Available online at www.jourcc.com

Journal homepage: www.JOURCC.com

Journal of Composites and Compounds

TZNT alloy for surgical implant applications: A systematic review

Shima Nasibi [a], Kiana Alimohammadi [b], Leila Bazli [c]*, Sara Eskandarinezhad [d], Ali Mohammadi [e], Niloufar Sheysi [e]

[a] *Materials Science and Engineering Department, School of Engineering, Shiraz University, Shiraz, Iran*
[b] *Faculty of Materials science and engineering, Khajeh Nasir Toosi University of Technology (KNTU), Tehran, Iran*
[c] *School of Metallurgy and Materials Engineering, Iran University of Science and Technology, Tehran, Iran*
[d] *Department of Mining and Metallurgical Engineering, Yazd University, Yazd, Iran*
[e] *Department of Pharmaceutical Chemistry, Tehran Medical Sciences, Islamic Azad University (IAU), Tehran ,Iran*

A B S T R A C T

Owing to its good mechanical properties, enhanced wear resistance, good biological properties, biocompatibility, low cytotoxicity, and great corrosion behavior, Ti-Nb-Ta-Zr (TZNT) alloy, as new β titanium alloy, has attracted considerable attention for surgical implant applications. The need for the improvement of the implant properties in the physiological environment can be fulfilled by using the β titanium alloy with low elastic modulus. Additionally, this alloy can inhibit the surgical implant fracture, infection, inflammation, and the reaction of soft tissue with particulate debris. Therefore, the aim of this paper is to review the properties and applications of TZNT alloy as a promising choice for surgical implant applications.

A R T I C L E I N F O R M A T I O N

Article history:
Received 31 May 2020
Received in revised form 8 June 2020
Accepted 23 June 2020

Keywords:
TZNT alloy
Surgical implant
β-titanium alloy
Biomedical applications

Table of contents

1. Introduction

Given the good performance including good biocompatibility, lower elastic modulus, excellent corrosion resistance, and high specific strength, Ti and its alloys are considered as the optimum materials for surgical implants [1]. With scientific advances, the third generation of titanium alloys as the new type of β alloys for biomedical applications has been developed such as Al-free Ti-Zr-Ta-Nb- and Ti-Zr-Mo-based alloys. The newly developed β titanium alloys have more advantages over conventional Ti alloys and are considered as more suitable materials for human-implant applications [2].

In the past few decades, Ti alloys, especially, Ti-6Al-4V alloy and commercially pure (cp) Ti, have been widely utilized in orthopedic implants due to their desirable biocompatibility, excellent corrosion properties, and promising mechanical performance. Based on the history of thermo-mechanical processing and material composition, titanium alloys have been divided into α, near-α, metastable β, stable β or α + β categories. Zr is a neutral stabilizer while elements such as Ta and Nb are isomorphs of β-stabilizers. Compared to cp titanium (α-Ti) and Ti-6Al-4V (α + β Ti), β-Ti alloys exhibit some enhanced characteristics [3].

* *Corresponding author:Leila Bazli; E-mail: leilabazli64@gmail.com*
DOR: 20.1001.1.26765837.2020.2.3.1.1
https://doi.org/10.29252/jcc.2.2.1

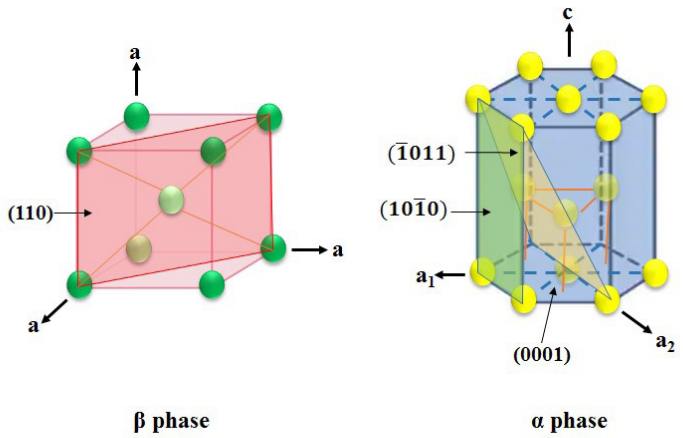

Fig. 1. Crystal structure of the α and β phases.

TNZT is a β-titanium quaternary alloy developed in recent years for orthopedic applications [4]. This alloy exhibits some promising properties including superior low elastic modulus [5-11] biocompatibility [12-16], good resistance to corrosion as well as the absence of toxic elements like vanadium and aluminum. The adverse tissue reaction and cytotoxicity resulting from V and Al have been extensively reported in the literature [3]. Complications caused by inflammation can be severe enough to make revision surgery necessary. Therefore, biomaterials and surface modification methods are required for the provision of the optimal infection resistance. In this regard, a comprehensive understating of the complicated interactions that occur at the interface of bone-implant is required. Two-thirds of implant-associated infections and revision surgeries have been reported to be due to the interaction of biomaterial with Staphylococcus and Staphylococcus aureus epidermis [17, 18]. Thus, investigations on the novel TNZT alloy with promising characteristics for surgical implant applications have attracted the attention of researchers.

2. Processing of β-titanium alloys

β alloys usually undergo a hot working process and the subsequent heat treatment. In the leaner β alloys, the α+β field is where the final hot working operation is conducted, while in the richer β alloys, it is preferentially performed in the β field. The heat treatment includes three steps: solution, quenching, and aging. If the solution treatment is performed above the temperature of β transus, the formed β grains will be coarse. On the other hand, the precipitation of the primary α_p phase occurrs when the solution treatment is performed just below the β transus. The crystal structure of the α and β phases are illustrated in Fig.1. The α_p volume fraction and shape is controlled by the heat treatment temperature and forging/rolling deformation, respectively. A needle-like α_p is formed when no working is done and by increasing the time of hot working the shape moves toward a spherical α_p shape [19].

An appropriate selection of deformation and temperatures initiating from the breakdown of ingot could control the size distribution and grain size of the β phase. It is possible to obtain small grain sizes by several deformation and recrystallization cycles [20].

A film-like α phase is preferentially precipitated in grain boundaries during the forging process, cooling process from β-forging, and final heat treatment. The suppression of the harmful precipitation of α in grain boundaries is possible by the high cooling rate from the beta phase region. If the cross-section is large, the grain boundary film can be broken by subsequent α/β-processing.

