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Engineering Nanostructured Thermal Spray Coatings for Biomedical Applications

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1. Thermal Spray Coatings

1.1 Thermal Spray Process

Thermal spraying comprises a group of processes wherein a feedstock material (usually a powder, but also in the form of a wire or rod) is heated and propelled as individual molten and/or semi-molten particles towards a substrate surface. Thermal spray torches are employed to deposit coatings on substrates. These thermal spray torches have a heat source, which can be (i) the combustion of a fuel gas (e.g., propylene and oxygen), (ii) a plasma gas (e.g., Ar/H_2) or (iii) an electric arc. At the heat source of the thermal spray torch the feedstock material is heated and changed to a jet of molten and/or semi-molten particles and is propelled towards the substrate surface via the expansion of the (i) combustion gases, (ii) plasma gases or (iii) compressed air. Basically, any material that is stable in its molten state can be deposited by thermal spray, which includes a wide range of metals, ceramics, polymers and cermets.

At impact with the substrate or previously deposited layers, the molten/semi-molten particles flatten and form thin lamellae (splats) that conform and adhere to the irregularities of the substrate surface and to each other. After impact, the splats cool down and resolidify very rapidly, generally before the arrival of the next impinging particle. The microstructure of a thermal spray coating is formed by the overlapping and interlocking of splats, thereby creating a lamellar structure. The coating is typically non-homogeneous, anisotropic and contains a combination of material originating from fully molten and semi-molten particles, as well as, pores, cracks (in ceramics) and oxides (in metals) [1].

Thermal spray coatings are normally deposited on metallic substrates, however, ceramic and plastic substrates may also be coated by this technique. Substrate preparation is of high importance. The substrate is generally prepared by grit-blasting the surface with alumina particles, which cleans the surface of contaminants, unwanted species (e.g., oxides) and provides microscopic asperities (roughness) to increase surface area and enhance coating adhesion. The bond between the coating and substrate may be mechanical (anchoring of the splats on the roughness of the substrate), chemical, metallurgical or a combination of these. The properties of thermal spray coatings are dependent on, among other things, the feedstock material, thermal spray process, thermal spray parameters and particle temperature and velocity in the thermal spray jet.

The two widely most employed thermal spray processes to spray feedstock powders today are air plasma spray (APS) and high velocity oxy-fuel (HVOF). The heat source of APS torches is based on a combination of plasma gases (e.g., Ar/H_2). The maximum temperature of a plasma jet is approximately 15,000°C, whereas, the particle speed generally varies from 150 to 300 m/s. This process is usually carried out in open air, however, it can be carried out inside a vacuum chamber, and then it is called vacuum plasma spray (VPS). Sometimes metals are sprayed by VPS in order to avoid particle oxidation from air during thermal spraying.

The heat source of HVOF torches is based on the combustion of a fuel gas (e.g., propylene and O_2). The maximum temperature of an HVOF jet is generally below 3,000°C, whereas, the particle speed generally varies from 600 to 800 m/s.

1.2 Biomedical Thermal Spray Coatings

There are approximately 435,000 total knee and hip joint replacements per year just in the USA. By the year 2030, a total of 730,000 total knee and hip joint replacement procedures per year is estimated only in the USA [2]. These implants are generally made of Ti-6Al-4V alloys, CoCr alloys or stainless steel. These materials have high mechanical strength, high corrosion resistance, good fatigue life and are extremely bioinert. Due to their high bioinertness they do not exhibit good biointeraction with the osteoblast cells once implanted in the human body; therefore another agent must be used in order to promote the osseointegration between the implant and the bone.

The first hip joint implants, which were developed during the 1960s, employed a cement to provide the fixation of the implant to the bone. These types of implants are called cemented implants. This technique is still employed today and the cement is based on an acrylic polymer called polymethylmethacrylate (PMMA). Uncemented implants were developed in the 1980s in an attempt to eliminate the possibility of part loosening and the breaking off of cement particles, which occurred more frequently in younger and active patients who had received cemented implants.

The state-of-the-art uncemented implants that are used today employ biocompatible thermal spray coatings, such as hydroxyapatite (HA) and titanium (Ti), to promote the osseointegration between the implant and the bone. HA is a calcium phosphate based material ($Ca_{10}(PO_4)_6(OH)_2$), which is the bone mineral found in human bodies. HA is highly biocompatible and bioactive in the human body. It is compatible with various tissue types and can adhere directly to osseous, soft and muscular tissue without an intermediate layer of modified tissue [3]. Due to this high bioactivity with human cells, synthetic HA powders are thermally sprayed onto the metallic implants. The thermal spray process employed is generally APS. Once the prosthesis is implanted, the osteoblast cells of the bones attach, grow and proliferate on the surface of these HA coatings, therefore promoting the necessary osseointegration. The HA coatings produced via APS for this application generally exhibit a thickness of 50 – 75 μm, an arithmetic mean roughness (R_a) of 7.5 – 9.5 μm, porosity of 1 – 10%, purity higher than 97%, crystallinity higher than 50% and bond strength between 20 – 30 MPa [3-6]. Figure 2 shows a typical example of a Ti-6Al-4V hip joint (stem and acetabular cup) coated with an HA thermal spray coating [7]. Figure 3 shows a typical artificial hip joint implant, like the one of Fig. 2, implanted in the human body [7]. The stem is implanted in the femur and the acetabular cup is implanted in the pelvis.

Titanium powders are generally thermal sprayed via VPS in order to avoid the oxidation of the Ti particles in air. Due to the lack of bioactivity between the titanium and the osteoblast cells, the osseointegration mechanism is different from that of HA coatings. The titanium thermal spray coatings are made highly porous. The large pores allow bone in-growth into the microstructure of the coating, filling the porosity of the coating, thereby promoting mechanical osseointegration. The titanium coatings produced via VPS generally exhibit thickness of 350 – 600 μm, arithmetic mean roughness (R_a) of approximately 30 μm, porosity of 15 - 40%, and bond strength of 25 MPa (minimum) [5, 8].

1.3 Nanostructured Thermal Spray Coatings

1.3.1 Enhanced Mechanical Performance of the Nanostructured Thermal Spray Coatings

It has been demonstrated by different authors that nanostructured thermal spray coatings exhibit enhanced mechanical performance when compared to their conventional counterparts [9-20]. Different characteristics have been observed, including, (i) higher wear resistance, (ii) higher bond strength with the substrate, (iii) higher resistance to delamination, (iv) higher toughness and (v) higher plasticity. In order to produce these types of coatings and achieve these properties, several important steps must be taken and are described in the reminder of this section.

1.3.2 Nanostructured Powders for Thermal Spray

As previously mentioned, thermal spray coatings are usually made from a powder feedstock. These powder particles typically exhibit a particle size distribution varying from 5 to 100 μm, i.e., the particles are microscopic. Individual nanostructured particles, i.e., smaller than 100 nm, cannot be thermally sprayed using the regular powder feeders employed in thermal spray. These tiny nanoparticles would clog the hoses that transport the powder particles from the powder feeder to the thermal spray torch.

