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PHYSICAL METALLURGY  
AND HEAT TREATMENT

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## $\beta$ -Ti-Based Alloys for Medical Applications

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**Abstract**—Titanium alloys have been used for medical purposes for over 60 years. They are employed in the manufacture of artificial heart valves, blood vessel stents, and endoprostheses of bones and joints (shoulders, knees, hips, and elbows); for the reconstruction of auricles; in facial surgery; and as dental implants. In first-generation materials (such as technically pure titanium or VT6 alloys), the matrix consisted of  $\alpha$ -Ti phase or a mixture of  $\alpha$  and  $\beta$  phases. Unfortunately, implants from first-generation materials require replacement after as early as 10–15 years of usage. This is due to the degradation of the implants and loss of contact with the bone. Recently, these materials have been replaced by  $\beta$ -titanium alloys, second-generation materials that make it possible to exclude the harmful effect of aluminum and vanadium ions released during the gradual corrosion of the implant, and their elastic modulus is closer to the values for living bone than those for  $\alpha$  and  $\alpha + \beta$  alloys. Important directions in the development of  $\beta$ -titanium alloys include increasing their mechanical strength, fatigue strength, corrosion resistance, and biocompatibility. New methods for the production and thermo-mechanical processing of titanium alloys, such as additive technologies or severe plastic deformation, are created and developed. Expensive alloying elements (such as tantalum, zirconium, or niobium) are very successfully replaced with cheaper ones (for example, chromium and manganese). As a result, the properties of titanium implants are gradually getting closer to those of human bone, and their service life is steadily increasing. In this regard, we have carried out a comparative analysis of  $\beta$ -titanium-based alloys for medical applications.

**Keywords:** titanium alloys,  $\beta$ -titanium, endoprostheses, implants, microstructure, biocompatibility

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### INTRODUCTION

To a certain extent, materials for the reconstruction of various elements of the human body have been known since ancient times. However, their widespread use in medicine began only after World War II. They significantly improve the quality and life expectancy of an increasingly aging world population. Currently, they are used in the manufacture of artificial heart valves, blood-vessel stents, and endoprostheses of bones and joints (shoulders, knees, hips, and elbows); for the reconstruction of auricles; in facial surgery; and as dental implants. The most common are endoprostheses for replacing vertebrae and knee and hip joints.

It is known that degenerative diseases such as arthritis deteriorate the mechanical properties of bones and joints due to excessive stress, as well as due to poor or absent normal biological self-healing processes, which is accompanied by unbearable pain and a decrease in or loss of joint function. At least 90% of the population over the age of 40 suffer in one way or another from such degenerative pathological changes in the musculoskeletal system, and the number of elderly people with this pathology has increased dramatically in recent years.

Artificial biomaterials make it possible to significantly expand the possibilities of therapy for pathological conditions such as osteoporosis, osteoarthritis,

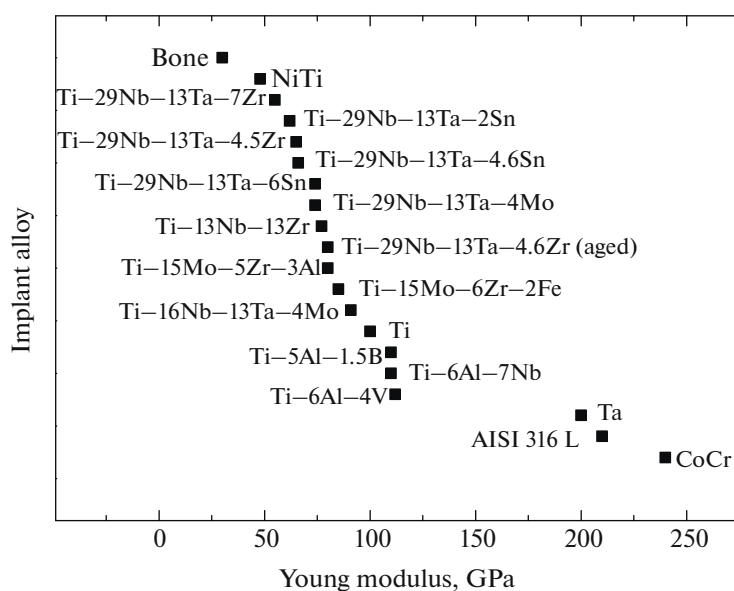


Fig. 1. Elastic modulus of biomedical alloys in comparison with natural bone.

and injuries. Another group of patients with high demand for surgical replacement of various elements of the skeleton with implants includes cancer patients with bone-tissue pathology resulting from primary neoplasms or metastases.

