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Biomedical titanium alloys and their additive manufacturing

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Abstract Titanium and its alloys have been widely used for biomedical applications due to their better biomechanical and biochemical compatibility than other metallic materials such as stainless steels and Co-based alloys. A brief review on the development of the β-type titanium alloys with high strength and low elastic modulus is given, and the use of additive manufacturing technologies to produce porous titanium alloy parts, using Ti–6Al–4V as a reference, and its potential in fabricating biomedical replacements are discussed in this paper.

Keywords Beta titanium alloys; High strength; Low elastic modulus; Additive manufacturing; Biomedical application

1 Introduction

About 90 % of the people above the age of 40 are afflicted with joint disease to different extent [1]. For patients suffering from arthritis, artificial implant fabricated from biomedical materials has helped to relieve much of the pain and improve their quality of life [2, 3]. All these treatments required orthopedic surgeries lead to an ever-increasing number of replacements [4]. Biomedical applications of materials are mainly based on the requirement of implants, which usually are used as different parts in human body, including heart valve prostheses, cardiac simulator, hip, knee, shoulder, elbow replacement prostheses, dental implants, intraocular lenses and stents [3, 5].

The ultimate goal of biomedical materials research is to achieve an implant which can last long time inside human body without failure or revision surgery [4, 6–8]. Of primary importance are properties of materials such as corrosion resistance in human body environment, high strength, low elastic modulus, good wear resistance and no cytotoxicity [3, 9–15]. So far, there are three common metals used for implants: stainless steel, Co-based alloys and titanium alloys [1, 16]. In particular, titanium alloys combine excellent mechanical properties in terms of low density, high strength, superior corrosion resistance, good biocompatibility and low modulus [3, 17, 18] and are of advantage in biomedical applications due to their great performance.

Commercially pure titanium (CP-Ti) and several alloys have been utilized as biomedical materials [4, 17, 19–23]. Although α + β-type Ti–6Al–4V is still the most commonly used [24–26], recent reports argued that V is toxic both in the elemental state and in the form of oxide, and there exists some correlation between V and Al ions released from the alloy and long-term health problems such as Alzheimer disease and neuropathy [27]. Moreover, Young's modulus of the alloy with a value of ~110 GPa is much too high to well match with surrounding bone with a modulus of less than ~30 GPa, thereby leading to the "stress-shielding" issue, one of the main origins of bone resorption and implant loosening [28–31]. It is therefore important to develop β-type titanium alloys with low elastic modulus and high strength [32–37].

Recently, the rapid growth of additive manufacturing (AM) technology adds another dimension to the development and manufacturing of implant [32–34]. Porous

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implants can be fabricated by AM systems directly without any machining procedure. Those implants have a series of advantages including low modulus, lightweight and the promotion of bone cell ingrowth [35]. In comparison with previous manufacturing methods, AM offers the advantages of accurate control of internal pore architectures and complex cell shapes, thus receiving extensive attention [36–38]. Till now, most of the reported AM systems employ selective laser melting (SLM) and electron beam melting (EBM). Both of them achieved high mechanical properties with multiple kinds of complex structure [35, 37, 39, 40]. The combination of AM technologies and the excellent properties of biomedical titanium materials would promote application in implants field [28]. In this paper, it is reviewed mainly the development of biomedical titanium alloys and their AM in terms of their performance as medical implants which require good mechanical and biocompatible properties.

2 Development of biomedical titanium alloys

Titanium and its alloys, which were pioneered in the late 1940s in the USA [41], have found wide application in aerospace, chemical and medical industries up to now [42–45]. The CP-Ti has good biocompatibility [46, 47], which allows its use as orthopedic and dental materials. However, its low strength, less than 500 MPa in general, limits wide applications. Although Ti–6Al–4V is the most frequently used titanium alloy in surgery, its elastic modulus is still much higher than that of bone tissue. To decrease modulus, many β-type titanium alloys composed of non-toxic and non-allergic elements have been developed [48].

