Novel TiNbTaZrMo high-entropy alloys for metallic biomaterials

Mitsuharu Todai, Takeshi Nagase, Takao Hori, Aira Matsugaki, Aiko Sekita, Takayoshi Nakano

A novel equiatomic TiNbTaZrMo high-entropy alloy (HEA) was developed as a new metallic biomaterial. The constituent elements of the HEA were biocomparable, and the HEA was designed based on parameters such as the mixing enthalpy ($\Delta H_{\text{mix}}$), the omega parameter ($\Omega$), the delta parameter ($\delta$), and the valence electron concentration (VEC) theory. The bcc solid solution phases with the different lattice constants were obtained in as-cast and annealed states. The HEA showed considerable strength with deformability and superior biocompatibility comparable to pure Ti. This study demonstrated the possibility of using HEAs as a new class of metallic biomaterials.

A wide variety of metallic biomaterials has been developed to date. However, there is a strong need for a new generation of metallic biomaterials with superior biocompatibility and mechanical properties to meet future demands of the medical field. Recently, a new class of structural materials, called high-entropy alloys (HEAs), has been developed [1–6]. These alloys consist of multicomponent elements with an approximately equiatomic ratio of various components for maximizing the configurational entropy, which stabilizes the solid solution phase. The complicated arrangement of different atomic species in HEAs is considered to give rise to a number of advantages over common and/or single-element-based alloys. These include the formation of a solid solution, which gives rise to deformability and a severely distorted lattice, which strengthens the material. HEAs may simultaneously realize superior mechanical properties and biocompatibility, which makes them suitable for use as a new class of metallic biomaterials. Among common metallic biomaterials, Ti-rich Ti–Nb–Ta–Zr (TNZ) alloys with a bcc phase have been widely investigated as superior Ti-based metallic biomaterials. The constituent elements of these alloys are non-toxic and allergy-free [7–10]. The combination of Ti, Nb, Ta, and Zr is favorable for the formation of a single solid solution phase in alloys based on the alloy design of HEAs (see Section S1 in the Supplementary material). In the present study, a novel TiNbTaZrMo HEA was designed from an equiatomic TiNbTaZr alloy, and the microstructure and biocompatibility of the TiNbTaZrMo HEA was investigated in order to clarify the possible use of HEAs as a new class of metallic biomaterials.

Various parameters have been suggested for predicting the formation of solid solution phases in multicomponent alloys and for the development of HEAs. In the present study, the heat of mixing ($\Delta H_{\text{mix}}$) [4–6, 11,12], delta parameter ($\delta$) (which determines the atomic-size difference in multicomponent alloys) [4–6,12–14], and omega parameter ($\Omega$) (defined by the combination of $\Delta H_{\text{mix}}, \Delta H_{\text{melt}}$, and the melting temperatures of the constituent elements) [5,6,14] were used. The possibility of forming a solid solution and the structure of the resulting solid solution in the equiatomic TiNbTaZr and TiNbTaZrX (X = Cr, V, Mo, W, Fe) alloys is discussed. The element X in these alloys was selected from elements in which a bcc-structured phase is formed at room temperature. The stability of fcc and bcc solid solutions in HEAs can be predicted by the valence electron concentration (VEC) parameter [15]. The HEA parameters of the TiNbTaZr and TiNbTaZrX (X = Cr, V, Mo, W, Fe) alloys are summarized in Table 1, along with those of typical HEAs such as a refractory TiNbTaZrHf HEA [16,17] and CoCrMnFeNi HEA [1] as a reference. The parameters of the atomic radius and $\Delta H_{m}$, which is the mixing enthalpy of an A–B (i = A, j = B, i ≠ j) binary system at an equiatomic composition ($A_{0.5}B_{0.5}$) for a liquid phase, were taken from literature [11]. Zhang et al. showed that solid solutions are formed in the alloys satisfying the criteria $-20 \leq \Delta H_{\text{mix}} \leq 5$, $\delta \leq 6.4$, and $12 \leq \delta \leq 17.5$ [4]. Guo et al. suggested that the following conditions are favorable for the formation of solid solutions: $-11.6 \leq \Delta H_{\text{mix}} \leq 3.2$ and $\delta \leq 6.6$ [12]. Yang et al. suggested that $\Omega \geq 1.1$ and $\delta \leq 6.6$ should be used as necessary conditions to predict the formation of solid solution phases [14]. Although some inconsistencies are observed between the above-mentioned criteria, the criteria are helpful in predicting the formation of solid solution phases in multicomponent alloys. The VEC parameters in the TiNbTaZr and TiNbTaZrX (X = Cr, V, Mo, W, Fe) alloys were found to be <5.0, indicating the strong bcc structure formation tendency of these alloys when a solid solution phase is obtained. According to the above-mentioned criteria, TiNbTaZr and TiNbTaZrX, ($X_1 = Mo, W$) show a high possibility for the formation of a solid solution, whereas TiNbTaZrX, ($X_2 = Cr, V, and Fe$) alloys are...
not expected to show superior solid-solution-forming ability because of the large value of $\delta$. Between W and Mo, Mo is preferred for the fabrication of metallic biomaterials because Mo has been selected in conventional metallic biomaterials such as Ti–15Mo–5Zr–3Al [20–22] and Co–Cr–Mo [23,24]. In the present study, the TiNbTaZr and TiNbTaZrMo alloys were newly focused, and the microstructure, mechanical properties and biocompatibility of TiNbTaZrMo were investigated in terms of using HEAs as a new class of metallic biomaterials.

