Formation, structure and properties of biocompatible TiZrHfNbTa high-entropy alloys

Yuan Yuan, Yuan Wu, Zhi Yang, Xue Liang, Zhifeng Lei, Hailong Huang, Hui Wang, Xiongjun Liu, Ke An, Wei Wu and Zhaoping Lu

ABSTRACT
Biocompatibility of HEAs in the TiZrHfNbTa system in which all the constituents are non-toxic and allergy-free was scrutinized systematically, and novel biomechanical materials with a unique combination of low modulus (57 GPa, almost half that of conventional biomedical titanium alloys), good mechanical biocompatibility and low magnetic susceptibility ($1.71 \times 10^{-6}$ cm$^3$ g$^{-1}$, similar to that of pure Zr) were successfully developed. Moreover, the underlying mechanisms responsible for phase formation and promising properties were explored. This work not only offers a series of novel bio-metallic materials with prominent properties for practical applications, but also shed light on understanding of phase formation and strengthening of HEAs in general.

1. Introduction
Metals and alloys are widely used as biomedical materials and therapeutic devices, especially as the replacement of hard tissues [1]. The most commonly used metallic biomaterials in the past decades include stainless steels (e.g. 316L SS and 304 SS), cobalt (Co)-chromium (Cr) alloys, and titanium (Ti) and its alloys [2]. However, Co-Cr alloys are too brittle and the famous Ti-6Al-4 V alloy still suffers from a large degree of biomechanical incompatibility due to their relatively high elastic modulus (about 90 GPa higher than that of human bones) and release of toxic ions (i.e. V and Al) into the body. When used as an implant, the titanium alloy overtakes a considerable part of the body loading because of the elastic modulus mismatch, which shields the bone from the necessary ‘stressing’ required to maintain its strength, density, and healthy structure. Such an effect, usually termed as ‘stress shielding’, eventually causes bone loss, implant loosening, and premature failure of prostheses [3]. Additionally, magnetic resonance imaging (MRI) diagnosis is greatly inhibited when conventional metallic biomaterials are implanted in the body due to their high magnetic susceptibility [4,5]. Exploring novel metallic materials concurrently possessing good biomechanical compatibility (e.g. a low Young’s modulus and good strength/ductility balance) and low magnetic susceptibility through innovative routes is urgently required for enabling their practical applications as biomedical components.
In recent years, a new alloy design concept, termed as high-entropy alloys (HEAs) which contain multiple principal elements with an atomic ratio ranging from 5 to 35 at.%, was proposed [6,7]. The basic idea is to utilize high mixing entropy and lattice disorder to enhance formation of solid solution phases [7,8]. The Young’s modulus of HEAs can be more easily adjusted than conventional alloys due to the large compositional variation [7], providing great possibility to design biomedical metallic materials with a low modulus. In a previous study, colony-forming units were proven to be considerably inhibited on HEA coatings, and the antibacterial rates for four different bacteria exceed 99.999%, indicating that HEAs have efficient antibacterial ability [9]. Ti, Zr, Hf, Nb and Ta elements are known to be fully non-toxic and allergy-free [3]. Moreover, the combination of these elements is favorable for the formation of a single solid solution phase [10]. Therefore, it is interesting and imperative, both scientifically and technologically, to fabricate HEAs composed of these five elements and explore their biocompatibility. In this paper, we report our successful development of promising biocompatible TiZrHfNbTa HEAs with a unique combination of low modulus, good mechanical biocompatibility and low magnetic susceptibility.

