Nanotechnologies for the Formation of Medical Implants Based on Titanium Alloys with Bioactive Coatings

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Abstract—The main approaches to the formation of modern functional materials for medical implants, including the principles of material choice on the criteria of their biochemical and biomechanical compatibility and their technological effectiveness, are represented in this review. Titanium alloys are considered the most prospective and extended materials for implants in traumatology, orthopedics, and stomatology. The trend over the last decade has been to exclude alloying components that may cause local allergic reactions on living tissues or general toxic effects on an organism from the structure of titanium alloys. One compromise to preserve high biochemical compatibility with the necessary increase in the mechanical properties of titanium alloys is based on the formation of submicrocrystalline (SMC) or nanostructured (NS) states in commercially pure titanium. The prospect of using SMC and NS titanium as a material for manufacturing implants is proven. An analysis of the results of experimental and theoretical research of the diffusion features on intergranular areas is carried out, and the role of diffusion-controlled processes in the formation of a microstructure of metals and alloys, as well as the microstructured state, is discussed. The efficiency of computer simulation on an atomic level in establishing the dependence of diffusion characteristics on intergranular areas from the average grain size and the structural state of internal boundaries of section is proven. A short description of simulation and semi-industrial methods of the formation of SMC and NS states in metals and alloys by means of severe plastic deformation—which are known as materials related to the "top-down approach," assuming the initial structure is crushed to nanosized components—is presented. Special attention is given to the recent developed of low-cost and high-efficiency technological schemes for the mass production of nanostructured titanium alloys for medical purposes, including radial-shift and screw rollings, along with a combination of traditional methods of mechanical-thermal processing, which make it possible to receive an assortment of the titanium and its alloys necessary for the mass production of medical implants and tools.

INTRODUCTION

One of the most important spheres of nanomaterial use in medicine is the formation of next-generation implants. The actual need for affordable implants (stomatological, traumatological, and orthopedic) in Russia exceeds the existing amount by 3–5 times. For example, the annual increase in the need for dental implants in Russia now reaches 30%. The market for the products under question is filled by foreign companies. The materials (mostly metals and alloys) used for implants need an increase in the biochemical and biomechanical compatibility with body tissues, an improvement of the functional characteristics, and the use of energy-efficient and ecologically pure technological processes in manufacturing.

The development of new structural and functional materials with improved characteristics is mainly determined by the results of fundamental studies of the formation of their structure and the nature of the physic-chemical processes that occur in materials under different operation conditions. A special role influencing the physical–mechanical, chemical, electrophysical, and other properties of materials is played by the internal surfaces of division (boundaries of grain (GB), subgrains, and phases) and by the free surfaces and pores and cracks that are connected with them. This is why the increase in the boundaries' length with a decrease of cristallites' size and the transition from usual polycrystalline materials to nanostructures lead to a principal change in the development of processes of thermal and electric transfer, plastic deformation and destruction, and degradation of structure.

Thus, it is an urgent problem to develop a complex approach to the formation of new innovative products in medicine: implants made of nanostructured materials with biocoatings, including all the stages of research, design, and development work, from fundamental research (that based on computer simulation), new technological and constructive solutions, and industrial production and metrological control. In this review we present the main results of developing and studying submicrocrystalline and nanostructured titanium and bioactive coatings whose practice in use as materials for implants in traumotology, orthopedics, and stomatology is expected in the nearest future.

NATURAL-SCIENCE ASPECTS OF NANOSTRUCTURED "BIOMETALS" USAGE IN MEDICINE

It is known that the functional reliability of medical implants and constructions used in traumotology, orthopedics, stomatology, and other medical spheres is, first of all, dependent on several mechanical properties shown in real working conditions in the living organisms whose surrounding tissues and biological liquids this material influences, as well as the organism as a whole. In connection with this, along with mechanical characteristics of metals such as strength, plasticity, resistance to cyclic loading, wearing capacity, etc., the biological and biomechanical compatibility of materials with living organisms is important. The problem of creating functional inorganic medical materials is an intensively developing field in cotemporary biomaterial science [1–12].

It is known that the tissues of living organisms may be presented as biopolymers. Bone tissue is a composite armored material whose strength may differ in local areas. Biopolymers, along with other organic polymers, are relaxation systems where thermodynamic equilibrium is established not momentarily but over the course of time [13]. All tissues in organisms reveal characteristics of viscoelasticity and viscoplasticity: relaxation under constant deformation, hysteresis under cyclic loading and unloading, and creep under constant stress [14–16]. An organic counterpart possesses elasticity and strong shape memory. Several mechanical characteristics close to those mentioned above may be revealed in metallic materials which possess a lower (close to that conformable for bone tissue) modulus of elasticity and the effect of shape memory in the temperature range of the vital activity of the living organism (Fig. 1) [8].

Taking into consideration the long-term use of implants in bodies, contemporary literature ranks biomechanical compatibility based on low-modulus properties and functionality connected with superelasticity and the effects of shape memory among the main critical factors of biomaterials applicability [8, 16]. The condition of biochemical compatibility of materials (lack of inflammatory tissue reactions) is considered standard. Even at the end of the previous century, materials with the latter character were divided into the so called "living" group (Ti and titanium alloys, Zr, Nb, Ta, and Pt), which does not significantly affect the surrounding biological tissues and liquids; the "incapsulated" group (Al, Fe, Mo, Ag, Au, stainless steels, and CoCr-alloys), from which the body protects itself by forming a "capsule"; and the "toxic" group (Co, Ni, Cu, V), which affects the body in a very negative way [17].

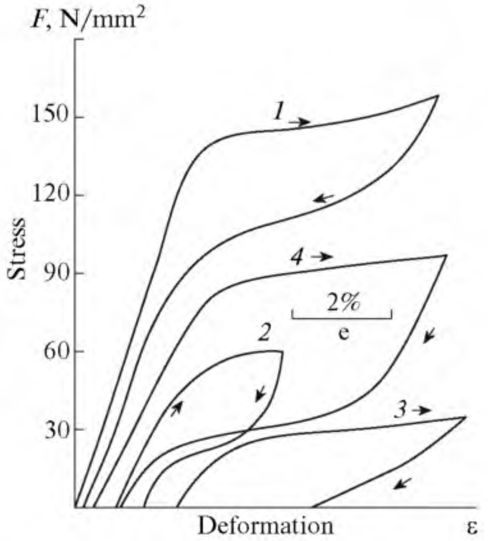

Fig. 1. Curves of loading–unloading different materials: (*1*) hair, (*2*) living bone tissue, (*3*) soft tissue, and (*4*) metallic superelastic alloy.

Of all the mentioned materials, steels are the strongest. Their mechanical properties are so high that it will be hard to fully abandon their use as materials for different (especially complex) constructions of medical implants any time soon. However, even high-alloy steel is insufficient from the point of view of biocompatibility. Implants made from alloy steel (including corrosion-resistant) in a corrosive medium—under interaction with biological liquids—lead to local inflammatory reactions in tissues and in some cases the body has toxic and allergic reactions. This is the reason for the constant search for new materials to use in medicine. Titanium and its alloys are the favorites among contemporary metal biomaterials. It was pointed out in [18] that the positive characteristics of titanium as a biomaterial are the following: high biocompatibility, good corrosion resistance, bioinertness, nonmagnetism, low thermal conduction, small coefficient of linear expansion, and lighter (in comparison with steel) specific weight. The high corrosion resistance of titanium is due to the quick formation on its surface of passive oxide film, which is firmly connected with main metal and precludes the contact of metal with a corrosion-active medium. Oxide film is formed on titanium surface under oxidation in the air, anodic oxidation, and by self-passivation, not only in strongly oxidizing but also in the neutral and subacid solutions.

Thus, titanium alloys fully correspond to the demands of biomaterials but are worse than steels in their level of yield stress and tensile stress, resistance to fatigue failure, and wear resistance.