The secondary α_s precipitation with fine distribution occurs at lower temperatures between 400 ˚C to 600 ˚C. Aging time and temperature besides the temperature of solution treatment could control the volume and size of the phase. Depending on the volume fraction of the precipitates and their size, a remarkable strengthening effect can be achieved. In richer beta alloys, inhomogeneous precipitation of α_s can be conducted, while in lean beta alloys it is homogeneous. In the case of rich beta alloys, grain boundaries are the first sites for precipitation and then the precipitates are formed in the grain leading to the creation of some local unaged areas. Generally, a more homogenous distribution of the α_s precipitates and an enhanced aging response can be obtained by cold work. To summarize, the control of the beta titanium alloys properties are influenced by β grain size, grain boundary α, the size, shape, and volume fraction of α_p and α_s [21, 22]. $\alpha_{p,}$ $\alpha_{s,}$ and grain boundary α are schematically illustrated in Fig. 2.

3. Mechanical properties

3.1. Tensile strength

Yield stresses in the range of 900 to 1400 MPa can be obtained by the aging of β titanium alloys. However, by increased aging, a significant reduction in ductility is observed in all β alloys. This is due to the larger difference between the yield stress of the aged β matrix soft and primary α as well as the increase of strain localization in the aged matrix that results in early crack nucleation [23]. Duplex aging processes have been used to improve the fatigue and toughness resistance in more highly β-stabilized alloys, which have inhomogeneous α_s precipitations. The duplex aging consists of "low/high" - or "high/low" aging steps, which allow obtaining higher strength in shorter time, compared to aging in just one step [24, 25].

The ductility of the alloys can also be influenced by primary α_p.

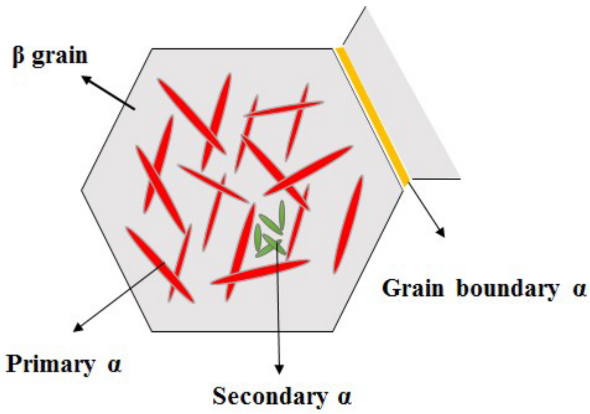

Fig. 2. Primary, secondary and grain boundary α.

The change from globular to acicular shape in primary α_p and also its coarsening, resulting from the processing, leads to the ductility reduction. This is due to the increased slip length or effective size of the soft primary α_p resulting in early crack nucleation [26]. Lower temperatures of solution heat treatment lead to the increase in the volume fraction of primary α_p and the reduction of ductility at a constant yield strength. For obtaining desirable yield stress, higher aging of the β phase with a larger volume fraction of soft α_p is required; however, this is in favor of crack nucleation. In other words, increased ductility and reduced yield strength is the consequence of the increased volume fraction of α_p at a constant aging treatment [27]. There is a correlation between the effects of grain boundary and grain size. Strength is not affected by these parameters; however, they can influence ductility. Because of the localized strain in the soft α film in the grain boundary, ductility is reduced resulting in the occurrence of crack nucleation and subsequent fracture in grain boundaries [28, 29]. In the case of intergranular crack nucleation, no conclusive explanation existed for the effect of the grain size on ductility.

3.2. Fracture Toughness

Fracture toughness is significantly reduced by increased aging. According to fractography analyses for ductility, the reason for this trend is an increase in localized strain and the strength difference between the aged matrix and the soft α_p [30]. Single-step aging has been replaced by duplex aging to improve toughness and strength [24]. Studies indicated that a combination of fine secondary α (resulting from low aging) and long, coarse primary α (resulting from high aging) forms a tortuous crack path leading to the increase in the toughness. Moreover, toughness will decrease when the shape of α_p phase transforms from elongated to globular shape [31]. Based on fractographic studies, a more pronounced crack deviation occurs when elongated α_p existed [32]. Increasing the volume fraction of α_p can also decrease toughness drastically at constant yield strength. An increase in the degree of matrix aging compensates for the higher volume fraction of soft α_p. The increased α_p volume fraction leads to an increase in toughness at constant aging [19].

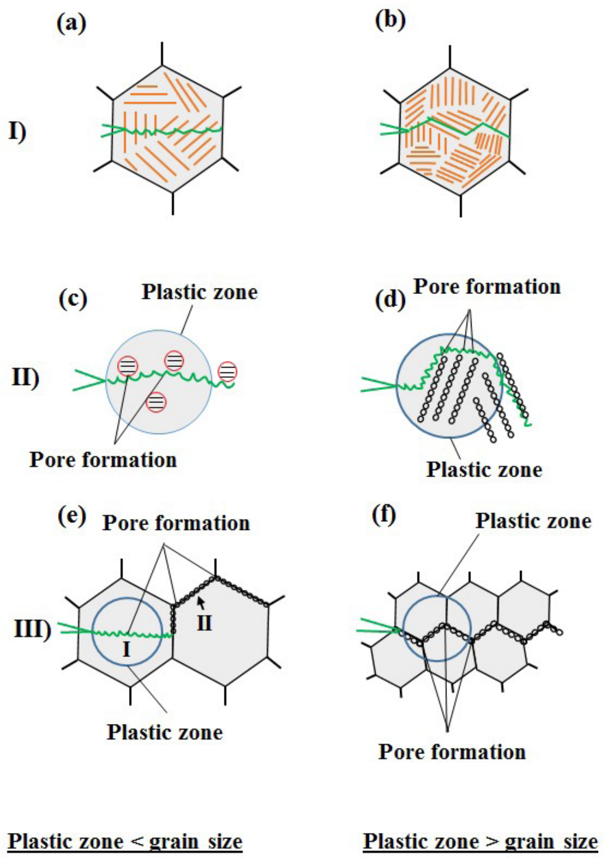

Fig. 3. Crack initiation and growth in β alloys.

