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Study and development of nanostructured metals for production of medical implants and equipment

Исследование и разработка наноструктурированных металлов для производства медицинских имплантатов и оборудования

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ABSTRACT

Nanostructured metals (Ti and Ti alloys, stainless steels, Mg alloys) with enhanced static and fatigue strengths are promising materials for medical implants [1]. The use of a combined severe plastic deformation (SPD) processing, including the recent equal channel angular pressing (ECAP)-Conform technique leads to significant strengthening of metallic materials due to their nanostructuring. In particular, the use of nanoTi rods with enhanced strength and fatigue life have enabled the fabrication of implants with improved design for dentistry and orthopedics. Furthermore, surface modification of nanoTi through chemical etching and bioactive coatings allows for considerable improvement of its biomedical properties. As a result of conducted studies, miniaturized dental implants and nanoTi plates with reduced thickness and enhanced osseointegration were manufactured and successfully tested in clinical trials.

KEYWORDS

Nanostructured metals; titanium; severe plastic deformation; medical implants; bioactive coatings.

АННОТАЦИЯ

Наноструктурные металлы (титан и титановые сплавы, нержавеющие стали, магниевые сплавы), имеющие повышенную статическую и усталостную прочность, являются перспективными материалами для медицинских имплантатов. Применение комбинированных методов интенсивной пластической деформации (ИПД), включающих недавно разработанный метод равноканального углового прессования (РКУП-Конформ), приводит к существенному упрочнению металлических материалов благодаря их наноструктурированию. Так, применение нанотитанового прутка с повышенными прочностными и усталостными характеристиками позволило изготовить имплантаты улучшенной конструкции для стоматологии и ортопедии. Более того, модификация поверхности нанотитана путем химического травления и формирования биоактивных покрытий позволила дополнительно повысить биомедицинские характеристики имплантатов. В результате проведенных исследований были изготовлены миниатюризированные дентальные имплантаты и пластины из нанотитана с уменьшенной толщиной, которые успешно прошли клинические испытания.

КЛЮЧЕВЫЕ СЛОВА

Наноструктурные металлы; титан; интенсивная пластическая деформация; медицинские имплантаты; биоактивные покрытия.

Introduction

In the past few years the nanostructuring of metals by severe plastic deformation (SPD) aimed at enhancing their properties has become a developed area of modern materials science and engineering [2]. With regard to medical applications, the creation of nanostructures in metals and alloys by SPD processing can improve both mechanical and biomedical properties. This paper describes the results of our recent investigations relating to titanium and its alloys that are the most extensively used to fabricate medical implants and other items. The examples demonstrate that nanostructured metals with advanced properties offer opportunities to create a new generation of medical devices with improved design and functionality [3].

1. Experimental Procedures

Rods of Grade 4 commercially pure (CP) titanium 12-mm in diameter, meeting all the specifications of the ASTM F67 standard for medical implants, were used in the study reported herein. The material impurity data was as following (in wt.%) 0.050% C, 0.20% Fe, 0.35% O_2, 0.007% N, 0.0020% H and the average grain size of the titanium rods in as-received condition equaled to ~25 μm. The rods were nanostructured via ECAP-C and drawing. The former processing technique is a comparatively recent modification of the standard ECAP method [4–6]. In the course of this process, a work-piece is forced through an ECAP die in a manner analogous to the Conform process, however in this case an upgraded ECAP design is applied for nanostructured materials to be produced with repeat-passes.

As-received Grade 4 Ti rods were subjected to ECAP-C in a die-set with a 120° intersection angle *Φ*, through the B_c route. Subsequent drawing was carried out to a reduction ratio of 85%. The deformation temperature was equal to 200 °C. The processing details are presented in Refs. [5, 6]. The final processed rods had a length of 3 m with the diameter from 3 to 6 mm.

The microstructure was analyzed by means of optical as well as transmission electron microscopy (TEM) in a JEOL JEM 2100 TEM with acceleration voltage 200 kV.

