J. Electrochem. Sci. Eng. **13(1)** (2023) 41-62; http://dx.doi.org/10.5599/jese.1424

Open Access : : ISSN 1847-9286
www.jESE-online.org

Review paper

Understanding cold spray technology for hydroxyapatite deposition

Gaurav Prashar[1] and Hitesh Vasudev[2,✉]

[1]*Department of Mechanical Engineering, Rayat Bahra Institute of Engineering and Nanotechnology, Hoshiarpur, Punjab, India*

[2]*Division of Research and Development, Lovely Professional University, Phagwara 144411, India*

Corresponding author: ✉*Hitesh.24804@lpu.co.in*

Received: June 23, 2022; Accepted: January 6, 2023; Published: January 31, 2023

Abstract

The standard method for applying hydroxyapatite (HAp) coatings to biomedical implants is plasma spraying. However, due to the high temperature of the plasma, these coatings frequently experience negative effects like evaporation, phase change, de-bonding, gas release, and residual stresses. This paper summarizes a revolutionary technique known as a cold spray (CS), which allows HAp coatings to be applied at temperatures well below their melting point. CS has several advantages over conventional high-temperature technologies, and it seems to be approaching parity with other older methods. When applied using the CS approach, the HAp coatings enhance bioactivity, increase corrosion resistance, and maintain the characteristics of calcium phosphate ceramics. This study aims to give a concise and comprehensive overview of HAp-based materials, including substituted-HAp and HAp/polymer composites, and their applications in bone tissue engineering. To better understand the advantages of CS technology, a comparison of CS, high-velocity oxy-fuel (HVOF), and plasma spray is given at the end. The perspective and difficulties were also highlighted.

Keywords

Cold spraying; high velocity oxygen fuel spraying; plasma spraying; hydroxyapatite coatings; 3D printing

Introduction

Aging is inevitable, as are its effects. The capacity of the human body to protect or mend tissue and cells is gravely impaired by toxins, genetic/hereditary anomalies, acute injuries, trauma, and illnesses. Since ancient times, those interested in medicine have considered the above-mentioned harmful components and how they affect the body. They have put a lot of effort into developing methods for keeping them in check. Thanks to evolutionary breakthroughs like thermal spray, science has advanced sufficiently to create methods for regaining function, correcting anomalies, and promoting healing in many human body parts. Technologies using thermal spray provided

versatility and adaptability in a range of biological applications. The various substrate and coating materials determined the technique that was used. Applications for replacement and repair both benefit from these tactics [1,2].

Bone is not consistently solid because it is made up of living bone cells arranged in a biomineral medium. This medium's surrounding intertwined cells are toughened to create bone. The majority of bone is composed of collagen fibres and an inorganic mineral in the form of small crystals [3]. About 30 % organic and 70 % inorganic components make up the biomineral medium of bone [4]. Osteopontin and other bone matrix proteins, non-collagenous proteins, lipids, and proteoglycan molecules make up practically all of the remaining 10 % of this organic segment [5]. The bone matrix proteins' ability to adhere to tissue and maintain mechanical strength is crucial.

Hydroxyapatite (HAp) ($Ca_{10}(PO_4)_6(OH)_2$) has been acknowledged for its good biocompatibility and efficiency in aiding biointegration for implants in soft tissue and osseous because of its similar composition to human bone [6,7]. Figure 1 shows the hexagonal crystal structure of HAp. The unit cell has 2 OH-, 10 Ca^{2+} and 6 PO_4^{3-} tetrahedra. The lattice parameters are as follows: $a = b = 0.943$ nm, $c = 0.688$ nm, and the a and b axes are at a 120° angle. Calcium and phosphorus, which have an atomic ratio of 1.67, make up the majority of natural bones. It is, therefore, commonly used in prosthetic joints, bones, dental implants, and other implant goods. It currently holds a prominent position in the field of biomaterials and has a lot of development potential [8-10].

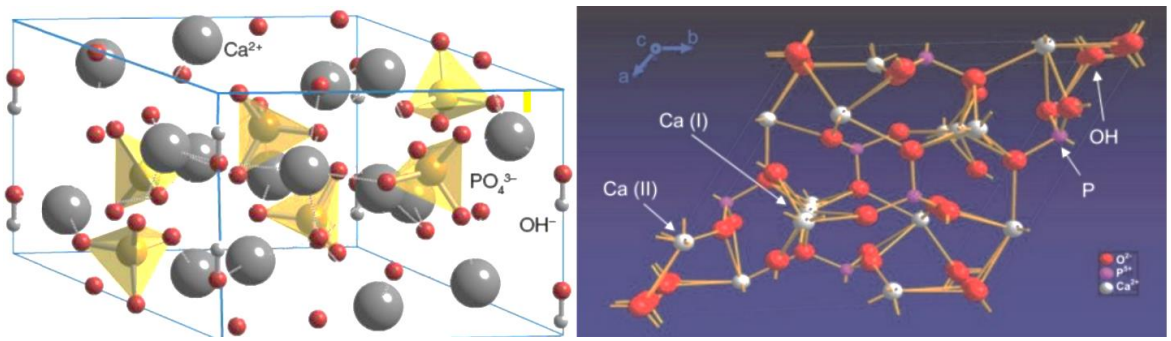

Figure 1. *HAp crystal structure [11]. Permissions under Attribution 4.0 International (CC BY 4.0)*

Figure 2 depicts the four key cells involved in bone regeneration and structure, including osteogenic, osteoblastic, osteocyte, and osteoclastic cells (together known as the basic multicellular unit).

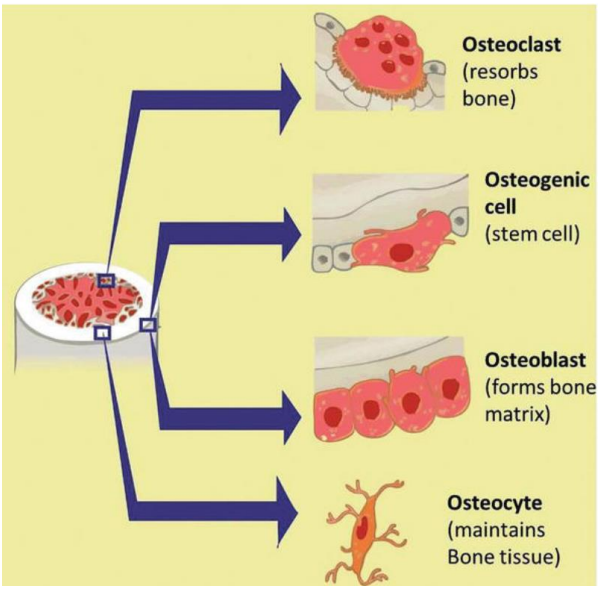

Figure 2. *Four important cells found in bone structure [12]. Permissions under (CC BY 4.0)*

Bone turnover is governed by the equilibrium between osteoblast and osteoclast activity, ensuring that neither too much bone is made nor too much bone is degraded. These cells both create and break down the bone matrix, which is made up of osteoid and HAp.

Metallic biomaterials have been utilized to replace biological implants since the nineteenth century. The mechanical properties of these metallic biomaterials, which satisfy the needs of human bone, have earned them the clinical success designation. When utilized as implants, the materials have significant downsides, such as releasing harmful and hazardous metal ions through wear and corrosion mechanisms after lengthy implantation. The bonding strength between human bone and metal implants is also believed to be limited due to the different components that make up both. Thus, it is hoped that the problems with biocompatible metallic biomaterials will be resolved by the development of metallic biomaterials with HAp coatings. The formation of HAp coating on metallic biomaterials improved their ability for load-bearing and substrate-coating adhesion while also increasing their resistance to corrosion. HAp possesses exceptional bond-binding capabilities (contrary to metals). Coating implants with a layer of HAp is one of the most common options due to its excellent biocompatibility and osteoconductive properties. Coated implants benefit from higher mechanical qualities and increased biocompatibility thanks to the union of a hard surface and a ductile substrate. The two most often used compositions across a range of biomedical applications are tricalcium phosphate (TCP) and HAp. The rate of HAp dissolution is significantly less than that of TCP. Because of its decreased dissolving rate, HAp is a good option for covering metallic implants.

Ti-6Al-4V is currently the most widely used metal alloy for orthopaedic applications due to its excellent properties [13]. The lower cytotoxicity associated with Ti-6Al-4V is due to vanadium ions leaching into the patient's bloodstream after an implant has been in place for a long time. vanadium ions can cause long-lasting disorders such as osteomalacia, Alzheimer's disease and neuropathy. As a result, they require the application of HAp coatings to alter the surface properties.

There are further reasons to be concerned with HAp since it limits the kinds of surface coating techniques that may be utilised to deposit it on Ti-6Al-4V for the therapeutic field as a result of its heat sensitivity and lack of plastic deformation. The development of new, commercially viable methods for generating HAp coatings on Ti-6Al-4V is constantly being researched. Several techniques have been used to successfully modify the metallic surface of Ti-6Al-4V alloy, including spraying it with a thin, continuous layer of HAp [13]. The manufacture of HAp coatings for commercial prosthetics using the plasma spraying method is well-established and permitted by FDA rules [14,15]. In spite of this, using greater working temperatures and rapid cooling (10-7-10-8 K/s) during plasma spray can alter the phase composition, increasing the likelihood of implant failure [16]. The development of amorphous phases and impurity phases like (-$Ca_3(PO_4)_2$, -$Ca_3(PO_4)_2$, $Ca_4P_2O_9$, and CaO) is mostly to blame for the greater dissolution rates in aqueous environments. Numerous authors have reported that the production of calcium phosphate phases (non-apatite, /-TCP) as a result of HAp disintegration at higher temperatures was observed between the 30.5 and 31.4° diffraction angles. Furthermore, there are issues with HAp coatings' poor mechanical characteristics, which restrict their clinical utility in orthopaedic applications [17]. These qualities include increased brittleness, wear, and less fracture toughness. The mechanical performance of HAp coatings must be increased as a result without compromising biocompatibility. In Table 1, the advantages and disadvantages of HAp coatings applied using various techniques are highlighted and discussed in-depth. It is also mentioned that wet deposition techniques are expensive and inappropriate because they cannot create thick, continuous HAp coatings. The adverse effects of HAp coatings made with

plasma spraying technology are accelerated resorption while in use and weak interface adhesion to the substrate.

