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Surface Modification of Titanium and Its Alloys for Biomedical Application

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Abstract. Titanium and its alloys have excellent properties and are promising biomaterial in medical engineering field. A bioactive surface on a Ti substrate is a prerequisite for great performance and long service life of implants. Based on the mechanism for inducing cell/tissue responses, three kinds of methods, namely morphological, physicochemical and biochemical methods, are reviewed in this paper. Hybrid methods that integrate individual methods or have additional functions are also discussed.

Introduction

Titanium occurs in abundance in the Earth's crust and owns superiority over other biomaterials, such as specific strength, thermal conductivity and biocompatibility [1-3]. Past decades have witnessed a great development of titanium and its alloys in biomedical area [4, 5]. To escape from the bone cement employed for fixation of implants, bioactive material has replaced the biologically inactive material in the bioengineering field. Thus, an idea implant should exhibit suitable mechanical properties while its surface should support cell growth and adhesion. A surface-modified Ti base implant is an engaging access to satisfying requirements on implants. Based on the inducing mechanism of interactions between implants and their surroundings in body, there are mainly three kinds of surface modification methods named as morphological, physicochemical and biochemical methods. In this paper these three classes of surface modification methods are discussed and some hybrid surface processing methods are also introduced.

Morphological Methods

It is observed that special surface morphology is preferable to cell adhesion and beneficial for cell proliferation. Efforts have been devoted into altering the surface morphology [6], such as surface roughness, surface free energy, wettability and hydrophility, and exploring the relationship between surface morphology and implant-tissue interactions.

Blasting was employed to adjust the surface roughness of Ti substrate [7]. Experimental results indicate that a rough surface is superior to a fine surface regarding cell adhesion and differentiation. Polishing and acid etching were also utilized to obtain different surface roughness on Ti samples [8]. In vitro experiments exhibit a low cell proliferation lever and a high differentiation degree on a coarse surface. Further, a comprehensive description of surface morphology, such as surface roughness, fractal dimension and wettability, was introduced. Then, polishing, blasting and etching were applied in different combinations to generate different surface morphologies [9]. In vitro studies disclose that fluctuating morphology with large fractal dimension and negative skewness is beneficial to cell adhesion.

Laser has also been introduced into bioengineering field [2, 10]. With advanced CAD system, a porous surface with proper pore arrangement can be produced to improve cell adhesion and boost mechanical lock of implants.

Glow discharge plasma uses magnetron discharge or radio frequency discharge to transfer momentum via ion bombardment [11, 12]. The surface of an implant can be cleaned and the surface energy can be increased through this method, given that surface energy affects cell responses.

Special morphology generated by proper methods releases the implants from bone cement. However, the fundamental mechanism between morphology and implant-surroundings interactions is still unclear. To further improve the performance of implants, some physical and chemical reactions on the implant surface are introduced.

Physicochemical Methods

In order to shorten healing time and improve cell-implant bonding strength, physical and chemical reactions on implant-surroundings interfaces that can induce cell/tissue activity have been introduced. The methods that generate a modified surface where cell/tissue activity is stimulated via moderate physical and chemical reactions are classified as physicochemical methods.

Alkali treatment and subsequent heat treatment, which alters the surface chemical components and generates a porous surface, found by Kim et al. [13], can improve the formation of a bone-like apatite layer and consequently the performances of the Ti implant. The two-step acid and alkali process have similar surface modification effect while avoids the heat treatment. Furthermore, pre-calcification can be used to accelerate deposition speed of Ca and P [13].

Sol-gel coating methods offer a good control of homogeneous chemical components and microstructure at low densification temperature. Common materials for coating include TiO_2, calcium phosphate, titania-hydroxyapatite composite and silica. The coating layer can accelerate the accumulation of calcium phosphate which will transfer to apatite [14]. Authors in literature [15] and [16] generated porous layers on Ti substrate with good bonding strength successfully through sol-gel methods. Figure 1 illustrates the generated coating layers.

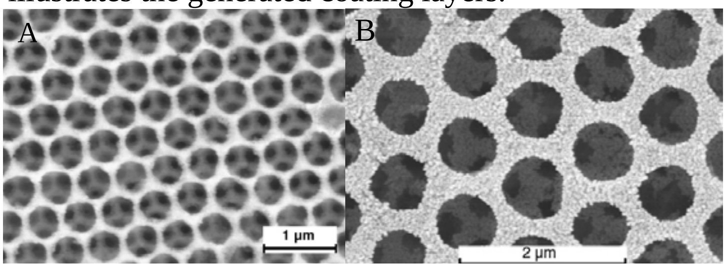

Fig. 1 Films generated by sol-gel methods in (A) [15] and (B) [16]

Oxidation that coats a bioactive TiO_2 layer on the Ti substrate is a promising approach to medical applications. With a mesoporous bioactive TiO_2 layer, the coating improves the accumulation of Ca and P, which subsequently transfer to hydroxyapatite [17, 18]. If increasing processing voltage to the breakdown limitation, reactions turn violent and accordingly the process is named as micro arc oxidation (MAO). Ca and P elements can be added in an elemental ratio of 1.67 which is equal to that of natural bones for boosting hydroxyapatite transformation. The structure and chemical components distribution of the coating can be controlled by process parameters and the general quality of coating is good.