The choice of biomaterials, as well as the design of products made from them, primarily depends on the field of medical application of the product being developed and the individual characteristics of the patient. The development of new materials is an interdisciplinary problem. It typically requires collaboration between materials scientists, engineers, biomedical product designers, bioengineering and cell technology specialists, and clinical practitioners. For a medical implant to serve for a long time and not cause rejection [1–3], it must have a number of important properties, such as the required mechanical properties, biocompatibility [4], high resistance to corrosion and abrasion [5], and the ability to integrate in the tissues of the human or animal body and not cause allergic reactions [6].

The aim of this work was to carry out a comparative analysis of  $\beta$ -titanium-based alloys for medical applications.

#### ADVANTAGES OF TITANIUM ALLOYS

Currently, surgical implants from metal alloys are designed using chromium–nickel stainless steel (316LSS), cobalt–chromium alloys, and titanium and its alloys [7–14]. However, it was found that elements such as nickel, cobalt, and chromium are gradually released from implants made of stainless steel and

cobalt–chromium alloys due to corrosion in fluids of the human body [15], which causes toxic effects [15].

In addition, both chromium–nickel stainless steels and chromium–cobalt alloys have a much higher elastic modulus compared to bone (Fig. 1). This leads to the insufficient transfer of mechanical stresses from the prosthesis to the bone and, as a consequence, to bone resorption and separation of the implant from the skeletal bones after several years of use. Fatigue fracture is also a problem (for example, in hip-joint prostheses, which undergo numerous loading and unloading cycles during usage over many years) [16].

Currently, titanium-based alloys are recognized as the best materials for prosthetics in clinical practice. This is due to the unique combination of properties of titanium and its alloys, such as high strength, low density (and therefore high specific strength), good corrosion resistance, inertness to the biological environment (that is, to the tissues surrounding the implant), increased biocompatibility, low elastic modulus, and high ability for integration with bones and other tissues [7–14, 17, 18]. Therefore, for example, the elastic modulus of titanium alloys ranges from 110 to 55 GPa, while for chromium–nickel stainless steels it is 210 and 240 GPa for a chromium–cobalt alloy (see Fig. 1). In other words, this is a very attractive property of titanium alloys.

The first attempts to use titanium for the manufacture of bone prostheses were made in the late 1930s. At that time, it was found that titanium is suitable for replacing femur bones in cats, along with other materials such as stainless steel or vitalium (an alloy of cobalt, chromium, and molybdenum). Nowadays,

implants are most often manufactured using a commercial-grade titanium and VT6 alloy (also called Ti–6Al–4V ELI or Ti64). Although the VT6 alloy was originally developed for aviation, its high corrosion resistance and biocompatibility have made it important for the biomedical industry as well.

In addition to the manufacture of implants, titanium alloys are widely used for other medical devices such as wheelchairs and removable limb prostheses. The range of application of titanium alloys in medicine is truly amazing. It includes dental implants and endoprostheses for facial surgery, hip joints, knees, shoulder joints, spine, elbow joints, and wrists; osteosynthesis elements for fixing bones (pins, screws, and plates); housings for cardiac pacemakers and artificial heart valves; surgical instruments; and parts of high-speed centrifuges for separating blood components [19–21].

Although commercially pure titanium and its VT6 alloys have gained an outstanding reputation for their high corrosion resistance and biocompatibility, the long-term operation of implants and prostheses made from these materials raises some concerns due to the gradual release of aluminum and vanadium ions. Thus, it was found that the release of aluminum and vanadium ions from the VT6 alloy can cause long-term health problems, stimulating the development of, for example, Alzheimer's disease, neuropathy, and osteomalacia (a systemic disease associated with softening of bones due to insufficient bone mineralization) [22].