The processing resulted in a large reduction in grain size, from the 25 μm equiaxed grain structure of the initial titanium rods to 150 nm after combined SPD and TMT processing, as shown in fig. 1. The selected area electron diffraction pattern, fig. 1 (*c*), further suggests that the ultrafine grains contained predominantly high-angle non-equilibrium grain boundaries with increased grain-to-grain internal stresses [4]. A similar structure for CP Ti can also be produced using a continuous SPD method, ECAP-Conform, combined with further drawing into long rods [180]. It was essential to produce homogeneous ultrafine-grained structure along the entire three-meter rod lengths to enable economical pilot production of implants and provide sufficient material for thorough testing of the mechanical and bio-medical properties of the nanostructured titanium.

The cylinder-shaped samples, 3 mm in diameter and of 15 mm gauge length were tensile-tested at room temperature in an INSTRON-type device with a primary strain rate of 10^{-3} s^{-1}. The tensile axis was parallel to the rod axis. Stress-controlled fatigue tests at ambient temperature were carried out to characterize the behavior of nanostructured (NS) and conventional coarse grain (CG) CP titanium at a load ratio of R $(\sigma_{min}/\sigma_{max}) = -1$. Rotational bending testing with a frequency of 50 Hz was performed.

Surfaces of mechanically-polished CG and NS samples of Grade 4 Ti were acid-etched in 30% HNO_3 + 3% HF+H_2O for 20 minutes. Surface topography was examined with a LSM-5-Exciter laser scanning microscope (LSM). Surface profiles were analyzed to determine the surface roughness parameter R_a and the size of etching dimples.

2. Results and Discussion

2.1. Design of Miniaturized Implants

There are simple rules when it comes to redesigning the devices in terms of the influence of changing materials, such as replacing CG Ti by nanostructured CP Ti. Fatigue performance must be retained with thorough account for the possibility of changing the device cross-sectional dimensions. The data on fatigue properties of nano Ti and initial Ti (table 1) [3] were used to calculate the design of dental implant with the diameter 2.4 and 2.0 mm (fig. 2, *a*) produced by the company «Timplant» s.r.o., Czech Republic [6, 7] and nanoTi mini-plates (fig. 2, *b*) from the company «Conmet», Moscow [29]. The implants were tested to demonstrate exceptionally high properties [3].

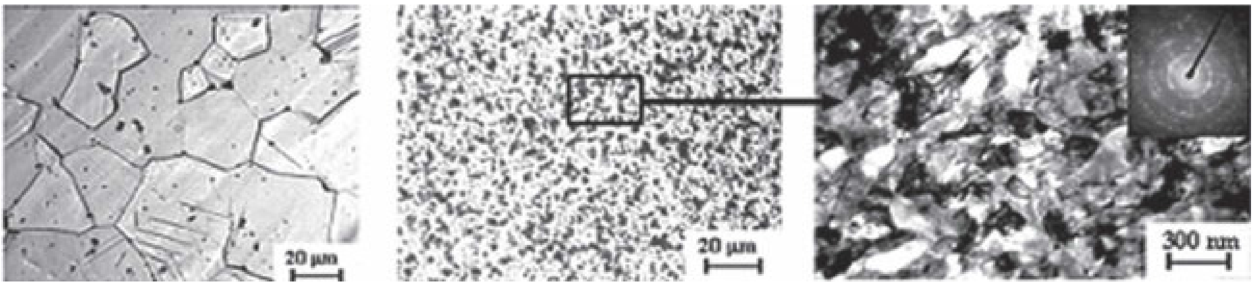


Fig. 1. Microstructure of Grade 4 CP Ti: *a* – the initial coarse grained rod; *b, c* – after ECAP + TMT (Optical and electron photomicrographs)

Рис. 1. Микроструктура титана CP4: *a* – исходный крупнозернистый стержень; *b, c* – после РКУП + ТМТ (оптические и электронные микрофотографии)

Table 1

Таблица 1

Mechanical properties of conventionally processed and nanostructured Grade 4 Ti produced by ECAP-C and drawing. Data on Ti-6Al-4V ELI alloy are presented to compare

Механические свойства предварительно обработанного и наноструктурированного Grade 4 Ti, произведенного ЕКАП-К и волочением. Для сравнения представлены данные по сплаву Ti-6Al-4V