Thermal spraying method sprays the molten material and generates a film on the target [12]. Depending on the heating source, there are flame spraying and plasma spraying, where the achievable temperature of the latter is much higher than that of the former. Coatings on Ti substrate generally have a porous structure and the coating process is highly efficient. However, when spraying hydroxyapatite, the touch of molten liquids on a cool substrate leads to sharp temperature drop and acts as quenching process. Consequently, it results in formation of amorphous calcium phosphate and reduction of crystallinity. Although thermal spraying has been applied in coating teeth root, knee and shoulder implants, the thermal mismatch between the coating and the substrate, which leads to poor bonding strength, limits its further application [19, 20].

Vapor deposition is commonly employed to generate films with different materials on various substrates [12]. The vapor deposition method is generally classified as chemical and physical vapor deposition based on whether chemical reactions happen or not during the process. Chemical vapor deposition owns better step coverage of film, therefore, is more suitable for coating complex substrates than physical vapor deposition. While, physical vapor deposition produces a coating layer with strong adhesion due to a low processing temperature, which reduces residual stress caused by thermal expansion mismatch between the coating layer and the Ti substrate.

Ion implantation bombards the substrate with energetic ions to adjust the surface properties [12]. Conventional beam-like ion implantation is a line-of-sight process, therefore, is difficult to handle complicated geometries. While the plasma immersion ion implantation forces the ion trajectory perpendicular to the surface of a substrate, which enables handling complex samples. A layer with graded composition and an obscure interface between the substrate and the coating layer can be produced by ion implantation. The bone components Ca and P were implanted into Ti substrate [21]. For different implantation subsequences, the Ca and P distribution and their peak value are different. However, significant thermal expansion mismatch introduced weak bonding strength is a main shortage.

Physicochemical surface modification methods utilize physical and chemical reactions to improve cell responses, and they generally have porous surface which brings a morphological effect benefiting implant’s performance. However, shortages such as the poor bonding strength should be overcome. Moreover, cost on equipment such as the heating source and the vacuum device limits the application of these methods.

Biochemical Methods

Biochemical methods utilize biomolecules to affect cell/tissue responses, which are a more direct way to impact implant-surroundings interactions than the morphological and physicochemical methods. As illustrated in literatures [22, 23], a morphologically, physically or chemically modified surface will first attract proper proteins, and then the proteins interact with relating bone cells [24]. Further, even using hydroxyapatite, it is translated bone-like hydroxyapatite that influences implant-surroundings interactions. While the induction time of translation from synthesized hydroxyapatites to bone-like hydroxyapatites is long. By contrast, biochemically modified surfaces drawing on biomolecules such as surface immobilized peptides, proteins and growth factors induce specific cell/tissue responses directly presenting significant potential.

Bioactive peptides include Arginine-Glycine-Aspartic (RGD) and Lysine-Arginine-Serine-Arginine (KRSR), etc. The RGD peptides, known as the shortest recognizable sequence of cells, can attract extracellular proteins, such as fibronectin, vitronectin, type I collagen, osteopontin and bone sialoprotein. While growth factors have influences on mitogenicity, osteoinduction and bone cell activity.

Biochemical surface modification methods relate to adsorption, retention and release of biomolecules. Dipping the prosthesis into a solution with biomolecules is a simple way of absorption of biomolecules on the surface. Covalent attachment, such as silane chemistry, self-assembled monolayers and plasma treatment, bonds biomolecules to the Ti surface via covalent bonds. Photochemistry is also utilized for grafting and controllable release of biomolecules on the Ti substrate. A proper coating layer acted as a connection between biomolecules and Ti substrate is explored to realize controllable release of biomolecules. Ethylene vinyl acetate (EVAc), poly (lactide-co-glycolide) acid and collagen are potential coating materials whereas calcium phosphate coating with micro porous structure is also a promising material for this intermediate coating.

Biologically modified surface draws on biological knowledge to guide the cell/tissue responses and owns promising potential. Exploring proper biomolecules and investigating into suitable methods for controllable adsorption, retention and release of these biomolecules still need further efforts.

Hybrid Methods

Attentions have been paid to integration of surface modification methods to overcome the each method's shortages and win a better performance than individual methods.