In addition, vanadium is highly toxic both in the elemental state and in the form of oxide,  $V_2O_5$ , which is present on the surface of products made of the VT6 alloy [23, 24]. It should be noted that titanium has low shear strength, which makes it not very desirable for the manufacture of screws, plates, and other similar fixing parts for osteosynthesis. In addition, titanium products wear out quickly if they rub against each other or other metal parts [25]. The operation of titanium alloys with a high coefficient of friction can lead to the formation of wear products (small metal particles or sawdust), which, in turn, cause an inflammatory reaction, pain, and loosening of implants due to osteolysis [26].

These disadvantages led to the fact that the service life of the implants made from first-generation biomedical materials was only 10–15 years. That prompted the developers of such materials to create new alloys for prostheses that would be more similar to human bones in terms of properties. As a result, new  $\beta$ -titanium-based alloys with a low elastic modulus were created which contain only alloying additives compatible with the human body and have elastic modulus close to that of the bone.

## PHASE COMPOSITION OF TITANIUM ALLOYS

Mechanical properties of a material, as well as its wear and corrosion resistance, are largely determined by its microstructure. In these terms, titanium alloys are very attractive, because a wide range of different microstructures can be obtained by changing the composition of this material and its thermomechanical processing. Titanium has two allotropic modifications:  $\alpha$ -titanium with a close-packed hexagonal structure at low temperatures and  $\beta$ -titanium with a body-centered cubic structure at temperatures above 883°C.

The temperature of  $\alpha$ – $\beta$  transformation in titanium alloys depends on the nature of alloying elements. Those that stabilize  $\alpha$ -titanium (aluminum, oxygen, nitrogen, etc.) are called “ $\alpha$  stabilizers.” The addition of these elements to titanium increases the  $\beta$ -transus temperature (that is, the temperature of transition from the  $\alpha + \beta$  region of the phase diagram to the  $\beta$  region). The elements that stabilize the  $\beta$  phase are called “ $\beta$  stabilizers” (these are vanadium, molybdenum, niobium, iron, chromium, etc.). Their addition to titanium, on the other hand, lowers the  $\beta$ -transus temperature. Under sufficiently rapid cooling, the  $\beta$  phase can remain metastable at room temperature and exist in alloys for an indefinitely long time.

Depending on the content of various phases, titanium alloys are divided into three main classes:  $\alpha$ ,  $\alpha + \beta$ , and  $\beta$ . In addition to  $\alpha$  and  $\beta$  phases, titanium has a high-pressure  $\omega$  phase, which can appear as metastable even at small [27–29] deformations of titanium alloys and also remain as metastable at atmospheric pressure and near-room temperature. The formation of the  $\omega$  phase is especially pronounced at large shear strains and high pressures [30–33].

## TRANSITION FROM $\alpha$ - AND $\alpha + \beta$ - TO $\beta$ -TITANIUM ALLOYS

VT6 is still the most widely used biomedical titanium alloy. It is usually supplied in the  $\alpha + \beta$  annealed state. Unfortunately,  $\alpha + \beta$ -titanium alloys, having a high elastic modulus, often lead to resorption of the bone that is in contact with the prosthesis, which destabilizes the area of implant consolidation, impairing its attachment to the bone. Therefore, much attention is paid to single-phase alloys with low elastic modulus and  $\beta$  microstructure, which are obtained by rapid cooling from high temperatures.

It was theoretically predicted that neodymium, zirconium, molybdenum, and tantalum are the most suitable alloying elements, the addition of which lowers the elastic modulus of  $\beta$  titanium without decreasing the strength of the alloy [34, 35]. It was also shown that small additions of these metals to titanium reduce the elastic modulus. If the concentration of these alloying elements is increased, the elastic modulus

increases due to the formation of the  $\omega$  phase and the precipitation of particles of the  $\alpha$  phase during aging [36, 37]. The most important property of these elements is their low toxicity, which makes them more attractive for the manufacture of implants [38].

Based on these considerations, metallurgists have developed a variety of biomedical titanium alloys containing titanium, niobium, tantalum, and zirconium. Among them, alloys such as Ti–29Nb–13Ta–4.6Zr and Ti–35Nb–7Zr–5Ta have been thoroughly studied [39–41].

