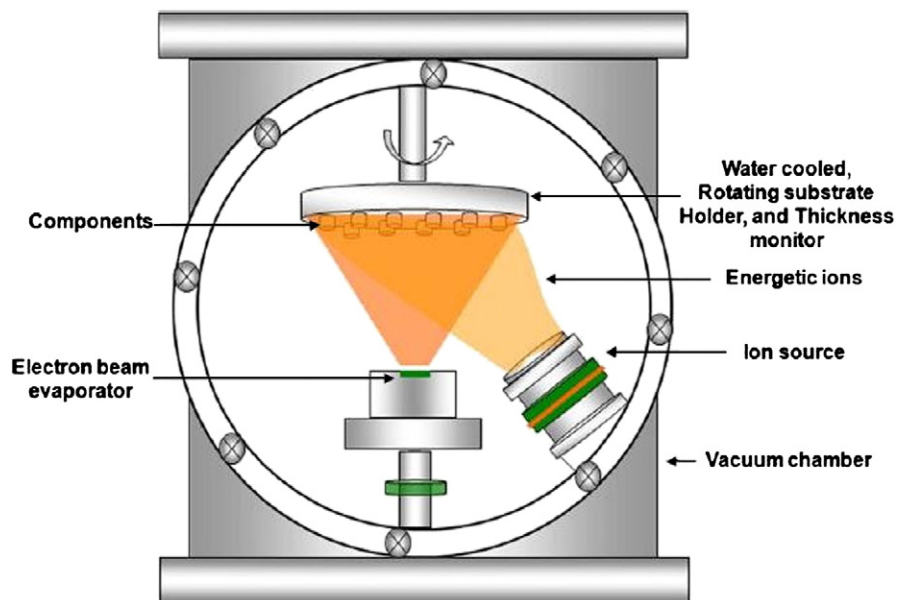


Fig. 4. Schematic diagram of IBAD system and process. The technology combines evaporation with concurrent ion beam bombardment to produce adherent dense coatings. Reprinted from [255] with authorization of Elsevier.

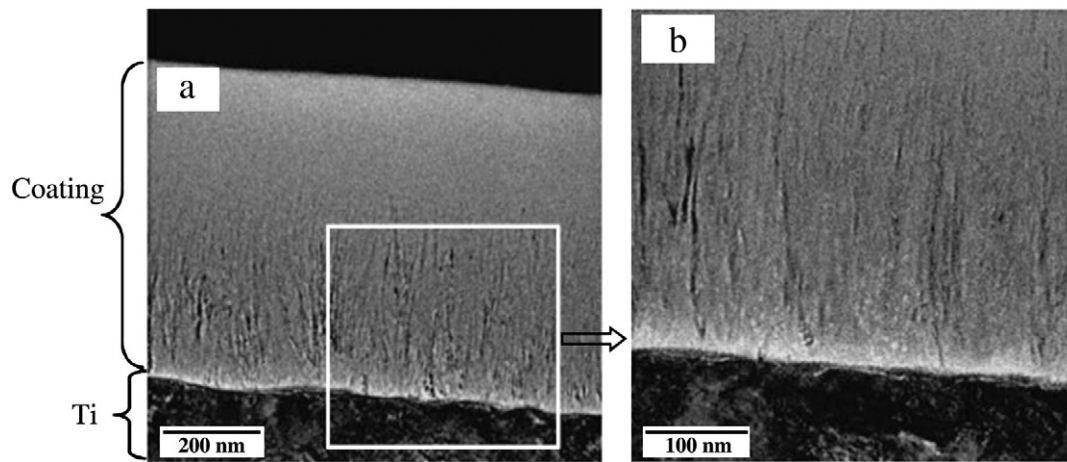


Fig. 5. TEM images of the cross-sections of IBAD CaP coatings: (a) is an image of cross-section including both Ti and coating; (b) is a higher-magnification image of the area showing interface and crystalline layer only.

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highly dense, uniform, continuous coatings without any micro cracks, surface and bulk porosity. These techniques allow maintaining an initial substrate surface roughness which makes the coatings beneficial in clinical trials where initial surface roughness of an implant should not be significantly influenced [10,14,49,57,58,99,111,138,147,161,253,254]. In the process of coating of porous materials it is very important that no surface porosity should be concealed for a further bone ingrowth. IBAD deposited CaP coatings are dense and pore-free, moreover, FG structure is found (Fig. 5a) [99]. The observations on the prepared IBAD coating cross-sections showed three distinct layers: a “mixed” crystalline interface layer adjacent to the Ti substrate, a crystalline bottom layer, and a mostly amorphous layer on the top surface (Fig. 5b). The typical patterns of the surface morphology of RF magnetron sputter deposited films are presented in Fig. 6. The surface morphology of these coatings can be significantly influenced by the variation of deposition control parameters, e.g. smooth (Fig. 6a) or nano/micro patterned (Fig. 6b) surface morphology can thus be obtained on the surface of the polished mirror-like silicon substrates.

The coatings prepared using PS and PLD techniques are rough, whatever initial surface roughness was prior to the coatings deposition (Fig. 7) [11,262]. The surface morphology of PS coatings consisted of many flat and smooth molten and unmolten submicrometric and micrometric splats with a significant number of thermally induced microcracks formed during the rapid cooling stage, as well as

spheroidized and partially melted fine particles, thus displaying a rough, irregular and inhomogeneous surface morphology (Fig. 7a) [32,108,125,153,162,179,220,228,237,245,246,263,264]. PLD produces very dense HA coatings with uniformly distributed droplets (0.5–5 μm) on the film surface (Fig. 7b). PS results in porous coatings [33,153,178,220] with the surface porosity of 0.2–1.6% [210], 11 vol.% [164], 18 vol.% [167] or $48.26 \pm 0.10\%$ in the case of LPS-porous coatings with a pore size range of 10–200 μm [41]. The porosities of SPS and LPS coatings are higher compared to powder plasma spraying (PPS) ones (Fig. 8). The as-deposited SPS coating reveals substantial porosity and a two-zone microstructure characterized in detail in the studies [30,37,223,224]: (i) a dense zone corresponding to well molten lamellae, similar to that observed in conventional PS coatings composed of HA as a major phase and decomposition phases such as tetra calcium phosphate (TTCP, $\text{Ca}_4(\text{PO}_4)_2\text{O}$) and CaO; and (ii) a sintered zone containing fine HA grains that correspond to the fine solids from the initial suspension [207]. The LPS process demonstrated far better control of the coating microstructure as compared to the conventional APS process, as both almost completely dense and highly porous microstructures without microcracks can be obtained by simply adjusting the solid content of the liquid precursor [41]. If annealing is applied, the surface morphology and roughness of HA coatings are reported to be dependent on the annealing temperature and time, and these changes were attributed to changes in the crystal structure and residual stress [10].

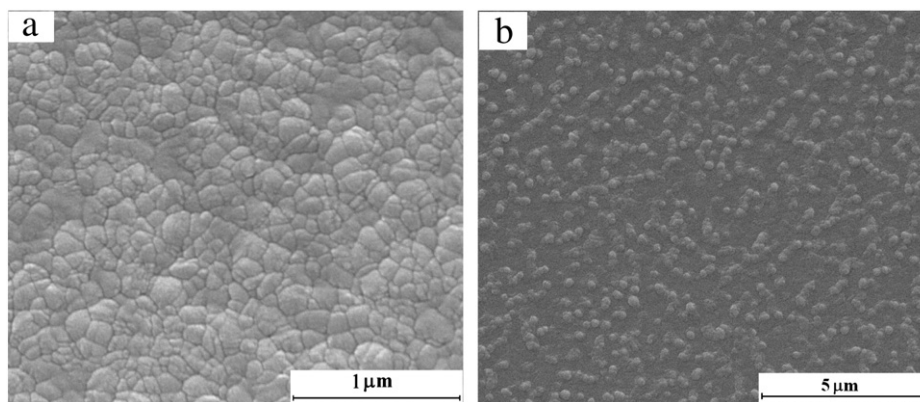


Fig. 6. The typical patterns of the surface morphology of RF magnetron sputter deposited coatings: (a, b) RF power – 290 W, deposition time 180 min, working atmosphere – argon. The substrate holder was grounded (a), and DC-bias of –100 V was applied (b). Nano/micro-patterned surface morphology is obtained under DC-substrate bias, while other deposition control parameters were kept constant.

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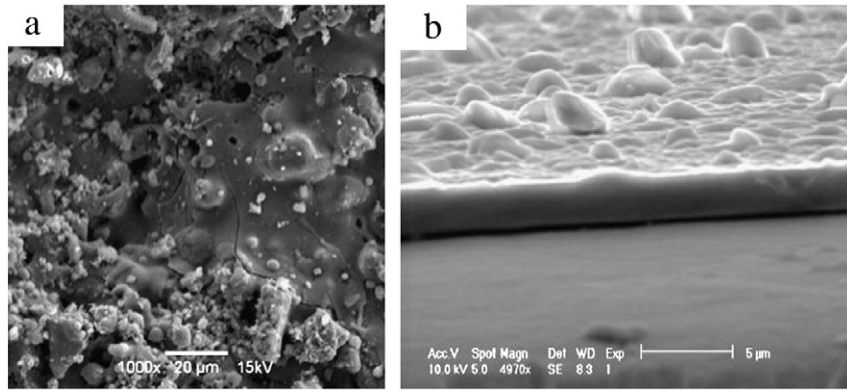


Fig. 7. Morphology of (a) PS and (b) PLD HA coatings. Reprinted from [108] with authorization of Springer and from [11] with authorization of Elsevier.