The developments of β-type biomedical titanium alloys can be divided roughly into two stages. In the first, more attention is paid to explore the lowest limit of elastic modulus. As shown in Fig. 1, many new alloys developed

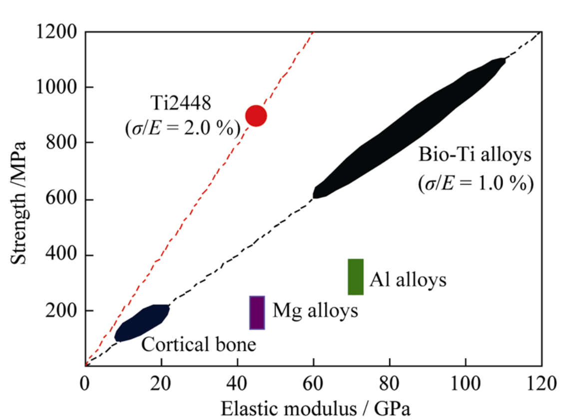

Fig. 1 Summary of developed β-type bio-Ti alloys: strength (σ) versus elastic modulus (E)

have lower modulus compared with Ti–6Al–4V. For example, Ti–13Nb–13Zr, Ti–15Mo and Ti–12Mo–6Zr–2Fe have modulus of ~80 GPa, while Ti–35Nb–5Ta–7Zr and Ti–29Nb–13Ta–4.6Zr developed more recently have modulus of ~60 GPa. The characteristic of this class of alloys is that with modulus decreasing, the strength decreases correspondingly (Fig. 1). This tendency is not unexpected from the principles of materials science which state that lower modulus corresponds to lower strength. The challenge of alloy development becomes how to improve strength while keeping the advantage of low modulus. Progress in this regard is expected to be very difficult because titanium alloys are much stronger than other metallic materials such as stainless steels and Al and Mg alloys (Fig. 1): their ratio of strength to modulus approaches ~1 %, about twice that of other metals.

In the second stage, efforts were made to develop alloys which are low in modulus but high in strength. An example of such alloys is Ti–24Nb–4Zr–8Sn (abbreviated as Ti2448 from its composition in weight percentage). The hot-rolled alloy has a strength-to-modulus ratio of ~2 % (Fig. 1), which is as high as that of brittle amorphous materials, and good ductility of ~20 % at room temperature. Its elastic modulus is about identical to Mg alloys, but its strength is ~5 times as high (Fig. 1).

The developed activities of the alloy in the second stage pointed to a route of exploring new alloys with lower elastic modulus. For titanium alloys containing single β phase or β plus a small content of ω phase in volume fraction, their elastic modulus versus the phase transformation temperature (T_β) from β phase to α phase shows a linear relationship (Fig. 2) [20], i.e., the alloy with higher T_β has lower modulus. Such a relation is valid for Ti–Nb-based alloys. This suggests that the lower limit of modulus in titanium alloys can be further decreased.

Extensive in vitro and in vivo tests of Ti2448 have been conducted in order to investigate the correlation of elastic matching between bone and implant to the bone healing behavior. For example, intramedullary nails made of the alloy were implanted into New Zealand white rabbits [49]. The results showed that the low modulus of Ti2448 leads to significant improvement in new bone formation in fractured rabbit tibiae compared with the control group of Ti–6Al–4V (Fig. 3) [49]. Clinical trials of a number of typical implants made of Ti2448, such as bone plates and spinal fixtures, have been completed in several qualified hospitals.

3 Additive manufacturing for biomedical application

AM, commonly known as 3D printing, is a process of joining materials to make objects from 3D model data as opposed to subtractive manufacturing methodologies. The

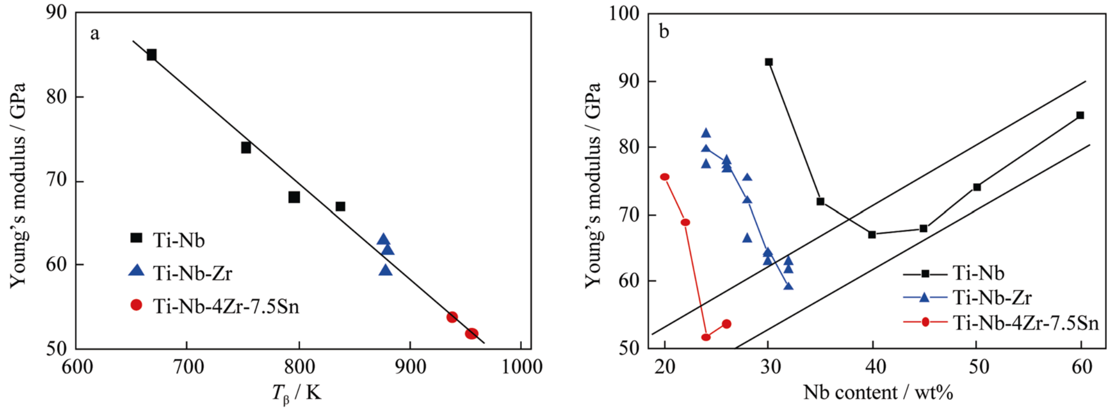

Fig. 2 Variations of Young's modulus with **a** T_β and **b** Nb content of Ti–Nb, Ti–Nb–(8, 10, 12)Zr and Ti–Nb–4Zr–7.5Sn alloys; alloys within region bounded by parallel lines in **b** containing almost single β phase and plot in **a** containing only data for these alloys