Table 1.*Various methods to deposit HAp coatings on metal implants with their merits and demerits [18]*

Methods	Thickness, µm	Demerits	Merits
Plasma spray	30-300	High temperatures encourage decomposition; quick cooling causes amorphous coatings; high temperatures hinder the simultaneous integration of biological agents; increased dilution rates; and poorly controlled physicochemical coating characteristics	Higher deposition rates result in improved biocompatibility, wear resistance, and corrosion resistance. In most cases, tensile adhesion strengths greater than 15 MPa are achievable
Cold spray	20-30	expensive process; no deposit of pure HAp powder	Less porosity, lower processing temperatures, no phase disintegration after spraying, better biocompatibility, wear and corrosion resistance, green process, encourages bone fusing, crystalline coatings; high strength of adhesion
Magnetron sputtering	0.5-3	expensive method; lower deposition rates; fast cooling produces amorphous coatings; High temperatures inhibit the simultaneous integration of biological agents	Heat-sensitive substrates will also be coated, and flat substrates will have uniform coating thickness, high adhesion strength and purity, low porosity, and dense coatings
Sol-gel technique	<1	Some procedures call for the use of expensive raw materials and controlled environments	Thin coatings, lower processing temperatures, an affordable procedure, the ability to cover complicated forms, and the incorporation of biological molecules
Biomimetic process	<30	Process takes a long time; pH consistency and replenishment are required	Less processing temperatures, the ability to create bone-like apatite, the ability to cover complicated forms, and the incorporation of biological molecules
Pulsed laser deposition	0.05-5	High temperatures make the simultaneous integration of biological agents impossible. Expensive procedure	improved adhesive strength; crystalline phase coatings; porous, dense coatings
Hot isostatic pressing	Up-to 2	Complex substrates can't be coated, coating demands high temperatures, thermal expansion mismatches, different elastic properties, is expensive, and encapsulating material removal/interaction; High temperatures prohibit biological agents from integrating at the same time	A dense covering may be created
Ion beam deposition	0.05-1	high-priced, amorphous coatings	Greater adhesive strength and homogeneous thickness of the coating that is created
Micro-arc oxidation	3-20	Every coating, with the exception of calcium orthophosphates, contains admixture phases	Simple, affordable, and eco-friendly coating technique that allows for covering of complicated geometries

One alternative is to use post-heat treatments (HT) on such HAp coatings to change amorphous HAp into crystalline phases [19]. Utilizing metallic porous-rough surfaces is another way to enhance mechanical properties through bone-in-growth interlocking [20]. A key factor in attaining long-term coating stability is coating dissolving behaviour. Two factors primarily affect how quickly coatings dissolve: (i) inborn material characteristics like composition and crystallinity and (ii) environmental factors like media composition and pH. It is well known that HA crystallinity has a significant impact on the tendency of HAp coatings to dissolve. Subsequent HAp phases like tricalcium phosphate, calcium oxide, tetracalcium phosphate, and amorphous calcium phosphate speed up the dissolution process [21,22]. The development of an amorphous calcium phosphate phase in the coating/substrate interface was found [23,24], which is detrimental to the coating's bond strength in in-vitro testing, even though high-velocity oxy-fuel (HVOF) produced more crystalline HAp coatings than plasma spray. HVOF crystalline HAp coatings were developed as an option to increase binding strength, and when exposed to simulated body fluids, they outperformed coatings without heat treatment [24]. On the other hand, osteoblastic differentiation was more pronounced in the presence of amorphous calcium phosphate. HAp coatings with graded crystallinity seem to be the best way to strike a balance between the biological properties of the deposited coatings and the adhesion strength of the crystalline coatings [25].

To manage the composition of HAp, low-temperature coating deposition techniques such as aerosol deposition [26,27] and nanoparticle deposition [28] were developed. On the other hand, these deposition techniques produced incredibly thin (nanometric) layers as a result of the reduced particle size. However, an additional HT of up to 400 °C was needed to prevent amorphous phases. The size of HA crystals increased from 16.2 to 29.3 nm under HT up to 400 °C, improving biological properties. On the other hand, HT beyond 400 °C led to a loss of biological features [18]. Furthermore, different HAp surface roughness was generated by altering the particle size distribution. So, cold spray (CS) was created as a substitute for HAp coating deposition.

Cold spray (CS)

CS, also known as cold-gas spraying, supersonic powder deposition, and kinetic spraying, is a relatively novel spraying technology. As new uncertainties develop and the inter-disciplinarity of research projects increases, it is difficult to forecast when or how the field of CS will reach its productivity plateau. Due to CS's green attributes, manufacturing must shift toward a sustainable future, which indicates an increasing necessity for its use. There will probably be more uses for CS in a greener world (which is the future). Due to the lack of fusion characteristics, the process has a smaller carbon footprint, and when other processes are put under pressure from high emissions, CS will fill a new market niche. A positive development is anticipated in the highly regulated biomedical field. However, as more process control and environmental compatibility will be required in the future, some spray methods are hitting their technological limits. As a result, we do anticipate increased interest in investigating process-specific certifications. Figure 3 shows the indicative hype cycle curve modified for the emergence and development of CS technology. Deformable metallic particles are fundamentally propelled toward a surface where they impact and form a coating after being fundamentally injected into a high-velocity stream travelling at up to 1200 m/s in an un-melted condition (often formed using a de-Laval) [30]. As a result, CS is a suitable approach for spraying compounds that are delicate to oxygen and temperature, producing deposits with the same chemical composition as the input. On the other hand, metals flex plastically when they strike a surface and bind to it by kinetic compaction [29]. Despite recent research addressing their deposition methods, which are

greatly influenced by the feedstock's characteristics, ceramics are more challenging to spray [31-34]. Because of this, CS makes it possible to spray customised coatings with the desired chemistry and microstructure, which is very helpful in the biomedical industry [35]. The CS keeps all the advantages of plasma spraying. However, pure HAp powder lacks plastic deformation, which is a need for any material that will be cold-sprayed. CS is unable to spray pure HAp powder on Ti-6Al-4V as a result. To solve the shortcomings of both CS and plasma spray techniques, biocomposite powders composed of a metal (often Ti) and HAp are employed in many studies.

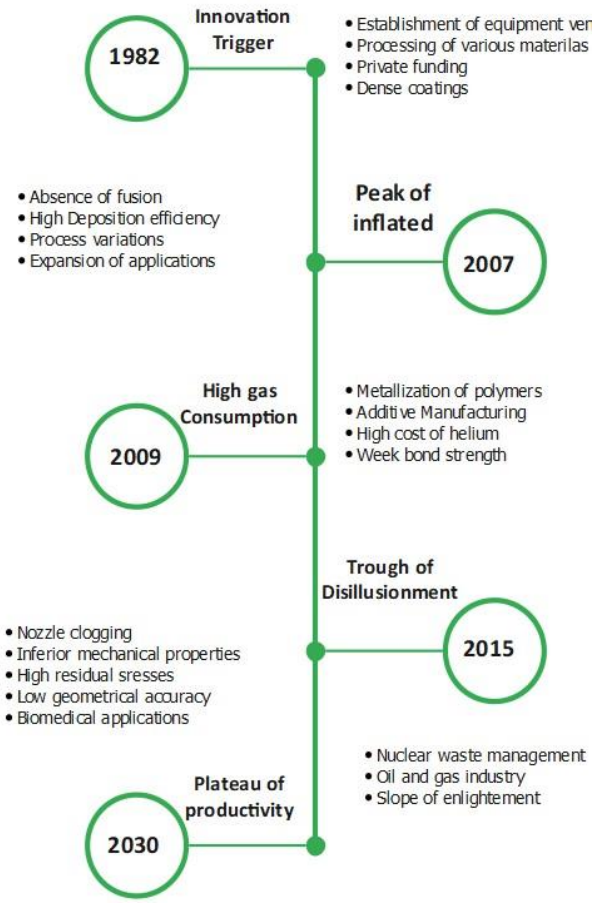

Figure 3. *Indicative hype cycle of the CS technique. Adapted form [29], Permissions under (CC BY 4.0)*

Much research has been done on HAp coatings sprayed using the plasma spray technique, and the majority of them are focused on the use and manufacture of HAp [36-39]. This is according to a recent survey of the literature. Both medical experts and material scientists are interested in the research of and application of HAp-based materials. We think that reading review articles is a simple and effective way for new researchers to get a thorough understanding of HAp right away. As a result, we make an effort to give a concise and comprehensive overview of HAp-based materials, Mg-doped HAp, Ag-doped HAp, and HAp/polymer composites in this study, as well as their applications in bone tissue engineering deposition via CS technology.

CS technology process parameters

The features of CS coatings are determined by the spraying process's settings. Correlations between coating attributes and spraying parameters must be developed in order to produce coatings with the appropriate characteristics. The specific process by which the solid particles deform and connect during CS is still not entirely understood by researchers and industry experts.

Un-melted particles undergo significant plastic deformation when they collide with a surface, which in the case of ductile materials like metals, causes the production of jets known as adiabatic shear bands (ASB). Even recrystallized areas and elongated grains at particle interfaces where temperatures were higher, a result of adiabatic shearing, are present in the microstructures of metals that are deposited by CS, and these microstructures have been fairly compared to those of materials that have been explosively fused and powder-compacted. CS can deposit non-ductile materials like ceramics onto ductile substrates, where embedded particles may be present.

For a material to deposit effectively onto a specific substrate, there is frequently a critical velocity (*V*c). The particle velocity must be higher than the critical velocity for effective deposition. But excessive speeds could cause the substrate's surface to erode. The CS gun parameters, such as the gas composition, preheat temperature, pressure, and nozzle shape, also affect the particle velocity. The *V*c is dependent on the intrinsic characteristics of the material being sprayed, *i.e.* the mechanical and physical characteristics like particle size, morphology, temperature, and substrate, as well as the density, melting point, and ultimate strength of the material. All of these factors must regularly be tuned for a successful deposition [40].

