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ASPECTS OF TITANIUM-IMPLANT SURFACE MODIFICATION AT THE MICRO AND NANO LEVELS

OBLIKE MODIFIKACIJE TITANOVIH IMPLANTATOV NA MIKROMETRSKEM IN NANOMETRSKEM NIVOJU

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The shape and chemical composition, as well as the macro- and microtopography, of an implant surface have been studied widely as the major factors that positively influence implant osseointegration. Titanium and titanium alloys have been used extensively over the past 20 years as biomedical materials in orthopedic and dental surgery because of their good mechanical properties, corrosion resistance, no cell toxicity, and very poor inflammatory response in peri-implant tissue, which confirms their high biocompatibility. Their favorable biological performance is attributed to a thin native oxide film that forms spontaneously on the titanium surface. It is well established that surface roughness plays an important role in implant fixation. Accordingly, some authors have indicated the existence of an optimal range of surface roughness.

The titanium surface can be either chemically or physically modified, or both, in order to improve biomaterial–tissue integration. Different treatments are used to modify the titanium surface. Hydroxyapatite coatings, preceded or not by acid etching, are used to create a rough, potentially bioactive surface. Oxide blasting treatments, either with or without chemical etching, are used to develop rough surfaces. Thick oxide films obtained by anodic or thermal oxidation have been used to accelerate the osseointegration process. The ideal microtopography of the surface is still unknown, however, because it is very difficult to associate surface properties with clinical results.

As more accurate knowledge is required, several Ti surfaces have been analyzed and the endosseous implant surface modified on the micro level has been thoroughly studied. Additionally, the production of gold (Au) nanoparticles to be added to the micron-scale modified surface has been performed. In this respect, an appropriate overview of our results is given.

Keywords: Ti implant, surface modification, microlevel, Au nanoparticles

Oblika, kemična sestava in makro- ter mikrotopografija površine implantata so bile raziskovane kot najpomembnejši dejavnik, ki pozitivno vpliva na kostni prirast. Titan in njegove zlitine se uporabljajo več kot 20 let kot biomedicinski material v ortopedski in zobni kirurgiji zaradi dobrih mehanskih lastnosti, odpornosti proti koroziji, zaradi celične netoksičnosti in majhne vnetne reakcije s periplantatnim tkivom, kar vse potrjuje njihovo biokompatibilnost. Ugodno biološko vedenje se pripisuje tanki naravni oksidni plasti, ki spontano nastane na površini titana. Znano je, da ima hrapavost površine pomebno vlogo pri pritrditvi implantata. Temu ustrezno so nekateri avtorji omenili obstoj nekega optimalnega območja hrapavosti površine.

Oblika površine titana se lahko spremeni kemijsko ali fizikalno ali na oba načina, kar poveča prirast biomateriala. Za spremembo oblike površine se uporablja več načinov. Hidroksiapatitna prekritja s predhodnim jedkanjem ali brez jedkanja s kislino se uporabljajo za tvorbo grobe, potencialno bioaktivne površine. Peskanje z oksidnim prahom s kemijskim jedkanjem ali brez njega se tudi uporablja za ustvarjanje grobe površine. Debele plasti oksida, nastale z anodno ali termično oksidacijo, se uporabljajo za pospešitev procesa kostnega prirastka. Idealna mikrotopografija površine je še vedno neznana, zato ker je težko uskladiti lastnosti površine s kliničnimi rezultati. Ker je potrebno boljše poznavanje, je bilo analiziranih več površin titana in modificirana površina implantata je bila na mikronivoju natačno preiskana. Dodatno so bili uporabljeni nanodelci zlata (Au) za dodatek na mikronivoju spremenjene površine. Ustrezen pregled doseženih rezultatov je predstavljen v tem prispevku.