Several authors [33, 34] have studied the role of grain boundary α and grain size. For instance, the fracture toughness of Ti-15-3 has been found to be reduced by beta grain refinement [35, 36]; while no effect was found for Ti-10-2-3 and Beta C [37]. It has been indicated that grain boundary α could lead to increase or decrease in fracture toughness, or it may has no effect on it. It has been reported that microstructures with very fine, recrystallized grains, and primary α_p decorated with grain boundary α show a drastic drop in fracture toughness in comparison with the microstructure with large grains [38].

To explain contradictory observations, one should consider different parameters including grain boundary, grain size, stress state, plastic zone size, and degree of aging [39]. In the following conclusions, the plastic zone is confined to the grain boundary α which acts as a low energy fracture path (Fig. 3).

The transgranular pre-fatigue crack will be the initiation of the fracture if the grain size is much larger than the plastic zone (large grain, high strength) [40]. Fracture toughness is not affected by grain boundary α in this fracture mode, because it is influenced by the intrinsic toughness of the aged matrix.

(II) The low energy path of soft grain boundary α can be the initiation site of cracks and its propagation when the beta grain size is much smaller than the size of plastic zone (low strength, small grain). For the transgranular fracture, smaller fracture toughness is obtained at constant yield stress. In the case of active grain boundary fracture mechanism, the increase in grain size results in more tortuosity in the crack path and the subsequent enhancement of toughness. When a broken up grain boundary α, called necklace, is formed instead of a continuous film, the cracks are still deflected; however, a higher energy path is provided and ductility is not reduced. Additionally, the plastic zone will be more confined to the grain boundary α film with an increase in matrix aging in the case of intergranular fracture, which will result in a lower toughness. Anisotropy in fracture toughness could be observed in stretched grains produced by forging due to the crack deviation effect and intergranular fracture.

(III) In the absence of grain boundary α, beta grain size does not influence toughness fracture due to transgranular fracture [19].

To sum up, a combination of maximum crack deviation and high-energy crack paths could result in an optimum toughness. This could be the combination of an aged matrix with acicular primary α_p or a large grain size with a broken up grain boundary α.

3.3. Fatigue

Beta alloys have good fatigue potential; for example, a cycle fatigue strength (HCF) of Ti-10-2-3 with large cross-section has been reported to be 700 MPa ($R= -1$, $K_t= 1$), which cannot be achieved for any other titanium alloys [41]. HCF strength can be increased by the increase in 0.2 % yield strength or aging. Some studies have also shown that the richer beta alloys exhibit a lower fatigue strength compared to leaner alloys. This is because α_s is heterogeneously precipitated in the richer beta alloys. Because of using a duplex aging, an increase in fatigue strength was obtained due to a more homogeneous α_s precipitation. Moreover, the results indicated that HCF strength could not exceed the upper limit by further aging. It can be concluded that at a higher strength, the soft regions such as primary α_p, zones without precipitates, or grain boundary α, which are fatigue cracks initiation sites, become more dominant. This is because the difference of strength between the aged matrix and these soft zones becomes higher. Additionally, the higher fatigue strength can be due to the localized slip in the aged matrix [42, 43].

It has been also shown that the fatigue strength of beta titanium alloys is enhanced by grain size reduction. It has been discussed that grain boundary α is the crack nucleation site. Similar to static properties, delayed crack nucleation occurs due to the reduction of the slip length of grain boundary alpha in smaller grain sizes. The studies on the effect of α/β deformation on fatigue strength after β-forging indicated that a higher ratio of high cycle fatigue strength to yield strength was observed in the purely β-forged condition in comparison with the beta+ alpha/beta-forged material with alpha/beta deformation higher than 30%. By an α/β deformation higher than 30%, high amounts of α grain boundary that were produced in the purely β-processed condition were effectively removed. This is also the reason why no further improvement of fatigue strength is observed in more than 30% α/β deformation. HCF strength is independent of the grain size effect in the case of grain boundary α suppression and the initiation of cracks from the aged matrix [19, 44, 45].

There is still a lack of data to understand and optimize the fatigue behavior; however, the obtained results already shed light on the fatigue resistance improvement approaches including homogeneous dispersion of secondary α, suppression, or reduction of grain boundary α, small grain size, and aging to an optimum level.

4. Properties of TZNT alloys

As mentioned, Ti alloys with metastable β structure, are good candidates for orthopedic applications due to high ductility, low elastic modulus, and the good corrosion resistance in the body environment [46, 47]. To avoid problems such as the stress shielding and the consequent osteoporosis, the difference between Young's moduli of bone and biomaterial should be reduced. Therefore, orthopedic materials are needed to have low Young's modulus. In general, Young's modulus of metastable β-Ti alloys is almost half of the Ti-6Al-4V alloy. By employing different methods such as conventional aging treatment [48, 49], severe plastic deformation [50], and the addition of alloying elements like Fe [23, 51], the strength of these alloys can be increased.

Zareidoost et al. [6] investigated the properties of different TZNT alloys by adding Ag (TZNT-Ag), Sn (TZNT-Sn), and Fe (TZNT-Fe) alloying elements. After suction casting, dendritic morphology was formed in the designed alloys; however, a more homogenous microstructure was obtained for the TZNT-Ag alloy. TZNT, TZNT-Ag, and TZNT-Fe consisted of the β phase, while TZNT-Sn showed separation of β-lean and β-rich regions in the alloy. Moreover, upon cold compressive deformation, very high ductility was obtained for the new TZNT alloys and TZNT-Ag showed the lowest Young's modulus around 65 GPa. Moreover, the ratio of compressive yield stress to Young's modulus was obtained in the range of 0.92-1.08% for all the prepared alloys. TZNT-Ag revealed the highest corrosion resistance in Ringer's solution.

In another study also conducted by Zareidoost et al. [52], as-cast $(Ti_{55}Zr_{25}Nb_{10}Ta_{10})_{99.5}$-$Fe_{0.5}$ alloy was cold-rolled and its effect on texture evolution and microstructure of the alloy was investigated. They reported that after different cold-rolling stages, hardness increased which was proposed to be related to grain refinement, the increase of microstrain, and the decrease of crystallite size. Additionally, it was indicated that the reduction of elastic modulus with the cold deformation increase was related to the texture evolution. Cold rolling up to 90% resulted in the increase in the intensity of α-fiber texture and the consequent increase in hardness and decrease in Young's modulus.