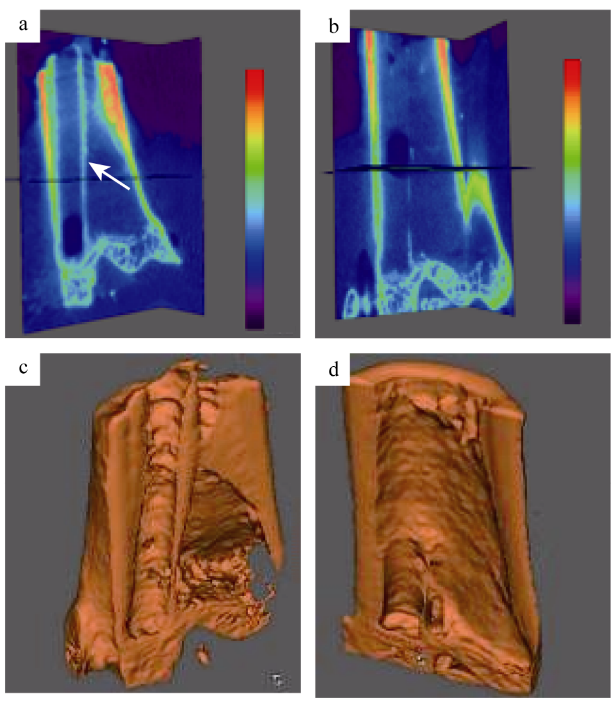

Fig. 3 Micro-computed tomography views in 2D (upper) and 3D (below) of **a**, **c** Ti2448 and **b**, **d** Ti–6Al–4V nails after implantation for 4 weeks in fractured rabbit tibiae, in which the newly formed bone being indicated by arrows

AM technique was established based on the principle of materials addition to build custom-designed components through computer-controlled self-assembly by melting powder layers using either a laser or an electron beam [34]. Such technique has attracted great attention in biomedical fields due to its advantages of producing prototypes or finalized parts rapidly and cost-effectively, providing accurate control over internal pore architectures and complex shapes.

AM methods using laser and electron beams as point source heating technologies have their origins in welding technologies. These power sources selectively fuse or melt the associated metal or alloy powder bed. This is also called powder bed fusion (PBF). Currently, two of the more representative AM techniques are outstanding: selective laser melting (SLM) and electron beam melting (EBM) [50]. In this part, the AM principles (including SLM and EBM), microstructure, mechanical properties of AM products and their application in biomedical fields are briefly discussed.

3.1 Selective laser melting

SLM system was first reported by Fraunhofer Institute ILT in 1995 in Germany [51]. Biomedical parts made of Ti–6Al–4V are among initial targets of SLM because this alloy has high strength, good corrosion resistance and acceptable cell response [51–53]. Unlike traditional manufacturing process, the SLM process is a layered technique fabricating component controlled by computer based on a 3D CAD model [37, 39, 52–54]. SLM systems use a laser source to input energy, and the laser beam is controlled by a mirror deflection systems focusing on the powder bed to melt the powders in selected area. The input energy can be up to 1 kW, and the mechanical movements of the scanning mirror permit accurate laser beam scanning up to scan rate of $\sim 15\ \mathrm{m \cdot s^{-1}}$ [55]. The thickness of the powder layer is normally between 20 and 100 μm [50]. The chamber is filled with pure argon gas to prevent parts from being oxidized [28]. So far, a wide range of metal powders including stainless steel [56], copper [57], cobalt alloys [58], aluminum alloys [59] and titanium alloys [53, 60] have been used for parts production. The SLM as-fabricated component with a complex geometry can acquire very good mechanical properties without any further treatment [40, 61, 62].

The properties of SLM as-fabricated specimen are critically determined by the process parameters including input energy, scanning speed, hatch space and layer thickness [39, 63]. Simchi [64] expressed the energy density (u) as:

$$u = P/vts \tag{1}$$

where P is the input power, v is the scanning speed, t is the layer thickness and s is the hatch space. A near full density component can be obtained by a group of optimized parameters which balance all factors above during SLM process. Kruth et al. [52] reported that a 99.9 % relative density part can be fabricated by SLM process.

