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Recent Advances in Processing and Application of Nanostructured Titanium for Dental Implants**

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The paper presents the results of developments of nanostructured Ti with enhanced strength in the form of long-length rods. Using the technique of ECAP-Conform and drawing, rods with record strength properties were obtained, with UTS 1 330 MPa and endurance limit based on 10^7 cycles of 620 MPa. The developed processing route is quite effective and can be implemented at the commercial scale. It is shown that the use of nano-Ti rods allows for creation of dental implants with improved design and a smaller diameter. Such modern miniature implants with the diameter of 2.4 and 2 mm were manufactured by the "Timplant" company and the results of successful clinical trials are presented.

1. Introduction

It is well known[1,2] that from the point of view of biocorrosion resistance, Ti 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 Ti orthopedic and dental implants. Furthermore, titanium is more light-weight than other surgical metals and produces fewer artifacts on computer tomography (CT) and magnetic resonance imaging.[3,4]

The static and fatigue strengths of titanium, however, are too low for commercially pure titanium (CP Ti) implants to be used in load-bearing situations. The addition of alloying elements allows for a significant improvement of the mechanical properties of titanium, but the typical alloying elements such as aluminum and vanadium are toxic. 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]

An alternative approach to overcome the problem of harmful ion release is to abandon the alloying concept altogether and to enhance the mechanical properties of pure titanium by nanoscale grain refinement using severe plastic deformation (SPD) processing.[6,7] The feasibility of strengthening different metals by nanostructuring through SPD techniques has been demonstrated in many studies.[6–9] In addition to improved mechanical properties, a more favorable cell response to nanostructured compared to coarse grained titanium has been reported.[10–12] Up to present several SPD techniques have been used for nanostructuring CP Ti including the most popular ones, i.e., high pressure torsion[13] and equal channel angular pressing.[14]

In the previous work,[12] nanostructuring CP Ti involved SPD processing by equal-channel angular pressing (ECAP) followed by thermally deformation treatment using forging and drawing to produce long-sized rods. Our present studies showed that the new modification of the equal-channel angular pressing into the ECAP-Conform (ECAP-C)

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technique in combination with subsequent drawing is the most effective way to produce long-length rods with an ultrafine-grained (UFG) structure.[13–15] Such rods are suitable for medical applications including that for dental implants. The advanced technology of production of long-length titanium rods with an UFG structure also can result in achieving high fatigue properties. This paper reports the results of the first developments of ECAP-C to produce nanostructured titanium (n-Ti) in the form of long-sized rods with superior mechanical and biomedical properties and demonstrates its applicability for dental implants.

2. Materials and Methods

The rods of Ti Grade 4 which met the requirements of the standard ASTM F67 for medical implants were chosen as the material for this investigation. The impurity content of the material was (wtpct) C – 0.052%, O_2 – 0.34%, Fe – 0.3%, N – 0.015%, Ti-balance. The average grain size of the as-received material was ≈25 μm. ECAP-C processing is a relatively new modification of conventional ECAP technique.[14,15] In this process, the principle used to generate the frictional force to push a work-piece through an ECAP die is similar to the Conform process while a modified ECAP die design is used so that the work-piece can be repetitively processed to produce UFG structures. Figure 1 illustrates the principle of the ECAP-C technique. A rotating shaft in the center contains a groove and the work-piece is fed into this groove. The work-piece is driven forward by frictional forces on the three contact interfaces with the groove so that the work-piece rotates with the shaft. However, the work-piece is constrained within the groove by a stationary constraint die; and this die also stops the work-piece and forces it to turn at an angle by shear as in a regular ECAP process. This set-up effectively makes the ECAP process continuous. Other ECAP parameters, such as the die angle and the strain rate, can also be easily incorporated into the facility. It is characterized by higher efficiency and lower wastage of the material. The angle of channels intersection was 120° that induced equivalent strain of ≈0.7 into billet per each ECAP-C pass.[15] Billets 500 mm in length and 11 × 11 mm^2 in cross section were subjected to ECAP-C processing at 200 °C, 6 passes. The billet after ECAP-C was subjected to drawing at 200 °C resulting in the production of a rod with a diameter of 6 mm.