2. Experimental

Ingots of six Ti-Zr-Nb-Ta alloys, (i.e. alloy 1: Ti25Zr25 Nb25Ta25; alloy 2: Ti31.67Zr31.67Nb31.66Ta3; alloy 3: Ti35Zr35Nb25Ta3; alloy 4: Ti45Zr45Nb5Ta3; alloy 5: Ti21.67Zr21.67Nb21.66Ta35; alloy 6: Ti15Zr15Nb15Ta35, and the numbers are in atomic percentage), ten Ta2HfZrTi (x = 0, 0.1, 0.2, 0.3, 0.4, 0.5, 0.6, 0.7, 0.8 and 1, and the numbers are in atomic ratio), five Nb2HfZrTi (x = 0, 0.2, 0.4, 0.8 and 1) and seven Ta4Nb2HfZrTi (x = 0, 0.2, 0.4, 0.5, 0.6, 0.8 and 1) alloys were synthesized by arc-melting a mixture of pure metals (purity > 99.9%) in a Ti-gettered high-purity argon atmosphere. The ingots were re-melted at least six times to ensure chemical homogeneity and eventually drop-cast into a mold with a dimension of φ10 mm × 60 mm. Phase identification was conducted using X-ray diffraction (XRD) with Cu Kα radiation and neutron diffraction at the VULCAN instrument, Oak Ridge National Laboratory Spallation Neutron Source (ORNL, SNS), USA. Microstructures were characterized by scanning electron microscopy (SEM) using a Zeiss Supra55 microscope operated at 15 kV with an energy dispersive spectrometer (EDS). Standard bright-field and diffraction patterns were obtained using a transmission electron microscope (TEM, Tecnai F30) operated at 300 kV. Both tension and compression tests were carried out on a CMT4105 universal electronic tensile testing machine with a strain rate of $1 \times 10^{-3}$ s$^{-1}$ at room temperature. The static Young’s modulus of all the specimens was determined by linearly fitting the elastic stage of tension stress–strain curves. The magnetization (M) as a function of applied magnetic field (H) was measured and recorded using a SQUID (Superconducting Quantum Interference Device, Quantum Design, USA) at room temperature, and its magnetic susceptibility, $\chi = M/H$, was obtained from the slope by linear fitting of the data.

3. Results and discussion

Phase identification was conducted by both XRD and neutron diffraction, and as an example, representative XRD traces and neutron diffraction patterns of six as-cast Ti-Zr-Nb-Ta alloys (i.e. alloy 1–6) are shown in Figure 1(a). As can be seen, all the reflection peaks on the curves obtained by both kinds of techniques can be indexed as the BCC lattice, indicating that those six alloys have a single BCC solid solution structure with no formation of any second phase. Figure 1(b–d) shows the corresponding SEM and TEM images of three typical HEAs, i.e. alloys 1, 4 and 6. Typical dendritic morphology is observed in the alloys enriched in Nb and Ta, i.e. alloys 1 and 6, whilst equiaxed grains are seen in alloy 4 with much less Ta (i.e. 5%). EDS results reveal that the dendritic phase is enriched in Ta and Nb while the inter-dendrite contains a high concentration of Ti and Zr, manifesting occurrence of elemental segregation during solidification of alloys 1 and 6. TEM bright field images and the corresponding selected area electron diffraction (SAED) patterns of these three alloys evidence no other crystalline phases and/or precipitates in the BCC matrix, which is consistent with the XRD and neutron diffraction results. Detailed structure characterization and analysis of the other alloys investigated in this study are not shown, but summary of their microstructure characteristics are listed in Table 1.

Figures 2(a,b) show room-temperature tensile and compressive true stress–strain curves of the aforementioned six Ti-Zr-Nb-Ta alloys. The present alloys exhibit high strength ranging from 690 to 1050 MPa, together with significant tensile ductility (> 10%). The static Young’s modulus deduced from the tensile stress–strain curves is estimated to be 89, 75, 69, 57, 93 and 135 GPa for alloys 1–6, respectively. The tensile properties including yield strength (YS), ductility (%) and Young’s modulus (E) of all the fabricated HEAs are also compiled in Table 1. Mechanical properties of the currently developed HEAs actually changed drastically when the alloy composition is altered, indicating that mechanical properties can be remarkably tailored even in the same HEA...
Figure 1. (a) XRD patterns of alloys 1–6. The inset shows neutron diffraction pattern of alloy 1 as an example. (b–d) SEM images and TEM bright-field photos of typical alloys 1, 4 and 6, respectively. The insets show the corresponding selected area electron diffraction (SAED) patterns.
Table 1. Phase constitution and mechanical properties for all the fabricated HEAs. ‘E’ denotes Young’s modulus while ‘YS’ represents yield strength.