3.2. The chemical composition and Ca/P ratio

The chemical composition of the outermost coating surface is important because it will be in direct contact with bone tissue and dissolves first at the initial stage of implantation. The X-ray photoelectron spectroscopy (XPS), X-ray fluorescence (XRF) or energy dispersive X-ray (EDX) survey analyses of CaP-based coatings typically reveal the presence of O, C, Ca, and P [10,13,57,58,101,111,138,184,245,265]. The EDX-mapping of PLD and RF magnetron sputter deposited films showed a homogeneous distribution of Ca and P on the film surface, proving the

absence of segregation phenomena which are usually responsible for the formation of the undesired second phases [179]. The Ca/P ratio is one of the main characteristics of a biocompatible film that depends on the applied deposition control parameters [8,10,111,266]. An overview of the Ca/P ratio of the coatings is presented in Table 2. It can be seen that CaP films with different Ca/P ratios, including that close to Ca/P = 1.67, which is typical for stoichiometric HA can be prepared using RF magnetron sputtering, PS, PLD, and IBAD techniques [71,111,156,159,196,242,267]. The reasons that can lead to the deviation in the coatings stoichiometry and subsequently to the different

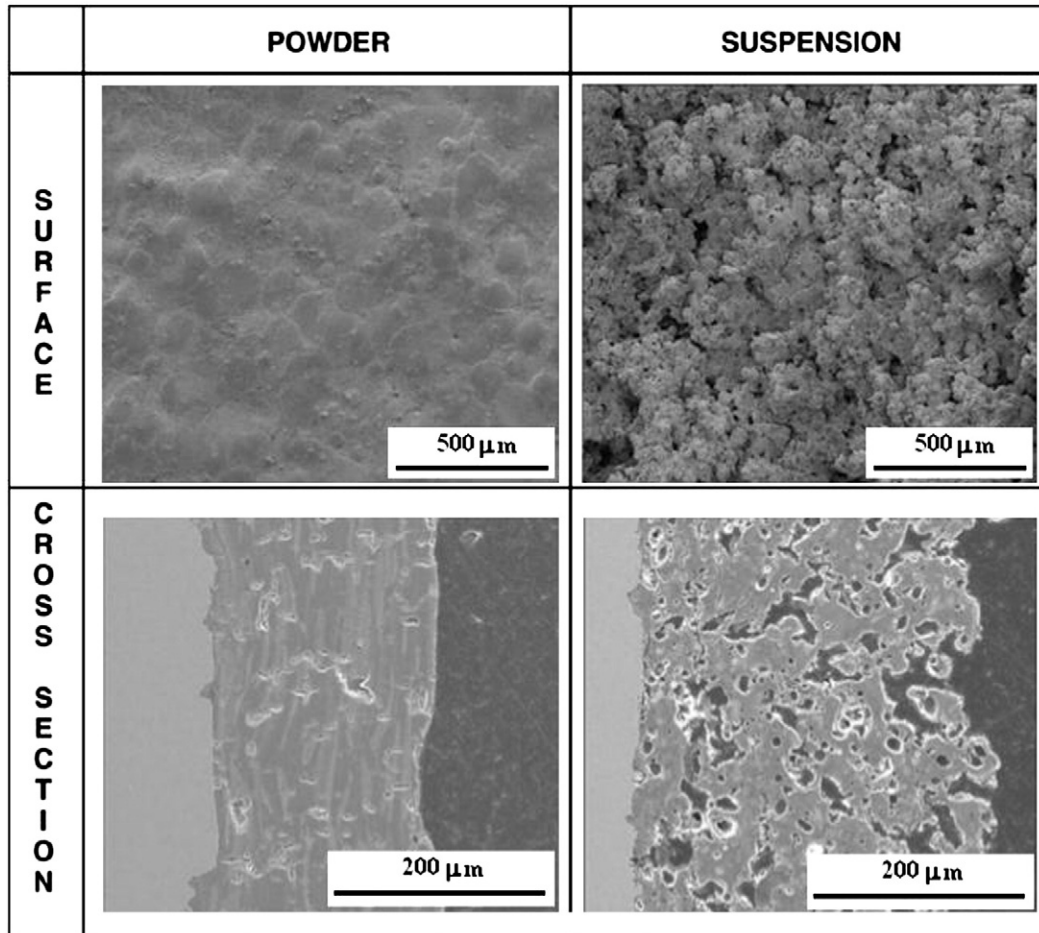


Fig. 8. The cross-section and surface of the coatings produced from a powder and suspension. Reprinted from [31] with authorization of Elsevier.

Table 2
The Ca/P ratio of the coatings prepared using plasma-based techniques.

Technique	Ca/P ratio	Deposition conditions or type of exposure	Type of the coating	Reference
RF magnetron sputtering	1.4	As-deposited in an inert atmosphere	HA	[179]
	1.55	As-deposited in an inert atmosphere with 20% O ₂		
	1.73 ± 0.08	As-deposited	HA	[49]
	1.6–2.6	As-deposited	HA	[10]
	1.1–1.2 and ~1.2–2.3	As-deposited and annealed at 900–1000 °C	HA	[64]
	~1.15	As-deposited in Ar atmosphere	CaP	[165]
	1.43, 1.53, 2.01	<i>In situ</i> annealed at 500, 600, 700 °C, respectively	Ca-P/TiO ₂	[54]
	1.67–1.75 and 1.56–1.65	As-deposited before and after 0.9% NaCl exposure	HA	[58]
	1.8	As-deposited in Ar atmosphere	B-type carbonated HA	[14]
	1.53–3.88	As-deposited	CaP, HA	[111]
PS	~1.67	As-deposited PS	HA	[238]
	1.5–2.2 and 1.4–1.7	As-deposited SPS before and after SBF	HA	[224]
	1.1–2.2	As-deposited SPS	HA	[223]
	1.7, ~2, ~4	As-deposited SPS (different areas)	CaP, HA	[30]
	1.36–1.68	After incubation in protein-free SBF	HA	[270]
PLD	1.62	As-deposited at room temperature	HA	[179]
	~1.9 to ~2.6	Deposited at room temperature to 500 °C	CaP	[264]
	~1.7	As-deposited at 650 °C in water vapor	HA	[159]
	1.83; 1.87	As-deposited at 500; 600 °C, respectively	fluorinated HA	[125]
	1.81; 2.1; 2.2	As-deposited at 30; 200–700; 750 °C, respectively	carbonated HA	[75]
	2.5; 2.62; 2.97; 3.16	As-deposited at different laser fluence	HA/CaP	[245]
	2.3; 2.34	Annealed at 1000 °C		
	~1.67	As-deposited	HA	[71]
	1.88, 2, 2.1, 2.2, 2.5	As-deposited at 200, 300, 350, 400, 500 °C, respectively	HA	[78]
	1.61 ± 0.07; 1.56 ± 0.14; 1.52 ± 0.15	As-deposited at 450–650; 400–600; 450–550 °C, respectively	CaP	[99,100]
IBAD	2–3.3	As-deposited	CaP	[149]
	2–3.6	As-deposited	CaP	[101]
	2.33 ± 0.01	As-deposited without silver	CaP	[98,100]
	2.95 ± 0.03	As-deposited with 2.34 ± 0.37 wt.% silver		
	2.19 ± 0.10	As-deposited with 6.29 ± 0.24 wt.% silver		
	3.09 ± 0.03	As-deposited with 13.53 ± 0.22 wt.% silver		

resorption rate *in vivo* and *in vitro* are presented below [8]. The sputtering of a multicomponent target, such as HA often resulted in a coating stoichiometry different from the bulk target (Table 2). As an example of the phenomenon, the Ca/P ratio from 1.51 ± 0.02 to 1.82 ± 0.02 revealed the formation of Ca₃(PO₄)₂ and CaO phases [268]. The components of the target such as hydroxide, oxygen, and hydrogen may not be completely transferred to the substrates owing to the low environmental pressure in the chamber. As a result, the composition of the coating may differ from that of the target material, depending on the type of sputtering system and the deposition parameters [10]. The difference in the Ca/P ratio between the HA target and the sputtered coatings is attributed to the preferential deposition of Ca ions and a possible significant loss of phosphorus ions, which may be pumped away before reaching the substrate or be re-sputtered out of the growing film by incoming ions or neutrals [10,13,61,91,103,165]. Different sputtering rates for calcium and phosphorus at the target can also affect the coatings Ca/P ratio. It could depend on the history of target processing that alters the target stoichiometry if sputtering rates are not identical for the different components [43,56]. Increase in Ca/P is also observed when annealing temperature is raised [54,64]. Ergun et al. provided evidence that Ca/P ratios should be maximized (up to 2.5) in nanoparticulate CaP formulations to increase osteoblast adhesion, a necessary step for the subsequent osteoblast functions such as new bone deposition [269].

During laser ablation the volatile species, such as P₂O₅, lead to a wider cone angle of ejection compared to the Ca-containing molecules. Hence, at lower chamber pressure (10^{-4} – 10^{-2} Torr), deposited films show a P deficiency [11]. Moreover, increase in substrate temperature or laser fluences results in higher Ca/P ratios compared to the target [125,264]. A quasistoichiometric transfer of the precursor compounds of HA fibroin from the solid target in the form of thin films was achieved using MAPLE [246]. In the case of the PS deposition process the difference in stoichiometry is commonly caused by powder decomposition in the plasma plume. It is typical for PS deposited films that the Ca/P ratio shows a gradient through the coating thickness as clearly visible in Fig. 9 [223]. Typically, the Ca/P profile

through the coatings thickness is found to be between 1.5 and 2.2 [163,270]. The presence of different phases through the coating thickness, including HA, TCP, TTCP, and CaO was confirmed by X-ray diffraction (XRD). The data presented in this section revealed that Ca- or P-deficient coatings with different properties for any particular clinical case can be prepared using plasma-assisted fabrication methods.

3.3. Phase composition and structure

The phase composition and structure, as well as the Ca/P ratio of the coatings depend on the deposition control parameters. Plasma-assisted fabrication allows the preparation of the CaP coatings of either amorphous or crystalline structure of a definite phase composition that along with the Ca/P ratio influences the coating behavior *in vitro* and *in vivo* [4,271,272]. Despite the utilization of a partially crystalline target RF magnetron sputtering [10,14,56,58,111,113,142,161,165,179,185,225,273], IBAD [5,91–93,98,99,101,138,149,254,256] and PLD [3,11,80,148,179,264] processes usually produce amorphous coatings or CaP compounds. It is also reported that when Si content is increased the XRD reflections referred to HA become less intense, a phenomenon that indicates a progressive loss of crystallinity along with the Si substitution [274]. It is generally known that the amorphous phase in CaP coatings easily dissolves and thus loses long-term stability in clinical use [126]. Since it is critical to maintain the integrity of HA coatings, controlling the heat-treatment temperatures and heating environment (air, water vapor) results in conversion of amorphous coatings to HA ones of different degrees of crystallinity [10,42,148]. Annealing *in situ* at 350–650 °C [56,68,81,148,242,257,274], 550 °C/1 h [14], 297–527 °C [57,58,111] or after deposition usually at the temperature of 320–700 °C in an inert gas, water vapor, air or vacuum enhances the films crystallinity [11,51,61,92,93,112,113,148,165,170,225,262,264,275–277]. Crystalline HA coatings were obtained during *in situ* annealing at 500, and 600 °C, as well as hybrid HA/TiO₂ films at 700 °C [54]. Bai et al. using IBAD reported that the coatings deposited in the

