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Review

Development of new metallic alloys for biomedical applications

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ABSTRACT

New low modulus β-type titanium alloys for biomedical applications are still currently being developed. Strong and enduring β-type titanium alloy with a low Young's modulus are being investigated. A low modulus has been proved to be effective in inhibiting bone atrophy, leading to good bone remodeling in a bone fracture model in the rabbit tibia. Very recently β-type titanium alloys with a self-tunable modulus have been proposed for the construction of removable implants. Nickel-free low modulus β-type titanium alloys showing shape memory and super elastic behavior are also currently being developed. Nickel-free stainless steel and cobalt–chromium alloys for biomedical applications are receiving attention as well. Newly developed zirconium-based alloys for biomedical applications are proving very interesting. Magnesium-based or iron-based biodegradable biomaterials are under development. Further, tantalum, and niobium and its alloys are being investigated for biomedical applications. The development of new metallic alloys for biomedical applications is described in this paper.

1. Introduction

Around 70–80% of implants are made of metallic biomaterials. Metallic biomaterials are remarkably important for the reconstruction of failed tissue, especially failed hard tissue, to improve the quality of life (QOL) of the patient. The demand for metallic biomaterials is increasing rapidly because the world population is getting increasingly older, and elderly people have a higher risk of hard tissue failure. The biological and mechanical biocompatibility of metallic biomaterials require much improvement. Furthermore, the biofunctionality of metallic biomaterials is at present inadequate, and needs to be improved.

Representative practical metallic biomaterials are stainless steels, cobalt (Co)–chromium (Cr) alloys, and titanium (Ti) and its alloys. Among these metallic biomaterials Ti alloys exhibit the highest biocompatibility, corrosion resistance, and specific strength (ratio of the tensile strength to density), compared with stainless steels and Co–Cr alloys. Co–Cr alloys exhibit the highest wear resistance and relatively higher strength compared with stainless steels and Ti alloys. Stainless steels generally exhibit higher ductility and cyclic twist strength compared with Co–Cr and Ti alloys. Stiffness is greatest for Co–Cr alloys, while it is the lowest for Ti alloys. Other metallic biomaterials, such as magnesium (Mg) alloys, iron (Fe), tantalum (Ta), and niobium (Nb) are also important, although their share of this field is small. Intensive research and development is being carried out globally on all kinds of metallic biomaterials. The elemental components of metallic biomaterials are basically non-toxic. Representative elements are Ti, Nb, Ta, molybdenum (Mo), and zirconium (Zr) [1,2]. In addition to these, Fe, tin (Sn), Co, hafnium (Hf), manganese (Mn), and Cr [3–7] have also been studied. Nickel (Ni) is a popular element for addition to stainless steels, and Co–Cr alloys are often used for biomedical applications. However, nowadays, Ni is widely recognized as a high risk element from the view point of incompatability problems [8–10]. Therefore, Ni is now avoided as much as possible as an additive in metallic biomaterials. Because of this Ni-free stainless steels [11] and Co–Cr alloys [12] have recently been developed. Vanadium (V)- and aluminum (Al)-free Ti alloys [10] were developed fairly early on in the realization of Ti alloys for biomedical applications, because of the toxicity of V [13] and issues with regard to Al causing Alzheimer's disease [14]. Al has since been proved not to be a cause of Alzheimer's disease [15], although it has been shown to be neurotoxic [16]. Recently improvements in mechanical biocompatibility in terms of properties such as the Young's modulus, strength/ductility balance, fatigue strength, fracture toughness, and wear resistance of metallic biomaterials have been achieved [17]. Among these properties control of the Young's modulus in particular has been extensively investigated because the much higher Young's moduli of metallic biomaterials compared with bone can lead to bone atrophy and poor bone remodeling [18], although implants need to exhibit structural stiffness. Therefore, low Young's modulus Ti alloys for use in replacing failed hard tissue (bone), such as artificial hip joints, bone plates, and spinal fixation rods, are required. Nowadays new concept metallic biomaterials such as Ti alloys with self-tunable Young's moduli for

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spinal fixation rods, and Ti and Zr alloys for removable implants are being investigated. Further, the creation of biofunctionalities such as bone conductivity and blood compatibility of metallic biomaterials through surface modification [19] are being widely investigated. Dental applications of metallic materials such as Ti alloys [20] and alloys of precious metals such as gold (Au) [21] and silver (Ag) [22] containing high amounts of platinum (Pt) and palladium (Pd) are also of interest. The authors hope that metallic materials for dental applications will be reviewed elsewhere in the future.

Representative topics in terms of new metallic biomaterials for implants for the reconstruction of hard tissue, as used mainly in orthopedic surgery, and for the reconstruction of soft tissues such as blood vessels are here described.