The defects will be generated as a result of imbalanced SLM parameters. As a result, the surface roughness and the mechanical properties will be affected [39, 65, 66]. Most likely, the defects are generated during SLM process, which might be caused by insufficient energy [28], balling effects [67], metal evaporation [40], heat-affected zone [68], thermal fluid dynamics [69] and atmospheric conditions [54]. It is necessary to study and solve these issues and then improve the SLM as-fabricated materials [70].

The technological feasibility of biomedical titanium alloys parts fabricated by SLM method was proved by previous researchers [28, 40, 60]. The powder materials from (α + β)-type titanium alloys such as Ti–6Al–4V [62, 71] and Ti–6Al–7Nb [72] and β-type titanium alloys such as Ti2448 [28] and Ti-21Nb-17Zr [73] have been produced to components successfully and studied systematically.

3.2 Electron beam melting

EBM is another AM system which is capable of producing fully dense part [50]. EBM shares the same working process and procedures as SLM. The main difference from the SLM is that the EBM uses an electron beam to replace the laser beam, and the electron beam continuously scans the powder bed, where the conversion of kinetic energy into internal energy occurs in a vacuum chamber. EBM systems generate a high-energy electron beam in a standard electron gun configuration operating at an accelerating potential of 60 kV. The scanning speeds for the EBM system are orders of magnitude greater than those for laser melting systems. Before producing, the electron beam preheats the substrate plate. The temperature increase can be up to 700 °C in order to reduce residual stresses and sinter the powder avoiding powder smoking [36, 50]. The above difference in beam energy input of SLM and EBM system results in the different microstructures and mechanical properties of SLM and EBM products. The densification rate and microstructural homogeneity of EBM as-fabricated parts with optimized parameters result in improvement of relative density of those as-fabricated parts.

Plenty of researches have been carried out to study the performance of EBM as-fabricated components and improve the properties of those samples. It was reported that a large number of implants including knee, hip joint, jaw and maxillofacial plate replacements had been manufactured successfully using EBM system [74–76]. Furthermore, titanium alloys, such as Ti–6Al–4V and Ti–24Nb–4Zr–8Sn, are attracting more interest due to their low density, high strength and good biological compatibility [38, 77–79]. The in vivo performance of Ti–6Al–4V EBM implant has been studied in detail [80]. The result showed that the osseous tissues were suitable ingrowth inside the EBM component.

3.3 Microstructure and mechanical properties of bulk Ti–6Al–4V

Ti–6Al–4V is a typical α+β dual-phase titanium alloy. Owing to its broad application prospect in orthopedic implant, Ti–6Al–4V parts built by SLM and EBM have been investigated extensively. Most investigations are focused on the comprehensive understanding of processing–microstructure–properties relationships. The microstructure of Ti–6Al–4V part fabricated by EBM generally consists of columnar prior β grains delineated by grain boundary α and a transformed α + β structure within the prior β grains (Fig. 4a) [81]. The mechanical properties were thought to be comparable to the wrought materials (Fig. 4c) [35]. The morphologies and mechanical properties are closely related to processing parameter, part size, orientation, location and post-heat treatment [82–85]. For example, variation of build temperature is seen to have a significant effect on the properties and microstructure of as-deposited samples [81]. Orientation was found to have no influence on ultimate strength (UTS) or yield strength (YS), whereas it has significant influence on elongation [82]. Prior-β grain size, α lath thickness and mechanical properties, including microhardness, were not found to vary as a function of distance from the build plate [82]. Part size, however, influences UTS, YS and elongation significantly [82]. A second thermal or hot isostatic pressing (HIP) treatment above T_{β} might result in the expected acicular Widmanstätten microstructure normally achieved through annealing, which corresponds to a different relationship between α lath thickness and mechanical properties [81, 84].

Owing to the fast cooling rate, the as-fabricated microstructure was dominated by columnar β grains and α′ martensites (Fig. 4b) [86]. The microstructure, roughness, densification and microhardness of Ti–6Al–4V parts were