In Russia commercially pure titanium VT1-0 and titanium alloys Ti-4A1-6V (BT 6), Ti-5Al-2Sn (BT 5-1) and Ti-2.5Al-5Mo-5V (BT16) are mostly used for the manufacture of implants. Foreign analogues of alloys

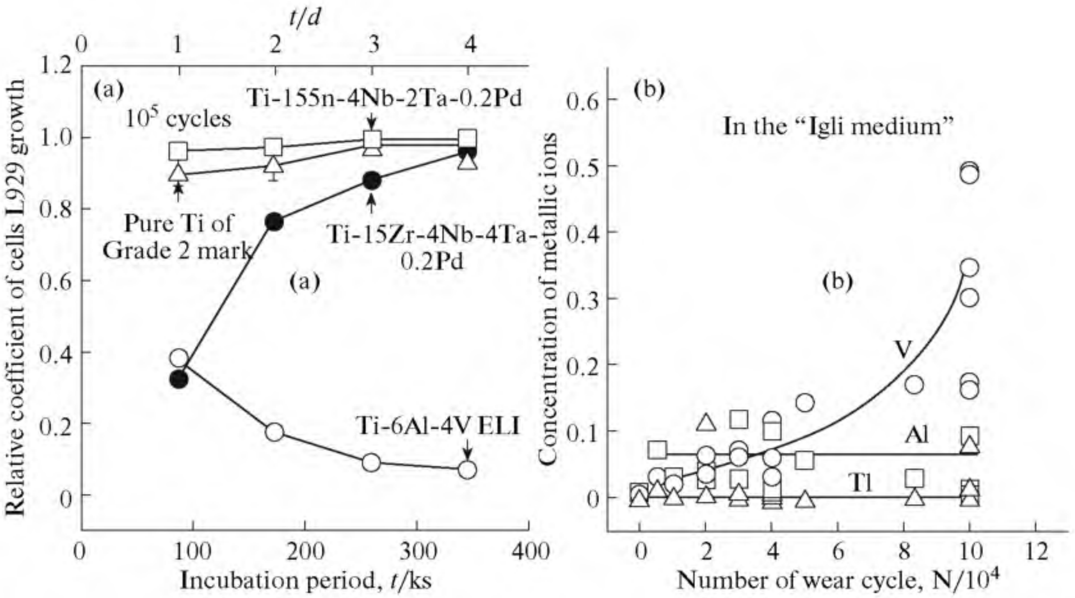

Fig. 2. The change in the relative growth speed of cell culture L929 with time after 10^5 cycles of friction of titanium alloys in contact with apatites ceramics in "Igli medium," (a) the dependence of concentration of metallic ions in the "Igli medium" on the number of cycles of alloy Ti-6Al-4V ELI wear in connection with apatites ceramics and (b) [22].

of our country are titanium alloys Grade-2 and Grade-4 (so called "commercially pure" titanium) and titanium alloy Ti-6Al-4V. Alloys based on Ti-5Al-7Nb and others are also widespread [16, 17].

The problem of the biological compatibility of implants is nowadays partially solved by the creation of both bulk and porous functional hyperlastic materials and constructions with shape memory on the basis of the intermetallic compound titanium nickelide [8, 19–21]. These alloys do not corrode in short work, because, under passivation in a biological medium, a layer of titanium oxide forms on its surface containing a certain amount of nickel. This why such alloys do not possess carcinogenic and allergic activity and are widespread in medicine.

In addition to titanium nickelide, most of the listed alloys contain alloying elements which are harmful for living organisms (Ni, Al, V, et al.). As of today it is generally inadmissible for implants to contain toxic elements. This is particularly based on experiments on the potential for cell survival in biological liquids (Eagle media) with wear products of titanium alloys in a friction pair with apatite ceramics, which is close in chemical content to natural bone [22]. It was demonstrated in the mentioned work that one of the most corrosion-resistant titanium alloys (Ti-6Al-4V)—both in wear test and after its finish—has a toxic influence on the cell cultures (osteoblasts) chosen in the experiment. This is in connection with the aluminum and, especially, vanadium appearing in the biological medium during the process of friction (Fig. 2). For alloys which do not contain the above-mentioned elements (including, first of all, pure titanium), no deviations from normal cell growth were detected.

It is known, wear is a critical process in the use not only of implants which constitute joints, but also of "simple" constructs of the "plate-screw" type. Micromobility in contacts in any constructs is inevitable in the moving functions of the body. Due to the elastic behavior of bone tissue and the bone in general in the beginning of osteosynthesis, the system "implant-bone" (titanium alloy–apatites ceramics in model [22]) may be itself a source of wear products and therefore may be a "supplier" of toxic ions in body tissues.

In the last 10–15 years, intensive studies were conducted which were aimed at developing metallic materials of a new generation for implants that include only titanium, tantalum, niobium, zirconium, and molybdenum, which have no negative impact on body tissues [17, 22–24]. From the listed materials β-metastable titanium alloys are of the most interest from the practical point of view. They possess the lowest elastic modulus close to the corresponding for bone tissue [23, 24]. Also, the mentioned alloys have a higher wear resistance index in biologically active mediums [25]. However, there are only a few works in contemporary literature devoted to the study of the shape memory effect and the superelasticity of such materials [16, 26] in spite of the fact that, for some of them, there is thermoelastic martensitic transformation on the state diagram.

However, introducing β-metastable titanium alloys as materials for medical implants is nowadays associated with significant problems connected with the impossibility of simultaneously combining high strength and wear properties with low elastic modulus. The metastable bcc lattice of titanium has low strength when the effective method of strengthening by ageing increases the Young modulus up to normal values. Also, there are many problems at the stage of casting such materials: the lack of ready mixtures for alloying (ligature) and the complexity of obtaining the precise chemical content and its homogenization in alloying. Nowadays, with the severe deficiency of affordable and available medical implants in the Russian market, approaches which assure the fast progress of ideas for creating highly technological productions subject to the present metallurgical and medical manufacturing are the most prospective.

One of this ideas was developed over the last decade by this author with collaborators that included replacing the titanium alloys widely used in medicine with high-strength SMC or NS unalloyed titanium (alloy VT1-0) [27].

It is known that the formation of submicrocrystlline (SMC) and nanostructured (NS) conditions in titanium alloys leads to a significant improvement of their mechanical properties, including those necessary for use as materials for medical implants [27, 28].

For example, the formation of the above-mentioned conditions in commercially pure titanium (VT1-0) by the impact of severe plastic deformation using methods of equal-channel angular pressing in an aggregate with cold rolling and annealing enables us to reach high homogeneity in grain-size distribution as opposed to a heterogenous band fine-grained structure formed in titanium rolling under usual conditions. Also, the localization of the deformation is suppressed in such a structure on the macro level. As a consequence, the strength level increases with the preservation of high plasticity and the endurance limit increases under cyclic loading [27]. In particular this let us obtain ultrafine high-strength titanium foils with thicknesses less than 10 μm, which are necessary for use in medical and technical products [29].

The peculiarity of submicrocrystalline and nanostructured states obtained in metals and alloys by the influence of severe plastic deformations is activization of diffusion [30]. A number of experiments show that the increase of diffusion influence on the structure evolution connected with the migration of grains boundaries, grainboundary segregation of impurity atoms, changes in micropores size, relaxation of internal stress, and isolation of secondary phase in such conditions is connected not only with the large area of grain regions but also with increased speed of diffusion in grain boundaries in comparison with macrocrystalline condition [30]. This peculiarity is a reason for the decrease in the temperature manifesting “high-temperature” diffusion-controlled mechanisms of plastic deformation, for example, such as grain boundary sliding up to a temperature close to room temperature [27]. The latter allows to use processes controlled by diffusion to achieve superplasticity and the controlled formation of structural-phase composition, which assure an increase in strength with the preservation or, in some cases, increase of plasticity under a sufficiently thermally stable structure. However, in order to use of the above-mentioned peculiarities, the dependencies that the diffusion characteristics, according to their grain regions, have on temperature, average size of grains, chemical composition, and structural state of internal boundaries need to be established. Interpreting the results of experiment in this case is very complicated due to, first and foremost, the complexity of the full description of the defective structure of SMC and NS materials obtained by the influence of plastic deformation. The latter is connected with the presence of unrelaxed residual stresses in such structure and, possibly, the heterogeneity of content and other peculiarities of observed heterosystems. These problems may be avoided by the abilities of contemporary computer simulation on an atomic level, which is actively used in the study of diffusion processes on the grain boundaries of metals [31]. The second section of this review is devoted to examining such investigations.

For natural reasons, the working temperature for titanium of medical use is the temperature of human body, with the exception of heating materials when sterilizing implants up to a temperature usually no higher than 200°C. For this reason, the problem of the thermal stability of a structure made out of common titanium and titanium alloys for medical use in the literature is not considered. However, activization of diffusion processes in SMC and NS titanium, requires a special study of this issue. At the same time, this very factor of diffusion penetrability may be purposefully used for the formation, for example, of a fine-dispersed precipitates which block the migration of grain boundaries and, for this reason, inhibit the development of the recrystallization process [27, 31, 32]. The simultaneous decrease in the resistance of low-temperature creep, which is connected with an increase in the diffusion penetrability, allows to decrease residual stresses in half-finished products up to safe level, for example, by conducting low-temperature prerecrystallization annealing after the whole cycle of technological redistribution of half-finished products.