Li et al. [53] compared the corrosion behaviors of Ti12.5Zr2.5Nb2.5Ta, Ti6Al7Nb, TA2, and Ti6Al4V in Ringer's solution using the potentiodynamic technique. According to the results, the corrosion resistance of TZNT was higher than that of TA2, Ti6Al7Nb, and Ti6Al4V. Ta_2O_5, Nb_2O_5, ZrO_2, and TiO_2 were the constituents of the passive film on the TZNT's surface. These oxides with the nobler equilibrium constants improve the stability of the passive film. Additionally, adding elements with low electrochemical reaction potentials, such as Ta, Nb, and Zr could lead to the reduction of the anode activity and improvement of passive properties.

5. TZNT alloys for biomedical applications

5.1 Application in orthopedic implants

One of the promising candidates for applications in the orthopedic field is titanium alloys containing Ta, Zr, and Nb with metastable β phase [54-59]. This is because of their high corrosion resistance in biological environments, high ductility, low elastic modulus, and excellent biocompatibility [60]. However, due to their relatively low strength, the use of these alloys for orthopedic implants is limited [51, 52, 59, 61].

Approximately one million hip replacements has been recorded since 2003 in Northern Ireland, Wales, and England according to the National Joint Registry (NJR) report. Ti alloys, mainly Ti6Al-4V, have been utilized for decades in implant applications where load-bearing properties are required. However, they have some limitations including corrosion, wear [62], infection, aseptic loosening, and adverse soft tissue reaction to debris particles resulting in implant failure and the need for revision surgeries [18, 62]. In terms of mechanical properties, low fracture toughness and low strength can result in implant fracture. The main reason for failure is the difference between the elastic modulus of implant and bone, which results in stress shielding and resorption of bone. Using materials with a modulus close to the human bone, such as TNZT, is a sensible solution to this problem. These β-Ti alloys contain no toxic elements and have lowest elastic modulus among the β-Ti family. On the other hand, the poor wear behavior of TNZT limits its application as a load-bearing part of hip implants [63]. Therefore, the improvement of the implant properties is required.

Laser surface nitriding of TNZT is a way to improve its biological response and mechanical properties. Titanium nitride has remarkable antibacterial properties and good biocompatibility. In this regard, Donaghy et al. [18] used laser nitriding to apply an antibacterial surface on TNZT alloys for hip implant applications. They used incremental laser power to prepare laser-nitrided surfaces on TNZT. According to the results, rougher surfaces with distinctive features were formed by laser nitriding. Regardless of laser power, the surface of implants could be tailored to become hydrophilic after laser nitriding. It was proposed that fiber laser nitriding in a high power regime could be employed for the formation of antibacterial surface patterns on TNZT. It was observed that the most effective laser power was 45W, which created an overlapping crescent shape. With increasing power, the overlapping crescent shape becomes more obvious. Accordingly, laser-nitrided surfaces provided the implant with a remarkable antibacterial effect while showing no special advantage to mesenchymal stem cell response.

The micro-scale abrasive wear property of Ti-35Nb-7Zr-6Ta alloy, as human-implant materials, in terms of load and sliding distance was studied by Zheng et al. [2]. The evaluation of micro-scale abrasive wear behavior of the alloy was carried out in distilled water and Hank's solution and the influence of sliding and load distance was studied. According to the results, the increase in the distance led to the increase in the wear volume of the TZNT alloy due to the greater damage, however, the same regularity was not seen in the wear volume with the increase in load. At different simulated body fluids, the wear occurred under the same sliding distance. The wear mechanism affected the wear appearance. In the wastage map, minor areas of low wastage were observed and the rest was medium wastage, and no high wastage was resent. The wastage map was attributed to the alloy wear volume under different conditions.

Acharya et al. [59] investigated the effect of the Zr addition to a Ti-Nb-Ta-O alloy in terms of the functional response and mechanical properties for orthopedic applications. By varying the processing technique, different crystallographic textures were observed in Ti-Nb-Ta-Zr-O and Ti-Nb-Ta-O. It was found that both alloys possessed low elastic modulus because they have beta microstructures, however, the lower elastic modulus belonged to the Ti-Nb-Ta-O alloy. This is due to its favorable orientation of crystals resulting from the absence of Zr in the structure. Because of the presence of oxygen atoms in interstitial sites, the values of tensile strength were noticeably high for both alloys. In comparison with Ti-Nb-Ta-O alloy, Ti-Nb-Ta-Zr-O showed higher strength revealing the hardening effect of Zr. Both alloys exhibited the satisfactory in vitro biological behavior and corrosion resistance. Additionally, improved osteoblast attachment and lower corrosion rate were observed in the Ti-Nb-Ta-Zr-O alloy. It was concluded that the functional response and mechanical properties of both alloys were promising, and marginal improvement in the performance of Ti-Nb-Ta-Zr-O alloy for orthopedic applications was shown due to the presence of Zr.

5.2 Application in dental implant

Dental implantology was first emerged in 1957 by Per-Ingvar Brånemark, a Swedish orthopedic surgeon [64]. He found that bone continued to grow adjacent to Ti, which could provide bone with the capability to adhere to the Ti metal effectively without rejection. The adherence of bone to implant is called "osseointegration" and it is an important indicator of success rates in dental implantology [65, 66]. In 1982, the United States Food and Drug Administration recommended Ti as a dental implant material. Since then, dental implant manufacturing companies have widely investigated the development of modern materials and the surface treatments to improve osseointegration and consequently, enhance the overall implant success [67-71].

A new binary alloy with the formulation of 13-17% zirconium and 83-87% titanium has recently been introduced in dentistry for producing narrow-diameter implants. It has been claimed that better mechanical characteristics (40% higher fatigue strength and tensile strength of 953 MPa) could be achieved by the application of this alloy in comparison with Ti-6Al-4V and cp Ti [72, 73]. Improved osseointegration can be obtained by adding Zr to Ti [65], and enhanced biocompatibility is shown compared to pure titanium [74].