In order to spray nanoparticles using regular powder feeders the individual nanostructured particles are agglomerated via spray-drying into microscopic particles. This process is usually employed when very fine materials such as nanostructured ceramic or cermet powders are to be thermal sprayed. Figures 4 and 5 show the typical morphology of conventional and nanostructured titania (TiO_2) powder particles for thermal spray systems [18]. The conventional particle is formed via fusing and crushing of the titania material (Fig. 4a). When this conventional particle is observed at high magnification it is not possible to identify any nanostructural character (Fig. 4b). The nanostructured titania particle produced for thermal spray is shown in Fig. 5. It exhibits the typical donut shape of spray-dried particles (Fig. 5a). When analyzed at higher magnifications it is possible to observe the nanostructure of the feedstock (Fig. 5b), i.e., each microscopic titania particle is formed via the agglomeration of individual titania particles smaller than 100 nm.

Nanostructured metallic powders can also be thermally sprayed. In this case, conventional microscopic metallic particles are usually milled in methanol or liquid nitrogen [21]. Due to the excessive plastic deformation of the metallic particles during milling, the submicron grains of the powders are destroyed and transformed into grains with diameters smaller than 100 nm [21].

1.3.3 Thermal Spraying Nanostructured Powders

The thermal spray process is intrinsically associated with the melting of particles. Without some particle melting it is extremely difficult to produce thermal spray coatings, particularly with ceramic materials. Some degree of melting is necessary to achieve a sufficient degree of particle adhesion and cohesion. This is a challenge for thermal spraying nanostructured powders; if all powder particles are fully molten in the thermal spray jet, all the nanostructural character of the powder particles will disappear, and therefore the thermal spray coating will not exhibit any nanostructured related property.

In order to overcome this challenge it is necessary to carefully control the temperature of the particles in the thermal spray jet, i.e., the temperature of the powder particles should be maintained such that is not much higher than the melting point of the material. The particles must be thermally sprayed in such a way to guarantee that part of the initial nanostructure of the feedstock will be embedded in the coating microstructure.

Nanostructured titania particles like that of Fig. 5 (VHP-DCS (5-20 μm), Altair Nanomaterials, Reno, NV, USA) were thermally sprayed using an HVOF torch (DJ2700-hybrid, Sulzer Metco, Westbury, NY, USA). During deposition, the temperature and velocities of the sprayed particles were monitored using a diagnostic tool (DPV 2000, Tecnar Automation, Saint Bruno, QC, Canada). The diagnostic tool is based on optical pyrometry and time-of-flight measurements to measure the distribution of particle temperature and velocity in the thermal spray jet. The average surface temperature and velocity of the thermally sprayed particles were 1874 ± 136°C and 635 ± 89 m/s [22]. As the melting point of titania is 1855°C [23], it is considered that part of the nanostructure of the titania powder was preserved and embedded in the coating microstructure, as will be seen in the next subsection.

It is important to point out that a new thermal spray process was launched by the end of the 1990s, and this new process is called cold spray. This process has a particular difference when compared to other thermal spray processes. In cold spray the powder particles are mixed with a heated gas (He, N_2 or air) at temperatures below 700°C (i.e., there is no particle melting) and accelerated to supersonic velocities on the order of 600 – 1000 m/s through a de Laval nozzle. The particles arrive at the substrate surface at these high speeds, plastically deform and adhere to the substrate surface [24]. This new process is still in its initial stage of development, but it may become very important in the future for allowing the spraying of nanostructured particles without any degree of melting, i.e., it will be possible to produce Ti coatings consisting of 100% nanostructured material. It is important to point out that cold spray is usually employed to spray metallic powders, due to their deformation capabilities.

1.3.4 Bimodal Microstructure of Nanostructured Thermal Spray Coatings

As previously stated, thermally sprayed nanostructured coatings are formed from nanostructured particles that were fully molten and semi-molten in the thermal spray jet: The particles that were fully molten in the spray jet lose the nanostructural character of the feedstock, whereas, the semi-molten particles retain some of their nanostructural features. Due to this characteristic, many authors describe these nanostructured thermal spray coatings as exhibiting a bimodal microstructure [9-13, 18-20]. A typical schematic (cross-section) of a microstructure of a nanostructured thermal spray coating is shown in Fig. 6. The semi-molten nanostructured particles (nanozones) are spread throughout the coating microstructure. The nanozones are found at (i) the coating/substrate interface, (ii) embedded in the coating microstructure and (iii) at the surface of the coating.

Figure 7a shows a low magnification view of the cross-section of the HVOF-sprayed nanostructured titania coating described in the previous section (1.3.3), which was deposited on a Ti-6Al-4V substrate. The coating is very dense and uniform, not exhibiting the typical lamellar structure of thermal spray coatings. It may be stated that this coating has an isotropic or bulk-like microstructure. When the coating of Fig. 7a is observed at higher magnifications (Fig. 7b) it is possible to observe the nanostructured zones, which were formed by semi-molten nanostructured particles that became entrapped in the coating microstructure. It is important to point out that these nanozones (Fig. 7b) are spread throughout the coating microstructure.

This bimodal microstructure is essential for the enhanced mechanical performance of these nanostructured coatings. The semi-molten nanostructured particles (nanozones) located at the coating/substrate interface and embedded throughout the coating microstructure act as crack arresters, thereby increasing the (i) bond strength of the coating, (ii) the resistance to delamination and (iii) the coating toughness [9-12, 18-20].

A practical example of the mechanism of crack arresting is found in Figs. 8 and 9. Figure 8 shows a crack propagation experiment carried out via Vickers indentation (5 kgf) on the cross-section of an HVOF-sprayed conventional TiO_2 coating. The Vickers indenter was aligned such that one of its diagonals would be parallel to the substrate surface. It is possible to observe that the cracks propagate parallel to the substrate surface beyond the limits of the picture [18]. Figure 9a shows a crack propagation experiment carried out via Vickers indentation (5 kgf) on the cross-section of an HVOF-sprayed nanostructured TiO_2 coating described in the previous section (1.3.3). In this case the Vickers indenter was also aligned such that one of its diagonals would be parallel to the substrate surface. It is also possible to observe that the cracks propagated parallel to the substrate surface but were arrested before the limits of the picture. It is important to point out that both pictures of Figs. 8 and 9a were taken at the same magnification. Therefore it can be observed that the nanostructured coating exhibits higher toughness and resistance to delamination when compared to the conventional one. By looking at the tip of the indentation crack of Fig. 9a at higher magnification, it is possible to notice that the crack is arrested after passing through a nanozone, which was formed by a semi-molten nanostructure particle (Fig. 9b) [18].

It is also important to point out that the nanostructured coating (Fig. 9) exhibited uniform crack propagation under Vickers indentation, i.e., four cracks with similar length propagating from the corners of the indentation impression, which is a typical characteristic of bulk materials and not thermal spray coatings. Therefore it may be stated that this nanostructured coating is so uniform that it is behaving like a bulk material, which is not the regular behaviour of a thermal spray coating.

