https://doi.org/10.1186/s10033-024-01064-y

Chinese Journal of Mechanical Engineering

REVIEW **Open Access**

Review on the Fabrication of Surface Functional Structures for Enhancing Bioactivity of Titanium and Titanium Alloy Implants

Heng Tang[1], Jiaxiang Xu[1], Bin Guo[1], Yansong Xie[1], Yalong Sun[2], Yanjun Lu[1*] and Yong Tang[1]

Abstract
Titanium and its alloys have been widely applied in many biomedical fields because of its excellent mechanical properties, corrosion resistance and good biocompatibility. However, problems such as rejection, shedding and infection will occur after titanium alloy implantation due to the low biological activity of titanium alloy surface. The structures with specific functions, which can enhance osseointegration and antibacterial properties, are fabricated on the surface of titanium implants to improve the biological activity between the titanium implants and human tissues. This paper presents a comprehensive review of recent developments and applications of surface functional structure in titanium and titanium alloy implants. The applications of surface functional structure on different titanium and titanium alloy implants are introduced, and their manufacturing technologies are summarized and compared. Furthermore, the fabrication of various surface functional structures used for titanium and titanium alloy implants is reviewed and analyzed in detail. Finally, the challenges affecting the development of surface functional structures applied in titanium and titanium alloy implants are outlined, and recommendations for future research are presented.

Keywords Surface functional structure, Titanium implant, Manufacturing technology, Bioactivity

1 Introduction

With the acceleration of the aging process of the population, as well as the continuous increase in bone cancer and traffic accidents, the repair and replacement of hard tissues such as bones and teeth are becoming increasingly important. As a result, demand for high-quality hard tissue replacement materials has also increased sharply. According to statistics, the global market size of biomedical materials and their products reached 191 billion US dollars in 2020, and its scale is expected to exceed 557.1 billion US dollars by 2026 [1], as shown in Figure 1. Figure 2 summarizes the global proportion of biomedical material products in 2020. As is evident from Figure 2, the orthopedic and cardiovascular medical fields have the largest demand, accounting for 37.5% and 36.1% of the global medical biomaterials market, respectively. As biomedical implant materials, the elastic modulus, fatigue strength, and biocompatibility are critical for tissue replacements and restorations. The strength of implant materials decides their loadbearing capability, while the biocompatibility determines the success of implantation surgery. Metal, ceramic and polymer materials are currently the three most commonly used materials in the field of biomedical implants. Among those, titanium and its alloys possess excellent mechanical properties, good corrosion resistance and biocompatibility, which are widely used in biomedical fields such as artificial joints, tooth root implants, and vascular stents [2].

The early and long-term stability of titanium implants after implantation is a key factor in determining their

*Correspondence:
Yanjun Lu
luyanjun@szu.edu.cn
[1] Guangdong Provincial Key Laboratory of Micro/Nano Optomechatronics Engineering, College of Mechatronics and Control Engineering, Shenzhen University, Shenzhen 518000, China
[2] School of Mechanical and Power Engineering, Zhengzhou University, Zhengzhou 450001, China

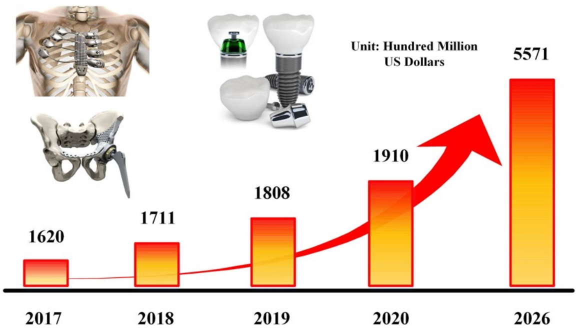

Figure 1 Trend chart of global sales scale of the biomedical materials and products industry

service life. The early stability of titanium and titanium alloy implants depends mainly on the mechanical forces formed on the surface and surrounding bone tissue. Roughening the surface of the implant can increase its contact area with the bone tissue, and a mechanical lock is formed between the implant and bone tissue, improving the early stability of the implant. The long-term stability of titanium and titanium alloy implants depends on the abilities of osteointegration, including mainly osteoconduction and osteoinduction [3–6]. However, this cannot actively induce osteogenesis because the surface of titanium and titanium alloy implants currently used in clinical practice is mostly biologically inert.

The functional surface consists of structures with various morphologies, scales and specific functions fabricated on the machined surfaces. It can improve the early and long-term stabilities of titanium and titanium alloy implants and effectively enhance their antibacterial properties, which has always been an active research topic in the biomedical field [7–9]. Studies have shown that the physical and chemical properties of titanium and titanium alloy implant surfaces can be significantly improved by fabrication of microstructures with different shapes and sizes, such as grooves and pits, on the surface of the implants. These microstructures can induce osteoblast migration and differentiation, and enhance the surface wettability of implants, thereby improving their biocompatibility and ensuring the implants firmly combine with the bone tissue. It is an effective method for solving the problems of poor osseointegration and weak antibacterial properties on the surface of implants [10–12]. The functional structure on the surface of titanium and titanium alloy implants is growing increasingly more complex for its wider use and higher performance demands.

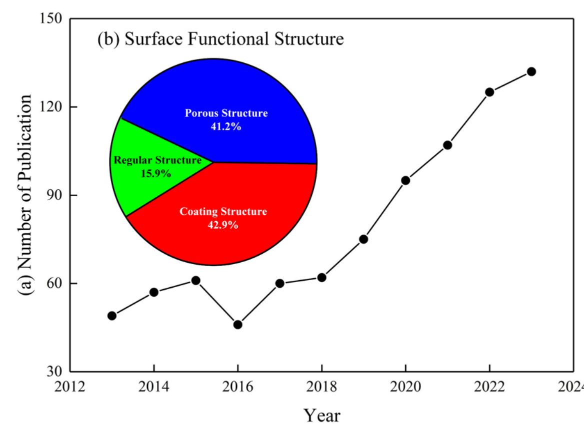

Figure 3 Worldwide research effort on the surface functional structure of titanium and titanium alloy implants in the past 10 years: (**a**) Number of publications per year, (**b**) The proportion of different types of surface functional structures

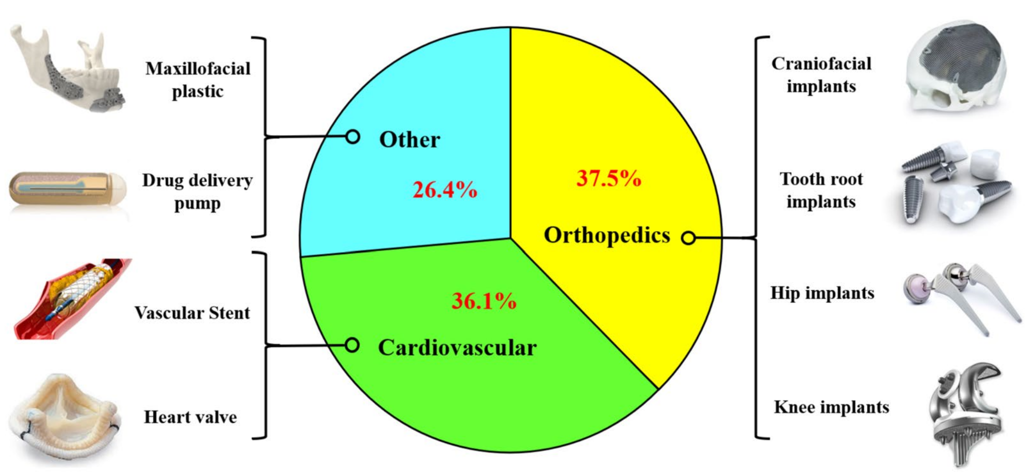

Figure 2 Global proportion of biomedical material products

Figure 3 summarizes the worldwide research on the surface functional structure of titanium and titanium alloy implants in the past 10 years. It can be seen from Figure 3 that the number of published papers in this research field shows an overall upward trend, and these researches mainly focuses on coating structure and porous structure (Figure 3(b)). In addition, the regular structure also attracted certain attention in recent years due to its good stability and simple preparation process.

The manufacturing techniques and methods used in fabricating surface functional structures have been the key factors that restrict the development of titanium and titanium alloy implants. However, to date, there has been no review of the fabrication and development of surface functional structures on titanium and titanium alloy implants. The objective of this literature review is to outline the worldwide research efforts on surface functional structures applied in titanium and titanium alloy implants and provide the reader with a better understanding of the current development status of surface functional structures as well as guide its future design and fabrication. In the first part of this review, the applications of surface functional structures on different titanium and titanium alloy implants are introduced. The second part summarizes the current manufacturing technologies of surface functional structures. The fabrication of various surface functional structures used for titanium and titanium alloy implants are reviewed and analyzed in the third part. Finally, the challenges affecting the development of surface functional structures for titanium and titanium alloy implants are outlined, and recommendations for future research are presented.

2 Application of Surface Functional Structure on Different Titanium Alloy Implants

The functional surface structure serves to strengthen light, enhance heat transfer, reduce resistance and wear-resistance due to its special geometric characteristics. It has been widely used in biomedicine, optical displays, 3C electronics (computer, communication, and consumer electronics) and other important fields [13, 14]. In recent years, the application of surface functional structures in the biomedical field has developed rapidly with the increasing demand for medical implants. The functional surface structures are vital for the development of implants with good biocompatibility. At present, the surface functional structure is applied widely in medical implants such as artificial joints, tooth root implants, vascular stents and heart valves [15–17].

2.1 Artificial Joint Implants

Hip and knee implants are the most widely used artificial joint implants in clinical practice. Irregular porous structures are often machined on the femoral surface of hip implants and the tibial joint pad surface of knee implants, as shown in Figure 4. This kind of structure can increase the contact area of the implant with human tissue, improving the binding strength of the implants, and providing a place for information exchange among cells [18]. In addition, structures such as micro-pits and micro-grooves, fabricated on the femoral head surface of hip implants, can store lubricants and collect wear scraps, significantly reducing the friction coefficient of the femoral head, as well as the wear between the femoral head and the acetabular shell [19–21].

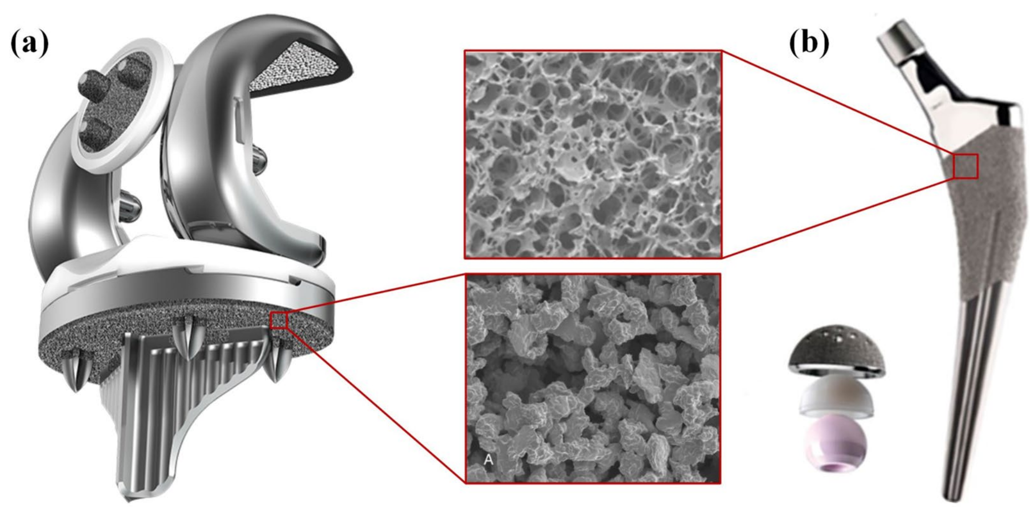

Figure 4 Surface of artificial joint implants: (**a**) Knee implants and (**b**) Hip implants

2.2 Tooth Root Implants

In the oral cavity, a root implant not only needs to resist the erosion caused by saliva, but also to bear the huge bite force. Under the environment of high loads, strong corrosion and multi-microorganisms, the binding force and antibacterial properties between the root implant and bone tissue have put forward higher requirements. Compared with tooth root implants with smooth surfaces, root implants with microstructures (grooves, pits, etc.) and silver coatings show good early osteogenesis performance and high bone tissue binding strength, which can significantly inhibit the growth of Staphylococcus aureus [22, 23]. Figure 5 shows the application of functional surface structure on the surface of tooth root implants.

2.3 Vascular Stents

With the growth of age and excessive intake of high fat, high cholesterol and other foods, people are prone to atherosclerosis and accumulation of arterial fat, which eventually lead to arterial blockage, insufficient blood supply to the heart and life-threatening. A vascular stent is a tiny metal mesh tube that is mainly used to treat clogged arteries and can be permanently inserted into the arteries. However, the surface of the stent may not adequately fuse with the vascular wall during implantation, increasing the risk of thrombosis and renarrowing of the blood vessels. Researchers have fabricated the structures such as micropores and micropits on the surface of vascular stents to increase the contact area between the stent and cells in the vascular wall, as depicted in Figure 6. This structure provides a place for the adhesion of cells to the vascular wall and the carrying of anticoagulant drugs, significantly improving the anti-hemagglutination, anti-proliferation, anti-inflammatory and biocompatibility of vascular stents [24–26].

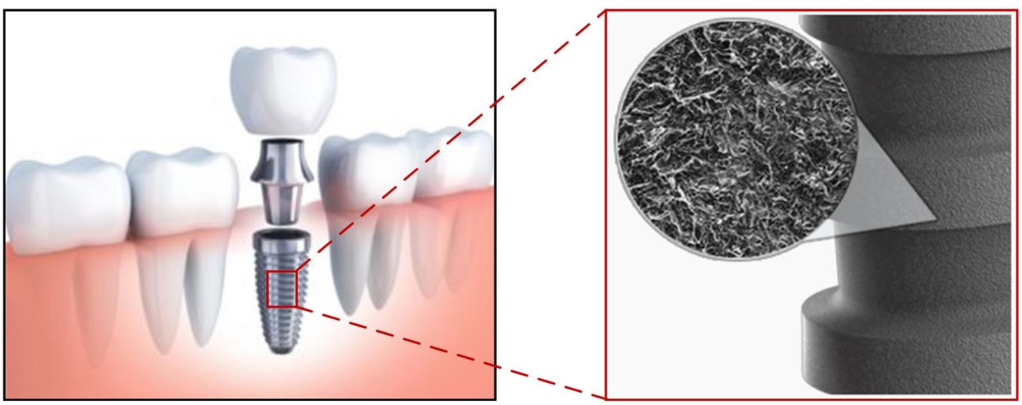

Figure 5 Tooth root implant and its surface microstructure

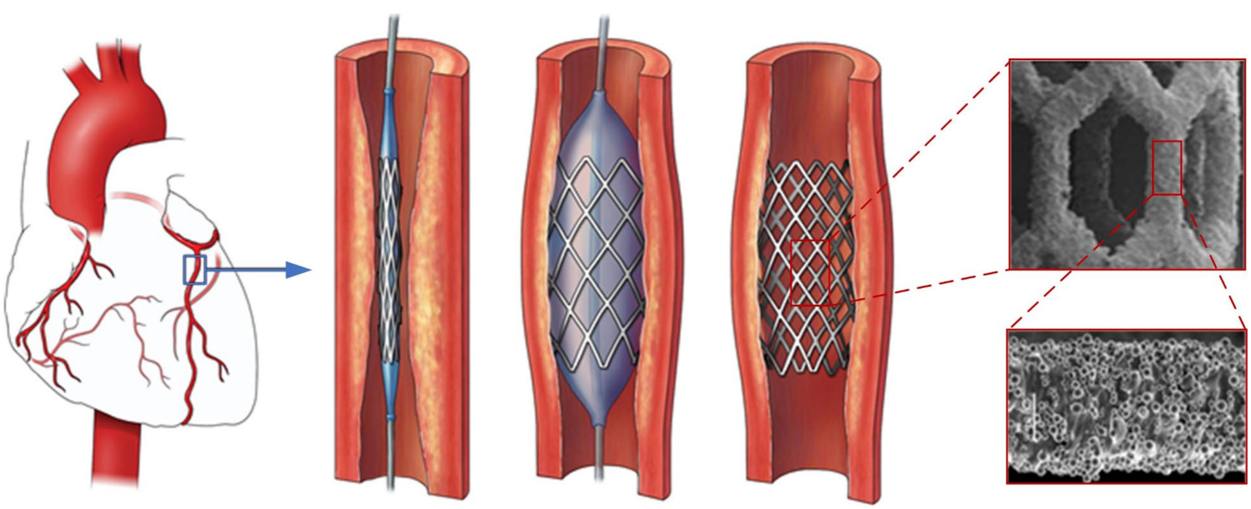

Figure 6 The vascular stent and its surface microstructure

2.4 Artificial Heart Valve

Heart valves are the key to ensuring normal blood circulation in the heart. At present, there are two types of artificial heart valve prostheses, including mechanical and biological prosthetic valves. Mechanical valves are widely used in artificial heart valves due to their excellent mechanical properties and long service life. Nonetheless, there is a higher risk of thrombosis and embolism on the surface. The risk of thrombosis and embolism can be effectively avoided by machining microstructures of specific shapes and sizes on the surface of the mechanical valves. Figure 7 shows a superhydrophobic structure fabricated on the surface of a mechanical valve. This structure can reduce the adhesion of blood to the surface of the mechanical valves, thereby reducing the risk of thrombosis and embolism [10, 27, 28].

