Development and study of medical implants made from nanostructured titanium

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Nanostructured Ti with enhanced static and fatigue strengths is a promising material for medical implants. The use of a combined Severe Plastic Deformation (SPD) processing, including the new Equal Channel Angular Pressing (ECAP)-Conform technique, leads to significant strengthening of Grade 4 titanium rods, due to material nanostructuring. The use of nano-titanium rods with enhanced strength and fatigue life enables the fabrication of implants with improved design for dentistry and orthopaedics. Miniaturized dental implants with diameters as small as 2 mm and nano-titanium plates with reduced thickness were manufactured and successfully tested in clinical trials.

Keywords: nanostructured titanium, severe plastic deformation, ECAP-Conform, fatigue strength, dental implants, bone plates, mini-implants

1. Introduction

It is well-known [1, 2] that from the point of view of biocorrosion resistance, titanium is superior to other surgical metals, due to the formation of a very stable passive layer of TiO_2 on its surface. Ti is intrinsically biocompatible and often exhibits direct bone apposition. Another favorable property of Ti is the low elastic modulus (twofold lower compared to stainless steel and Co–Cr), which results in less stress shielding and associated bone resorption around titanium orthopedic and dental implants. Furthermore, titanium is more light-weight than other surgical metals and produces fewer artifacts on computer tomography and magnetic resonance imaging [3, 4]. However, the static and fatigue strengths of titanium are too low for commercially pure (CP) titanium implants to be used in load-bearing situations. For example, small-sized systems and designs from plates and screws are often used in the maxillofacial area of a skull [4–6]. Depending on the injury type and the location of the device within the bone, loads on such implants can vary from 200 to 700 N [2]. The maximal load for a 1-mm-diameter screw can be 900 MPa, which is significantly higher than the ultimate tensile strength of commercially pure Ti [7] and requires the use of a stronger Ti alloys or stainless steel [1, 2, 5]. Alloying with aluminum and vanadium allows for a significant improvement of the mechanical properties of titanium, however both elements are potentially toxic, have mutagenic actions on cells and can cause neurological conditions (e.g., Alzheimer's disease). Therefore, much effort is being directed toward the development of V- and Al-free Ti alloys. The research on titanium alloys composed solely of non-toxic elements has been under way for several years [3–5]. A promising way to enhance the mechanical strength of titanium is by nanostructuring - grain refinement to the nanosized range—by severe plastic deformation (SPD) [6–10]. Our recent studies have shown that the application of such severe plastic deformation processing techniques as equal-channel angular pressing combined with Conform, i.e. the ECAP-Conform (ECAP-C) technique, with subsequent drawing is currently the most effective way to produce long-length nanostructured rods with enhanced strength[11, 12]. These studies demonstrate the promising outlook for nano-Ti as a biomaterial for dental implants [13, 14]. In addition to high static strength, nanostructured titanium exhibits enhanced

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fatigue resistance [14, 15], exceeding the level of Ti-6Al-4V ELI used in osteosynthesis devices. This opens up new horizons for miniaturization of nano-Ti implants.

The present paper demonstrates the possibility of obtaining high-strength bar-shaped nanostructured pure titanium semi-finished products through the use of ECAP-C technology for the development of medical products with improved design. Examples of mini-implants fabrication and their use in dentistry and orthopaedics are also presented.

2. Materials and methods

2.1. Material and processing

12-mm diameter rods of Grade 4 titanium meeting all the requirements of ASTM F67 were used in this investigation. The impurity content of the material was (in wt %) 0.050% C, 0.200% Fe, 0.350% O_2, 0.007% N and 0.002% H. The average grain size in the as-received conditions was ~25 μm. The nanostructuring process was implemented via ECAP-C and drawing. ECAP-C processing is a relatively new modification of the conventional ECAP technique [11–13]. In this process, the principle of frictional force generation required to push a work-piece through an ECAP die is similar to the Conform process, but a modified ECAP die design is used here so that the work-piece can be repetitively processed to produce a nanostructured material.

The as-received 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 rate of 85%. The deformation temperature was 200°C. The processing details are presented in [16].

