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RESEARCH ARTICLE

Characteristics of Biocompatible Coatings on Dental Implants

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Abstract

The purpose of this article is to give an overview of various biocompatible modifications of the implant surface and factors that mainly affect processes at the implant-bone interface. This review summarizes and explains the factors that are currently recognized as important for dental implants osseointegration: body materials and coatings, topography, hydrophilicity and polarity of the implant surface. Implant body materials (titanium, zirconium) are designed to provide mechanical stability. Their effect on bone cells can be improved with the help of surface treatment with various materials that include calcium phosphates, strontium, bio-glass, and diamond-like carbon. Surface topography can be changed using various methods, for example, plasma spraying, sandblasting, acid etching and microarc oxidation to increase bone contact with the implant. The hydrophilicity and polarity of the surface of the implants shows a significant cell adhesion effect. At the present time the currently used dental implant materials are showing satisfactory clinical results, ongoing research on innovative surfaces is necessary to improve and accelerate the of dental implant osseointegration.

Key words: *Dental implants, Implant body materials, Biocompatible coatings, Osseointegration.*

Introduction

Loss of teeth not only disrupts the structural, functional and aesthetic view of the maxillofacial region, but also often leads to serious psychosocial consequences and a decrease in the quality of life. One of the most effective solutions for this problem is dental implants. Since the 18th century dentists have already had the idea of using intraosseous implants, but the procedure almost always resulted in infection of the surgical wound and rejection of the implants. Only the discovery of effective antiseptics significantly reduced the risk of infection of surgical wounds and determined the success of dental implantology.

Initially, the clinical goal was the development of an optimal design (both in shape and geometry) to avoid implant rejection, inflammatory processes caused by a chewing load on the implant [1, 2].In the 50-60s of the 20th century there were several major studies in this area. In 1951, titanium was proposed as a material for implants. In 1952, P.I. Branemark noted that in the bone bed, a traumatically prepared and exactly matching the shape of the titanium structure, there is a strong "fusion" between the metal surface and the bone. This process is called osseointegration. In 1959, the Italian dentist S. Tramonte proposed the design screw implant, following in 1962 the French doctor R. Chercheve offered a design of a corkscrew implant. In 1965, P.I. Branemark created a collapsible design screw implant consisting of intraosseous part and bolted it to the base of the head (abutment). In 1969, Linkow invented the plate implant. In addition to implants of helical, cylindrical and plate forms, a number of implants of a combined form were proposed in the 70s.

Together with its clinical use, dental implantation has made through a significant development path. Their use for functional and aesthetic rehabilitation of patients in need of tooth replacement is constantly increasing [3, 4].This is due to the significant advantages of dental implantology compared to traditional prosthetics (crowns, bridges), such as no need to grind adjacent healthy teeth, reliable fixation and a long service life,

slowed jaw bone atrophy and aesthetics. Implants don't cause discomfort, have no effect on speech, do not require food restrictions. In addition, there are a smaller number of contraindications for the installation of dental implants and now a wider range of patients can have them installed. The disadvantages are the high cost and the long duration of the procedure for updating the dentition, two-stage implantation is currently used. In some cases, it takes up to about six months for the whole process. In addition, it is likely that the implants will not take root in the jaw.

Recent success rate of implant engraftment is about 95% in the upper jaw and 97% in the lower jaw after 10 and 15 years of observation, respectively [5, 6].Despite the high level of successful cases, studies are still aiming at increasing clinical efficacy in more difficult conditions, such as poor bone quality [7], implantation site deterioration due to age-related bone changes [8], accelerated postoperative healing and implants osseointegration.

For the success of osseointegration, it is currently not enough that the implant is safe for the surrounding tissue and ignored by living tissue. The implant material should evoke the desired tissue response. The osseointegration processes occur at the bone, dental implant interface, and therefore, the characteristics of the coating of dental implants and their biocompatibility with bone tissue have a key role in these processes.

In modern dental implantology, one of the leading areas is the study of various materials and technologies for development of dental implant coatings with improved biocompatibility. The purpose of this article is to overview available biocompatible modifications of the implant surface and factors affecting the processes at the implant-bone interface.

Materials for Dental Implants

Before considering the dental coatings, we will take a quick look on the materials for their manufacture, because they are a substrate for biocompatible coatings. Currently, the most commonly used are the endosseous screw implants (intraosseous screw implants) directly inserted into the alveolar bone.