TZNT is considered as another new promising Ti alloy for surgical implants. This alloy benefits from the unique advantage of the elasticity modulus closer to the human bone than that of conventional Ti alloys as well as admission strain (0.65%) near to human bones (0.67%). The incorporation of alloying elements such as Ta, Nb, and Zr enhances the alloy corrosion resistance and no adverse tissue reactions or toxicity is observed [74-76].

Wang et al. [77] conducted osseointegration studies on Ti–Nb–Zr–Ta–Si titanium alloy for dental implant materials. For the preparation of the alloy, high-energy ball milling was used and subsequently, reactive sintering was performed. Based on the results, compared to cp Ti implants, the prepared Ti alloy implants exhibited a higher rate of mineral apposition after four weeks of healing. It was suggested that the prepared alloy implants showed osseointegration comparable to cp Ti implants. Additionally, a more favorable rate of mineral apposition was promoted by the Ti alloy implants compared to cp Ti implants. It was concluded that the prepared TZNT alloy could be considered as an alternative material for dental implants due to improved mineral matrix apposition rate and establishment of a close direct contact compared to cp Ti implants.

The corrosion resistance of Ti−Nb−Ta−Zr−Fe (TNTZF) alloy, which is currently utilized as replacement materials for dental implants, artificial hip joints, and other hard tissues, was studied by Xu et al. [78]. Compared to Ti–6Al–4V ELI alloy, TNTZF alloy showed wider passive region, passive current density with more stability, lower corrosion current density, and higher corrosion potential indicating its better corrosion resistance. Additionally, in contrast to Ti–6Al–4V ELI alloy, pitting corrosion was not indicated on its surface passive film. The surface passive film on TNTZF alloy was found to be composed of TiO, ZrO_2, Ta_2O_5, NbO_2, Nb_2O_5, and Ti_2O_3 oxides in the TiO_2 matrix. These oxides provide the passive film of TNTZF with more stability and protective ability compared to Ti−6Al−4V ELI alloy leading to its superior corrosion resistance.

6. Conclusions and future insights

As elements such as titanium, niobium, zirconium, and tantalum exhibit good corrosion resistance and excellent biocompatibility in the physiological environments, they are incorporated in the initial Ti alloy (e.g., TZNT). Nb and Ta are also β-stabilizing alloying elements. Moreover, Zr plays a β-stabilizer role in titanium alloys containing Nb and/or Ta. Owing to their excellent physicochemical properties, low density, high corrosion resistance, and good biocompatibility, TZNT alloy have been used as a surgical implant material. Additionally, the low elastic modulus of TZNT alloy can provide protection from adverse soft tissue reaction to debris, inflammation, infection, and consequent implant failure. In conclusion, the development of TZNT alloy can lead to the achievement of a more promising candidate for application in surgical implants.

It has been found that improvement of properties, particularly in surgical implants, can be achieved by using TZNT alloy. Additionally, there is the possibility to fabricate special implant material and enhance the properties of these alloys to promote the surgical implants' advantages and reduce the risk factors, and consequently, the surgical implant failure. Thus, it is expected that this novel implant material should be improved owing to the optimal properties offered by TZNT implants. Meanwhile, these implants will be considered as alternatives to Ti-based and Zr-based implants in dental and orthopedic implantology.

Acknowledgments

The authors received no financial support for the research, authorship and/or publication of this article.

Conflict of Interest

All authors declare no conflicts of interest in this paper.

REFERENCES

[1] E. Sharifi Sedeh, S. Mirdamadi, F. Sharifianjazi, M. Tahriri, Synthesis and Evaluation of Mechanical and Biological Properties of Scaffold Prepared From Ti and Mg With Different Volume Percent, Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry 45(7) (2015) 1087-1091.

[2] Z. Zheng, Z. Wang, W. Huang, Influence of load and sliding distance on the micro-scale abrasive wear behavior of TZNT alloy, Journal of the Chinese Advanced Materials Society 4(1) (2016) 82-90.

[3] L.C. Donaghy, R. McFadden, C.G. Smith, S. Kelaini, L. Carson, S. Malinov, A. Margariti, C.-W. Chan, Fibre Laser Treatment of Beta TNZT Titanium Alloys for Load-Bearing Implant Applications: Effects of Surface Physical and Chemical Features on Mesenchymal Stem Cell Response and Staphylococcus aureus Bacte-rial Attachment, Coatings 9(3) (2019).

[4] L. Zhou, T. Yuan, J. Tang, J. He, R. Li, Mechanical and corrosion behavior of titanium alloys additively manufactured by selective laser melting – A comparison between nearly β titanium, α titanium and α + β titanium, Optics & Laser Technol-ogy 119 (2019) 105625.

[5] M. Sowa, M. Parafiniuk, C.M.S. Mouzêlo, A. Kazek-Kęsik, I.S. Zhidkov, A.I. Kukharenko, S.O. Cholakh, E.Z. Kurmaev, W. Simka, DC plasma electrolytic oxidation treatment of gum metal for dental implants, Electrochimica Acta 302