2.2. Microstructure observation

The microstructure of ECAP-processed rods was analyzed by optical microscopy and by transmission electron microscopy (TEM) in a JEOL JEM 2100 TEM operating at an accelerating voltage of 200 kV. For optical metallography, the samples were mechanically polished and etched in a solution of 4% hydrofluoric acid and 20% perchloric acid in distilled water. TEM foils were cut out by the electrospark method, mechanical thinned down to 100 μm and subjected to electrolytic polishing using a "Tenupol-5" setup. A solution of 5% perchloric acid, 35% butanol and 60% methanol was used for electropolishing.

2.3. Static and fatigue testing

Mechanical tensile tests were conducted in an INSTRON-type testing machine, at room temperature with an initial strain rate of 10^{-3} s^{-1}. Cylindrical samples with a gauge length of 15 mm and a diameter of 3 mm were tested. Ambient temperature stress-controlled fatigue tests of nanostructured and conventional commercially pure titanium were performed using the rotational bending loading scheme with a frequency of 50 Hz, at the load ratio $R(\sigma_{min}/\sigma_{max}) = -1$.

2.4. Producing miniaturized dental implants

Rods of high-strength nanostructured Grade 4 Ti produced by the ECAP-C process followed by drawing, were subjected to grinding, in order to produce the required surface quality and tolerance. 2.4-mm-diameter screw implants Nanoimplant® with a thread and the intraosseal part length of of 8, 10, 12 and 14 mm were manufactured from nano-Ti by "Timplant'" s.r.o. in Ostrava, Czech Republic (www.timplant.cz/en/). The implant has a polished gingival part with a cone top above it. The developed implant is made from pure titanium and, therefore, it does not contain any toxic alloying elements (like V or Al) and elements classified as allergens (like Ni, Co, or Cr). The clinical performance of Nanoimplants® was statistically evaluated basing on the 2-year follow-up information supplied by five dental surgeons from the state and private dental clinics.

2.5. Geometrical parameters of nano-Ti mini-plates

As known that simplified rules for designing devices are used in case of material change: fatigue strength retention with change of its cross section. In order to determine the critical minimal sizes of a plate depending on the loading conditions, the following conditions should be fulfilled [1]: for tension/compression, the cross section area of a plate

$$A \geq F_{max}/\sigma_f, \tag{1}$$

for bending, the axial resistance moment:

$$W \geq Mb_{max}/\sigma_f, \tag{2}$$

where σ_f is the material fatigue endurance limit; F_{max} and Mb_{max} are the maximal applied force and the bending moment, respectively.

In this work the standard sizes of a mini-plate from commercially pure Ti designed by the "Conmet" company [18] are taken as the base sizes according to ASTM F 67-00. In order to determine the coefficient of the cross section area reduction, the fatigue endurance limit of Ti Grade 4 was measured in the initial coarse-grained $\sigma_{f(CG)}$ and nanostructured $\sigma_{f(NS)}$ states, respectively (section 2.3). Knowing the values of $\sigma_{f(CG)}$ and $\sigma_{f(NS)}$, one can calculate the fatigue strength ratio in accordance with the formula [1]:

$$K_r = \sigma_{f(CG)}/\sigma_{f(NS)}. \tag{3}$$

Then, using formulas (1) and (2) for both loading schemes (tension/compression and bending), the main criterion in the cross section area reduction in the nano-Ti plate will be the following ratios [1]: for tension/compression

$$A_{(NS)} \geq A_{(CG)} * K_r, \tag{4}$$

for bending:

$$W_{(NS)} \geq W_{(CG)} * K_r. \tag{5}$$

The new sizes of nano-Ti Grade 4 plates are chosen (see below), using the estimated values of the fatigue strength ratio K_r.