Ključne besede: Ti-implantat, sprememba oblike površine, mikronivo, nanodelci Au

1 INTRODUCTION

According to the European Association of Biomaterials, materials that are developed to be implanted into human tissues are called biomaterials and need to have a high biocompatibility. Biocompatibility of the material assumes that the material is not associated with any local or systemic damage to the organism, whereas the biological environment, in which the material is implanted, does not cause any changes to the material itself. Biomaterials must not show any toxic, allergogenic, cancerogenic or radioactive activity. Additionally, within the tissue-implant interaction, any kind of material damage, due to corrosion, dissolving or biodegradation, is not allowed.

Dental implants (**Figure 1**) are widely used in modern dental practice as a substitute for lost dentition.

Shape, chemical composition, as well as the macro- and microtopography of the implant surface, have been widely studied as major factors that positively influence implant osseointegration. Ossseointegration is a biological phenomenon associated with a direct structural and functional contact between a vital bone and non-vital implant, without connective tissue insertion.[1] Titanium and titanium alloys have been commonly used over the past 20 years as biomedical materials in orthopedic and

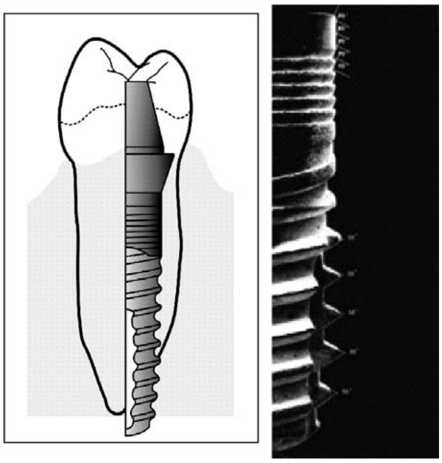


Figure 1: Dental implant
Slika 1: Zobni implantat

dental surgery because of their good mechanical properties, corrosion resistance, cell toxicity absence, as well as very poor inflammatory response in peri-implant tissues, which confirms a high biocompatibility[1].Their favorable biological performance is attributed to a thin native oxide film that is spontaneously formed on the titanium surface. The titanium surface can either be chemically or physically modified, or both, in order to improve the biomaterial–tissue integration.

2 IMPLANT-SURFACE MODIFICATION

The shape of a dental implant has been thoroughly studied, providing scientists and clinicians with implants of adequate macrodesign with different dimensions that enable proper osseointegration. The most widely used implants are screw-shaped endosseous implants, either with parallel walls or with a tapered (root-like) design. The further development of biomaterials in modern implantology is associated with implant micro-design improvement, leading to the creation of different concepts of implant-surface modification.

It is well established that surface roughness plays an important role in implant fixation. Compared to initially used implants with machined polished surfaces, implants with rough surfaces have shown superior results, while enhancing bone apposition and regeneration on the bone-to-implant contact. The distribution of the surface roughness of successfully implanted and clinically biofunctional materials is shown in **Figure 2**. The surface roughness that is manipulated to have a range from 1 μm to 50 μm is associated with an excellent implant survival rate.[2] Accordingly, some authors indicated the existence of an optimal range of surface roughness.[3,4] It is considered that a moderate surface roughness, i.e. 1.5–5μm, has a positive influence in the healing process and implant primary stability.

For implant-surface modification, mechanical, chemical and physical methods are applied, as well as their combination. Mechanical methods, including machining, grinding, polishing, and blasting, involve physical treatment, shaping, or the removal of the material's surface. The objectives of mechanical surface modification are to obtain specific surface topographies and roughness, to remove surface contamination, and/or to improve the adhesion in subsequent bonding steps. Chemical methods involve chemical treatment, electrochemical treatment (anodic oxidation), sol–gel, chemical vapor deposition (CVD), and biochemical modification. During the above-mentioned treatments, electrochemical or biochemical reactions occur at the interface between titanium and a solution. Physical methods, during which chemical reactions do not occur, are thermal spraying and physical vapor deposition. The formation of a surface-modified layer, films or coatings on titanium and its alloys are mainly attributed to thermal, kinetic, and electrical energy.