(2019) 10-20.
[6] A. Zareidoost, M. Yousefpour, A study on the mechanical properties and cor-ro-sion behavior of the new as-cast TZNT alloys for biomedical applications, Ma-teri-als Science and Engineering: C 110 (2020) 110725.
[7] S. Li, T.-h. Nam, Superelasticity and tensile strength of Ti-Zr-Nb-Sn alloys with high Zr content for biomedical applications, Intermetallics 112 (2019) 106545.
[8] S.F. Jawed, C.D. Rabadia, Y.J. Liu, L.Q. Wang, P. Qin, Y.H. Li, X.H. Zhang, L.C. Zhang, Strengthening mechanism and corrosion resistance of beta-type Ti-S. Nasibi et al. / Journal of Composites and Compounds 2 (2020) 62-6867Nb-Zr-Mn alloys, Materials Science and Engineering: C 110 (2020) 110728.
[9] Y.P. Sharkeev, V.A. Skripnyak, V.P. Vavilov, E.V. Legostaeva, A.A. Kozulin, A.O. Chulkov, A.Y. Eroshenko, O.A. Belyavskaya, V.V. Skripnyak, I.A. Gluk-hov, Special Aspects of Microstructure, Deformation and Fracture of Bioinert Zirconi-um and Titanium-Niobium Alloys in Different Structural States, Russian Physics Journal 61(9) (2019) 1718-1725.
[10] T. Kokubo, S. Yamaguchi, Simulated body fluid and the novel bioactive ma-terials derived from it, Journal of Biomedical Materials Research Part A 107(5) (2019) 968-977.
[11] A. Vladescu, M. Badea, S.C. Padmanabhan, G. Paraschiv, L. Floroian, L. Gaman, M.A. Morris, J.-L. Marty, C.M. Cotrut, Chapter 15 - Nanomaterials for medical applications and their antimicrobial advantages, in: A.-M. Holban, A.M. Grumezescu (Eds.), Materials for Biomedical Engineering, Elsevier2019, pp. 409-431.
[12] A.S. Konopatsky, S.M. Dubinskiy, Y.S. Zhukova, V. Sheremetyev, V. Brai-lovski, S.D. Prokoshkin, M.R. Filonov, Ternary Ti-Zr-Nb and quaternary Ti-Zr-Nb-Ta shape memory alloys for biomedical applications: Structural fea-tures and cyclic mechanical properties, Materials Science and Engineering: A 702 (2017) 301-311.
[13] V.T. Nguyen, M. Qian, Z. Shi, T. Song, L. Huang, J. Zou, A novel quaternary equiatomic Ti-Zr-Nb-Ta medium entropy alloy (MEA), Intermetallics 101 (2018) 39-43.
[14] X. Meng, X. Wang, Y. Guo, S. Ma, W. Luo, X. Xiang, J. Zhao, Y. Zhou, Bio-compatibility Evaluation of a Newly Developed Ti-Nb-Zr-Ta-Si Alloy Im-plant, Journal of Biomaterials and Tissue Engineering 6(11) (2016) 861-869.
[15] T. Nagase, M. Todai, T. Hori, T. Nakano, Microstructure of equiatomic and non-equiatomic Ti-Nb-Ta-Zr-Mo high-entropy alloys for metallic biomaterials, Journal of Alloys and Compounds 753 (2018) 412-421.
[16] X. Song, C. Xiong, F. Zhang, Y. Nie, Y. Li, Strain induced martensite stabi-liz-ation in β Ti-Zr-Nb shape memory alloy, Materials Letters 259 (2020) 126914.
[17] W.F. Oliveira, P.M.S. Silva, R.C.S. Silva, G.M.M. Silva, G. Machado, L.C.B.B. Coelho, M.T.S. Correia, Staphylococcus aureus and Staphylococ-cus epidermidis infections on implants, Journal of Hospital Infection 98(2) (2018) 111-117.
[18] C. Lubov Donaghy, R. McFadden, S. Kelaini, L. Carson, A. Margariti, C.-W. Chan, Creating an antibacterial surface on beta TNZT alloys for hip implant applications by laser nitriding, Optics & Laser Technology 121 (2020) 105793.
[19] C. Leyens, M. Peters, Titanium and Titanium Alloys: Fundamentals and Ap-plications, Wiley2006.
[20] G. Welsch, R. Boyer, E.W. Collings, Materials Properties Handbook: Ti-tani-um Alloys, ASM International1993.
[21] A.P. Mouritz, Introduction to Aerospace Materials, Elsevier Science2012.
[22] I. Polmear, D. StJohn, J.-F. Nie, M. Qian, 7 - Titanium Alloys, in: I. Pol-mear, D. StJohn, J.-F. Nie, M. Qian (Eds.), Light Alloys (Fifth Edition), But-ter-worth-Heinemann, Boston, 2017, pp. 369-460.
[23] I. Kopova, J. Stráský, P. Harcuba, M. Landa, M. Janeček, L. Bačákova, New-ly developed Ti–Nb–Zr–Ta–Si–Fe biomedical beta titanium alloys with increased strength and enhanced biocompatibility, Materials Science and Engineering: C 60 (2016) 230-238.
[24] R. Santhosh, M. Geetha, V. Saxena, M.N. Rao, Effect of duplex aging on microstructure and mechanical behavior of beta titanium alloy Ti–15V–3Cr–3Al–3Sn under unidirectional and cyclic loading conditions, International Journal of Fatigue 73 (2015) 88-97.
[25] A.E. Chaikh, P. Schmidt, H.J. Christ, Fatigue properties of duplex-aged Ti 38-644 metastable beta titanium alloy, Procedia Engineering 2(1) (2010) 1973-1982.
[26] M.J. Donachie, Titanium: A Technical Guide, 2nd Edition, ASM Interna-tion-al2000.
[27] Y. Ren, S. Zhou, W. Luo, Z. Xue, Y. Zhang, Influence of primary α-phase volume fraction on the mechanical properties of Ti-6Al-4V alloy at different strain rates and temperatures, IOP Conference Series: Materials Science and Engi-neer-ing, IOP Publishing, 2018, p. 022022.
[28] Y. Chen, Z. Du, S. Xiao, L. Xu, J. Tian, Effect of aging heat treatment on mi-crostructure and tensile properties of a new β high strength titanium alloy, Jour-nal of alloys and compounds 586 (2014) 588-592.