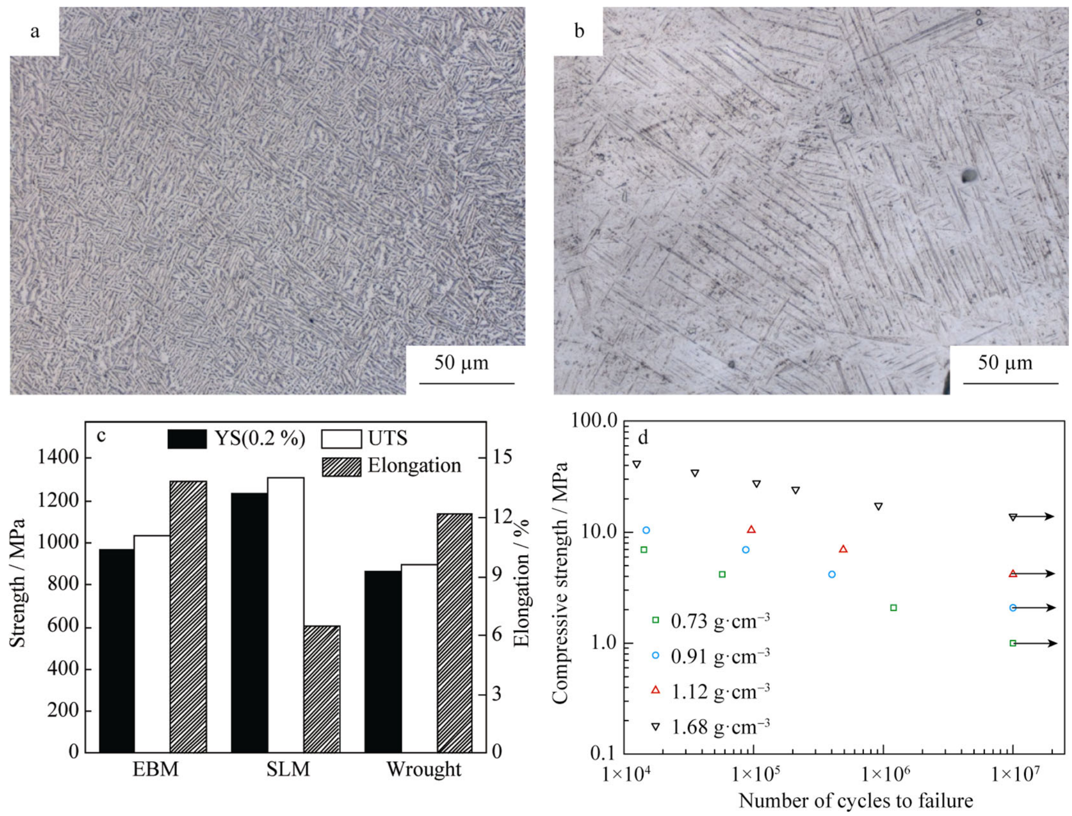

Fig. 4 Optical micrographs of **a** EBM and **b** SLM Ti–6Al–4V alloy and **c** tensile and **d** fatigue properties of EBM and SLM Ti–6Al–4V alloys

also a strong function of processing parameters. An excellent Ti–6Al–4V part with high microhardness and smooth surface can be manufactured by SLM using a preferable laser power of 110 W and scanning speed of 0.4 $m \cdot s^{-1}$, for which the build density can be comparable to that of the bulk alloy [87]. The porosity level generally decreases with the increase in laser power and laser scanning speed [84, 86]. Owing to the hard martensite, the as-fabricated products show very high tensile strengths but poor ductility with elongation of generally smaller than 10 % (Fig. 4c) [88]. The horizontally built samples show even lower elongation than vertically built samples, whereas the strength does not show obvious difference [84, 86]. The fatigue life of SLM product is significantly lower compared with that of wrought material. This reduction in fatigue performance was attributed to a variety of issues, such as microstructure, porosity, surface finish and residual stress (Fig. 2d) [89–91]. HIP treatment can considerably improve ductility and close most of pores formed during the build process [86, 89], significantly improving their fatigue strength so as to be comparable to the wrought alloys [91, 92].

Figure 5 illustrates an example of Ti–6Al–4V biomedical components fabricated using EBM system. It is apparent that near shape products can be achieved with significant machining reduction, and a finish by machining is required before the clinical application.

3.4 Microstructure and mechanical properties of porous Ti–6Al–4V

Titanium and its alloys with open cellular structures and foams possess low modulus, matching that of human bone and the capability to provide space for bone tissue ingrowth to reach a better fixation, which have been thought as a good choice for the replacement of the dense implant and received extensive attention [33]. Recently, AM using EBM and SLM methods has been applied successfully to fabricate titanium cellular meshes and foams (Fig. 6a) [33, 93]. Compared with the previous methods, it offers advantages of accurate control of internal pore architectures and complex cell shapes, thus receiving extensive attention. In this part, it is reviewed the current activities of design, mechanical properties and applications of EBM/SLM Ti–6Al–4V reticulated meshes.