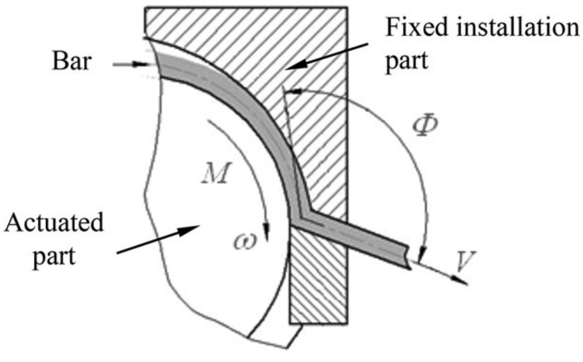

Fig. 1. The principle of ECAP-C technique.

The microstructure was analyzed by the optical and transmission electron microscopies (TEM). For optical metallography, the sample surface was polished mechanically and etched in chemical solution consisting of hydrofluoric acid – 4%, perchloric acid – 20%, and distilled water – 76%. Samples for TEM studies were cut out by the electrospark method. After mechanical thinning down to 100 mm, they were subjected to electrolytic polishing using a "Tenupol-5" set. Electropolishing was conducted using chemical solution consisting of perchloric acid – 5%, butanol – 35%, and methanol – 60%. The microstructure was investigated in a JEOL JEM 2100 TEM operating at an accelerating voltage of 200 kV.

Mechanical tensile tests were conducted at room temperature with the initial strain rate of 10^{-3} s^{-1} using an INSTRON-type testing machine. Cylindrical samples with a gauge length of 15 mm and a diameter of 3 mm were tested. Investigation of the Ti Grade 4 tensile properties carried out in accordance to STM E8-13a. Ambient temperature stress controlled fatigue tests of nanostructured and conventional CP titanium were performed at a load ratio $R(\sigma_{min}/\sigma_{max}) = -1$ and rotational bending loading scheme with a frequency of 50 Hz. The fatigue tests were performed according to ASTM-E466.

The rods of high-strength nanostructured Ti (Grade 4) produced by ECAP-C processing followed by drawing were subjected to grinding for the required surface quality and tolerance. Screw implants with the thread Nanoimplant and a diameter of 2.4 mm and a length of the intraosseal part 8, 10, 12, and 14 mm were manufactured from new Ti in Timplants.r.o. in Ostrava, Czech Republic (http://www.timplant.cz/cs/). The implant has a polished gingival part with a cone top above it.[16] The developed implant is made from pure Ti and, therefore, it does not contain any toxic alloying elements (like V) and elements classified as allergens (like Ni, Co, or Cr). The nanoimplant observation was evaluated on the base of supplied information of five dental surgeons from the state and private dental clinics, where the nanoimplants were inserted during the two-year period. Statistical method was used to evaluate the supplied data.[17]

3. Results and Discussion

Nanostructuring involved SPD processing by equal-channel angular pressing via the Conform scheme followed by drawing to produce 6 mm diameter bars with a 3 m length using the new facilities of spin-off company "NanoMeT" (http://www.nano-titanium.com).

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 ECAP-Conform and drawing processing, as shown in Figure 2. The selected area electron diffraction pattern, Figure 2c, further suggests that the

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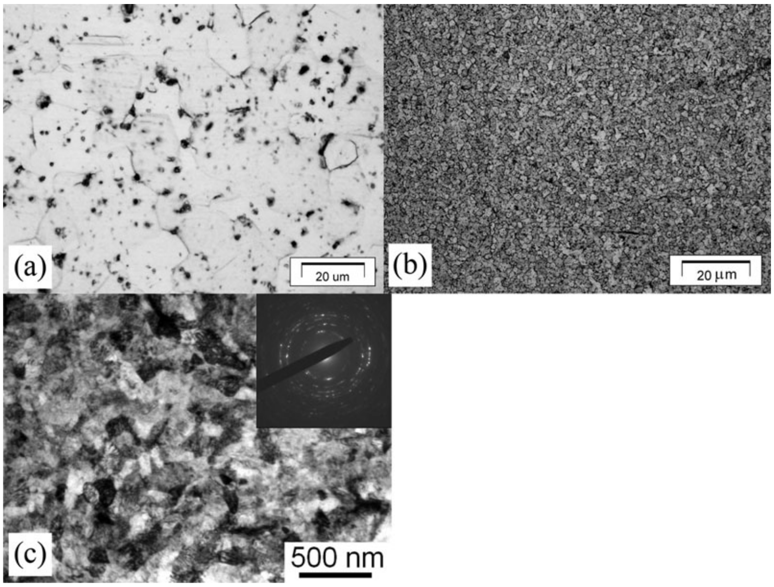