One of the most important conditions for a well-grounded prediction of stability of the structure and the mechanical properties of titanium under conditions of long-term operation in a biological medium is to consider its interaction with hydrogen. The latter is known can diffuse into the material from the environment and worsen the mechanical properties up to embrittlement near-surface layers, which is encountered for titanium and titanium alloys used nowadays, including that of medical use. We may expect that SMC and NS state formation allows to reduce the influence of hydrogen due to a significant increase in the extent of grain boundaries in the submicro- and, especially, nanostructure. In such structures, incoming hydrogen is known to be redistributed by many traps, i.e., nonequilibrium grain boundaries and deformation defects. This allows to avoid achieving and exceeding the maximum solubility of hydrogen in a crystal lattice. For this reason we may expect that the hydrides particles, if they appear, will be smaller and uniformly distributed in the material volume, mostly in grain boundaries. From the point of view of hydrogen brittlement, such a state of the hydride phase is the least dangerous, and it allows to increase the value of the maximum permissible concentration of hydrogen in titanium and its alloys. However, the problem of SMC and NS influence on the interaction of titanium alloys with hydrogen in the process of operation has not yet been studied very well and needs to be investigated, Based on the results of fundamental research on the formation and evolution of SMS and NS states (obtained by the influence of severe plastic deformation) in commercially pure titanium (alloy VT1-0), which does not contain any alloying elements harmful for a living body, showed the possibility of and methods for reaching strength properties under static and cyclic loading which correspond to the level of alloyed titanium alloys commonly used in medicine [29, 33, 34]. The strength properties that were reached make it possible to use unalloyed SMC and NS titanium as medical implants in traumatology and orthopedics [35].

However, most methods of formation of the abovementioned states using the influence of severe plastic deformation (which will be discussed in the third section of the article) are inefficient and significantly increase the cost of the materials. Metals and alloys in SMC and NS states, as a rule, have lower thermal stability, high strength, and reduced plasticity when there is no special thermal treatment. This restricts the possibility of processing them using pressure when obtaining the necessary industrial assortment of half-finished products, and it increases the labour input of making products on an automatic mill in mass production.

In connection with the aforesaid, the development of highly effective and low-cost technology for obtaining an industrial assortment of half-finished products of SMC and NS titanium and alloys on its basis with improved mechanical and functional characteristics for manufacturing medical products in commercial production is an urgent problem. Nowadays, as part of the large set of projects under the federal target program “Nanoindustry and Nanomaterials” with the topic “The Development of Experimental Industrial Technologies of Forming Next-Generation Medical Implants on the Basis of Titanium Alloys,” such technology was elaborated, and shaped sections and rods made out of commercially pure titanium (alloy VT1-0) with SMC structures were manufactured. At the industrial base of one of the participating organizations of the project (SUE All-Russian Research and Design Institute of Medical Instruments (Kazan)), a pilot batch of implants for traumotology (plates and screws) were manufactured from the mentioned materials. These products successfully underwent preclinical tests and the whole set of products is now undergoing clinical tests. The third section is devoted to describing these works.

As was mentioned above, another urgent question of medical material science is developing technology for the formation of bioinert and bioactive coatings. Bioactive coatings include polymers, metal oxides (e.g. TiO_2, Al_2O_3) and some other types of ceramic compounds. Bioactive coatings not rejected by an organism, but they also speed up the growth of bone tissue, thus promoting the quickest implantation in the body. Bioactive coatings include calcium-phosphate (tribasic calcium phosphate, hydroxylapatite, et al.) and fluorine-apatite ceramics.

RESULTS OF EXPERIMENTAL AND THEORETICAL STUDIES OF GRAIN BOUNDARY DIFFUSION IN SUBMICROCRYSTALLINE AND NANOCRYSTALLINE METALS

To analyze the results of diffusion experiments in microcrystalline, SMC, and NS materials, the diffusion coefficient on grain boundaries D_{GB} and diffusion coefficient by triple junction D_{TJ} [36] are introduced. In this case D_{GB} and D_{TJ} are parameters of the diffusion model using GB and TJ, which are presented in model as homogeneous phase and their values are determined by a square of the diffusion displacement of atoms $\Delta\vec{r}_i$ according to the Einstein relation for a diffusion coefficient in a three-dimensional medium $D = \sum_{i=1}^{N}(\Delta\vec{r}_i)^2/(6Nt)$. Here, N is the number of atoms in the corresponding phase and t is the time of the atoms. In the range of large amounts of time, the tilt of the dependency of the average square atoms on time is supposed to be constant for the studied area. But D_{GB} and D_{TJ} do not have physical sense out-of-frame of chosen diffusion models along GB and TJ. Therefore, for a diffusion description in NS materials, independent from the model presentation about the structure of GB and TJ, the following characteristics were introduced [37]: ζ_{GB} is the average excess of the sum of atoms squares per time unit connected with the formation of grain boundaries and reckoned to the grain boundaries square unit and ζ_{TJ} is the average excess of the sum of atoms squares per time unit reckoned to the length unit of triple junction. These characteristics are determined through the rate of the increase in ΔZ, where the excess of the sum of the diffusion displacement of atoms squares accumulated in NS sample for the time t; this is presented as sum of the contribution of GB and TJ ($\Delta Z/t = \zeta_{GB}A_{GB} + \zeta_{TJ}l_{TJ}$), where A_{GB} and l_{TJ} is the total area of grain boundaries and the total length of triple joints in NS materials respectively.

It follows from the Einstein relation that the introduced characteristics of GB and TJ are connected with

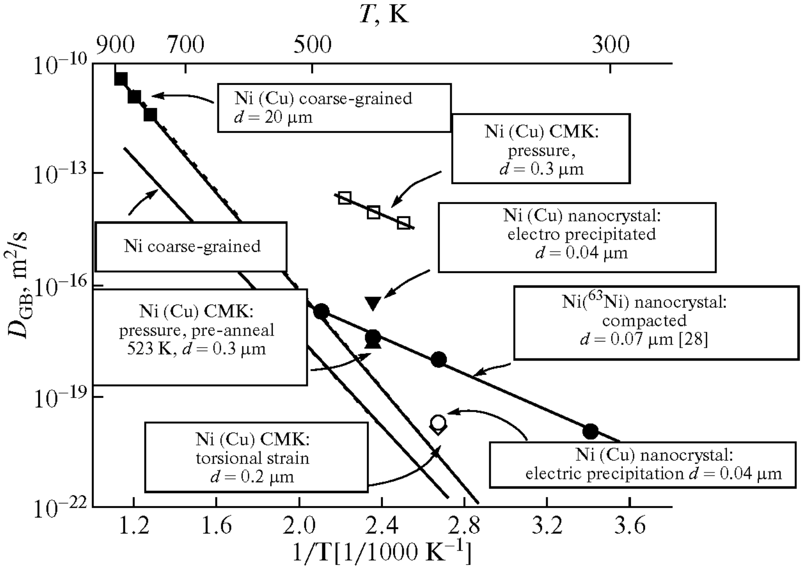

Fig. 3. Arrhenius dependence of coefficients of grain boundary self-diffusion of nickel and heterodiffusion of copper in nickel with a different structure [25].

corresponding diffusion coefficients D_{GB} and D_{TJ} by relations $(D_{GB} - D_V)\delta = (\Omega/6)\zeta_{GB}$ and $(D_{TJ} - D_V)R^2 = (\Omega/6\pi)\zeta_{TJ}$ if we accept that GB and TJ are homogeneous phases in material in a form of plate with a thickness δ and a cylinder with radius R respectively. Here D_V is a diffusion coefficient in grains volume and Ω is the average volume per one atom. This relation allows to compare the coefficient of grain boundary diffusion D_{GB} determined from the analysis of diffusion experiments discussed below and the excess in the sum of atoms squares estimated from the results of molecular-dynamic simulation of diffusion processes in grain boundaries.

