Reconstruction of Load-bearing Defects in Oncology by Using Nanomodification of Implants

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ABSTRACT

Different coating procedures enlarging biocompatibility factors of implants were developed.

Depending on the construction type (stable or rolling) different nanostructured thin films and coatings in the system Ti-Ca-P-C-O-N are applied using magnetron sputtering.

The effectiveness of implants considered in comparison with a control group of implants without nanostructured modification and with thin films produced by alternative methods can be proved by experimental models.

The combination of excellent mechanical properties with biocompatibility and non-toxicity makes nanostructured films promising candidates to be used for various medical applications.

Keywords: reconstructive, nanostructured, coatings, implants, biocompatibility

1 AIMS

The primary aim of this work was to increase the effectiveness of reconstructive operations performed for reconstruction of functional and anatomical defects of supporting structures.

The second aim was to increase indications for radical tumor treatment by use of biocompatible implants.

2 ACTUALITY

Radiotherapy and chemotherapy accompanying surgical treatment sharply reduce the recovery abilities of organism which leads to loss of 10 - 15 % of the plastic material during soft-tissue self-reconstruction in locomotors apparatus, limbs and jaw-face region.

Defects of supporting structures should be replaced by implants. Advanced biomaterials to be used in load-bearing applications must possess high hardness, excellent fatigue and tensile strength, superior corrosion and wear resistance, good biocompatibility and non-toxicity. While metals and alloys meet many of these requirements, the interfacial bonding between the metallic surface and the surrounding bone is poor or does not exist at all. An effective way to promote the formation of bone-like layer on the implant surface is the deposition of multifunctional bioactive coating.

3 INNOVATION

By means of nanotechnological approach different coating procedures enlarging biocompatibility factors of implants were developed.

Recently, CaO- and ZrO_2-doped Ti-based multicomponent thin films have been deposited and evaluated as perspective biomaterials to be used in load-bearing medical applications [1-3]. Hydroxyapatite ($Ca_{10}(PO_4)_3(OH)_2$) and calcium phosphate ceramics are widely used as a bioactive interface between the bulk metal implant and the surrounding tissue because of its close similarity to the chemical and mineral components of teeth and bone. The low strength, low fracture toughness, and poor impact resistance of hydroxyapatite coatings restrict their application as heavy-loaded implants. Only little data regarding investigation of the feasibility of ($Ca_{10}(PO_4)_3(OH)_2$)-doped Ti-based multicomponent coatings for medical applications is available

4 MATERIALS AND METHODS

4.1 Materials

$TiC_{0.5}$+10%($Ca_{10}(PO_4)_6(OH)_2$) composite target was synthesised using the combined force SHS-pressing technology, as described elsewhere [4]. The target was subjected to magnetron sputtering in a gaseous mixture of argon and nitrogen. The diameter of the target was 125 mm and the target to substrate distance was 100 mm. The total pressure, P, was maintained at 0.2 Pa, and the nitrogen partial pressure was kept constant at 14% of the total pressure. Ti-Ca-P-C-O-N coatings, 0.7-0.8 µm thick, were deposited on single crystal silicon (100), Ni-based alloy and Ti medical nets without substrate bias for 60 min. Prior to deposition, the surface of substrate was sputter cleaned by low energy ion etching with argon using an additional ion source operated at a fixed energy of 1.5 keV. The adhesion between the Ti-Ca-P-C-O-N coating and substrate was achieved by deposition of a thin titanium sublayer for 2 min using Ti target. During deposition of the Ti-Ca-P-C-O-N coating, the substrate temperature was kept constant at 200. The microstructure and elemental composition of coatings were investigated by means of X-ray diffraction (XRD), transmission electron microscopy (TEM) (Figure 1), X-ray photoelectron spectroscopy (XPS) and energy-dispersive X-ray spectroscopy (EDS). The coatings were also characterized in terms of their hardness H, elastic modulus E, and elastic recovery W_e using a Nano Hardness Tester (CSM Instruments, Switzerland). The tribological properties of the coatings were evaluated using a conventional ball-on-disc tribometer (CSM Instruments, Switzerland) under normal loads of 1 N with 3-mm diameter Al_2O_3 ball (H=20 GPa, E=390 GPa) as a counterpart material. Sliding speed was 10 cm/s. Adhesion strength (critical load, L_c) was measured by means of a scratch tester (CSM Instruments, Switzerland) using acoustic emission fluctuations and optical microscopy to confirm the starting point of adhesion failure.