Fig. 2. Microstructure of Grade 4 CP Ti: (a) the initial coarse grained rod; (b) and (c) cross-section rod after ECAP-C + drawing (optical (a and b) and TEM (c) pictures).

ultrafine grains contained predominantly high-angle grain boundaries.

A similar structure for CP Ti can be produced in small discs using other SPD techniques, for example, high pressure torsion (HPT) as studied in detail.[18] 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. It is important to note that the homogeneous UFG structure was also typical for 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 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 10% elongation to failure) normally seen after usual rolling or drawing.

The high value of ultimate tensile strength (UTS) in Ti after ECAP + Dr almost twice exceeds that in the initial state and is even higher with increasing the degree of straining from 75 to 85% during drawing. As is known, for conventional techniques of deformation processing such as rolling, extrusion, or drawing, with increasing the accumulated strain and microstructural refinement a visible strength growth can be observed but also considerable reduction in the ductility takes place. 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 high volume of low-angle grain boundaries.

At the same time, the use of SPD techniques allows for the formation of UFG structure featuring homogeneity, large volume of high-angle grain boundaries and lack of pronounced texture. Such ultrafine-grained structure may provide the combination of high strength through the Hall-Petchrelation[19,20] and sufficient ductility[18,21,22] because the origin of grain boundaries in the UFG materials plays an important role in determining the level of mechanical properties. In the studies on UFG Ti[18,23] 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. 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.[7,21]

The results of the present study demonstrate that the formation of ultrafine-grained structure during SPD in Ti leads also to considerable increase of fatigue endurance as compared with the initial state. The corresponding fatigue endurance limit is 590 MPa after ECAP-C and subsequent drawing to 75% in comparison to 380 MPa in the as received condition (Figure 3). Similar tendency was observed in our previous works on conventional ECAP.[24,25]

Table 1 also shows that the fatigue strength of nanostructured CP titanium at 10^7 cycles is almost two times higher than conventional CP titanium and exceeds that of the Ti-6Al-4V alloy.[5,26] The ratio $\sigma_{-1}/\sigma_{UTS} = 0.47$ is close to the same value for CG Ti. Increasing of the fatigue strength of CP titanium depends on tensile strength, that is a feature of titanium as opposed to fcc wavy slip materials.[25] This to some extent may be related with the difficulty of dislocation cross slip in the hcp

Table 1. Mechanical properties of conventionally processed and nanostructured CP Grade 4 Ti produced by ECAP-C and drawing (ECAP-C + Dr).

Processing/treatment conditions	UTS [MPa]	YS [MPa]	Elongation [%]	Reduction area [%]	Fatigue strength at 10^7 cycles
Conventional Ti as received	700	530	25	52	340
n-Ti ECAP-C + Dr(75%)	1 255	1 200	12	45	590
n-Ti ECAP-C + Dr(85%)	1 330	1 267	11	48	620
Annealed Ti-6Al-4V ELI	940	840	16	45	530

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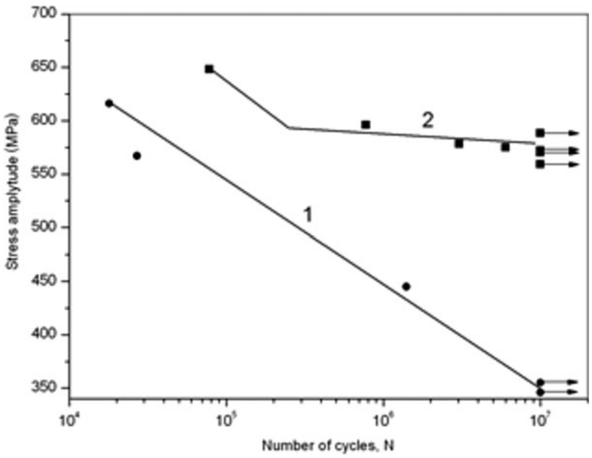