In practice, different treatments are used to modify the titanium surface. Hydroxyapatite coatings, preceded or not by acid etching, are used to create a rough,

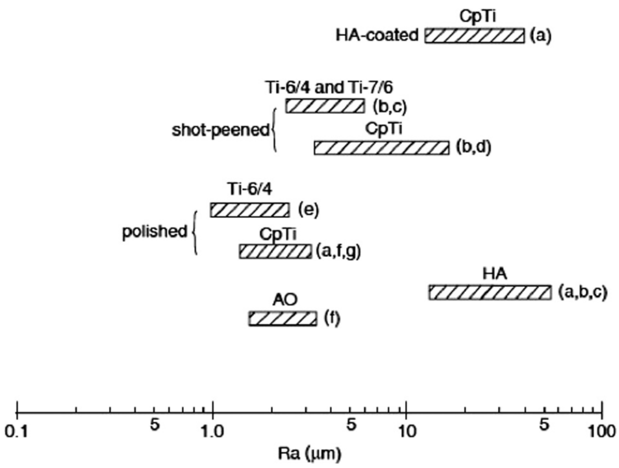


Figure 2: Distribution of implant surface roughness[4]
Slika 2: Pregled hrapavosti površine implantata[4]

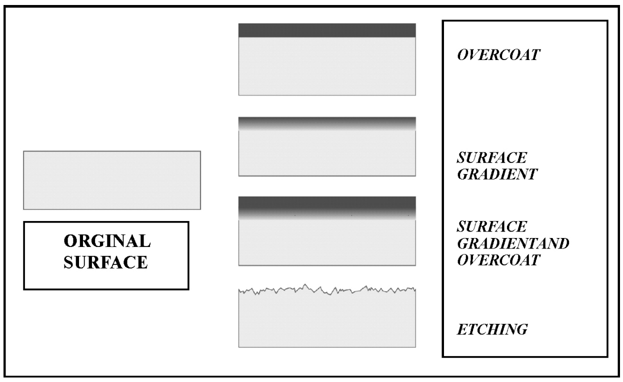


Figure 3: Schematic representations of different plasma methods to modify the surfaces of biomaterials[6]
Slika 3: Shematičen prikaz različnih plazemskih metod za modifikacijo biomaterialov[6]

potentially bioactive surface. Oxide blasting treatments, either with or without chemical etching, are used to develop rough surfaces, and thick oxide films obtained by anodic or thermal oxidation have been used to accelerate the osseointegration process. However, other characteristics, such as oxide thickness, oxide crystallinity and ions present in the external layer, may also influence the bone bonding.

Therefore, the ideal microtopography of the surface is still unknown, because it is very difficult to associate surface properties with clinical results. Although more accurate knowledge is required, different surfaces have been submitted to controlled clinical trials and are commercially available.

3 MICROSTRUCTURED SURFACES

As stated above, implant-surface modification aims to increase the surface roughness and the surface for bone-to-implant contact. Implant surface design affects the amount of osseointegration. A surface topography on the micrometer scale can increase the bone-to-implant contact because of its enhanced biomechanical properties, providing an environment for easier contact osteogenesis, as well as signals for the cell interactions.

It has been shown[5] that an implant surface modified on the micron-level is associated with a faster and increased osseointegration and bone-to-implant contact, when compared to polished Ti surfaces.

In implant surface topography engineering, artificial surface roughening is achieved with a combination of two different processes:

– Coating of the implant surface with an additional layer
– Implant surface erosion with blasting or etching protocols

Plasma-surface modification (PSM) is an efficient and economical surface-treatment technique with the unique advantage that the surface properties and biocompatibility can be enhanced selectively, while the bulk attributes of the materials remain unchanged (**Figure 3**).[6]

Laser-surface modification or laser-surface texturing presents a relatively novel and popular technique of surface modification. Its advantages are associated with precise, targeted and guided surface roughening, controlling the roughening dimension. with a controlled surface, roughening an adequate micron-scale topography can be obtained, in respect to the bone cells' shape, structure and orientation.[7]

4 NANOSTRUCTURED SURFACES

In recent years there has been a growing interest in the possible influence of nanostructured implant surfaces on bone healing and apposition. The nanoscale modification of a Ti implant surface can modify both the topography and the chemistry of the surface itself.