Despite the efficient fabrication of metal, ceramic, and polymeric coatings onto a variety of substrates employing CS, ceramic coatings still pose a challenge due to their intrinsic brittleness. Metal-ceramic feedstock powder combinations have been sprayed by CS, increasing coating properties such as wear and hardness [41]. The studies done on bioceramic coatings using the CS process will be covered in the following section.

Bioceramic coatings *via* CS

Particularly bioactive ceramic coatings emphasise their strong relationship to living tissues following implantation. When seeking fixation, bioactive fixation results in a stronger relationship than mechanical fixation. HAp-coated prostheses offer superior options than cemented joints in terms of fixation and microparticle migration reduction [42]. But just now, inquiries are being made.

HAp biocoatings

Low temperature-related factors have previously been predominantly associated with the benefits of CS over conventional thermal spray techniques. Because CS is defined by lower temperatures, undesirable evaporation processes, residual stresses, or phase transitions are prevented [14,43,44]. Despite the fact that HAp coatings have been found to promote rapid and increased attachment strength, the long-term durability of the fixation has been acknowledged to be a challenge in thermal spray procedures. CS is proposed as an alternative to obtaining HAp coatings with higher density and controlled crystallinity. The HAp CS approach differs from other low-temperature deposition techniques, such as sol-gel deposition, atomic layer deposition, solution deposition, and biomimetic deposition, in that it is an easy and inexpensive way to create coatings with precise microstructures at low temperatures. Contrary to popular opinion, several techniques have been employed to blast an implant's metal surface with HAp particles [45-49], and they have been made even more successful by addressing a shot-penning pathway [50]. In fact, the vacuum cold spray, also known as aerosol deposition, and nanoparticle deposition systems, which were established in the 1990s and 2000s, respectively, have been compared to the ceramics industry's CS. Although the acceleration of sub-micrometer-sized particles is necessary for aerosol deposition, low vacuum conditions are necessary for supersonic flow control. On the other hand, bonding in a nanoparticle deposition system is assumed to be caused by the dissipation of the particles' kinetic energy. Several

plasticity traits have been observed, and it appears that employing sub-micrometeric feedstock particles is also essential [51-53]. Dense HAp coatings on Ti have been produced using this method [54-55]. Numerous numerical and virtual investigations have been carried out to establish the best CS of HAp parameters. Zhang *et al.* [56] looked at the factors impacting HAp particle acceleration using the computational fluid dynamics programme FLUENT. The modelling results showed that the HAp particle accelerates when its throat and exit diameters have expansion ratios within the optimal range of 1.5-4. Additionally, HAp particle velocity rises as HAp particle size decreases until a minimum of 5 m, at which point it abruptly decelerates, with 5-20 μm particle size being acceptable for CS spray. HAp particle velocity increases as gas pressure rises, particularly from 0.2 MPa to 0.6 MPa. Using the Taguchi technique, Singh [57] optimised the HAp conditions in the CS. They discovered the effects of each element's percentage contribution on the exit particle velocity of the HAp powder, which was as follows in descending order: gas type, particle size, gas entry pressure, particle temperature, and gas entry temperature are the order of importance. They also realised how those variables interacted could affect the result [58]. For instance, it was discovered that increasing gas pressure and the temperature of the feedstock particle increased the particle's velocity, whereas increasing the diameter of the HAp particle caused the particle's velocity to decrease and had a greater effect than the respective effects of increasing gas pressure, the temperature of the gas, and the temperature of the particles. Therefore, HAp particle velocity is inversely related to particle size despite the increase in gas temperature and pressure. Mg has been suggested as a replacement biomaterial due to its simple degradability and nearly comparable mechanical characteristics to bone. The benefits of using magnesium as an implant are further bolstered by its appealing biological properties [59,60]: a) Mg metal is biodegradable by corrosion in body fluid; b) Mg^{2+} is a vital element for the body; c) magnesium can help form new tissues; d) density, modulus of elasticity, and yield strength of magnesium are closer to the bone tissue. Because of this, Mg-based alloys offer excellent properties, but the biomedical implant industry hasn't yet used them effectively [61]. They have so far been studied for the production of cardiovascular stents, bone fixation materials, and porous scaffolds for bone healing. However, the biggest obstacle to their use in medicine is their corrosion behaviour. Another issue mentioned is the production of hydrogen due to corrosion. When there is a considerable development of hydrogen gas, Mg cannot be absorbed by the body, causing a balloon effect. As a result, developing coatings or performing surface treatments is crucial [62]. In order to reduce the pace of degradation, which might happen rather quickly, it is advantageous to cover the magnesium alloy with HAp. HAp contributes to accelerating the biodegradation of magnesium alloys. Plasma spraying of Mg alloys has not gotten much attention due to Mg low melting temperature. Additionally, when plasma is sprayed on HAp, it may transform into various calcium phosphate phases. These modifications in chemistry and crystallinity commonly affect HAp's distinctive bioactive properties as well as its adhesion to the implant [63-64]. CS has provided a solution to both difficulties [65]. In simulated physiological fluid, the rate of biodegradation of AZ51 coated with HAp utilising CS coating technique was examined. The findings show that the coated alloy is bioactive and biodegradable, qualifying it for possible use as biodegradable orthopaedic implants.

In a different work, Hasniyati *et al.* [66] alter the CS technique to offer a novel method for coating HAp onto an Mg substrate at a low temperature. An XRD phase study showed that the HAp coatings underwent no phase changes throughout processing. The stand-off distance, substrate surface roughness, substrate temperature, and the number of sprays are just a few of the CS process variables whose effects are examined in this article in relation to the features of the HAp coating on the preheated Mg substrate. The findings that were chosen for optimization only contained physical

parameters, such as coating thickness, nano-hardness, and coating modulus. The response optimizer claims that at a standoff distance of 22 mm, a surface roughness of 649.2 grit, and a substrate heating temperature of 496 °C, good HAp coatings with 46 μm coating thickness, 436.5 MPa hardness, and 43.9 GPa coating modulus were attained. As a result, it is frequently utilised to improve bioactivities and corrosion resistance on Mg surfaces.

On poly(ether ether ketone) (PEEK) substrates, CS has developed pure HAp coatings to give materials bioactivity while avoiding the weak characteristics of ceramic substrates and the stress shielding effect that frequently develops between bone and metallic materials [67]. Incorporating HAp into polymeric biomaterials is one of the best approaches to increase biocompatibility. However, to regulate or produce various calcium phosphate phases, HAp ceramic coatings require either an expensive vacuum deposition method or an HT at a high temperature to encourage the crystallisation of the coating layer. When it comes to polymeric biomaterials, HT at a higher temperature causes polymers to distort, which eventually impairs the performance of the polymer and limits its usage as a biomaterial. Furthermore, a vacuum deposition procedure at lower temperatures may deform polymer surfaces and injure polymer surfaces, which is not suitable. It also requires high production expenses to increase productivity. CS overcomes the limitations of a number of conventional coating processes and makes it possible to cover the surfaces of polymeric biomaterials while maintaining the intrinsic properties of both the polymer and the powder. CS also has low production costs and high productivity. HAp, bioglass mixtures, bioglasses that have crystallised, and bioglasses containing CaO, SiO_2, and P_2O_5 as main components are all claimed as bioactive coatings in this patent [67]. Lee et al. study of the bioactivity of HAp coatings on PEEK substrates by CS [68] revealed that these coatings were uniform and firmly adhered without distorting the substrate material. The HAp-PEEK material might be applied in therapeutic settings in the upcoming years to hasten recuperation.

HAp-composite coatings

HAp has poor mechanical qualities and is fragile. Due to the inherently brittle character of HAp, particularly when applied to the common metallic prostheses, such as Ti and SS, due to the inelastic deformation that results in failure fragmentation, direct deposition of a thick layer of HAp by CS with good adhesion strength is still challenging. To better understand this behaviour, numerous investigations on the analysis of HAp failure mechanisms during dynamic impacts are being conducted [69-70]. The application of metal-HAp and polymer-HAp composite powders is therefore actively pursued. HAp can have better mechanical and bioactive qualities by adding more Zn [71]. Given that Zn has a low melting temperature, the optimum method for depositing HAp/Zn composites on Mg alloys is CS. When plasma is used to spray it, it will oxidise at a high temperature. CS HAp [72-74], HAp/Ti [75,76], and HAp/Ta [77] composite coatings can improve the bioactivities of metals and stop HAp breakdown. The results showed that compared to pure Ti coating, cold-sprayed HAp/Ti composite coating had a larger corrosion current and lower corrosion resistance. However, a post-spray HT can greatly improve the corrosion resistance of the HAp/Ti composite coating. In addition, a post-spray HT treatment of up to three times boosted the mechanical properties of the 20 wt.% HAp/Ti composite coating (microhardness and ultimate shear strength). However, according to the published studies [75-77], interface cracks between ceramic and metal particles in HATi and HAp/Ta are inevitable because of their significant mechanical and thermal expansion coefficient differences, which may be harmful to the substrates' ability to resist corrosion.

A Zn-HAp/Zn double-layer coating made of a Zn underlayer and a HAp/Zn upper layer may be able to simultaneously achieve corrosion resistance and bioactivity. Yao et al. cover the AZ91D alloy with a Zn-HAp/Zn double-layer coating using the CS method. Potentiodynamic polarization and EIS experiments revealed that the CS Zn-HAp/Zn double-layer coatings enhance the bioactivity and corrosion resistance of the Mg alloy substrates [78].

Other endeavours, such as HAp-graphenenano-sheet (GN) and doping HAp with silver, have been made to ease concerns regarding the long-term performance of HAp-composite coatings [79-80]. It has been shown that adding GN is very suitable for load-bearing applications and demonstrates very acceptable biocompatibility. The GN-containing HAp coatings significantly increased the osteoblast cells' adhesion and proliferation, most likely because the serum proteins fibronectin and other crucial components adsorb quickly.