3 Manufacturing Technologies of Surface Functional Structure Applied in Titanium Alloy Implants

At present, the manufacturing technologies used in fabricating surface functional structures for titanium and titanium alloy implants can be divided into traditional machining methods, non-traditional machining methods and other new machining methods. The traditional machining methods mainly include turning, milling and grinding, etc. The non-traditional machining methods mainly include chemical processing, electrochemical processing and laser processing, etc. Other new processing methods are primarily plasma spraying, magnetron sputtering and metal 3D printing, etc.

3.1 Traditional Machining Methods

Traditional machining methods, including turning, milling and grinding, have been widely used in surface functional structure machining of titanium and titanium alloy implants due to their high efficiency and low cost. Figure 8 shows the microstructure of titanium and titanium alloy implant surfaces fabricated by turning, milling and grinding, respectively. Among these, the turning processing is the first machining method used for fabricating the microgroove structure on the surface of titanium and titanium alloy implants. The milling processing, which has the advantages of high machining accuracy and ability to fabricate complex curved surfaces, is the most widely used technology in the manufacture of microstructures on the surface of titanium and titanium alloy implants [29–31].

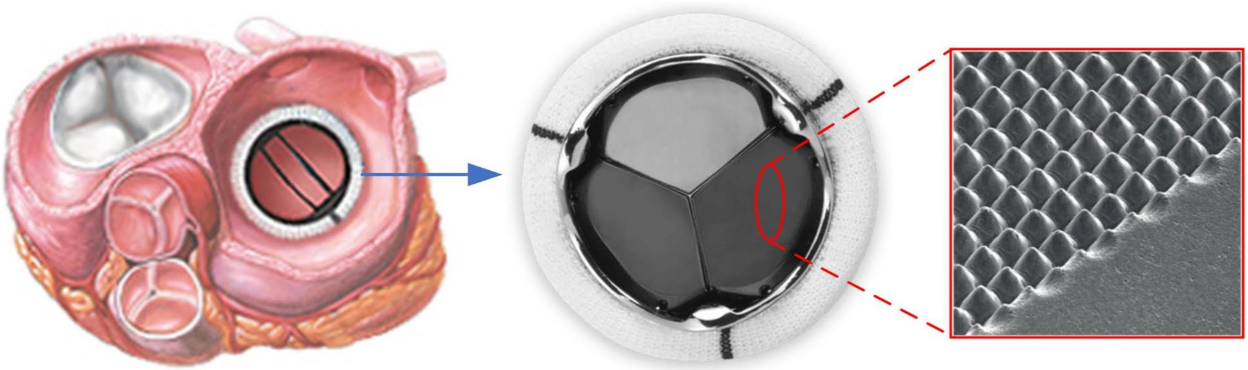

Figure 7 Superhydrophobic structures on the surface of artificial mechanical valves [28]

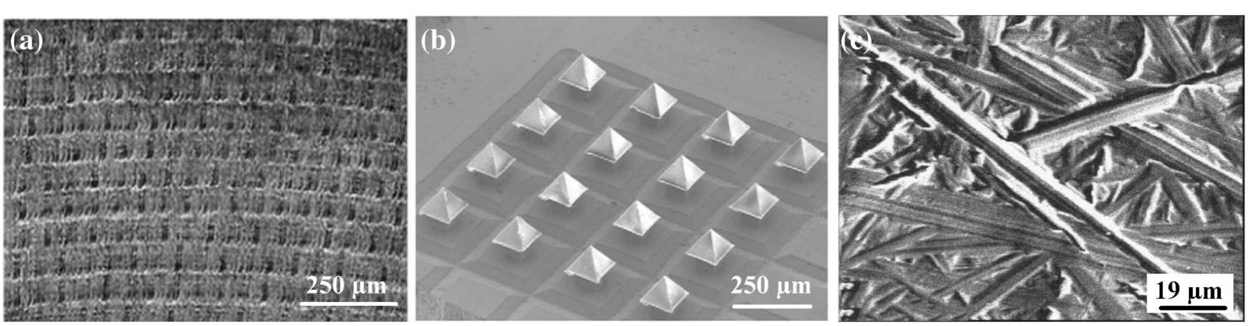

Figure 8 Microstructures of titanium and titanium alloy implants surface fabricated by different machining methods: (**a**) Turning [32], (**b**) Micro milling [30], and (**c**) Grinding [31]

3.2 Non-traditional Machining Methods

Non-traditional machining methods can be used to fabricate some structures on metal surfaces that are difficult to fabricate and process by traditional machining methods. At present, the chemical etching, electrochemical processing and laser processing are the most widely used non-traditional machining methods in manufacturing the microstructures on the surface of titanium alloys. Figure 9 shows the microstructures fabricated by these three machining methods on the surface of titanium alloy implants. The electrochemical etching is mainly used for machining porous structures with good wear resistance and corrosion resistance. Higher surface porosity and hydrophilicity of porous structures can enhance the tissue-bonding ability of the titanium and its alloy surface [33–35]. Laser processing, which has the advantages of high machining efficiency and good controllability, is mainly used for fabricating micro-groove structures. The surface of the grooves fabricated by laser processing can generate a rough laminar microstructure, which is conducive to improving the stability of the implant after implantation in the human body [36].

3.3 Other New Machining Methods

With the increasing demand for titanium and titanium alloy implants with different surface functional structures, traditional and non-traditional machining methods are difficult to satisfy the processing requirements. New machining methods such as plasma spraying, magnetron sputtering, and metal 3D printing have been applied to fabricate surface functional structures for titanium and titanium alloy implants. The plasma spraying and magnetron sputtering are mainly used for machining the coating structures on titanium and titanium alloy implant surfaces. The methods both have high spraying efficiency, and the machined coating structures are uniform with strong adhesion, making them extremely suitable for the fabrication of coating structures on the surface of titanium and titanium alloy implants [37, 38]. Metal 3D printing technology is chiefly used to manufacture porous titanium and titanium alloy implants with complex structures due to its short production cycle, high material utilization rate and efficient forming of complex structures [39–42]. Figure 10 exhibits the microstructures fabricated on the surface of titanium and titanium alloy implants using plasma spraying, magnetron sputtering, and metal 3D printing techniques, respectively. Table 1 summarizes the different manufacturing

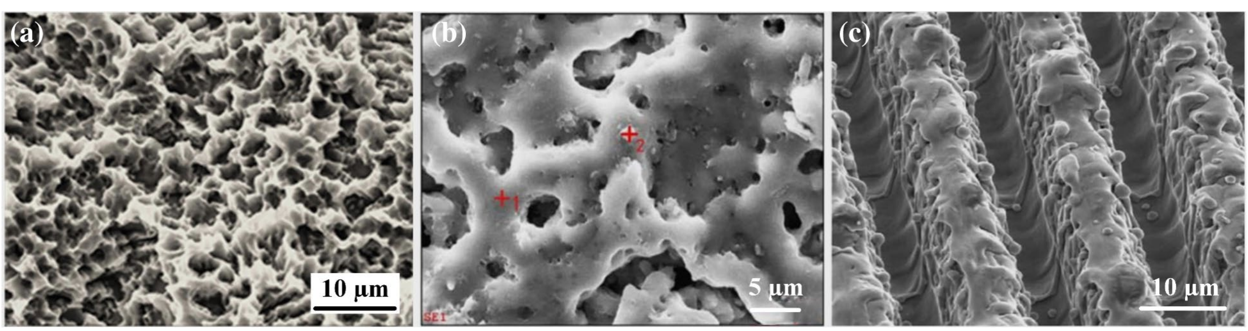

Figure 9 Microstructures fabricated on the surface of titanium alloy implants using different non-traditional machining methods: (**a**) Chemical etching [33], (**b**) Electrochemical processing [35], and (**c**) Laser processing [36]

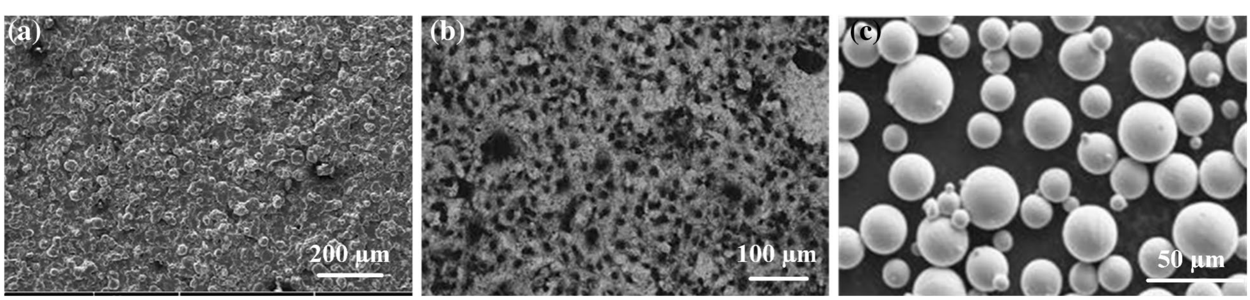

Figure 10 Functional structures fabricated on the surface of titanium and titanium alloy implants using different machining methods: (**a**) Plasma spraying [37], (**b**) Magnetron sputtering [38], and (**c**) Metal 3D printing technology [39]

Table 1 Characteristics of different manufacturing methods on titanium and its alloys surface

Classification	Manufacturing technologies	Advantages	Disadvantages	Structure type
Traditional machining methods	Turning	Low cost, high efficiency	Unable to turn the complex curved body	Microgrooves, Micro pits
	Grinding	High processing efficiency, low cost, good processing quality	Low surface roughness	Microgrooves
	Micro milling	High processing accuracy, good operability, good surface regularity	High equipment and maintenance costs	Microgrooves, Micro pits
Non-traditional machining methods	Anodic oxidation	High coating hardness, good wear resistance	High cost, low efficiency, small aperture	Porous structure
	Micro-arc oxidation	Uniform coating, high bonding strength, large aperture	Large capacity refrigeration equipment is required	Porous structure
	Chemical etching	High processing efficiency, no stress, simple operation	Chemical solution pollutes the environment	Microgrooves, Micro pits
	Laser processing	Fast processing speed, small deformation	Equipment is expensive and energy is uneven	Microgrooves, Micro pits
Other new machining methods	Metal 3D printing	Free molding, low cost, loose and porous surface	Powder particle dissociation leads to infection and failure	Porous structure
	Plasma spraying	High spraying efficiency, low cost, simple operation	Carrier gas is expensive	Coating structure
	Magnetron sputtering	Fast deposition speed, high bonding strength	Anode requires high consumption	Coating structure

technologies of surface functional structures applied in titanium and titanium alloy implants, as well as the advantages and disadvantages of each technology and the types of various structures.

4 Fabrication of Surface Functional Structure on Titanium and Titanium Alloy Implants

There are many types of surface structures on titanium and titanium alloy implants, which have different morphologies and sizes. According to the different surface structural morphology of titanium and titanium alloy implants, it can be divided into three categories: coating structure, regular structure and porous structure. At present, scholars have carried out a large number of studies in fabricating surface functional structures on titanium alloy implants, and some achievements have been achieved. The research on the fabrication of coating structure, regular structure and porous structure on the surface of titanium and titanium alloy implants are summarized and reviewed as follows.

4.1 Coating Structures

The surface of early titanium alloy implants is smooth and the biological activity is low. After implantation, it would release metal elements that are harmful to the human body, leading to metal poisoning in serious cases. Coating structures can effectively prevent direct contact between the metal surface and biological tissue. Preparing a bioactive coating on the surface of titanium alloy implants, can not only activate the bioactive factors on the implant surfaces, but also effectively improve the corrosion resistance and wear resistance, which is the transitional layer between human tissue and implant. At present, hydroxyapatite coating and titanium dioxide coating are the two most commonly used coating structures on the surface of titanium and titanium alloy implants.

4.1.1 Hydroxyapatite Coating

Hydroxyapatite (HA) is a natural calcium phosphate that is the main constituent of teeth and bones. Hydroxyapatite coating has the osteoinduction to provide a bone-friendly surface for titanium alloy implants, which can enhance osteoblast activity. However, it also has the defects of high brittleness, weak antibacterial, low bonding strength with metal substrate, and is easy to shed after long-term implantation. It is an effective method to improve the binding strength and antibacterial performance of HA coating by doping functional elements on the coating surface. Currently, the element doping methods of HA coating can be divided into single-element doping and multi-element doping.

Elements such as tantalum, strontium and fluorine are commonly used in single-element doping. Lu et al. [43] fabricated Ta-HA coating with a microporous structure doped with tantalum elements using plasma spraying technology, and the surface characteristics and mechanical properties of the coating were tested. The experimental results showed that the surface roughness and wettability of Ta-HA coating were significantly improved, and the minimum contact angle was 13.2°. The bonding strength of Ta-HA coating with metal substrate was obviously better than that of HA coating. Tao et al. [44] prepared Sr-HA coating doped with strontium element by electrochemical deposition techniques, and tested the effects of Sr content on the bonding strength of the implant. The results showed that when the Sr content was 20 %, the titanium implant coated with Sr-HA coating showed the best osseointegration performance. The maximum push-out force ratio and bone area ratio were about 2.25 and 3.35 times that of HA coating, respectively. Subsequently, Li et al. [45] fabricated Mg-HA coating doped with magnesium element on the surface of titanium substrates by the sol-gel dip-coating method. The histomorphometry and biomechanical testing revealed that the bone-implant contact and bone area ratio of Mg-HA-coated titanium implants increased by 2.25 and 1.35 times, respectively. The maximum push-out force increased by 1.54 times. Zhong et al. [46] fabricated Zn-HA coating doped with zinc element on titanium substrates by electrophoretic deposition techniques, and the effect of zinc content on alkaline phosphatase activity related to osteogenic properties was studied. The results showed that the Zn-HA coating had better osteogenic properties than HA coating when the zinc content was 5%, and its alkaline phosphatase content was 1.61 times that of the HA coating. Lou et al. [47] fabricated La-HA coating doped with lanthanum element on titanium substrates by the sol-gel dip-coating method, the La-HA coating was mainly composed of rod-like particles. The effect of lanthanum content on the bonding strength and alkaline phosphatase activity of the coatingwas studied. The results showed that when the content of La was 20%, the bonding strength and alkaline phosphatase activity of La-HA coating was 1.08 and 1.11 times as that of HA coating, respectively.

Although single-element doping can improve the performance of HA coating, it has limited functionality. Multi-element doping is developed on the basis of single-element doping. Compared with single-element doping, it has the advantages of high binding strength, good antibacterial property and biocompatibility, which is the main method of HA coating modification at present. Vu et al. [48] fabricated HA coating doped with various chemical substances (ZnO, SiO_2 and Ag_2O) on titanium substrates by plasma spraying technology. Experiments in vitro showed that ZnO could induce osteogenesis, SiO_2 could promote angiogenesis and Ag_2O could inhibit bacterial production. Compared with HA coating, Zn/Si/Ag-HA coating had similar performance on bonding strength and maximum push-out force, and had larger proportion of total bone formation and bone mineralization of 1.24 and 2.91 times, respectively. The Zn/Si/Ag-HA coating also showed great hydrophilicity, and the minimum contact angle was 40°, which was 51.7% smaller than untreated surface. Ke et al. [2] fabricated HA coating doped with MgO and Ag_2O on titanium alloy substrates by using plasma spraying technology. The experimental results indicated that the strength of the doped HA coating improved by 52% more than that of the HA coating without doping. In addition, MgO could induce osteogenesis and the Ag_2O had obvious inhibitory effect on Escherichia coli and Staphylococcus aureus. Huang et al. [49] first prepared a layer of titanium dioxide nanotube structure on the surface of titanium substrate by anodic oxidation technology, and then deposited a HA coating doped with F element and Ag element on the surface of titanium dioxide nanotube by electrodeposition technology, and studied the bonding strength, antibacterial efficacy, wettability and in vitro bioactivity of F/Ag-HA coating. The results showed that the addition of fluorine elements can significantly enhance the adhesion of the coating to the titanium substrate. The bonding strength of F/Ag-HA coating is about 1.39 times that of HA coating. F/Ag-HA coating can significantly inhibit the growth of Staphylococcus aureus. Compared with HA coating, the wettability of the F/Ag-HA coating was significantly reduced, and the contact angle was 110°, which mainly depended on the dandelion-like aggregates on the surface of the needle-like nanocrystals, as shown in Figure 11. The results of in vitro bioactivity showed that the alkaline phosphatase activity of F/Ag-HA coating was about 1.47 times that of HA coating.

HA coating is a bioactive coating with the ability to induce osseointegration effectively between the implant and the bone interface. However, HA coating has the disadvantages of high brittleness, low fatigue strength and weak bonding strength, and its inconsistency of thermal expansion coefficient in metal matrix leads to the low long-term survival rate of HA coating implants. The bonding strength of coating and implant plays a decisive role in the service life of the implant. Figure 12 summarizes the maximum bond strength enhancement ratio of HA coatings doped with different elements. It could be seen that most of the doped functional elements played a certain role in promoting the bonding strength of coating and implants. HA coating doped with single-element tends to have larger bonding strength, while HA coating doped with multi-element has multifunctional properties.