2. Titanium and its alloys

The biocompatibilities of Ti (pure Ti) and its alloys are the highest among the main metallic biomaterials, such as stainless steels and Co–Cr alloys. Ti alloys also exhibit a high specific ratio (i.e. tensile strength divided by density) and good corrosion resistance. Therefore, Ti alloys have attracted a great deal of attention for biomedical applications. Early in the development of Ti alloys for biomedical applications V-free TI alloys such as Ti–6Al–7Nb [23] and Ti–5Al–2.5Fe [24] were developed, because, as already stated above, V in a practical Ti–6Al–4V ELI was toxic. Then V- and Al-free Ti alloys, such as Ti–Zr-based and Ti–Sn-based alloys [25], were developed, because Al was once thought to be a cause of Alzheimer's disease (although it has since been proved that this is not the case). Recently the problem of stress shielding has received a lot of attention in the case of implants made of metallic materials [18]. Stress shielding is the inhomogeneous transfer of stress between the implant and bone. Stress is predominantly transferred through the implant because the Young's modulus of implants made of metallic materials is generally much higher than that of bone. This leads to bone absorption, which results in loosening of the implant or refracture of the bone after removal of the implant. Therefore, metallic biomaterials with a similar modulus to that of bone, i.e. low modulus metallic biomaterials, are required. The modulus of Ti alloys is the lowest among the main metallic biomaterials [1]. The elastic modulus of the $(\alpha + \beta)$-type Ti alloy Ti–6Al–4V (~110 GPa) is much lower than those of stainless steel and Co-based alloys (~180 and 210 GPa, respectively). Ti alloys are grouped into α-type, $(\alpha + \beta)$-type, and β-type alloys. The modulus of β-type Ti alloys is lower than those of the α-type and $(\alpha + \beta)$-type alloys because the crystal structure of the α phase, which is the main component phase of α-type Ti alloys, is hexagonal closed-packed (hcp), while that of the β phase, which is the main component phase of β-type Ti alloys, is body-centered cubic (bcc). The density of atoms in the lattice is lower for the bcc structure. Thus the development of low modulus β-type Ti alloys for biomedical applications was begun, and is still progressing.

2.1. Low modulus titanium alloys

Low modulus Ti alloys developed for biomedical applications are all β-type alloys composed of non-toxic elements. The first low modulus β-type Ti alloy developed for biomedical applications was Ti–13Nb–13Zr [26]. The alloys Ti–12Mo–6Zr–2Fe (TMZF) [27], Ti–15Mo [28], Ti–16Nb–10Hf (Tiadyne 1610) [2], Ti–15Mo–5Zr-3Al [29], Ti–35.3Nb–5.1Ta–7.1Zr (TNZT) [30], and Ti–29Nb–13Ta–4.6Zr (TNTZ) [3] were also developed early on. Since then many low modulus β-type Ti alloys have been developed or are being developed. Very recently low modulus β-type Ti alloys composed of low cost elements such as Fe, Cr, Mn, Sn, and Al have been proposed to reduce the consumption of high cost elements such as the rare metals Nb, Ta, Mo, and Zr. Examples of these alloys include Ti–10Cr–Al [31], Ti–Mn [7], Ti–Mn–Fe [32], Ti–Mn–Al [33], Ti–Cr–Al [34], Ti–Sn–Cr [35], Ti–Cr–Sn–Zr [36], Ti–(Cr, Mn)–Sn [37], and Ti–12Cr [38].

The low modulus β-type Ti alloys used for biomedical applications are listed in Table 1 [39]. The Young's moduli of each of the β-type Ti alloys are shown in Fig. 1 [26–30,38,40–55], together with an indication of the processing and measurement methods employed. Tensile tests seem to give slightly lower Young's modulus values than free resonance or ultrasonic methods, while the

Table 1
Selected low modulus β-type titanium alloys for biomedical applications.

β-type titanium alloys	ASTM Standard	ISO Standard	JIS Standard
Ti–13Nb–13Zr	ASTM F 1713	–	–
Ti–12Mo–6Zr–2Fe (TMZF)	ASTM F 1813	–	–
Ti–12Mo–5Zr–5Sn		–	–
Ti–15Mo	ASTM F 2066	–	–
Ti–16Nb–10Hf (Tiadyne 1610)	–	–	–
Ti–15Mo–2.8Nb–0.2Si	–	–	–
Ti–15Mo–5Zr–3Al	–	–	JIS T 7401-6
Ti–30Ta	–	–	–
Ti–45Nb	AMS 4982	–	–
Ti–35Zr–10Nb	–	–	–
Ti–35Nb–7Zr–5Ta (TNZT)	Task Force F-04.12.23	–	–
Ti–29Nb–13Ta–4.6Zr (TNTZ)	–	–	–
Ti–35Nb–4Sn	–	–	–
Ti–50Ta	–	–	–
Ti–8Fe–8Ta	–	–	–
Ti–8Fe–8Ta–4Zr	–	–	–
Ti–35Nb–2Ta–3Zr	–	–	–
Ti–22.5Nb–0.7Zr–2Ta	–	–	–
Ti–23Nb–0.7Ta–2.0Zr–1.2O (Gum Metal)	–	–	–
Ti–28Nb–13Zr–0.5Fe (TNZF)	–	–	–
Ti–24Nb–4Zr–7.9Sn (Ti2448)	–	–	–
Ti–7.5Mo	–	–	–
Ti–12Mo–3Nb	–	–	–
Ti–12Mo–5Ta	–	–	–
Ti–12Cr	–	–	–
Ti–30Zr–7Mo	–	–	–
Ti–30Zr–3Mo–3Cr	–	–	–