Substituted HAp coatings

HAp coatings are a very promising alternative to conventional calcium phosphate coatings. In addition to accelerating biomechanical fixation, the replaced HAp coatings would be designed to help with a number of pathological problems like infection and osteoporosis. Orthopaedic prostheses, dental implants, and macroporous scaffolds have all received replaced HAp coatings in the past, expanding their uses for bone regeneration therapy. Because of the variety of elements and ions discovered in the past 50 years that have therapeutic effects, the research of substituted HAp coatings is currently a field of study that is constantly developing. The crystalline structure of HAp also facilitates ion incorporation through substitutive and interstitial processes. These features have led to novel circumstances in which coatings not only hasten bone repair following early implantation but also actively treat illnesses. In conjunction with the recently discovered additively produced metallic scaffolds, substituted HAp coatings are expanding the therapeutic applications of metallic implants from their typical substitutive functions towards bone regeneration goals. The recent combination of substituted HAp and nanostructures has also opened up new prospects in coatings for orthopaedic applications [81-83].

The bioactive behaviour of stoichiometric HAp can be improved by substituting the cationic and anionic sublattices. The anions like F- or C- can exhibit the same oxidation state as OH^-, as can the cations like Sr^{2+}, Ag^+, Cu^{2+}, and others. In order to offer HAp additional properties like osteoinduction or antibacterial action, ionic substitutions are used. HAp can have several ionic substitutions that add utility by improving its composition or crystalline structure, for as, by making it antimicrobial or osteoinducing [84]. For instance, it's conceivable that CO_3^{2-} in biological apatites will be substituted for PO_4^{3-} (type B) or OH^- (type A). The structures of substituted and unsubstituted HAp are shown in Figure 4.

Cationic substitutions in HAp coatings

We have already covered cationic Mg-HAp and Zn-HAp substitution coatings in the preceding section. Other cationic replacements in HAp coatings, such as copper, strontium, and silver, are covered in this section. Finally, investigations on HAp coatings replaced with Co^{2+}, Na^+, Mn^{2+}, and Ce^{3+} were also discussed.

The human body does not contain the metal element of silver, with the exception of inadvertent contamination (Ag). Ag^+, a powerful antibacterial agent, is added to HAp coatings to prevent infections of dental and orthopaedic implants. Ag^+ antibacterial impact is related to its capacity to bind to microbial DNA, which stops bacterial reproduction. Feng et al. [85] showed that the Ag-substituted HAp coatings on implants had good antibacterial characteristics. Ag^+ ions can also be used as a dependable bioactive delivery mechanism for the slow release of antibiotics by being

included in HAp coatings with micropores [86]. HAp-Ag/PEEK coatings were successfully applied to glass using CS by Sanpo *et al.* [80] at room temperature. By using EDX analysis, it was determined that the HAp-Ag/PEEK concentrations in the original powders and as-sprayed coatings were identical. According to the study, CS may deposit ceramic materials (HAp-Ag), nanophases, and composite powders (HAp-Ag/PEEK), all while conserving and eliciting coating functionality (Bio) that is comparable to that of the starting material

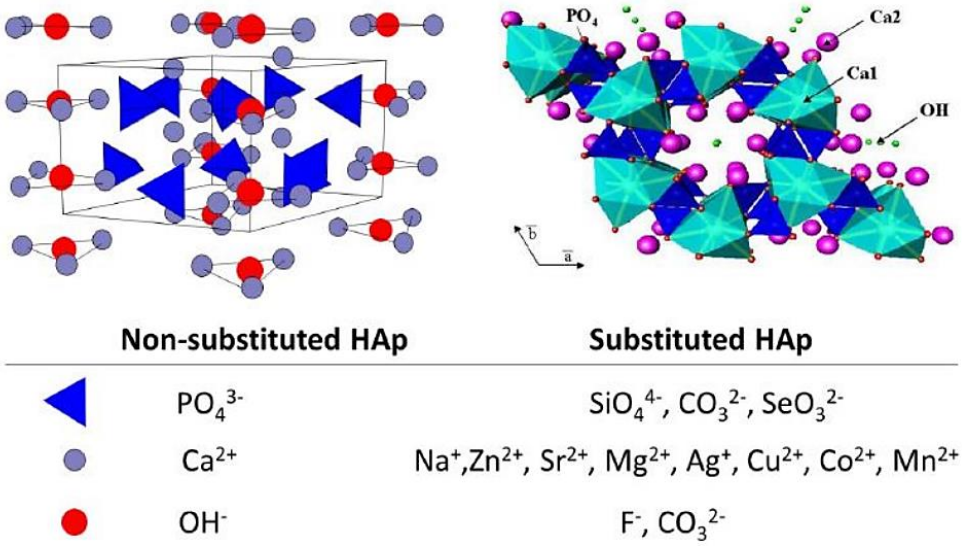

Figure 4. *Structure of non-substituted and substituted HAp [84]. Permissions under (CC BY 4.0)*

Strontium is considered non-essential to human health. An average adult human carries 0.14 g of strontium. It is primarily found in the mineral phase of bones, especially in regions where bone turnover is more pronounced [87]. The main cause behind Sr incorporation into CaPs was its inhibitory effect on bone resorption and augmentation of bone growth in osteoporotic patients. Sr^{2+} for Ca^{2+} substitution in CaPs has been proven in numerous studies to increase osteoblast activity and decrease osteoclast development [88-89]. Sr^{2+} expands the HAp unit cell and increases the cell volume because it has a larger ionic radius than Ca^{2+} (112 *vs.* 99 pm). The Sr-low HAp wettability and strong Sr concentration would provide good corrosion resistance for metallic substrates [90].

Copper (Cu), as the trace element, is necessary for most living organisms. An adult human weighing 70 kg contains about 0.15 g of copper. Cu deficiency is a serious problem, especially in babies, and in cases of acute deficiency can result in anaemia, irregular bone formation, and fractures. However, toxicity brought on by too much Cu can build up in the liver and brain. In persons with Wilson syndrome, copper accumulation can lead to gradual deterioration of the liver and neurological tissue. Cu^{2+} cations have been added to HAp bone grafts in order to provide antibacterial and bactericidal action, angiogenic potential, and the capacity to boost the activity of osteoblastic cells [91-93]. A group of academics have proposed a technique for incorporation that substitutes Cu^{2+} for Ca^{2+} [94-95]. The advantages of Cu-rich HAp have been disputed because of this cation's cytotoxicity. When there is a large concentration of Cu precursors, CuO can form, which seriously compromises cell viability. There aren't many investigations on Cu-HAp coatings because the majority of the prepared Cu-HAp has been purchased as powders. Cu-HAp coatings have been produced using plasma spraying, but they did not outperform HAp that has not been substituted [96].

In addition to the aforementioned examples, substituted HAp coatings containing Co^{2+}, Na^{+}, Mn^{2+}, and Ce^{3+} are also described in a small number of studies. Therefore, it is occasionally impossible to provide a detailed description and discussion. Similar to Co-HAp coatings, there aren't

many studies on them. Co-HAp coatings were recently produced by electrodeposition on $Ti_{22}Nb_6Zr$ alloy [97]. This study shows that adding Co^{2+} improves corrosion resistance even though no biological effects have been studied.

Additionally, it has been discovered that coatings consisting of sodium-substituted hydroxyapatite (Na-HAp) offer better corrosion resistance. However, no inference could be made regarding the presence of Na^+ in the ceramic component because the crucial comparison with unsubstituted HAp was not performed [98].

Mn-HAp coatings on stainless steel have most recently been applied by Ananth *et al.* [99]. This bilayer coating improved the mechanical characteristics, the efficiency of metal ion leach-out, bioactivity, and biocompatibility as well as corrosion resistance. However, when paired with coatings other than calcium phosphates, Mn^{2+} may not always have favourable benefits.

There has recently been a rise in interest in HAp replaced with rare earth elements. Examples include the substitution of Ce^{3+} or Ce^{4+} in HAp, which has proven to have antibacterial activity [100]. Collagen and Ce-HAp have recently been applied to Ti substrates as coatings. The resulting Ce-HAp coatings had bactericidal rates for *E. coli* and *S. aureus* of 92.61 and 73.59 %, respectively.

Anionic substitutions in HAp coatings

A 70 kg adult contains 2.6 g of the essential trace element fluor. Despite the importance of biological role of F^-, little is understood about its biochemical action. In the bones and teeth, where it isoelectronically replaces OH^- in HAp, the majority of the F^- is present. F^- anions are also found in the intracellular compartment at much lower levels and in external fluids at very low concentrations (micromolar levels). F^- is incorporated into the HAp structure, which results in a tougher structure and a slower rate of dissolution [101]. F-HAps coatings have been made using a variety of methods, includeing slip coating and sol-gel [102,103]. Whether fluoride has beneficial or harmful biological effects on osteoblast cells is a topic of intense discussion. The best bonding strength on Ti substrates, the lowest rate of dissolution, and the most tolerable biological activity were, however, demonstrated by coatings with medium F^- concentrations and OH^- substitutions in the range $Ca_{10}(PO_4)_6(OH)_{0.75\text{-}1}F_{1.25\text{-}1}$. The carbonated ($CO_3^{2-}$)-HAp coating is the second anionic substitution. The inclusion of CO_3^{2-} in the HAp structure contributes to maintaining consistent bone regeneration through cycles of dissolution-crystallization. CO_3^{2-}-HAp coatings are more soluble than HAp and are, therefore, likely to elicit a greater osteogenic response, despite the fact that the durability of the coating can be substantially damaged. Another technique for enhancing the stability of C-HAp coatings is the development of composites employing biocompatible polymers.

Comparison of CS HAp coating with plasma and HVOF spray

HAp coatings were applied to Ti6Al4V alloy substrates using a mix of thermal spray processes, including atmospheric plasma spray, HVOF, and CS. Surface properties such as topography, microstructure, phase composition, wettability, and crystallinity were evaluated to test cell response. For in-vitro tests, primary human osteoblasts were utilised. With the operating temperature of the thermal spray methods being lowered, the HAp coatings showed an increase in HAp crystallinity from 62.4 to 89 % and an increase in hydrophilicity from 32 to 0° [104]. The CS process has shown maximum crystallinity followed by APS and HVOF process (CS > APS > HVOF).