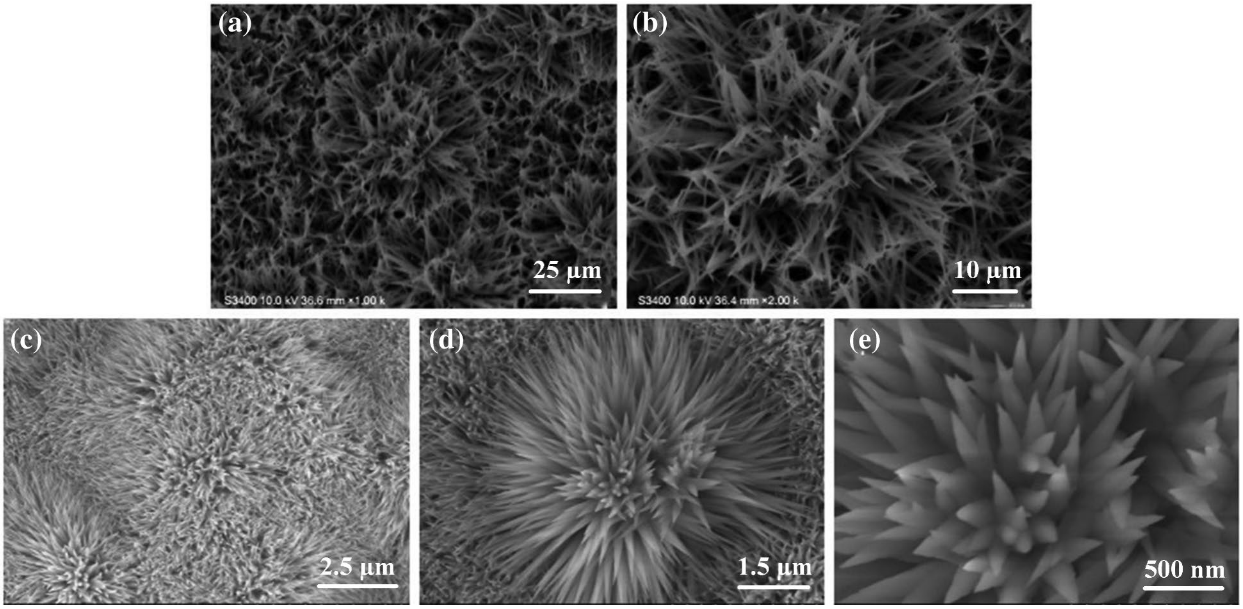

Figure 11 Microstructure of HA coating and F/Ag-HA coating: (**a**, **b**) Low and high magnification images of HA coating, (**c**–**e**) Low and high magnification images of F/Ag-HA coating [49]

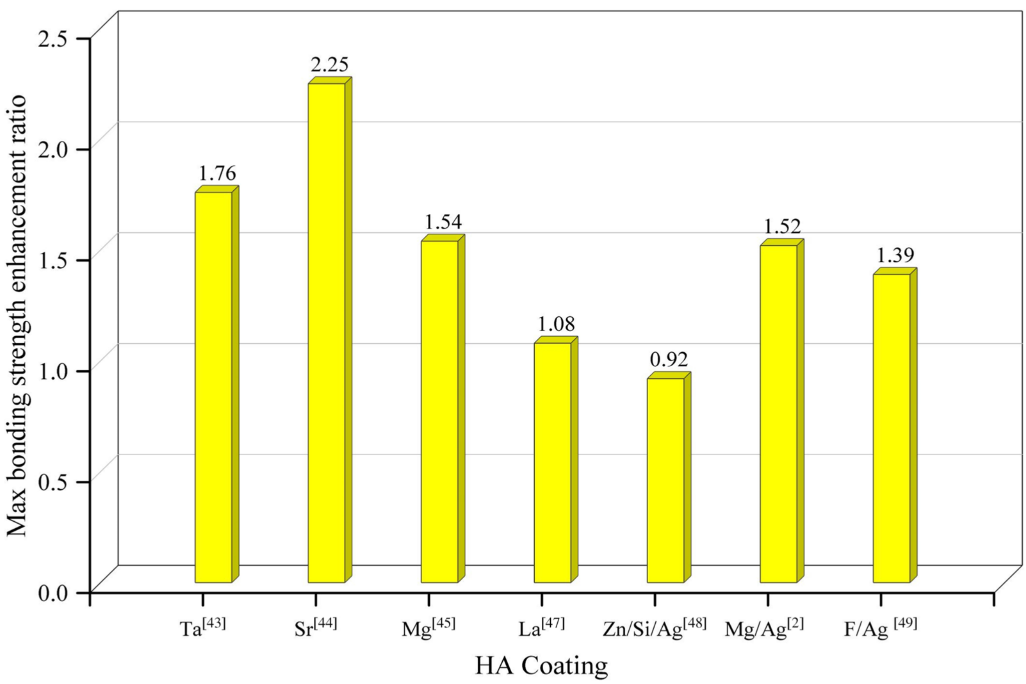

Figure 12 The maximum bonding strength enhancement ratio of HA coatings doped with different elements

4.1.2 Titanium Dioxide Coating

Titanium dioxide (TiO_2), as a common oxide on the surface of titanium and its alloys, has good corrosion and wear resistance properties, and is often used as a surface coating structure for titanium alloy implants. Compared with HA coating, TiO_2 coating has higher binding strength with substrate, but it is not suitable for long-term implantation in human body due to their relatively weak osseointegration and antibacterial properties.

In order to improve the osseointegration and antibacterial properties of titanium dioxide coating, some researchers doped corresponding functional elements to improve its performance. Kang et al. [50] prepared a copper-doped titanium dioxide coating on the surface of titanium substrate by micro-arc oxidation technology. The surface morphology is similar to a crater-like microporous structure. The effects of different copper contents on the wettability, antibacterial properties and osteogenic ability of the coating were studied. In vitro antibacterial experiments indicated that Cu-TiO_2 coating could significantly inhibit the growth of Staphylococcus aureus and Porphyromonas gingivalis. The wettability test results showed that when the copper content was 0.5%, and the minimum contact angle of the Cu-TiO_2 coating was 43°. The results of osteogenic ability experiments showed that when the copper content was 1%, the alkaline phosphatase activity of the Cu-TiO_2 coating was about 1.94 times that of TiO_2 coating. Zhao et al. [51] prepared silicon-doped TiO_2 coating on the surface of titanium substrate by micro-arc oxidation technology, and its surface morphology was microporous, as shown in Figure 13. Firstly, the effect of silicon content on the roughness of Si-TiO_2 coating was studied, and the effect of Si-TiO_2 coating on osteogenic activity and alkaline phosphatase activity was studied. The experimental results showed that the surface roughness of the coating prepared by micro-arc oxidation technology has a significant increase compared with the smooth titanium surface, while the effect of Si content on the roughness is not obvious. With the increase of Si content, the osteogenic activity of Si-TiO_2 coating was enhanced, and the alkaline phosphatase activity was 1.59 times that of TiO_2 coating. Kang et al. [52] prepared Zn-doped TiO_2 coating on the surface of titanium substrate by micro-arc oxidation technology. The surface morphology of Zn-doped TiO_2 coating was crater-like. The effects of zinc content on the wettability, antibacterial properties and osteogenic activity of Zn-TiO_2 coating were studied. Antibacterial experiments indicated that Zn-TiO_2 coating had a significant inhibitory effect on Staphylococcus aureus and Porphyromonas gingivalis. The contact angle test showed

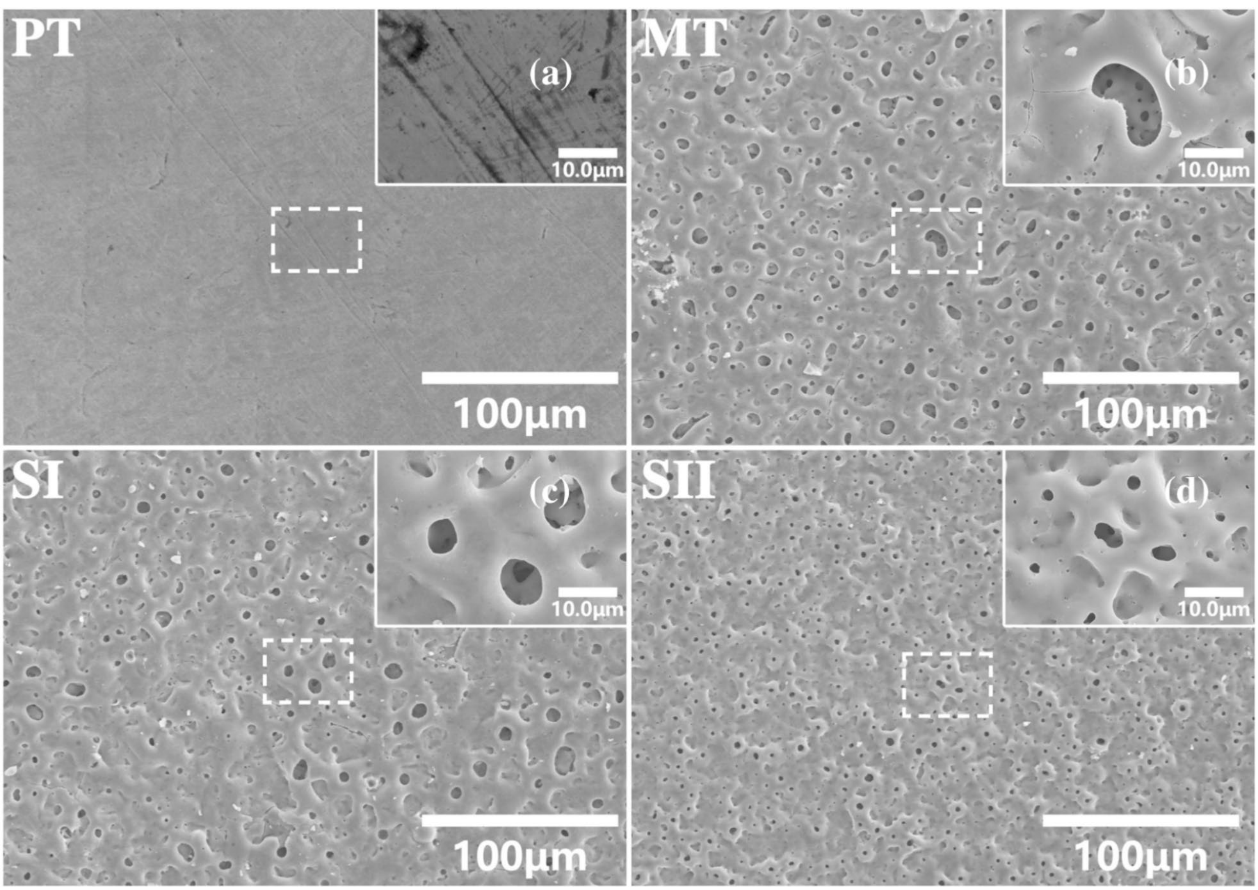

Figure 13 Surface morphologies of different coatings: (**a**) Smooth titanium surface, (**b**) TiO_2 coating, (**c**) 5% Si-TiO_2 coating and (**d**) 10% Si -TiO_2 coating [51]

that the maximum contact angle of the Zn-doped TiO_2 coating was 48.5°, which showed limited influence on the wettability of the TiO_2 coating, but the osteoblast activity of Zn-TiO_2 coating was about 1.34 times that of TiO_2 coating.

Zhang et al. [53] prepared Y-doped TiO_2 coating on the surface of titanium alloy substrate by micro-arc oxidation. The surface is mainly composed of micropores and micro/nano structures, as shown in Figure 14. The antibacterial properties and osteogenic activity of Y-TiO_2 coating were studied. The results of antibacterial experiments showed that Y-TiO_2 coating could significantly inhibit the growth of Staphylococcus aureus and Escherichia coli. The results of in vitro osteogenesis experiments showed that the osteoblasts and alkaline phosphatase activity of Y-TiO_2 coating were about 2.03 and 1.34 times as that of TiO_2 coating, respectively. Zhang et al. [54] prepared a manganese-doped TiO_2 coating on the surface of titanium substrate by micro-arc oxidation. The surface contains a large number of micron and nano pores, and studied the antibacterial properties, wettability and osteogenic activity of Mn-TiO_2 coating. The results of wettability experiment showed that doping Mn element would reduce the wettability, and the contact angle was 85.4°. The results of antibacterial experiments showed that Mn-TiO_2 coating could significantly inhibit the growth of Staphylococcus aureus. The results of in vitro osteogenesis experiments showed that the osteoblasts and alkaline phosphatase activity of Mn-TiO_2 coating were about 1.78 and 1.52 times that of TiO_2 coating, respectively. Zhou et al. [55] prepared fluorine-doped TiO_2 coating on the surface of titanium substrate by micro-arc oxidation. The surface contains microporous structure and nanoparticles, and studied the effect of F content on the antibacterial properties and osteogenic activity of TiO_2 coating. The results of antibacterial experiments showed that when the F content was 6%, the F-TiO_2 coating had the best antibacterial properties and could significantly inhibit the growth of Staphylococcus aureus and Escherichia coli. The results of in vitro osteogenesis experiments showed that the maximum push-out force, bone-implant contact area and alkaline phosphatase activity of F-TiO_2 coating were about 2.23, 2.31 and 4 times that of TiO_2 coating, respectively. Zhou et al. [56] prepared a cobalt-doped TiO_2 coating on the surface of titanium substrate by micro-arc oxidation, which contains microporous

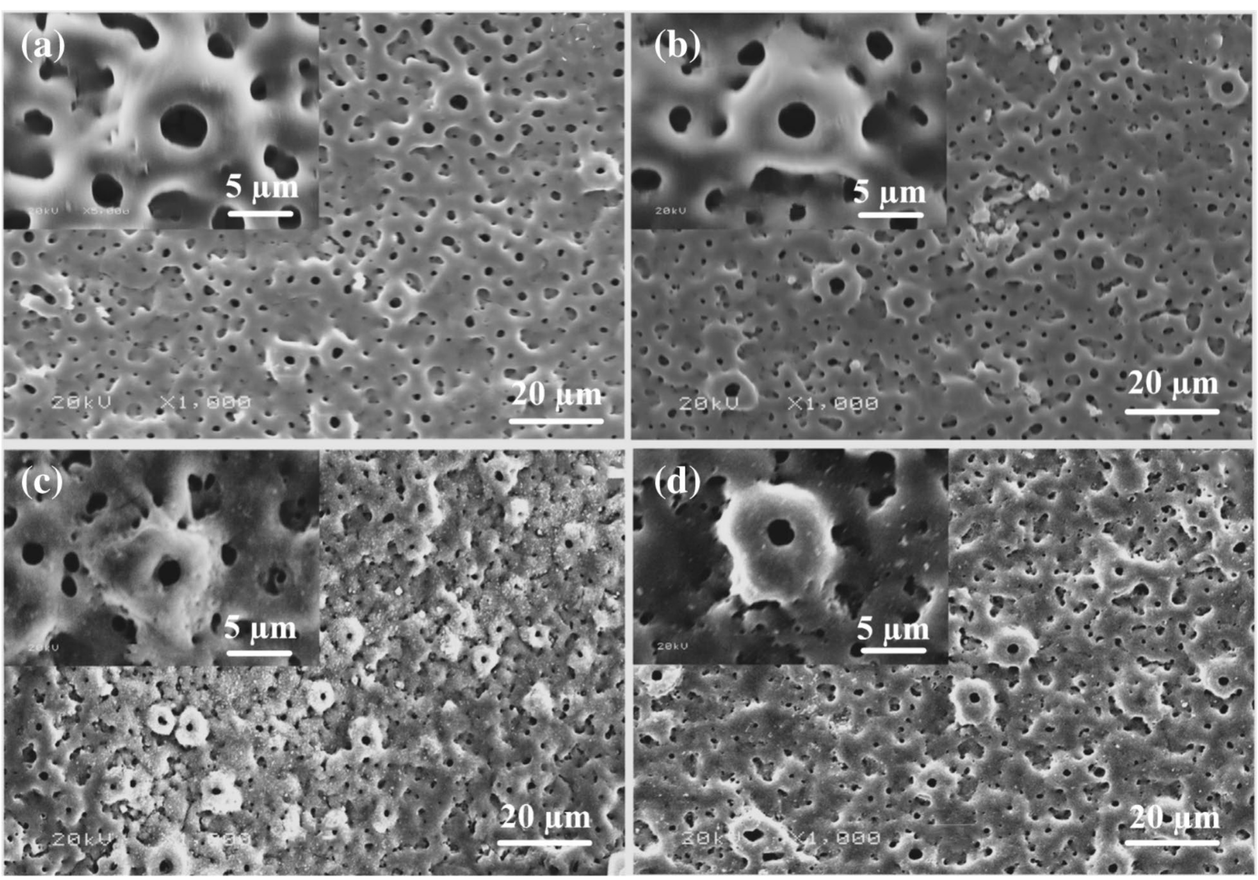

Figure 14 Surface morphologies of different coatings: (**a**) TiO_2 coating, (**b**) 3% Y-TiO_2 coating, (**c**) 6% Y-TiO_2 coating and (**d**) 9% Y-TiO_2 coating [53].

structure and nanoparticles, and studied the effect of Co content on the roughness, wettability and osteogenic activity of Co-TiO_2 coating. The experimental results showed that the F content does not significantly change the roughness and wettability of the Co-TiO_2 coating. When the Co content was 7%, the optimal contact angle of the Co -TiO_2 coating was 44.6°. The results of in vitro osteogenesis experiments showed that the osteoblast activity and alkaline phosphatase activity of Co-TiO_2 coating were about 1.55 and 2.22 times that of TiO_2 coating, respectively. Due to the double-layer function of boron in promoting osteogenesis and bacteriostasis, Sopchenski et al. [57] prepared boron-doped B-TiO_2 coating on the surface of titanium substrate by micro-arc oxidation technology. Antibacterial experiments indicated that B-TiO_2 coating could significantly inhibit the growth of Staphylococcus aureus and Pseudomonas aeruginosa. In addition, Yetim et al. [58] studied the corrosion behavior of Ag-TiO_2 coating doped with silver in a simulated cell solution. The corrosion test results showed that the Ag-TiO_2 coating has higher corrosion resistance than the undoped TiO_2 coating.