### FEATURES OF BEHAVIOR OF MULTICOMPONENT $\beta$ -TITANIUM ALLOYS

Recently developed metastable  $\beta$ -titanium alloys include Ti–Mo–6Zr–2Fe (TMZF), Ti–15Mo–5Zr–Al, Ti–15Mo–3Nb–3O, TIMETAL 21SRx, and Ti–13Nb–13Zr [42–45]. In addition to niobium, tantalum, and zirconium, molybdenum, tin, and hafnium are now employed as alloying elements for biocompatible titanium alloys [46]. Not so long ago, inexpensive alloying elements such as chromium and manganese began to be used to reduce the cost of medical Ti alloys [46].

There are ongoing intensive studies of  $\beta$ -titanium alloys, which will make it possible to understand the influence of alloying elements, machining parameters, and heat-treatment modes on the phase transformations, microstructure formation, elastic modulus, and deformation behavior of these materials. The optimal chemical composition of titanium alloys is selected not only experimentally, but also with the help of theoretical studies using, for example, the method of molecular orbitals [46, 47] or *ab initio* calculations [48]. Therefore, the Ti–29Nb–13Ta–4.6Zr alloy, commonly referred to as TNTZ, was developed using the method of alloy design based on the *d*-electron concentration [47]. The main goal of all these studies was to create biomedical alloys with the required mechanical properties capable of long-term operation as implants and bone prostheses.

Subsequently,  $\beta$ -titanium alloys with low and variable Young's modulus were developed, such as Ti–12Cr and Ti–11Cr–0.2O. They are used, in particular, in the manufacture of rods for fixing the spine elements [49, 50].  $\beta$ -titanium alloys with low Young's modulus and high zirconium content, such as Ti–30Zr–7Mo [51], Ti–30Zr–5Cr [52], and Ti–30Zr–3Cr–3Mo [52], were developed for the manufacture of removable implants. Titanium alloys with a zirconium content above 25 wt % prevent the formation of calcium phosphate on the surface [53]. This means that the adhesion of such alloys to the bone is low, which facilitates the removal of temporary titanium implants after they provide bone healing and are no

longer needed (for example, for fixing the bone fragments of the facial skeleton).

Other titanium–zirconium alloys used as temporary implants include, for example, Ti–Zr–Nb [54], Ti–Zr–Nb–Ta [55], and Ti–Zr–Al–V [56]. Young's modulus of  $\beta$ -titanium alloys Ti–30Zr–7Mo, Ti–30Zr–3Cr–3Mo, and Ti–30Zr–3Cr–3Mo can be varied within wide limits. These materials are mainly in demand as rods for surgical operations on the spine.

The aforementioned  $\beta$ -titanium alloys with low Young's modulus, which are used in medicine (apart from Ti–Cr alloys), contain a large amount of costly alloying elements such as niobium, tantalum, molybdenum, and zirconium. Therefore, it became necessary to create titanium alloys with low Young's modulus and inexpensive alloying additions. In accordance with these requirements, the Ti–Mn [57], Ti–Mn–Fe [58], Ti–Mn–Mo [59], and Ti–Mn–Al [60] alloys were created. Such inexpensive materials include Ti–10Cr–Al [61], Ti–Cr–Al [62], Ti–Sn–Cr [63], Ti–Cr–Sn–Zr [64, 65], and Ti–12Cr [66], which contain high concentrations of affordable elements such as manganese, chromium, and tin. A recently developed method makes it possible to produce gradient implants with a variable chromium concentration (and variable mechanical properties) by means of additive technologies (layer-by-layer laser deposition) [67].

High-entropy<sup>1</sup> biocompatible materials were developed based on multicomponent alloys Ti–Nb–Ta–Zr–Mo and Co–Cr–Mo [68]. They make it possible to overcome the limitation of classic metallic biomaterials while increasing the mechanical hardness and biocompatibility. These formulations show higher biocompatibility than commercially pure titanium and are suitable for use as prosthetic implants with a variety of functions [68].

Typically,  $\beta$ -titanium alloys are annealed in the  $\beta$  region to form a solid solution based on the  $\beta$  phase and then aged to decompose metastable phases and achieve high strength. Correct heat treatment makes it possible to obtain a number of various structures in  $\beta$ -titanium alloys, in particular, the equiaxed (as opposed to lamellar) grain structure has very attractive properties. It was found to have the best combination of mechanical properties in  $\alpha + \beta$  alloys.