The parameters of grain boundary diffusion (diffusion coefficients and energy of diffusion activation), as a rule, are formed from experimental profiles of distribution by the depth of the layer concentration or concentration in the grain boundary (GB) of diffusant (impurities or isotope) after diffusion annealing under conditions when volume diffusion is “frozen” ($D_V = 0$) and there is no outflow of the diffusant from the boundaries to the volume of grains. The main results of the experimental studies of grain boundary diffusion in SMC materials obtained by influence of plastic deformation and in NS and SMC materials obtained by electric deposition according to [30, 38–44] are show in Fig. 3 in comparison with coefficients of grain diffusion D_{GB} and their temperature dependence for coarse-grained polycrystals. Experiments showed that D_{GB} for polycrystalls in coarse-grained and in NS and SMC states may coincide or differ by 1–5 orders of magnitude. The fluctuation of D_{GB} under the same temperature in different experiments is 2–3 orders of magnitude. The value of activation energy of grain boundary diffusion Q_{GB} in SMC metals determined in [30, 40, 43, 44] from the temperature dependence D_{GB} were 1.5–2 times less than the corresponding values for coarse-grained states and close in their values to the diffusion activation energies on free surface. The increased diffusion rate up to 1–2 orders of magnitude in material with fine grains is indicated by indirectly estimating the parameters of grain boundary diffusion from data on the study of diffusion-controlled processes such as plastic deformation on the mechanism of grain boundary sliding and activated recrystallization in SMC and coarse-grained polycrystals [37].

The increase of diffusion speed in SMC metals is qualitatively explained by contemporary views on the structure of GB in them. Numerous researches indicate that the SMC structure of metallic materials formed by the method of severe plastic deformation is characterized along with small size of grains by the extremely nonequilibrium state of GB. Boundaries in such state have a high density of defects with deformation origins and higher energy and surplus volume than the minimum under given conditions, and they create distortions in the border zone of the crystal lattice [45, 46]. This explains the increase in the grain boundary diffusivity by such GBs. The degree of nonequilibrity of the GBs of submicrocrystalline structure is determined by the material characteristics and method and conditions of acquisition. Therefore the detected dispersion of D_{GB} values at the same temperature in different experiments may be connected with the different degree of nonequilibrity of GB [37].

In spite of the great volume of experimental information about grain boundary diffusion and the diffusion-controlled processes in materials with an average grain size of less than 100 nm, this data is insufficient for providing a definite answer to the question about

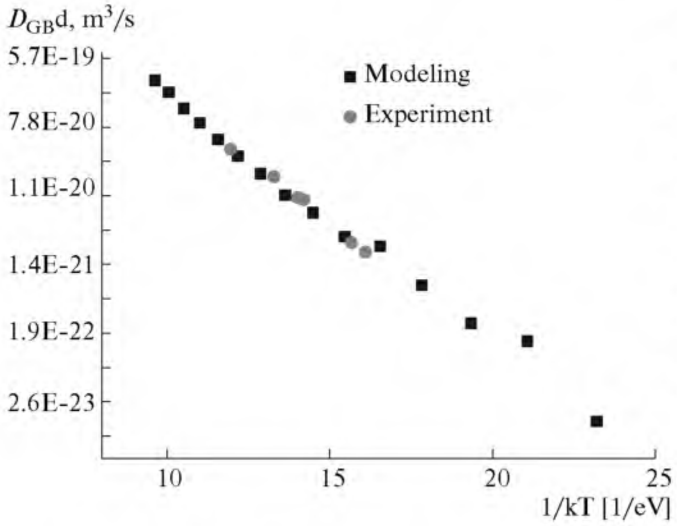

Fig. 4. Assessed and experimental values of parameters of Arrhenius dependence of $D_{GB}\delta$ on temperature for highly pure copper.

whether principal differences in the diffusion parameters of GB in SMC, NS, and coarse-grained states exist. It became possible to overcome this problem using a computer experiment with the example of molecular-dynamic simulation of nanocrystalline copper, which enables to establish correct information about the parameters of grain boundary diffusion.

Figure 4 shows the results of an analysis of molecular-dynamic simulation of coarse-grained NS-copper and diffusion experiments in highly pure coarse-grained copper conducted for crossing temperature ranges. It is clearly seen from the figure that diffusion characteristics from independent approaches conform well. This testifies, first of all, about the coincidence of diffusion characteristics by GB in NS and coarse-grained copper at a high temperature; secondly, it confirms the validity both of the data of computer simulation and results of diffusion experiments obtained in [47].

The direct simulation of diffusion processes in SMC materials on atomic level obtained of the influence of plastic deformation is impossible because of the complexity of their atomic structure and relative large size of the grains. However, methods of computer simulation on an atomic level allows to establish general regularities in the changes of GB characteristics with an increase in the excessive volume δV connected with GB from the studies of model bicrystals. Establishing such regularities allows to interpolate the results of simulation in the case of SMC materials using experimental values of excessive volume δV in them. This approach was taken in [31] for an estimation of the correlation between coefficients of GB diffusion in SMC materials obtained by SPD and without such processing. The assessment from indirect measurements of diffusion coefficients and from results of computer simulation on an atomic level [31] confirm the data from direct measurements about the fact that, in the SMC condition, the effective diffusion coefficients exceed those corresponding for coarse-grained condition by several degrees. It is necessary to point out that the increase of diffusion mobility of atoms in GB of SMC is directly connected with the increase of GB energy in these materials, whereas, in NS materials obtained, e.g., by compaction, the energy of the GB of grains coincides with that in coarse-grained condition [48, 49]. This conforms to the equality of diffusion characteristics of GB in NS and coarse-grained conditions. Because of this, in NS materials obtained by compaction, the increase of the effective diffusion coefficients may apparently be connected only with the influence of triple junction. The displacement of atoms that belong to triple junction increases with the decrease in the average size of grains.

As a result, an analysis of the results of the present diffusion experiments and computer simulation shows that the main peculiarity of diffusion in submicrocrystal materials obtained by the influence of plastic deformation—in comparison with nanocrystallic metals obtained by compaction and coarse-grained metals—is, the increased diffusion penetrability of grain boundaries, which is connected with their nonequilibrium state formed in the process of severe plastic deformation. There is no dependence of diffusion coefficient in the grain boundaries on their average size in the absence of the mentioned structural condition.

In NS-titanium, the largest number of atoms is in GB, which creates conditions for the significant influence of diffusion in grain boundaries on the evolution and stability of the microstructure of this material, especially in the process of plastic deformation when, as was discussed above, the diffusion penetrability of GB is increased. Other than the process of isolation of dispersed phases, which have a determining value for GB consolidation, diffusion in grains boundaries transfers the excessive volume formed as a result of plastic deformation to its effective flow (triple junction). This increases the accumulation of micropores and thus decreases its influence on the degradation of mechanical properties of NS titanium and its alloys. Conducted studies of diffusion on grain boundaries in titanium by methods of computer simulation have recently been limited to considering some grain boundaries [50]. It may be expected that using methods for a diffusion study of the nanocrystalline condition, which was discussed above using copper as an example, will make it possible in the future to establish diffusion characteristics on grain boundaries and triple junction in NS titanium too.

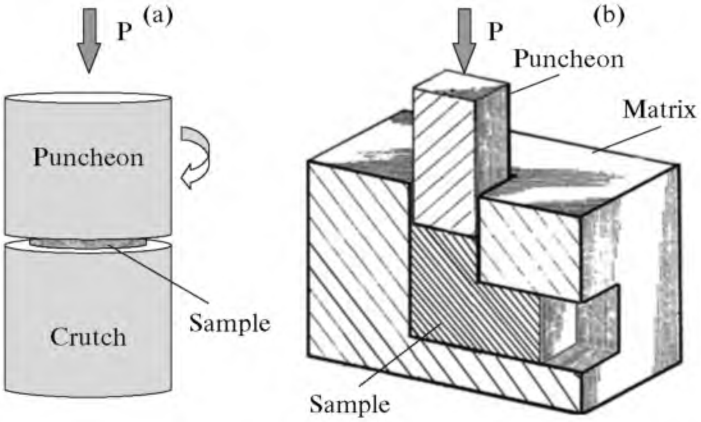

Fig. 5. (a) Intensive plastic deformation by torsion under high pressure and (b) intensive plastic deformation by equal channel angular pressure.

METHODS OF THE FORMATION OF SUBMICROCRYSTALLINE AND NANOSTRUCTURED CONDITIONS IN TITANIUM

Fundamental researches on the regularities of formation of cellular and fragmented structures with the formation of high angle boundaries of grains in the course of process of (large) plastic deformation under usual and higher temperatures [51–55] conducted in the 1980s and 1990s greatly determined the progress in the development of contemporary gaining methods of SMC and NS materials and alloys using the influence of plastic deformations [27, 46, 56–58].