The function of single element doping is relatively single, and multi-element doping can make up for the limitations of single element doping. Zhao et al. [59] prepared a titanium dioxide coating doped with zinc and strontium elements (MT-Zn/Sr) on a titanium substrate surface using micro-arc oxidation technology, where Zn and Sr were evenly distributed in the coating. The antibacterial and adhesion experiments showed that MT-Zn/Sr coating not only had good antibacterial activity, which could inhibit the proliferation of Staphylococcus aureus, but also promoted the early osseointegration between titanium implants and bone tissue. Wang et al. [60] prepared Zn/Zr-TiO_2 coating doped with zinc and zirconium on the surface of titanium alloy by magnetron sputtering-microarc oxidation composite method, and its surface is rich in microporous structure. The corrosion resistance, antibacterial properties and osteogenic properties of Zn/Zr-TiO_2 coating were studied. The results of corrosion and antibacterial experiments showed that the corrosion resistance and antibacterial ability of Zn/Zr-TiO_2 coating were better than that of TiO_2 coating. The osteoblast activity of Zn/Zr-TiO_2 coating was about 1.41 times that of TiO_2 coating. Lv et al. [61] prepared TiO_2 coating doped with zinc and silver on the surface of titanium substrate by micro-arc oxidation, and studied the antibacterial properties and biocompatibility of Zn/Ag-TiO_2 coating. The results of antibacterial experiments showed that the antibacterial rates of Zn-TiO_2, Ag-TiO_2 and Zn/Ag-TiO_2 coatings were 92.6 %, 96.2 % and 97.8 %, respectively. In vitro biocompatibility experiments showed that the osteoblast activity and alkaline phosphatase activity of Zn/Ag-TiO_2 coating were 1.51 and 1.24 times that of TiO_2 coating, respectively. Zhao et al. [62] prepared porous Si/Ag-TiO_2 coating doped with silicon and silver on the surface of titanium substrate by micro-arc oxidation, and studied the wettability, antibacterial properties and mineralization of osteoblasts of Si/Ag-TiO_2 coating. The contact angle measurement data showed that the contact angle of SiAg-TiO_2 coating was 73.4°, which decreased by 12.22 %, and the wettability was improved. The results of osteogenic performance test showed that the total bone formation of SiAg-TiO_2 coating was about 1.43 times that of TiO_2 coating and had a good antibacterial effect. He et al. [63] prepared Cu/Si-TiO_2 coatings doped with copper and silicon on the surface of titanium substrate by micro-arc oxidation, and studied the antibacterial and osteogenic properties of different coatings. The experimental results showed that the coating doped with Cu element inhibit the growth of Staphylococcus aureus, but it will also seriously restrict the assembly of the cytoskeleton. Doping Si element can not only improve the cytotoxicity caused by Cu element, but also significantly promote cell proliferation and differentiation.

Through the above research, it can be found that the TiO_2 coating on the surface of implants is mainly prepared by micro-arc oxidation technology. It has a larger bonding strength with titanium substrate than HA coating. However, the weak surface biocompatibility of TiO_2 coating is not conducive to inducing new bone formation. The biocompatibility of the TiO_2 coating can be effectively improved by depositing different functional elements, thereby enhancing cell vitality. To a certain extent, higher cell viability leads to better biocompatibility of the implant. Figure 15 summarizes the cell viability enhancement ratio of TiO_2 coating doped with different elements. It can be seen that the cell viability was significantly enhanced by the functional elements in most studies. In addition, the TiO_2 coating doped with multi-element has certain antibacterial properties.

4.2 Regular Structure

Coating structure has the disadvantages of a complex fabrication process, fast dissolution rate and easy fracture, which is not conducive to long-term implantation in the human body. Regular structure means that regular microstructures such as micro-grooves and micro-pits are directly machined on the surface of titanium alloy implants to improve their osseointegration and antibacterial properties.

4.2.1 Micro-groove Structure

The micro-groove structure is simple and easy to be machined, and is widely used on the surface of medical

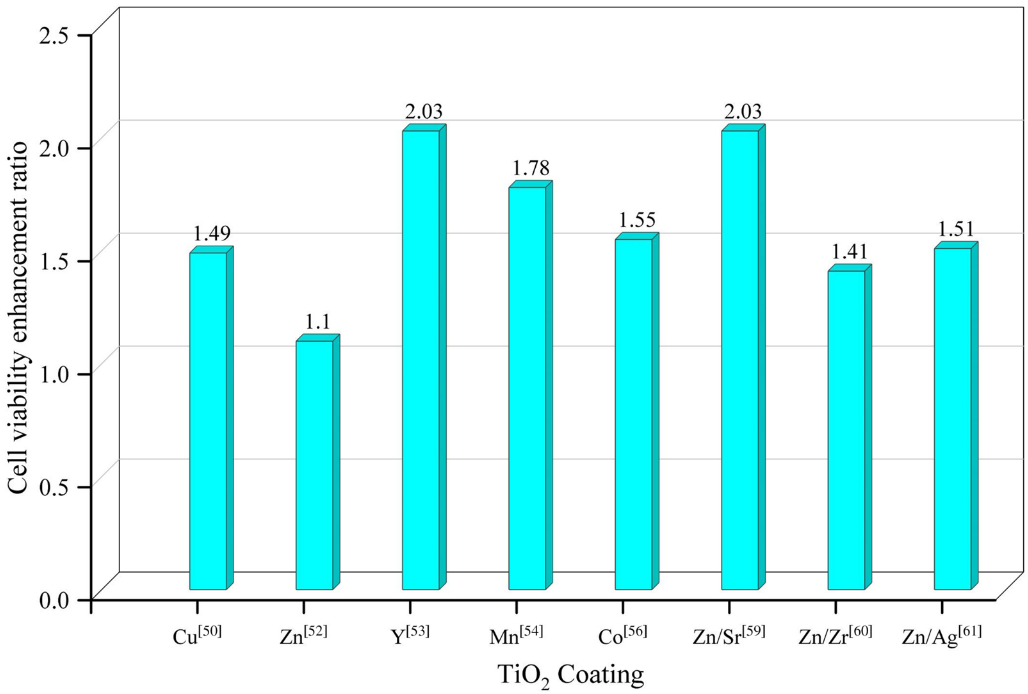

Figure 15 Cell viability enhancement ratio of TiO_2 coating doped with different elements

instruments. At present, the machining methods of micro-groove structures mainly include turning processing, laser processing and micro-milling, etc.

Turning is one of the most widely used traditional machining methods, which has the advantages of high processing efficiency and low cost. It was first used for micro-groove structure machining on the surface of titanium alloy implants. Luthen et al. [64] prepared different surface structures on the surface of titanium substrate by polishing, turning and sandblasting, and studied the effects of surface structures with different roughness on cell proliferation and differentiation. The experimental results showed that the surface obtained by turning can effectively promote cell proliferation and differentiation compared with the surface prepared by polishing and sandblasting. In recent years, a new machining method has been applied to the processing of micro-groove structures. Zamani et al. [65] used ultrasonic assisted turning technology to prepare a microgroove structure with special micro-textures on the surface of titanium substrate, and studied the cell adhesion properties of this special surface. The results indicated that the microgroove surface prepared by ultrasonic assisted turning technology promoted the expression of osteoblast integrin and the adhesion of osteoblast fibrin. Sajjady et al. [32] prepared a nano-scale microgroove structure on the surface of titanium alloy by three-dimensional elliptical vibration turning, as shown in Figure 16. The hydrophilicity and roughness test results showed that the micro-grooved surface processed by three-dimensional elliptical vibration turning has stronger hydrophilicity (minimum contact angle was 30.7°) and the most suitable roughness compared with the micro-grooved surface processed by non-vibration turning, which can effectively improve the osteogenesis of the titanium alloy implant surface.

Laser processing has many advantages, such as good processing controllability, fast forming speed and the ability to process complex structures on the metal surface [66], which is often used in the fabrication of micro-groove structures on the surface of titanium alloy implants. Conserva et al. [67] used laser processing technology to fabricate micro-groove structures with different sizes on the surface of titanium alloy implants, and carried out cell adhesion experiments. It was found that micro-grooves with a width of 8 μm significantly promoted cell proliferation and differentiation. Wang et al. [68] first prepared a microgroove structure (Ti-G) on the surface of titanium alloy by laser processing technology, and then prepared a graphene oxide coating (Ti-G-GO) on the microgroove surface by chemical assembly technology, as shown in Figure 17. The wettability test showed that the minimum contact angle of the Ti-G-GO titanium alloy implant surface was 33°, indicating that the microgroove and graphene oxide coating structure can improve the hydrophilicity of the titanium alloy implant. The results of in vitro cell

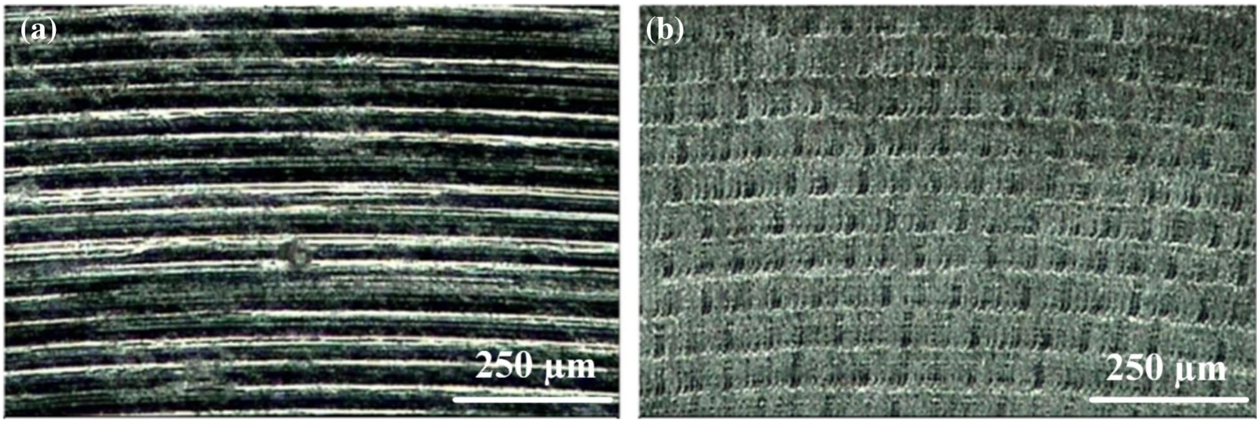

Figure 16 Micro-grooved surface processed using different turning methods [32]: (**a**) Non-vibration turning, and (**b**) Three-dimensional elliptical vibration turning

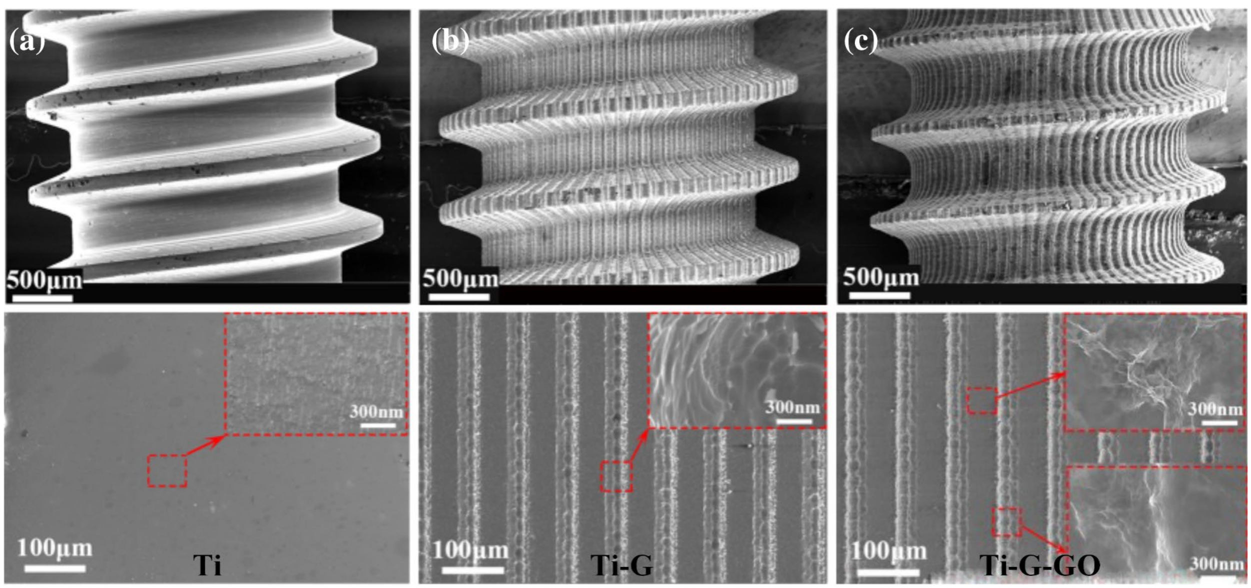

Figure 17 Micro-grooves fabricated by laser processing and chemical assembly techniques [68]: (**a**) Smooth Ti group, (**b**) Micro-groove group: Ti-G, and (**c**) Micro-grooved group with graphene oxide coating: Ti-G-GO

biological activity test showed that the cell viability and alkaline phosphatase activity of Ti-G-GO were 1.41 and 2.05 times higher than those of the smooth Ti group, respectively. Veiko et al. [69] fabricated three kinds of microgrooves on the surface of titanium alloy implants by laser processing technology, including open grooves, grids and closed grooves, as shown in Figure 18. The results of wettability study showed that the three microgrooves had superhydrophilicity. The results of osteogenic properties showed that the alkaline phosphatase activity of the open groove was the best, which was 44.94 times that of the smooth titanium alloy implant. Zheng et al. [70] prepared microgrooves with different widths and depths on the surface of titanium alloy implants by laser processing technology, and studied the effects of groove width and depth on its wettability and osteogenic properties. The results of wettability test showed that with the increase of groove width and depth, the wettability of titanium alloy implant surface was improved, and the contact angle decreased from 65.7° to 45°. The experimental results of osteogenic properties showed that the alkaline phosphatase activity of the groove surface with a width of 30 microns was 5.34 times that of the smooth surface.

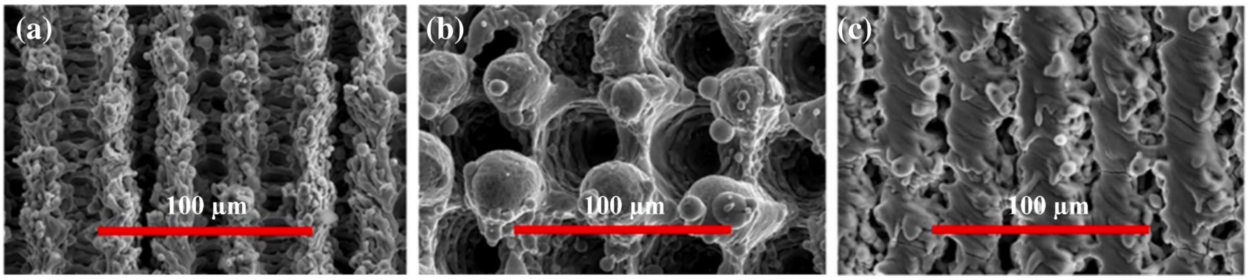

Figure 18 Three kinds of micro-groove structures were fabricated by laser processing (the scale bar is 100 µm) [69]: (**a**) Opened groove structure, (**b**) Grid groove structure, and (**c**) Close groove structure

With the development of laser processing technology, femtosecond laser processing technology has the advantages of small pulse width, high peak power and small heat-affected zone, which has been gradually applied in the machining of micro-grooves on the surface of titanium alloy. Fasasi et al. [36] prepared grooves with a depth of 1 to 14 µm by femtosecond laser processing. The effect of groove depth on cell adhesion was investigated and experimental results indicated that the micro-grooves with a depth of 8 to 12 µm presented the best early osseointegration performance, in which bone tissue mainly proliferated on the groove ridge and migrated along the groove direction. Sun et al. [71] used femtosecond laser processing technology to fabricate an array of micro-groove structures on the implant surface, as shown in Figure 19, and carried out the roughness and hydrophilicity tests. The experimental results indicated that the micro-groove structures increased the roughness and hydrophilicity of the material, and promoted the proliferation and differentiation of osteoblasts, leading to good osseointegration performance. The contact angle of the implant surface processed by femtosecond laser was 48.8°, which was decreased by 46.8% compared with the polished surface.