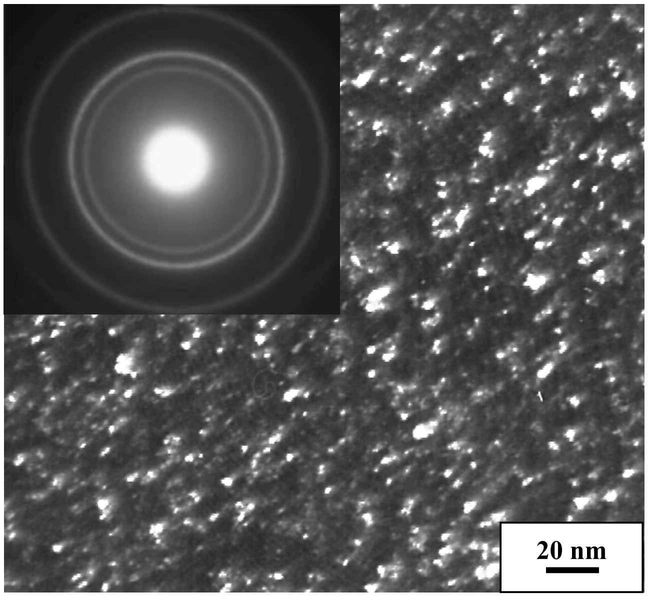

Figure 1. Dark-field TEM micrograph (plain-view) of Ti-Ca-P-C-O-N coating.

4.2 Methods

Two groups of rats each comprises four animals (average weight about 170 g) were formed. All the rats were anaesthetized with relanium (0,5 ml intraperitoneous) and ketamin (0,4 ml intramuscular). All rats underwent craniotomy resulting in a round calvarian bone defect with a diameter of 3-4 mm: the skin of the head was incised to expose the calvaria and defect was created and the bone fragments were removed.

The defects in experiment presented were critical size defects [5], which would have healed by fibrous union rather than bone formation.

Those defects were substituted by titanium implants (Figure 2).

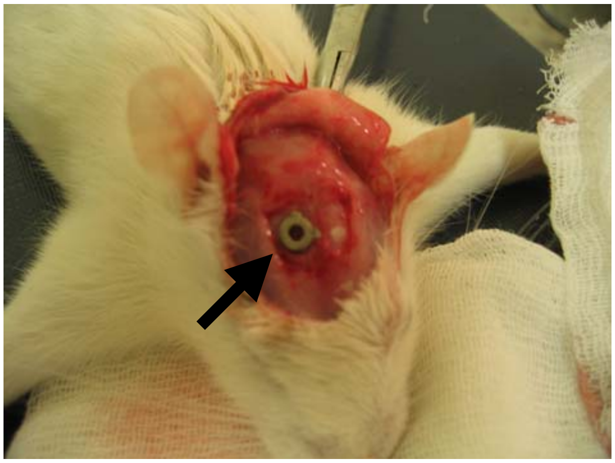

Figure 2. Step of operation: Substitution of calvarian bone defect by titanium mash implant (marked by arrow).

Three of four implants for each group of animals did have ($Ca_{10}(PO_4)_3(OH)_2$)-doped Ti-based multicomponent coatings. The fourth one was not coated for control purposes. After confirming that there was no bleeding the wound was closed with sutures. To confirm the implants stability X-ray examinations were performed 1, 15 and 30 day after implantation (Figure 3).