Arc-melted ingots were prepared by mixing lumps of the pure elements. To achieve a homogeneous distribution of the constituent elements in the alloy, the alloy was melted 10 times and maintained in a liquid state for approximately 300 s during each melting event. The annealed samples were obtained by vacuum annealing at 1273 K for 168 h. The microstructure and constituent phases of the ingots were investigated by X-ray diffraction (XRD) analysis, optical microscopy (OM), scanning electron microscopy (SEM), electron probe microanalysis (EPMA), and transmission electron microscopy (TEM). Rectangular specimens for compression testing with dimensions of approximately 2 mm × 2 mm × 5 mm were cut from the ingots by electron discharge machine. Compression tests were conducted using an Intron-type testing machine at nominal strain rate of 1.67 × 10$^{-2}$ mm s$^{-1}$.

Table 1

| Alloys                    | $\Delta S_{\text{mix}}$ [J mol$^{-1}$ K$^{-1}$] | $\Delta H_{\text{mix}}$ [kJ mol$^{-1}$] | $\delta$ | $\Omega$ | VEC | Phase            | References |
|---------------------------|-----------------------------------------------|----------------------------------------|----------|----------|-----|------------------|------------|
| TiNbTaZr                  | 1.42 R                                       | 2.5                                    | 5.3      | 11.6     | 4.50| bcc              | Present study |
| TiNbTaZrMo                | 1.61 R                                       | −1.8                                   | 5.9      | 19.7     | 4.80| bcc1 + (bcc2)    | Present study |
| TiNbTaZrW                 | 1.61 R                                       | −3.2                                   | 5.8      | 11.5     | 4.80| bcc1 + (bcc2)    | [18]       |
| TiNbTaZrV                 | 1.61 R                                       | 0.3                                    | 6.7      | 101      | 4.60| bcc              | [19]       |
| TiNbTaZrCr                | 1.61 R                                       | −3.7                                   | 8.2      | 8.9      | 4.80| Compounds        | [19]       |
| TiNbTaZrFe                | 1.61 R                                       | −10.1                                  | 8.4      | 3.2      | 5.20|                  |            |
| TiNbTaZrHf                | 1.61 R                                       | 2.7                                    | 5.5      | 12.4     | 4.40| bcc              | [16,17]   |
| CoCrMnFeNi                | 1.61 R                                       | 3.2                                    | 1.1      | 7.4      | 8.80| fcc              |            |