A number of methods to obtain SMC and NS materials using the influence of plastic deformation have been developed recently. Using these methods allows to form submicro- and nanostructure in volume metallic samples and workpieces using significant deformation under pressure at a usual temperature or higher. For example, the structure may be significantly ground as a result of cold or warm rolling or drawing, when the maximal degree of deformation is limited by the plasticity resource of materials. However, such structures are mainly of a granulated–subgranulated mixture where most of the boundaries are the borders of cells and dislocations subboundaries with low angle disorientation. At the same time, it is possible to form an ultrafine-grained structure with a grain size of about some deciles of micron under pressure. Therefore, for the formation of submicro- and nanostructures in volume samples, it is necessary to use special schemes of deformation, which allows to achieve large plastic deformations without material destruction (with the degree of true deformation accumulation $e >$ 10) under moderate temperatures. It is necessary to use specially developed optimal regimes of plastic deformation. To achieve these principles, throughout the last decade known schemes of mechanical deformation were used and new special schemes were developed, like high pressure torsion, equal channel angular pressure (ECAP), continuous equal channel angular pressure (ECAP-conform), equal channel multiangular pressure, pressure with multiple change of deformation axis, screw extrusion, batch hydroextrusion, multiple roll welding, et al. Most of the applied and fundamental results of SMC and NS states formation in volume samples of metals and alloys, including intermetallides, were obtained using three of the methods listed above: high pressure torsion, equal channel angular pressure, and extrusion with a multiple change in the deformation axis [27, 57].

High pressure torsion and equal channel angular pressure (ECAP) belong to so called methods of severe plastic deformation (SPD). The construction of the torsion arrangement under high pressure is a development of famous Bridgman anvil [59]: the sample put between two puncheons is contracted under applied pressure (P) in several GPa. The lower puncheon rotates and the skin-friction force deforms the sample by shift (Fig. 5a). This method was used to study the phase transformation at conditions of intensive deformations [60, 61] and peculiarities of structural evolution after such an influence. The formation of submicro and nanostructures with nonequilibrium large-angle boundary of grains was also revealed [62]. This made it possible to look at this method in the same way as at a new method of getting nanostructured materials. It is possible to get a “true” nanostructured condition with a grain size of less than 100 μm, but they are samples with small geometries (diameter 10–20 mm and thickness 0.2–0.5 mm).

The ECAP method, which deforms massive samples by a simple shift, was elaborated in the 1970s years in order to subject materials to larger plastic deformations without a change in the cross section of samples with the aim of its recurrent deformation [63]. This method was developed and applied for the first time in the beginning of the 1990s in order to get structures with submicrone and nanomentric grain sizes [27, 57]. ECAP is based on the fact that the workpiece is repeat-

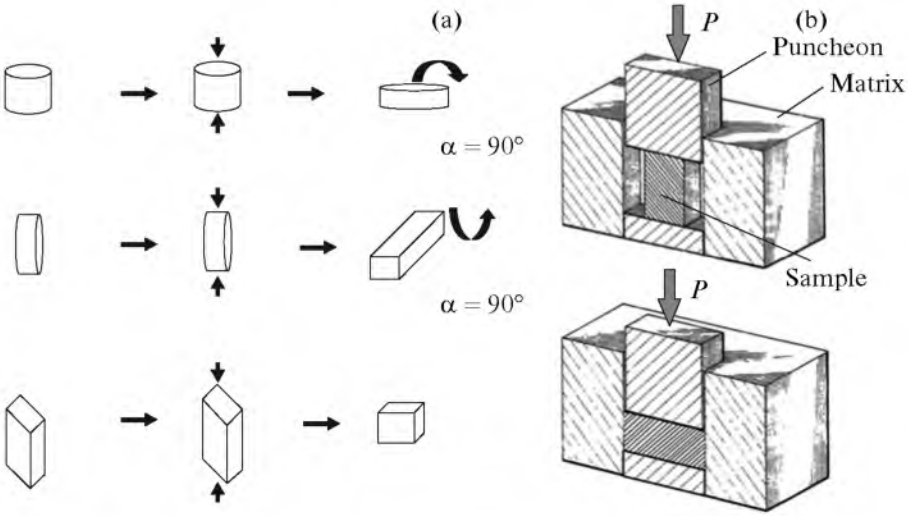

Fig. 6. (a) Scheme of free uniform pressure under high pressure and (b) scheme of uniform pressure while changing the deformation axis using press-forms.

edly pressed in a special gear though two channels with similar cross-sections which are crossed, usually under the angle $\varphi = 90°$ or at another angle.

The process of ECAP is mostly known as a method for the formation of SMC and NS states. However, from a practical point of view, it is labor- and resource-consuming (expensive materials and complex equipment) and also inefficient if the process for producing a long-length workpiece is large-scale. Therefore attempts to improve it are being made [64, 65].

A method for inclusive extrusion or pressure with a multiple change in the deformation axis was offered for the formation of submicro- and nanostructured states in massive samples of titanium alloys [66–68].

Inclusive pressure is based on the use of multiply repeating open forging: an upset-broach with the change in axis of the applicable deforming force [27]. With such a technological scheme, the homogeneity of deformation by the sample is usually lower than with ECAP or high pressure torsion. But this method of influence using large plastic deformations allows to obtain SMC and NS states in sufficient fragile materials because the first cycles of processing with pressure are conducted under higher temperatures when a small specific load on press gear is sufficient. In the next cycles, deformation occurs with the graded temperature decrease. Such a deformation scheme allows to lower the grain size on each stage without crack formation, because material plasticity usually increases with the decrease in grain size. At least this rule is kept for the deformation intervals under moderate and higher temperatures. The use of this method allows to to carry out this process to obtain larger samples.

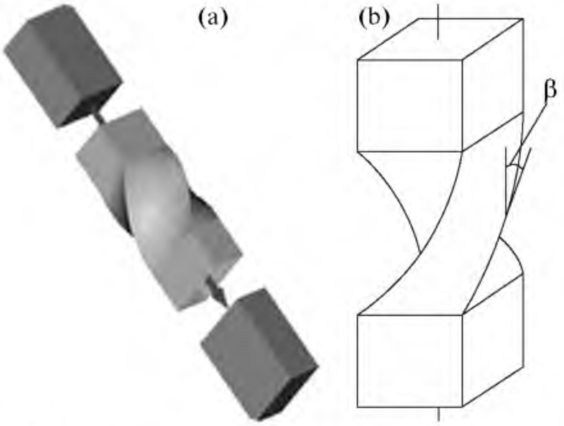

Fig. 7. Schemes of (a) screw extrusion and (b) screw channel under screw extrusion.

The disadvantage of this method is that the coefficient of material used does not exceed 60–80%. In order to increase the coefficient, it was decided to use die tooling (Fig. 6). In such a deformation scheme, the value reaches 95–98%.

The idea of using a screw scheme of deformation for the formation of nanostructured state was presented in [70] and carried out in the form of screw extrusion. The essence of this method is that a prismatic workpiece is forced through the matrix with the screw channel (Fig. 7). The angle β of the slope of the screw line to the extrusion axis changes in the matrix height; in its beginning and ending regions, it reaches zero. The geometric peculiarities of the matrix channel lead to the following: in the process of extrusion though it, the identity of the initial and final forms and sizes of the workpiece under treatment is preserved. This, in its turn, allows to conduct multiple extrusions with the aim of accumulating high levels of plastic deformation. Unfortunately, this method has the same disadvantages as ECAP. It is, first of all, a complex

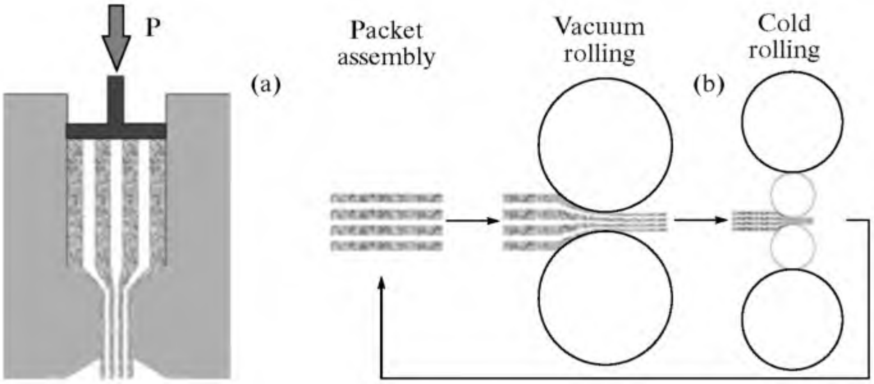

Fig. 8. Schemes of (a) batch hydroextrusion and (b) multiple roll welding.

structure of gear, very labor-consuming, and there are difficulties in obtaining long workpieces.