| Alloys       | Structure | E (GPa) | YS (MPa) | Elongation (%) |
|--------------|-----------|---------|----------|----------------|
| Ti-Zr-Nb-Ta  | Alloy 1   | BCC     | 89       | 970            | 23             |
|              | Alloy 2   | BCC     | 75       | 790            | 29             |
|              | Alloy 3   | BCC     | 69       | 780            | 26             |
|              | Alloy 4   | BCC     | 57       | 690            | 24             |
|              | Alloy 5   | BCC     | 93       | 1050           | 12.7           |
|              | Alloy 6   | BCC     | 135      | 970            | 12.5           |
| TaxHfZrTi    | x = 0    | HCP     | 111      | 822            | 13.6           |
|              | x = 0.1  | HCP     | 105      | 890            | 5.3            |
|              | x = 0.2  | HCP     | 97       | 1020           | 5.08           |
|              | x = 0.3  | HCP + BCC | 80      | 225            | 13.96          |
|              | x = 0.4  | HCP + BCC | 76      | 365            | 30.26          |
|              | x = 0.5  | HCP + BCC | 79      | 683            | 29             |
|              | x = 0.6  | HCP + BCC | 74      | 738            | 21.73          |
|              | x = 0.7  | BCC     | 77       | 1046           | 14.31          |
|              | x = 0.8  | BCC     | 85       | 1120           | 4.63           |
|              | x = 1    | BCC     | 86       | 1367           | 4.07           |
| NbxBxFzrTi   | x = 0    | HCP     | 111      | 822            | 13.6           |
|              | x = 0.2  | HCP + BCC | 118     | 906            | 0.73           |
|              | x = 0.4  | BCC     | 82       | 744            | 11.9           |
|              | x = 0.8  | BCC     | 79       | 718            | 16.2           |
|              | x = 1    | BCC     | 83       | 728            | 18.7           |
| TaxNbxBfZrTi | x = 0    | HCP     | 111      | 822            | 13.6           |
|              | x = 0.2  | HCP + BCC | 71     | 480            | 32.5           |
|              | x = 0.4  | BCC     | 78       | 800            | 10             |
|              | x = 0.5  | BCC     | 85       | 850            | 13             |
|              | x = 0.6  | BCC     | 73       | 880            | 19             |
|              | x = 0.8  | BCC     | 93       | 890            | 18             |
|              | x = 1    | BCC     | 103      | 1200           | 12             |

Figure 2(c) shows the comparison of tensile properties between our fabricated HEAs and the conventional biomedical titanium materials [11]. Noted that the Young’s modulus of alloys 2, 3, 4 and Ta0.5HfZrTi (red column in Figure 2(c)) is only half that of conventional biomedical titanium alloys such as Ti-15Mo (annealed) and Ti-35.3Nb-5.1Ta-7.1Zr whose Young’s modulus is on the lower side among all titanium bio-implant alloys [11]. Therefore, the currently developed HEAs, especially alloys 2, 3, 4 and Ta0.5HfZrTi, possess a good combination of low Young’s modulus, high strength and ductility, in comparison with those of the conventional bio-implant titanium materials [11]. Particularly, Ti-Zr-Nb-Ta HEAs exhibit really decent mechanical properties under compression, i.e. high compressive strength (800–1200 MPa) and large compressive plasticity (> 40%) (Figure 2(b)).

Young’s modulus has been known as one of the intrinsic nature of materials, and the crystalline structures have a dramatic effect on its value, e.g. the BCC structure generally has a lower Young’s modulus in comparison with HCP structures in the same group [12]. Therefore, effects of crystalline structures on Young’s modulus of the group IV (Ti, Zr, Hf) HEA alloys are worthy to be investigated at the first place. The valence electron concentration (VEC) is the dominant factor in controlling the phase structure and stability for many intermetallic alloys such as (Fe, Co, Ni)3V [13] and NbCr2-based Laves phase alloys [14]. In addition, VEC also plays a decisive role in the stability of Ti alloys [12] and some FCC and BCC solid-solution HEAs [15]. However, whether the VEC criterion holds in the current HEA systems still needs to be verified. VEC for a multi-component alloy can be defined as the weighted average from VEC of the constituent components: $VEC = \sum_{i=1}^{n} c_i (VEC)_i$, where $(VEC)_i$ is the VEC for the individual element (Table 2)
Figure 3. Dependence of Young’s modulus and crystalline phase structure on VEC in all the HEAs investigated.