In comparison to HVOF and CS HAp coatings, higher surface micro-features were apparent in plasma spray HAp coatings. Cells onto plasma spray HAp coatings displayed speedier attachment by adopting osteoblastic morphology as opposed to the rounded cell shape seen on CS HAp coatings at 1 day of cell growth. HVOF HAp coatings showed acceptable cell attachment despite the enlarged

filopodia of cells on plasma spray HAp coatings. The HAp coatings with higher crystallinity, however, showed increased cell proliferation and differentiation after fourteen days of cell culture (HVOF and CS techniques). It is thought that moderate surface wettability and surface microfeatures both encourage cell adherence. HAp crystallinity and crystal size are hypothesised to have a substantial effect on cell proliferation and differentiation. Table 2 lists the characteristics of the three coatings.

Table 2. *Properties of of APS, HVOF and CS*

Properties	APS	HVOF	CS
Thickness, μm	84.5 ± 6.1	68.6 ± 6.0	45 ± 20
Microroughness, μm	5.8 ± 0.4	4.2 ± 0.4	12 ± 1
Crystallinity, %	62.4	82	89
Porosity, %	21-23	11-15	*

Poor adherence of HAp plasma coatings is one of the main problems with coated prostheses, which could lead to failure and have catastrophic consequences for the patient. But tensile adhesion tests of CS Ti-HA coatings exhibited greater values when compared to PS coatings and other thermal spray procedures with FDA certification.

Some patents on the development of CS coatings

The cold spraying of HAp coatings was the subject of a straightforward patent filing in China [105]. For prosthetic joints and dental roots, "baked" 28-53 μm HAp powder is used during the treatment. The method allows for producing HAp coatings with a high degree of crystallinity and strong biological stability while preventing pyrolysis of HAp and minimising hydroxyl group loss. A method for spraying pacemakers, clips, bioresorbable stents, and orthopaedic support devices is described in a patent [106]. The method of mixed coatings deposition via CS route, from which the stents are EDM-machined, is specifically covered in the document. The material porosity is specified as 0.2 % or less due to the CS deposition process. From biocompatible metals, ceramics, metal alloys, and polymers, CS processing is used to produce porous starting materials that can later be processed into porous medical devices like stents. The porous substrates and coatings have the potential to hold a medication or therapeutic ingredient [107].

Conclusion and future trends

The performance of the CS HAps coating is the main topic of the current review. Little oxidation or deterioration, as well as little microstructural change, occurs during the deposition of spray materials. This technique may be preferable to conventional thermal spray techniques because it may create dense coatings while maintaining the phase composition and feedstock material chemistry. Studies on CS coatings are emerging in the orthopaedics field (for internal fixation systems and prostheses as well as for antibacterial applications). Research on HAp coatings is continually developing in order to produce implant surfaces that offer a balance between cell adhesion and minimum cytotoxicity, mechanical properties, and functionalization. Despite being a fairly developed field, surface engineering advancements have the potential to help the biomedical industry overcome a number of obstacles. Following is a summary of the key points:

- It is necessary to establish correlations between the coating properties and the CS spraying parameters in order to produce HAp coatings with the desired characteristics. Particle velocity must be greater than the critical velocity for effective deposition.

- When compared to materials created using conventional production methods, CS produces porous, mechanically robust structures that are 40 % more powerful.
- On samples of magnesium alloy, HAp coatings have been produced utilising a quick and effective CS processing approach, and the structures are especially well suited for fabricating biomedical parts like replacement joints because of their tiny size and porosity. In order to reduce the pace of degradation, which might happen rather quickly, it is advantageous to cover the magnesium alloy with HAp. HAp contributes to accelerating the biodegradation of magnesium alloys.
- By controlling the temperature and pressure of the CS coating conditions, the HAp layer was uniformly coated on the PEEK implants surface. These coatings proved to be uniform and firmly adhering without distorting the substrate material in any way.
- It is preferable to strengthen HAp coatings with Zn, Ti, Ta, Ag, and GN or replaced HAp coatings in order to enhance their mechanical qualities. The HAp structure's ability to allow for different ionic replacements during CS gives it an advantage over currently available plasma-sprayed coatings.
- The incorporation of ions with antibacterial properties to lower the risk of infection is a priority research field in the near future for the development of new coatings.
- •3D printing is a further industry 4.0 transforming thrust area. It's also important to highlight the emergence of metallic implants produced via 3D printing. Widespread clinical applications and mass production are still in their infancy because the majority of the existing investigations are still in the research stage. However, it is possible that 3D printing technology, which is being integrated with artificial intelligence, the internet, and big data, will become more common in the field of metals and medicinal equipment and eventually a crucial part of the digital economy and the production of medical devices.
- To the best of the authors' knowledge, relatively little research has been done on the CS approach for fabricating 3D porous structures, yet it is a more efficient method than selective laser melting and binder jet due to its rapid deposition rate.
- One potential drawback is the mass production's relatively high cost of the CS coatings. Helium gas processing is expensive, and CS requires a thermal source for higher deposition rates. Additionally, it has the ability to deposit coatings with lower HAp contents. Since there aren't many studies in this field, it will be possible to enhance the amount of HAp in coatings in the future using laser-enabled CS techniques.
- There is potential for improving coating quality and deposition efficiency by combining low-pressure cold spraying with aerosol deposition techniques. Future research in aerosol CS will examine bioactivity studies, potential pathogen reactions to the coated surface, process parameter optimization, and more.

References

[1] G. Prashar, H. Vasudev, Thermal sprayed composite coatings for biomedical implants: A brief review, *Journal of Thermal Spray and Engineering* **2** (2020) 50-55. https://doi.org/10.52687/2582-1474/213

[2] G. Prashar, H. Vasudev, L. Thakur, A. Bansal, Performance pf Thermally Sprayed Hydroxyapatite Coatings for Biomedical Implants: A Comprehensive Review, *Surface Review and Letters* **30(01)** (2022) 2241001. https://doi.org/10.1142/S0218625X22410013

[3] V. Uskoković, I. Janković-Častvan, V. M. Wu, Bone mineral crystallinity governs the orchestration of ossification and resorption during bone remodeling, *ACS Biomaterials Science & Engineering* **5** (2019) 3483-3498. https://doi.org/10.1021/acsbiomaterials.9b00255

[4] D. Wang, J. Jang, K. Kim, J. Kim, C.B. Park, "Tree to Bone": Lignin/Polycaprolactone Nanofibers for Hydroxyapatite Biomineralization, *Biomacromolecules* **20** (2019) 2684-2693. https://doi.org/10.1021/acs.biomac.9b00451

[5] C. Hu, D. Ashok, D. R. Nisbet, V. Gautam, Bioinspired surface modification of orthopedic implants for bone tissue engineering, *Biomaterials* **219** (2019) 119366. https://doi.org/10.1016/j.biomaterials.2019.119366

[6] Z.-Y. Qiu, Y. Cui, X.-M. Wang, *Natural Bone Tissue and Its Biomimetic*, in: *Mineralized Collagen Bone Graft Substitutes*, Elsevier, 2019, pp. 1-22. https://doi.org/10.1016/B978-0-08-102717-2.00001-1

[7] S. Türk, İ. Altınsoy, G. Çelebi Efe, M. Ipek, M. Özacar, C. Bindal, Effect of Solution and Calcination Time on Sol-gel Synthesis of Hydroxyapatite, *Journal of Bionic Engineering* **16** (2019) 311-318. https://doi.org/10.1007/s42235-019-0026-3

[8] R. Narayanan, S.K. Seshadri, T. Y. Kwon, K. H. Kim, Calcium phosphate-based coatings on titanium and its alloys, *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **85B** (2008) 279-299. https://doi.org/10.1002/jbm.b.30932

[9] B. A. Jerri Al-Bakhsh, F. Shafiei, A. Hashemian, K. Shekofteh, B. Bolhari, M. Behroozibakhsh, In-vitro bioactivity evaluation and physical properties of an epoxy-based dental sealer reinforced with synthesized fluorine-substituted hydroxyapatite, hydroxyapatite and bioactive glass nanofillers, *Bioactive Materials* **4** (2019) 322-333. https://doi.org/10.1016/j.bioactmat.2019.10.004

[10] R. Radha, D. Sreekanth, Mechanical and corrosion behaviour of hydroxyapatite reinforced Mg-Sn alloy composite by squeeze casting for biomedical applications, *Journal of Magnesium and Alloys* **8** (2020) 452-460. https://doi.org/10.1016/j.jma.2019.05.010

[11] E. Fiume, G. Magnaterra, A. Rahdar, E. Verné, F. Baino, Hydroxyapatite for Biomedical Applications: A Short Overview, *Ceramics* **4** (2021) 542-563. https://doi.org/10.3390/ceramics4040039

[12] R. Setiawati, P. Rahardjo, *Bone Development and Growth*, in: Osteogenesis and Bone Regeneration, IntechOpen, 2019. https://doi.org/10.5772/intechopen.82452

[13] S. Bose, S. Tarafder, A. Bandyopadhyay, *Hydroxyapatite coatings for metallic implants,* in: Hydroxyapatite (Hap) for biomedical applications, Woodhead Publishing, (2015) pp. 143-157. https://doi.org/10.1016/B978-1-78242-033-0.00007-9

[14] L. Sun, C. C. Berndt, K. A. Gross, A. Kucuk, Material fundamentals and clinical performance of plasma-sprayed hydroxyapatite coatings: A review, *Journal of Biomedical Materials Research* **58** (2001) 570-592. https://doi.org/10.1002/jbm.1056

[15] E. Mohseni, E. Zalnezhad, A. R. Bushroa, Comparative investigation on the adhesion of hydroxyapatite coating on Ti-6Al-4V implant, *International Journal of Adhesion and Adhesives* **48** (2014) 238-257. https://doi.org/10.1016/j.ijadhadh.2013.09.030

[16] Y. C. Tsui, C. Doyle, T.. Clyne, Plasma sprayed hydroxyapatite coatings on titanium substrates Part 2: optimisation of coating properties, *Biomaterials* **19** (1998) 2031-2043. https://doi.org/10.1016/S0142-9612(98)00104-5

[17] H.-W. Kim, G. Georgiou, J. C. Knowles, Y.-H. Koh, H.-E. Kim, Calcium phosphates and glass composite coatings on zirconia for enhanced biocompatibility, *Biomaterials* **25** (2004) 4203-4213 https://doi.org/10.1016/j.biomaterials.2003.10.094