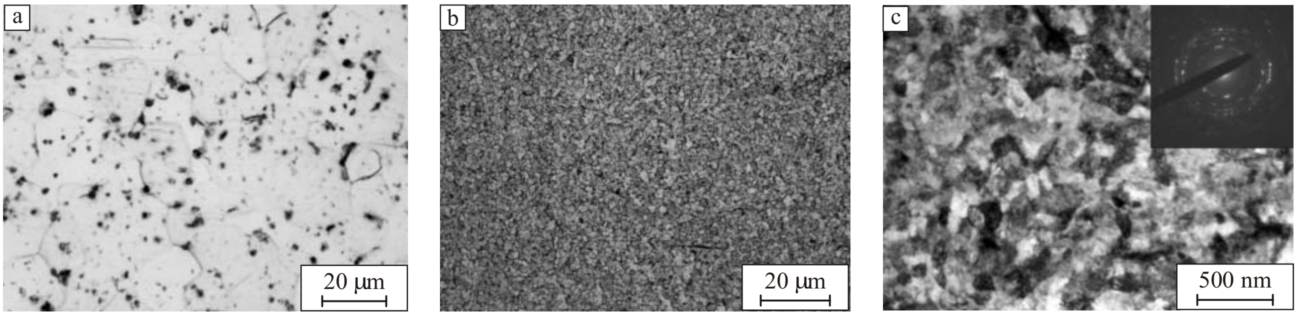

Fig. 1. Microstructure of Grade 4 CP Ti: (a) the initial coarse-grained rod; (b) and (c) cross section of the rod after ECAP-C + drawing (optical (a), (b) and TEM (c) images).

2.6. Allowable bending strengths of the standard and a mini-plate

In plates, bending stresses are dominant [1], therefore, a comparative evaluation of the bending strength was performed [19, 20] for the standard plate from a conventional CG Ti and for a plate from nanostructured Ti with a reduced cross section. Cyclic fatigue tests of Ti mini-plates were carried out using the ElectroPuls E3000 system with a clamping device for holding the plate on one side [20]. The plate was bent plastically at a constant deflection value of 3 mm. The load frequency was 30 Hz. The tests were conducted to failure, with a relevant number of cycles to failure N. Three plates were tested in each state. As a plate is fixed only on one side during testing, in these loading conditions (single-sided support), the axial resistance moment can be calculated according to the formula [21]:

$$W = bh^2/6, \quad (6)$$

where b and h are the width and thickness of the plate, respectively.

Having determined σ_f for CG and NS Ti Grade 4, the applied bending moment Mb (bending strength) is estimated from ratio (2) for both plate types during testing.

3. Results

3.1. Microstructure and mechanical properties

Nanostructuring involved severe plastic deformation processing via ECAP-Conform followed by drawing to produce 3 m long rods, using the facilities of the «NanoMeT» company (Ufa, Russia) [22]. This 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 a combined processing by ECAP-Conform and drawing, as shown in Fig. 1.

The selected area electron diffraction pattern, Fig. 1(c), further suggests that the ultrafine grains contained predominantly high-angle grain boundaries. A similar structure for commercially pure Ti can be produced in small discs using other severe plastic deformation techniques, for example—high-pressure torsion (HPT) as studied in detail in [15]. In the present work it was essential to produce a homogeneous ultrafine-grained structure throughout a three-meter long rod to enable a pilot production of implants and provide sufficient material for thorough testing of the mechanical and bio-medical properties of nanostructured titanium. It is important to note that a homogeneous UFG structure was also typical for the longitudinal section of the rods, but here a small elongation of the grains was observed (elongation coefficient <1.4). Table 1 illustrates the mechanical property benefits attainable by nanostructuring of commercially pure titanium, for example, the strength of the nanostructured titanium is nearly twice that of conventional commercially pure titanium. Notably, this improvement has been achieved without the drastic ductility reductions (to below 10% elongation to failure) normally observed after usual rolling or drawing.

The ultimate tensile strength (UTS) of Ti after ECAP + Drawing is almost twice that of the initial state; even higher UTS values are obtained with increasing the degree of straining from 75 to 85% during drawing. In conventional techniques of deformation processing, such as rolling, extrusion or drawing, the visible strength growth achieved by increasing the accumulated strain and microstructure refinement is accompanied by considerable reduction in ductil-

Table 1. Mechanical properties of conventionally processed and nanostructured Grade 4 Ti produced by ECAP-C and drawing.

