Multiscale Phenomena in Surfaces *Research Summary*

Characteristics of Hemocompatible TiO_2 Nano-films Produced by the Sol-gel and Anodic Oxidation Techniques

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Hemocompatible films can be obtained by different techniques which must produce a smooth surface and a desired combination of crystal structure including rutile and anatase structures. Two of the simplest techniques include sol-gel and anodic oxidation. The characteristics of the films associated with the process variables are presented. The most important characteristics of the films are thickness, structure, roughness, and mechanical properties such as adhesion and wear resistance.

INTRODUCTION

Significant advances in biomedical technology in recent decades have greatly improved the health and social integration of people of all ages. One of these technologies is in the field of implants with different functions in the body, such structural materials (e.g., bone implants) or critical functional devices (e.g., heart valves and pacemakers). This progress required advances in materials technology, and efforts are continuing in the search for better materials to improve performance. There is a requirement of biocompatibility which, in the case of devices in contact with blood, is hemocompatibility. This short review presents some advances in the production of hemocompatible titanium alloys coated with titanium dioxide.

COATINGS

Coatings of metals and alloys are widely used to incorporate or improve tribological, biological, corrosion, or aesthetic properties into a component. The choice of the substrate material and type of coating for implants is a complex issue and depends on many aspects, such as the place in the body where they are implanted and where they must have full biocompatibility, such as tissue integration, hemocompatibility, and tribological and mechanical properties adequate to the desired performance.[1]

In the case of tribological properties, wear resistance and a low friction coefficient of a coating increase the lifetime of a component.[2] The tribological properties necessary in the coating are associated with those needed in the specific device implanted on humans. The required properties are also related to the type of tissue with which the device is in contact, where the coating must integrate and also have the mechanical and tribological performance according to the specific requirements. For instance, in hip and dental implants the device is in contact with both hard (cortical bones) and soft tissue (trabecular bones and muscles). In other cases, like in heart valves, stents, hemodialysis equipment, and pacemakers the most important property is hemocompatibility, where the device must be biologically inert in the blood stream.[3]

How would you…

…describe the overall significance of this paper?

This paper presents a review of two of the most simple techniques to produce hemocompatible nano-films and their characterization, particularly thickness and crystal structure. The techniques are sol-gel dip coating and anodic oxidation and the film is titanium oxide.

…describe this work to a layperson?

The need of new and better hemocompatible materials for use in prosthetic human devices require the investigation of alternatives such as those presented in the paper. Titanium dioxide is a good candidate and the methods to produce these protective films are discussed. The methods are simple and efficient.

Tribological thin coatings can be produced by physical or chemical methods and the process must produce a coating which must satisfy certain conditions like the relation between hardness of the coating and the substrate, the thickness, the surface roughness, adhesion, and size and hardness of the debris produced by wear,[4] which in the case of orthopedic implants are most demanded.

In the case of implanted mechanical heart valves, hemocompatibility becomes the most relevant requirement in which the wear and fracture fatigue in the moving hinge are also of major concern because failure could be fatal.

TITANIUM AND TiO_2 COATING

Titanium and its alloys are among the most used material in bone implants as well as heart valve parts,[5,6] stents, hemodialysis equipment, and pacemakers.[3] The use of titanium alloys is expected to increase in the future due to their superior biocompatibility, corrosion resistance, and specific strength compared to other metallic alloys.[6] Pure Ti, Ti-6Al-4V, and vanadium- and aluminum-free titanium alloys containing non-toxic elements like Nb, Ta, and Zr have tensile strength between 500 and 1000 MPa, elongation between 10 and 20%, and module of elasticity between 55 and 85 MPa.[6]

However, titanium may be dissolved by physiological fluids releasing ions in vivo and may be accumulated in adjacent tissues or transported to distant organs by the blood stream.[7] This indicates that the oxide layer of TiO_2 formed naturally is not sufficiently protective under wear and therefore additional coating must be deposited in order to

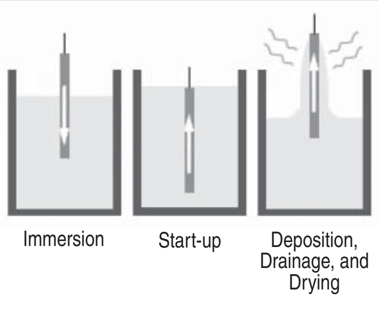

Figure 1. Steps of the sol-gel dip-coating technique.

improve the tribological properties and also improve hemocompatibility of the implant.