It is known that one more method for obtaining NS material is batch hydroextrusion and multiple roll welding based on the use of diffusion welding in the process of deformation (Fig. 8) [71–73]. The principle of these methods lies in the primary packet assembly from a certain number of plates and vacuum rolling (extrusion) under high temperature and the subsequent cold rolling or extrusion for the accumulation of large plastic deformations with thinning up to a depth equal to the depth of one of the initial plates that composes the composite material. The use of such methods allows to obtain new constructional and functional materials consisting of dissimilar metals and alloys, for example, nano laminated plastic [73].

Thus, the processing methods using the influence of plastic deformation that were developed over the last few decades are based mainly on the idea of form preservation of the model sample under the accumulation of bog plastic deformation.

Using the result of research devoted to the problem of achieving ultimate grain grinding in metallic materials with the influence of plastic deformations is hindered by the complex difficulties connected with the cost of processing and efficiency. Also, there are difficulties in further altering nanostructured half-finished products up to the necessary product mix of industrial assortment (plates, sticks, et al.) with the condition of nanostructure preservation, that is, without heating to higher temperatures. In this connection the authors of many technological works returned to searching for the classical method of metal processing by pressure, which can be used for nanostructure formation. The abilities of so called "conform" process [74] were analyzed first. This is a process of "winding" a stick on a drum of the rolling mill due to the friction force with the resulting extrusion. This process was simplified to the case of even channels (an equal section of the entering and exiting rod) with angular deformation (the extrusion under a 90° angle in the direction of the stick's movement around a circle). As a result, the "ECAP-Conform" method was obtained [65]. The universality and adaptability of ECAP extrusion were lost, but new abilities of gaining a long stick appeared. Also, other difficulties were preserved: the complexity of the process and the cost and wear of the gear.

The most actual problem is that of the efficiency and productivity of methods of processing using the influence of plastic deformations in cases when it is necessary to get samples of an industrial assortment. One example is getting commercially pure SMC and NS-unalloyed titanium to use in medicine.

Despite of numerous works conducted earlier on the formation of submicro- and nanostructures in VT1-0 alloy by various methods, the low-cost and efficient low-tonnage manufacture of VT1-0 alloy in SMC and NS states was able to be carried out in the works of the author et al. only using traditional methods of metal processing with pressure. The combination of radial-shift rolling and screw and longitudinal rolling has been adopted before for rolling hard-to-deform alloys on the basis of wolfram and molybdenum [74]. These methods are widespread and studied in detail [75–77]. But they were not examined in literature on material science from the point of view of defining optimal paths and temperature–rate intervals of deformation, the sequence of the use of these methods to the task of deliberate creation, and the further elimination of the heterogeneity of processing half-finished product sections while gaining submicrocrystalline and nanostructured states in small plates or rods, for example, for alloys on the basis of titanium.

Usage mills of radial-shift and screw rollings is urgent also because the product of deformational processing is a stick with high geometric accuracy. Such mills are standardized for the production of rods of any diameter from the workpieces of quite a wide range. The usage of mentioned rolling methods is based on the use of a three-high mill with mushroom-shaped or cup-shaped rollers (Fig. 9) [74, 75], which allows to achieve large degrees of deformation by one pass (with a reduction of 1.2–5.0). Also, in the screw rolling, the scheme of a stress condition close to uniform com-

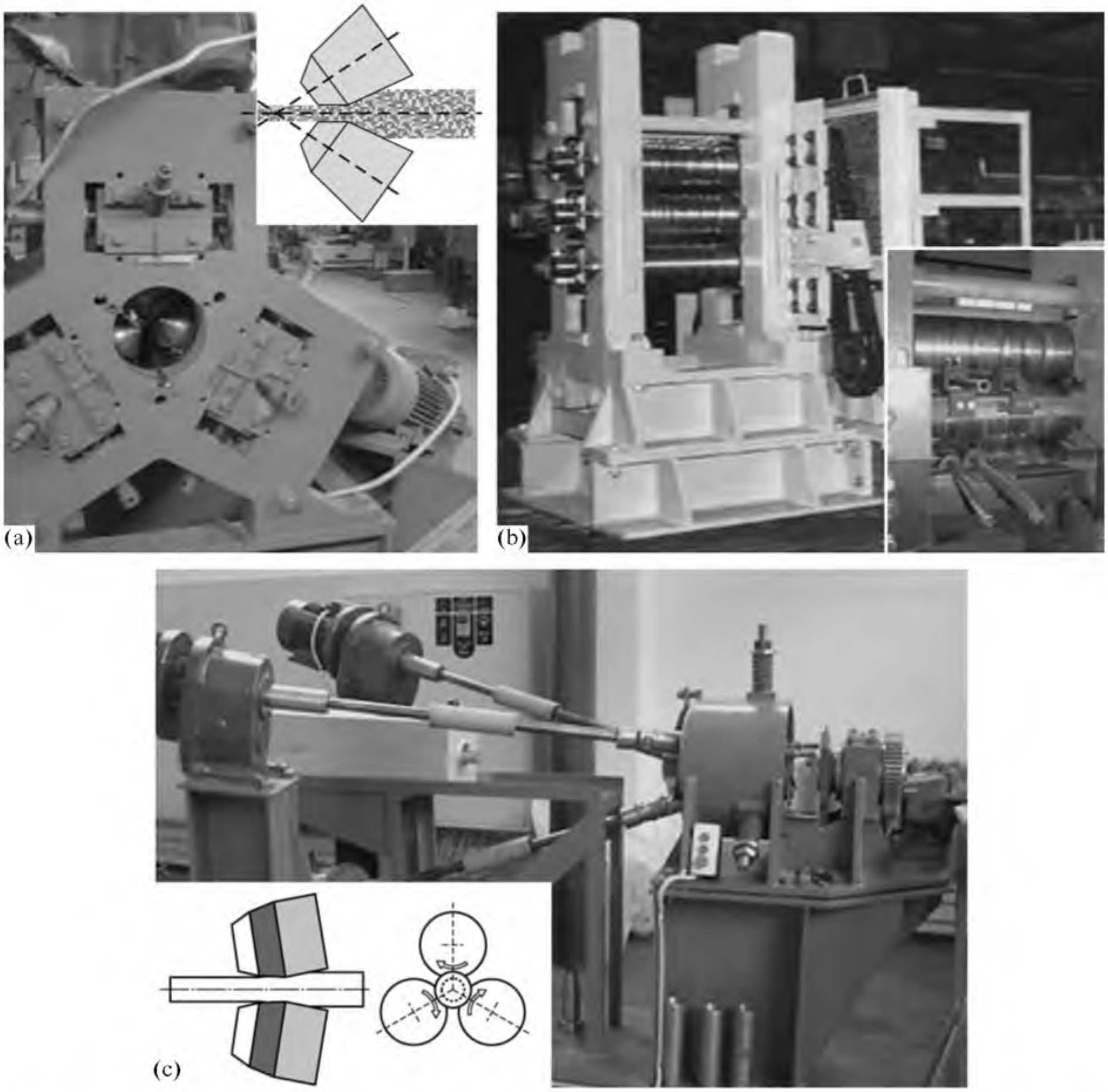

Fig. 9. (a) Mill of longitudinal rolling MISIS-10, (b) mill of screw rolling TRIO-450, and (c) mill of radial-shift rolling RSP14-40.

pression with large shear deformation is achieved. The most intensive shear deformations are localized in the zone of metal slip line cross–circular zone of the cross-section, which is characteristic for a three-high scheme. Using such a scheme allows to carry out the process with a large reduction in one pass and process hard-to-deform materials [74].