Processing/treatment conditions	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

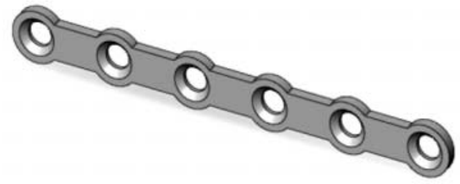

Fig. 2. Image of a mini plate with six holes made from nanostructured Ti Grade 4.

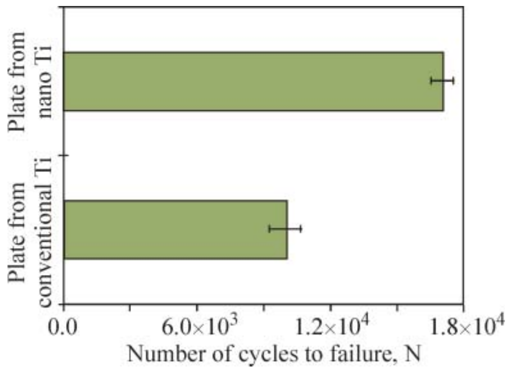

Fig. 3. Fatigue life of the standard plate and plate from nano-Ti with a reduced cross section area. [32].

ity. This is due to the fact that these processing techniques result in a subgrain type of microstructure, which is characterized by pronounced metallographic and crystallographic textures as well as by high volume of low-angle grain boundaries.

At the same time, the use of severe plastic deformation processing allows for the formation of a UFG structure featuring homogeneity, a large volume of high-angle grain boundaries and a lack of a pronounced texture. Such an ultrafine-grained structure may provide the combination of high strength through the Hall-Petch relation and sufficient ductility [23–25], because the origin of grain boundaries in UFG materials plays an important role in determining the level of mechanical properties. In the studies on UFG Ti [15, 26] it was shown that the formation of high-angle, non-equilibrium grain boundaries may provide the processes of intergranular sliding during severe plastic deformation already at room temperature, thus considerably influencing the material deformability and ductility level. An increase of accumulated strain and volume of high-angle grain boundaries in the UFG Ti structure leads to a change of the dominant deformation mechanisms due to the increasing contribution of grain boundary sliding and rotation [7, 23].

The results of the present study demonstrate that the formation of an ultrafine-grained structure during severe plastic deformation in Ti leads also to a considerable increase of fatigue endurance as compared with the initial state. The fatigue endurance limit is 590 MPa after ECAP-C and subsequent drawing to 75% in comparison to 380 MPa in the as-received condition (Fig. 3). A similar tendency was observed in our previous works on conventional ECAP [27, 28].

Table 1 also shows that the fatigue strength of nanostructured commercially pure titanium at 10^7 cycles is almost two times higher than that of conventional commercially pure titanium and exceeds that of the Ti-6Al-4V alloy [3, 29] The ratio σ_{-1}/σ_{UTC} = 0.47 is close to the corresponding value for CG Ti. Increasing of the fatigue strength of commercially pure titanium depends on tensile strength that is a feature of titanium as opposed to FCC wavy slip materials showing degradation in strain-controlled cyclic properties [28]. This may be related, to some extent, to the difficulty of dislocation cross slip in the H commercially pure lattice, i.e. the fatigue life of titanium depends on various parameters of UFG structure such as the size and shape of grains and the type of boundaries. Twinning does not play a key role in the cyclic deformation of UFG titanium, and fatigue mechanisms are likely to be related to grain boundaries. The results of microstructural studies and mechanical characteristics of Ti Grade 4 after severe plastic deformation show that the ECAP-Conform technique and drawing lead to formation of a homogeneous UFG structure with equiaxed grains both in the transverse and longitudinal sections of the rods that mostly have high-angle boundaries. The rods along the entire length have a uniform distribution of tensile properties, as confirmed by the relevant tests of samples taken from the rods of different batches. The evaluation of the uniformity was performed by the coefficient of variation in accordance with ASTM E8-95à.