Processing/ treatment terms	UTS, MPa	YS, MPa	Elongation, %	Reduction of area, %	Fatigue strength at 10^7 cycles
Conventional Ti (as-received)	700	530	25	52	340
nano-Grade 4	1330	1267	11	48	620
Annealed Ti-6Al-4V ELI	940	840	16	45	530

a

b

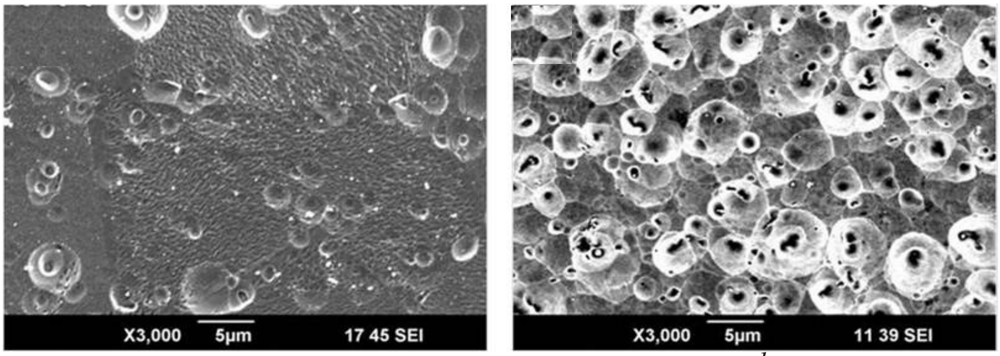
Fig. 2. 2.0 mm diameter Nanoimplant [7] from NS Grade 4 Ti in a panoramic X-ray radiograph after surgery (*a*) and the image of a miniplate with six holes made from NS Grade 4 Ti (*b*)

Рис. 2. Наноимплантат диаметром 2,0 мм [7] из наноструктурированного Grade 4 Ti на панорамном рентгенограмме после операции (*a*) и изображение мини-пластины с шестью отверстиями из NS Grade 4 Ti (*b*)

2.2. Surface modification of nanoTi implants

Surface properties are an important aspect of an implant design to ensure effective osseointegration. Pure Ti has very low bioactivity (i.e. bioinert material) and it does not bond directly to the human bone [8]. Extensive studies have shown that grain refinement down to the nanoscale in CP Ti can stimulate various bone-forming cell types to adhere and proliferate with increased efficiency [8–12]. Additional surface modification can further improve bioactivity of implants made from nano Ti. Two main approaches of surface modifications are studied in our works: chemical etching and deposition of bioactive coatings [3, 13–18].

The topography of etched surfaces is strongly determined by etching solution and etching time. Different solutions, such as acidic (H_2SO_4/H_2O_2) or basic (NH_4OH/H_2O_2) Piranha solutions can be used for etching of CP Ti [18] resulting in different surface topographies. Manipulation with etching time can substantially modify the surface topography and this effect is more pronounced in the nano Ti, as it has been very recently demonstrated in fig. 3 [18].



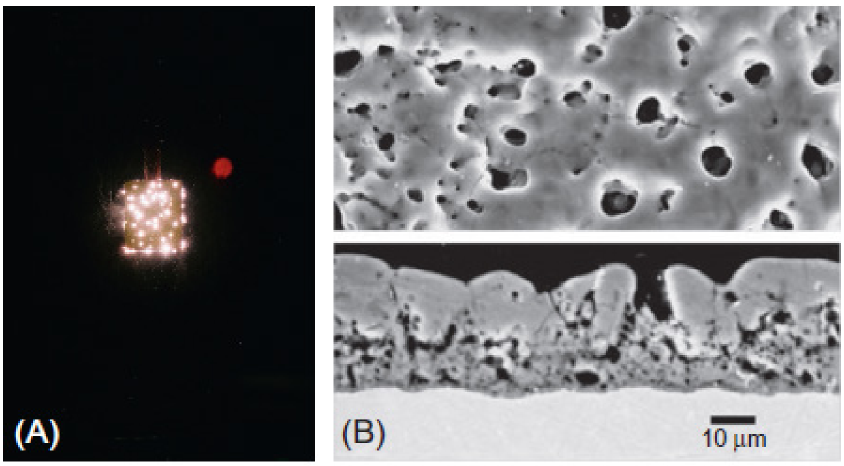
a *b*

Fig. 3. Surface of CG and NS samples of Grade 4 Ti after mechanical polishing and etching in the mixture of acids 30% HNO_3 + 3% HF+H_2O for 20 minutes: *a* – CG Ti surface; *b* – nano-Ti surface. SEM images