The so called "loosening" of the central zone of the rod, which composes up to 20% of the cross section of the material, is thought to be one of the negative factors of the screw-rolling influence on the structure of material. A study of the structure of this zone and an assessment of the flow of materials showed that simple stress deformation, which leads to stitch structure and, in critical situations, to pore formation and metal loosening, occurs in the center of the stick [74]. However, the formation of pores and cavities occurs only when there is a large (more than a critical value) deformation level by one pass. The selection of rational rates (trajectories and temperature-speed intervals) of deformation is different for each material and its intermediate structure and allows to not only successfully carry out the process of form formation without internal and external defects of the half-finished product but also to use the advantages of screw rolling in structure elaboration due to achieving the intensive shear component of deformation [78]. This is successfully used in the metallurgy manufacture of rolled sections, including titanium alloys [75]. In our works we succeeded in obtaining a homogenous globular submicro-

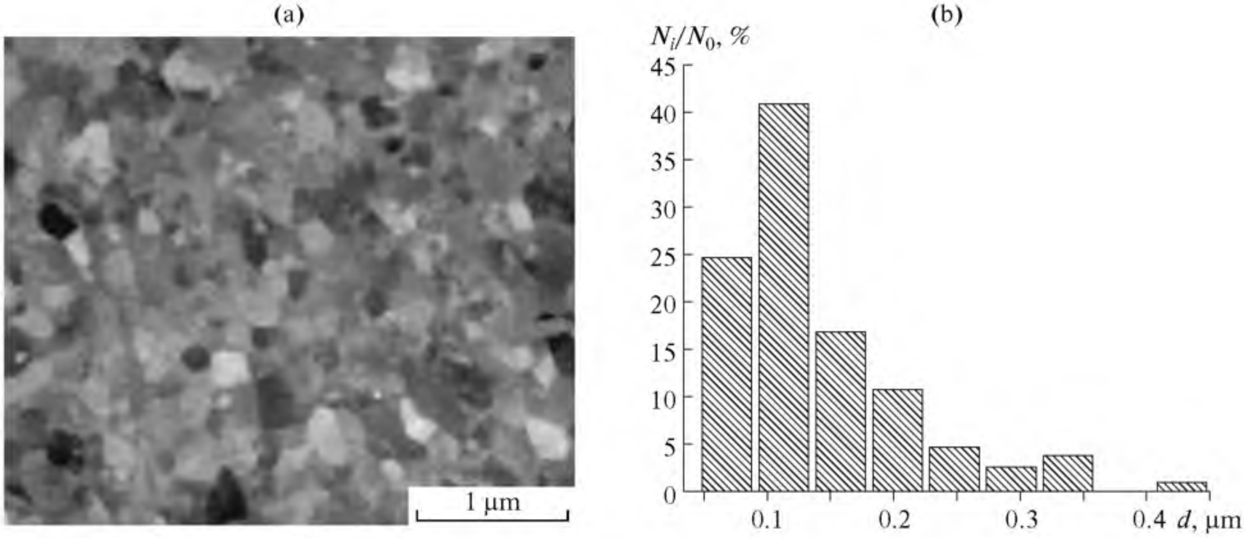

Fig. 10. (a) Typical submicrocrystalline structure and (b) histogram of grains distribution by sizes of titanium VT1-0 processed by combination of redial-shift, screw, and sort rolling. (N_i is the number of grains of i interval and N_0 is the total number of grains).

crystalline structure with an average grain size of ~150 μm (Fig. 10) in sticks with small diameters (6–8 mm) from commercially pure titanium (alloy VT1-0) with a high level of mechanical quality (table) by a combination of redial-shift, screw, and longitudinal rolling. The size of structural elements in such titanium is changed usually in the range from 0.05 to 0.5 μm (the share of nanosized grains is about 35%). The discussed method of processing using special conditions of deformations allows to gain a more homogeneous nanostructure in which the size of structural elements are in range from 30 to 300 μm and the average size is 90 nm (Fig. 11); the share of grain smaller than 100 nm is 64%.

The tensile strength of commercially pure titanium VT1-0 in nanostructured states obtained by a combination of redial-shift, screw and longitudinal rolling corresponds to titanium alloy VT6, as can be seen from the table. The most interesting results were obtained in a torsion test of finished implants (screws for ostheosynthesis). In Fig. 12 the dependencies of the torsional moment on the rotation angle in the torsion tests of screws for ostheosynthesis with a diameter of 4.5 mm formed from the alloy VT16 (alloy of system Ti-Al-V-Mo) and the above-mentioned titanium VT1-0 are presented. According to the tests results, screws from nanostructured titanium demonstrate very high plasticity (the maximal angle before destruction in torsion). The plasticity of NS titanium is an important indicator of the reliability of screws made from such material, because during real medical operations, screws from ordinary titanium alloys often beak. Tests conducted earlier on low- and high-cycle fatigue showed that submicrocrystalline and nanostractured alloy VT1-0 has fatigue resistance on the level of alloy VT6 [27]. Recent data shows that pure SMC-titanium has quite high fatigue resistance, including on samples with cuts [79]. The obtained results make it possible to consider nanostructured titanium VT1-0 as a substitute for alloys VT6 and BT16, as well as for imported Grade-4 alloy used in stomatology.

It is known that half-finished products with submicrocrystalline structure made by influencing severe plastic deformation under medium temperatures are characterized by high internal stress, the sources of which are grain boundaries of a deformation nature, dislocation, and dislocational subboundaries. The presence of such stress may lead to the buckling of products and is a serious obstacle for their usage in medicine. The easiest way to relieve the internal stress

Mechanical characteristics of titanium alloys used in medicine

	Grade-4*	BT1-0**	BT1-0 nanostructural condition	BT6**
Ultimate strength, MPa	700	460	950	970
Plasticity, %	28	27	18	17

Notes: * Producer Perryman Co, Huston, USA.
** Producer OAO Korporatsiya VSMPO-AVISMA, Verkhnyaya Salda, Russia.

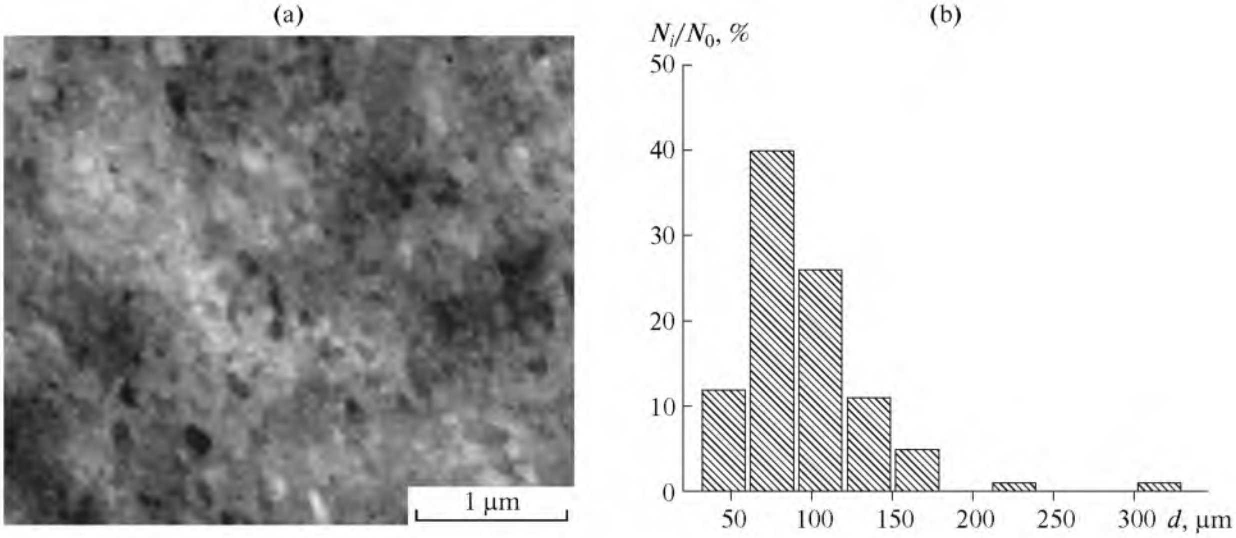

Fig. 11. (a) Microstructure and (b) histogram of the distribution of titanium VT1-0 (by grain sizes) processed in maximum temperature–speed under deformation in a combination of radial-shifts crew and sort rolling (N_i is the number of grains of i interval and N_0 is the total number of grains).

in metal in half-finished products is by heating and aging under certain temperature; the efficiency of annealing increases with the temperature growth, but for SMC- and NS metals it is possible to carry out annealing only under temperatures lower than in the beginning of the recrystallyzation process.

It is shown on Fig. 13 that, in the deformed state, commercially pure titanium VT1-0 is characterized by high residual stress of the first type, which significantly decreases as a result of annealing under T ~ 350–370°C. Such annealing does not lead to a decrease of mechanical properties (using the example of microhardness), but also some strengthening happens apparently due to the processes of aging (this effect was discussed before in [32]). In [32] it is shown that the effect under question is connected with the release of microcarbides-type particles with an ordered placement of Ti–C layers.