Fig. 3. Fatigue properties of Ti Grade 4 1 in the as-received condition, 2 after ECAP-C with drawing to 75%.

lattice, i.e., fatigue life of Ti depends on various parameters of UFG structure such as size and shape of the grains and type of the boundaries. Twinning does not play a key role in the cyclic deformation of UFG titanium, and fatigue mechanisms are likely related to the grain boundaries. The results of microstructural studies and mechanical characteristics of Ti Grade 4 after SPD show that the ECAP-Conform technique and drawing lead to the formation of homogeneous UFG structure with near-equiaxed grains both in the transverse and longitudinal sections of the bars that mostly has high-angle boundaries. Bars along the entire length have a uniform distribution of tensile properties, as confirmed by the relevant tests of samples taken from the bars of different batches. Evaluation of the uniformity was performed by the coefficient of variation in accordance with ASTM E8-95a.

As it follows from the results in Table 1, the combined deformation processing of Ti using ECAP-Conform with drawing allows obtaining a good combination of high strength and ductility what demonstrates the effectiveness of this approach. The developed approach of the combined thermo-mechanical treatment is already applied by "NanoMeT" (http://www.nano-titanium.com), which serves as the basis for the pilot production of nano-Ti rods with increased strength certified in accordance with ISO 9001:2008. The company's products meet the requirements of GOST 26877-91 for the manufacture of medical implants.

3.1. Dental Implants

The development of SPD technology to produce the nanostructured Ti with enhanced mechanical properties made it possible to fabricate dental implants with lower diameters. The results computational analysis,[27,28] demonstrate that these low-radius implants with a diameter of 2.4 mm can withstand loads similar to those carried by the implants of conventional design with a diameter of 3.5 mm made from coarse-grained Ti.

Another positive side of the low-radius implant is that it allows for minimization of medical intrusion, thus, making the implantation procedure less traumatic. Reducing the implant radius leads to less injuries of bone tissue.[29] Implants of lower radius can be inserted to the patients with thin alveolar bone, i.e., the cases when the use of conventional implants with coarse-grained structure is impossible or requires additional surgery followed by bone augmentation.

The implants from n-Ti showed also better biological properties in comparison with the coarse grained Ti.[17] Increased cell survival rate and enhanced cell adhesion on the surface of nanostructured Ti was also reported in ref.[12,30]. As was earlier established in ref.,[12] the colonization of fibroblasts on the surface on Ti Grade 4 increases significantly after nanostructuring. Clinical observation of the patients demonstrated that enhanced biological properties of nano-Ti contributes to the rapid implant survival and about 70% of nano-Ti implants could be loaded immediately after inserting. The most frequent prosthetics are the bridges over 2–4 implants. For hybrid overdentures it is of advantage to use metallic bars (dolber bar) for better retention and support of prosthetic appliance.[31] Results of inserted nanoimplants are presented in Table 2.

The number of inserted n-Ti implants with a diameter of 2.4 mm constituted 491, of which 96% (471 implants) were inserted immediately ($t < 48$ h). Low-radius implants made of n-Ti make it possible to insert a group of implants up to 5 or more units (Table 2) in a short period of time. The cases of complications requiring the implant removal are very rare – 11 cases were reported, which is 2.2% of the total number of the inserted implants. These figures are considerably lower than those common for dental practice.[1,29] Complications were caused by the processes of tissue inflammation around the implant, which can result in the progressive destruction of the bone tissue surrounding the implant.[31] Due to different

Table 2. Evaluation results of 491 inserted nanoimplants dia 2.4 mm with 97.8% fruitfulness.

Total patient	250	NANO Implants evaluation Results	
Total NANO implants	491		
Loading timing	Total immediate loaded ($t < 48$ h):	Total early loaded ($t < 7$ days):	Total lost
SUM	473	7	11
Crowns and bridges:			
Single implant post	35	5	1
Implant groups (2–4 implants)	292	2	7
Implant groups (>5 implants)	136	0	3
Over dentures	10	0	0

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reaction of living tissues, such cases do still happen in modern dentistry and may be reduced by creating bioactive coatings on the surface of implants that enhance the recovery of bone tissue around the implants and increase their biocompatibility. Our work on this issue is still in progress with the aim to create the bioinert and bioactive coatings for titanium implants.