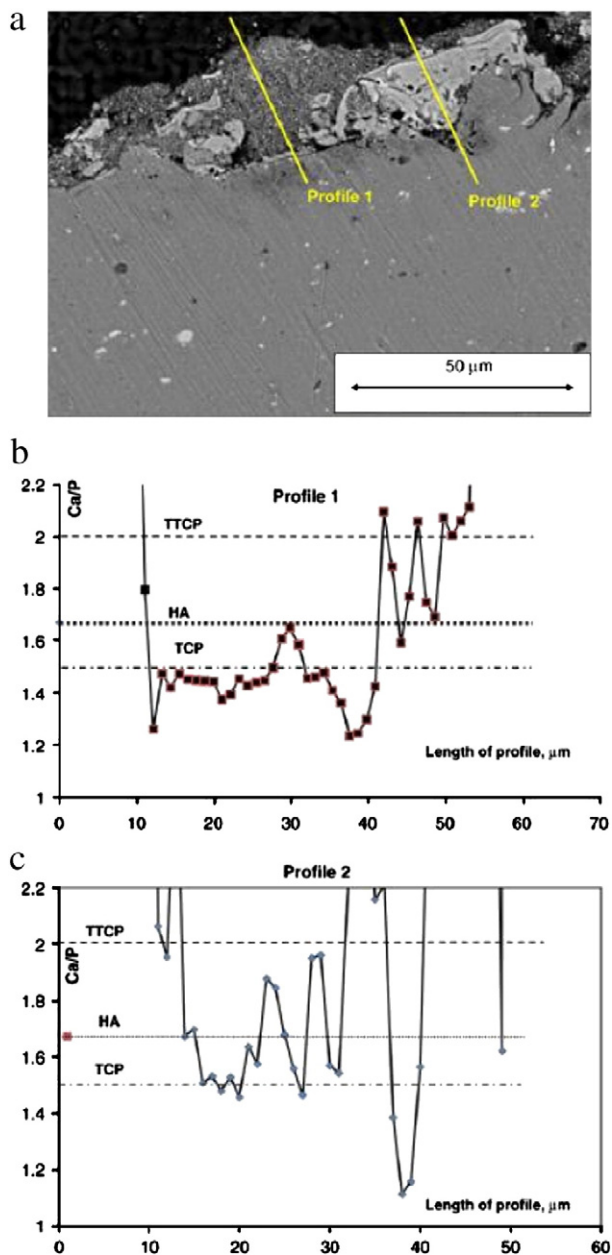


Fig. 9. SEM (backscattered electrons) of two characteristic zones in suspension plasma sprayed HA, (a) and the profiles Ca/P obtained with electron microprobe analyzer along porous zone (b) and dense zone (c). Reprinted from [223] with authorization of Elsevier.

temperature range of 400–650 °C had a multiphase structure: α - $\text{Ca}_2\text{P}_2\text{O}_7$, $\text{Ca}_4\text{O}(\text{PO}_4)_2$, β -TCP, CaHPO_4 , β - CaP_2O_6 [99]. If the temperature was excessive, cracks could be seen at the interface and delamination occurred [240]. The failure of the interface and the increasing propagation of cracks at high temperature are attributable to the recrystallization and related to the change in the HA specific volume, which is likely to trigger increasing stresses in the system.

Several laser treatments were performed with the purpose of increasing the HA crystallinity at the surface of plasma sprayed titania-HA FG coating [151]. After being post-treated by water vapor (WVT), a few impurities including the β -TCP and the TTCP phases still remained in the WVT coatings [163]. However, electric polarization in alkaline solution (PAS) resulted in coatings composed of only HA and amorphous phase. The sharpening of three strongest HA peaks ($2\theta = 31.8^\circ$, 32.2° , 32.9° , ICDD, # 9-432) and the decreasing of amorphous calcium phosphate (ACP) ‘hump’ (2θ from about 28°

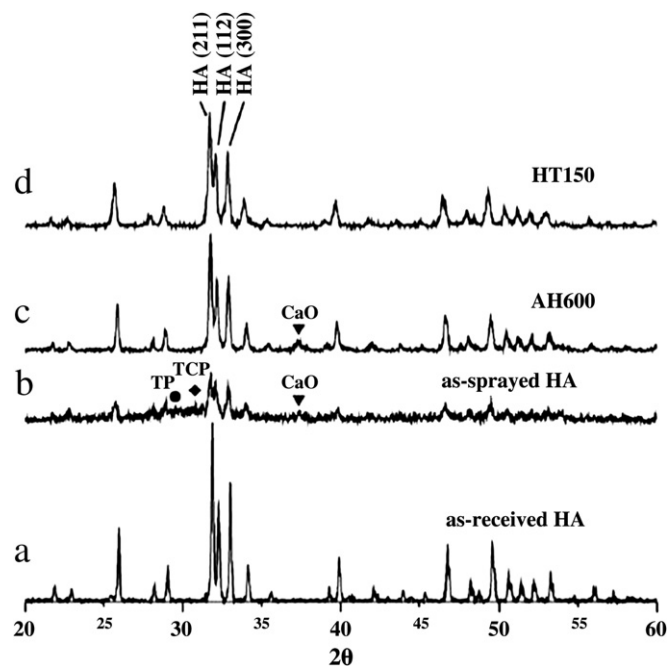


Fig. 10. The XRD-patterns of the as-received HA powder (a), as-sprayed HA coatings (b), air heat-treated (AH600) coatings (c) and hydrothermally-treated (HT150) coatings (d). The crystallinity and phase purity of HA increased with hydrothermal treatment. Reprinted from [263] with authorization of Elsevier.

to 31°) indicate that the plasma sprayed HA coatings significantly crystallized by heat treatment in air and hydrothermal treatment (Fig. 10c, d) in comparison to as-sprayed coatings (Fig. 10b). An XRD-pattern of as-received precursor powder is also presented (Fig. 10a) [263]. However, CaO remained within the coating layer heat-treated at 600 °C in air because CaO cannot easily be converted into HA without abundant water molecules present in the heating atmosphere. CaP films were crystallized under hydrothermal conditions in distilled water at 100–170 °C [78,161]. CaO is significantly eliminated through the hydrothermal treatment of the coatings at 150 °C [263]. The overall amount of CaO phase should be relatively small and meet the relevant requirement of ISO 13779-2:2008, the industry standard for HA coatings applied to surgical implants [18].

The as-deposited HA coatings of a sufficient crystallinity were also prepared by RF magnetron sputtering [57,58,111,278], and PLD [242]. The high intensity of the (002) peak at $25.78^\circ 2\theta$ indicates a preferred crystallographic orientation of HA thin films (Fig. 11). No other high-temperature phases like β -TCP, TTCP, or crystalline CaO which can

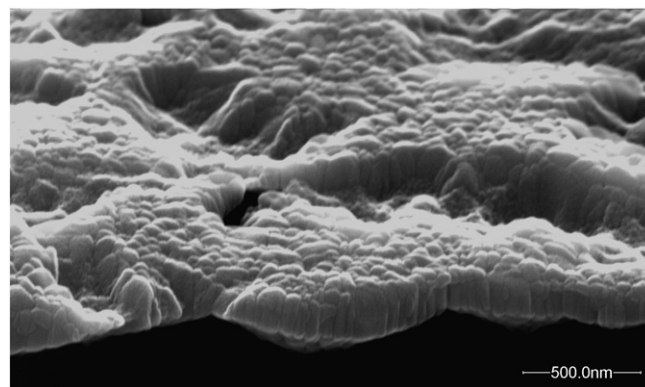


Fig. 11. A cross-section pattern of RF magnetron sputter deposited CaP film after etching in 0.1 mol HCl solution. Unpublished results, reprinted with authorization of Mrs. M. Surmeneva (Tomsk Polytechnic University) and Prof. M. Epple (University of Duisburg-Essen).

occur in the plasma spray process are found [57]. The (002) texture is a common phenomenon when RF magnetron sputtering is used [14,57,62,111,161,170,265,279], and is also found in case of PLD [11,159] and PS deposited films [31,250]. Thin highly crystalline nanometer thick HA films were prepared using right angle RF magnetron sputtering approach [49,53,280]. These coatings show some advantages over conventionally sputtered films in which ambient temperature deposition yields nanocrystalline and nearly stoichiometric HA coatings under appropriate conditions, thereby avoiding the need for *in-situ* or *ex-situ* annealing.

Sputtering process in an inert atmosphere results in a partly dehydroxylated as-deposited HA coating [57,111,165] which was also found in PS [108] and IBAD films [99]. The dehydroxylation led to the large loss of the OH⁻ group, which results in the formation of oxyapatite (OAp) or oxyhydroxyapatite (OHAp) in the coating and affects their structural integrity [108]. The presence of water vapor in the LPS process would suppress the dehydroxylation in the high temperature plasma jet. Therefore, the LPS coatings showed a sharp and strong OH⁻ group absorption band, indicating structural integrity which was absent in the APS coatings [40,41].

A highly crystalline HA coating was formed by PLD at 1.5 mbar water-vapor pressure on commercially pure Ti [159]. The HA/CaP coatings structure deposited by PLD mostly depends on the KrF laser fluences [245]. Samples deposited at 2.4 J cm⁻² were partially amorphous and had rough surfaces with many droplets, while higher laser fluences (29.2 J cm⁻²) showed higher level of crystallinity and lower roughness of the obtained surfaces. The various CaP-phases synthesized using PLD techniques include α -TCP, β -TCP, TTCP, octacalcium phosphate (OCP), ACP, and crystalline HA [13]. Katayama et al. used two excimer lasers to develop a new HA coating method [71]. One laser beam from KrF laser, the ablation laser, is used for the ablation of a HA target. The other beam from ArF laser, the assist laser, is used to irradiate a Ti substrate surface during formation of the HA coating and allows the formation of a crystalline HA coating with improved adhesion strength to the Ti substrate.

A HA powder particle injected into the hot plasma jet of an APS system by a blast of inert carrier gas (Ar) suffers thermal decomposition during its flight along the trajectory that is determined to a large extent by the plasma power, grain size, density and velocity of the particles, as well as the kinematic viscosity and the density of the plasma gas [108,117,209,240,270,281,282]. The XRD analysis showed that the microstructures of the PS coating were mainly composed of HA, ACP and some minute phases of α -TCP or β -TCP, TTCP and CaO [3,22,32,37,40,41,117,137,160,163,173,218,220,223,224,237,240,263,270,282]. When LPS (or SPS) is used ACP, HA, α -TCP, β -TCP, CaO phases are also found [30,32,40,41,223]. After being heat-treated at 650 °C for 1 h, the APS heated, LPS-dense heated and LPS-porous heated coatings are nearly composed of HA and CaO [41]. It was revealed by Gross et al. that the powder feedstock produced a dense, oriented coating (preferable crystallite orientation (002)), whereas the suspension led to a porous randomly oriented coating [31]. Saber Samandari et al. reported that the coating was free of decomposition phases and had a preferred orientation with c-axis perpendicular to its surface [33]. It is possible to prevent the powder decomposition by using supersonic plasma nozzles [2]. No TTCP or CaO phases were found in such coatings; they showed higher crystallinity and phase stability due to the relatively short exposure time of HA particles in the plasma in comparison to those prepared by using a normal plasma nozzle. The impurity phases of HA were influenced by the hydrogen (H₂) flux which controlled the decomposition of HA in the plasma flux [240]. The lower is the H₂ flux, the higher is the crystallinity and the lower CaO content. The experiment performed on the CaP coatings deposited on Ti6Al4V with TiN buffer layers reveals that the addition of magnesium into HA improves the crystallinity of deposited layer [247]. FA coatings prepared under the same deposition control parameters showed better crystallinity than HA

coatings [126]. Substitution of the hydroxyl ion by fluoride in the HA lattice renders the CaP thermally more stable. The results suggest that FA coating has the potential to show stability in long-term clinical use [271]. It is shown in this section that plasma-assisted fabrication methods allow the preparation of CaP coatings with different phase composition and structure which is important in both short- and long-term clinical applications.