Their osseointegration provides strong structural support in the long run [3, 9].Materials for dental implants meet several requirements: no toxicity and corrosion, strength, manufacturability, physical properties close to natural tissues, etc. Material inconsistency in at least one of the parameters reduces the implant functional value and its lifetime. The optimal combination of material characteristics ensures its biocompatibility (including biomechanical one) [10, 11].

There are 3 groups of biocompatible implant materials:

- Biotolerant (stainless steel, cobalt-chromium alloys (CCA), silver-palladium alloys, polymers from which non-absorbable barrier membranes are made).
- Bioinert (titanium and its alloys, zirconium, corundum ceramics, tantalum, etc.).
- Bioactive (hydroxyapatite, tricalcium phosphate, bio-metals, absorbable barrier membranes).

All biotolerant materials exhibit satisfactory biocompatibility, but have no osteoconductive properties, i.e. they are not able to provide adhesion of proteins and bone cells on their surface. Therefore, there is no physicochemical bond between the surface of the implant and the bone matrix, which leads to the connective tissue accumulation or fibrous capsule.

Such indirect contact is called fibro-osseointegration, which happens due to distant osteogenesis. Currently, these materials are rarely used for dental implants. Bioactive non-biological materials take part in the ion exchange and metabolism of the bone matrix. The bone tissue replaces them partially or completely during its regeneration. They are often applied to the surface of implants to improve their biocompatibility.

Bioinert implant materials own pronounced osteoconductive properties, since their surface can provide a physicochemical bond with the bone matrix, but with no inclusion into the metabolism of bone tissue no degradation throughout the entire period of interaction. On their surface, a stable oxide

film is formed, which causes the glycosamines and other proteins adsorption that are necessary to trigger osteogenesis. As a result of this interaction of bone tissue and the implant, direct contact (ankylosis) forms over time, i.e. the process of osseointegration occurs, which is based on contact osteogenesis. Implantologists tend to use bioinert metal implants. Titanium implants show the most favorable tissue response. The advantage of titanium is its lightness, strength, ductility, and high biocompatibility [12, 13].

The main reason for Ti biocompatibility is the rapid oxidation process. After implant insertion, granulocytes involved because severe oxidative stress at the implantation site due to overproduction of oxygenated derivatives such as H_2O_2. Lysis of H_2O_2 into reactive oxygen species and subsequent incorporation into the surface causes a thickening of the titanium dioxide (TiO_2) layer on the implant [14]. Bone matrix calcium and phosphorus ions get into this porous layer together with oxygen-containing derivatives, which leads to a highly dynamic boundary between the bone and the implant.

The oxide layer prevents the direct contact between the metal and the environment and acts as a protective layer, thus minimizing the ions release [15].Two types of titanium implants used are the commercially pure titanium (CP Grade 1-4, contamination with other elements is the lowest in grade 1 and highest in grade 4) and titanium alloys [16].

Several in vitro studies have been conducted to prove biocompatibility and lack of hemolytic activity on various Ti alloys, such as alloys with niobium (Nb), zirconium (Zr), molybdenum (Mo), tantalum (Ta) and hafnium (Hf) [17, 19].Studies showed that the zirconium owns good biocompatibility, improving the adhesion and proliferation of osteoblasts [20].

According to histomorphometric studies, the surface of ZrO_2, compared to titanium, a significant improvement in bone healing in the lower jaw was observed in dwarf pigs [21].The titanium zirconium alloy (commercially called Roxolid) developed by the Straumann Institute AG (Basel, Switzerland) and containing 13-17% zirconium (TiZr) showed improved mechanical properties compared to pure Ti [22].

Despite ongoing research on titanium alloys for dental use, commercially pure titanium still is the most widely used material for implant dentistry, with zirconium popularity is increasing [23, 25].

Features of Various Biocompatible Surfaces of Dental Implants

If the mechanical implants properties (Young's modulus, fatigue, etc.) depend on the material of which the implant is made, then the biological effects at the bone. Dental implant interface are strictly related to the implant surface and its properties [26].The process that takes place on the "bone-dental implant" border was described by P.I.

Branemark and was called the osseointegration. Branemark defined osseointegration as "the obvious direct attachment of living bone tissue to the implant surface without the introduction of a layer of connective tissue" [27].Today, the biological aspects of the dental implant osseointegration are described in detail by the Blood clot retraction theory [28], according to which there is a successive change of three stages, reflecting the gradual regeneration of the bone:

- Osteoconduction, when the osteoblasts are attracted and migrate to the surface of the implant through the remainder of the blood clot around it;
- Osteoinduction - bone formation happens as a result of bone matrix mineralization when osteogenic cells reach the implant surface;
- Bone remodeling - a long process with cycles of resorption and bone formation, stabilizing no earlier than 18 months after the operation of dental implantation.