Although femtosecond laser processing technology improves the machining accuracy, the expensive equipment limits its wide application. In recent years, micro-milling technology has been widely used in the fabrication of micro-groove structure on the surface of titanium alloy due to its advantages of high machining accuracy and low cost. Wang et al. [72] first machined micro-grooves with a depth of 80 µm and a spacing of 120 µm on the surface of titanium alloy by micro-milling technology, and then processed nanoflower structures on the surface of the micro-grooves by alkali thermal reaction, and fabricated a micro-groove-nanoflower composite structure with micro/nano bipolar morphology. The results indicated that the composite micro/nanostructures could reduce the contact angle (the minimum value was 17.9°) and enhance the hydrophilicity of surface, which could effectively improve the biological activity of titanium alloy implant surface and promote cell adhesion and proliferation. Wan et al. [73] proposed a nanotube-modified micro-groove structure to improve the osteogenesis and antibacterial properties of titanium alloy implants. They first machined micro-grooves with a depth of 40 µm on the surface of titanium alloy using micro-milling technology, and then processed titanium dioxide nanotubes (TiO_2) structure on the surface of

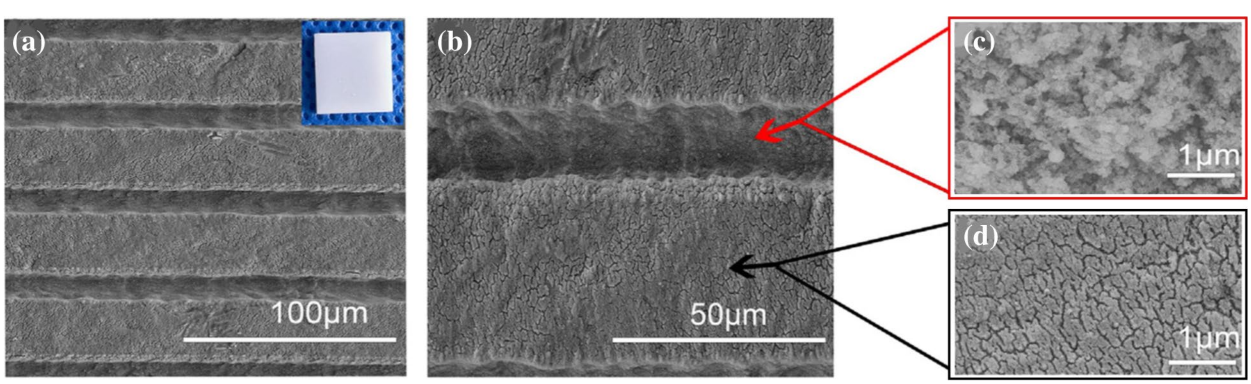

Figure 19 Surface topography of micro-groove structures fabricated using femtosecond laser processing [71]: (**a**, **b**) Micro-grooves, (**c**) Internal groove structure, and (**d**) Groove spacing structure

the micro-grooves using anodic oxidation technology to fabricate a micro-groove with a surface structure of nanotubes, as shown in Figure 20. Compared with the micro-grooves, the micro-grooves with nanotube structure could improve the osteogenic properties of titanium alloy implants and effectively inhibited bacterial reproduction. The nanotube structure could also enhance the hydrophilicity of surface, and water contact angle decreasing from 67.3° to 60.3°.

Subsequently, Wang et al. [74] used the same processing method to fabricate ordered TiO_2 nanotube structures on the surface of the titanium alloy implants, which were located on the surface of groove ridges. The synergistic effect of micro-grooves and TiO_2 nanotubes decreased the contact angle of the implant surfaces from 78.5° to 17.5°, which significantly improved the hydrophilicity of the implants. Cell adhesion experiments indicated that these structures improved the corrosion resistance of titanium alloy implants and could effectively promote osteoblast differentiation.

Micro-groove structure increases the surface area of implants, provides sites for osteoblast growth and protein adsorption, and enhances the adhesion tension between cells and implants. In addition, micro-groove structure has a contact guidance function, which induces cells to grow along the groove direction. At present, micro-groove structures on the surface of titanium and titanium alloy implants are mainly prepared by laser processing and micro-milling. Micro-milling has the advantages of low processing cost and high processing accuracy. However, the surface processed by micro-milling is hydrophobic, so an extra process of surface hydrophilicity modification such as electrochemical or chemical treatment is required. Laser processing technology is the most widely used method for the preparation of micro groove structures on titanium and titanium alloy implants, for its advantages of the simple preparation process, fast forming speed, and the ability to process micro grooves with micro/nano composite structure at one time.

4.2.2 Micro-pit Structures

Micro-pit structures are also one of the commonly used structures on the surface of titanium alloy implants. Currently, the key area of research is finding ways to adjust

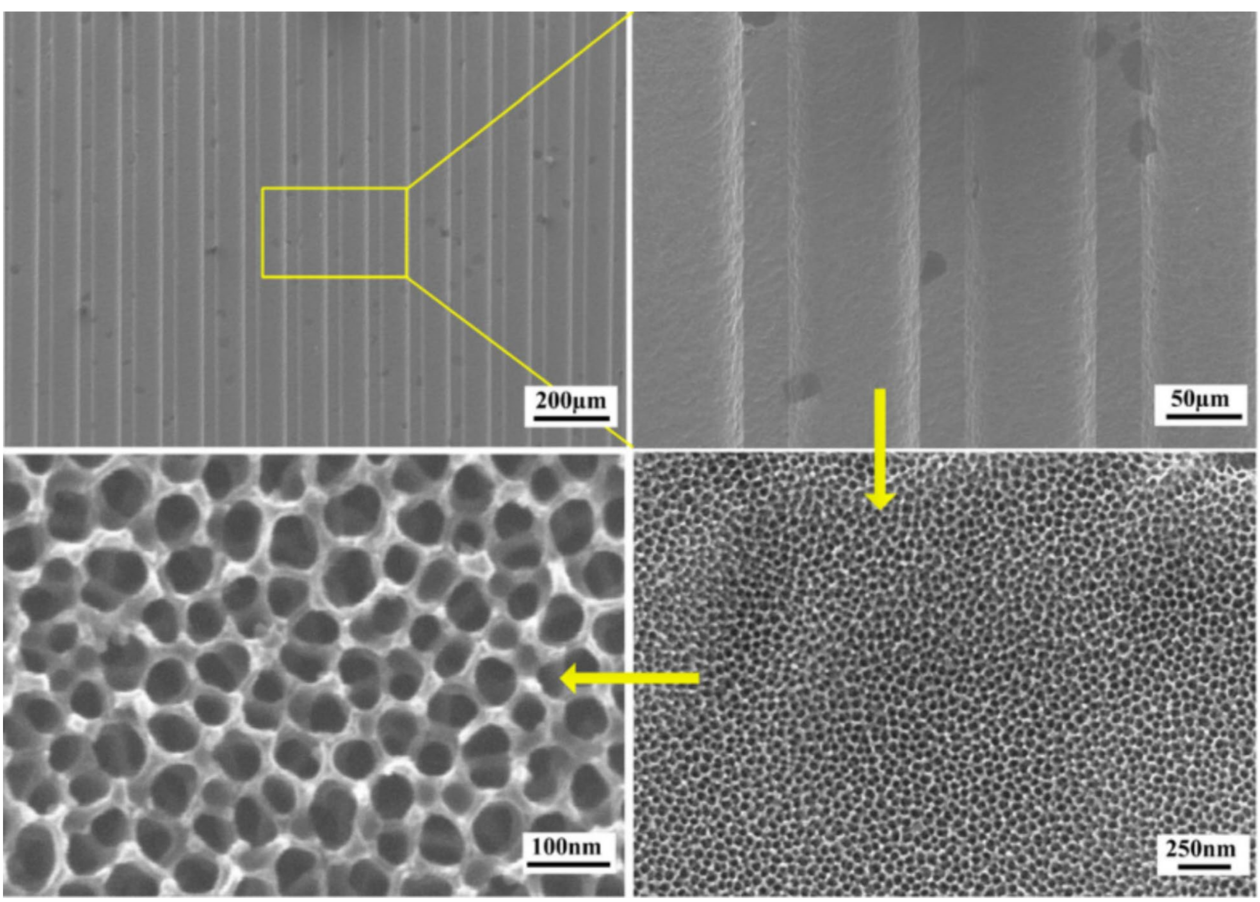

Figure 20 Surface topography of titanium alloy implants with micro-grooves of nanotube structure [73]

the osteogenesis performance of the implant surfaces by changing the structural size of micro-pits.

Dumas et al. [75] processed three biomimetic micro/nano structures on the surface of titanium alloy implants by femtosecond laser according to the surface structure morphology of bone: nano-ripples in the pits, nano-ripples around the pits and only nano-ripples, as shown in Figure 21. The results indicated that the adhesion of osteoblasts on the surface of three kinds of structures was enhanced by the surface containing both micro-pits and nano-ripples compared with the surface without pits. The surface with both micro-pits and nano-ripples was more hydrophilic than the polished surface, and the contact angle decreased from 37.4° to 30.1°. Zhang et al. [76] first prepared micro-pit array structures with diameter of 140 μm and depth of 35 μm on the surface of titanium alloy by laser processing, and then fabricated a nanoscale pit structure in the pits by acid etching. The results of cell adhesion experiments indicated that compared with the surface without pits, the pits with micro and nano scales could effectively improve the biocompatibility and osseointegration of titanium alloy implants. Subsequently, they [77] used the same method to prepare micro-pits with a diameter of 150 μm and a depth of 50 μm on the surface of titanium alloy implants, and studied their biological activity in simulated body fluid. The experimental results showed that the micro-pits with micro/nano structures had better osteogenic properties than the polished surface.

Zwahr et al. [78] first processed micro-pits with a diameter of 50 μm on the surface of titanium alloy by laser, and then fabricated nanoscale pit morphology in micro-pits by femtosecond laser, as shown in Figure 22. The surfaces were hydrophilic (with a contact angle of 32°). The antibacterial and wear experiments indicated that the micro/nano composite pit structure had good antibacterial performance, which could effectively inhibit the increment of Escherichia coli. In

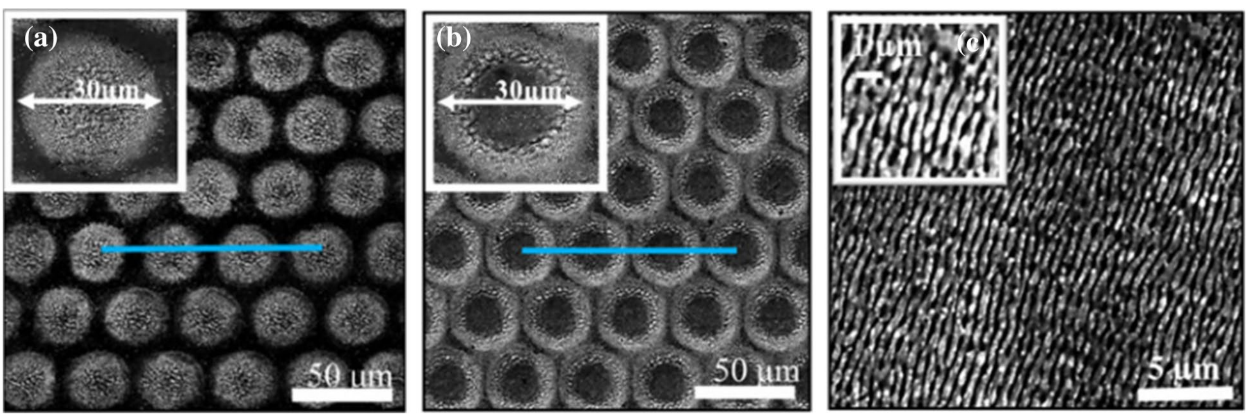

Figure 21 Micro-pit structures fabricated by femtosecond laser processing [75]: (**a**) Nano-ripples in the pits, (**b**) Micro-pits with nano-ripples around the pits, and (**c**) Only nano-ripples

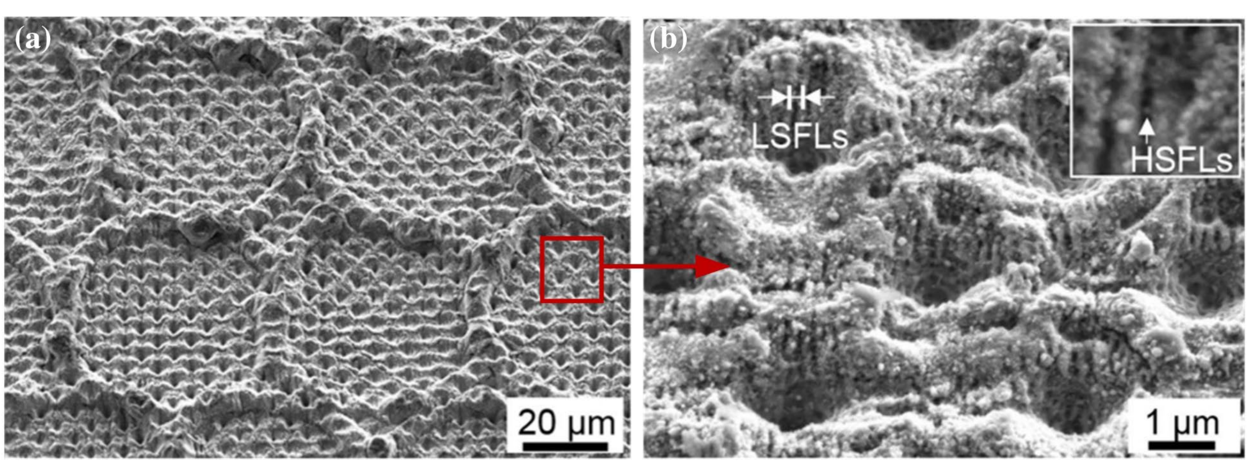

Figure 22 Micro/nano-scale pits fabricated by laser processing [78]: (**a**) Micro-scale pits, and (**b**) Nano-scale pits.

addition, compared with the surface of micron-level pits, the wear performance of the surface was greatly improved. Lin et al. [79] first fabricated a series of regular micro-pits on the surface of titanium alloy by femtosecond laser, and then deposited hydroxyapatite coating (HA) on the surface of micro-pits by chemical vapor deposition technology to prepare the structural surface of micro-pits with HA coating. It was found that the contact angle of micro-pits with HA coating (31°) was much lower than the contact angle of untreated surface (77°), presenting good hydrophilicity, which could effectively promote osteoblast differentiation. Wang et al. [80] prepared a new structure containing micro-pits and nano-pits on the surface of titanium substrate by combining sand blasting, acid etching and chemical oxidation, and studied its wettability and corrosion resistance. The experimental results of wettability showed that the micro/nano pits on the surface of titanium implants increase the roughness of titanium matrix, which showed that the wettability of titanium matrix was improved, and the contact angle decreased from 79.2° to 73.2°. In addition, compared with the polished titanium surface, the corrosion resistance of the titanium substrate with micron and nanometer pits is significantly improved. Zhang et al. [81] used a combination of electrochemical oxidation and acid etching to prepare a micro/nano composite micro-pit structure on the surface of titanium substrate, and studied the effect of this structure on cell adhesion and proliferation. The results of wettability experiments showed that the micro-pit structure of the micro/nano composite level made the surface of the titanium matrix super-hydrophilic, and the contact angle was less than 5°. Besides, compared with the polished titanium substrate surface, the micro/nano composite micro-pit structure significantly promoted cell proliferation and differentiation.

Micro-pit structure on the surface of titanium and titanium alloy implants is mainly prepared by laser processing. Micro-pits with micro/nano composite structures fabricated by laser processing can significantly improve the hydrophilicity and biological activity of implants. The combination of micron and nanometer morphology effectively reduces the stage of osteoblast growth, accelerates the process of osseointegration, and avoids the risk of implant rejection. In addition, the micro/nano composite structure can promote the inward growth of cells, which significantly increases the binding force between the implants and human tissue.

4.3 Porous Structures

Compared with coating and regular structure, porous structure has the advantages of low bulk density, large specific surface area and good energy absorption, which can reduce the stress shielding between titanium and titanium alloy implants and bone tissue and improve their osseointegration performance. The TiO_2 nanotube structure prepared by anodic oxidation on the surface of titanium and its alloy and the surface porous structure formed by metal 3D printing are the main forms of porous structure of titanium and titanium alloy implants.