TiO_2 is the natural selection for coating a titanium prosthesis. The methods to produce films of TiO_2 reported in the literature include thermal oxidation, anodic oxidation, magnetron sputtering, cathodic arc deposition, plasma immersion ion implantation (PIII), ion beam-enhanced deposition (IBED), and the sol-gel process.[7,8]

The choice of the method depends on the type of implant and surface requirements according to the tissue and cells in contact and its lifetime expectancy which result in design parameters. There is no general theory for process selection and the performance of a given coating must be proven under conditions as close as possible to the final application.[2]

In particular a rough porous film of TiO_2 on titanium has been proven to have good osseointegration.[9] In some cases surface modification produced by sandblasting,[9,10] acid etching,[9,10] a combination of both,[9,10] deposition of calcium phosphate, or hydroxyapatite coatings by ion implantation can also improve biocompatibility.[10] The process route may include first, the treatment of the titanium alloy substrate surface and then, production of the coating by one of the most accessible methods such as thermal or anodic oxidation or the sol-gel technique. On the other hand, hemocompatibility requires smooth surface finishing; in such cases the substrate surface must be smooth since a thin film may reproduce the roughness of the substrate. In some cases, such as in dental applications, rough and smooth surfaces are required in different parts of the implant.[9]

HEMOCOMPATIBILITY

According to Buddy D. Ratner,[11] "There is no clear consensus as to which materials are 'blood compatible'," and "There are no standardized methods to asses blood compatibility." Nevertheless a hemocompatible material could be defined one with a surface that is unable to activate the platelet coagulation system or generate alteration or damage in the blood components.[3]

In this case the surface plays a crucial role, as properties must be maintained during the whole process until it reaches the surgery room and during service in the human body. The qualification of the hemocompatibility is performed by in-vitro and in vivo testing. In vitro investigations include clotting time measurements, platelet adhesion, and hemolysis analysis.[12] In vivo testing requires the implantation of the component in animals and then in humans with a rigorous protocol.

In general the main factors affecting hemocompatibility are surface roughness, superficial energy, corrosion resistance, and surface electric charge.[1,3] Roughness increases the surface contact area with blood and may favor blood coagulation[13] and very smooth surface roughness (3–4 nm) inhibits thrombogenicity.[14] Measurement of clotting time on rutile coating, grown by thermal oxidation, shows that the anti-clotting properties increase when the coating thickness increase from 40 nm to 350 nm.[15]

At present there is substantial effort to produce suitable TiO_2 coatings which have been demonstrated to have better blood compatibility than low-temperature isotropic pyrolitic carbon (LTIC), which is widely used in the production of mechanical heart valves,[5,16] and also diamond-like carbon (DLC) films.[17,18] The TiO_2 has shown to have better hemocompatibility properties due to its semiconductor properties.[18]

The films can be deposited by the techniques mentioned above. In the cases of IBED[11,16] and PIII[18,19] the techniques permit doping of the films with others elements which may modify beneficially the physical structure of the material and the physicochemical properties due to changes in the electrical double layer between the surface and the biosystem.[1]

In the case of TiO_2, the crystal struc-

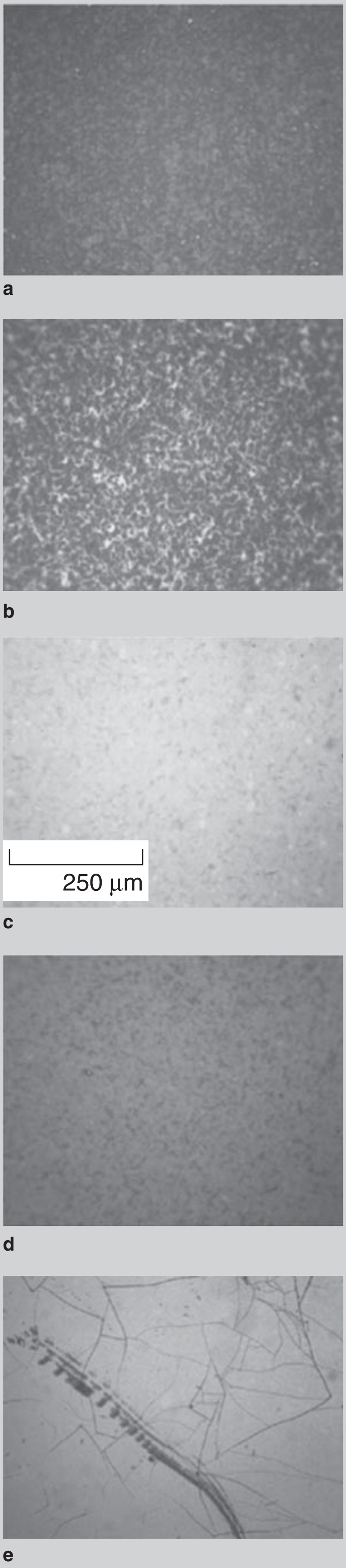

Figure 2. Colors of the coatings as the thickness increases, are (a) violet blue, (b) light blue, (c) yellow, (d) purple, (e) green.[21]