[18] S. V. Dorozhkin, Calcium orthophosphate coatings, films and layers, *Progress in Biomaterials* **1** (2012) 1. https://doi.org/10.1186/2194-0517-1-1

[19] A. Singh, G. Singh, V. Chawla, Influence of post coating heat treatment on microstructural, mechanical and electrochemical corrosion behaviour of vacuum plasma sprayed reinforced hydroxyapatite coatings, *Journal of the Mechanical Behavior of Biomedical Materials* **85** (2018) 20-36. https://doi.org/10.1016/j.jmbbm.2018.05.030

[20] A. M. Vilardell, N. Cinca, I. Pacheco, C. Santiveri, S. Dosta, I. G. Cano, J. M. Guilemany, M. Sarret, C. Muller, Hierarchical structures of anodised cold gas sprayed titanium coatings, *Transactions of the IMF* **96** (2018) 71-78. https://doi.org/10.1080/00202967.2018.1419625

[21] F. Fazan, P. M. Marquis, Dissolution behavior of plasma-sprayed hydroxyapatite coatings, *Journal of materials science: Materials in Medicine* **(12)** (2000) 787-792. https://doi.org/10.1023/A:1008901512273

[22] L. Sun, C. C. Berndt, K. A. Khor, H. N. Cheang, K. A. Gross, Surface characteristics and dissolution behavior of plasma-sprayed hydroxyapatite coating, *Journal of Biomedical Materials Research* **62** (2002) 228-236. https://doi.org/10.1002/jbm.10315

[23] K. A. Gross, C. C. Berndt, H. Herman, Amorphous phase formation in plasma-sprayed hydroxyapatite coatings, *Journal of Biomedical Materials Research* **39** (1998) 407-414. https://doi.org/10.1002/(SICI)1097-4636(19980305)39:3<407::AID-JBM9>3.0.CO;2-N

[24] J. Fernández, M. Gaona, J. M. Guilemany, Effect of Heat Treatments on HVOF Hydroxyapatite Coatings, *Journal of Thermal Spray Technology* **16** (2007) 220-228. https://doi.org/10.1007/s11666-007-9034-7

[25] M. Gaona Latorre, Recubrimientos biocompatibles obtenidos por Proyección Térmica y estudio in vitro de la función osteoblástica, PhD thesis, *Universitat de Barcelona* (2007) http://hdl.handle.net/2445/36451

[26] B. D. Hahn, D. S. Park, J. J. Choi, J. Ryu, W. H. Yoon, K. H. Kim, C. Park, H. E. Kim, Dense Nanostructured Hydroxyapatite Coating on Titanium by Aerosol Deposition, *Journal of the American Ceramic Society* **92** (2009) 683-687. https://doi.org/10.1111/j.1551-2916.2008.02876.x

[27] D. Park, I. Kim, H. Kim, A. H. K. Chou, B. Hahn, L. Li, S. Hwang, Improved biocompatibility of hydroxyapatite thin film prepared by aerosol deposition, *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **94B** (2010) 353-358. https://doi.org/10.1002/jbm.b.31658

[28] M. S. Kim, D. M. Chun, J. O. Choi, J. C. Lee, K. S. Kim, Y. H. Kim, C. S. Lee, S. H. Ahn, Room temperature deposition of TiO2 using nano particle deposition system (NPDS): Application to dye-sensitized solar cell (DSSC), *International Journal of Precision Engineering and Manufacturing* **12** (2011) 749-752. https://doi.org/10.1007/s12541-011-0099-3

[29] D. Guo, M. Kazasidis, A. Hawkins, N. Fan, Z. Leclerc, D. MacDonald, A. Nastic, R. Nikbakht, R. Ortiz-Fernandez, S. Rahmati, M. Razavipour, P. Richer, S. Yin, R. Lupoi, B. Jodoin, Cold Spray: Over 30 Years of Development Toward a Hot Future, *Journal of Thermal Spray Technology* **31** (2022) 866-907. https://doi.org/10.1007/s11666-022-01366-4

[30] G. Prashar, H. Vasudev, L. Thakur, *Thermal Spraying Fundamentals: Process Applications, Challenges, and Future Market,* in: *Thermal Spray Coatings*, CRC Press, 2021, 1-36. https://www.taylorfrancis.com/chapters/edit/10.1201/9781003213185-1/thermal-spraying-fundamentals-gaurav-prashar-hitesh-vasudev-lalit-thakur

[31] N. Cinca, A. M. Vilardell, S. Dosta, A. Concustell, I. Garcia Cano, J. M. Guilemany, S. Estradé, A. Ruiz, F. Peiró, A New Alternative for Obtaining Nanocrystalline Bioactive Coatings: Study of Hydroxyapatite Deposition Mechanisms by Cold Gas Spraying, *Journal of the American Ceramic Society* **99** (2016) 1420-1428. https://doi.org/10.1111/jace.14076

[32] A. M. Vilardell, N. Cinca, I. G. Cano, A. Concustell, S. Dosta, J. M. Guilemany, S. Estradé, A. Ruiz-Caridad, F. Peiró, Dense nanostructured calcium phosphate coating on titanium by cold spray, *Journal of the European Ceramic Society* **37** (2017) 1747-1755. https://doi.org/10.1016/j.jeurceramsoc.2016.11.040

[33] M. Yamada, H. Isago, K. Shima, H. Nakano, M. Fukumoto, *Deposition of TiO_2 Ceramic Particles on Cold Spray Process*, in *Thermal Spray 2010: Proceedings from the International Thermal Spray Conference*, B. R. Marple, A. Agarwal, M. M. Hyland, Y.-C. Lau, C.-J. Li, R. S. Lima, G. Montavon (Eds.), 2010, pp. 172-176. https://doi.org/10.31399/asm.cp.itsc2010p0172

[34] D. Seo, M. Sayar, K. Ogawa, SiO_2 and $MoSi_2$ formation on Inconel 625 surface via SiC coating deposited by cold spray, *Surface and Coatings Technology* **206** (2012) 2851-2858. https://doi.org/10.1016/j.surfcoat.2011.12.010

[35] A. M. Vilardell, N. Cinca, A. Concustell, S. Dosta, I. G. Cano, J. M. Guilemany, Cold spray as an emerging technology for biocompatible and antibacterial coatings: state of art, *Journal of Materials Science* **50** (2015) 4441-4462. https://doi.org/10.1007/s10853-015-9013-1

[36] D. Arcos, M. Vallet-Regí, Substituted hydroxyapatite coatings of bone implants, *Journal of Materials Chemistry B* **8** (2020) 1781-1800. https://doi.org/10.1039/C9TB02710F

[37] G. Molino, M.C. Palmieri, G. Montalbano, S. Fiorilli, C. Vitale-Brovarone, Biomimetic and mesoporous nano-hydroxyapatite for bone tissue application: a short review, *Biomedical Materials* **15** (2020) 022001. https://doi.org/10.1088/1748-605X/ab5f1a

[38] G. Choi, A.H. Choi, L.A. Evans, S. Akyol, B. Ben-Nissan, A review: Recent advances in sol-gel-derived hydroxyapatite nanocoatings for clinical applications, *Journal of the American Ceramic Society* **103** (2020) 5442-5453. https://doi.org/10.1111/jace.17118

[39] S. Awasthi, S. K. Pandey, E. Arunan, C. Srivastava, A review on hydroxyapatite coatings for the biomedical applications: experimental and theoretical perspectives, *Journal of Materials Chemistry B* **9** (2021) 228-249. https://doi.org/10.1039/D0TB02407D

[40] H. Singh, T. S. Sidhu, S. B. S. Kalsi, Cold spray technology: future of coating deposition processes, *Frattura Ed Integrità Strutturale* **6** (2012) 69-84. https://doi.org/10.3221/IGF-ESIS.22.08

[41] J. M. Miguel, S. Vizcaíno, S. Dosta, N. Cinca, C. Lorenzana, J. M. Guilemany, Recubrimientos de materiales compuestos metal-cerámico obtenidos por nuevas tecnologías de proyección térmica: Proyección fría (CGS) y su resistencia al desgaste, *Revista de Metalurgia* **47** (2011) 390-401. https://doi.org/10.3989/revmetalm.1045

[42] G. Lewis, Properties of acrylic bone cement: State of the art review, *Journal of Biomedical Materials Research* **38** (1997) 155-182. https://doi.org/10.1002/(SICI)1097-4636(199722)38:2<155::AID-JBM10>3.0.CO;2-C

[43] Y. C. Tsui, C. Doyle, T. W. Clyne, Plasma sprayed hydroxyapatite coatings on titanium substrates Part 1: Mechanical properties and residual stress levels, *Biomaterials* **19** (1998) 2015-2029. https://doi.org/10.1016/S0142-9612(98)00103-3

[44] M. Villa, S. Dosta, J. Fernández, J. M. Guilemany, La proyección fría (CGs): Una alternativa a las tecnologías convencionales de deposición, *Revista de Metalurgia* **48** (2012) 175-191. https://doi.org/10.3989/revmetalm.1111

[45] K. Ishikawa, Y. Miyamoto, M. Nagayama, K. Asaoka, Blast coating method: New method of coating titanium surface with hydroxyapatite at room temperature, *Journal of Biomedical Materials Research* **38** (1997) 129-134. https://doi.org/10.1002/(SICI)1097-4636(199722)38:2<129::AID-JBM7>3.0.CO;2-S

[46] P. O'Hare, B.J. Meenan, G.A. Burke, G. Byrne, D. Dowling, J. A. Hunt, Biological responses to hydroxyapatite surfaces deposited via a co-incident microblasting technique, *Biomaterials* **31** (2010) 515-522. https://doi.org/10.1016/j.biomaterials.2009.09.067

[47] U. Gbureck, A. Masten, J. Probst, R. Thull, Tribochemical structuring and coating of implant metal surfaces with titanium oxide and hydroxyapatite layers, *Materials Science and Engineering: C* **23** (2003) 461-465. https://doi.org/10.1016/S0928-4931(02)00322-3