However, a necessary condition for successful osseointegration of the dental implant is its coating biocompatibility. Initially, biocompatible coatings were described as chemically and biologically inert materials that are safe for tissues and the whole body, with no inflammation, rejection, necrosis, and apoptosis.

Further development of clinical practice led to the following principle: material should still enter into specific interactions with the body, and not just be ignored by the surrounding living tissue.

The material should evoke the desired tissue response, ensuring its effective engraftment. An important property of the implant surface is its topography. This term refers to the presence of pits, craters, protrusions and grooves on the surface of the implant, which can be described as surface roughness.

A number of researchers have proved that the rough surface of titanium dental implants has greater energy and wettability compared to a smooth surface [29, 30].The presence of roughness, pores or depressions, of a certain size, on the surface of the intraosseous part of the dental implant promotes protein adsorption, mechanical attachment of fibrin and collagen fibers to the surface of the material, adhesion of osteogenic cells, fibro and osteoblasts, as well as the synthesis of specific proteins and growth factors. As a result, it allows achieving an increase in bone integration area.

The relief can significantly increase the specific surface area of the implant interacting with the bone, which increases the strength of its integration with the bone and reduces the level of mechanical stress in the surrounding structural units of the bone [13].The surface roughness index is calculated by the profile (line), or by the surface (area). To calculate the roughness of the profile, use the value Rz - the difference between the highest and lowest points on the surface, and Ra - the average value of the surface height that can be quantitatively measured at the micro-scale (Ra 1-100 μm) or nanoscale (Ra 1-100 nm) levels.

However, the roughness parameters of the three-dimensional region (Sa, Sq) are more significant since thanks to micro- and nanotopography, the area of contact between the implant and the tissue increases, which contributes to the further interaction of the cell with the implant [13]. Most surfaces of dental implants produced at present have moderate surface roughness with complex microtopography (Sa 1-2 μm) [31].

Various technologies can be used to create the rough surface of titanium dental implants: plasma spraying of titanium powder, anodizing, acid etching, sandblasting acid etching, microarc oxidation, modification with carbon-oxygen (CO), laser processing. For the commercial production of dental implants, most manufacturers use varieties of sandblasting acid etching. The most commonly used are Straumann's SLA (Sand blasted, Largegrit, Acid-etched) surfaces in various modifications (SA Osstem implants, NanoTec Alpha Bio implants, etc.) and RBM (Resorbable Blast Media).

The SLA surface is formed as a result of rough sandblasting with corundum particles (aluminum oxide Al2O3), due to which macro-roughness of the titanium surface is achieved. Then, for several minutes, intensive etching in an acid bath with a mixture of HCl and H2SO4 at an elevated temperature follows. The main advantage of the SLA surface, which has won its widespread recognition, is well-developed porosity with craters of 2-5 microns in diameter, which, as established, play an important role in the process of osseointegration.

However, the SLA surface formation process has unavoidable disadvantages: acid etching does not completely remove aluminum oxide particles from the surface after blasting, and more intense etching, which may be able to remove these particles, can lead to a weakening of the subsequent adhesion of bone tissue to the implant.

The RBM technique is that the implant surface is sandblasted with Beta-Tricalcium phosphate (Ca3O8P2) particles of a certain density, mass and size. After mechanical treatment, the surface is etched in organic low concentrated acid, leaving the surface clean (without $Ca_3O_8P_2$ particles remaining), without changing the structure of the titanium “pattern”.

Nevertheless, the RBM surface has a drawback that reduces its marketing attractiveness: its topography, although rough, does not have structurally organized craters that are considered responsible for good osseointegration of the SLA. In general, as shown above, all methods of transforming the surface of dental implants are aimed mainly at increasing the adhesion area of the implant with the bone, i.e. to increase the degree of roughness [32].

However, roughness is far from the only surface parameter of dental implants that affects the success of osseointegration. It reflects only the physics of the surface of dental implants, but surface chemistry also plays an important role in the early stages of

reparative osteogenesis, which is why there is a need to develop dental implants with bioactive coatings that contain bioactive ions on their surface that stimulate osteogenesis. Important surface properties that determine biocompatibility are its hydrophilicity and polarity.