2. Enhanced Biocompatibility of Nanostructured Materials

It has been demonstrated that nanostructured materials, such as, alumina (Al_2O_3), titania (TiO_2), HA, Ti, Ti-6Al-4V and Co28Cr6Mo exhibit enhanced biocompatibility with osteoblast cells (i.e., bone cells) when compared to their conventional counterparts [25-30]. This enhanced biocompatibility is translated into higher cell reproduction and adhesion on the surface of these materials, which are very important characteristics for making implants with improved bioperformance and longevity. Webster et al. [28], explained this better performance of the nanostructured material as the effect of the nanotexture or nanoroughness of these materials on the adsorption of the adhesion proteins like fibronectin. This phenomenon was experimentally observed by Dalby et al. [31]. Adhesion proteins like fibronectin mediate the adhesion of anchorage-dependent cells (such as osteoblasts) on substrates and coatings [32]. These adhesion proteins are initially adsorbed on the surface of an implant almost immediately upon its implantation in the human body. When the osteoblast cells arrive at the implant surface they "see" a protein-covered surface that will connect with the transmembrane proteins (integrins) of the osteoblast cells [32]. It is important to point out that these proteins, such as fibronectin, exhibit nanosized lengths and structures [33].

It is interesting to note that the surface of a nanostructured material (nanosized grains) will exhibit predominantly nanoscale features, like nanoroughness, whereas, the surface of a conventional material (microsized grains) will tend to exhibit more microsized features [26]. It has been proven that the interaction or the adsorption of a nanosized protein (e.g., fibronectin) to a nanotextured surface will be more effective than that provided by a microtextured one [28, 31]. Proteins were placed on substrate surfaces containing (i) essentially flat regions (no roughness) and (ii) nanoprotuberances. It was observed that the proteins tended to attach and anchor on the nanoprotuberances, whereas, no significant attachment was noted for the flat regions [34, 35]. Therefore nanostructured materials, containing regions on their surfaces exhibiting nanotexture, has the potential as the next generation of biomedical materials, with the attributes of exhibiting enhanced cell proliferation and adhesion.

3. Engineering the New Generation of Biomedical Thermal Spray Coatings for Uncemented Implants

3.1 Current Problems of HA Thermal Spray Coatings

HA coatings thermally sprayed via APS can be considered as one of the state-of-the-art materials used today to promote osseointegration of the implant to the bone in uncemented implants [36]. HA thermal spray coatings have been successfully used since the 1980s in thousands of patients. Despite the success with this coating, there are still drawbacks concerning its application.

HA thermal spray coatings may fail by (i) aseptic loosening or (ii) osteolysis. Concerning aseptic loosening, Lai et al. [37] and Reikeras and Gunderson [6] observed that following implantation in humans the HA coatings dissolved over a period of 10 years. They observed that after HA dissolution, the bone did not necessarily interlock with the metallic implant surface. Lai et al. [37] also established a relationship between the amount of residual HA on acetabular cups and the stability of the cup. It was found that when the percentage of residual HA covering the surface was less than 40% the implant tended to become unstable. Reikeras and Gunderson [6] and Manley et al. [38] observed that some HA coatings did not exhibit dissolution and interlocked very well with the bone, however, the HA coatings were not able to withstand the stresses generated due to the activity of the patients and failed by delamination. Lai et al. [37] and Shen et al. [39] also observed that the initial dissolution of the HA may weaken the structure of the coating, causing it to delaminate.

Osteolysis may also lead to the failure of HA thermal spray coatings. According to Silver et al. [40], the activities of macrophages and osteoclasts, which are present during osteolysis, may lower the pH of the environment surrounding the bone to values equal to or less than 3.6. It is known that HA thermal spray coatings when immersed in simulated body fluid (SBF), which has the pH of the human blood (7.4), exhibit a decrease in the values of hardness, elastic modulus and bond strength due to the HA dissolution [41]. At a pH of 3.6 or lower it is expected that the impact on the integrity of HA thermal spray coatings would be negative, due to an accelerated dissolution. Lai et al. [37], Reikeras and Gunderson [6], Blacha [42] and Bloebaum et al. [43] observed a correlation between the osteolysis and the failure of HA thermal spray coatings. Bloebaum et al. [43] also observed that the osteolysis can generate particulates of HA via dissolution that may migrate to polyethylene inserts of the hip joints leading to a third-body wear and contributing to an accelerated failure of the implant.

3.2 Nanostructured Thermal Spray Coatings for Biomedical Applications

Biomedical thermal spray coatings, such as HA and Ti, due to their previous successes, will continue to be employed in the coming years as important agents to promote osseointegration in uncemented implants. However, despite this success the current implants are not yet optimized. The average longevity of the implants, in general, ranges from 12 to 15 years [2]. The life expectancy in countries like the USA and Canada is close to 80 years [44, 45]; and this number is increasing. As the longevity of the current implants is about 15 years, it means that many of those who receive an implant at age 65 or below will require at least one revision surgery. Consequently, the next generation of implants will be required to be (i) more biocompatible and (ii) mechanically superior when compared to those of the current generation of implants. Patients implanted with these new generation of prosthesis should have shorter hospitalization times and lower rates of revision surgeries. These improvements translate into an improvement in the quality of life and reduced medical costs.

It was previously stated that nanostructured thermal spray coatings have been shown to exhibit enhanced mechanical performance, such as (i) higher bond strength, (ii) higher toughness and (iii) higher resistance to delamination, when compared to the current conventional thermal spray coatings. It was also previously stated that the cell cultures on nanostructured materials, such as alumina (Al_2O_3), titania (TiO_2), HA, Ti, Ti-

6Al-4V and Co28Cr6Mo, have exhibited higher cell reproduction rates and adhesion strength on the surface of these materials when compared to that of conventional ones. Therefore engineering thermal spray coatings to contain nanostructured features for application in the biomedical field is a new approach and a promising new area that is in its initial stage of development. These coatings may represent the next generation of thermal spray coatings for uncemented implants. Such materials offer the possibility of improved performance by combining the good mechanical characteristics imparted by the nanostructured thermal spray coatings and the enhanced biocompatibility of nanotextured surfaces.

3.3 Nanostructured TiO_2 Thermal Spray Coatings for Biomedical Applications

Due to the above-mentioned problems, new higher performance alternatives to HA thermal spray coatings for biomedical applications are required. It is hypothesized that a good coating/material to replace HA thermal spray coatings would have to exhibit three main characteristics: (i) be non-toxic and non-absorbable by the human body, (ii) have excellent mechanical performance and (iii) have good biocompatibility with the osteoblast cells.

Nanostructured titania thermal spray coatings may be an interesting alternative to HA thermal spray coatings. Titania is a non-toxic material and non-absorbable by the human body. It has been shown that nanostructured titania thermal spray coatings exhibit excellent mechanical performance [13, 18-20]. It also has been demonstrated that nanostructured titania (bulk) has enhanced biocompatibility with osteoblast cells [25-29]. Therefore HVOF-sprayed nanostructured titania coatings are being considered as alternatives to HA coatings thermally sprayed via APS [22, 46].