[29] C. Bo, S. Bing, L. Dong, Effect of heat treatment on microstructure and me-chanical properties of laser melting deposited TC17 titanium alloy, Chinese J La-sers 41(4) (2014) 0403001.
[30] G. Srinivasu, Y. Natraj, A. Bhattacharjee, T. Nandy, G.N. Rao, Tensile and fracture toughness of high strength β Titanium alloy, Ti–10V–2Fe–3Al, as a func-tion of rolling and solution treatment temperatures, Materials & Design 47 (2013) 323-330.
[31] S. Sadeghpour, S. Abbasi, M. Morakabati, S. Bruschi, Correlation between al-pha phase morphology and tensile properties of a new beta titanium alloy, Mate-ri-als & Design 121 (2017) 24-35.
[32] V.K. Saxena, V. Radhakrishnan, Effect of phase morphology on fatigue crack growth behavior of α-β titanium alloy—A crack closure rationale, Metallurgical and materials transactions A 29(1) (1998) 245-261.
[33] S. Ankem, C. Greene, Recent developments in microstructure/property re-la-tionships of beta titanium alloys, Materials Science and Engineering: A 263(2) (1999) 127-131.
[34] J. Tiley, T. Searles, E. Lee, S. Kar, R. Banerjee, J. Russ, H. Fraser, Quanti-fi-cation of microstructural features in α/β titanium alloys, Materials Science and Engineering: A 372(1-2) (2004) 191-198.
[35] Y. Kawabe, S. Muneki, Strengthening capability of beta titanium alloys, Beta Titanium Alloys in the 1990's1993.
[36] E. Breslauer, A. Rosen, Relationship between microstructure and mechanical properties in metastable β titanium 15–3 alloy, Materials science and technology 7(5) (1991) 441-446.
[37] J. Ferrero, J. Wood, P. Russo, Microstructure/Mechanical property rela-tion-ships in bar products of Beta-C trademark (Ti-3Al-8V-6Cr-4Mo-4Zr), Beta Titani-um Alloys in the 1990's1993.
[38] C. Sauer, G. Lütjering, Influence of α layers at β grain boundaries on me-chan-ical properties of Ti-alloys, Materials Science and Engineering: A 319 (2001) 393-397.
[39] J.W. Foltz, B. Welk, P.C. Collins, H.L. Fraser, J.C. Williams, Formation of grain boundary α in β Ti alloys: its role in deformation and fracture behavior of these alloys, Metallurgical and Materials Transactions A 42(3) (2011) 645-650.
[40] C.M. Branco, L.G. Rosa, Advances in Fatigue Science and Technology, Springer Netherlands2012.
[41] R. Boyer, Applications of beta titanium alloys in airframes, The Miner-als, Metal & Materials Society(USA) (1993) 335-346.
[42] G. Lütjering, J. Albrecht, C. Sauer, T. Krull, The influence of soft, preci-pi-tate-free zones at grain boundaries in Ti and Al alloys on their fatigue and frac-ture behavior, Materials Science and Engineering: A 468 (2007) 201-209.
[43] M. Niinomi, Mechanical biocompatibilities of titanium alloys for biomedi-cal applications, Journal of the mechanical behavior of biomedical materials 1(1) (2008) 30-42.
[44] S. Shekhar, R. Sarkar, S.K. Kar, A. Bhattacharjee, Effect of solution treatment and aging on microstructure and tensile properties of high strength β titanium al-loy, Ti–5Al–5V–5Mo–3Cr, Materials & Design 66 (2015) 596-610.
[45] C. Tan, X. Li, Q. Sun, L. Xiao, Y. Zhao, J. Sun, Effect of α-phase morphology on low-cycle fatigue behavior of TC21 alloy, International Journal of Fatigue 75 (2015) 1-9.
[46] J. Gao, Y. Huang, D. Guan, A.J. Knowles, L. Ma, D. Dye, W.M. Rainforth, Deformation mechanisms in a metastable beta titanium twinning induced plasticity alloy with high yield strength and high strain hardening rate, Acta Materialia 152 (2018) 301-314.
[47] M.A.-H. Gepreel, Improved elasticity of new Ti-alloys for biomedical ap-pli-cations, Materials Today: Proceedings 2 (2015) S979-S982.
[48] S. Bahl, A.S. Krishnamurthy, S. Suwas, K. Chatterjee, Controlled nanoscale precipitation to enhance the mechanical and biological performances of a metas-ta-ble β Ti-Nb-Sn alloy for orthopedic applications, Materials & Design 126 (2017) 226-237.
[49] C. Xiong, P. Xue, B. Sun, Y. Li, Effect of annealing temperature on the mi-cro-structure and superelasticity of Ti-19Zr-10Nb-1Fe alloy, Materials Science and En-gineering: A 688 (2017) 464-469.
[50] V. Cojocaru, D. Raducanu, T. Gloriant, D. Gordin, I. Cinca, Effects of cold-rolling deformation on texture evolution and mechanical properties of Ti–29Nb–9Ta–10Zr alloy, Materials Science and Engineering: A 586 (2013) 1-10.
[51] J. Stráský, P. Harcuba, K. Václavová, K. Horváth, M. Landa, O. Srba, M. Janeček, Increasing strength of a biomedical Ti-Nb-Ta-Zr alloy by alloying with Fe, Si and O, Journal of the Mechanical Behavior of Biomedical Materials 71 (2017) 329-336.
[52] A. Zareidoost, M. Yousefpour, Effect of cold rolling on the microstructure and texture evolution of as-cast (Ti55Zr25Nb10Ta10)99.5-Fe0.5 alloy, Materials