Figure 3. X-ray picture of implant (marked by arrow).

Animals from the first group were sacrificed after 15 days of implantation, from the second one – after 30 days.

4.3 Results

The elemental composition was determined from XPS data and is shown in Table 1. Although XPS did not show any noticeable signal from phosphorus, the presence of P was confirmed by EDS (Figure 1). The coatings showed a cubic B1 NaCl-type structure with a weak planar (111) texture. The coatings were characterised by a very small grain size that ranged from 4 to 10 nm (Figure 2). The coatings showed high hardness 27 GPa, reduced Young's modulus 240 GPa and high percentage of elastic recovery 66%. The Ti-Ca-P-C-O-N coatings also showed stable low friction coefficient of about 0.21 both in air and under physiological solution (PS) that is significantly lower than that of TiC and TiN films. The wear rate of the coatings was within the range of $(3.3\text{-}5.2)\times10^{-6}$ $mm^3N^{-1}m^{-1}$ in ambient air and $7.1\text{x}10^{-6}$ $mm^3N^{-1}m^{-1}$ under PS (100 ml H_2O + 0.9 g NaCl). No any noticeable wear of counterpart material was registered in both cases. The evolution of coating adhesion showed that although some small cracks have formed at low loads of 4.3 N, the substrate itself was only visible inside the track when the load was higher than 40 N (Figure 4). From these tests, it can be concluded that the adhesion strength is high because the coating deforms plastically without detaching from the substrate.

Elemental composition, at%					
Ti	Ca	P	C	O	N
41.7	1.8	<1	16.4	12.6	26.5

Table 1. Elemental composition of the Ti-Ca-P-C-O-N coatings.

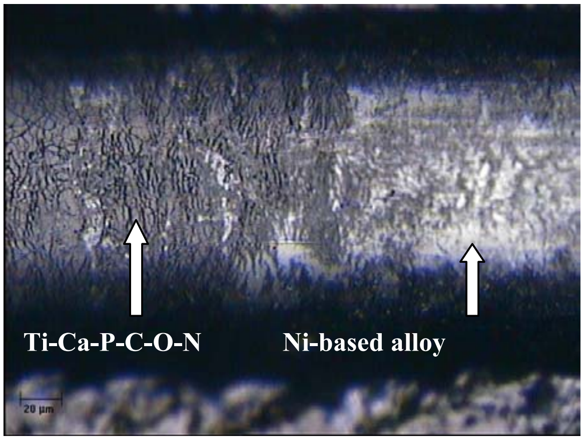

Figure 4. Typical failure of scratch test at a critical load of 40 N.

Animals from the first and the second groups were clinically observed and physically examined. After wounds healing (2-3 days after implantations) no changes in rats behavior were found.

Animals – members of the first group have lived 15 days, of the second one - 30 days. Their basic biological functions were close to normal.

X-ray investigations showed an absence of the patalogical periostal reaction around the implants.

Area of operation exploration allowed to do conclusion, that the wounds were healed by first intension; there were no inflammatory reactions around them at the moment of examination.

Calvarian bone supporting function restoration is evident on thorough palpation with firm pressure.

Histological investigations for all the rats after treatment are in progress now.

5 CONCLUSIONS

The effectiveness of implants considered in comparison with a control group of implants without nanostructured modification can be proved by experimental models.

The use of nanostructured modification of medical implants can genuinely influence and provide control over the processes of biointegration. The combination of excellent mechanical properties with biocompatibility and non-toxicity makes nanostructured films promising candidates to be used for various medical applications.

A comparison of Ti-Ca-P-C-O-N coatings with the properties of bulk materials (metals and alloys, ceramics) and thin films produced by alternative methods shows a noticeable advantage from the view point of the whole combination of physical, mechanical and tribological properties.

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