So far, more than 7 000 of dental implants made from nanostructured titanium with a diameter 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 Czech Republic. Until now not a single case of rupture or breakage of this n-Ti implant is known. Therefore, it can be stated that the implant with a diameter of 2.4 mm made of n-Ti with UTS of 1 255 MPa is sufficiently safe for use as a dental implant. The calculations and experimental results show that the use of already available nanostructured titanium with UTS of 1 330 MPa may securely reduce the diameter of the implant down to 2.0 mm (Figure 4).

Below are the results of clinical studies[29,32,33] illustrating the examples of use of low-diameter implants in dentistry.

3.2. Indication of Nanoimplants

If the alveoli has a width of 6 mm or more, it is possible to use n-Ti implant with a diameter of 3.5 mm. Nano-Ti implants with a 2.4 mm diameter are most frequently used in the cases of lack of transversal dimension of processus alveolaris, i.e., in the cases of a narrow alveoli (4.5–6 mm). In the cases of a very narrow alveoli (below 4.5 mm) there is an option of splitting the alveoli and introducing n-Ti implant with possible augmentation.[32,33] In certain circumstances this surgical intervention may be replaced by using a 2.0 mm diameter n-Ti implant.

Another indication group represents situations of insufficient mesiodistal interdental and interradicular dimension. A typical example is anodontia of upper teeth number two. This situation occurs quite often and requires an orthodontist. However, orthodontic treatment does not always ensure the formation of a required gap of at least 7 mm wide, which is necessary when using the classical implant of a 3.5 mm diameter. This is when a 2.4 mm diameter n-Ti implant can be applied, for which a gap of 4.5–5 mm is quite sufficient.

In cases of a narrow alveoli the following surgical procedures may be considered for pre-implantologic evaluation:[29,32]

i) guided bone regeneration;
ii) bone splitting – splitting of alveolus;
iii) onley's augmentation by use of cortico-spongious graft;
iv) osseo-distraction.

Onley's augmentation of larger scale or osseo-distraction are the treatments of high demand that are realized on the wards of maxillofacial surgery under general anaesthesia. In the case of extensive onley's augmentation it is necessary to remove the graft from the iliaca bucket—from spinailliaca anterior superior or from a skull—osparietale. These operations are not always acceptable to the patient as treatment options.

In the simplest case, it is possible to offer thin n-Ti implants as full-fledged and fully loadable pillars due to their strength and excellent anchor surface. Indications for n-Ti implants in the lower jaw are the same as those for classical wider implants, such as solo pillar, shortened dental arch, interstitial pillar, total defect including the immediate loading.

The same also applies for the upper jaw in the case of a good bone density D2 and good vertical dimension. It follows that maxilla are less suitable in the side sections. The length of the fixture is very important. Following certain studies on the subject, for example, the work of French authors Saadoun-Le Gall, thin implants fixtures shorter than 10 mm are not recommended for use. The variety of length for n-Ti implants is 8, 10, 12, and 14 mm.[16]