[16]. Figure 3 shows Young’s modulus of the current HEAs as a function of VEC. A careful examination of Figure 3 suggests that the VEC criterion can be used to predict phase constitution in the current HEA system, i.e. from single HCP, to mixed HCP and BCC, and to single BCC with increasing BCC stabilizers of Nb and Ta. At VEC ≥ 4.18, a single BCC phase was formed, whilst when 4.09 ≤ VEC < 4.18, mixed BCC and HCP phases co-existed and a single HCP phase would be formed at VEC < 4.09. It is evident that as the VEC value decreases from 4.18, the HCP structure stabilizes and its formation subsequently leads to an increase of Young’s modulus, as shown in Figure 3. Thus the trend is due to the fact that the Young’s modulus in the <100> direction of BCC crystals is usually reduced by lowering c_{11} − c_{12} [12] which is generally decreased with decreasing of d + s electrons (i.e. the valence electrons for transitional metals) in BCC metals [17]. Therefore, a low Young’s modulus can be achieved by controlling the VEC value around 4.18 to obtain a small c_{11} − c_{12} value while maintaining the BCC structure simultaneously.

Table 2 shows σ_{0.2} values for pure elements at room temperature [18]. Yield strengths of the six Ti-Zr-Nb-Ta HEAs (alloy 1–6) estimated from rule of mixture of the yield strength of pure elements, i.e. (σ_{0.2})_{mix} = \sum_{i=1}^{n} c_i(σ_{0.2})_i, where c_i is the molar ratio and (σ_{0.2})_i is yield strength value of each constituent element, is 221, 235, 235, 214, and 215 MPa, respectively, which are much smaller than the experimental values (i.e. 970, 790, 780, 690, 1050 and 970 MPa, respectively). Senkov et al. [18] firstly attempt to predict solid-solution strengthening effect in the multicomponent TaNbHfZrTi HEA [19]. Here, the HEA is considered as a pseudo-binary solid solution. By doing so, atomic misfit and modulus misfit of the HEAs were estimated and finally their contribution to strength was determined theoretically. The atomic radius [20] and shear modulus [18] of the pure elements are given in Table 2. It should be noted that the BCC crystal lattice has eight nearest-neighbor atoms while the HCP crystal lattice has twelve nearest-neighbor atoms. Considering the largest difference in atomic size of Zr and Hf with the rest elements, to assess the contribution from lattice distortion, all the fabricated HEAs are taken as pseudo-binary solid solutions, defining the Ti, Nb, Ta as solvents and Zr plus Hf as solutes. For the calculation of modulus misfit, the largest modulus distortion appears in the vicinity of Ta element for the alloys containing Ta, while pairing of Ti atoms with other elements provides the largest modulus misfit for the alloys without Ta element, e.g. HfZrTi and Nb_xHfZrTi (x = 0, 0.2, 0.4, 0.8 and 1) HEAs. For clarity, we summarize a column chart (Figure 4) to directly show the strength contributions from lattice distortion Δσ_{dr}, modulus distortion ΔG and (σ_{0.2})_{mix} based on the ‘rule of mixtures’ using the Senkov’s model for all the fabricated single BCC and HCP HEAs. It is apparent that the calculated data (σ_{0.2})_{cal} is good agreement with the experimental values (σ_{0.2})_{exp} (solid circle), especially for equiatomic HEAs. It can be easily seen from the chart that the solid strengthening from the modulus misfit and the atomic size misfit is almost the same in the currently developed HEA systems with less Ta addition. While the high yield strength in the HEAs with lots of Ta addition mainly associates

| VEC | σ_{0.2} (MPa) | r (pm) | G (GPa) |
|-----|---------------|--------|---------|
| Ti  | 4  | 195     | 141.8   | 44      |
| Zr  | 4  | 280     | 155.1   | 33      |
| Hf  | 4  | 240     | 154.1   | 30      |
| Nb  | 5  | 240     | 142.9   | 38      |
| Ta  | 5  | 170     | 143.0   | 69      |

Figure 4. The calculated strength contributions from lattice distortion Δσ_{dr}, modulus distortion ΔG and (σ_{0.2})_{mix} based on the ‘rule of mixtures’. The solid circle represents experimental yield strength.
with the large modulus misfit, and therefore, to further increase the yield strength, addition of the elements with a larger modulus misfit with the constituent elements, such as Mo and W, should be considered. In addition, it has been reported previously [21], the yield strength of dual-phase (mixed HCP and BCC phases) HEAs depends on the constituent phase and their volume fractions, but here such aspects are not discussed.