Owing to fast cooling rate of the thin and isolate struts, both EBM and SLM mesh struts primarily consist of α′ martensite in as-processed parts (Fig. 6b) [94, 95]. The

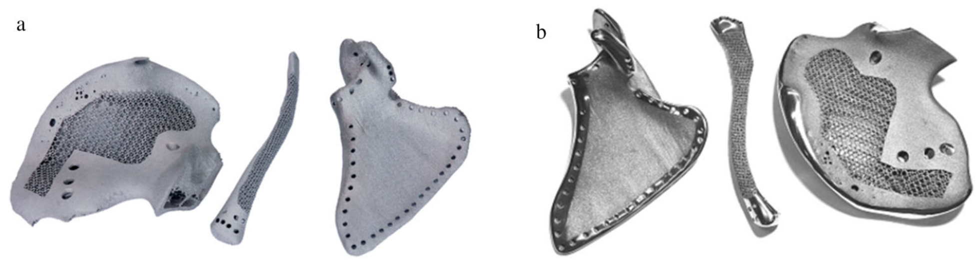

Fig. 5 Examples of experimental biomedical replacements produced by EBM layer manufacturing: **a** as-manufactured components and **b** finished component

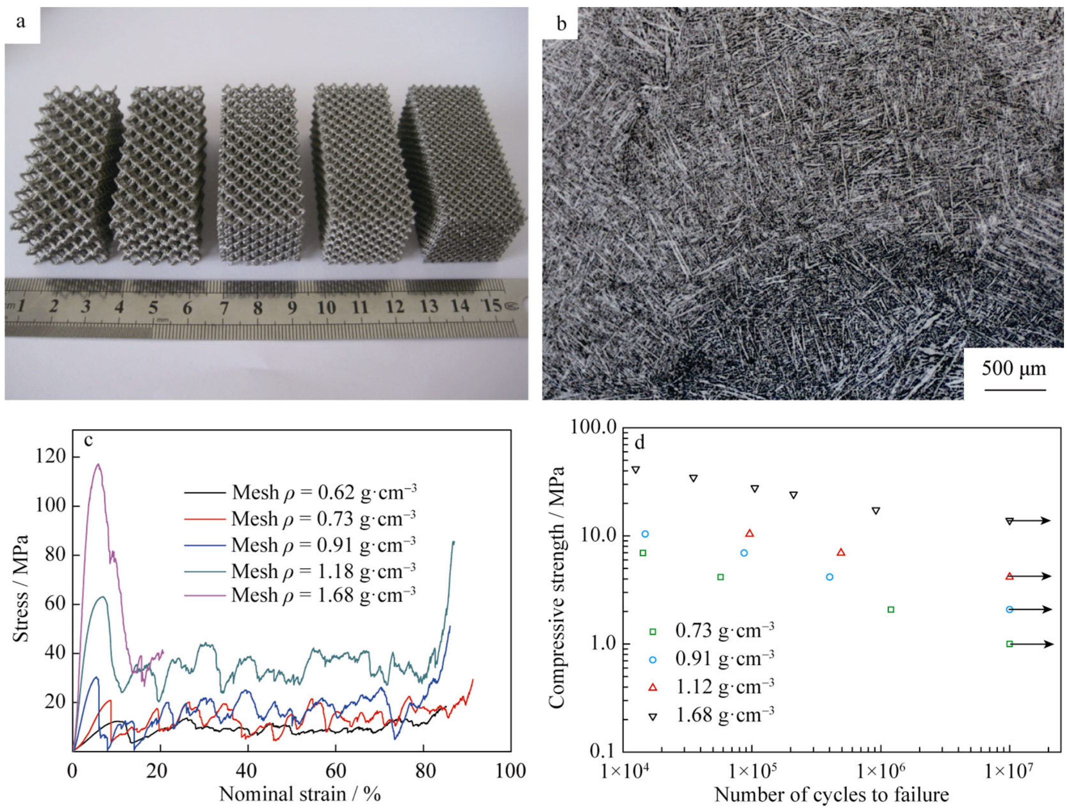

Fig. 6 Macroscopic image of reticulated Ti–6Al–4V meshes **a**, microstructure of Ti–6Al–4V mesh struts **b**, and compressive **c** and fatigue **d** properties of reticulated Ti–6Al–4V meshes

surfaces of the mesh struts are very rough [36]. Such phenomenon is due to powder particles partially melted and sintered to the surface. The struts may be thinner/thicker than those defined by CAD models for SLM/EBM technique resulting from the processing conditions, which results in larger/smaller pores and a higher/lower experimental porosity of fabricated meshes [36, 96, 97].