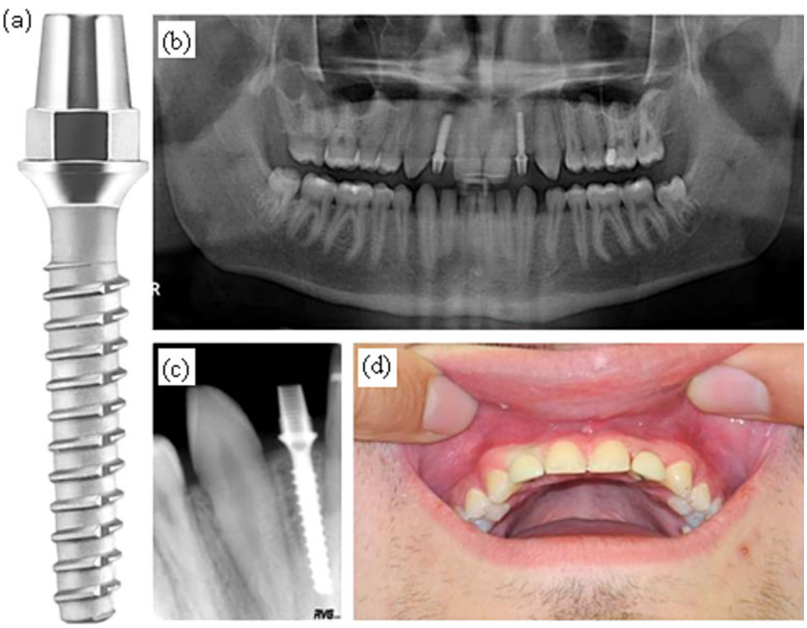

Fig. 4. Implant dia 2.0 mm from nanostructured Ti (a) and X-ray photos after surgery (b) and control photo after incorporation of implants (c), implants with final metalceramics crowns (d).[25]

3.3. New Nanoimplant of 2.0 mm Diameter

Further, another implant prototype with a diameter of 2.0 mm was developed in the framework of VINAT project.[27,28] The implant was manufactured from newly processed dn-Ti with an increased strength (UTS 1 330 MPa, Table 1). For the first time the implant of a reduced diameter was produced from commercially pure Ti and not Ti alloy.

The prototype of an implant with a diameter of 2.0 mm was surgically inserted to a patient (male, age 18) with the history of a long orthodontic treatment subject to his consent.[32] The patient lacked the basis of his own natural teeth in the areas 12 and 22. After examination it was decided that in the area 22 (the second tooth

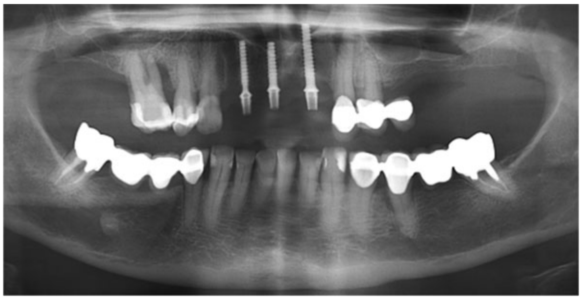

Fig. 5. Ortopantomogram of implanted nanoimplants, left dia 2.0 mm, right two implants of dia 2.4 mm.

on top left) did not have a suitable bone and that he would not have a 2.4 mm dia implant inserted into this locality due to lack of transverse dimensions of the bone.

The radiograph analysis determined that the 2.0 implant would be suitable for the treatment of the aforementioned patient and that the bone was sufficiently wide for this diameter 2.0 mm. As a result, a low radius implant (2.0 mm) was inserted (between teeth 11 and 13). Another implant of 2.4 mm diameter was inserted to the right side position 22–left side of the X-ray (Figure 4b). The patient left the dental office with two nanoimplants and two provisional crowns made on the day of implantation (Figure 4b and c). After 6 weeks, final metalceramic crowns were fixed over the implants (Figure 4d).

Another case of inserted implant dia 2.0 mm in combination with two nanoimplants of dia 2, 4 is shown on Figure 5. Figure 6 demonstrates the third case and step-by-step procedure of implantation performed to a woman (age 42) after orthodontic treatment, with narrow bone and little space between teeth. The teeth braces can be seen in the picture.

4. Summary and Conclusions

The results of this work testify to the fact that the new SPD processing by ECAP-C and drawing opens new possibilities in the development of nanostructured Ti with enhanced strength in the form of long-length rods for medical application and first of all provides new horizons for dentistry. It has been evidenced from producing and clinical study of dental implants of improved construction with lower diameters of 2.4 and 2.0 mm that were successfully tested on the patients.

During the period of monitoring another batch of 2.0 mm diameter implants was applied and regularly checked by the dentist—with the same principally convergent results.

Thus, the 2.0 mm diameter implant provides the patient with an opportunity of a relatively simple method of implantation. Otherwise, these patients would have to pass a different, more difficult and risky surgery, such as alveolar splitting or augmentation.[29,32]

After a 6-month monitoring of the thin implant in the patient's mouth it can be stated that the implant withstands normal physiological loads without any problems and the process of osseo-integration runs in the manner that is usual for the implants Nanoimplant with diameter of 2.4 mm.