3.4. Mechanical performance

3.4.1. Adhesion strength

The mechanical properties of CaP-based coatings determine the overall success of an implant [57]. The mechanical properties of the coatings depend on many parameters such as density, phase and chemical composition, and crystallinity [268]. An overview of CaP coatings adhesion strength is presented in Table 3. The investigations of the coating bond strength is typically performed according to ISO 4624 (pull-off test) [210], ASTM C633 (tensile adhesion test) [41,116,159,160,167,263], ASTM F-1147-05 (tensile adhesion test) [283] or DIN 50,161 (shear strength) [117]. The ISO 13779-2:2008 standard requirement for tensile adhesion strength of HA coatings in the surgical implant application is 15 MPa [18,41,121]. Another technique to study thin films adhesion strength is the scratch test [11,37,103,134,148,166,168,221,223,284,285]. The scratch test is performed with reference to ISO 20502:2005(E) [242,286]. In most papers concerning PLD films the adhesion strength is determined by the scratch test method and the authors conclude that this type of coating is highly adherent to the substrate [11,73]. Furthermore, as-deposited and annealed at 350 °C PLD deposited HA films exhibited excellent adhesion to Ti6Al4V alloy substrates [148]. The coatings with improved adhesion strength obtained by PS of HA suspension are reported [223]. Roy et al. revealed that the adhesion strength of PS coatings decreased when either the plate power was reduced (from 28 to 22 kW) or the working distance was increased (from 90 to 130 mm) [2]. Surface modification by grit blasting with Al₂O₃ particles and subsequent wet blasting with mixed HA/Ti particles followed by PS of both 100 μ m thick HA/Ti mixed bond coat and then HA-top coat was successfully applied. Specimens could survive up to 10 million cycles at stress amplitude of 200 MPa, which can be compared with the maximum stress in bones during running or jumping: the order of 100 MPa [39]. Many authors reported that adhesion strength could still be enhanced using different interlayers such as TiO₂/Ti/TiN [3,54,64,68,73,74,116,156,159,160,170–172,178,240–242,247,273,287–289], ZrO₂ [172], HA/Ti bond coat [28,39,82], HA/SiO₂ [203], Al₂O₃ [77,172], Al₂O₃/TiO₂ [283], carbon nanotubes (CNTs) [290], Al₂O₃-CNT [153], fluoridated HA/CNT composite [45] as well as HA/(ZrO₂ + Y₂O₃) [142]. These interlayers can reduce the mismatch of thermal expansion coefficients between HA and substrates or increase the surface area of the material, wettability and heat conductivity and provide reinforcement via rebar mechanism, as in the case of Al₂O₃-CNT composite, thus increasing the coatings bonding strength without affecting biocompatibility. Sima et al. reported that bond strength of the carbonated HA structures was successfully increased by ~24% when an intermediate CHA_xTi_{1-x} (x = 0–1) composite buffer layer was introduced [14]. In the case of annealed (550 °C/1 h) graded RF magnetron sputter deposited coatings, the failure occurred within the glue layer at 84.80 \pm 0.78 MPa without damaging the film integrity. Since this value represents the bonding limit of the epoxy adhesive as confirmed by the manufacturer, the true coating-substrate adhesion strength could be even higher. The adhesion strength was increased in the case of FG atmospheric plasma sprayed HA/ZrO₂ coating [218]. Bioceramic composite coatings of HA reinforced with bioinert Al₂O₃ and CNTs were synthesized with significantly improved fracture toughness up to 300% by providing reinforcement via the 'rebar' mechanism [153]. A 3-D TiN dendrite network provided extra surface area and a locking mechanism for the adhesion joint

Table 3
A summary of CaP-based coatings adhesion strength.

Technique	Adhesion strength, MPa		Type of exposure	Type of the coating	Reference
	Pull-off	Tensile			
RF magnetron sputtering		~35	As-sputtered and annealed at 600 °C	Graded HA/Ti	[441]
	>60		As-sputtered and air heat-treated	ACP, and OAp	[277]
	~40		Heat treated in vacuum	OAp	
	68.5 ± 3.74		As-deposited	carbonated HA	[14]
PS	84.8 ± 0.78		Annealed 550 °C/1 h		
	~30		As-deposited	HA PMMA	[179]
	~16–25		As-deposited APS	HA	[210]
		29.8	Laser gas nitrided Ti followed by PS	HA	[160]
		16.1	Grit-blasted Ti followed by PS		
		~13	As-deposited MIPS	HA	[167]
		4.8–24	As-deposited supersonic PS	HA	[2]
		16.7	As-deposited VPS	Ti/Si-HA	[116]
		25.6	As-deposited VPS with TiO ₂ bond layer		
		21	LENS™ followed by RF induction PS	HA on the LENS™ prepared Ti-HA/TCP composite layer	[82]
		32.4 ± 1.0	As-sprayed	HA	[263]
PLD		38.9 ± 1.0	Hydrothermally-treated at 150 °C		
		37.1 ± 1.8	Air heat-treated at 600 °C		
		20.10 ± 2.11	As-deposited LPS	Dense HA	[41]
		17.56 ± 0.92		Porous HA	
			As-deposited	HA PMMA	[179]
		~8	As-deposited (mirror surface)	HA	[159]
		~11	As-deposited (grit-blasted surface)		
		~16	As-deposited (nitrided + etching)		
		~30–40	As-deposited at 500–600 °C	HA	[442]
		>58	As-deposited at 455 °C	HA	[250]
IBAD		31.1 ± 13.1	As-deposited at 500–520 °C (ground Ti)	HA	[248]
		21.1 ± 5.3	As-deposited at 500–520 °C (polished Ti)		
		68.3 ± 17.8	As-deposited at 625–715 °C	HA	[147]
		85–89	Substrate temperatures from 650 to 400 °C over 6 h	FG CaP	[99]
		83–88	Substrate temperature was 550 °C for the first 4 h	Ag-HA	[98]
		85	and 450 °C for the last 2 h	FG HA	

[73,159,160]. The bonding strength of the HA coating on the laser gas nitrided substrate was 1.8–2 times higher than that on the grit-blasted substrate (Table 3) [160]. “Remelting” of the coating (using Nd:YAG laser technology) with different current and voltage parameters to melt the HA coating and alloy it with base material to solve the problem concerning poor mechanical properties was developed [20].

IBAD deposited coatings showed a superior bond strength of the coating that can be attributed to the presence of the intermixed interface layer and dense CaP coatings [89,98,102,253,255,291]. The sputtering process was reported to produce dense, uniform and continuous coatings with a high coating-substrate bonding strength [10,57]. These coatings have been reported to possess significantly higher coating-metal interfacial bonding strength compared to PS coatings [10]. Pichugin et al. using the scratch-test observed that the as-sputtered coatings of the thickness less than 1.6 µm on Ti did not delaminate until the indenter reached the substrate-coating interface. The typical failure mechanisms of RF magnetron sputter deposited coatings of different thicknesses are presented in Figs. 12a, b. The mode of damaging the CaP coating with the thickness greater than 1.6 µm differed from that of the thinner CaP coatings. The destruction of the coatings with the thickness less than 1.6 µm occurred only after its perforation (Fig. 12a), whereas thicker coatings collapsed by exfoliation, splits and chips along the scratching direction (Fig. 12b). According to the results of acoustic emission and friction coefficient tests all coatings with a thickness up to 2.7 µm had a high adhesion strength to Ti and NiTi, which is in good agreement with the data reported by other authors (Table 3). The reason for a high adhesion strength is a thin oxide layer of TiO₂ that promotes a formation of a strong covalent bond between the substrate and CaP coating with the energy above 0.5 eV [57]. It was discussed that different oxide phases can be formed on Ti or Ti6Al4V prior to the CaP film growth by PLD in water vapor atmosphere [11,71,78], which can degrade the coating adhesion strength. When CaP films are deposited by RF

magnetron sputtering in argon atmosphere, there is only a scarce quantity of oxygen atoms available that limit the substrate oxidation. As a result HA/TiO₂ hybrid coatings can be formed, where a TiO₂ layer provides stability and appropriate biofunctionality [54,292]. Berezhnaya et al. reported that 0.2 µm thick TiO₂ interlayer in the HA/Ti system inhibited Ti oxidation, and the reaction intermediates formed during high temperature heat treatment (900–1000 °C) enhance the adhesion between the Ti and HA [64]. The combination of PLD and post-deposition annealing allows fabrication of pure, adherent, crystalline HA coatings on Ti6Al4V with good mechanical and biocompatible properties due to lower processing temperature (300 °C/4 h), which restricts the formation of Ti-oxide at the interface between the coating and the substrate [11]. Laser-assisted laser ablation method for high-quality HA coating onto Ti substrate was developed [71,293]. Thus, the experimental data summarized in this section reveal that plasma-assisted fabrication allows preparation of CaP coatings with the adhesion strength that meets the requirements of the standard [16,18]. Moreover, the adhesion strength of the coatings is higher compared to that of solution-based coatings [4].