Types of surface modifications (**Figure 4**) on the nanolevel are:[8]

A) Self-assembled monolayers, which can induce chemical and topographical surface modification, resulting in novel physical and/or biochemical surface properties
B) Deposition and chemical modification techniques on the nanoscale ($x \leq 100$ nm), which can realize a distribution on the micron-scale ($y \geq 100$ nm)
C) Compaction techniques applied on the nanoscale ($x \leq 100$ nm), which can realize a distribution on the nanoscale
D) Isotropic surfaces on the nanoscale ($x \leq 100$ nm), obtained by subtractive and additive methods. The distribution can occur either on the nano- or on the micron-scale.

Possible methods developed in surface modification on the atomic (nano) level are:

– Self-assembling of monolayers
– Physical approach (particle compaction, ion-beam deposition)
– Chemical approach (acid etching, peroxidation, NaOH oxidation or anodisation)
– Nanoparticle deposition (sol-gel, crystalline deposition)
– Lithography

Regarding cell behavior in the contact with nano-modified surfaces, different cell reactions, such as protein adsorption, cell adhesion, cell proliferation or cell differentiation and spreading can be expected.

In comparison to conventional micrometer-structured surface modification, three types of nano-stuctured surface modifications have been developed so far:

Surface coating with a nano-structured diamond layer (diamond-like carbon, DLC). Increased mechanical properties in terms of hardness, wear resistance, corrosion resistance and longevity, as well as better biocompatibility have been achieved. The layers are applied to the implant surface by CVD.

Surface coating with nanoparticles of hydroxyapatite (HA) or crystalline calcium phosphate (CaP), which enhances both the contact to the bone and to the metal. When compared to microparticle coatings of the same

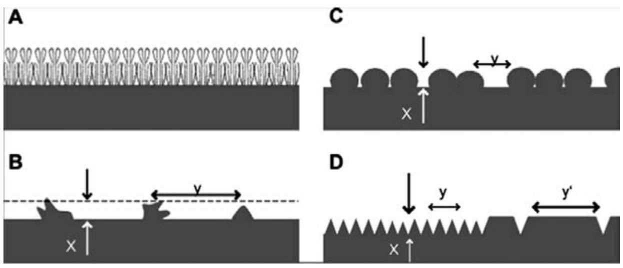


Figure 4: Nanoscale surface modification[8]
Slika 4: Modifikacije površine na nanonivoju[8]

materials, the abrasion and loosening of the particles is decreased, thus diminishing the negative properties of these materials. It has been proved that nanoparticles of HA improve the osteoblast adhesion, proliferation and mineralisation

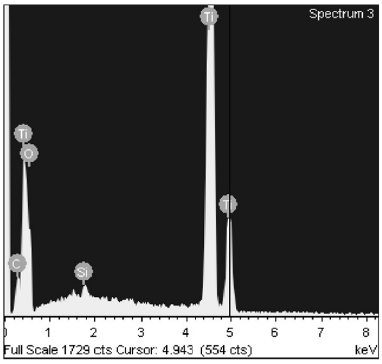
A surface coating of ceramic fused to metal materials, increases the chemical bonding, which results in a better hardness and wear resistance

Regarding all the above stated, surface modification on the nanolevel can be achieved by using different techniques and materials. One of the possibilities is the use of a dental alloy with a high gold content because of the exceptional biological compatibility of gold and its high electrochemical resistance, functionality and longevity.[9,10] Gold is compatible with gingival tissues and is not susceptible to oxidation and the accumulation of dental plaque.