It is important to note that researchers did not pay attention to the thermomechanical processing of biomedical titanium alloys for a long time. The first work on the effect of thermomechanical treatment on the formation of an equiaxed structure in the Ti–13Nb–13Zr alloy was carried out only in 2001 [69]. In that work, the authors also examined the formation of an equiaxed grain structure in two other  $\beta$ -titanium alloys, Ti–13Nb–20Zr and Ti–20Nb–20Zr. The

<sup>1</sup> High-entropy materials are multicomponent alloys without a main component in which concentrations of various metals are comparable to each other.

choice of a suitable “window” for their heat treatment made it possible to obtain fine equiaxed grains, while in the Ti–13Nb–13Zr alloy, the same conditions give rise to a mixture of large equiaxed and elongated grains. The presence of niobium in these alloys made it possible to process them at low temperatures, which, in turn, led to the formation of a structure of fine equiaxed grains [69, 70]. The concentrations of alloying elements were chosen so that they did not exceed 20 wt %, since their further increase could lead to the formation of the  $\omega$  phase, which increases the strength and elastic modulus of the alloy.

The elastic modulus of  $\beta$ -titanium alloys depends on the amount of  $\beta$ -phase present in the microstructure. Aging of  $\beta$ -titanium alloys leads to an increase in hardness and elastic modulus due to the release of small particles of the  $\alpha$  phase; however, the presence of such particles does not always lead to an increase in these indicators, which depend both on the origin of the  $\alpha$  phase and on other parameters of the microstructure. For example, aging of the Ti–34Nb–9Zr–8Ta (TNZT) alloy leads to a decrease in strength and elastic modulus. This was explained by the dissolution of the ordered B2 phase [22]. After homogenization, the B2 phase has a higher hardness than after aging.

In contrast to TNZT, in the Ti–29Nb–13Ta–4.6Zr alloy, both the strength and the elastic modulus increase with aging. This is due to the release of small particles of the  $\alpha$  phase from the  $\omega$  phase in the  $\beta$  matrix. It is interesting to note that the strength decreases in the case of the Ti–15Mo alloy, while the elastic modulus increases [22]; the decrease in strength is due to the fact that this material does not contain nanoparticles of  $\omega$ -phase precipitates during aging, and the increase in the elastic modulus is explained by a large volume fraction of fine particles of the  $\alpha$  phase.

Interesting opportunities for modifying the microstructure of  $\beta$ -titanium alloys follow from the phenomenon of the so-called wetting of grain boundaries by interlayers of the second solid phase [71–74]. In titanium-based alloys, this phenomenon is observed, as a rule, in the two-phase  $\alpha + \beta$  region of the phase diagram [71, 75–79]. At high temperatures, the  $\alpha$  phase almost completely wets all grain boundaries in the  $\beta$  phase, forming so-called fringes, and, as the temperature decreases, the fraction of boundaries in the  $\beta$  phase completely wetted by the  $\alpha$ -phase interlayers gradually decreases [75–79].

## FATIGUE STRENGTH

Young’s modulus of  $\beta$ -titanium alloys, as a rule, reaches minimum values if they contain only the  $\beta$  phase. This can be achieved by annealing the alloy in the  $\beta$ -solid solution region, followed by rapid cooling from a temperature above the transformation into the  $\beta$  phase (it is also called the  $\beta$ -transus temperature).

The static tensile strength and dynamic (fatigue) strength of  $\beta$ -titanium alloys with low Young’s modulus and single-phase  $\beta$  structure are generally low. Therefore, there is a need to increase these strength characteristics while maintaining low values of Young’s modulus and sufficient plasticity.