3.4.2. Nanohardness and Young's modulus

Nanoindentation technique is typically used to study the nanohardness (*H*) and Young's modulus (*E*) of CaP-based coatings according to Oliver and Pharr's method [294]. The fracture toughness of the HA coatings [164] and the scratch hardness [185] can also be studied. Hardness is a property related to yield strength and can be useful to predict the strength of the coating, stress state within the coating, and the abrasion resistance on the coating surface [295,296]. An overview of thin films nanohardness and Young's modulus is presented in Table 4. A large range observed in nanohardness values of PS deposited films is attributed to the presence of porosity, surrounding amorphous areas, and HA (unmolten particle cores and recrystallized HA). The data revealed that little attention is paid nowadays to

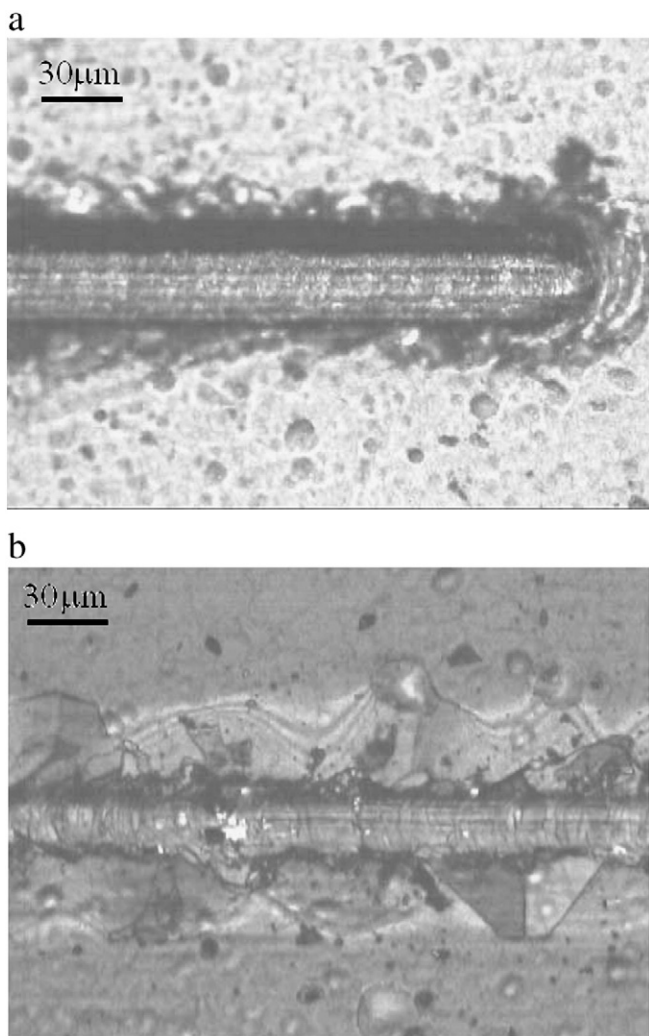


Fig. 12. Light-microscopic images of scratch tests on a CaP coating (thickness (a) 1.6 μm and (b) 2.7 μm) on Ti. The images (a) and (b) were taken at 2 N and 0.66 N, respectively. The coating (a) was not damaged during the scratch test experiment but merely impressed into the substrate. There are the tracks of a deformative wave ahead of the scratching direction. The coating (b) was clearly damaged during the scratch test experiment. There are clear signs of exfoliation and bursting of the CaP coating. Reprinted from [57] with authorization of Elsevier.

investigations of nanohardness and Young's modulus of both RF magnetron sputter deposited and IBAD deposited CaP coatings. Dinda et al. showed that crystalline films were mechanically more resistant and presented higher hardness and Young's modulus compared to amorphous HA films [11]. The typical patterns obtained by nanoindentation of SPS coatings are presented in Fig. 13a [31]. A wide range in the values of nanohardness and Young's modulus is attributed to high film porosity (Fig. 13b). The porosity leads to a decrease in the hardness and elastic modulus of the bulk coating, but site specific indentations on dense areas in the SPS coating revealed greater values (5 ± 0.2 vs 4 ± 0.2 GPa), possibly due to finer grain size and crystal orientation. The nanohardness and Young's modulus of the MIIPS coatings measured according to DIN 50359-1 (H -3.5 GPa, and E -80 GPa) were much reduced compared to bulk sintered HA material (6 and 125 GPa, respectively) due to the coating porosity of ~ 18 vol.% [167].

The selection of powder type (spray-dried or sintered) and particles size leads to different mechanical properties within the coating [33]. Nanoindentation testing showed a non-uniform stress state throughout the HA coating. A spray-dried powder provides a lower hardness and elastic modulus when unmolten particle cores are included in the coating. Meanwhile, recrystallized areas are intermediate

in hardness [295]. The flame spray process produced a residual stresses, as revealed by an increase in hardness from the interface towards the coating surface. The surface exhibited a higher hardness suggesting a compressive stress state at the surface, but a tensile stress at the Ti-HA interface. It should be pointed out that all plasma-assisted techniques can cause a shift of the Bragg peaks of the HA. This is most probably attributed to the lattice compression of HA due to the presence of residual stress [11,297]. The residual stresses of PS coating arise from intrinsic or deposition stresses which are generated during the cooling of sprayed particles to the substrate temperature after solidification or because of differential thermal contraction arising during post-fabrication cooling down [33,110,224,276,297]. The thermal expansion coefficient of sintered HA is larger than that of either Ti6Al4V alloy or pure Ti ($\sim 14 \cdot 10^{-6} \text{K}^{-1}$ [110,216], $(8.4\text{--}8.9) \cdot 10^{-6} \text{K}^{-1}$ [110,216,298], $8.5 \cdot 10^{-6} \text{K}^{-1}$ [299], respectively), hence HA will be in a tensile stress state after being cooled from the elevated temperature. It has been recently reported that HA coating spraying on the hollow rotational substrate with back cooling jet would lead to a higher temperature in HA coating than substrate during PS and result in the tensile residual stress in the HA coating. On the contrary, HA coating with front cooling jet displayed a much lower temperature than the non-hollow substrate and hence the compressive residual stress occurred [22]. The change in apatite composition due to dehydroxylation will also modify the resulting stress condition [33]. Stress conditions can cause CaP coatings delamination in the experiments *in vivo* or *in vitro* and be a reason of implant failure shortly after surgery; therefore, they should be avoided. It was mentioned in Section 3.4.1 that different interlayers between CaP-based coating and a substrate can reduce the mismatch of thermal expansion coefficients, thus avoiding stress state formation. Other reliable and inexpensive ways are still a challenge for the research community for the nearest future.

3.5. Requirements of HA coatings of implants

The cytotoxicity of implanted metals is a major concern in the biomedical field and is still an object of debate [300]. Ions and/or debris released from an implanted material can in fact provoke adverse immune and inflammatory reactions that can ultimately defeat the purpose of the biomedical device. It is commonly accepted that Ti and its alloys are biocompatible. However, some Ti alloys show a certain degree of cytotoxicity due to the alloying elements [301]. For example, Al and V were associated with neurological disorders [302]. In addition, high levels of Cr, Ni and Co raise the risk of carcinogenicity [301]. While these effects are known, it is important to enhance biocompatibility of metallic implants [23]. Biocompatibility refers to the ability of a material to perform with an appropriate host response, in a specific application [303,304]. Hence biocompatibility is neither a single event nor a single phenomenon but is meant to be a collection of processes involving different but interdependent interaction mechanisms between a material and a living tissue (for further details see Williams [305] and Heimann [23]).

Osteoconduction is defined as the process of bone ingrowth from local osseous tissue onto surfaces. The original definition was not strictly restricted to biomaterials [306,307]. However, the contemporary concept of an osteoconductive material is the one where bone formation is promoted to appose and conform to its surface, when the material is placed into a bone, by virtue of its composition, shape, or surface texture [308]. In effect, these materials act as receptive scaffolds that facilitate enhanced bone formation. Purely osteoconductive biomaterials, e.g. HA, are not usually associated with a bone formation outside the bone [309].

Osteogenic materials are defined as those that contain living cells and are capable of differentiating into bone. *Osseointegration* is defined as the 'process whereby clinically asymptomatic rigid fixation of alloplastic materials is achieved and maintained in bone during functional loading' [310–314]. From a histological point of view, this is generally interpreted as the intimate apposition of bone tissue to

Table 4

The nanohardness and Young's modulus of CaP-based coatings. * – the data were calculated from Hv by the author.

Method	Hardness, GPa	Young's modulus, GPa	Type of the coating	Reference
RF magnetron sputtering	~10	~110	as-deposited HA	[57]
	–	~131–163	HA after annealing at 550 °C at 1 hour	[268]
	4.5–5.2	130–155	TiN/HA composite	[445]
	5	130	TiN/HA composite	[170]
	10 ± 1	147 ± 10	HA after annealing at 550 °C at 1 hour	[446]
	~3.4–4	~125	as-deposited HA	[171]
	~5–5.2	~140	as-deposited HA with TiN buffer layer	
	10–12	–	as-deposited HA	[447]
	1.5 ± 0.3	48 ± 6	Amorphous phase	[295]
	3.0–7.7	–	Crystalline HA	
	~3.5	~80	MIPS HA	[167]
	–	23.3 ± 0.8	As-sprayed HA	[263]
	–	33.2 ± 0.8	Hydrothermally treated HA at 150 °C	
	–	26.8 ± 1.5	Air heat-treated HA at 600 °C	
	3–5	~28.4	As-deposited SPS HA at 50 mm, and 27 kW	[37]
PS	–	~15.6	As-deposited SPS HA at 60 mm, and 30 kW	
	~3–3.4*	~56–62	As-deposited APS HA	[210]
	9.8 ± 1.9*	–	Laser processed HA	[82]
	4.5	~120	Small HA particles (20–40 µm)	[33]
	3.9	~111	Medium HA (40–60 µm)	
	3.5	~108	Large sized HA particles (60–80 µm)	
	5	~10–130	SPS HA	[31]
	4–4.5	~40–70	PPS HA	
	2.0 ± 0.4	82 ± 11	As-deposited HA at 650 °C, and 5 J cm ⁻²	[81]
	2.9 ± 0.5	92 ± 11	As-deposited HA at 650 °C, and 7 J cm ⁻²	
	10	–	Fluorinated HA deposited at 400 °C	[125]
	12–13	–	Fluorinated HA deposited at 500–600 °C	
	3.48	91.24	Unannealed HA films	[148]
	5.2	110	Amorphous CaP	[11]
	5.9	140	Crystalline HA	
PLD	1.9 ± 0.1	70 ± 17	As-deposited at 400 °C HA	[77]
	5–8	–	Amorphous carbonated HA deposited at 30–500 °C	[75]
	28 ± 3	–	Crystalline carbonated HA deposited at 700 °C	
	1.79 ± 0.8	53 ± 15	As-deposited at 400 °C HA	[74]
	1.25 ± 0.6	58 ± 15	As-deposited at 400 °C HA on Ti/TiN followed by WPT at 400 °C/6 h	
	–	–	As-deposited at 450–600 °C FG CaP	[99]
	–	–		
	–	–		
IBAD	~5–6.5	~90–100		

the implant without intervening fibrous tissue [315,316]. The phenomenon of osseointegration was first described by Brånemark et al. in 1977 [317] and first defined by Albrektsson et al. in 1981 [102,307,312]. *Osteoinduction* is defined as the process by which osteogenesis (*i.e.* new bone formation from osteocompetent cells in connective tissue or cartilage) is induced [308,310]. In effect, this phenomenon features in most bone healing processes, and osteoinductive materials provide a biological stimulus for induction, recruitment, stimulation, and differentiation of primitive, undifferentiated, and pluripotent stromal cells into osteoblasts or preosteoblasts, the initial cellular phase of a bone-forming lineage. The original definition of osteoinductive materials by Marshall Urist states that these biomaterials are capable of inducing bone to form when placed into an extraskeletal site [307,318]. Osteoinductive materials include autografts, demineralized bone matrix (DBM), and specific bone morphogenetic proteins (BMPs) that naturally form bone within the skeleton as well as extraskeletally [307,309,319,320]. The ideal bone regeneration system will be fashioned from an osteoinductive replacement material that elicits an appropriate cellular response with the aid of bioactive factors to allow healing and osseous regeneration.