Fig. 1 shows the microstructure analysis results of the TiNbTaZrMo alloy, together with the XRD pattern of a quaternary TiNbTaZr alloy as a reference. Fig. 1a shows the XRD patterns of the TiNbTaZr and TiNbTaZrMo alloys. The TiNbTaZr alloy shows sharp diffraction peaks, indicated by the index●, and all peaks were identified as a bcc solid solution phase. The lattice constant of the bcc phase in the TiNbTaZr alloy evaluated by XRD was 0.332 nm, which is in good agreement with that estimated by the linear combination of pure elements (i.e., Vegard’s law [25], 0.336 nm). From the XRD pattern of the TiNbTaZrMo alloy, the two peaks indicated by the indexes● and ○ can be seen in the as-cast state. The constituent phases in the as-cast TiNbTaZrMo alloy were identified as a main bcc solid solution phase with a lattice constant of 0.325 nm (●) and a minor bcc phase with a lattice constant of 0.333 nm (○). The XRD patterns did not indicate the formation of any intermetallic compound phases or bcc-based ordered phases. These results suggest that the as-cast specimens for the TiNbTaZr and TiNbTaZrMo alloys had bcc solid solutions without any inclusions. The annealing did not lead the decomposition of bcc solid solution phases to other phases and the formation on intermetallic compounds in TiNbTaZrMo alloy, and stimulates the slight change in minor
The room-temperature engineering stress vs. plastic strain curves of the TiNbTaZrMo HEAs in the as-cast and annealed states obtained during compression testing are given in Fig. 2. The inset shows the 0.2% proof stress (σ_{0.2}) of the TiNbTaZrMo HEAs in the as-cast and annealed states, together with those of refractory TiNbTaZrHf HEA [16,17] and Ti-6Al–4V [26] as references. The as-cast and annealed TiNbTaZrMo HEAs show high σ_{0.2} of >1000 MPa. The values of σ_{0.2} in the annealed TiNbTaZrMo HEAs are higher than those of the refractory TiNbTaZrHf HEA and Ti-6Al–4V alloys. The annealing was effective in improving the deformability of the TiNbTaZrMo HEA, which may be related to the grain coarsening and/or redistribution of the constituent elements in the main-dendrite and inter-dendrite regions. The TiNbTaZrMo HEA shows high yield strength and good deformability.

Fig. 3 shows the osteoblasts cultured for 24 h on SUS316L (Fig. 3a), CP-Ti (Fig. 3b), and TiNbTaZrMo HEA in the as-cast (Fig. 3c) and annealed (Fig. 3d) states. The osteoblasts on the surfaces of the as-cast and annealed TiNbTaZrMo HEAs show a widespread morphology, which is quite similar to the morphology of the cells on CP-Ti. In
contrast, the osteoblasts on SUS316L show a relatively small, less wide-spread morphology. Cell spreading plays a significant role in cellular functions involving migration, proliferation, and protein synthesis. The obtained results indicate that the osteoblasts on the TiNbTaZrMo HEAs with and without annealing, as well as on CP-Ti, have a significant advantage in bone matrix formation. The cell density analyzed after 24 h cultivation quantitatively revealed that the osteoblasts on the as-cast and annealed TiNbTaZrMo HEAs had a significantly increased number of cells as compared to SUS316L. Notably, the as-cast TiNbTaZrMo HEA showed excellent biocompatibility comparable to that of CP-Ti. Moreover, the significantly superior biocompatibility of the annealed TiNbTaZrMo HEA as compared to CP-Ti is demonstrated for the first time (Fig. 3e). This indicates that the grain coarsening and/or redistibution of the constituent elements in the annealed TiNbTaZrMo HEA possibly accelerated the osteoblast adhesion. The combination of a Ti oxide layer and a Zr oxide layer in a TNTZ alloy has been shown to exhibit excellent biocompatibility [27]. Furthermore, a Ti–30Zr–7Mo alloy was reported to have shown a significantly increased number of cells as compared to CP-Ti, allowing the formation of a Zr oxide layer, as well as a Ti oxide layer [28]. Taken together, the excellent biocompatibility in the TiNbTaZrMo HEA obtained in this study may be due to the particular oxide layer based on the complicated arrangement of constituent metallic elements. Further research is necessary for clarifying the origin of the excellent biocompatibility in the TiNbTaZrMo HEA, which will be reported in future works. These results clearly indicate that the HEA shows potential as a new class of metallic biomaterials.

In conclusion, a novel equiatomic TiNbTaZrMo HEA composed of biocomparable elements was successfully developed as a metallic biomaterial. Two bcc solid solution phases were obtained in the TiNbTaZrMo HEA. An equi-axis fine dendrite structure was observed in the ingots. The HEA showed excellent biocompatibility compared to that of pure Ti, together with superior mechanical properties, indicating the possibility of using HEAs as a new class of metallic biomaterials.

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Appendix A. Supplementary data

Supplementary data to this article can be found online at http://dx.doi.org/10.1016/j.scriptamat.2016.10.028.

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