3.3.1 Superior Mechanical Performance of Nanostructured TiO_2 Coatings

HVOF-sprayed nanostructured titania coatings were produced according to the conditions described in an earlier section (1.3.3) and their mechanical properties were compared to those of HA. Table 1 shows a comparison of Vickers hardness values of HVOF-sprayed nanostructured titania coatings and HA. The Vickers hardness of the HVOF-sprayed nanostructured titania coating was found to be 61% higher than that of the bulk (sintered) HA and more than 3 times that of a plasma sprayed HA (Table 1) [47, 48]. This shows that the nanostructured titania coating exhibits higher cohesive strength, which is an important property for a long-term performance implant.

The bond strength values (ASTM C633 [49]) of the HVOF-sprayed nanostructured titania coating and various HA thermal spray coatings (deposited on Ti-6Al-4V substrates) found in the literature [50-55] are listed in Table 2. The mechanical strength of the nanostructured titania coating is higher than the mechanical strength of the epoxy glue used during the bond strength test of the ASTM standard C633. Therefore during the tensile test for bond strength, the epoxy glue breaks (fails) before the coating at 77 MPa, i.e., the bond strength value (adhesion to the substrate) of the nanostructured titania coating is higher than 77 MPa. As can be seen in Table 2, the bond strength value of the HVOF-sprayed nanostructured titania coating is at least 2.5 times that of the highest bond strength value shown for an HA thermal spray coating.

These mechanical characteristics are very desirable when engineering an implant for increased longevity. It is important to point out that, unlike HA, titania does not dissolve in the human body. Therefore these improved mechanical properties of the HVOF-sprayed nanostructured titania coating should remain intact through the years after implantation in the human body.

3.3.2 Nanotexture on the Coating Surface

It was previously stated that nanostructured thermal spray coatings exhibit semi-molten nanostructured particles (nanozones) spread throughout their microstructures.

Nanozones found at the coating/substrate interface and embedded in the microstructure help to enhance the mechanical performance of the coatings.

These nanozones can also be found at the coating surface (Figure 6). Figure 10 shows a nanozone at the surface of the HVOF-sprayed nanostructured titania coating engineered as described in an earlier section (1.3.3). It is hypothesized that these nanozones located at the coating surface may enhance the interaction of the nanosized adhesion proteins (e.g., fibronectin) with the coating surface, and consequently the proliferation and adhesion of cells, like the osteoblast cells, as described by Webster et al. [25-29] and experimentally observed by Dalby et al. [31].

Therefore, in addition to the superior mechanical performance, the nanostructured thermal spray coatings may also exhibit a superior biocompatibility when compared to the conventional ones. The conventional thermal spray coatings would tend to exhibit mainly microirregularities on their surfaces, features that may be less effective for interlocking with the nanosized adhesion proteins. A schematic of the enhanced biocompatibility of nanostructured thermal spray coatings is shown in Fig. 11. It is important to point out again that this is a hypothesis, not yet experimentally confirmed for nanostructured thermal spray coatings.

3.3.3 Preliminary Osteoblast Cell Culture

HVOF-sprayed nanostructured titania and APS HA coatings were deposited on Ti-6Al-4V discs. Osteoblast cells, obtained from rat calvaria, were cultured on the surface of these coatings for SEM analysis (7-day culture) and alkaline phosphatase activity (15-day culture) in order to compare the degree of cell proliferation and adhesion on these two types of coatings. It is important to point out that the same number of cells was initially seeded on both coatings in order to produce valid statistical results and comparison. The detailed information about the in vitro testing is described elsewhere [46].

Figures 12 and 13 show the SEM analysis of the comparison of an osteoblast cell culture (obtained from rat calvaria) carried out during 7 days on the surface of the HVOF-sprayed nanostructured titania and APS HA coatings (both coatings deposited on

Ti-6Al-4V substrates). The osteoblast cells completely covered the surface of the nanostructured titania coating, whereas, the surface of the HA coating was partially covered [22].

After a 15-day culture the cells were stained for alkaline phosphatase activity shown as a red stain over the coatings. The percentage of the coating covered in red is a measure of the osteoprogenitor's ability to adhere, proliferate, and differentiate toward the osteoblast lineage. The results can be found in Figs. 14-16 [46]. Figure 16 quantifies the relative intensity of red staining on the surface of the coatings measured from a threshold.

All the preliminary results of Figs. 12-16 indicated the same trend, i.e., the HVOF-sprayed nanostructured titania coatings exhibit a degree of osteoblast cell proliferation and adhesion equivalent or superior to that of HA APS coatings.

Therefore the initial mechanical evaluation and preliminary cell culture results indicated that these HVOF-sprayed nanostructured titania coatings may become an interesting alternative to HA thermal spray coatings for uncemented implants. The combination of the (i) good chemical stability of titania in the human body, (ii) the excellent mechanical performance of the nanostructured titania coatings and (iii) the excellent bioperformance of nanostructured titania may help to lead towards to increased implant life. Of course, more in-depth investigation and testing remains to be performed with this coating in order to prove that it can be successfully implanted in human beings.

4. Final Considerations

In addition to nanostructured titania, nanostructured HA thermal spray coatings may bring important improvements to the field of biomedical coatings. The good biocompatibility of HA could be enhanced by the presence of the nanostructural character, in addition, an improvement of the mechanical performance of these coatings could be expected due to the effect of the nanozones.

The possibility of cold spraying nanostructured Ti also seems very promising. By using cold spray (i.e., no particle melting) it will be possible to produce Ti coatings consisting of 100% nanostructured material.

One of the challenges of the coming years will probably be the production of biomedical coatings (using thermal spray or other techniques) exhibiting a strong nanostructural character on their surfaces in order to become more biomimetic with the human cells.

It is important to point out again that the idea of combining the enhanced mechanical performance of nanostructured thermal spray coatings with the improved biocompatibility of the nanostructured materials is new and consequently much work is still required to more fully investigate this potential. In fact, this is an open field with many possibilities and opportunities for development and application.

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Table 1: Vickers microhardness values of the HVOF-sprayed nanostructured titania coating, plasma sprayed HA and bulk (sintered) HA.

Material	Indentation load	Vickers hardness
HVOF Nano TiO_2	300 g	824 ± 40 (n = 10)
Bulk (sintered) HA	300 g	513 ± 52 [47]
HVOF Nano TiO_2	100 g	851 ± 30 (n = 10)
Plasma spray HA	100 g	275 ± 40 [48]

Table 2: Comparison of bond strength values (ASTM C633) for the nanostructured titania coating and various HA thermal spray coatings available in the literature (substrate: Ti-6Al-4V).