Low magnetic susceptibility is required for biomaterials so that MRI diagnosis is not interfered. The magnetic variation versus the applied magnetic field of three typical HEAs (i.e. alloys 1, 4 and 6) at room temperature is shown in Figure 5(a), and the data of pure Zr is included for comparison. Similar to pure Zr, all the alloys show a linear trend, which is indicative of typical paramagnetic behavior. The magnetic susceptibility (χ) can be then derived from the slope by linear fitting of these data. Figure 5(b) shows the comparison of χ value of three HEAs (∼2.45 × 10⁻⁶, 2.58 × 10⁻⁶ and 1.71 × 10⁻⁶ cm³ g⁻¹, respectively) with that of representative conventional biomedical Co-Cr alloys (e.g. Co-Cr-Mo, ∼7.7 × 10⁻⁶ cm³ g⁻¹) [2] and Ti-based alloys (e.g. Ti-6Al-4 V, ∼3.5 × 10⁻⁶ cm³ g⁻¹ and Ti-6Al-7Nb, ∼3 × 10⁻⁶ cm³ g⁻¹) [2]. It is clear that the currently developed HEAs, especially alloy 6 possesses low magnetic susceptibility (1.71 × 10⁻⁶ cm³ g⁻¹), similar to that of pure Zr (1.67 × 10⁻⁶ cm³ g⁻¹), indicating the present HEAs have great potential to suppress artifacts in MRI measurements. It is noted that the small deviation between our experimental result (1.67 × 10⁻⁶ cm³ g⁻¹) and literature reported χ value (1.33 × 10⁻⁶ cm³ g⁻¹) for pure Zr [22] may be due to experimental errors such as elemental purity, experimental method and testing environment. To better understand origins of magnetization behavior, it is interesting to verify whether the magnetic susceptibilities obey Vegard’s rule of mixture, i.e. whether a given magnetic susceptibility of the ‘mixture’ χmix is a compositional average of the properties χi of the constituent elements, χmix = ∑ciχi. The magnetic susceptibility at 20°C of pure Ti [22], Zr [22], Nb [22] and Ta [22] is 3.35 × 10⁻⁶, 1.33 × 10⁻⁶, 2.30 × 10⁻⁶ and 0.85 × 10⁻⁶ cm³ g⁻¹, respectively. Deviation of the experimental values χexp from the ROM values χmix can thus be calculated using the expression Δχ = (χexp − χmix)/χmix as 25, 14 and 6% for alloy 1, 4 and 6, respectively, suggesting that the rule of mixture does not hold for the magnetic susceptibility in the present HEAs. This observation implies that in addition to compositional average of magnetic susceptibilities, there may exist strong complex coupling effects from the multiple constituents in the disordered structures.

4. Conclusions

A series of HEAs with different lattice structures, from a single HCP, to a mixture of HCP + BCC, and finally to a BCC structure were designed in the TiZrHfNbTa HEA systems. Highly biocompatible HEAs with a unique combination of low Young’s modulus, high strength and ductility, and low magnetic susceptibility were developed. Our analyses indicate that VEC plays an important role in phase stability and Young’s modulus of these HEAs: single HCP or BCC phase was formed when VEC < 4.09 and > 4.18, respectively, and the mixed HCP and BCC phases were formed in-between. A low Young’s modulus can be achieved by controlling the value of VEC around 4.18 and simultaneously maintaining the BCC structure. Large modulus misfit based on solid solution model was found to mainly contribute to the significantly enhanced yield strength. The low magnetic susceptibility of the developed HEAs is related to the chemical disordering and lattice distortion. Current understanding and implications governing biocompatibility provide important guidelines for developing promising biomedical HEAs with enhanced overall properties.

Disclosure statement

No potential conflict of interest was reported by the authors.
Funding
This research was supported by National Natural Science Foundation of China [grant numbers 11790293, 51871016, 51671018, 51671021, and 51531001], 111 Project (B07003), International S&T Cooperation Program of China [grant number 2015DFG52600], the Program for Changjiang Scholars and Innovative Research Team in University of China (IRT_14R05) and the Projects of SKL-AMM-USTB (2016Z-04, 2016–09 and 2016Z-16). Y. W. acknowledges the financial support from the Top-Notch Young Talents Program and the Fundamental Research Funds for the Central Universities.