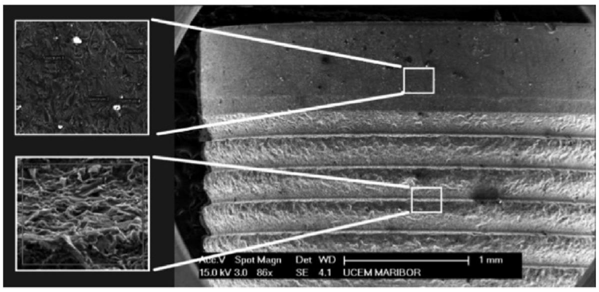
5 RESULTS

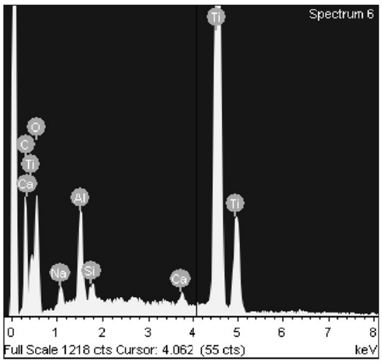
Several samples of endosseus implants commonly used in modern dental practice were submitted for SEM analysis. The implant macrodesign shows two parts of an implant, a collar and implant body with threads. Both parts were analyzed using SEM microscopy and the analysis of their chemical composition.

The microstructure of the implant surface is shown in **Figure 5**. Since the chemical analysis showed a higher content of Na, Al, C, O and Ca at the implant body, compared to the implant neck, it can be concluded that the surface was modified by blasting techniques with Al_2O_3 and SiC.



Spectrum	C	O	Na	Al	Si	Ca	Ti	V
Spectrum 3	2.17	18.55			0.44		78.84	
Max.	2.17	18.55	0.00	0.00	0.44	0.00	100.00	2.91





Spectrum	C	O	Na	Al	Si	Ca	Ti	Total
Spectrum 6	8.96	22.10	0.72	2.45	0.45	0.57	64.74	100.00
Max.	8.96	22.10	0.72	2.45	0.45	0.57	64.74	

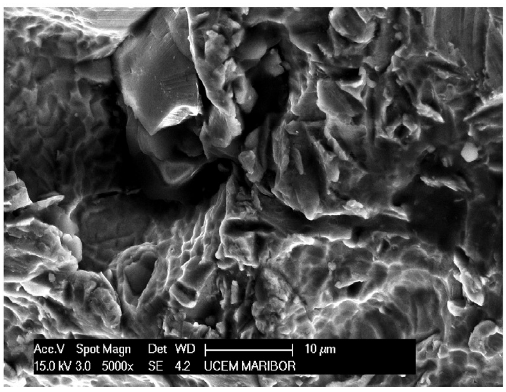
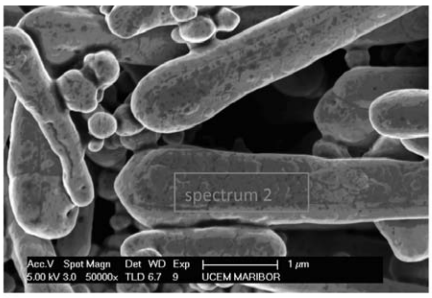
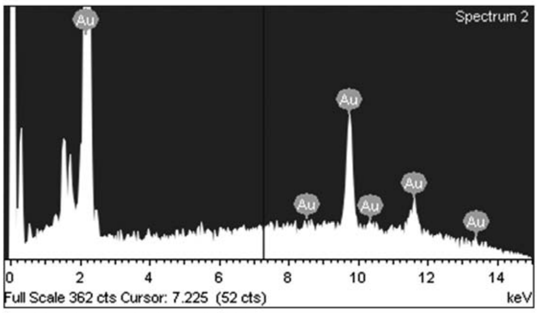