Material	Powder	Process	Bond strength (MPa)
TiO_2	Nanostructured	HVOF	>77 (n = 5)
HA	Conventional	APS	23 ± 4 [50]
HA	Nanostructured	HVOF	24 ± 8 [51]
HA	Conventional	APS	13 ± 1 [52]
HA	Conventional	APS	14 ± 2 [53]
HA	Conventional	HVOF	31 ± 2 [54]
HA	Conventional	APS	27 ± 2 [55]

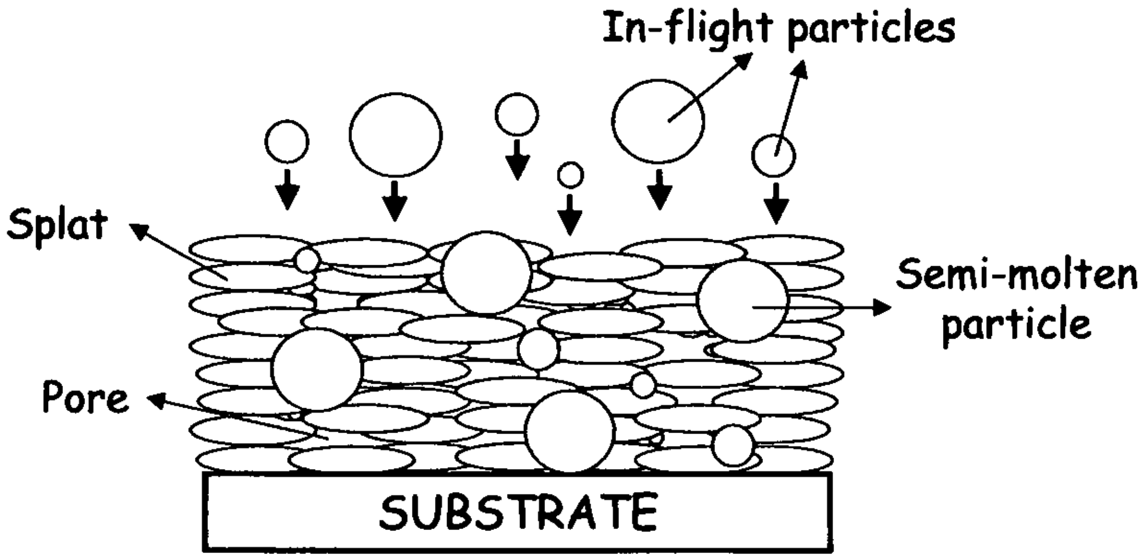

Figure 1 – Schematic of the lamellar microstructure of a thermal spray coating (cross-section) consisting of splats, semi-molten particles and pores.

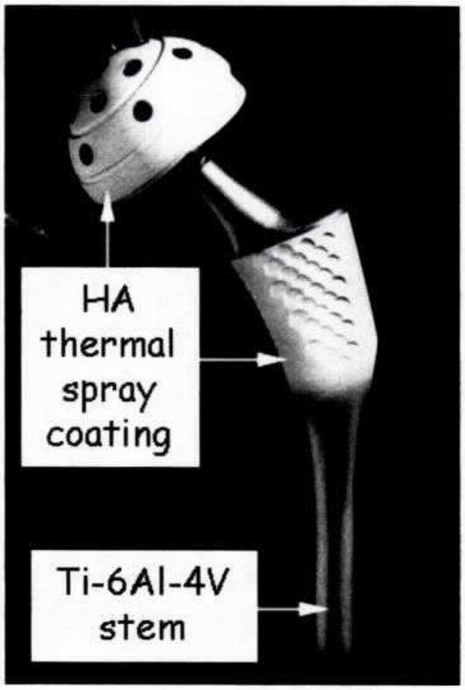

Figure 2 – Typical Ti-6Al-4V hip joint (stem and acetabular cup) coated with an HA thermal spray coating (International Orthopaedics, 25, 2001, 17-21, C. J. M. Oosterbos, A. I. A. Rahmy, A. J. Tonino, Fig. 1, with kind permission of Springer Science and Business Media) [7].

Figure 3 – Typical artificial hip joints implanted in the human body. The stem is implanted in the femur and the acetabular cup is implanted in the pelvis (International Orthopaedics, 25, 2001, 17-21, C. J. M. Oosterbos, A. I. A. Rahmy, A. J. Tonino, Fig. 4, with kind permission of Springer Science and Business Media) [7].

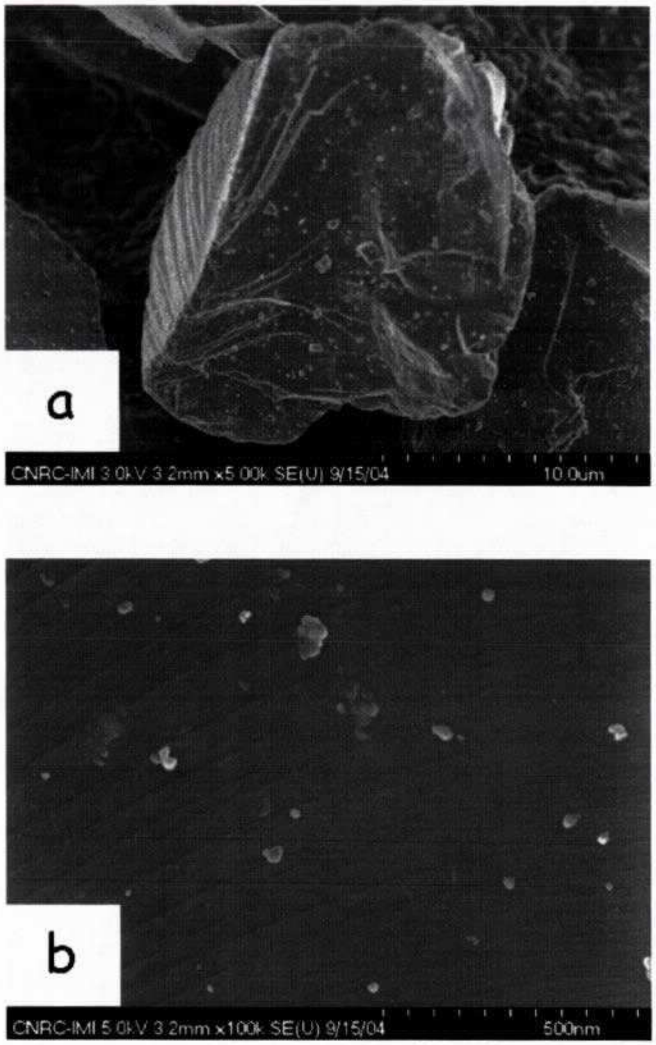

Figure 4 – (a) Conventional titania thermal spray powder particle for thermal spray. (b) Particle of (a) observed at higher magnification; absence of nanostructural character (Reprinted from Materials Science and Engineering A, 395, R. S. Lima and B. R. Marple, Enhanced Ductility in Thermally Sprayed Titania Coating Synthesized Using a Nanostructured Feedstock, 269-280, 2005, with permission from Elsevier) [18].

