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Nanostructured Titanium for Biomedical Applications

By *Ruslan Z. Valiev,* Irina P. Semenova, Vladimir V. Latysh, Henry Rack, Terry C. Lowe, Jiri Petruzelka, Ludek Dluhos, Daniel Hrusak* and *Jarmila Sochova*

Metallic materials, for example, stainless steel, titanium and its alloys, and tantalum, are widely used for medical implants in trauma surgery, orthopedic and oral medicine.[1–3] Successful incorporation of these materials for design, fabrication and application of medical devices require that they meet several critical criteria. Paramount is their biocompatibility as expressed by their relative reactivity with human tissues. Another is their ability to provide sufficient mechanical strength, especially under cyclic loading conditions to ensure the durability of the medical devices made therefrom. Finally the material should be machinable and formable thereby enabling device fabrication at an affordable cost. In this paper we show that nanostructured commercial purity titanium produced by severe plastic deformation (SPD) opens new avenues and concepts for medical implants, providing benefits in all areas of medical device technology.

Numerous clinical studies of medical devices fabricated from commercial purity (CP) titanium for trauma, orthopaedic and oral medicine has proven its excellent biocompatibility.[3] However the mechanical strength of CP titanium is relatively low compared to other metals used in biomedical devices. Whereas the strength of this material can be increased by either alloying or secondary processing, for example rolling, drawing, *etc.*, these enhancements normally come with some degradation in biometric response and fatigue behaviour. Recently it has been shown that nanostructuring of CP titanium by SPD processing can provide a new and promising alternative method for improving the mechanical properties of this material.[4–8] This approach also has the benefit of enhancing the biological response of the CP titanium surface.[9]

This paper reports the results of the first developments and studies of nanostructured titanium (n-Ti), produced as long-sized rods with superior mechanical and biomedical properties and demonstrates its applicability for dental implants. The effort was conducted using commercially pure Grade 4 titanium [C – 0.052 %, O_2 – 0.34 %, Fe – 0.3 %, N – 0.015 %, Ti-bal. (wt. pct.)]. Nanostructuring involved SPD processing by equal-channel angular pressing[10] followed by thermo-mechanical treatment (TMT) using forging and drawing to produce 7 mm diameter bars with a 3 m length. 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 combined SPD and TMT processing, as shown in Figure 1. The selected area electron diffraction pattern, Figure 1(c), further suggests that the ultra fine grains contained predominantly high-angle non-equilibrium grain boundaries with increased grain-to-grain internal stresses.[11]

A similar structure for CP Ti can be produced in small discs using other SPD methods, for example – high pressure torsion (HPT) as studied in detail.[8] In the present work it was essential to produce homogeneous ultrafine-grained structure throughout a three-meter length rod to enable the pilot production of implants and provide sufficient material for thorough testing of the mechanical and bio-medical properties of the nanostructured titanium.

Table 1 illustrates mechanical property benefits attainable by nanostructuring of CP titanium, for example, the strength of the nanostructured titanium is nearly twice that of conventional CP titanium. Notably this improvement has been achieved without the drastic ductility reductions (to below

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[*] *Prof. R. Z. Valiev, Dr. I. P. Semenova*
Institute of Physics of Advanced Materials
Ufa State Aviation Technical University
12 K. Marx str., Ufa 450000 Russia
E-mail: RZValiev@mail.rb.ru

Dr. V. V. Latysh
Innovation Scientific and Technical Center «Iskra»
81 Pushkin str.
Ufa 450077 Russia

Prof. H. Rack
School of Materials Science and Engineering
Clemson University
Clemson, SC 29634 USA

Dr. T. C. Lowe
Los Alamos National Laboratory
Los Alamos
NM 87545 USA

Prof. J. Petruzelka
FS, VŠB – Technická univerzita Ostrava
tr. 17 listopadu 15
Ostrava-Poruba, CZ 708 33
E-mail: jiri.petruzelka@vsb.cz