The static strength of  $\beta$ -titanium alloys annealed above the transus line can be improved by cold deformation processes, which include, in particular, intense cold rolling [80], forging [81], compression [81], and severe plastic deformation (SPD), including high-pressure torsion (HPT) [82]. These types of treatment do not increase Young’s modulus and make it possible to maintain good ductility. However, the methods of intensive cold machining fail to improve the fatigue strength without increasing Young’s modulus [83]. Therefore, in order to improve the dynamic (fatigue) strength of  $\beta$ -titanium alloys for medical use (TNTZ type), it is necessary to introduce a enough secondary phases, such as  $\alpha$  and  $\omega$ , into the  $\beta$  matrix. The separation of particles of these phases can be achieved by suitable thermal or thermomechanical treatment, as well as by additional aging immediately after cold machining [84]. It is also possible to add ceramic particles of titanium diboride or yttrium oxide to the alloy [85], although this increases Young’s modulus.

On the other hand, solid solution hardening can be achieved using lightweight, inexpensive, and safe interstitial alloying elements such as oxygen. Oxygen alloying can increase both the fatigue strength and the tensile strength of the TNTZ alloy. The maximum number of fatigue loading cycles before the fracture of the oxygen-doped TNTZ alloy can be achieved in the range of oxygen concentrations from 0.16 to 0.7 wt % [86]. The fatigue strength of the TNTZ alloy increases with an increase in the oxygen concentration due to the formation of a martensite phase because of deformation, where the thickness of martensite plates decreases as the oxygen concentration increases:

Oxygen concentration, wt %	0.1	0.5	0.7
Thickness of martensite plates, nm	240	90	30

Thus, the addition of oxygen increases the strength of the material due to grain refinement and solid solution strengthening. In turn, this leads to an increase in the fatigue strength of the TNTZ alloy. Moreover, there is an optimal balance between tensile strength and elongation even at a high oxygen concentration of 0.7 wt % [87, 88]:

Oxygen concentration, wt %	0 (VT6 *)	0.1	0.3	0.5	0.7
Young’s modulus, GPa	105	58	63	68	75
Maximum tensile strength, MPa	950	300	720	930	1050
Maximum elongation, %	15	26	12	14	18

\* Provided for comparison

IN VITRO BIOCOMPATIBILITY OF β-TITANIUM-BASED ALLOYS

The activity of human osteoblasts cultured on TNTZ alloy was examined in its various states [89]:

- (i) after annealing in the single-phase β region (TNTZ<sub>ST</sub>);
- (ii) after additional aging, which followed annealing in the single-phase region, when the alloy has a coarse-grained structure (TNTZ<sub>AT</sub>);
- (iii) after additional processing by high-pressure torsion (HPT), which leads to grain refining (TNTZ<sub>AHPT</sub>).

The number of human osteoblasts that attached to TNTZ<sub>ST</sub>, TNTZ<sub>AT</sub>, TNTZ<sub>AHPT</sub>, and VT6 alloys after 6-h incubation at 24°C is given below [89]:

Substrate	TNTZ <sub>ST</sub>	TNTZ <sub>AT</sub>	TNTZ <sub>AHPT</sub>	VT6
Cell count	10 500	10 900	17 500	11 000

It can be seen that, among the substrates studied, the number of adhered human osteoblasts was the highest for the TNTZ<sub>AHPT</sub> alloy. There was no statistically significant difference in the number of adhered cells on the remaining substrates.

We also studied the viability of cells on substrates of β-titanium alloys Ti–12Cr and Ti–Mn with low Young’s moduli [90]. Below are the values of the density of living cells MC3E3-E1 (their count per 1 mm<sup>2</sup>), which were cultivated on these substrates for 86 400 s [90]:

Substrate	Stainless steel 316L	VT6	TNTZ	Ti–12Cr
Cell count/mm <sup>2</sup>	110 ± 10	140 ± 20	170 ± 30	190 ± 10

The highest density of adhered cells was on the Ti–12Cr substrate. It significantly exceeded the performance of stainless steel and the VT6 alloy, being similar to that of the TNTZ alloy.

Further, the cytotoxicity was investigated on substrates of technical grade titanium, the Ti–(6–18)Mn alloy, commercially pure manganese, and the VT6 alloy. A polystyrene (PS) substrate was used as a control. MC3T3-E1 cells were incubated for 24 h. After calculating the ratio of living cells on the surface of the test materials to the control, no significant differences in cytotoxicity were found between the Ti–(6–18)Mn alloys and other materials [91]:

PS	1.21
Technically pure titanium	0.94
Ti–6Mn	0.80
Ti–9Mn	0.83
Ti–13Mn	0.88
Ti–18Mn	0.80
Technically pure manganese	0.75
VT6	1.0

Thus, values of the cytotoxicity of Ti–(6–18)Mn alloys are comparable to those for titanium and the VT6 alloy (although for the Ti-18 alloy, wt% Mn is lower than the values for commercially pure titanium and the VT6 alloy). The cytotoxicity value for the commercially pure manganese alloy was much lower than for commercially pure titanium and the VT6 alloy.