Mechanical properties of SLM/EBM meshes have been investigated extensively. The as-fabricated SLM/EBM meshes have comparable compressive strength and elastic modulus to those of trabecular and cortical bone (Fig. 6c) [12, 36, 98]. Owing to hard α′ martensite contained in struts, the meshes exhibit brittle deformation behavior (Fig. 6c), which can be avoided by adjusting the coupling of the buckling and bending deformation of struts [99]. Relative strength and density of EBM/SLM Ti–6Al–4V meshes follow a linear relation as described by the well-known Gibson–Ashby model, but its exponential factors are deviated from the ideal value of 1.5 derived from the model [36]. Both stress relief heat treatment and a HIP treatment result in the lamellar microstructure of the equilibrium $\alpha + \beta$ phases of the mesh struts, leading to a lower compressive strength but higher ductility compared with as-processed martensitic parts [100]. The effective modulus was not significantly influenced by the thermal treatments [100].

For long-term application of metallic cellular structures in human body, fatigue strength is very important and should be considered carefully. For reticulated meshes fabricated by EBM/SLM technique, their fatigue lives are mainly determined by uniform deformation of the entire specimens, while their failures are characterized by rapid strain accumulation [36]. The underlying mechanism of fatigue failure appears to be the interaction between the cyclic ratcheting and the fatigue crack initiation and propagation, while the former plays a dominant role in fatigue life. Owing to hard and brittle α' martensite contained in the Ti–6Al–4V struts, their fatigue endurance ratios ranged in 0.1 and 0.2 (Fig. 6d), which are much lower than that of the bulk alloy (about 0.6) [36, 100].

The biocompatibility of SLM/EBM Ti–6Al–4V meshes has been investigated extensively. Warnke et al. [101] fabricated the porous Ti–6Al–4V scaffolds using SLM and evaluated the tissue ingrowth and the influence of pore size on their biocompatibility. Heinl et al. [77] and Li et al. [102] fabricated cellular Ti and Ti–6Al–4V parts by the selective EBM technique, and their results showed that by chemical surface modification using HCl and NaOH, the bioactivity of the surface was improved and the modified surface is expected to enhance the fixation of the implant in the surrounding bone as well as to improve its long-term stability. Guo et al. developed a porous Ti cage and compared its spinal fusion efficacy with a polyetheretherketone (PEEK) cage in a preclinical sheep anterior cervical fusion model [103]. The in vivo test indicated that the porous Ti cage fabricated by EBM could achieve fast bone ingrowth and it had better osseointegration and superior mechanical stability than the conventional PEEK cage, demonstrating great potential for clinical application (Fig. 7) [103, 104].

3.5 Ti2448 alloy fabricated by AM technique

Low-modulus β titanium alloys comprising non-toxic and non-allergic elements are currently being developed for the next generation of metallic implant materials. Recently, some β-type titanium alloys fabricated using SLM and EBM have been reported. Murr et al. fabricated solid, prototype components using atomized, pre-alloyed Ti2448 powder by EBM and studied their microstructure and mechanical properties [38]. X-ray diffraction (XRD) analyses showed that they had bcc β phase microstructure, and transmission electron microscopy (TEM) analyses