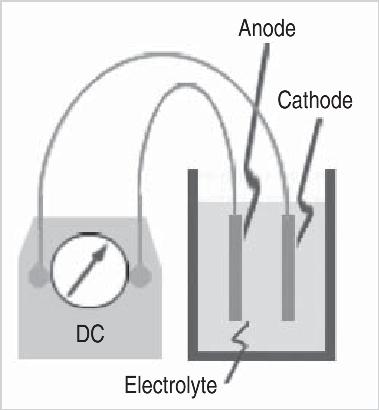

Figure 3. Schematic of the anodic oxidation set-up.

ture of the film is also very important. For instance, the dissolution of titanium metal ions from rutile is one order of magnitude lower than that from anatase.[15] So far, a mixed composition of each crystal structure, rutile and anatase, is preferable for blood compatibility.[18] Research is ongoing to produce nanofilms with these characteristics employing two accessible methods based on sol-gel and anodic oxidation techniques which are presented next.

SOL-GEL DIP-COATING AND ANODIC OXIDATION TECHNIQUES

The sol-gel dip-coating and anodic oxidation techniques are two of the most inexpensive and reliable techniques available today.

Sol-gel Dip-coating

The sol-gel dip-coating technique consists of three main steps as illustrated in Figure 1: immersion of a substrate to be coated in a sol containing particles of the coating material; start-up and withdrawal of the substrate at slow velocity to permit drainage of the sol; and drying of the film. The next step consists of the heat treatment for crystallization.[8,20] With this technique it is possible to control the film thickness by the withdrawal velocity, number of layers, sol concentration and sol aging time and crystal structure by heat treatment and thickness.[8,14,20]

Coatings between 25 and 205 nm were obtained and x-ray diffraction analysis determined that the crystal structure is a combination of anatase and rutile phases where the rutile phase increases with the heat treatment temperature.[8,14]

Table I. Color and Thickness of the Anodic Oxide Films Obtained at Different Voltages[30]

V	Color	t [nm]
10	Golden	27.21
20	Purple	48.00
30	Light blue	70.46
40	Light green	92.25
50	Yellow	112.64

The thicknesses of the coatings are associated qualitatively with the color due to light interference, which can be observed by the naked eye (Figure 2).[8]

Anodic Oxidation

The anodic oxidation technique schematically shown in Figure 3 is simple to mount and has been extensively applied and studied.[8, 22–29] The anode is made of the metal or alloy to be coated and the cathode is made of a noble metal like platinum, both immersed in an electrolyte. Oxidation occurs by reactions such as those proposed for titanium and the oxide could be formed by either constant voltage or current. The following reactions have been proposed in the literature:[28]

- Ti / TiO_2 interface: $Ti \Leftrightarrow Ti^{+2} + 2e^-$
- TiO_2 / electrolyte interface: $2H_2O \Leftrightarrow 2O^{2-} + 4H^+$ (oxygen ions react with titanium to form oxide); $2H_2O \Leftrightarrow O_2$ (gas) $+ 4H^+ + 4e^-$ (oxygen gas evolves)
- In both interfaces: $Ti^{+2} + 2O^{2-} \Leftrightarrow TiO_2 + 2e^-$

The process can be controlled by the following parameters: concentration of the electrolyte, current density, anodic voltage, temperature, agitation speed, time and surface area ratios of cathode to anode. In a 1M H_2SO_4 solution used as electrolyte and using different constant voltages (V) it is possible to produce coatings of different thickness (t) as with the sol-gel technique. The relation among voltage, color, and thickness is shown in Table I[30] and Figure 4.[31]

It has been found that thickness and crystal structure are related.[24] Although that relationship is unclear, the possible sequence is amorphous/unknown, anatase, anatase and rutile and rutile phases as thickness increases. Anatase and rutile could alternatively be obtained by heat treatment.[29]