TiO_2 nanotube structure on the surface of titanium alloy implants can not only improve the osseointegration, but also promote the proliferation and differentiation of osteoblasts by regulating the tube length and diameter of TiO_2 nanotube. Mansoorianfar et al. [82] prepared TiO_2 nanotube arrays with a diameter of about 90–97 nm, a thickness of about 20–30 nm and good uniformity on the surface of titanium alloy by anodic oxidation, as shown in Figure 23. In vitro cell culture, when the voltage is lower than 60 V, the prepared TiO_2 nanotubes showed the best cell activity, and the TiO_2 nanotube surface (contact angle was 36°) showed stronger hydrophilicity than

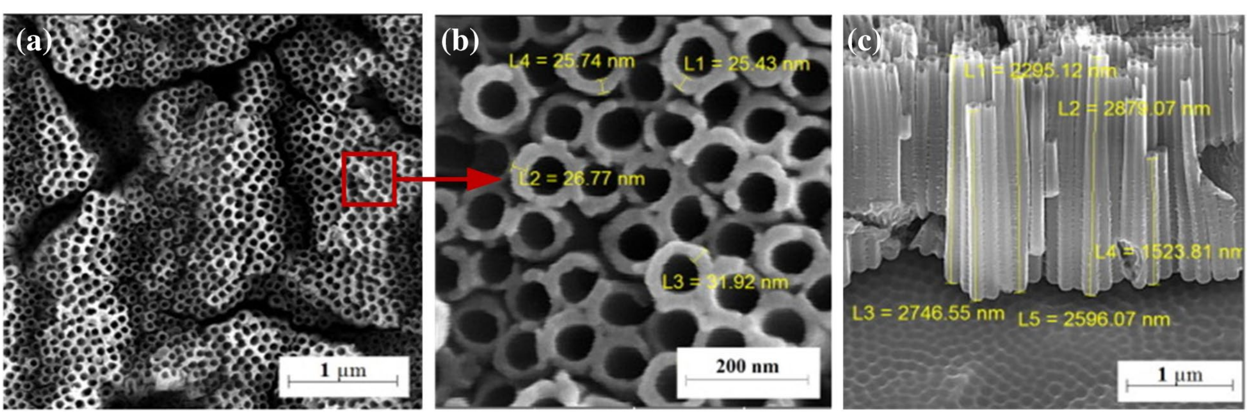

Figure 23 Structure of TiO_2 nanotubes prepared by anodic oxidation [82]: (**a**) TiO_2 nanotubes at low magnification, (**b**) TiO_2 nanotubes at high magnification, and (**c**) Lateral structure of TiO_2 nanotubes

the untreated surface (contact angle was 73.5°). Park et al. [83] studied the effects of TiO_2 nanotubes with different diameters (15–100 nm) on the proliferation and differentiation of osteoblasts. It was found that TiO_2 nanotube with a diameter of 15 nm were beneficial to osteoblast differentiation. When the diameter of TiO_2 nanotube exceeded 50 nm, the proliferation and adhesion of the cells were hindered, and the formation of osteoblast protein was blocked on the tube with a diameter of 100 nm. Wang et al. [84] first prepared TiO_2 nanotubes with a diameter of about 50–90 nm on the surface of titanium substrate by anodic oxidation technology, and then prepared a tantalum (Ta) coating on the surface of TiO_2 nanotubes by plasma spraying. The results of wettability experiments showed that the contact angle of Ta/TiO_2 nanotubes with Ta coating was significantly reduced to 10.7°, which was more hydrophilic than ordinary TiO_2 nanotubes. The results of cell adhesion experiments in vitro also showed that Ta/TiO_2 nanotubes had a strong ability to induce osteoblast proliferation and differentiation. Zhao et al. [85] firstly prepared TiO_2 nanotube structure on the surface of a titanium substrate by anodic oxidation method, and then introduced silicon (Si) element into TiO_2 nanotube by plasma injection method to prepare Si-TiO_2 nanotube structure doped with Si element. The results of wettability experiments showed that the hydrophilicity of Si-TiO_2 nanotube titanium implants doped with Si was significantly improved compared with polished and TiO_2 nanotube titanium implants, and the contact angle reduced from 65° to 11.3°. In addition, Si-TiO_2 nanotube titanium implants can promote osteoblast proliferation and differentiation. Hu et al. [86] first prepared TiO_2 nanotube structure on the surface of titanium substrate by anodic oxidation method, and then deposited nano-calcium phosphate on TiO_2 nanotube by electrochemical deposition method to prepare nano-calcium phosphate TiO_2 nanotube structure. The wettability test results showed that the nano-calcium phosphate TiO_2 nanotube titanium implant exhibited super-hydrophilicity compared with sandblasting, polishing and TiO_2 nanotube titanium implants, and the contact angle decreased from 73.4° to 14.5°. Besides, nano-calcium phosphate TiO_2 nanotube titanium implants can significantly inhibit the growth of Streptococcus sanguinis. Zhao et al. [87] firstly prepared TiO_2 nanotube structure with a diameter of about 87.17 nm and a length of about 1.32 μm on the surface of titanium substrate by anodic oxidation method, and then deposited zinc ions in TiO_2 nanotubes by electrochemical deposition method to prepare Zn-doped Zn-TiO_2 nanotube structure. The Zn-TiO_2 nanotube titanium implants could significantly promote osteoblast proliferation and differentiation. Saha et al. [88] combined anodic oxidation method and electrophoretic deposition method to prepare TiO_2 nanotube structure coated with silk fibroin on the surface of titanium alloy substrate. The results of wettability experiments showed that the wettability of TiO_2 nanotube titanium implants was significantly improved compared with polished titanium implants, and the contact angle was 42.1°. The wettability of TiO_2 nanotube titanium implants coated with silk fibroin was not significantly improved. The results of osteoblast adhesion experiment showed that the alkaline phosphatase activity of TiO_2 nanotube titanium implants coated with silk fibroin was 2.23 times that of TiO_2 nanotube titanium implants, which significantly promoted the proliferation and differentiation of osteoblasts. Wang et al. [89] prepared a TiO_2 nanotube structure with a diameter of about 30–50 nm on the surface of titanium substrate by acid etching and anodic oxidation, and studied the wettability and osteogenic properties of the micro/nano composite structure. The experimental results showed that compared with the polished surface and the pure micro-treated surface, this micro/nano composite structure can provide greater roughness, surface energy and better hydrophilicity, and the water contact angle was reduced from 73.3° of the polished surfaces to 23.3°.

TiO_2 nanotube arrays also show unique superiorities in supporting ions and carrying drugs. Yao et al. [90] first prepared a TiO_2 nanotube structure with a diameter of about 80 nm and a length of about 200 nm on the surface of titanium substrate by anodic oxidation, and then deposited penicillin and calcium phosphate simultaneously in TiO_2 nanotubes by co-precipitation method. Osteoblast adhesion experiments showed that the TiO_2 nanotube structure on the surface of titanium matrix significantly promoted the adhesion and differentiation of osteoblasts. The results of drug release study showed that the TiO_2 nanotube structure on the surface of titanium matrix could release drug molecules for about 3 weeks, and had a significant antibacterial effect. Wang et al. [91] first prepared TiO_2 nanotube structure with a diameter of about 80 nm and a length of about 2 microns on the surface of titanium substrate by anodic oxidation method, and then introduced copper and magnesium ions into TiO_2 nanotubes by hydrothermal treatment. The results of wettability experiments showed that the hydrophilicity of TiO_2 nanotube structure loaded with Cu and Mg ions on the surface of titanium substrate was significantly improved compared with that of TiO_2 nanotube structure without loaded ions, and the contact angle decreased from 91.7° to 58.8°. The results of antibacterial experiments showed that the TiO_2 nanotube structure loaded with ions could significantly inhibit the growth of Escherichia coli and Staphylococcus aureus. Savoji et al. [92] prepared TiO_2 nanotube arrays that could support ions by anodic oxidation. The experimental results showed that TiO_2 nanotube arrays loaded with Ag, Cu and Sr plasma could be used as antibacterial agents for continuous release of antibacterial drugs in organisms. It is possible to achieve intelligent release by controlling the temperature and pH value of electrolyte solution. Chen et al. [93] first processed TiAg thin films on the surface of titanium alloy by magnetron sputtering technology, and then prepared TiO_2 nanotube arrays loaded with Ag ions by anodic oxidation. It was found that the structure still kept good antibacterial activity and osseointegration after loading for 60 hours. Zhao et al. [94] fabricated TiO_2 nanotube structures on the surface of titanium alloy by anodic oxidation, and then implanted Si ions inside the nanotubes by plasma injection technology to prepare TiO_2 nanotube structures loaded with Si ions. After two weeks of culture in rat femur, it was found that the binding strength of nanotubes loaded with Si ions to bone tissue was increased by 54% compared with TiO_2 nanotubes. Popat et al. [95] fabricated a TiO_2 nanotube structure with a diameter of 80 nm and a length of 400 nm on the surface of titanium alloy by anodic oxidation, as shown in Figure 24. The release rate of gentamicin and its effect on epidermal adhesion of Staphylococcus aureus were studied by loading gentamicin 200, 400 and 600 μg into TiO_2 nanotube. The results showed that the drug-loaded nanotube structure had strong antibacterial and osteogenic properties. In addition, it is able to load drugs with different qualities and control their release rate by varying the length and diameter of the nanotubes.

Metal 3D printing technology can not only produce titanium alloy implants with complex structure, but also form porous structures on the surface of implants that are conducive to improving the osseointegration, which has been widely used in medical implant manufacturing in recent years [96]. Laser selective melting (SLM) and electronic melting (SEBM) are two of the most commonly used metal 3D printing technologies for machining porous structures.

Molinari et al. [97] fabricated porous titanium alloy implants with porosity ranging from 47.8% to 82.6% by using SLM technology, and mechanical properties and cell adhesion tests were carried out. The experimental results showed that porous titanium implants with porosity between 65% and 75% had the best strength and osseointegration. Zaharin et al. [98] used SLM technology to fabricate porous titanium alloy implants with porosity ranging from 57.48% to 79.36%. It was found that, the mechanical properties of implants were close to natural bone when the porosity was approximately 70%. Pei et al. [39], combined with computer-aided design, fabricated the bionic porous titanium implant with tetrahedral shape by using laser selective melting technology, as shown in Figure 25. The pores on the surface of the implant were evenly distributed and the pore size was about 630 μm, which could effectively promote cell adhesion and host bone tissue embedding.

Zhang et al. [99] used SEBM technology to fabricate porous titanium alloy with porosity ranging from 61.44% to 79.65%, and found that its elastic modulus was lower approximately 91% to 96% than that of dense titanium alloy, and its surface had good osseointegration. Warnke et al. [100] used SLM technology to fabricate porous titanium alloy implants with pore sizes of 0.45 to 1.2 mm. Osteoblast culture experiments in vitro showed that osteoblasts on the surface of implants grew the most vigorously when the pore size was 0.5 to 0.6 mm, and could fill the entire pore. When the pore size was greater than 0.7 mm, the number of osteoblasts on its surface began to decrease. Taniguchi et al. [101] prepared porous structural implants with pore sizes of 0.3 to 0.9 mm by using SLM technology. After implantation in rabbits for a

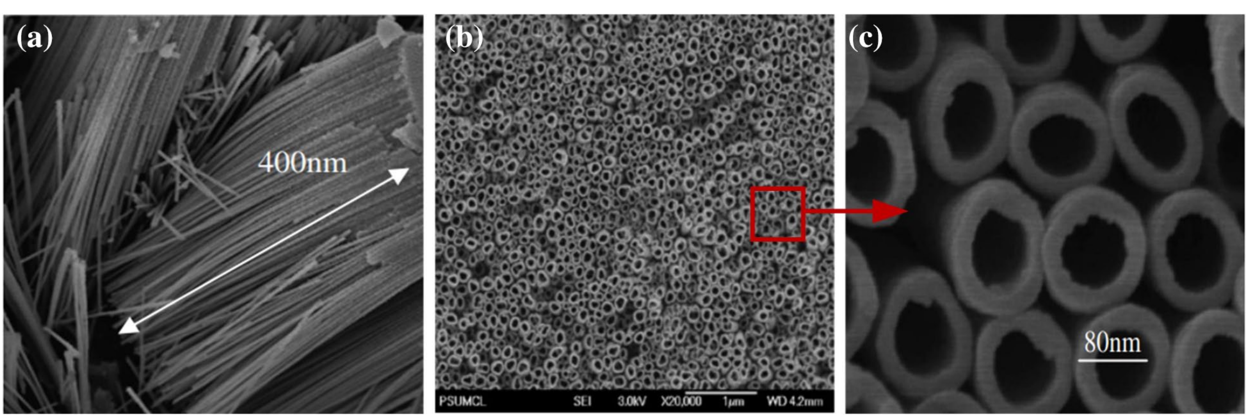

Figure 24 Structure of TiO_2 nanotubes prepared by anodic oxidation [95]: (**a**) Fracture surface of TiO_2 nanotube sample, (**b**) TiO_2 nanotubes at low magnification, and (**c**) TiO_2 nanotubes at high magnification

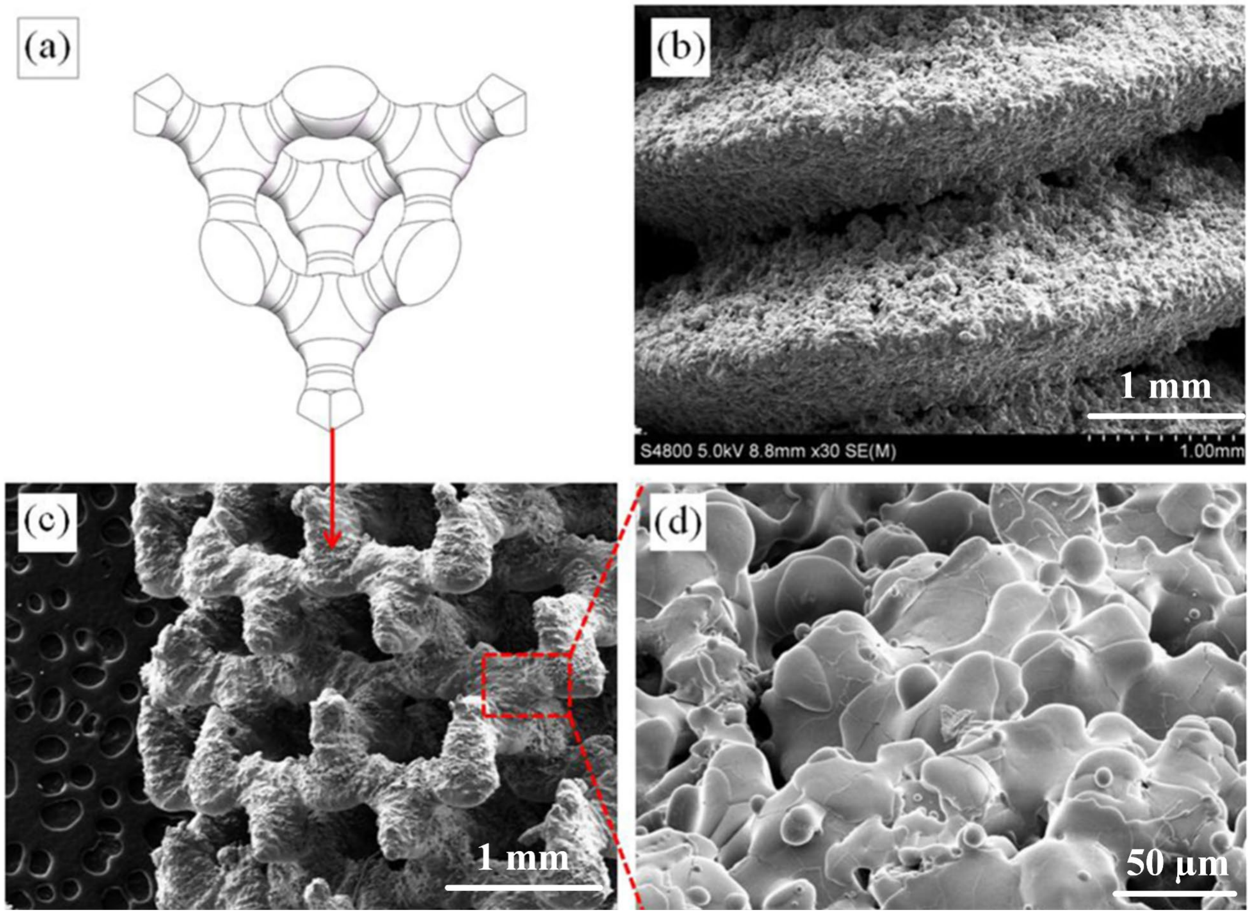

Figure 25 Tetrahedral porous structure prepared by 3D printing technology [39]: (**a**) CAD model of basic pore unit, (**b**) SEM photo of screw section of prosthesis, (**c**) Cutaway view of pores, and (**d**) Porous structure

period of time, it was found that compared with porous implants with diameters of 0.3 mm and 0.9 mm, the porous implants with a diameter of 0.6 mm were more conducive to the growth of bone tissue and had stronger binding ability with bone tissue.

As the above review reveals, the TiO_2 nanotubes prepared by anodic oxidation on the surface of implants have micro/nano composite structure, which is similar to the natural bone. It has a significant effect on the adsorption of protein and the proliferation and differentiation of osteoblasts due to larger surface area, higher hydrophilicity and surface energy. TiO_2 nanotubes, as nanomaterial with multidimensional regulatory capabilities, can regulate the osseointegration process by adjusting the diameter, length and thickness. However, current research mainly focus on the influence of diameter, and the researches on other parameters are obviously insufficient. In addition, TiO_2 nanotubes are prepared on smooth titanium surfaces in most current studies, but there are still challenges in the preparation of TiO_2 nanotubes on surfaces of threaded or irregular morphology. Metal 3D printing technology can prepare porous implants with complex structures, and is suitable for the development of medical implants in the future. Blood vessels and bone growth can be induced in the internal space of the porous structure, which is conducive to the interlocking between the tissue and the implant. Besides, elastic modulus of implant can be adjusted by porous structure to reduce stress shielding. However, molten particles may remain on the surface of the implant, resulting in allergic reactions after implantation. The high production cost also limits the further development and large-scale application of implant 3D printing technology. The characteristics and processing methods of various surface functional structures of titanium alloy implants are summarized in Table 2.