In relation to the described above, the CaP-based coatings should be tailored to exhibit prescribed biological attributes for each specific application. The key requirements of the CaP coatings of implants and specific functions are summarized in Table 5 (re-designed based on [150,321,322]). The dissolution of the CaP coating is an important requirement to induce the precipitation of bone-like apatite on the implant surface [227]. More details about standard orthopedic specifications of HA bioceramics for surgical implants can be found elsewhere [323,324]. The extensive overviews on *in vitro* and *in vivo* evaluation of thin CaP coatings are presented elsewhere [67,325].

3.6. Biological assessments *in vitro*

Biological assessments allow modeling a biocompatible coating behavior in a human organism. *In vitro* laboratory models often consist of evaluating the effects of novel surfaces *versus* control surfaces on cell cultures [215,326]. The significant number of papers on biological assessments of the CaP-based coatings are done *in vitro* in SBF [3,37,71,81,117,129,133,178,182,218,221,224,276,327–331], Hanks' solution [94,159,160,178,231], fetal bovine serum (FBS) solution [54], buffering fluid (BF) [129], saline solution [58,277], phosphate buffered saline (PBS) [149,277], or fast calcification solution [163]. The dissolution of CaPs at soaking in SBF is a process which depends mainly, for the given fluid, on phase content and crystallinity; morphology (porosity, size of lamellas); and residual stresses pattern [224]. The CaP coatings and ceramics are degradable, with the following order of relative solubility CaO ≫ α-TCP > β-TCP > ACP > TTCP > OHAp/OAp ≫ HA [3,10,163,209,270]. PS deposited coatings dissolve quicker than stoichiometric HA does; since the high temperature process melts the HA powder and transforms it into new phases that lack the original hydroxyl (OH⁻) group [152]. Many large cracks propagate along the whole coating surface exposed to SBF [129,160,162,218], and other experimental media [159]. The deposition of calcium ions and the formation of phosphate layer when exposed to SBF are believed to be crucial to initiate the growth of bone-like apatite on biocompatible implants [160]. The incubation of the as-deposited HA coatings in SBF leads to the transformation of ACP to crystalline phases. OAp readily transforms in the presence of fluid back to HA [152,332]. It should be stressed that the formation of a secondary HA layer during the immersion in SBF is only a necessary, but not a sufficient effect for biocompatible behavior.

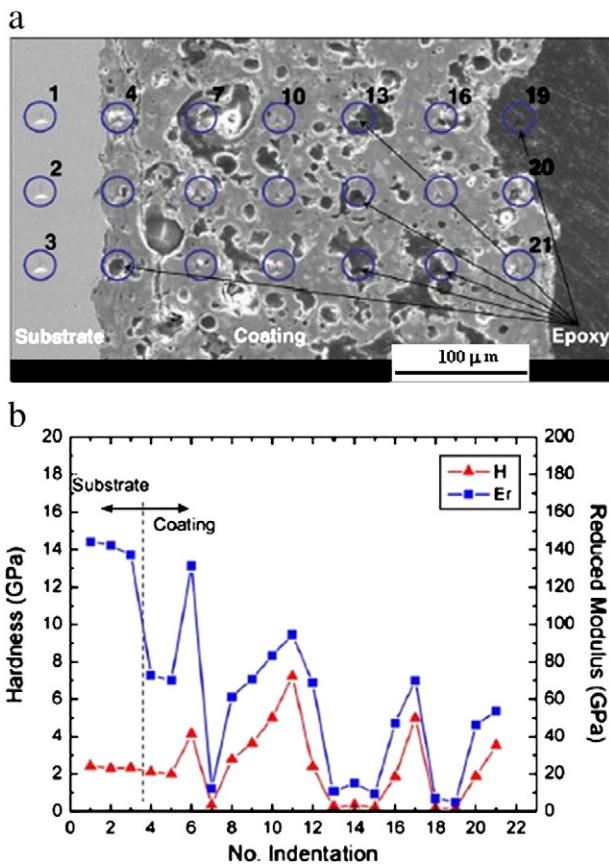


Fig. 13. Nanoindentation with 150 mN in a SPS coating, as seen in (a) a cross-section showing the indentation locations, and (b) the corresponding values of hardness and elastic modulus.

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The biological trials using different cell lines *in vitro* revealed that the CaP coating enhanced the cellular adhesion, proliferation and differentiation, in order to promote bone regeneration [2,14,49,51,78,82,99,102,117,150,158,177,179,225,251,278,326,333–338], and antibacterial activity [80,130,339] when compared to uncoated substrates. The cells seeded on the surface of a material coated with CaP synthesize a number of osteoblastic phenotypic proteins and promote the secretion of extracellular matrix (ECM). Alkaline-phosphatase (ALP) is the major marker characteristic of osteoblasts. ALP is regarded as an early marker for osteoblast differentiation, and it is generally accepted that as the specific activity of ALP in a population of bone cells increases, there is a corresponding shift to a more differentiated state [340]. Osteoblasts also produce osteocalcin, which binds calcium, concentrating local calcium levels further [307]. The CaP-based films typically increase the ALP activity, osteocalcin, and protein levels of different cell lines [48,121,338,341,342].

Table 5

Key requirements of CaP coatings of implants and specific functions.

Requirement	Definition/function
Biocompatibility	Ability of a material to perform with an appropriate host response in a specific application [305,443]
Bioactivity	Ability to interact with the surrounding bone and soft tissues
Osteoconductivity	Ability to provide scaffold for the formation of new bone [444]
Dominant crystalline phase	Prevent resorption (dissolution) of the coating in body fluids [17,18]
Amorphous phase	Promote early osseointegration [17,18]
Dissolution of HA	Programmed dissolution rate in body fluids to match the <i>in vivo</i> healing process
Defined elemental composition	Match elemental composition of bone mineral phase [17]
Specific surface morphology of interfacial matrix (interface 2)	Enable osteoblasts attachment and differentiation, and bone material ingrowth (fixation to the bone)
Interfacial stability and strong adhesion to an implant (interface 1)	Prevent mechanical failures under load bearing conditions [16,18]
Therapeutic capabilities	Templates for the <i>in situ</i> delivery of drugs and growth factors at the required times [438]

Some studies reported that heat-treatment enhanced the cells activity on the surface of CaP coatings [41,69,99,343]. The MTT and enzyme-linked immunosorbent assay (ELISA) results indicated that the cell proliferation and differentiation of the APS, LPS-dense and LPS-porous coatings were enhanced after heat treatment [41]. The LPPS-porous coatings after heat treatment (650 °C for 1 h) had the best osteoblastic MG-63 cell proliferation and differentiation compared to APS, LPPS-dense HA coatings. Bai et al. showed that FG IBAD coatings deposited at 450 °C promote more numerous cells attachment locations when compared to uncoated Ti and the FG coatings deposited at 400 °C [99]. The reason for better cell activity can be the following: post-heat treated HA coatings exhibit higher crystallinity, a rougher surface and more nanoparticles than as-deposited coatings [262,341,343].

Different CaP-based composites were tested *in vitro* [124,290]. The deposition of alendronate modified HA thin films by MAPLE technique yields coatings with enhanced bioactivity able to promote osteoblast-like cells (MG63) differentiation and inhibit osteoclast proliferation [124]. Osteosarcoma SaOs2 cells cultured 72 h on HA silk fibroin films prepared by MAPLE showed increased viability, good spreading and normal cell morphology [246]. HA coating combined with BMP-2 gene has better biological activity. The osteoconductivity of BMP-2 gene modified rat bone marrow mesenchymal stem cells on HA-coated substrates was mediated by the modulation of osteoblast differentiation and mineralization [344].

3.6.1. Influence of strontium, silicon, and silver on CaP film performance *in vitro*

Different dopants such as strontium (Sr), silicon (Si), and silver (Ag) in CaPs significantly affect the coatings biological performance *in vitro* [72,80,108,116,117,122,123,127,130,345–351,448,449]. Antibacterial effect of Ag is reported for plasma sprayed [127,130,351], RF magnetron sputter deposited [350], IBAD deposited [90,98], and PLD deposited [72,80] Ag-HA coatings. Feng et al. showed that impregnating HA films with Ag results in excellent antibacterial properties against gram-positive and gram-negative bacteria [349]. Chen et al. studied the *in vitro* cytotoxicity of co-sputtered Ag-containing HA coatings [350]. A significantly reduced number of *Staphylococcus epidermidis* and *Staphylococcus aureus* on the Ag-HA surface was achieved without remarkable differences in the *in vitro* cytotoxicity compared with HA surface.

The presence of Sr (3–7 at.%) in HA thin films can enhance the positive effect of HA coatings on osteointegration and bone regeneration of MG63 osteoblast-like cells, and prevent undesirable bone resorption [122,123]. Significantly increased values of ALP activity, osteocalcin, type I collagen and osteoprotegerin/TNF-related activation-induced cytokine receptor ratio, and considerably reduced values of osteoclast proliferation, were observed.

Tang et al. using *in vitro* cell culture demonstrated the highest human osteoblast cells growth on Si-HA coatings (0.73–0.82 wt.% Si) compared to HA [108]. Plasma spraying of Si-HA coatings (0.8 wt.% Si) over Ti substrates demonstrates increased metabolic activity and ALP regarding human bone marrow derived osteoblastic cells proliferation

and differentiation, comparing to HA coatings [117]. Thian et al. also reported improved cell growth on a magnetron sputter deposited 0.8 wt.% Si-containing HA over Ti surfaces, comparing to uncoated ones [112,119,348]. Xiao et al. using human serum albumin (HSA) revealed that the incorporation of silicon (up to 1.22 wt.%) in HA can lead to significant improvements in the bioactive performance of HA [116]. The incorporation of silicate groups (SiO_4^{4-}) into the HA lattice leads to a tetrahedral distortion. This creates some hydroxyl site vacancies, which in its turn decreases the apatite structure stability and increases the reactivity [108]. The silicate ions substitution into HA crystal lattice is believed to significantly influence the surface wettability and increases the surface charge that results in the enhancement of protein expression, namely of ALP, type 1 collagen, and osteocalcin [347]. A critical review of silicon influence on CaP performance has been recently published [352].