Another important result of this tech-

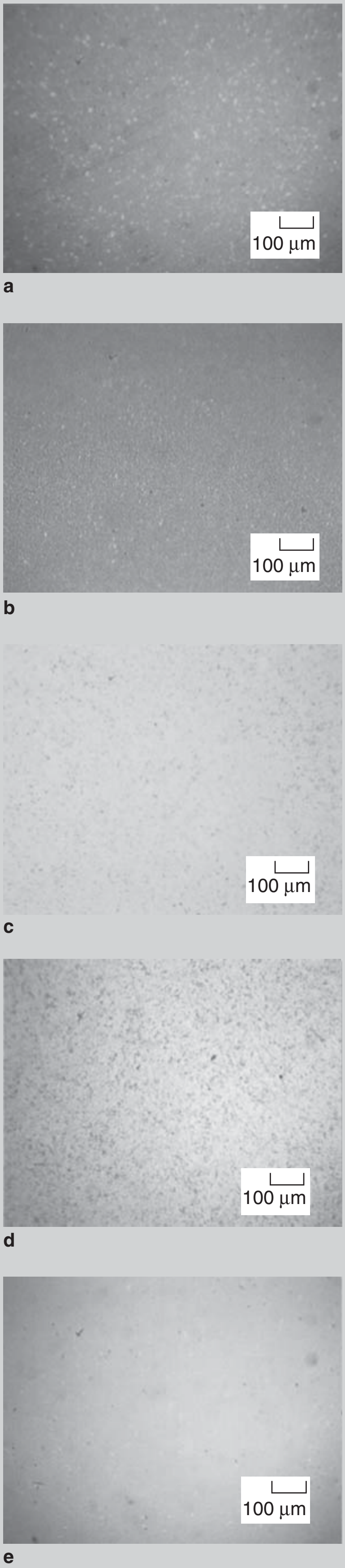

Figure 4. Appearance at each applied voltage: (a) 10 V, (b) 20 V, (c) 30 V, (d) 40 V, (e) 50 V.[31]

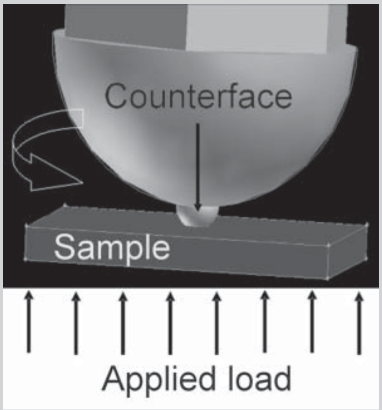

Figure 5. The system of ball-on-flat contact used for the wear test.[21]

nique is that at higher voltages the film increases porosity and therefore be suitable for osseointegration.[27,31] It has also been found that the thickness depends on the texture of the substrate and could vary from grain to grain.[25,32]

ADHESION AND WEAR PROPERTIES

Implants in a blood stream such as a heart valve or a stent not only must satisfy hemocompatibility criteria but also must have certain mechanical properties according to the required performance. In the case of heart valves the TiO_2 coating must have a good adhesion and moving parts must wear at a rate comparable with the expected valve lifetime.

Assays were performed on TiO_2 coatings obtained by both techniques using a scratch test to measure adhesion[33] and a ball-on-flat test for wear. In the case of adhesion an increasing load applied at a 2N/mm rate and up to 10N did not produce failure of anodic oxide films in the whole range of thicknesses listed in Table I. In the case of sol-gel dip-coatings the coating adhesion increases with the number of deposited layers and temperature of the heat treatment.[34]

In the wear tests, a rotating ball-on-flat device was used in order to approximate the movement of a pivot in a prosthetic heart valve, as shown in Figure 5. Lubricated tests were performed, employing a 6.35 mm in diameter glass ball as counterface. A constant 7 rpm and 1 N in load[8,35] were chosen to perform the test; this value exceeds more than 50 times the stress calculated on the valve pivot. Optical microscopy was used to characterize the film before and after the wear test.

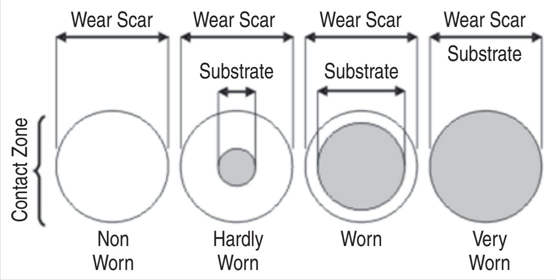

Figure 6. Wear scar categories utilized in the tests.[34]

As a measure of wear, a qualitative scale has been proposed and utilized as shown in Figure 6,[35] where the shaded area is the area of the coating which has been removed due to wear. It is found that tri-layer films are more resistant when each layer has a high temperature heat treatment that assures the crystallization of them.

CONCLUSIONS

Coating continues to be a very active area of research with a substantial amount of effort directed to produce better implants, in particular those which require hemocompatibility properties. Titanium alloys coated with titanium oxide nano-films is one of the suitable combinations for implants where hemocompatibility properties are required as well as good mechanical and tribological behavior.

Anodic oxidation and sol-gel techniques, which are two of the most simple to implement and control, can be used to produce nano-films with mechanical and tribological properties with overall qualities to build implants. Testing of the coatings requires specific systems which reproduce as much as possible the in-vivo conditions.

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