The wettability of titanium and titanium alloy implants plays an important role in protein adsorption, osteoblast proliferation and differentiation [102]. To a certain extent, high wettability can promote

Table 2 The characteristics and processing methods of various surface functional structures

Structure type	Processing methods	Advantages	Disadvantages	Application
Coating structures	Plasma spraying	High binding strength and good abrasion resistance	Expensive carrier gas and low spray rate	Tooth root implants, joint implants
	Magnetron sputtering	Fast deposition speed and good uniformity	High anode consumption and high demand for gas ionization rate	Tooth root implants, joint implants
	Micro-arc oxidation	Uniform coating, high bonding strength, large aperture	Uncontrollable coating thickness	Tooth root implants, joint implants
Regular structures	Laser processing	Fast processing speed, small deformation, with secondary structure	Expensive equipment and uneven energy	Tooth root implants, joint implants
	Micro milling	High processing accuracy, good operability, surface rules	High equipment and maintenance costs	Tooth root implants
	Turning	Low cost, high efficiency	Unable to turn the complex curved body	Tooth root implants
Porous structures	Chemical etching	High processing efficiency, no stress, simple operation	Chemical solution pollutes the environment	Tooth root implants, vascular stents
	Anodic oxidation	High hardness, good wear resistance, and strong adsorption capacity	High cost, low efficiency, small aperture	Tooth root implants, vascular stents
	Metal 3D Printing	Free forming, low cost, loose and porous surface	Powder particle dissociation leads to infection and failure	Joint implants, vascular stents

the biocompatibility of titanium and titanium alloy implants. Functional structure can be fabricated on the surface of implants to improve the hydrophilic properties, thereby increasing the capillary force and prompting the implant surface wetting of tissue fluid. According to Wenzel [103] model formula, for hydrophilic surfaces, the greater the degree of surface roughness, the smaller the contact angle of the surface, and the better the surface hydrophilicity [104]. Figure 26 summarizes the contact angles of three types of surface functional structures on the surface of titanium and titanium alloy implants. The average contact angles

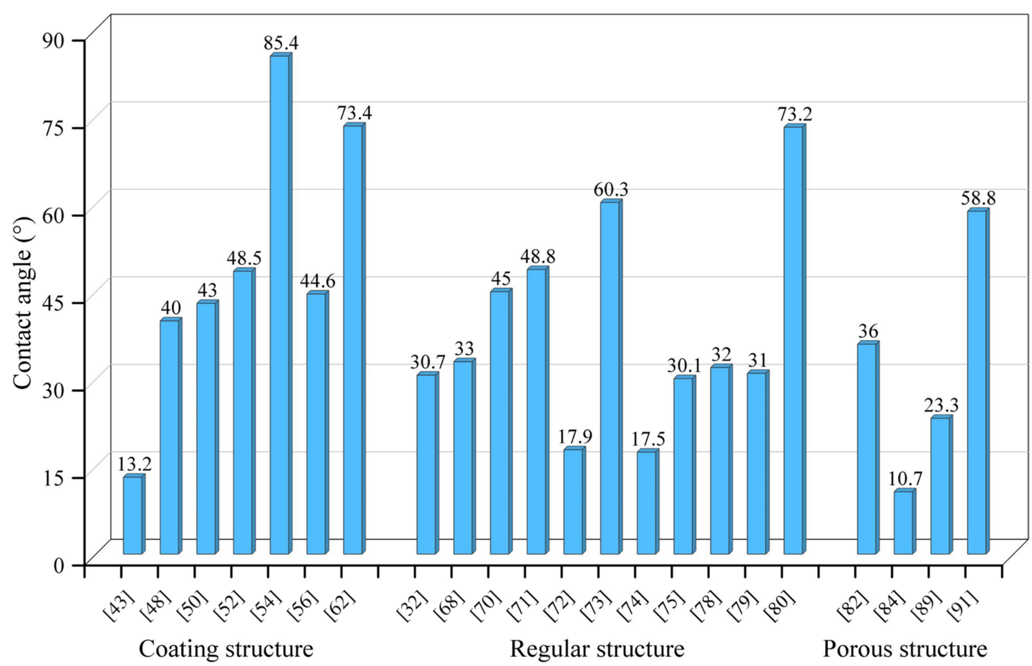

Figure 26 Contact angle of various surface functional structures

of coating structure, regular structure and porous structure are 49.7°, 38.1°and 31°, respectively. Compared with coating structure and regular structure, porous structure on implant surfaces provides more micro/nano composite interfaces, resulting in higher roughness and better hydrophilicity. However, the mechanical strength of implants is inevitably weakened by internal pores, which is not conducive to long-term implantation. The coating structure has relatively lower hydrophilicity but better flexibility, in which different biological needs of implants can be satisfied by certain functional elements. In addition, the regular structure possesses good biocompatibility due to the synergistic effect of biomechanical properties and hydrophilicity.

Alkaline phosphatase (ALP) activity measurement is mainly used to detect the differentiation of osteoblasts and cell viability. Figure 27 summarizes the ALP activity enhancement ratio of three types of surface functional structures on implants compared with polished titanium samples. The average ALP activity enhancement ratios of coating structure, regular structure and porous structure were 1.92, 1.68 and 1.44, respectively. In general, these three types of surface functional structures on the surface of titanium and titanium alloy implants significantly promote osteoblast differentiation compared with polished titanium samples. Besides, the bone growth and the repair of the defect tissue can be stimulated by doping functional elements, resulting in higher biological activity of coating structure.

5 Conclusions and Recommendations

With the aging of the population, the increase of bone cancer and the frequent occurrence of traffic accidents, the demand for titanium and titanium alloy implants is increasing, and higher requirements are put forward for the functional structure of the surface. The surface functional structures of titanium and titanium alloy implants include coating structure, regular structure and porous structure. The early osseointegration of implants and bone tissue can be accelerated due to the high biological activity of coating structure, but its long-term stability is limited by the relatively weak bonding strength with titanium matrix. This shortcoming can be compensated by the regular structure for its good biomechanical properties and contact guidance ability, which increases the mechanical interlocking with tissues and improves the long-term stability of implants. Compared with the coating structure and the regular structure, the porous structure provides extra contact area and better wettability. Besides, specific functions can be implemented by porous structure including carrying antibacterial drugs and reducing stress shielding. However, the strength of porous structure implants is easily affected by the internal pores. The prepared surface functional structure should comprehensively consider the functions of biological activity, bonding strength and antibacterial properties due to the complexity of the human environment. With the rapid development of surface functional structure manufacturing technology, titanium and titanium alloy implants with a single surface functional structure

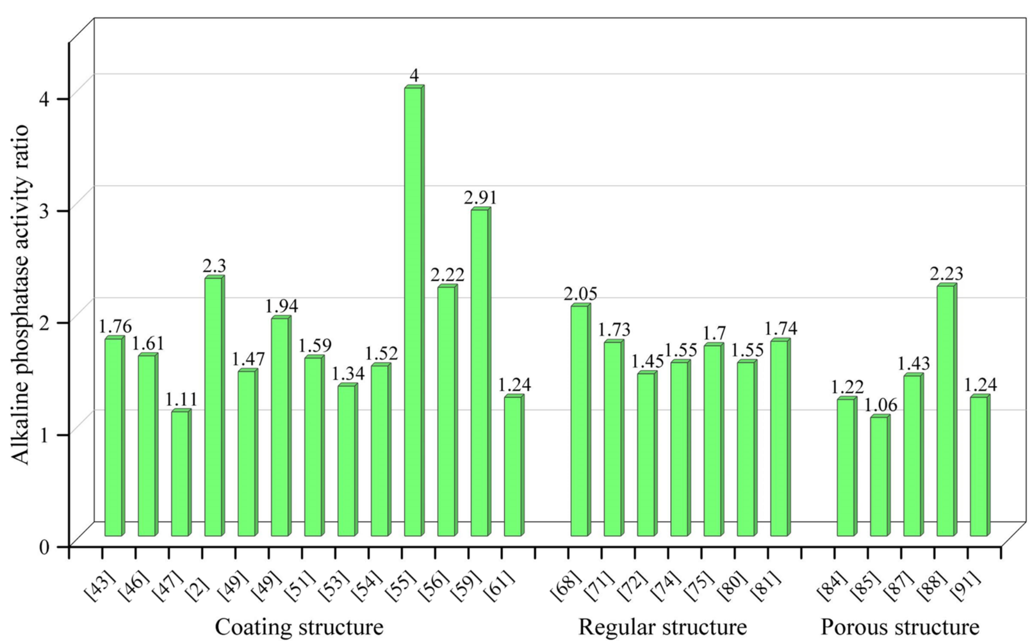

Figure 27 Different types of surface functional structure ALP activity enhancement ratio

are no longer suitable for complex human implantation environments. The preparation of implants with multi-functional structural surfaces has gradually become the main research direction in the future. Combined with the current research status and demand characteristics of the surface functional structure of titanium and titanium alloy implants, the following aspects can be studied in the future:

(1) Natural bone is composed of micron-scale bone plate and nano-scale collagen fiber. In the manufacturing of bionic bone structures, the fabrication of micro/nano two-stage structures is conducive to obtaining good biocompatibility. However, due to the limitations of current manufacturing technology, it is difficult to fabricate structures with micro-scale and nano-scale at the same time, which needs to be further expanded in future research.
(2) At present, researches on the surface functional structures of implants mainly focuses on the single osteogenic or antibacterial property, while there are few researches on the micro/nano two-stage composite structures with both properties, which need to be further studied.
(3) With the continuous development of metal 3D printing technology, the fabrication of titanium alloy implants using the metal 3D printing technology is the focus of future research. However, the surface quality of implants fabricated by 3D printing is difficult to guarantee due to lots of molten particles formed on the surface. Therefore, the surface of implants can be treated with chemical etching, electrochemical processing and other methods to remove molten particles, improving the surface biocompatibility of implants.
(4) Stress shielding is an important problem in biomedical implantation, which is caused by the different elastic modulus between implants and bone tissue. The elastic modulus of commonly used titanium alloy implants is higher than that of bone tissue, it is easy to cause stress shielding phenomenon after implantation, resulting in shedding of implants. Although the titanium alloy implants with elastic modulus close to natural bone tissue can be fabricated by metal 3D printing technology through adjusting its porosity, larger porosity will affect the strength of implants. Therefore, how to make the elastic modulus of titanium alloy implants closer to bone tissue under the condition of ensuring the strength is the focus of future research.
(5) With the development of biomaterials, protein materials have also been applied to implant coating for their higher biocompatibility. Protein coating can reduce the rejection reaction between implants and human tissue, accelerating the adhesion and proliferation of new cells. However, it cannot withstand the high temperature and high pressure during the preparation process. Therefore, how to fabricate stable and reliable protein coating will be a hotspot of future research.
(6) The durability of surface functional structures on titanium and titanium alloy implants should be improved. The surface functional structure of the implant may gradually fail with increasing working time, leading to implantation failure. Therefore, more attention needs to be paid to durability when designing the surface functional structure on implants.

Acknowledgements
Not applicable.

Author contributions
HT, JX and YL contributed to conceptualization; HT and YS provided methodology; BG, JX and YX performed investigation; HT, BG and JX performed writing original draft; all authors performed writing review and editing; HT and YT contributed to funding acquisition; YT performed supervision. All authors read and approved the final manuscript.

Funding
Supported by National Natural Science Foundation of China (Grant Nos. 52235011, 51905352), Shenzhen Municipal Excellent Science and Technology Creative Talent Training Program (Grant No. RCBS20210609103819021), Guangdong Provincial Basic and Applied Basic Research Foundation (Grant No. 2023B1515120086), and Shenzhen Municipal Science and Technology Planning Project (Grant No. CJGJZD20230724093600001).

Availability of Data and Materials
All data generated or analyzed during this study are included in this published article.

Declarations

Competing Interests
The authors declare no competing financial interests.

Received: 28 November 2023 Revised: 25 June 2024 Accepted: 27 June 2024
Published online: 05 August 2024

References
[1] www.qianzhan.com/analyst/detail/220/210105-8c76dc30.html.
[2] D Ke, A A Vu, A Bandyopadhyay, et al. Compositionally graded doped hydroxyapatite coating on titanium using laser and plasma spray deposition for bone implants. *Acta Biomaterialia,* 2019, 84: 414-423.
[3] H Chouirfa, H Bouloussa, V Migonney, et al. Review of titanium surface modification techniques and coatings for antibacterial applications. *Acta Biomaterialia*, 2019,83: 37-54.
[4] M Kaur, K Singh. Review on titanium and titanium based alloys as biomaterials for orthopaedic applications. *Materials Science and Engineering C-Materials for Biological Applications*, 2019, 102: 844-862.
[5] E Zhang, X T Zhao, J I Hu, et al. Antibacterial metals and alloys for potential biomedical implants. *Bioactive Materials*, 2021, 6(8): 2569–2612.

[6] R Shi, J Zhang, J Tian, et al. An effective self-powered strategy to endow titanium implant surface with associated activity of anti-biofilm and osteogenesis. *Nano Energy,* 2020, 77: 105-201.

[7] B L Tao, W K Zhao, C C Lin, et al. Surface modification of titanium implants by ZIF-8@Levo/LBL coating for inhibition of bacterial-associated infection and enhancement of in vivo osseointegration. *Chemical Engineering Journal,* 2020, 390: 124621.

[8] T Albrektsson, A Wennerberg. On osseointegration in relation to implant surfaces. *Clinical Implant Dentistry and Related Research,* 2019, 21: 4-7.

[9] X Y Zhang, G N Zhang, M Z Chai, et al. Synergistic antibacterial activity of physical-chemical multi-mechanism by TiO_2 nanorod arrays for safe biofilm eradication on implant. *Bioactive Materials,* 2021,6(1): 12-25.

[10] J C M Souza, M B Sordi, M Y Kanazawa, et al. Nano-scale modification of titanium implant surfaces to enhance osseointegration. *Acta Biomaterialia,* 2019, 94: 112–131.

[11] B Rena, Y Wana, C Liuc, et al. Improved osseointegration of 3D printed Ti-6Al-4V implant with a hierarchical micro/nano surface topography: An in vitro and in vivo study. *Materials Science and Engineering C-Materials for Biological Applications,* 2021, 118: 111505.

[12] R Wang, M Shi, F Y Xu, et al. Graphdiyne-modified TiO_2 nanofibers with osteoinductive and enhanced photocatalytic antibacterial activities to prevent implant infection. *Nature Communications,* 2020, 11(1): 4465.

[13] Y L Sun, Y Tang, S W Zhang, et al. A review on fabrication and pool boiling enhancement of three-dimensional complex structures. *Renewable and Sustainable Energy Reviews*, 2022 162: 112437.

[14] Y L Sun, H M Li, J Y Chen, et al. Hierarchical sintered porous surfaces with enhanced pool boiling heat transfer performance for high-power cooling applications. *Applied Thermal Engineering,* 2024, 249: 123368.

[15] P Wang, X W Li, S M Luo, et al. Additively manufactured heterogeneously porous metallic bone with biostructural functions and bone-like mechanical properties. *Journal of Materials Science and Technology,* 2020, 62: 173-179.

[16] J Lin, J T Hu, W Wang, et al. Thermo and light-responsive strategies of smart titanium-containing composite material surface for enhancing bacterially anti-adhesive property. *Chemical Engineering Journal,* 2020, 407: 125783.

[17] L Yuan, S Ding, C Wen. Additive manufacturing technology for porous metal implant applications and triple minimal surface structures: A review. *Bioactive Materials,* 2019, 4: 56-70.

[18] C L Tan, C Deng, S Li, et al. Mechanical property and biological behaviour of additive manufactured TiNi functionally graded lattice structure. *International Journal of Extreme Manufacturing,* 2022, 4(4): 045003.

[19] H Ito, K Kaneda, T Yuhta, et al. Reduction of polyethylene wear by concave dimples on the frictional surface in artificial hip joints. *International Journal of Nanomedicine,* 2000, 15(3): 332-338.

[20] B Sagbas, M N Durakbasa. Effect of surface patterning on frictional heating of vitamin E blended UHMWPE. *Wear,* 2013(1-2), 303: 313-320.

[21] M Tarabolsi, T Klassen, F Mantwill, et al. Patterned CoCrMo and Al_2O_3 surfaces for reduced free wear debris in artificial joint arthroplasty. *Journal of Biomedical Materials Research Part A,* 2013,101(12): 3447-3456.

[22] A S Alagl, M Madi, S Bedi, et al. The effect of er, Cr: YSGG and diode laser applications on dental implant surfaces contaminated with acinetobacter baumannii and pseudomonas aeruginosa. *Materials,* 2019, 12(13): 2073.

[23] A I Nicolas-Silvente, E Velasco-Ortega, I Ortiz-Garcia, et al. Influence of the titanium implant surface treatment on the surface roughness and chemical composition. *Materials,* 2020, 13(2): 314.

[24] R Wessely, J Hausleiter, C Michaelis, et al. Inhibition of neointima formation by a novel drug-eluting stent system that allows for dose-adjustable, multiple, and on-site stent coating. *Arteriosclerosis Thrombosis and Vascular Biology,* 2005, 25(4): 748-753.

[25] S Borhani, S Hassanajili, S H Ahmadi, et al. Cardiovascular stents: overview, evolution, and next generation. *Progress in Materials Science,* 2018, 7: 175-205.

[26] J W Park, C A Song, H G Kang, et al. Integration of a three-dimensional-printed titanium implant in human tissues: case study. *Applied Sciences-Basel,* 2020, 10(2): 553.

[27] G Vigano, G H Ten Brink, M Groenendijk, et al. Laser texturing of a st. jude medical regent TM mechanical heart valve prosthesis: the proof of concept. *Interactive Cardiovascular and Thoracic Surgery,* 2021, 33(6): 986-991.

[28] M P Prabhakaran, J Venugopal, S Ramakrishna. Electrospun nanostructured scaffolds for bone tissue engineering. *Acta Biomaterialia,* 2009, 5(8): 2884-2893.

[29] P Huang, H Li, W Zhu, et al. Effects of eco-friendly cooling strategy on machining performance in micro-scale diamond turning of Ti–6Al–4V. *Journal of Cleaner Production,* 2020, 243: 118526.

[30] S Filiz, L Xie, L E Weiss, et al. Micromilling of microbarbs for medical implants. *International Journal of Machine Tools and Manufacture,* 2008, 48(3-4): 459-472.

[31] K Anselme, P Linez, M Bigerelle, et al. The relative influence of the topography and chemistry of TiAl6V4 surfaces on osteoblastic cell behaviour. *Biomaterials,* 2000, 21(15): 1567-1577.

[32] S A Sajjady, M Lotfi, S Amini, et al. Improving the surface energy of titanium implants by the creation of hierarchical textures on the surface via three-dimensional elliptical vibration turning for enhanced osseointegration. *Proceedings of the Institution of Mechanical Engineers Part H-Journal of Engineering in Medicine,* 2019, 233(12): 1226-1236.