As follows from the results in Table 1, the combined deformation processing of Ti using ECAP-Conform with drawing allowed us to obtain a good combination of high strength and ductility which demonstrates the effectiveness of this approach. The developed approach of combined thermomechanical treatment (ECAP-Conform + drawing) is already being used by the “NanoMeT” company. “NanoMeT” serves as the basis for the pilot production of nano-Ti rods with an increased strength, certified in accordance with ISO 9001:2008. The company’s products meet the requirements of the GOST 26877-91 standard for the manufacture of medical implants.

The development of the severe plastic deformation technology to produce nanostructured titanium with enhanced mechanical properties has made it possible to fabricate dental implants with lower diameters. According to the results of computational analysis [30, 31], these thin implants with a diameter of 2.4 mm can withstand loads similar to those carried by implants of the conventional design with a diameter of 3.5 mm made from coarse-grained Ti.

3.2. Nano-Ti plates for maxillofacial surgery

To produce implants from nanostructured Ti, a plate for maxillofacial surgery designed by the "Conmet" company (Moscow, Russia) (see Fig. 2) was used [18].

In accordance with formula (5), knowing the fatigue endurance limit values of the conventional and nano-Ti (Table 2), one can calculate the coefficient K_r, and the axial resistance moment W. This enables determining the minimal cross section area of the nano-Ti plates allowing the retention of the item's fatigue strength. The results of cross section area calculation of the nano-Ti plate are listed in Table 2 [32]. Only the plate thickness is changed, while the width and diameter are kept unchanged (as in the standard item).

It can be seen that the reduction of the plate thickness from 0.9 to 0.7 mm fulfills the conditions of ratios (4) and (5). Using the fatigue endurance limit values σ_f for Ti Grade 4 and taking into account the axial resistance moment W values of the plate with the standard and reduced sizes, the maximum bending moment Mb_{max} (bending strength) is determined in accordance with ratio (2), which equals to 140 MPa for CG Ti and 145 MPa for nano-Ti. This testifies to the fact that the reduced cross section area should not lead to strength reduction of the plate during bending. The experimental values of the fatigue life of plates after bending tests are presented in Fig. 3.

The standard plates withstood 17000± 500 cycles to failure, whereas the nano-Ti plate with the reduced cross section withstood considerably more cycles—105000± 800. This result suggests the enhanced bending strength of the nano-Ti plate despite its reduced thickness, which is an important advantage over the standard item made from conventional Ti.

3.3. Nano-Ti dental implants

The reduced radius of an implant makes its implantation a less invasive and less traumatic procedure. Implants with a reduced radius can be installed in patients with a thin alveolar bone, for whom the use of conventional CG Ti implant is impossible or requires additional intervention followed by bone augmentation.

The implants from nano-Ti exhibited better biological properties compared to the coarse-grained Ti [33]. Increased cell survival and enhanced cell adhesion on the surface of nanostructured titanium were reported in [13, 34]. Previously, it was found that the colonization of fibroblasts on the surface of titanium Grade 4 increases significantly after nanostructuring and chemical etching [13]. Seeing patients in a clinical setting has shown that increasing the biological properties of nano-titanium contributes to the rapid engraftment of the implant and most of nano-Ti implants could be loaded immediately after inserting [22].The number of the inserted nano-Ti implants with a diameter of 2.4 mm which were inserted immediately (t <48 hours) is equal to 96% of these nano-Ti implants (471 implants). Using nano-Ti implants with a small diameter allows for insertion of several implants (5 or more) in a short time. The cases of complications that require removal of the implant are very rare after implantation: only 11 cases (2.2% of the total implant number) were reported. These values are considerably smaller than those commonly reported in dental practice [1, 35]. Complications were caused by tissue inflammation around the implant, which can result in progressive destruction of the bone tissue surrounding the implant [36]. Different patients can have different predispositions for tissue reaction, and complications still happen in dental implantology. Creating a bioactive coating on the implant surface can increase biocompatibility and enhance the recovery of bone tissue around the implant. The creation and investigation of bioinert and bioactive coatings on nano-titanium implants is currently underway.