Letters 259 (2020) 126876.
[53] J. Li, L. Zhou, Z. Li, Corrosion behaviors of a new titanium alloy TZNT for surgical implant application in Ringer's solution, Rare Metals 29(1) (2010) 37-44.
[54] W. Weng, A. Biesiekierski, Y. Li, C. Wen, Effects of selected metallic and in-terstitial elements on the microstructure and mechanical properties of beta titanium alloys for orthopedic applications, Materialia 6 (2019) 100323.
[55] W. Weng, A. Biesiekierski, J. Lin, S. Ozan, Y. Li, C. Wen, Impact of the rare earth elements scandium and yttrium on beta-type Ti-24Nb-38Zr-2Mo-base alloys for orthopedic applications, Materialia 9 (2020) 100586.
[56] S. Acharya, A.G. Panicker, V. Gopal, S.S. Dabas, G. Manivasagam, S. Su-was, K. Chatterjee, Surface mechanical attrition treatment of low modulus Ti-Nb-Ta-O alloy for orthopedic applications, Materials Science and Engineering: C 110 (2020) 110729.
[57] W. Xu, X. Lu, J. Tian, C. Huang, M. Chen, Y. Yan, L. Wang, X. Qu, C. Wen, Microstructure, wear resistance, and corrosion performance of $Ti_{35}Zr_{28}Nb$ alloy fabricated by powder metallurgy for orthopedic applications, Journal of Materials Science & Technology 41 (2020) 191-198.
[58] J. Ureña, E. Tabares, S. Tsipas, A. Jiménez-Morales, E. Gordo, Dry sliding wear behaviour of β-type Ti-Nb and Ti-Mo surfaces designed by diffusion treatments for biomedical applications, Journal of the Mechanical Behavior of Biomedical Materials 91 (2019) 335-344.
[59] S. Acharya, A.G. Panicker, D.V. Laxmi, S. Suwas, K. Chatterjee, Study of the influence of Zr on the mechanical properties and functional response of Ti-Nb-Ta-Zr-O alloy for orthopedic applications, Materials & Design 164 (2019) 107555.
[60] I. Çaha, A.C. Alves, P.A.B. Kuroda, C.R. Grandini, A.M.P. Pinto, L.A. Rocha, F. Toptan, Degradation behavior of Ti-Nb alloys: Corrosion behavior through 21 days of immersion and tribocorrosion behavior against alumina, Corrosion Science 167 (2020) 108488.
[61] S. Ozan, J. Lin, Y. Li, Y. Zhang, K. Munir, H. Jiang, C. Wen, Deformation mechanism and mechanical properties of a thermomechanically processed β Ti–28Nb–35.4Zr alloy, Journal of the Mechanical Behavior of Biomedical Materials 78 (2018) 224-234.
[62] S.K. Kolawole, W. Hai, S. Zhang, Z. Sun, M.A. Siddiqui, I. Ullah, W. Song, F. Witte, K. Yang, Preliminary study of microstructure, mechanical properties and corrosion resistance of antibacterial Ti-15Zr-xCu alloy for dental application, Journal of Materials Science & Technology 50 (2020) 31-43.
[63] C.L. Donaghy, R. McFadden, G.C. Smith, S. Kelaini, L. Carson, S. Malin-ov, A. Margariti, C.-W. Chan, Fibre laser treatment of beta TNZT titanium alloys for load-bearing implant applications: Effects of surface physical and chemical features on mesenchymal stem cell response and Staphylococcus aureus bacterial attachment, Coatings 9(3) (2019) 186.
[64] K. Zhang, Q. Van Le, Bioactive Glass Coated Zirconia for Dental Implants: a review, Composites and Compounds 2(1) (2020).
[65] L. Bazli, H. Nargesi khoramabadi, A. Modarresi Chahardehi, H. Arsad, B. Malekpouri, M. Asgari Jazi, N. Azizabadi, Factors influencing the failure of dental implants: A Systematic Review, Composites and Compounds 2(1) (2020).
[66] F. Sharifianjazi, A.H. Pakseresht, M. Shahedi Asl, A. Esmaeilkhanian, H. Nar-gesi khoramabadi, H.W. Jang, M. Shokouhimehr, Hydroxyapatite Con-solidated by Zirconia: Applications for Dental Implant, Composites and Compounds 2(1) (2020).
[67] J. Diaz-Marcos, 9 - Bone response to decontamination treatments for dental biomaterials, in: A. Piattelli (Ed.), Bone Response to Dental Implant Materials, Woodhead Publishing2017, pp. 163-184.
[68] L. Gaviria, J.P. Salcido, T. Guda, J.L. Ong, Current trends in dental implants, J Korean Assoc Oral Maxillofac Surg 40(2) (2014) 50-60.
[69] S. Rahimi, F. SharifianJazi, A. Esmaeilkhanian, M. Moradi, A.H. Safi Samgh-abadi, Effect of SiO_2 content on Y-TZP/Al_2O_3 ceramic-nanocomposite proper-ties as potential dental applications, Ceramics International 46(8, Part A) (2020) 10910-10916.
[70] M. Nejati, M.R. Rahimipour, I. Mobasherpour, A.H. Pakseresht, Micro-struc-tural analysis and thermal shock behavior of plasma sprayed ceria-stabilized zir-conia thermal barrier coatings with micro and nano Al_2O_3 as a third layer, Surface and Coatings Technology 282 (2015) 129-138.
[71] A.H. Pakseresht, A.H. Javadi, E. Ghasali, A. Shahbazkhan, S. Shakhesi, Eval-uation of hot corrosion behavior of plasma sprayed thermal barrier coatings with graded intermediate layer and double ceramic top layer, Surface and Coatings Technology 288 (2016) 36-45.
[72] E.H. Jazi, R. Esalmi-Farsani, G. Borhani, F.S. Jazi, Synthesis and Charac-ter-ization of In Situ Al-$Al1_3Fe_4$-Al_2O_3-TiB_2 Nanocomposite Powder by Mechanical Alloying and Subsequent Heat Treatment, Synthesis and Reactivity in Inorganic, Metal-Organic, and Nano-Metal Chemistry 44(2) (2014) 177-184.
[73] A. Esmaeilkhanian, F. Sharifianjazi, A. Abouchenari, A. Rouhani, N. Parvin, M. Irani, Synthesis and Characterization of Natural Nano-hydroxyapatite Derived from Turkey Femur-Bone Waste, Applied Biochemistry and Biotechnology 189(3) (2019) 919-932.
[74] S. Bhasin, E. Perwez, S. Sachdeva, R. Mallick, Trends in prosthetic bioma-te-rials in implant dentistry, Journal of the International Clinical Dental Research Organization 7(3) (2015) 148-159.
[75] A. Brizuela, M. Herrero-Climent, E. Rios-Carrasco, V.J. Rios-Santos, A.R. Pérez, M.J. Manero, J. Gil Mur, Influence of the Elastic Modulus on the Osseointe-gration of Dental Implants, Materials 12(6) (2019).
[76] Y. Kirmanidou, M. Sidira, M.-E. Drosou, V. Bennani, A. Bakopoulou, A. Tsouknidas, N. Michailidis, K. Michalakis, New Ti-Alloys and Surface Mo-di-fications to Improve the Mechanical Properties and the Biological Response to Orthopedic and Dental Implants: A Review, BioMed Research International 2016 (2016) 2908570.
[77] X. Wang, X. Meng, S. Chu, X. Xiang, Z. Liu, J. Zhao, Y. Zhou, Osseointegra-tion behavior of novel Ti–Nb–Zr–Ta–Si alloy for dental implants: an in vivo study, Journal of Materials Science: Materials in Medicine 27(9) (2016) 139.
[78] Y.-f. Xu, Y.-f. Xiao, D.-q. Yi, H.-q. Liu, L. Wu, J. Wen, Corrosion behavior of Ti–Nb–Ta–Zr–Fe alloy for biomedical applications in Ringer's solution, Transactions of Nonferrous Metals Society of China 25(8) (2015) 2556-2563.