[48] L. O'Neill, C. O'Sullivan, P. O'Hare, L. Sexton, F. Keady, J. O'Donoghue, Deposition of substituted apatites onto titanium surfaces using a novel blasting process, *Surface and Coatings Technology* **204** (2009) 484-488. https://doi.org/10.1016/j.surfcoat.2009.08.014

[49] C. O'Sullivan, P. O'Hare, N. D. O'Leary, A. M. Crean, K. Ryan, A. D. W. Dobson, L. O'Neill, Deposition of substituted apatites with anticolonizing properties onto titanium surfaces using a novel blasting process, *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **95B** (2010) 141-149. https://doi.org/10.1002/jbm.b.31694

[50] G. D. Byrne, L. O'Neill, B. Twomey, D. P. Dowling, Comparison between shot peening and abrasive blasting processes as deposition methods for hydroxyapatite coatings onto a titanium alloy, *Surface and Coatings Technology* **216** (2013) 224-231. https://doi.org/10.1016/j.surfcoat.2012.11.048

[51] D. M. Chun, S. H. Ahn, Deposition mechanism of dry sprayed ceramic particles at room temperature using a nanoparticle deposition system, *Acta Materialia* **59** (2011) 2693-2703. https://doi.org/10.1016/j.actamat.2011.01.007

[52] D. M. Chun, J. O. Choi, C. S. Lee, S. H. Ahn, Effect of stand-off distance for cold gas spraying of fine ceramic particles (<5μm) under low vacuum and room temperature using nanoparticle deposition system (NPDS), *Surface and Coatings Technology* **206** (2012) 2125-2132. https://doi.org/10.1016/j.surfcoat.2011.09.043

[53] J. Akedo, Aerosol Deposition of Ceramic Thick Films at Room Temperature: Densification Mechanism of Ceramic Layers, *Journal of the American Ceramic Society* **89** (2006) 1834-1839. https://doi.org/10.1111/j.1551-2916.2006.01030.x

[54] B. D. Hahn, D. S. Park, J.bJ. Choi, J. Ryu, W.bH. Yoon, K.bH. Kim,C. Park, H.bE. Kim, Dense nanostructured hydroxyapatite coating on titanium by aerosol deposition, *Journal of the American Ceramic Society* **3** (2009) 683-687. https://doi.org/10.1111/j.1551-2916.2008.02876.x

[55] D. S. Park, I.-S. Kim, H. Kim, A. H. K. Chou, B.-D. Hahn, L.-H. Li, S.-J. Hwang, Improved biocompatibility of hydroxyapatite thin film prepared by aerosol deposition, *Journal of Biomedical Materials Research Part B: Applied Biomaterials* **94B(2)** (2010) 353-358. https://doi.org/10.1002/jbm.b.31658

[56] L. Zhang, W. T. Zhang, Numerical Investigation on Particle Velocity in Cold Spraying of Hydroxyapatite Coating, *Advanced Materials Research* **188** (2011) 717-722. https://doi.org/10.4028/www.scientific.net/AMR.188.717

[57] R. P. Singh, Numerical evaluation, optimization and mathematical validation of cold spraying of hydroxyapatite using Taguchi approach, *International Journal of Engineering Science and Technology* **3** (2011) 7006-7015. http://www.ijest.info/docs/IJEST11-03-09-080.pdf

[58] R. P. Singh, U. Batra, Effect of cold spraying parameters and their interaction an hydroxyapatite deposition, *Journal of Applied Fluid Mechanics* **4** (2013) 555-561. https://doi.org/10.36884/jafm.6.04.21277

[59] Y. W. Song, D. Y. Shan, E. H. Han, Electrodeposition of hydroxyapatite coating on AZ91D magnesium alloy for biomaterial application, *Materials Letters* **62** (2008) 3276-3279. https://doi.org/10.1016/j.matlet.2008.02.048

[60] G. Song, Recent Progress in Corrosion and Protection of Magnesium Alloys, *Advanced Engineering Materials* **7** (2005) 563-586. https://doi.org/10.1002/adem.200500013

[61] F. Witte, N. Hort, C. Vogt, S. Cohen, K. U. Kainer, R. Willumeit, F. Feyerabend, Degradable biomaterials based on magnesium corrosion, *Current Opinion in Solid State and Materials Science* **12** (2008) 63-72. https://doi.org/10.1016/j.cossms.2009.04.001

[62] J. E. Gray, B. Luan, Protective coatings on magnesium and its alloys — a critical review, *Journal of Alloys and Compounds* **336** (2002) 88-113. https://doi.org/10.1016/S0925-8388(01)01899-0

[63] A. Choudhuri, P. S. Mohanty, J. Karthikeyan, *Bio-ceramic composite coatings by cold spray technology,* in *Thermal Spray 2099: Proceedings from the International Thermal Spray*

Conference., Las Vegas, Nevada, USA, May 4–7, 2009, pp 391-396. https://doi.org/10.31399/asm.cp.itsc2009p0391

[64] J. Weng, Q. Liu, J.G.C. Wolke, X. Zhang, K. Degroot, Formation and characteristics of the apatite layer on plasma-sprayed hydroxyapatite coatings in simulated body fluid, *Biomaterials* **15** (1997)1027-1035. https://doi.org/10.1016/S0142-9612(97)00022-7

[65] A. C. W. Noorakma, H. Zuhailawati, V. Aishvarya, B. K. Dhindaw, Hydroxyapatite-Coated Magnesium-Based Biodegradable Alloy: Cold Spray Deposition and Simulated Body Fluid Studies, *Journal of Materials Engineering and Performance* **22** (2013) 2997-3004. https://doi.org/10.1007/s11665-013-0589-9

[66] M. Hasniyati, H. Zuhailawati, R. Sivakumar, B. K. Dhindaw, S. N. F. M. Noor, Cold spray deposition of hydroxyapatite powder onto magnesium substrates for biomaterial applications, *Surface Engineering* **31** (2015) 867-874. https://doi.org/10.1179/1743294415Y.0000000068

[67] J. H. Noh, D. W. Kim, An J. S. An, H. R. Chang, D. H. Kim, K. S. Hong, D. K. Chin, Method for modifying the surface area of a bioinert material, US Patent 0009341 A1, January 12, 2012 https://patents.google.com/patent/WO2010093130A2/en

[68] J. H. Lee, H. L. Jang, K. M. Lee, H.-R. Baek, K. Jin, K. S. Hong, J. H. Noh, H.-K. Lee, In vitro and in vivo evaluation of the bioactivity of hydroxyapatite-coated polyetheretherketone biocomposites created by cold spray technology, *Acta Biomaterialia* **9** (2013) 6177-6187. https://doi.org/10.1016/j.actbio.2012.11.030

[69] M. W. Chen, J. W. McCauley, D. P. Dandekar, N. K. Bourne, Dynamic plasticity and failure of high-purity alumina under shock loading, *Nature Materials* **5** (2006) 614-618. https://doi.org/10.1038/nmat1689

[70] A. K. Mukhopadhyay, K. D. Joshi, A. Dey, R. Chakraborty, A. Rav, S. K. Biswas, S. C. Gupta, Shock deformation of coarse grain alumina above Hugoniot elastic limit, *Journal of Materials Science* **45** (2010) 3635-3651. https://doi.org/10.1007/s10853-010-4409-4

[71] W.-Y. Li, C.-J. Li, G.-J. Yang, Effect of impact-induced melting on interface microstructure and bonding of cold-sprayed zinc coating, *Applied Surface Science* **257** (2010) 1516-1523. https://doi.org/10.1016/j.apsusc.2010.08.089

[72] A. M. Vilardell, N. Cinca, N. Garcia-Giralt, S. Dosta, I. G. Cano, X. Nogués, J. M. Guilemany, Functionalized coatings by cold spray: An in vitro study of micro- and nanocrystalline hydroxyapatite compared to porous titanium, *Materials Science and Engineering: C* **87** (2018) 41-49. https://doi.org/10.1016/j.msec.2018.02.009

[73] M. R. Hasniyati, H. Zuhailawati, R. Sivakumar, B. K. Dhindaw, Optimization of multiple responses using overlaid contour plot and steepest methods analysis on hydroxyapatite coated magnesium via cold spray deposition, *Surface and Coatings Technology* **280** (2015) 250-255. https://doi.org/10.1016/j.surfcoat.2015.09.006

[74] Q.-Y. Chen, Y.-L. Zou, X. Chen, X.-B. Bai, G.-C. Ji, H.-L. Yao, H.-T. Wang, F. Wang, Morphological, structural and mechanical characterization of cold sprayed hydroxyapatite coating, *Surface and Coatings Technology* **357** (2019) 910-923. https://doi.org/10.1016/j.surfcoat.2018.10.056

[75] M. Gardon, A. Concustell, S. Dosta, N. Cinca, I. G. Cano, J. M. Guilemany, Improved bonding strength of bioactive cermet Cold Gas Spray coatings, *Materials Science and Engineering: C* **45** (2014) 117-121. https://doi.org/10.1016/j.msec.2014.08.053

[76] X. Zhou, P. Mohanty, Electrochemical behavior of cold sprayed hydroxyapatite/titanium composite in Hanks' solution, *Electrochimica Acta* **65** (2012) 134-140. https://doi.org/10.1016/j.electacta.2012.01.018

[77] J. Tang, Z. Zhao, H. Liu, X. Cui, J. Wang, T. Xiong, A novel bioactive Ta/hydroxyapatite composite coating fabricated by cold spraying, *Materials Letters* **250** (2019) 197-201. https://doi.org/10.1016/j.matlet.2019.04.123

[78] H.-L. Yao, Z.-H. Yi, C. Yao, M.-X. Zhang, H.-T. Wang, S.-B. Li, X.-B. Bai, Q.-Y. Chen, G.-C. Ji, Improved corrosion resistance of AZ91D magnesium alloy coated by novel cold-sprayed Zn-HA/Zn double-layer coatings, *Ceramics International* **46** (2020) 7687-7693. https://doi.org/10.1016/j.ceramint.2019.11.271

[79] Y. Liu, Z. Dang, Y. Wang, J. Huang, H. Li, Hydroxyapatite/graphene-nanosheet composite coatings deposited by vacuum cold spraying for biomedical applications: Inherited nanostructures and enhanced properties, *Carbon* **67** (2014) 250-259. https://doi.org/10.1016/j.carbon.2013.09.088