Plasma sprayed synthesized hydroxyapatite coating presents chemical and structural similarity to natural hydroxyapatite while has poor bonding strength and unwanted components produced at the high processing temperature. Additionally, micro arc oxidation can produce a layer with graded distribution of calcium and phosphate while the peak amount of these elements is limited. Therefore, two methods are integrated to generate a coating layer with abundant Ca and P [25]. A hydroxyapatite coating was first coated on the Ti substrate by an electron beam evaporation method, and then, the sample was treated by micro arc oxidation. The experimental results show that cell proliferation on the hybrid coating is similar to that on the micro arc oxidized Ti. Further, the alkaline phosphatase (APL) test results show that cell activity on the new coating is significantly higher than that on solely micro arc oxidized Ti and commercially pure Ti. Figure 2(A) shows the cross sectional view of the hybrid coating and Figure 2(B) shows the APL activity on the hybrid coating and other two comparing surfaces.

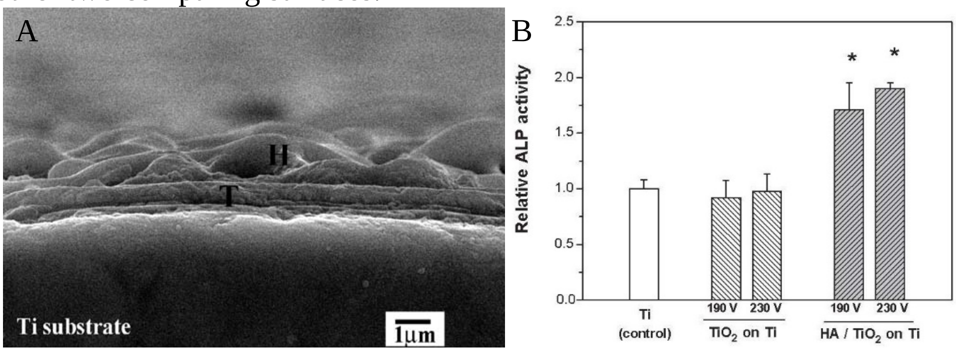

Fig. 2 (A) SEM cross sectional view of the hybrid coating; (B) APL activity on different surfaces

Commonly used hydroxyapatite not only promotes the bone growth but also attracts germs colonization [26]. Moreover, there is little blood and lymphatic circulation around the bones, which causes difficulty in transferring drugs to the implants area. Therefore, a coating that acts as a drug hauler has been investigated [27]. A sol-gel derived silica xerogel for controllable release of antibiotic pharmacy (tetracycline hydrochloride, TCH) was coated on an oxidized Ti surface. Micro arc oxidation and anode oxidation were employed respectively to generate oxidized porous surfaces with different pore sizes as the container of silica xerogel. Drug releasing period can be last for 7 days while the morphology of silica xerogel did not change. Figures 3 exhibit (a) the anode oxidized Ti and (b) the TiO_2 coating filled with xerogel/TCH.

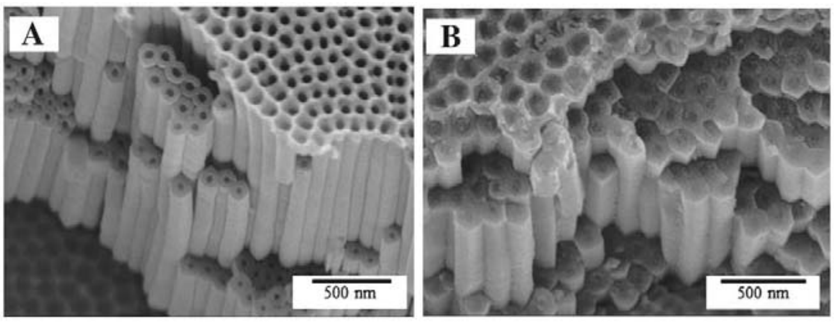

Fig. 3 SEM images of the anode oxidized Ti before (A) and after (B) silica xerogel/TCH infiltration

A mesoporous titanium dioxide coating produced by an evaporation induced self-assembly method was utilized to deliver cephalothin [16]. In vitro experiments show that cell viability on the mesoporous oxidized surface is higher indicating a better biocompatibility than pure Ti and solely oxidized Ti.

Hybrid methods have two meanings. The first is integrating individual methods that overcome individual's shortages and gain better performance than each own method. The second is adding additional functions to the implant, such as resistant of infection and inflammation. Hybrid methods present a bright outlook on surface modification with more careful consideration for better performance of the implant than before.

Summary

Surface modification improves the performance of Ti implants. Morphological methods boost relating cells' adhesion and growth by the surface morphology, while physicochemical methods impact cells' activity via moderate physical and chemical reactions on the surface with special morphology. By contrast, biochemical methods employ biomolecules to guide the cell/tissue responses directly. Further, hybrid methods integrate individual methods and add additional functions to the implant owning bright prospect.

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