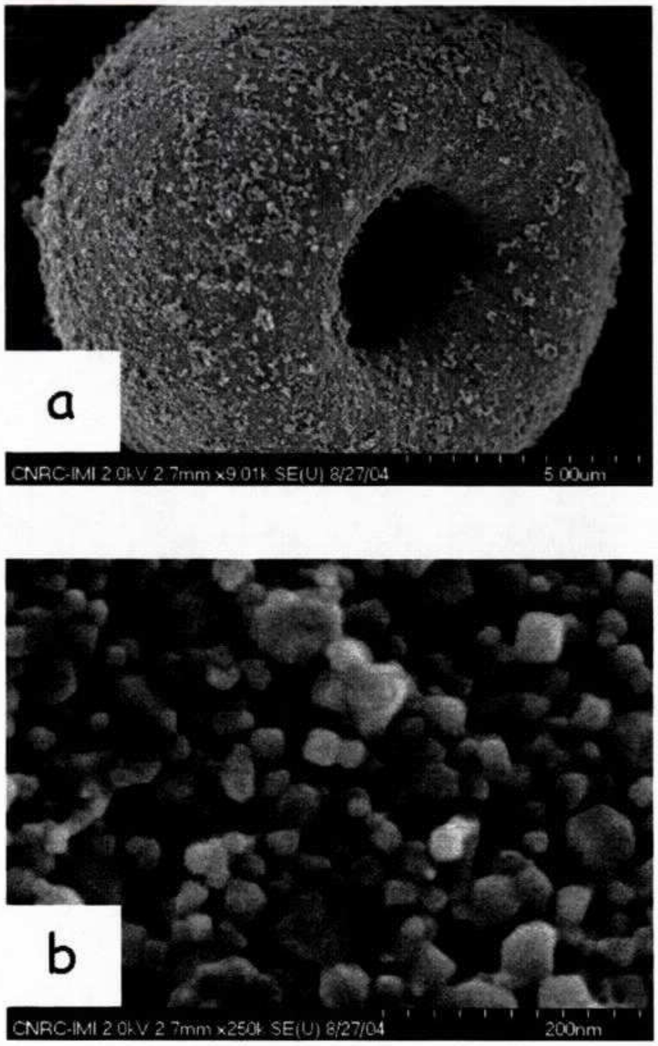

Figure 5 – (a) Titania powder particle for thermal spray formed by the agglomeration of individual nanosized particles of titania. (b) Particle of (a) observed at higher magnification; individual nanosized titania particles smaller than 100 nm (Reprinted from Materials Science and Engineering A, 395, R. S. Lima and B. R. Marple, Enhanced Ductility in Thermally Sprayed Titania Coating Synthesized Using a Nanostructured Feedstock, 269-280, 2005, with permission from Elsevier) [18].

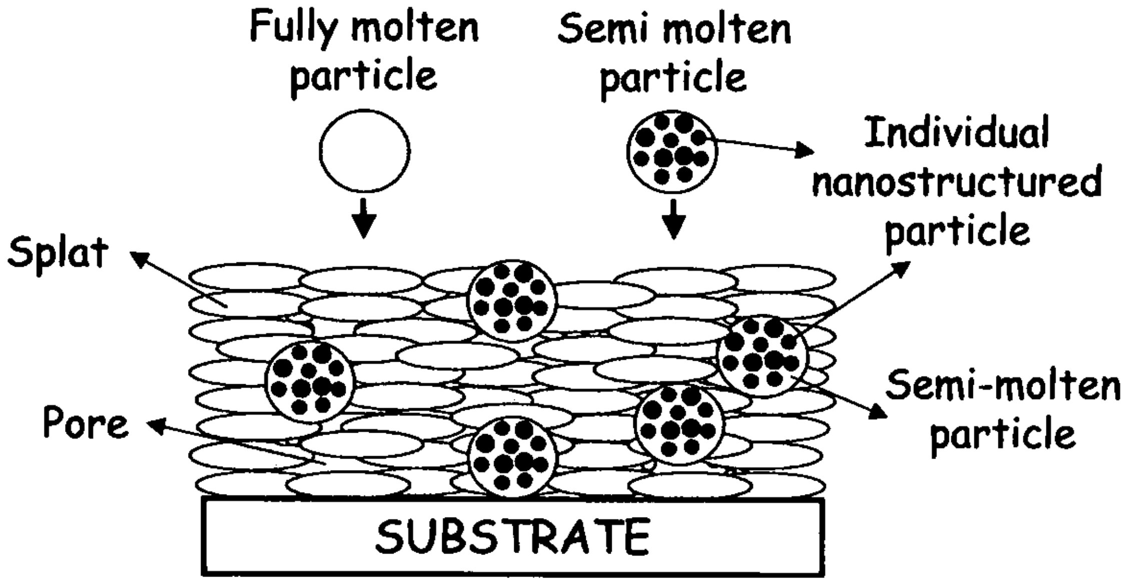

Figure 6 – Typical schematic (cross-section) of the bimodal microstructure of nanostructured thermal spray coatings, formed by nanostructured particles that were fully molten and semi-molten in the thermal spray jet.

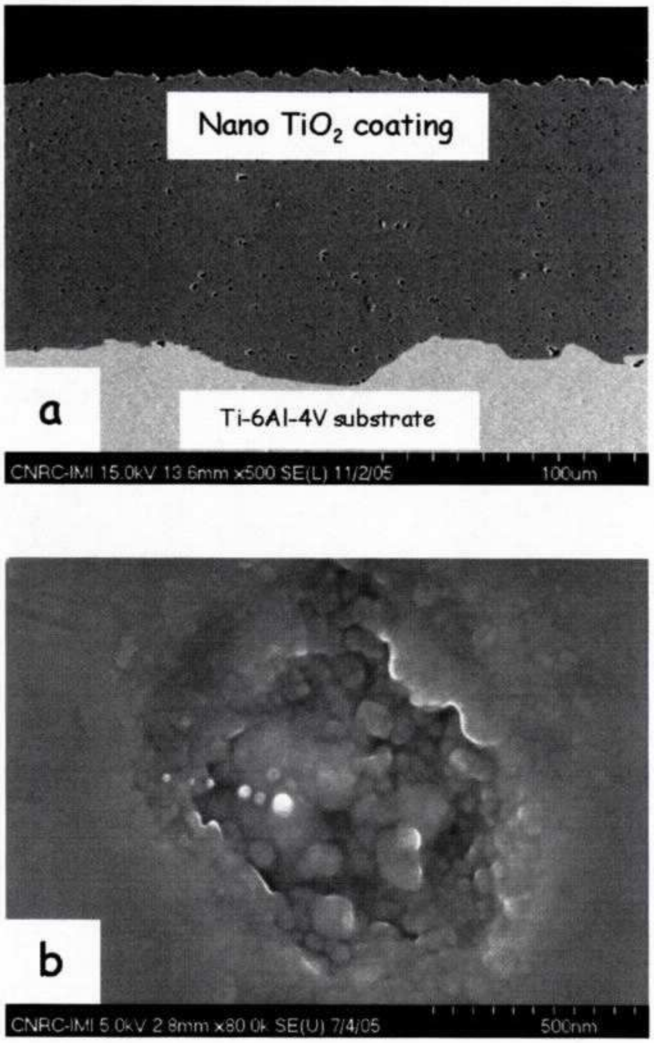

Figure 7 – (a) Low magnification view of the cross-section of the HVOF-sprayed nanostructured titania coating deposited on a Ti-6Al-4V substrate. (b) Coating of (a) observed at higher magnification; semi-molten nanostructured TiO_2 agglomerate (nanozone).