So far, more than 7000 dental implants made from nanostructured Grade 4 titanium with diameters of 2.4 and 3.5 mm, as well as several implants with a new diameter of 2.0 mm, were inserted in several clinics of the Czech Republic. Until now, not a single case of mechanical failure of this nano-Ti implant is known. Therefore, it can be stated that the implant with a diameter of 2.4 mm made of nano-Ti with UTS of 1255 MPa is sufficiently safe for use as a dental implant. The calculations and experimental results show that by using the already available nanostructured titanium with UTS of 1330 MPa, it is possible to safely reduce the implant diameter to 2.0 mm (Fig. 4). This makes it possible to use nano-Ti implants even in the case of a very narrow alveolar bone—less than 4.5 mm.

More detailed results of the clinical studies are presented in [35, 37, 38]. These examples illustrate the use of implants with a reduced diameter in dental practice.

Table 2. Sizes of a base plate from CG and NS Ti Grade 4 [32]

Plate	Fatigue strength limit σ_f, MPa	Strength ratio, K_r	Geometrical sizes of a plate				Axial resistance moment, W
		$K_r = \sigma_{f(CG)}/\sigma_{f(NS)}$	Length L, mm	Area in the central part A, mm^2	Thickness h, mm	Width b, mm	$W = bh^2/6$, mm^3
Ti plate	340	0.6	46.4	2.7	0.9	3	0.40
nano-Ti plate	620		46.4	2.1	0.7	3	0.25

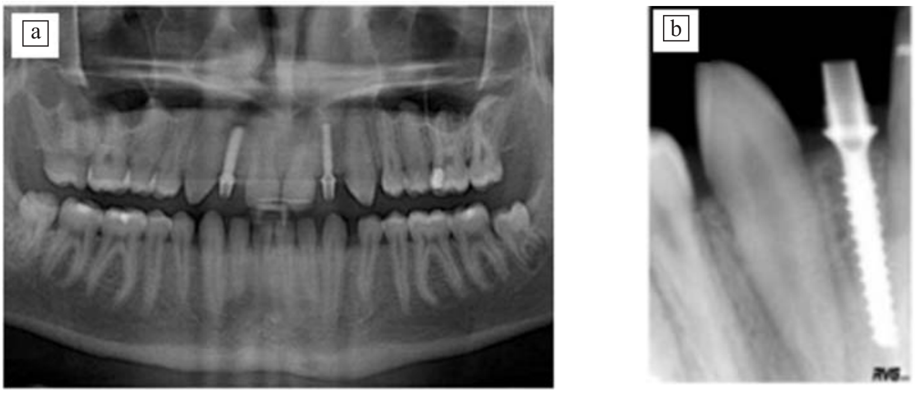

Fig. 4. 2.0 mm diameter Nanoimplant® (www.timplant.cz/en/) from nanostructured Ti Grade 4 on X-ray photos after surgery (a), the right one, and the control photo after incorporation of the implant (b).

4. Conclusions

It follows from the presented results that nanostructured Grade 4 titanium is a very promising material for medical applications. Nanostructured Ti is a metal of high purity that does not contain any other elements that could be potentially harmful to the body. At the same time, nano-Ti possesses high static and fatigue strength coupled with high ductility and exhibits good machinability. The future research on nanostructured Ti should be focused on achieving even higher ultimate and yield strengths accompanied by reduction of the modulus of elasticity, to bring it closer to the modulus of elasticity of the jaw-bone [30].

The results testify that ECAP-C combined with drawing provides new possibilities for the development of long-length nanostructured Ti rods with enhanced strength for medical applications. The excellent clinical performance of nano-Ti dental implants with smaller diameters of 2.4 and 2.0 mm and improved design opens new horizons for dental implantology and gives hope to patients who are currently not candidates for conventional-size dental implants.

Nanostructuring of commercially pure Ti by severe plastic deformation processing produces a material with mechanical properties superior to those of the Ti-6Al-4V alloy. Such nano-Ti is a promising material for creating miniature implant designs, e.g., plates for maxillofacial surgery that can withstand the same loads as the standard items.

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