BIOCOMPATIBILITY IN VIVO

In vivo trials of the TNTZ alloy of the femoral head endoprosthesis were carried out on Suffolk sheep [92]. This endoprosthesis was implanted into the animal by pressing into the remnant of the femur. Unfortunately, the experimental animal died three years after the implantation due to traumatic bleeding and intestinal obstruction. The endoprosthesis was removed during the dissection of the animal and cut to examine its composition and determine the metal content in the bone surrounding the prosthesis. The concentration of alloying elements of the titanium alloy in the liver and kidneys, as well as in the soft tissues of the animal, was measured.

X-ray images of the prosthesis in the femur, as well as the femur cut around the center of the prosthesis, showed that the prosthesis was congruent and well anchored in the bone; that is, endoprosthetics was successful. The concentration of metallic elements was measured in the liver and kidneys, as well as in the bone tissue forming the acetabulum and the cortical layer of the distal femur. Apart from the titanium and zirconium contained in the food of the experimental animal, no other foreign metal elements in the liver and kidneys of the sheep were found. Niobium and tantalum were present in the inner cortical region of the femur. It is assumed that the release of metal ions occurred mainly where the experimental animal’s bone contacted the prosthesis.

Thus, prosthetics with the experimental product did not lead to the accumulation of metallic elements in the liver and kidneys, leaving the structure of these organs unchanged. The results of these experiments in vivo proved the biocompatibility of the rod made of the TNTZ alloy with low Young’s modulus. Moreover, excellent compatibility was also demonstrated in experiments on the implantation of intramedullary rods and plates for the fixation of bone fragments in a model tibia fracture in Japanese white rabbits [93].

Below are the data on the relative area of contact with the bone in the Ti–12Mn alloy and commercially pure titanium 12, 52, and 98 weeks after implantation into the condyles of the femur of Japanese white rabbits [94]:

Duration, weeks	12	52	98
Ti–12Mn, %	11	28	30
Technically pure titanium, %	12	33	31

It can be seen that, in all the three cases, the value of the contact of the Ti–12Mn alloy with the bone was close to the value for commercially pure titanium. However, one should note a small amount of dissolved manganese ions in the surface layer of implants made of the Ti–12Mn alloy in the area of contact with the bone. These data made it possible to prove the biocompatibility of inexpensive  $\beta$  alloys of titanium with manganese in a concentration of less than 12 wt % in vivo.

## CONCLUSIONS

The development of titanium alloys that reproduce the properties of living tissue is one of the most interesting and in-demand issues in current research and healthcare.

Medical titanium alloys based on  $\beta$ -Ti are increasingly replacing the first-generation alloys based on  $\alpha$ -Ti or a mixture of  $\alpha + \beta$ -phases (such as commercially pure titanium or VT6 alloys). Implants made from the first-generation materials sometimes require replacement after as early as 10–15 years of use, and they gradually release aluminum or vanadium ions into the body. In  $\beta$ -titanium alloys, the elastic modulus is lower than that of  $\alpha$ - and  $\alpha + \beta$  alloys, which is closer to that in living bone.

The development of new  $\beta$ -titanium alloys makes it possible to increase the mechanical strength, fatigue strength, corrosion resistance, and biocompatibility of implants. New methods for production and thermo-mechanical processing of titanium alloys, such as additive technologies or severe plastic deformation, are created and developed.

Expensive components of  $\beta$ -titanium alloys (such as tantalum, zirconium, or niobium) are being replaced step by step with cheaper ones (such as chromium and manganese). As a result, the service life of titanium implants is steadily increasing, and their characteristics are gradually approaching those of human bone.

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## CONFLICT OF INTERESTS

The authors declare that they have no conflicts of interest.

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