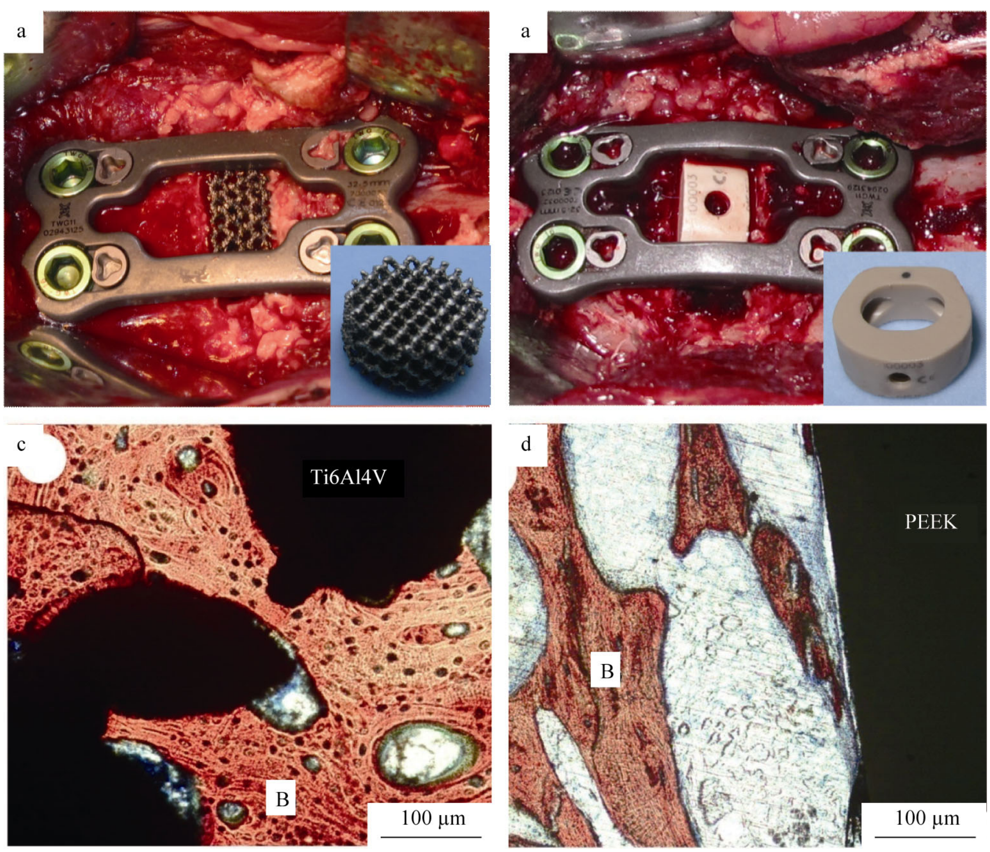

Fig. 7 Macro-images of porous EBM **a** Ti–6Al–4V cage and **b** PEEK cage used in animal test; histological images of **c** porous EBM cage and **d** PEEK cage over post-surgery recovery time

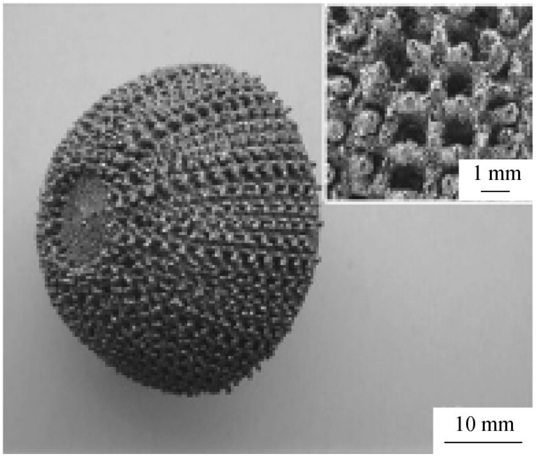

Fig. 8 An example of precise acetabular cup produced by SLM using Ti2448 powders with laser power of 200 W and a laser scan speed of 550 mm·s^{-1}; inset showing fine-scale scaffold that has been created on surface, which is aimed at enhancing bone ingrowth

found that the β phase had plate morphology with space of ~100–200 nm. Vickers hardness values were tested to be on average 2.0 GPa for the precursor powder and 2.5 GPa for the solid EBM-fabricated products.

Zhang et al. [28] produced biomedical β type Ti2448 components using SLM. The density and microhardness generally increase with laser scan speed decreasing, which corresponds to a higher laser energy density. Near full density parts (>99 %) can be obtained at a laser power of 200 W and with a scan speed range of 300–600 mm·s^{-1}. Compared with material prepared by conventional processing routes, SLM processing produces samples with similar mechanical properties but without pronounced superelastic deformation due to the high oxygen content of the starting powder. An example of an acetabular hip cup with complex outer scaffold has been manufactured (Fig. 8) [28]. Liu et al. [40] presented an optimal porous structure with 85 % porosity fabricated by Ti2448. The relative density was affected by scanning speed and input energy. A 99.3 % relative density specimen was achieved at 750 mm·s^{-1} with an input power of 175 W. The compressive strength reaches 51 MPa with a ductility of 14 %. The results above indicate that Ti2448 is suitable for artificial implant.

4 Conclusion

The emphasis of this review is on the recent progress in biomedical titanium development and achievement brought about by additive manufacturing. Beta-type biomedical titanium alloys are preferred materials for medical implants due to their low modulus, excellent biocompatibility, high corrosion resistance and high strength compared with stainless steel and Co-based alloys. Efforts to further improve biocompatibility and reduce modulus of titanium alloys had been made. A new generation of β-type biomedical titanium alloys consisting of non-toxic elements possessed low elastic modulus.

The development of new biomedical titanium alloys coupled with the application of additive manufacturing technologies brought about new opportunities in the biomedical industry. Many researches exhibited the excellent performance of AM technologies in fabricating artificial replacements in terms of complex structure, high mechanical properties and the promotion of bone cell ingrowth. Further investigations need to be done to improve the roughness of implants manufactured by AM systems. Design and fabrication of graded porous structure with gradient modulus to reduce the stress concentration of implants is an important future research direction.

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