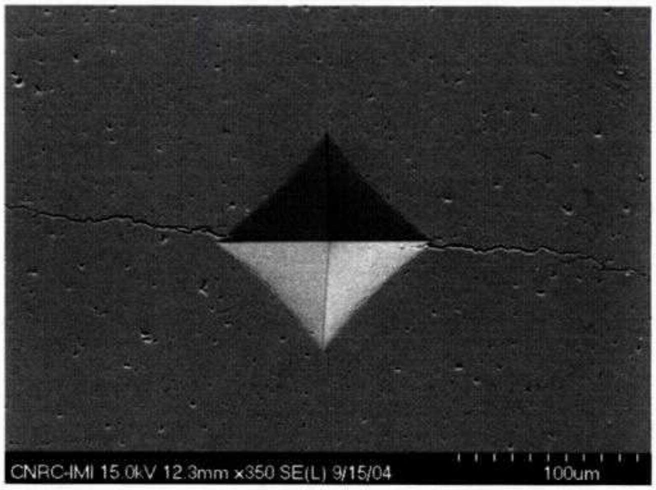

Figure 8 – Vickers indentation impression (5 kgf) and crack propagation in the cross-section of an HVOF-sprayed conventional TiO_2 coating (Reprinted from Materials Science and Engineering A, 395, R. S. Lima and B. R. Marple, Enhanced Ductility in Thermally Sprayed Titania Coating Synthesized Using a Nanostructured Feedstock, 269-280, 2005, with permission from Elsevier) [18].

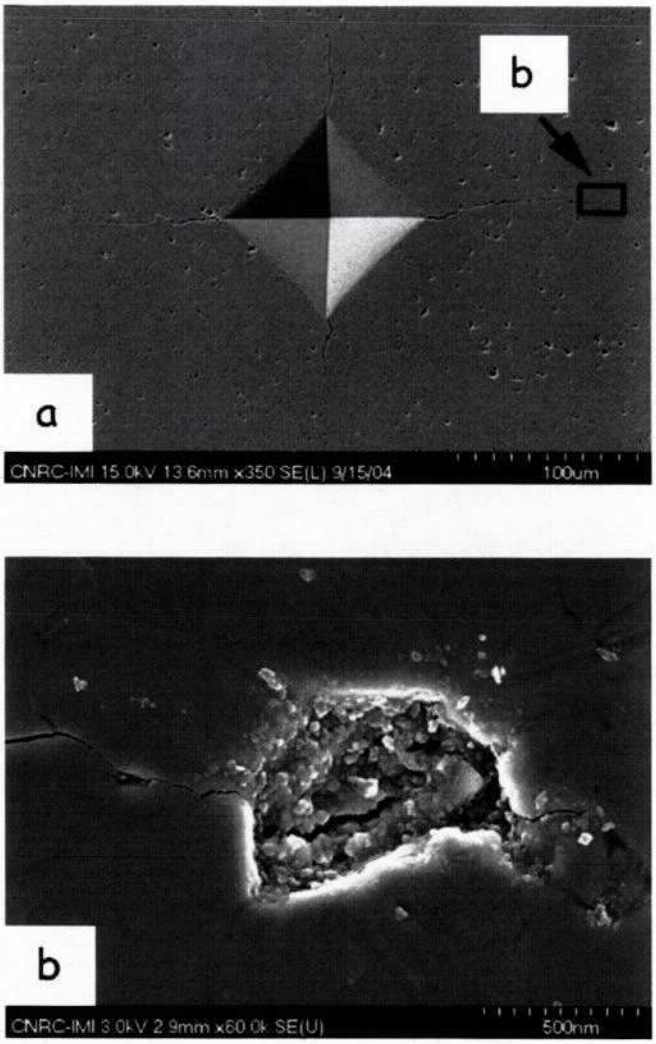

Figure 9 – (a) Vickers indentation impression (5 kgf) and crack propagation in the cross-section of an HVOF-sprayed nanostructured TiO_2 coating (Reprinted from Materials Science and Engineering A, 395, R. S. Lima and B. R. Marple, Enhanced Ductility in Thermally Sprayed Titania Coating Synthesized Using a Nanostructured Feedstock, 269-280, 2005, with permission from Elsevier) [18]. (b) Vickers indentation crack being arrested by passing through a nanozone in the coating (Reprinted from Journal of Thermal Spray Technology, R. S. Lima and B. R. Marple, Superior Performance of High-Velocity Oxyfuel-Sprayed Nanostructured TiO_2 in Comparison to Air Plasma-Sprayed Conventional Al_2O_3-$13TiO_2$, 14(3), 2005, 397-404, reprinted with permission of ASM International®) [20].

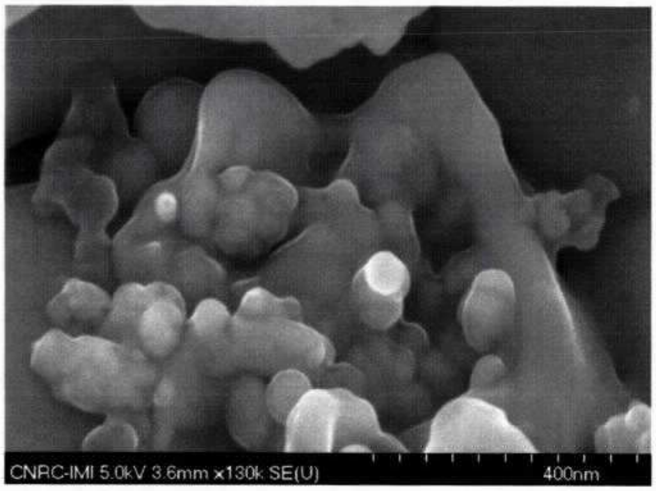

Figure 10 – A nanozone on the surface of the HVOF-sprayed nanostructured titania coating formed by a semi-molten nanostructured particle (Reprinted from R. S. Lima, B. R. Marple, H. Li, K. A. Khor, Biocompatible Nanostructured High Velocity Oxy-Fuel (HVOF) Sprayed Titania Coating, Thermal Spray 2006: Science, Innovation and Application, (Eds.) B. R. Marple, M. M. Hyland, Y.-C. Lau, R. S. Lima, and J. Voyer, ASM International, Materials Park, Ohio, USA, reprinted with permission of ASM International®) [22].

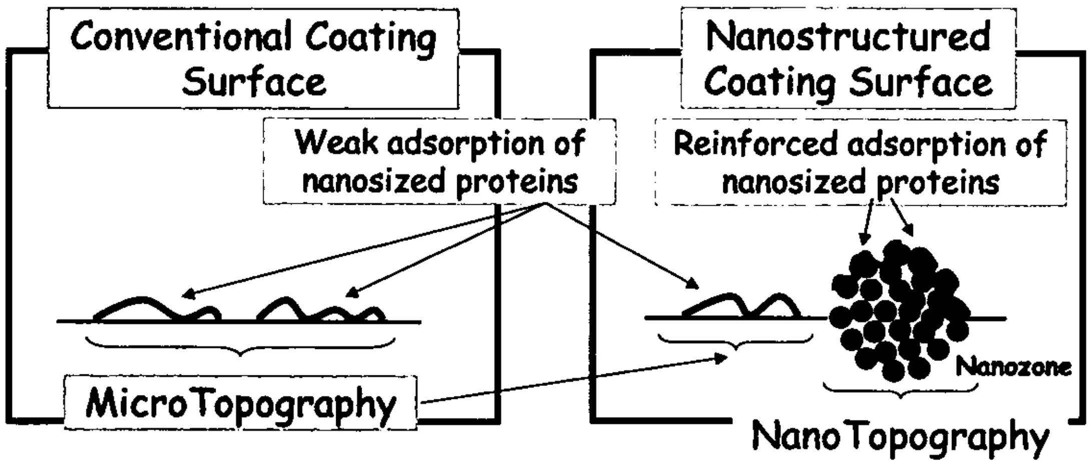

Figure 11 – Schematic of the surface of a conventional and a nanostructured thermal spray coating. The nanosized adhesion proteins (e.g., fibronectin) would tend to exhibit better interlocking with the nanozones located at the surface of the nanostructured coating.