Рис. 3. Поверхность образцов крупнозернистого и наноструктурированного Grade 4 Ti после механической полировки и травления в смеси кислот 30% HNO_3 + 3% HF+H_2O в течение 20 минут: *a* – крупнозернистый Ti; *b* – наноструктурированный Ti. Растровая электронная микроскопия

Biocompatible coatings can also essentially facilitate integration of the nano Ti implants into a human bone [16, 17]. Presently, the research into synthesis of biocompatible coatings integrating the inorganic (Ca-, P-containing phases) and organic (biologically active and bioinert molecules) components on titanium implants appears to be topical state of the art [19, 20].

During the last decade, significant attention is attracted to Ca-, P-containing coatings obtained by the method of plasma electrolytic oxidation (PEO) [21, 22]. PEO process is an expansion of the traditional anodizing into the high voltages up to 600 V; these voltages promote microdischarges within the coating (fig. 4); this results in its resoldifying and intensive growth [22, 23]. This method is applicable to both CG and UFG titanium [14, 24]. The coatings obtained by this method contain stable titania (rutile and anatase) tightly attached to the surface because of the process mechanism including electrochemical oxidation and numerous melting and crystallizing events at the microdischarge sites. This coating formation mechanism helps to develop coatings with regulated porosity, with the pore size from 0.1 to 10 μm [25]. This coating morphology provides gradual change of the elasticity modulus from the metallic implant to the bone; this enhances their biomechanical compatibility. High surface area of the PEO coating promotes osteoblast attachment on the implant surface. Applying varying pulse polarity during PEO and introduction of bioactive particles into the electrolyte helps to incorporate the anions and cations of the electrolyte into the coating; this provides Ca-, P-containing bioactive crystalline phases within the coating: hydroxyapatite, tricalciumphosphate, tetracalciumphosphate, perovskite [25]. Adhesion of the PEO coatings is higher than of the other coating types.



a *b*

Fig. 4. Photographs of microdischarges on the sample surface during PEO process (*a*); SEM image of PEO Ca-, P-containing coating on titanium, top view (above) and cross-section (below) (*b*) [22, 25]

Рис. 4. Фотографии микроразрядов на поверхности образца в процессе плазменного электролитического окисления (*a*); изображение плазменного электролитического окисления Ca-, P-содержащего покрытия на титане, вид сверху (наверху) и поперечное сечение (снизу) (*b*) [22, 25]

3. Summary and Conclusions

Thus, nanostructured Grade 4 titanium appears to be the material with a very high potential for medical applications as its elements have no harmful effects on humans. It should be noted that nanostructured CP Ti also imparts good machinability. Additional research on nanostructured Ti is foreseen to even further increase ultimate strength and yield strength as well as to develop a way to reduce the effective modulus of elasticity that could come close to the modulus of elasticity of jaw-bone [3].

The recent results have shown also that ECAP-C with subsequent drawing provides new opportunities in the development of nanostructured Ti, providing the ability to enhance the strength uniformly in long-length rods that can be machined into dental implants and other devices for medical applications. Nanostructuring of CP Ti by SPD processing produces a material with mechanical properties superior to those of Ti-6Al-4V. The application of nano-Ti in maxillofacial surgery can be promising for producing miniature implant designs, in particular plates that will endure the same loads as the conventional items.

Chemical etching and deposition of bioactive coatings can be utilized for surface modification in nanostructured Ti. Nanostructured CP Ti with modified surfaces can show improved functional properties such as improved surface bioactivity and reduced Ti ion release into human body. This makes nanostructured Ti an attractive material for manufacturing implants. The clinical significance of these research results [7, 26–28].

A number of biomedical researches have been already made to date, which shows that further biological studies are still needed. This applies also to other nanostructured metals (stainless steel, Co-Cr alloys, magnesium alloys etc.), which are now actively developing for biomedical applications [1].

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