J. Sochova, Dr. L. Dluhos
Timplant®, Sjednocení 77
Ostrava – Polanka, CZ 725 25

Dr. D. Hrusak
FN Plzen
Alej Svobody 80
Plzen CZ 323 00 – Czech Republic

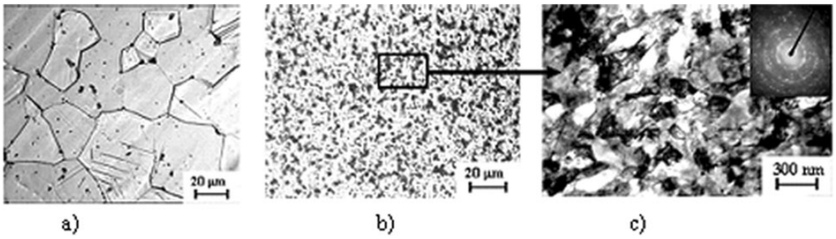

Fig. 1. Microstructure of Grade 4 CP Ti: a) the initial coarse grained rod; b, c) after ECAP + TMT (Optical and electron photomicrographs).

Table 1. Mechanical properties of conventionally processed and nanostructured CP Grade 4 titanium.

State	Processing/treatment conditions	UTS, MPa	YS, MPa	Elongation, %	Reduction Area, %	Fatigue strength at 10^6 cycles
1	Conventional Ti As received	700	530	25	52	340
2	nTi ECAP + TMT	1240	1200	12	42	620
3	annealed Ti-6Al-4V ELI	940	840	16	45	530

10 % elongation to failure) normally seen after rolling or drawing.

Further room temperature, laboratory air fatigue studies of nanostructured and conventional CP titanium were performed per ASTM E 466-96 at a load ratio R ($\sigma_{\min}/\sigma_{\max}$) = 0.1 and loading frequency of 20 Hz. Table 1 also shows that the fatigue strength of nanostructured CP titanium at 10^6 cycles is almost two times higher than conventional CP titanium and exceeds that of the Ti-6Al-4V alloy.[1,2]

Cytocompatibility tests utilizing fibroblast mice cells L929 were undertaken to verify the previously reported benefits of nanostructured CP titanium *vis à vis* conventional coarse grained CP Ti. This study was performed as described elsewhere,[12] with hydrofluoric acid surface etching being performed prior to cell exposure. Figure 2 shows the etched conventional and nanostructured titanium surfaces, respectively. The differences in surface roughness of these materials are easily seen, a homogeneous and nanometer-sized roughness being apparent for nanostructured titanium compared with the much coarser structure for etched CP Grade 4 titanium.

The cell attachment investigation shows that fibroblast colonization of the CP Grade 4 titanium surface dramatically increases after nanostructuring, Figure 3. For example, the surface cell occupation for conventional CP Ti was 53.0 % after 72 hrs in contrast to 87.2 % for nanostructured CP Grade 4 (Tab. 2). The latter observations also confirm the previous studies,[9,13,14] showing that cell-adhesion on nanostructured titanium is greater than on conventional CP Grade 4 titanium. This result suggests that a high osteointegration rate should be expected with nanostructured CP Grade 4 titanium when compared to conventional titanium.

One objective of this effort was to design, fabricate and implant a nanostructured CP Grade 4 titanium dental post to clinically demonstrate the benefits associated with nanostructuring outlined previously. Toward this end, a reduced diameter implant post Nanoimplant® was designed and fabricated. This implant sustains the same load as a conventional 3.5 mm-diameter titanium implant, the former having the added capability of being used as a pillar in cases of insufficient thickness of the alveolar bone.

The certified system of Timplant® manufactured to standard EN ISO 13485:2003 was used during development of the Nanoimplant® implant. The implants are shown in Figure 4, the nanoimplant intraosseal diameter 2.4 mm, having a strength equivalent to the conventional of 3.5 mm diameter implant.