It follows from the presented results that nanostructured titanium (n-Ti) is a promising material for medical applications and that in future it will have its parameters continuously improved and adapted to the requirements of individual applications. In support of this statement it should be noted that n-Ti is metal of high purity and good machinability, which does not contain any other elements that could be even potentially harmful to the body.

It is worth focusing the future research of n-Ti on achieving even higher ultimate strength and yield strength in dependence on reduction of the modulus of elasticity, which could approach the modulus of elasticity of jaw-bone.[27] Recent studies show[31] that nanostructured β-Ti alloys processed by SPD quite satisfy these requirements and the use of such alloys in dental implants with improved design and functionality is rather promising.

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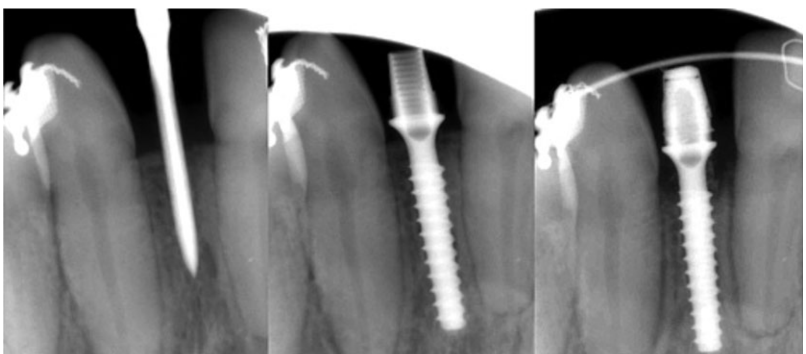

Fig. 6. Digital radiovisiography—state during bone preparation left, implant after insertion-middle, Implant with provisional crown-right.

[1] D. M. Brunette, P. Tengvall, M. Textor, P. Thomsen (Eds.), *Titanium in Medicine*, Springer-Verlag, Berlin **2001**, 1019.
[2] N. Soumya, B. Banerjee, in *ASM Handbook*, Vol. 23 (Ed: R. Narayan), ASM International, Materials Park, OH 2012, pp. 6–17.
[3] M. Niinomi, *Mater. Trans.* **2008**, *49*, 2170.
[4] M. Geetha, A. K. Singh, R. Asokamani, A. K. Gogia, *Prog. Mater. Sci.* **2009**, *54*, 397.
[5] M. Niinomi, *Metall. Mater. Trans. A* **2001**, *32*, 477.
[6] R. Z. Valiev, R. K. Islamgaliev, I. V. Alexandrov, *Prog. Mater. Sci.* **2000**, *45*, 1.
[7] R. Z. Valiev, *Nat. Mater.* **2004**, *3*, 511.
[8] M. J. Zehetbauer, Y. T. Zhu (Eds.), *Bulk Nanostructured Materials*, Wiley-VCH Verlag GmbH & Co. KGaA Weinheim **2009**, p. 850.