ORCID
Zhi Yang http://orcid.org/0000-0002-1297-7981
Zhaoping Lu http://orcid.org/0000-0003-1463-8948

References
[1] Li X, Wang C, Zhang W, et al. Fabrication and characterization of porous Ti6Al4V parts for biomedical applications using electron beam melting process. Mater Lett. 2009;63(3):403–405.
[2] Li H, Zhou F, Li L, et al. Design and development of novel MRI compatible zirconium-ruthenium alloys with ultralow magnetic susceptibility. Sci Rep. 2016;6:24414.
[3] Song Y, Xu D, Yang R, et al. Theoretical study of the effects of alloying elements on the strength and modulus of β-type bio-titanium alloys. Mater Sci Eng A. 1999;260(1):269–274.
[4] Shafiei F, Honda E, Takahashi H, et al. Artifacts from dental casting alloys in magnetic resonance imaging. J Dent Res. 2003;82(8):602–606.
[5] Olsrud J, Lätt J, Brockstedt S, et al. Magnetic resonance imaging artifacts caused by aneurysm clips and shunt valves: dependence on field strength (1.5 and 3T) and imaging parameters. J Magn Reson Imaging. 2005;22(3):433–437.
[6] Yeh JW, Chen SK, Lin SJ, et al. Nanostructured high-entropy alloys with multiple principal elements: novel alloy design concepts and outcomes. Adv Eng Mater. 2004;6(5):299–303.
[7] Zhang Y, Zuo TT, Tang Z, et al. Microstructures and properties of high-entropy alloys. Prog Mater Sci. 2014;61:1–93.
[8] Yuan Y, Wu Y, Tong X, et al. Rare-earth high-entropy alloys with giant magnetocaloric effect. Acta Mater. 2017;125:481–489.
[9] Wu WH, Yang CC, Yeh L. Industrial development of high-entropy alloys. Ann Chim-Sci Mat. 2006;31(6):737–747.
[10] Todai M, Nagase T, Hori T, et al. Novel TiNbTaZrMo high-entropy alloys for metallic biomaterials. Scr Mater. 2017;129:65–68.
[11] Niinomi M. Mechanical properties of biomedical titanium alloys. Mater Sci Eng A. 1998;243(1):231–236.
[12] Ikehata H, Nagasako N, Furuta T, et al. First-principles calculations for development of low elastic modulus Ti alloys. Phys Rev B. 2004;70(17):174113.
[13] Liu C. Physical metallurgy and mechanical properties of ductile ordered alloys (Fe, Co, Ni)3V. Int Meter Rev. 1984;29(1):168–194.
[14] Zhu J, Liaw P, Liu C. Effect of electron concentration on the phase stability of NbCr 2-based Laves phase alloys. Mater Sci Eng A. 1997;239–240:260–264.
[15] Guo S, Ng C, Lu J, et al. Effect of valence electron concentration on stability of fcc or bcc phase in high entropy alloys. J Appl Phys. 2011;109(10):103505.
[16] Guo S, Liu C. Phase stability in high entropy alloys: formation of solid-solution phase or amorphous phase. Prog Nat Sci-Mater. 2011;21(6):433–446.
[17] Chan KS. A computational approach to designing ductile Nb-Ti-Cr-Al solid-solution alloys. Metall Mater Trans A. 2001;32(10):2475–2487.
[18] Senkov O, Scott J, Senkova S, et al. Microstructure and room temperature properties of a high-entropy TaNbHfZrTi alloy. J Alloys Compd. 2011;509(20):6043–6048.
[19] Labusch R. A statistical theory of solid solution hardening. phys. Status Solidi B. 1970;41(2):659–669.
[20] Koželj P, Vrtnik S, Jelen A, et al. Discovery of a superconducting high-entropy alloy. Phys Rev Lett. 2014;113(10):107001.
[21] Wang SP, Xu J. Tizrnbtamo high-entropy alloy designed for orthopedic implants: As-cast microstructure and mechanical properties. Mater Sci Eng C. 2017;73:80–89.
[22] Taniguchi S, Tebble R, Williams D. The magnetic susceptibilities of some transition metal alloys and the corresponding density of states curves. Proc R Soc Lond A. 1962;265(1323):502–518.