To date over 250 Nanoimplants® have been implanted, most of them as immediate load implants, with all results indicating the excellent primary stability of Nanoimplants® when compared to other implant types [http://www.timplant.cz/e_stomatolog.asp]. For example, a 55-year-old male with edentulous mandible and maxilla was treated by insertion of conical implants laterally and Nanoimplants® in the narrow anterior part. Primary retention of all implants was very good; on the day of surgery the patient received a complete provisional bridge. Post-operation healing at the surgery site occurred without complications, with subsequent attachment of a definitive metalloceramic bridge completing the treatment.

Thus, nanostructuring of titanium by SPD processing has made material with significantly superior mechanical performance when compared to conventional CP Grade 4 titanium.

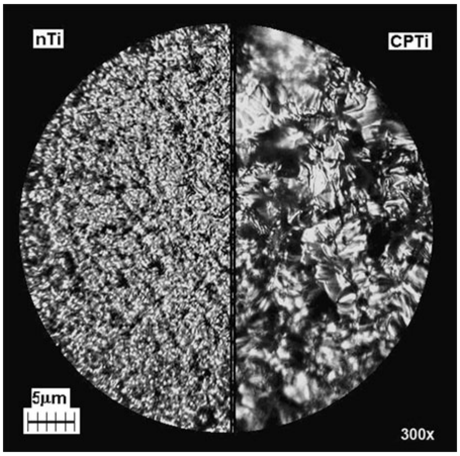

Fig. 2. Surface relief after hydrofluoric acid treatment of nanostructured (left) and CP Grade 4 titanium (right) surfaces.

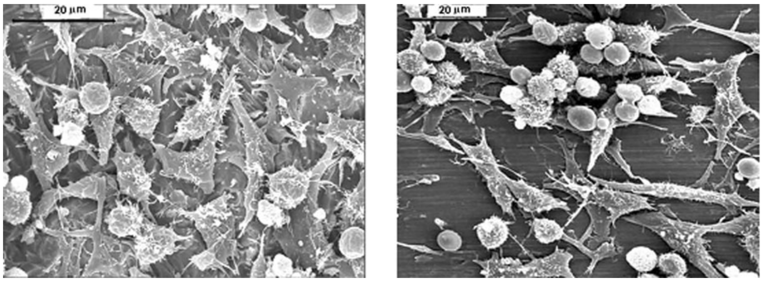

Fig. 3. Occupation of the mice fibroblast cells L929 after 24 hours; Nanostructured (left) and conventional (right) CP Grade 4 titanium.

Table 2. Surface cell occupation for conventional and nanostructured CP Grade 4 titanium.

Material	Surface treatment	Occupied surface [pct.] after 72 hours
CP Gr. 4 Ti	Machining, followed by hydrofluoric acid etching	53.0
Nanostructured Gr. 4 Ti		87.2

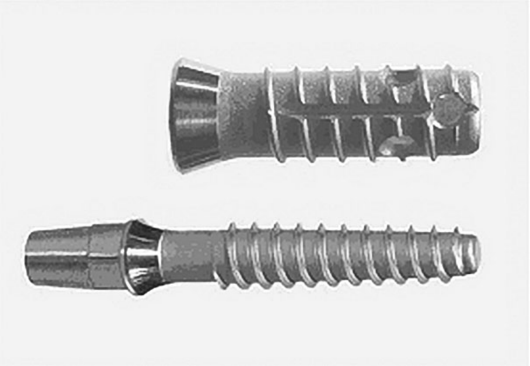

Fig. 4. 3.5 mm diameter Timplant® (above) and 2.4 mm diameter Nanoimplant® (below).

Furthermore, cytocompatibility studies with fibroblast mice cells L929 have indicated that the nanostructured Ti surface has significantly higher cell colonization, suggesting more rapid osseointegration. Nanostructured (Nanoimplants®) implants have been successfully designed and fabricated. Clinical trials with over 250 patients, most of them receiving immediate load implants, have shown no adverse effects, preliminary results being extremely encouraging. Further clinical studies are presently underway with an enlarged, 1000 patient, population.

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