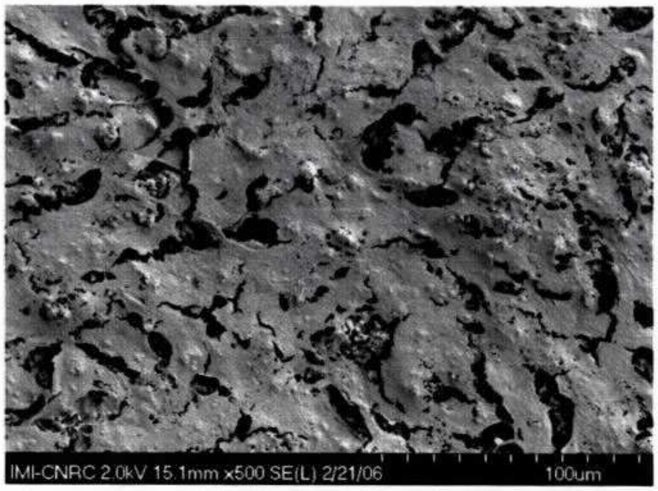

Figure 12 – Osteoblast cells (obtained from rat calvaria) cultured during 7 days on the surface of the HVOF-sprayed nanostructured titania coating (Ti-6Al-4V substrate). The osteoblast cells completely covered the coating surface.

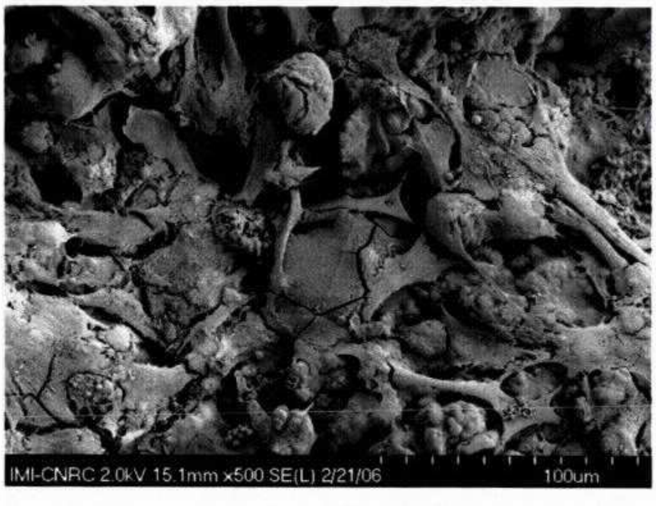

Figure 13 - Osteoblast cells (obtained from rat calvaria) cultured during 7 days on the surface of the APS HA coating (Ti-6Al-4V substrate). The osteoblast cells partially covered the coating surface.

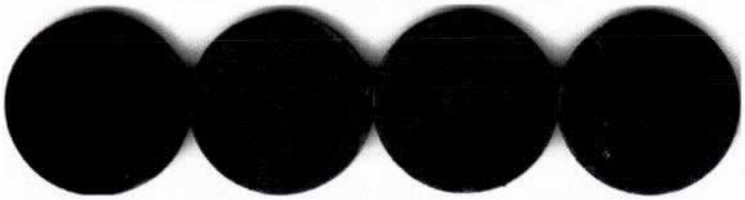

Figure 14 - Osteoblast cells (obtained from rat calvaria) stained for alkaline phosphatase activity (shown in red) after 15-day culture on the surface of the HVOF-sprayed nanostructured titania coatings (Reprinted from R. S. Lima, B. R. Marple, H. Li, K. A. Khor, Biocompatible Nanostructured High Velocity Oxy-Fuel (HVOF) Sprayed Titania Coating, Thermal Spray 2006: Science, Innovation and Application, (Eds.) B. R. Marple, M. M. Hyland, Y.-C. Lau, R. S. Lima, and J. Voyer, ASM International, Materials Park, Ohio, USA, reprinted with permission of ASM International®) [22].

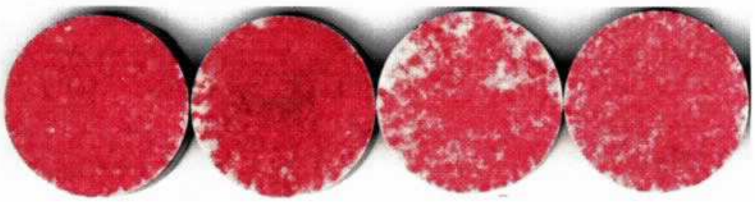

Figure 15 - Osteoblast cells (obtained from rat calvaria) stained for alkaline phosphatase activity (shown in red) after 15-day culture on the surface of the APS HA coatings (Reprinted from R. S. Lima, B. R. Marple, H. Li, K. A. Khor, Biocompatible Nanostructured High Velocity Oxy-Fuel (HVOF) Sprayed Titania Coating, Thermal Spray 2006: Science, Innovation and Application, (Eds.) B. R. Marple, M. M. Hyland, Y.-C. Lau, R. S. Lima, and J. Voyer, ASM International, Materials Park, Ohio, USA, reprinted with permission of ASM International®) [22].

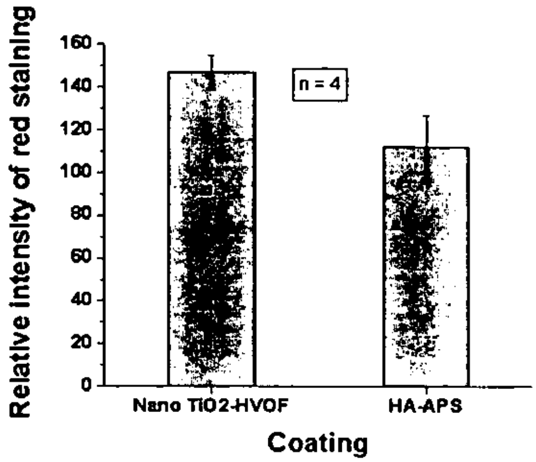

Figure 16 - Relative intensity of red staining for the osteoblast cells on the surface of the HVOF-sprayed nanostructured titania and APS HA coatings after a 15-day cell culture (Reprinted from R. S. Lima, B. R. Marple, H. Li, K. A. Khor, Biocompatible Nanostructured High Velocity Oxy-Fuel (HVOF) Sprayed Titania Coating, Thermal Spray 2006: Science, Innovation and Application, (Eds.) B. R. Marple, M. M. Hyland, Y.-C. Lau, R. S. Lima, and J. Voyer, ASM International, Materials Park, Ohio, USA, reprinted with permission of ASM International®) [22].