3.6.2. Influence of surface topography on CaP film performance *in vitro*

Surface factors, such as chemistry, energy, roughness and crystallinity that influence the cell response to a biomaterial have recently attracted much attention [5,102,342,343,348,353]. Surface chemistry and nanotopography play a major role in the osseointegration of implants, and hence plasma-assisted deposition represents a powerful tool for producing surfaces that would allow us to understand, modulate and elicit the desired reactions on the tissues surrounding implants, and that would eventually lead to more satisfactory tissue regeneration [83,139,354]. The microtopography creates an environment, so-called niches, favorable for cells and cell ECM interactions, and increases production of growth factors [278,354–356]. It provides increased differentiation of osteogenic cells, resulting in high activity of ALP and osteocalcin synthesis [357,358]. The RF magnetron sputter deposited CaP coating improved the ALP activity of SaOS-2 cells and it should be noted that the CaP coating enhances the osteogenic differentiation of osteoblasts on the surface of the blast-treated Ti plate [342].

The differences in the coating properties were seen to have a significant influence on the nature of the protein adsorption [54]. Cairns et al. reported that the influence of surface topography on osteoblast-like cells (MG63) adhesion, proliferation and differentiation in the presence of an adsorbed fibronectin (FN) layer [51]. The use of protein ad-layer in combination with different surface topographies has allowed for a more detailed assessment of the attendant response *in vitro*. Osteoblast-like cell response to the various sample types has confirmed the ability of the FN layer on CaP thin films to improve cell adhesion and early osteoblast differentiation. The results illustrated that FN layers on the CaP thin films with microstructure and a nano-scale surface roughness results in up-regulated focal adhesion assembly and enhanced early cell differentiation.

Most surfaces currently available have random topography with a wide range of thicknesses, from nanometers to millimeters. The exact biological role of these features is unknown because of the absence of standardized surfaces with repetitive topography at the nano-sized level (e.g. pits with fixed diameters and depth, lanes with controlled profiles). Such controlled or standardized surfaces might help to understand the interactions between specific proteins and cells [137]. So far, there exist few studies that have investigated the importance of nanometer structures on implant integration in bone but the few that exist indicate nanometer structures to have an impact on early bone healing [261,359]. However, the optimal size and distribution of nanometer particles or pores applied on implant surfaces is still unknown [139].

3.7. Animal studies *in vivo*

The challenge in implant research is the capability of the surface to guide cells colonization and differentiation. Cell migration, adhesion, and proliferation on implant surfaces are a prerequisite to initiate

the tissue regeneration [359]. Following *in vitro* laboratory tests for the general safety of new biomaterials' surfaces, laboratory *in vivo* models are the next step in biocompatibility testing complexity [215]. CaP coatings increase the surface roughness of implants and are used to promote osseointegration [120,158]. The effect of different dopants such as strontium (Sr) [120], silicon (Si), zinc (Zn), and others in CaPs on the coatings biological performance *in vivo* is presented in the review of Habibovic et al. [345].

Most animal studies at early implantation times (typically 2–6 weeks) including RF magnetron sputter deposited [63,277,360–362], PLD deposited [158], PS deposited [25,232,238,354,363–365], and IBAD coated [101,215,252,254,366,367] CaP-based thin films on Ti and Ti6Al4V implants demonstrated higher biomechanical fixation [63,238,277,354,361,364,366], healing capacity [232,366], bone-implant contact (BIC) [25,63,215,252,277,354,360,362,364,365,368], and antibacterial activity [130] when compared with non-coated implants.

The following animal studies at longer implantation times (from 6 weeks to 27.5 months) including RF magnetron sputter deposited [50,342,361,369,370], PS deposited [106,107,143,163,237,363,364,371–374], IBAD deposited [215,253,259,260], PLD deposited [143,375,376] also reported higher biomechanical fixation [106,163,215,322,361,363,368–373,377–379], healing capacity [106,253,379,380], BIC [107,195,237,253,259,260,342,369,370,374–376,381] when compared with non-coated implants. Though, it is worth noting that the difference in BIC between an HA-coated implant and an uncoated one was not significant [50,143,375,376].

The thickness of the coating, which promotes better biological response, has been investigated [382]. Histomorphometric and biomechanical testing at early implantation times showed that IBAD deposited coating thickness of 300–500 nm resulted in increased biological response when compared with a 20–50 nm coating thickness at early implantation times control surface implants (alumina-blasted/acid-etched (AB/AE) Ti alloy implants) [101,254]. Though, ultra thin (20–50 nm) bioceramic coating deposited by IBAD onto previously AB/AE substrates presented biocompatible and osteoconductive properties *in vivo* [138], a 20–50 nm thick bioceramic CaP coating onto previously AB/AE substrates did not improve the biomechanical fixation and the BIC at early implantation times *in vivo* [254]. Furthermore, it was demonstrated that the *in vivo* performance of the 300–500 nm thickness IBAD deposited coating was comparable to plasma sprayed HA [215]. Ultra-thin RF magnetron sputter deposited 0.1 μm thick amorphous CaP coating on dental implants can combine the positive effects of CaP during the early stage of osseointegration without causing the impairment of the later stages [50]. Peraire et al. reported that while 50 μm thick plasma sprayed HA implants showed considerable instability and reduction in thickness after 24 weeks, but no statistical difference to the Ti group, the 2 μm thick HA PLD group showed much higher amount of bone apposition than the other two groups, without signs of degradation or dissolution [143].

Attempts to identify the structure of the coating which promotes better osseointegration were performed. The 0.1 μm thick amorphous CaP is likely to be degraded rapidly, which is in agreement with the results obtained by Wolke et al. that 0.1 μm thick CaP coatings disappeared within 1 week of implantation [383]. The fast dissolution of the ultra-thin CaP coating and the subsequent almost similar surface of the implants can also explain the same osseointegration after 27.5 months independent from surface modification [50,384]. An increase in the percentage of the BIC was demonstrated in Ti cylinders coated with an ACP coating after 8–12 weeks following their implantation in the mandibles of beagle dogs [342]. Vercaigne et al. installed Ti oxide (TiO_2) grit-blasted implants provided with RF magnetron sputter deposited, amorphous/crystalline CaP coatings of different thickness [0.1 μm (CaP0.1), 1 μm (CaP1), 4 μm (CaP4); R_a : 1.3–2.1 μm] in the trabecular bone of the femoral condyle of goats and compared mechanical anchorage as well as bone-implant response [369]. Compared with the uncoated, grit-blasted surface, the mean BIC percentages for CaP 1 and

CaP 4 were statistically higher after 6 as well as after 12 weeks. A similar improving effect of crystalline sputtered HA coatings on the BIC was observed by Mohammadi et al. in rabbit studies [362].

Dissolution of plasma sprayed HA coatings observed *in vivo* has a positive effect on osteoconductive properties of the CaP-based coatings [106,354,374,385,386]. However, the observations of a nonuniform and partial degradation of CaP plasma sprayed coatings after implantation [354,387–389] and a relationship between fragments from fractured coatings and adverse cellular reactions in the interfacial bone, were suggested to adversely affect the long-term integration [354,387,390]. Another aspect is the propensity of materials to contribute to established infection [391]. There are studies reporting no effect of the coating, some of them are controversial [5,101,392]. Moura et al. suggested that the presence of a bioactive ceramic IBAD deposited 300–500 nm thick coating on a rough AB/AE substrate did not favor the events related to *in vitro* osteogenesis compared to the smoother as-machined surface and the moderately rough AB/AE surfaces [5], whereas Coelho et al. found positively modulated bone healing *in vivo* at early implantation times of the IBAD deposited 300–500 nm thick coating [101]. The studies raising concerns on long-term performance of HA coatings are discussed by Lima et al. [212]. Furthermore, the plasma sprayed HA coating did not improve either bone integration or pull-off strength of unloaded-pedicular screw in spine [392]. Though sufficient experimental data are available in the literature that signify the influence of the CaP-based coatings on bioactivity of the implants, the absence of the standardized technological procedures and different equipment used for preparation of the coatings leads to the occurrence of CaP films with different surface roughness, composition and chemistry, which makes it difficult to compare the results obtained by different authors.

3.7.1. Clinical trials *in vivo*

The replacement of a tooth and bone with metal implants and plates is one of the most frequently used and successful surgical procedures. The introduction of modern implants started with the work of Brånemark, who observed in 1969 that a piece of Ti embedded in a rabbit bone became firmly attached and difficult to remove [393]. This led to Brånemark's careful characterization of interfacial bone formation at Ti implant surfaces, and the demonstration of excellent osseointegration [315,322,394]. Dental implants based on the Brånemark's work were introduced in 1971 [395]. The total hip replacement was first developed by Charnley in 1962, with stainless steel used for the stem and the attached ball [9,322,396]. After the decades of subsequent research in industry and academia, implants have evolved, with a high percentage of survival rate and longevity. In 2003, more than 700,000 dental-implant procedures were performed in the United States and more than 1.3 million procedures in Europe [322,397]. Approximately 1 million artificial hips and knees are implanted each year in the United States, as reported in 2006 [398]. Hip and knee replacements have a success rate of more than 90%, and dental implants of 90–95% [399]. Dental implants have a long and successful history. The percentage of failures is very low, approximately 5%, most likely due to infection, rejection, accelerated bone loss, and poor osseointegration with the loosening of the implant [399]. The most frequent cause for failure is insufficient bone formation around the biomaterial immediately after implantation [322,400]. Therefore, these are the areas where improvements are needed.

In clinical practice bioceramic HA coatings are being routinely applied to Ti and Ti6Al4V alloy orthopedic prostheses and dental implants by PS [23,127,133,137,158,209,215,221,230,233,235,316,354,357,359,401–403]. IBAD is also used to apply either HA coatings to dental implants [260] or antimicrobial coatings to catheters and other devices [90]. Extensive review on clinical performance of plasma sprayed medical implants has been given by Sun et al. [4]. Most clinical studies are optimistic about the long-term performance of HA-coated prostheses [168,215,403]. Clinically, HA-coated implants show less subsidence on

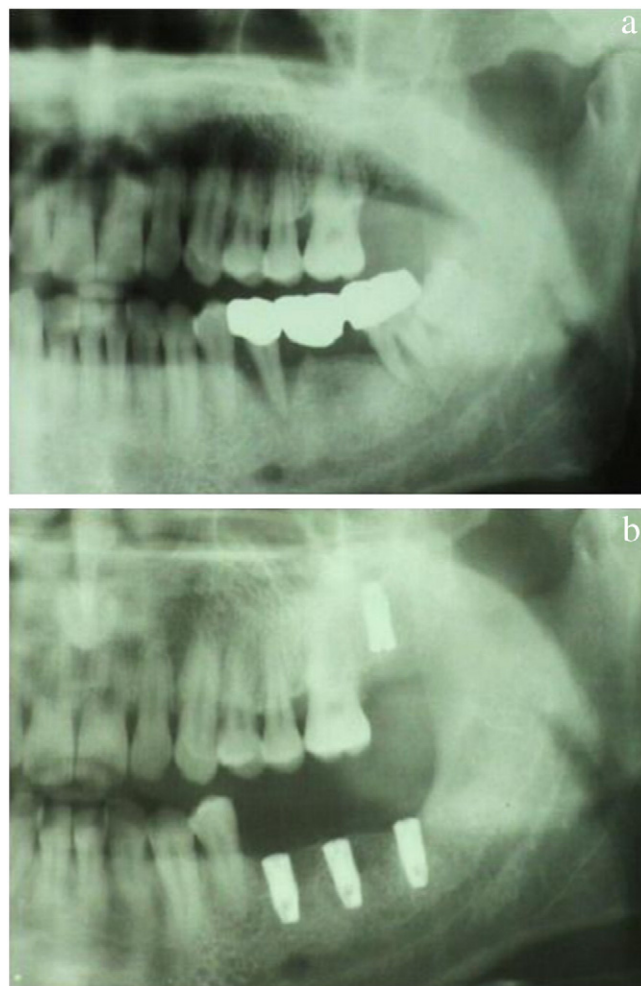


Fig. 14. Radiographs before (a) implantation in a patient and (b) 1-year after. Reprinted from [104] with authorization of Elsevier.

roentgen stereophotogrammetric analysis, which may reduce the risk of the development of implant aseptic loosening [49]. The HA coating appeared to increase the prosthesis (press-fit femoral stems) surface roughness on a microscopic level that was mechanically important [404]. The addition of the HA coating improved immediate postimplantation stability through mechanical means, before biological action.