DOI: 10.1002/adem.201500212

[9] Y. Estrin, A. Vinogradov, *Acta Mater.* **2013**, *61*, 782.
[10] Y. Estrin, E. P. Ivanova, A. Michalska, V. K. Truong, R. Lapovok, R. Boyd, *Acta Biomater.* **2011**, *7*, 900.
[11] T. N. Kim, A. Balakrishnan, B. C. Lee, W. S. Kim, B. Dvorankova, K. Smetana, J. K. Park, B. B. Panigrahi, *J. Mater. Sci. Mater. Med.* **2008**, *19*, 553.
[12] R. Z. Valiev, I. P. Semenova, V. V. Latysh, H. Rack, T. C. Lowe, J. Petruzelka, L. Dluhos, D. Hrusak, J. Sochova, *Adv. Eng. Mater.* **2008**, *10*, B15.
[13] G. I. Raab, R. Z. Valiev, T. C. Lowe, Y. T. Zhu, *Mater. Sci. Eng. A* **2004**, *382*, 30.
[14] R. Z. Valiev, T. G. Langdon, *Prog. Mater. Sci.* **2006**, *51*, 881.
[15] D. V. Gunderov, A. V. Polyakov, I. P. Semenova, G. I. Raab, A. A. Churakova, E. I. Gimaltdinova, I. Sabirov, J. Segurado, V. D. Sitdikov, I. V. Alexandrov, N. A. Enikeev, R. Z. Valiev, *Mater. Sci. Eng. A* **2013**, *562*, 128.
[16] C. Arnold, D. Hrušák, L. Dluhoš, *StomaTeam CZ* **2007**, *1*, 26.
[17] D. Hrušák, L. Dluhoš, in *XIXth Congress of the European Association for Cranio-Maxio-Facial Surgery*, Bologna, Italy, Sept. 9th-12th **2008**. *Abstrakt Journal of Cranio-Maxillofacial Surgery*, Vol. 36, Supplement 1, September 2008, s. S260. ISSN: 1010–5182.
[18] V. Sergueeva, R. Z. Valiev, A. K. Mukherjee, *Scripta Mater.* **2003**, *49*, 669.
[19] T. G. Langdon, *Acta Mater.* **2013**, *61*, 7035.
[20] Y. Estrin, A. Vinogradov, *Acta Mater.* **2013**, *61*, 782.
[21] R. Z. Valiev, I. V. Alexandrov, T. C. Lowe, Y. T. Zhu, *J. Mater. Res.* **2002**, *17*, 5.
[22] F. Dalla Torre, R. Lapovok, J. Sandlin, P. F. Thomson, C. H. J. Davies, E. V. Pereloma, *Acta Mater.* **2004**, *52*, 4819.
[23] R. Z. Valiev, A. P. Zhilyaev, T. G. Langdon, *Bulk Nanostructured Materials: Fundamentals and Applications*, John Wiley BT & Sons, Inc. Hoboken, NJ **2013** /2014, p. 456.
[24] V. V. Stolyarov, I. V. Alexandrov, Yu. R. Kolobov, M. Zhu, Y. Zhu, T. Lowe, Enhanced fatigue and tensile mechanical properties of titanium processed by severe plastic deformation. Proceedings of the Seventh Int. Fatigue Congress, Beijing, P. R. China, (Eds: X. R. Wu, Z. G. Wang), Higher Education Press, 8–12 June, **1999**, v.3, 1435–1440.
[25] A. Y. Vinogradov, V. V. Stolyarov, S. Hashimoto, R. Z. Valiev, *Mater. Sci. Eng. A* **2001**, *318*, 163.
[26] R. Boyer, G. Welsch, E. Collings (Eds.), *Materials Properties Handbook: Titanium Alloys*, ASM International, Materials Park, OH **1994**, p. 1998.
[27] L. Dluhoš, J. Petruželka, Manufacturing of functional prototype of implantable medical appliance. Final project report, Project ViNaT, Contract No.: 2953 22, Virtual nanotitanium: Theoretical analysis, design and virtual testing of biocompatibility and mechanical properties of titanium-based nanomaterials, Fp7, 1/ 2014.
[28] L. Mishnaevsky, Jr., E. Levashov, R. Z. Valiev, J. Segurado, I. Sabirov, N. Enikeev, S. Prokoshkin, A. V. Solov'yov, A. Korotitskiy, E. Gutmanas, I. Gotman, E. Rabkin, S. Psakh'e, L. Dluhoš, M. Seefeldt, A. Smolin, *Mater. Sci. Eng.* R **2014**, 81, 1.
[29] P. Lovecký, J. Strecha, L. Dluhoš, *Nanoimplantáty. Stomatológ XXI* **2011**, *3*, 30.
[30] S. Faghihi, F. Azari, A. P. Zhilyaev, J. A. Szpunar, H. Vali, M. Tabrizian, *Biomaterials* **2007**, *28*, 3887.
[31] S. Gatina, I. Semenova, M. Janecek, J. Strasky, *Mater. Sci. Eng.* **2014**, *63*, 1.
[32] V. Březina. Protokol o zkoušce číslo 31a. Zkouška kolonizace povrchu. B.P. Medical, Brno 20. 10. **2011**.
[33] V. Březina. Protokol o zkoušce. protokol č. Z13 Kolonizace. 4 str. 18. b. **2012**. Jihočeská univerzita v Českých Budějovicích, Laboratoř tkáňových struktur. Zadavatel: Timplant s.r.o.