Figure 5: Micron-scale implant surface on SEM
Slika 5: SEM-posnetek površine implantata na mikrometrskem nivoju

a)



b)



Element	*weight%*	*atom%*
Au M	*100,00*	*100,00*
Total	*100,00*	

Figure 6: Structural analysis: a) SEM micrograph of Au fibers, b) spectrum of EDS analysis marked as "spectrum 2" in **Figure 6a**. (Quantification spectrum for the rectangular area in **Figure 6a**.)
Slika 6: Strukturna analiza: a) SEM-posnetek Au niti, b) spekter EDS-analize, označen kot "spekter 2" na **sliki 6a** (kvantifikacija spektra za pravokotno površino na **sliki 6a**)

At the bottom of **Figure 5** the magnified part of the implant body is presented. It is clearly seen that the surface morphology is ranging within the micrometer scale. At the microlevel up to 10 μm, an interesting surface morphology, presenting diluted spaces, as well as surface shells, represents an adequate platform for the osteoblast cell adhesion and spreading. The main author's idea was whether the addition of nanoparticles onto the presented micrometer-scale surface morphology would result in benefits, such as faster cell attachment, spreading and differentiation. On the nanolevel, we have managed to obtain ideal gold (Au) nanoparticles and nanofibers, as shown in **Figure 6**. Gold (Au) nanoparticles and nanofibers were formed by ultrasonic spray pyrolysis.[11,12]

The nanoparticles could be added to the implant surface by: (i) spray deposition techniques or (ii) plasma deposition techniques. Good nanoconfiguration of the particles could improve the cell activity on the implant surface, whereas nanofibers can serve as an additional matrix for bone cells, thus improving osseointegration and the bone-to-implant contact.

6 DISCUSSION AND CONCLUSIONS

The classical protocol of osseointegration was based on the success of the uncoated cpTi, treaded root-form implant. Long-term clinical data support the use of this material as an ideal dental implant. Ti is osseoinductive and it may create physical-chemical bonds with the bone. However, current data substantiate the use of a variety of implant surface biomodifications, coatings, as well as geometries to attain osseointegration.

Therefore, the next step in the upgrading of the quality of the implant surfaces was the addition of coatings onto the implant in the following ways: a) metal-to-metal; b) ceramic-to-metal; and c) biologically active molecules on metal, on ceramics or diverse functional carriers. Ti has been used to date as a biological substrate for many osteoconductive and osteoinductive, inorganic or organic coatings: ceramics of different kinds, glass, adhesion proteins, extracellular bone matrix proteins, growth factors and cytokines. The primary goal of the coated implants was to combine the benefit of a bioactive surface layer with the properties of the substrate, i.e., the strength of the underlining metal.

As described above, the particle size of the coating layer, or surface topography, plays one of the key roles in terms of material properties and its behavior in contact with living tissues.

Implant surface properties, such as micro-roughness and nano-roughness, are essential components to be discussed in terms of implant osseointegration, as well as bone-to-implant contact. An interesting fact is that different structures of the implant surface are to be found on the micrometer and nanometer scale. It has been noticed that a smooth surface on the microlevel is not necessarily smooth on the nanolevel. Nevertheless, an arranged surface structure shown on the microscale does not have to be arranged when observed within the nanoscale.[10]

Since a stronger and faster bone response is found in the nano-modified implant surfaces, which has to be taken into consideration is the possible coating detachment and its behavior within the tissue, in the period of time. It also has to be studied whether the nanoscale modification can alter the surface reactivity.

The biological properties of gold (Au) and gold alloys have already been confirmed and found an important place in dental prosthodontics.[9] Nevertheless, there is limited data on their use as a substrate layer in implantology. A substrate production in forms of nanoparticles and nanofibers of Au,[11,12] and its addition to an implant surface, is a complex method that could result in an ideal surface topography. The effect of an Au nanolayer could be extraordinarily positive due to its biocompatible properties and, additionally, associated with the positive effects of nanosurfaces.

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