The radiographs of a patient before and after the implant treatment in mandibular are shown in Fig. 14 [104]. Before the treatment, the patient suffered from the fixed restoration with inflammation. There existed much bone loss around the abutment teeth (Fig. 14a), so the restoration was loosened and needed to be extracted. The CaP IBAD coated implants were placed to restore the loss of teeth. After 1-year functional loading, the implants were well maintained with osseointegration and there wasn't any inflammation or bone loss around the implants (Fig. 14b). The retrieval of HA-coated oral implants after 10 years of functional loading in a mandible have revealed maintained coating and high implant–bone contact [354,405]. A meta-analysis on the survivability of the HA-coated dental implants showed that the long-term effect (up to 10 years) of the HA-coated implants is certain and affirmative to clinical use [406]. Two human HA-coated dental implants were retrieved after a 14-year loading period [407]. No acute or chronic inflammatory cell infiltrate was found in the peri-implant tissues. No signs of coating infection, fatigue, or failure were observed. The clinical (Baleia Hospital, Brasil) evaluation performed on of HA-coated fixation pins after a 4 year period showed a very good HA thermal spray coating biocompatibility with a human tissue such as bone and muscle [168]. An inflammatory reaction occurred in only 3% of HA-coated fixation

pins; whereas 30% of non-coated fixation pins did produce the inflammatory reaction. A manual extractive force 10 times greater in HA coating pins shortly after surgery indicates that there is better integration between bone and the HA coating than in the case of non-coated pins [168]. Saithna in his review reported that there had been significantly less pin loosening in the HA-coated groups although the definition of loosening was based on different criteria [15].

Recent clinical orthopedic studies indicate that there is no clear advantage to using HA coatings either for a femoral stem or an acetabular cup of hip implants [408–413]. The situation with dental implants is no different; there are contradicting reports on the effectiveness of the HA coatings [414–416]. A problem is the variability in the composition and microstructure of both experimental and commercially available HA-coated oral implants [354]. The clinical survival data reported for the HA coatings on oral implants were similar to those reported for non-coated Ti [417]. One of the major concerns with plasma sprayed coatings is the possible delamination of the coating from the surface of the Ti implant and the failure at the implant–coating interface despite the fact that the coating is well-attached to the bone tissue. The discrepancy in dissolution between various phases that make up the coating has led to delamination, particle release and thus the clinical failure of implants [137,414,418]. The CaP coatings have also been reported to be at a higher risk for failure, due to peri-implant diseases, when compared with non-coated devices [4,107,316,419–421]. Thus, the issue of coating practical utility is not fully resolved. Further investigation of the CaP coatings prepared using plasma-assisted methods is required to provide a better understanding of the long-term clinical performance of these films [133].

4. The most important challenges and critical issues

Future research should concentrate on both the improvements in the CaP coating deposition process and investigation of their characteristics. It is known that all plasma-based processes, such as PS, PLD, RF magnetron sputtering and IBAD, are line-of-sight techniques, therefore, additional measures should be taken to prepare a uniform coating on implants with a complex geometry. Plasma-assisted techniques can cause the dehydroxylation of HA during biocompatible film deposition [2,58,99,108,111]. Therefore, if a coating of pure HA is to be deposited the addition of water vapor into the deposition system should become commonplace. A possible effect of water vapor on the CaP coating adhesion strength should be taken into account [11,71,78]. A potential drawback of the novel processing techniques for CaP film deposition is its relatively high cost for a large scale production. Therefore, to decrease processing time and make thin coatings manufacturing commercially viable, it is desirable to process the thinnest coating that would significantly increase the biological response [215]. Large amount of coatings have been applied to metallic implants with a variety of surface modification techniques, however, few studied coatings have multi-functions and few of them have come into clinical use. The organic–inorganic hybrid coatings may be a prospective challenge [422]. Much attention should be paid to FG CaP-based coatings with an amorphous top layer and a crystalline layer underneath [3]. This allows adjusting the coating resorption rate to the rate at which new bone grows at early stages, when it is of the most importance for the bone mineralization process. The amorphous regions may act like cement, promoting the cohesion between the crystalline regions and the adhesion to the substrate [240]. According to the International Organization for Standardization, the crystalline content of HA shall be not less than 45% and the maximum allowable level of other crystalline phases shall be 5%, with the balance being amorphous [108].

It is known that the study of the bioactivity of the CaP-based coatings is usually performed using SBF solution [37,155,224,331]. However, the method itself may provide at best incomplete information, primarily because it is determined only by solution supersaturation,

irrespective of biological processes [423]. The misinterpretation of the outcome of such tests might result in the misunderstanding of the true effects and behavior of materials intended for use in embedded biological contexts. The mechanisms involved in the formation of the interface between the coating and bone may differ drastically from those in pure inorganic SBF. Beside the physico-chemical interactions, adsorption of proteins to the surface and substrate specific cell activity also influences the structure of the interface under biological conditions. Thus, one can obtain more information on the biological behavior of these coatings by the way of *in vitro* assessments in bone cell culture including tests to determine the levels of ALP and osteocalcin [273].

Although it is generally accepted that HA and CaP coatings deposited by plasma-assisted fabrication methods improve bone strength and the initial osseointegration rate, the optimal coating properties required to achieve maximum bone response are yet to be determined. A better understanding in structure–property relationship would provide good guidelines for implant designs [178]. Moreover, there are only a limited number of *in vivo* studies available in the open literature [5,50,101,107,130,138,158,163,233–235,238,254,277,392,402,424,425]. The *in vivo* testing should demonstrate stability in biological environment for up to 1 month, which corresponds to the initial healing phase of the implants [152]. The limitations on such experiments may be attributed to any of the following reasons [13]: i) difficulty in selecting a suitable animal model so as to simulate the actual mechanical loading and unloading conditions the implant might undergo in a human body environment; ii) the need to sacrifice a large number of animals, since most of these experiments demand a statistical analysis to validate the results; iii) high cost and long time frame of clinical testing these experiments demand; iv) lack of coordination among material scientists and biologists and thereby an insufficient understanding of this interdisciplinary subject; v) serious ethical concerns on the use of animals for experimental studies, as they are subjected to painful procedures or toxic exposures in the course of a test.

Another concern about HA coatings is their adhesion to metal substrates, which is influenced by the coating properties, the substrate superficial roughness, and, most of all, the residual stresses. The difference between the coefficient of thermal expansion of HA and that of Ti/Ti alloys is relevant and may result in dangerous thermal residual stresses. The HA coating–metal substrate adhesion may be improved by the introduction of a proper bond coat, such as TiO₂/Ti/TiN and some other interlayers (see Section 3.4.1, and [426]). Moreover, they prevent direct contact between the HA and the metal substrate which is likely to act as a catalyst for the thermal decomposition of the HA. It also reduces the release of metal ions from the metal substrate (e.g., NiTi [44,58,450], Ti and cobalt-chromium alloys [427], and Ti6Al4V [428]) and reduces the fatigue phenomena caused by the cyclic loading–unloading stresses under service conditions [240].

As was already mentioned plasma-assisted fabrication allows the preparation of the coatings with nano/micro scaled surface topography, which plays a crucial role in the further targeted protein and cell adhesion. The influence of surface chemistry modifications and topography at a nano/micro scale level on biological response, as well as hydrophilicity, surface charge, and wettability should be studied more carefully [5,13,51,145,221,277,347,354,359,429–436]. Despite the extensive literature in the field of osseointegrated surfaces, the lack of hierarchical approach and standardized parameters makes it difficult to evaluate the significance of the effect that the numerous topographic and chemical modifications have on implant performance [435].

Biphase CaP coatings prepared by plasma-assisted fabrication consisting of a mixture of β -TCP and HA at various ratios are promising in the sphere of bone defects repairing rather than in pure HA or β -TCP [4]. The HA is considered the most stable phase and a non-biodegradable bone replacement material, while β -TCP is biodegradable and significantly more soluble in body fluid than HA. Their physicochemical properties, such as crystallinity, determine surface

reactivity *in vivo* which is important for chemical and cell-mediated degradation of the material, and also for the osteogenic differentiation of endogenous cells, so-called osteoinduction [437].

To conclude, future investigations of plasma deposited CaP-based coatings should address [10,102,321,322,438]: i) the effect of coatings crystallinity (including the importance of low crystallinity), chemical composition and surface topography on the cell differentiation, ii) therapeutic capabilities of the coating (templates for the *in situ* delivery of drugs and osteoinductive agents (peptides, hormones and growth factors) at the required times), and iii) long-term *in vivo* clinical trials to optimize coating properties, continue the preclinical research to provide additional understanding of bone responses to the coated implant surfaces of different properties.

5. Conclusions

This review summarizes some of the latest achievements in the field of plasma-assisted fabrication of CaP-based coatings prepared using the most frequently applied techniques: PS, RF magnetron sputtering, PLD, and IBAD. It is aimed at significant reduction of the problems associated with implant failures in the short run. The presented techniques encourage the preparation of the coatings with tailored characteristics. There can be deposited either dense, homogeneous, pore-free and high adherent biocompatible coatings with tailored stoichiometry that can prevent leaching of toxic ions (e.g., nickel) from the metal to the surrounding tissues or rough and porous coatings that can stimulate new bone osteogenesis. The main advantages and limitations of the described techniques to deposit CaP-based coatings are presented as well as the most important challenges and critical issues are highlighted.

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