[33] B Kim, J S Kim, Y M Park, et al. Mg ion implantation on SLA-treated titanium surface and its effects on the behavior of mesenchymal stem cell. *Materials Science and Engineering C-Materials for Biological Applications,* 2013, 33(3): 1554-1560.

[34] R Smeets, B Stadlinger, F Schwarz, et al. Impact of dental implant surface modifications on osseointegration. *Biomed Research International,* 2016, 16: 6285620.

[35] Y Lian, X Dai, J Zhang. Characterization of micro-arc oxidation coatings on Ti6Al4V with addition of SiC particle. *Materials Research Express,* 2020,7(1): 016438.

[36] A Y Fasasi, S Mwenifumbo, N Rahbar, et al. Nano-second UV laser processed micro-grooves on Ti6Al4V for biomedical applications. *Materials Science and Engineering C-Materials for Biological Applications,* 2009, 29(1): 5-13.

[37] L Guehennec, A Soueidan, P Layrolle, et al. Surface treatments of titanium dental implants for rapid osseointegration. *Dental Materials,* 2007, 23(7): 844-854.

[38] S Rodil, P Silva-Bermudez, A Almaguer-Flores, et al. Biomedical coatings prepared by magnetron sputtering. *Frontiers in Bioengineering and Biotechnology,* 2016, 1: 01672.

[39] X Pei, B Zhang, Y Fan, et al. Bionic mechanical design of titanium bone tissue implants and 3D printing manufacture. *Materials Letters,* 2017, 208: 133-137.

[40] M Regis, E Marin, L Fedrizzi, et al. Additive manufacturing of trabecular titanium orthopedic implants. *Mrs Bulletin,* 2015, 40(2): 137-144.

[41] Z Yuan, B Tao, Y He, et al. Remote eradication of biofilm on titanium implant via near-infrared light triggered photothermal/photodynamic therapy strategy. *Biomaterials,* 2019, 223: 119479.

[42] Z Q Gao, J Yin, P Liu, et al. Simultaneous multi-material embedded printing for 3D heterogeneous structures, *International Journal of Extreme Manufacturing,* 2023, 5(3): 035001.

[43] R J Lu, X Wang, H X He, et al. Tantalum-incorporated hydroxyapatite coating on titanium implants: its mechanical and in vitro osteogenic properties. *Journal of Materials Science-Materials in Medicine,* 2019, 30(10): 111.

[44] Z S Tao, B L Bai, X W He, et al. A comparative study of strontium-substituted hydroxyapatite coating on implant's osseointegration for osteopenic rats. *Medical Biological Engineering Computing,* 2016, 54(12): 1959–1968.

[45] X D Li, Y F Li, Y L Liao, et al. The effect of magnesium-incorporated hydroxyapatite coating on titanium implant fixation in ovariectomized rats. *International Journal of Molecular Sciences,* 2014, 29(1): 196-202.

[46] Z Y Zhong, J Ma. Fabrication, characterization, and in vitro study of zinc substituted hydroxyapatite/silk fibroin composite coatings on titanium for biomedical applications. *Journal of Biomaterials Applications,* 2017, 32: 399-409.

[47] W W Lou, Y W Dong, H L Zhang, et al. Preparation and characterization of lanthanum-incorporated hydroxyapatite coatings on titanium substrates. *International Journal of Molecular Sciences,* 2015, 16(9): 21070-21086.

[48] A A Vu, S F Robertson, D Ke, et al. Mechanical and biological properties of ZnO, SiO_2, and Ag_2O doped plasma sprayed hydroxyapatite coating

for orthopaedic and dental applications. *Acta Biomaterialia,* 2019, 92: 325-335.

[49] Y Huang, G Song, X Chang, et al. Nanostructured Ag^{+}-substituted fluorhydroxyapatite-TiO_2 coatings for enhanced bactericidal effects and osteoinductivity of Ti for biomedical applications. *International Journal of Nanomedicine,* 2018, 13: 2665-2684.

[50] B Kang, D Lan, C Yao, et al. Evaluation of antibacterial property and biocompatibility of Cu doped TiO_2 coated implant prepared by micro-arc oxidation. *Frontiers in Bioengineering and Biotechnology,* 2022, 10: 941109.

[51] Q Zhao, X Li, S Guo, et al. Osteogenic activity of a titanium surface modified with silicon-doped titanium dioxide. *Materials Science and Engineering C-Materials for Biological Applications,* 2020, 110: 110682.

[52] B B Kang, D M Lan, L Liu, et al. Antibacterial activity and bioactivity of Zn-Doped TiO_2 coating for implants. *Coatings,* 2022, 12(9): 1264.

[53] B P Zhang, B Li, S T Gao, et al. Y-doped TiO_2 coating with superior bioactivity and antibacterial property prepared via plasma electrolytic oxidation. *Materials and Design,* 2020, 192: 108758.

[54] X X Zhang, Y Lv, F Shan, et al. Microstructure, corrosion resistance, osteogenic activity and antibacterial capability of Mn-incorporated TiO_2 coating. *Applied Surface Science,* 2020, 531: 147399.

[55] J H Zhou, B Li, Y Han. F-doped TiO_2 microporous coating on titanium with enhanced antibacterial and osteogenic activities. *Scientific Reports,* 2018, 8: 17858.

[56] J H Zhou, L Z Zhao. Hypoxia-mimicking Co doped TiO_2 microporous coating on titanium with enhanced angiogenic and osteogenic activities. *Acta Biomaterialia,* 2016, 43: 358–368.

[57] L Sopchenskia, S Cogob, M F Dias-Ntipanyjb, et al. Bioactive and antibacterial boron doped TiO_2 coating obtained by PEO. *Applied Surface Science.* 2018, 458: 49–58.

[58] T Yetim. An investigation of the corrosion properties of Ag-doped TiO_2-coated commercially pure titanium in different biological environments. *Surface & Coatings Technology,* 2017, 309: 790–794.

[59] Q Zhao, L Yi, L Jiang, et al. Surface functionalization of titanium with zinc/strontium-doped titanium dioxide microporous coating via micro-arc oxidation. *Nanomedicine-Nanotechnology Biology and Medicine,* 2019, 16: 149-161.

[60] R Y Wang, X J He, Y Gao, et al. Antimicrobial property, cytocompatibility and corrosion resistance of Zn-doped ZrO_2/TiO_2 coatings on Ti6Al4V implants. *Materials Science and Engineering C,* 2017, 75: 7–15.

[61] Y Lv, G Y Cai, X X Zhang, et al. Microstructural characterization and in vitro biological performances of Ag, Zn co-incorporated TiO_2 coating. *Ceramics International,* 2020, 46(18): 29160–29172.

[62] Q M. Zhao, J S Wu, Y K Li, et al. Promotion of bone formation and antibacterial properties of titanium coated with porous Si/Ag-doped titanium dioxide. *Frontiers in Bioengineering and Biotechnology,* 2022, 10: 1001514.

[63] X J He, G N Zhang, H Y Zhang, et al. Cu and Si co-doped microporous TiO_2 coating for osseointegration by the coordinated stimulus action. *Applied Surface Science,* 2020, 503: 144072.

[64] F Lüthen, R Langeb, P Beckerc, et al. The influence of surface roughness of titanium on β1- and β3-integrin adhesion and the organization of fibronectin in human osteoblastic cells. *Biomaterials,* 2005, 26(15): 2423-2440.

[65] M Zamani, M Farahnakian, S Elhami. Employment of ultrasonic assisted turning in the fabrication of microtextures to improve the surface adhesion of the titanium implant. *Proceedings of the Institution of Mechanical Engineers Part B-Journal of Engineering Manufacture,* 2021, 235(12): 1-9.

[66] K Sugioka. Hybrid femtosecond laser three-dimensional micro-and nanoprocessing: a review. *International Journal of Extreme Manufacturing,* 2019, 1(1): 012003.

[67] E Conserva, U Consolo, P Bellini. Adhesion and proliferation of human dental pulp stem cells on a laser microtextured implant surface: an in vitro study. *Oral Health and Care,* 2018, 3(4): 1-6.

[68] C Wang, H Hu, Z Li, et al. Enhanced osseointegration of titanium alloy implants with laser microgrooved surfaces and graphene oxide coating. *ACS Applied Materials and Interfaces,* 2019, 11(43): 39470-39483.

[69] V Veiko, Y Karlagina, T Itina, et al. Laser-assisted fabrication and in vitro verification of functionalized surface for cells biointegration. *Optics and Laser Technology,* 2021, 138: 106871.

[70] Q C Zheng, L L Mao, Y T Shi, et al. Biocompatibility of Ti-6Al-4V titanium alloy implants with laser microgrooved surfaces. *Materials Technology Advanced Performance Materials,* 2022, 37(12): 2039–2048.

[71] Y Sun, J Sun, X Wu, et al. Mechanism of zirconia microgroove surface structure for osseointegration. *Materials Today Advances,* 2021, 12: 100159.

[72] T Wang, Y Wan, Z Liu. Effects of superimposed micro/nano-structured titanium alloy surface on cellular behaviors in vitro. *Advanced Engineering Materials,* 2016, 18(7): 1259-1266.

[73] Y Wan, T Wang, Z Wang, et al. Construction and characterization of micro/nano-topography on titanium alloy formed by micro-milling and anodic oxidation. *International Journal of Advanced Manufacturing Technology,* 2018, 98(1-4): 29-35.

[74] G Wang, Y Wan, B Ren, et al. Bioactivity of micropatterned TiO_2 nanotubes fabricated by micro-milling and anodic oxidation. *Materials Science and Engineering C-Materials for Biological Applications,* 2019, 95: 114-121.

[75] V Dumas, A Guignandon, L Vico, et al. Femtosecond laser nano/micro patterning of titanium influences mesenchymal stem cell adhesion and commitment. *Biomedical Materials,* 2015, 10(5): 055002.

[76] R Zhang, Y Wan, X Ai, et al. Preparation of micro-nanostructure on titanium implants and its bioactivity. *Transactions of Nonferrous Metals Society of China,* 2016, 26(4): 1019-1024.

[77] R Zhang, Y Wan, X Ai, et al. Fabrication of micro/nano-textured titanium alloy implant surface and its influence on hydroxyapatite coatings. *Journal of Wuhan University of Technology-Mater. Sci. Ed,* 2016, 31(2): 440-450.

[78] C Zwahr, R Helbig, C Werner, et al. Fabrication of multifunctional titanium surfaces by producing hierarchical surface patterns using laser-based ablation methods. *Scientific Reports,* 2019, 9(1): 6721.

[79] X Lin, X Li, G Li, et al. Micro-dot-matrix induced by femtosecond laser on titanium surface for Ca-P phase deposition. *Applied Surface Science,* 2020, 499: 143925.

[80] G S Wang, Y Wan, Z Q Liu. Construction of complex structures containing micro-pits and nano-pits on the surface of titanium for cytocompatibility improvement. *Materials,* 2019, 12(17): 2820.

[81] Y M Zhang, X K Wang, Y X Li, et al. Cell osteogenic bioactivity mediated precisely by varying scaled micro-pits on ordered micro/nano hierarchical structures of titanium. *Regenerative Biomaterials,* 2022, 9: rbac046.

[82] M Mansoorianfar, M Tavoosi, R Mozafarinia, et al. Preparation and characterization of TiO_2 nanotube arrays on Ti6Al4V surface for enhancement of cell treatment. *Surface and Coatings Technology,* 2017, 321: 409-415.

[83] J Park, S Bauer, K Mark, et al. Nanosize and vitality: TiO_2 nanotube diameter directs cell fate. *Nano Letters,* 2007, 7(6): 1686-1691.

[84] F Wang, C Li, S Zhang, et al. Tantalum coated on titanium dioxide nanotubes by plasma spraying enhances cytocompatibility for dental implants. *Surface and Coatings Technology,* 2020, 382: 125161.

[85] X J Zhao, L N You, T Wang, et al. Enhanced osseointegration of titanium implants by surface modification with silicon-doped titania nanotubes. *International Journal of Nanomedicine,* 2020, 15: 8583–8594.

[86] X C Hu, R G Xu, X L Yu, et al. Enhanced antibacterial efficacy of selective laser melting titanium surface with nanophase calcium phosphate embedded to TiO_2 nanotubes. *Biomedical Materials,* 2018, 13(4): 045015.

[87] H Zhao, W H Wang, F Liu, et al. Electrochemical insertion of zinc ions into self-organized titanium dioxide nanotube arrays to achieve strong osseointegration with titanium implants. *Advanced Materials Interfaces,* 2022, 9(16): 2200312.

[88] S Saha, K Pramanik, A Biswas. Silk fibroin coated TiO_2 nanotubes for improved osteogenic property of Ti6Al4V bone implants. *Materials Science & Engineering C,* 2019, 105: 109982.

[89] F Wang, L Shi, W X He, et al. Bioinspired micro/nano fabrication on dental implant–bone interface. *Applied Surface Science,* 2013, 265: 480-488.

[90] C Yao, T J Webster. Prolonged antibiotic delivery from anodized nanotubular titanium using a co-precipitation drug loading method. *Journal of Biomedical Materials Research Part B-Applied Biomaterials,* 2009, 91B(2): 587-595.

[91] B B Wang, Z Z Wu, S Wang, et al. Mg/Cu-doped TiO_2 nanotube array: A novel dual-function system with self-antibacterial activity and excellent cell compatibility. *Materials Science & Engineering C,* 2021, 128: 112322.

[92] M T Savoji, X X Zhu. Temperature- and pH-controlled encapsulation and release of guest molecules from invertible carriers. *Polymer,* 2015, 68: 35-40.
[93] Y Chen, A Gao, L Bai, et al. Antibacterial, osteogenic, and angiogenic activities of $SrTiO_3$ nanotubes embedded with Ag_2O nanoparticles. *Materials Science and Engineering C-Materials for Biological Applications,* 2017, 75: 1049-1058.
[94] X Zhao, T Wang, S Qian, et al. Silicon-doped titanium dioxide nanotubes promoted bone formation on titanium implants. *International Journal of Molecular Sciences,* 2016, 17(3): 292.
[95] K C Popat, M Eltgroth, T J LaTempa, et al. Decreased staphylococcus epidermis adhesion and increased osteoblast functionality on antibiotic-loaded titania nanotubes. *Biomaterials,* 2007, 28(32): 4880-4888.
[96] A N Chen, J Su, Y J Li, et al. 3D/4D printed bio-piezoelectric smart scaffolds for next-generation bone tissue engineering. *International Journal of Extreme Manufacturing,* 2023, 5(3): 032007.
[97] A Molinari, J Klarin, F Johansson. Mechanical properties of porous structures produced by selective laser melting of a Ti6AL4V alloy power. *Journal of the Japan Society of Powder and Powder Metallurgy,* 2018, 65(8): 481-485.
[98] H Zaharin, A Abdul Rani, F Azam, et al. Effect of unit cell type and pore size on porosity and mechanical behavior of additively manufactured Ti6Al4V scaffolds. *Materials,* 2018, 11(12): 2402.
[99] C Zhang, L Zhang, L Liu, et al. Mechanical behavior of a titanium alloy scaffold mimicking trabecular structure. *Journal of Orthopaedic Surgery and Research,* 2020, 15(1): 1489.
[100] P H Warnke, T Douglas, P Wollny, et al. Rapid prototyping: porous titanium alloy scaffolds produced by selective laser melting for bone tissue engineering. *Tissue Engineering Part C-Methods,* 2009, 15(2): 115-124.
[101] N Taniguchi, S Fujibayashi, M Takemoto, et al. Effect of pore size on bone ingrowth into porous titanium implants fabricated by additive manufacturing: An in vivo experiment. *Materials Science and Engineering C-Materials for Biological Applications,* 2016, 59: 690-701.
[102] Z J Jia, P Xiu, M Li, et al. Bioinspired anchoring AgNPs onto micro-nanoporous TiO_2 orthopedic coatings: Trap-killing of bacteria, surface-regulated osteoblast functions and host responses. *Biomaterials,* 2016, 75: 203-222.
[103] R N Wenzel. Resistance of solid surfaces to wetting by water, Industrial and engineering chemistry. *Industrial and Engineering Chemistry,* 1936, 28: 988-994.
[104] H Tang, J X You, Y Tang, et al. Pool boiling heat transfer performance of micro-embossing molds for the fabrication of polymer wicks. *Physics of Fluids,* 2024, 36(2): 023346.

Heng Tang born in 1989, he is currently an associate professor at *College of Mechatronics and Control Engineering, Shenzhen University, China*. His research interests include advanced manufacturing of surface functional structures and its mechanism.

Jiaxiang Xu born in 1998, he is currently a master candidate at *College of Mechatronics and Control Engineering, Shenzhen University, China*.

Bin Guo born in 1996, he is currently a master candidate at *College of Mechatronics and Control Engineering, Shenzhen University, China*.

Yansong Xie born in 1998, he is currently a master candidate at *College of Mechatronics and Control Engineering, Shenzhen University, China*.

Yalong Sun born in 1994, he is currently an assistant professor at *School of Mechanical and Power Engineering, Zhengzhou University, China*. His research interests include design and manufacturing of surface functional structures and its application.

Yanjun Lu born in 1987, he is currently an associate professor at *College of Mechatronics and Control Engineering, Shenzhen University, China*. His research interests include precision manufacture of micro-structure.

Yong Tang born in 1962, he is currently a professor at *College of Mechatronics and Control Engineering, Shenzhen University, China*. His research interests include manufacturing theory of surface functional structures; thermal control and packaging of semiconductor devices