[80] N. Sanpo, M. L. Tan, P. Cheang, K. A. Khor, Antibacterial Property of Cold-Sprayed HA-Ag/PEEK Coating, *Journal of Thermal Spray Technology* **18** (2009) 10-15. https://doi.org/10.1007/s11666-008-9283-0

[81] H. Qiao, G. Song, Y. Huang, H. Yang, S. Han, X. Zhang, Z. Wang, J. Ma, X. Bu, L. Fu, Si, Sr, Ag co-doped hydroxyapatite/TiO 2 coating: enhancement of its antibacterial activity and osteoinductivity, *RSC Advances* **9** (2019) 13348-13364. https://doi.org/10.1039/C9RA01168D

[82] H. Qiao, Q. Zou, C. Yuan, X. Zhang, S. Han, Z. Wang, X. Bu, H. Tang, Y. Huang, Composite coatings of lanthanum-doped fluor-hydroxyapatite and a layer of strontium titanate nanotubes: fabrication, bio-corrosion resistance, cytocompatibility and osteogenic differentiation, *Ceramics International* **44** (2018) 16632-16646. https://doi.org/10.1016/j.ceramint.2018.06.090

[83] Y. Huang, W. Wang, X. Zhang, X. Liu, Z. Xu, S. Han, Z. Su, H. Liu, Y. Gao, H. Yang, A prospective material for orthopedic applications: Ti substrates coated with a composite coating of a titania-nanotubes layer and a silver-manganese-doped hydroxyapatite layer, *Ceramics International* **44** (2018) 5528-5542. https://doi.org/10.1016/j.ceramint.2017.12.197

[84] H. Shi, Z. Zhou, W. Li, Y. Fan, Z. Li, J. Wei, Hydroxyapatite Based Materials for Bone Tissue Engineering: A Brief and Comprehensive Introduction, *Crystals* **11** (2021) 149. https://doi.org/10.3390/cryst11020149

[85] Q. Ling Feng, T. Nam Kim, J. Wu, E. Seo Park, J. Ock Kim, D. Young Lim, F. Zhai Cui, Antibacterial effects of Ag-HAp thin films on alumina substrates, *Thin Solid Films* **335** (1998) 214-219. https://doi.org/10.1016/S0040-6090(98)00956-0

[86] M. Shirkhanzadeh, M. Azadegan, G. Q. Liu, Bioactive delivery systems for the slow release of antibiotics: incorporation of Ag+ ions into micro-porous hydroxyapatite coatings, *Materials Letters* **24** (1995) 7-12. https://doi.org/10.1016/0167-577X(95)00059-3

[87] S. Dahl, P. Allain, P.. Marie, Y. Mauras, G. Boivin, P. Ammann, Y. Tsouderos, P.. Delmas, C. Christiansen, Incorporation and distribution of strontium in bone, *Bone* **28** (2001) 446-453. https://doi.org/10.1016/S8756-3282(01)00419-7

[88] N. D. Ravi, R. Balu, T.S. Sampath Kumar, Strontium-Substituted Calcium Deficient Hydroxyapatite Nanoparticles: Synthesis, Characterization, and Antibacterial Properties, *Journal of the American Ceramic Society* **95** (2012) 2700-2708. https://doi.org/10.1111/j.1551-2916.2012.05262.x

[89] C. Capuccini, P. Torricelli, E. Boanini, M. Gazzano, R. Giardino, A. Bigi, Interaction of Sr-doped hydroxyapatite nanocrystals with osteoclast and osteoblast-like cells, *Journal of Biomedical Materials Research Part A* **89A** (2009) 594-600. https://doi.org/10.1002/jbm.a.31975

[90] Y. Li, S. Shen, L. Zhu, S. Cai, Y. Jiang, R. Ling, S. Jiang, Y. Lin, S. Hua, G. Xu, In vitro degradation and mineralization of strontium-substituted hydroxyapatite coating on magnesium alloy synthesized via hydrothermal route, *Journal of the Ceramic Society of Japan* **127** (2019) 158-164. https://doi.org/10.2109/jcersj2.18170

[91] G. Borkow, J. Gabbay, Copper as a Biocidal Tool, *Current Medicinal Chemistry* **12** (2005) 2163-2175 https://doi.org/10.2174/0929867054637617.

[92] C. Wu, Y. Zhou, M. Xu, P. Han, L. Chen, J. Chang, Y. Xiao, Copper-containing mesoporous bioactive glass scaffolds with multifunctional properties of angiogenesis capacity, osteostimulation and antibacterial activity, *Biomaterials* **34** (2013) 422-433. https://doi.org/10.1016/j.biomaterials.2012.09.066

[93] A. Ewald, C. Käppel, E. Vorndran, C. Moseke, M. Gelinsky, U. Gbureck, The effect of Cu(II)-loaded brushite scaffolds on growth and activity of osteoblastic cells, *Journal of Biomedical Materials Research Part A* **100(9)**(2012) 2392-2400. https://doi.org/10.1002/jbm.a.34184

[94] M. Pujari, P. N. Patel, Strontium-copper-calcium hydroxyapatite solid solutions: Preparation, infrared, and lattice constant measurements, *Journal of Solid State Chemistry* **83** (1989) 100-104. https://doi.org/10.1016/0022-4596(89)90058-3

[95] S. Shanmugam, B. Gopal, Copper substituted hydroxyapatite and fluorapatite: Synthesis, characterization and antimicrobial properties, *Ceramics International* **40** (2014) 15655-15662. https://doi.org/10.1016/j.ceramint.2014.07.086

[96] A. V. Lyasnikova, O. A. Markelova, O. A. Dudareva, V. N. Lyasnikov, A. P. Barabash, S. P. Shpinyak, Comprehensive Characterization of Plasma-Sprayed Coatings Based Silver- and Copper-Substituted Hydroxyapatite, *Powder Metallurgy and Metal Ceramics* **55** (2016) 328-333. https://doi.org/10.1007/s11106-016-9809-9

[97] R. Drevet, Y. Zhukova, S. Dubinskiy, A. Kazakbiev, V. Naumenko, M. Abakumov, J. Fauré, H. Benhayoune, S. Prokoshkin, Electrodeposition of cobalt-substituted calcium phosphate coatings on $Ti_{22}Nb_6Zr$ alloy for bone implant applications, *Journal of Alloys and Compounds* **793** (2019) 576-582. https://doi.org/10.1016/j.jallcom.2019.04.180

[98] K. Prem Ananth, J. Sun, J. Bai, Superior corrosion protection and in vitro biocompatibility of Na-HAp/CS composite coating on PoPD-coated 316L SS, *Materials Today Chemistry* **10** (2018) 153-166. https://doi.org/10.1016/j.mtchem.2018.08.001

[99] K. Ananth, J. Sun, J. Bai, An Innovative Approach to Manganese-Substituted Hydroxyapatite Coating on Zinc Oxide-Coated 316L SS for Implant Application, *International Journal of Molecular Sciences* **19** (2018) 2340. https://doi.org/10.3390/ijms19082340

[100] Y. Lin, Z. Yang, J. Cheng, Preparation, Characterization and Antibacterial Property of Cerium Substituted Hydroxyapatite Nanoparticles, *Journal of Rare Earths* **25** (2007) 452-456. https://doi.org/10.1016/S1002-0721(07)60455-4

[101] E. O. López, A. L. Rossi, B. S. Archanjo, R. O. Ospina, A. Mello, A. M. Rossi, Crystalline nano-coatings of fluorine-substituted hydroxyapatite produced by magnetron sputtering with high plasma confinement, *Surface and Coatings Technology* **264** (2015) 163-174. https://doi.org/10.1016/j.surfcoat.2014.12.055

[102] M. Caligari Conti, G. Xerri, F. Peyrouzet, P. S. Wismayer, E. Sinagra, D. Mantovani, D. Vella, J. Buhagiar, Optimisation of fluorapatite coating synthesis applied to a biodegradable substrate, *Surface Engineering* **35** (2019) 255-265. https://doi.org/10.1080/02670844.2018.1491510

[103] B. León, M. Albano, L. Garrido, E. Ferraz, A. Rosa, P. Tambasco de Oliveira, Processing, structural, and biological evaluations of zirconia scaffolds coated by fluorapatite,

International Journal of Applied Ceramic Technology **15** (2018) 1415-1426. https://doi.org/10.1111/ijac.12904

[104] A. M. Vilardell, N. Cinca, N. Garcia-Giralt, S. Dosta, I. G. Cano, X. Nogués, J.M. Guilemany, In-vitro comparison of hydroxyapatite coatings obtained by cold spray and conventional thermal spray technologies, *Materials Science and Engineering: C* **107** (2020) 110306 https://doi.org/10.1016/j.msec.2019.110306.

[105] S. Ban, L. Cui, D. He, J. Jiang, X. Li, Z. Wang, L. Zhao, Q. Zhao, Z. Zhou, Preparation method for Making Hydroxyl Apatite Coating Through Cold Spraying, Involves Spraying Dried Hydroxyl Apatite Powders onto Matrix of Biomedical Implanted Metal Material Using Cold Spraying Device, CN101591777-B, 2011. https://patentimages.storage.googleapis.com/cc/8a/aa/bd755411df0fe3/CN101591777B.pdf in Chinese

[106] R. Mongrain, O. F. Bertrand, S. Yue, O. Bertrand, Intermixed Particulate Material Used in Bioresorbable stent comprises cathodic Particles Made of Cathodic Material and Anodic Particles Made of Anodic Material Bound to Each Other, where the Materials Form a Galvanic Couple, WO2013163747-A1, 2013 https://patentimages.storage.googleapis.com/b3/10/dd/d63c1cc8515ff1/WO2013163747A1.pdf

[107] P. A. Kramer, Manufacturing Medical Device e.g. Drug Eluting Stent, Guide Wires, Lead Tips, Catheters, Markers Involves Forming Porous Substrate from Biocompatible Material Using Spray Process and Processing Porous Substrate INTO Medical Device, US7514122-B2, 2009. US7514122-B2, 2009 https://portal.unifiedpatents.com/patents/patent/US-7514122-B2