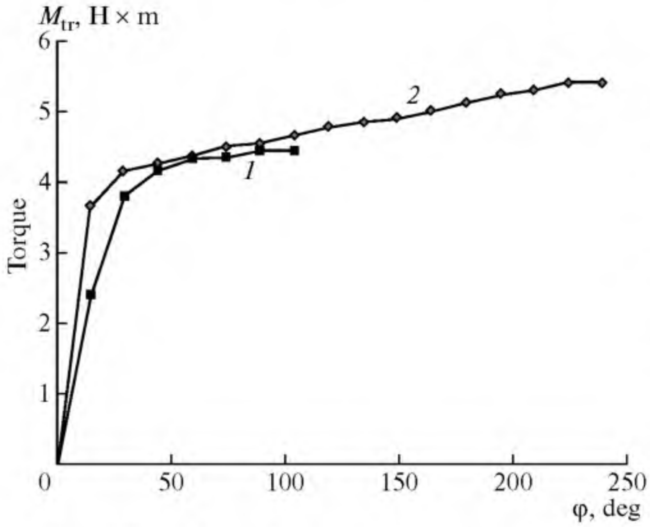

Fig. 12. Dependence of the torsional moment on the rotation angle in experiments on screw torsion for the ostheosynthesis with a diameter of 4.5 mm. (*1*) Alloy BT16 in hard-grain condition. (*2*) Commercially pure titanium VT1-0 in nanostructured condition.

Low-cost and highly efficient technological processes developed on the basis of the above-described methods of making shaped sections and round sticks from titanium VT1-0 with nano- and submicrosrystal structures are now used in the technology of making a pilot batch of materials for medical implants as part of program of the federal program on the topic “Development of Pilot Technologies for the Formation of Next-Generation Medical Implants on the Basis of Titanium Alloys,” which, as was mentioned above, are now undergoing clinical tests (Fig. 14).

Nowadays works on developing methods to form calcium-phosphate coatings on submicrocrystalline and nanostructured titanium and its alloys are being conducted in several research organizations in Russia as a part of above-stated project [80, 81]. Methods of synthesizing nanocrystalline hydroxilapatites and electrolytes on their basis are being developed with this aim [82, 83]. Compositional biocoatings, which are being developed in the Center of nanostructured Materials and Nanotechnologies at Belgorod State University and are deposited on nanostructured titanium by the method of microarch oxidation, have successfully undergone their initial screening in solutions with nanohydroxilapatites at the Gertsen Cancer Research Institute, Moscow. The in vivo laboratory studies of the physiology of adaptive processes at Belgorod State University showed that biocoatings in a

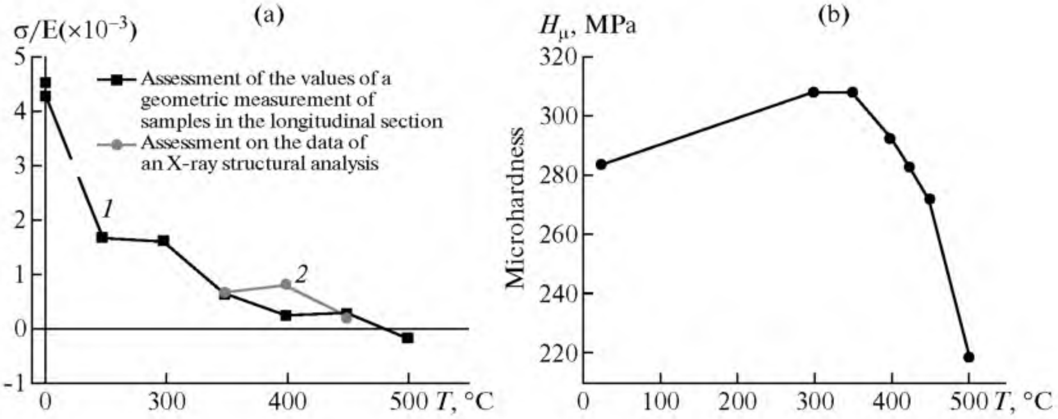

Fig. 13. (a) Dependence of the values of residual stress on the annealing temperature assessed by values of geometric measurement of samples in lengthway cut (*1*) and by data of X-ray structural analysis (*2*); (b) value of microhardness.

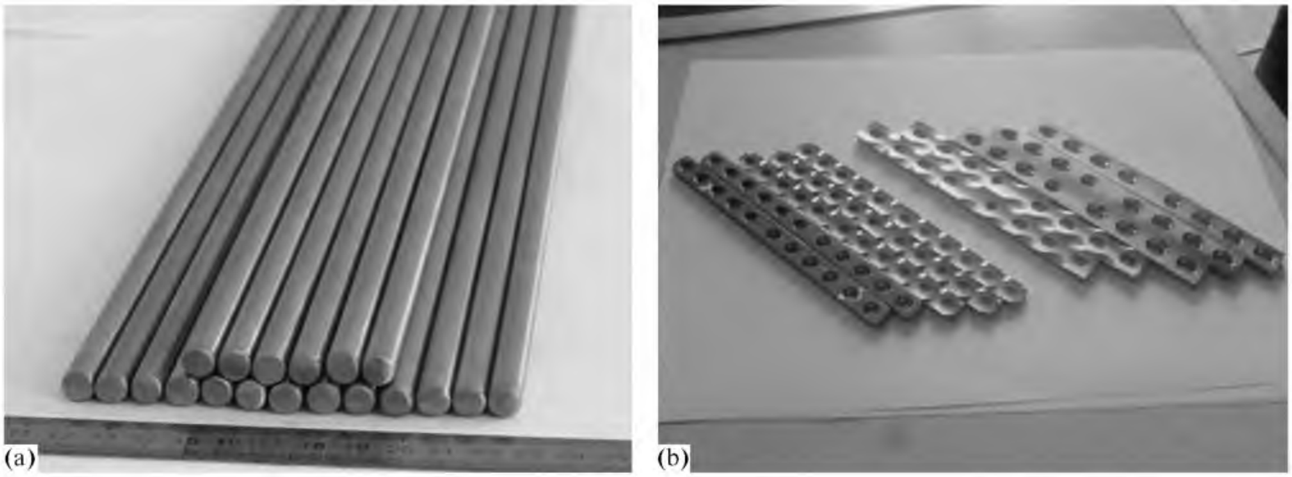

Fig. 14. (a) Trial set of sticks of submicrocrystalline technical titanium VT1-0 for manufacture of medical implants; (b) trial set of plates for traumatology manufactured from submicrocrystalline technical titanium VT1-0.

surgical procedure are not rejected in the body. This is indicated by the lack of activation of the immune system demonstrated by data on C-reactive protein concentration and interleukin1β concentration in the plasma of animals after implantation. The results obtained allow us to recommend implants on the basis of SMC and NS titanium with microarc calcium–phosphate bioactive coatings for conducting clinical tests.

CONCLUSIONS

An analysis of the main approaches for making modern functional materials for medical implants has been carried out. The principles of choosing materials by the criteria of their biochemical and biomechanical compatibility were examined. One of the most prospective and wide-spread materials for traumatology, orthopedics, and stomatology implants are titanium alloys. The most optimal variant for preserving high biochemical compatibility while increasing mechanical properties to a level corresponding to alloyed high-strength titanium alloys is to form submicrocrystalline or nanostructured states in commercially pure titanium which does not contain alloying substances that are harmful for a living body. The prospect for its use as material for medical implants was proven be the recently reached level of service characteristics.

An analysis of the results of experimental and theoretical studies of the peculiarities of diffusion by grain regions was conducted, and the role of diffusion-controlled processes in the formation and evolution of submicrocrystalline and nanostructured state was revealed. The efficiency of computer simulation on an atomic level in establishing the dependencies of diffusion characteristics by grain regions on the average grain size and structural states of internal boundaries is outlined.

The contemporary methods of forming submicrocrystalline and nanostructured states in metals and alloys obtained under the influence of plastic deformation were considered. It was shown that an industrial assortment of titanium and titanium alloys needed for serial manufacturing medical implants and instruments may be obtained using recently developed low-cost technological methods of metal processing by pressure, including radial-shift and screw rolling in combination with traditional methods of mechanical thermal processing.

A number of methods of microarc deposition of coatings using electrolytes with nanohydroxylapatites (with crystal sizes less than 100 nm) for the formation of nanocrystalline bioactive coatings on the surface of medical implants were discussed.

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