For example, the Osstem TSIII CA implant has a chemically active Calcium SA surface, the hydrophilic properties of which are preserved by packing the implant in an ampoule with $CaCl_2$ solution, this overcomes such a lack of SLA surfaces as hydrophobicity. The chemically modified hydrophilic surface of TS III CA, in contrast, attracts water. This means that immediately after installation, a layer of blood and proteins forms on the surface of the implant, which accelerates the process of osseointegration.

The chemically modified surface of TS III CA implants has a positive charge due to treatment with Ca ions, which leads to more intensive adsorption of negatively charged proteins (more than three times in comparison with chemically unmodified surfaces). More intense protein adsorption stimulates platelet activity, which in turn leads to earlier formation of the fibrin network and the attachment of osteoblasts to the implant surface, and, as a result, accelerates the formation of a new bone. Most often, tricalcium phosphate, hydroxyapatite and tetracalcium phosphate act as bioactive coatings [33].

Calcium phosphate ($Ca_3 (PO_4)_2$) forms the basis of the inorganic component in the bones. Hydroxyapatite (HA) is the most stable form of calcium phosphate [34, 35].HA coating accelerates the initial rate of osseointegration due to the release of Ca and PO4 ions into the surrounding tissues, which leads to the formation of a chemical bond between the implant and bone without the intervention of a layer of connective tissue [36].

$Ca_3 (PO_4)_2$ can be resorbed by osteoclasts, which, in turn, activate osteoblasts with the formation of a new bone [37].However, coatings with $Ca_3 (PO_4)_2$ are not without such a disadvantage as peeling of the coating from a titanium substrate. To overcome this drawback, various methods of applying $Ca_3 (PO_4)_2$ to a titanium implant substrate have been tried.

During titan plasma spraying (TPS), coatings are formed that usually contain 60-70% of HA [38].It was found that this coating technique accelerates the healing of wound tissue, which occurs along with bone formation [39].Pulse laser deposition (PLD), ion beam and radio frequency (RF) sputtering methods have been studied, but these methods are too expensive for widespread clinical use.

More economical and effective methods are immersion of implants in simulated biological fluids (SBF) after preliminary treatment with hydroxyl or oxide groups, or immersion of implants in a gel containing calcium and phosphorus (Sol-gel) [12].Experiments were carried out on the use of Bioactive glass (BG) as a dental implant coating, which is a glass ceramic consisting of 45% SiO_2, 24, 5% NaO_2, 24, 5% CaO and 6% P_2O_5 [40].

BG is a bioactive material because it is capable of forming a layer of carbonate-substituted hydroxyapatite-like (HCA) structures on the surface in contact with biological fluids. This positive effect gives high biocompatibility of BG and ensures tight bone contact with the implant without the intervention of fibrous tissue [41]. However, BG slowly decomposes to HCA and has low mechanical strength. Therefore, their chemical modifications were proposed, such as partial or complete substitution of SiO_2 for B_2O_3 to generate borosilicate from borate bioactive glasses [42] or substitution of SiO_2 for P_2O_5 to produce phosphate glasses [43].

In vitro and animal studies comparing the effectiveness of BG coatings with HA [44] have shown that dental implants coated with silicate bioactive glass have the ability to achieve osseointegration comparable to HA coating after insertion into the jawbone of a person. A promising material for use in bioactive coatings is strontium. This is due to the fact that it is able to replace calcium in bone tissue. Currently, the possibility of using strontium on metal implants is being actively studied.

In vitro experiments showed cell proliferation and attachment to the surface, and in vivo stimulation of bone formation was comparable to HA coatings [45]. It was also established that the inclusion of strontium in the titanium dioxide layer improves the implant osteoconductivity [46], studies on the

incorporation of strontium in the titanium dioxide layer have demonstrated an improvement in the osteoconductivity and healing rate of the implant due to an increase in bone tissue deposits on its surface and, as a result, closer contact bones with an implant. High hardness, wear resistance and corrosion resistance, low coefficient of friction, chemical inertness drew attention to diamond-like carbon (DLC) coatings as promising for use on intraosseous implants. However, studies of DLC coatings are still insufficient [47, 48].

Conclusion

Dental implants must be functional, biocompatible, successfully and quickly integrate with bone tissue, to ensure a high aesthetic result of implantation. The materials from which the implant is made determine its mechanical properties-strength, fatigue, etc. The nature and intensity of the biological processes taking place at the "implant-bone" border depends on the parameters of the implant surface, its topography, hydrophilicity, and the materials from which it is formed.

It is the features of the implant surface that determine its biocompatibility and affect the implant osseointegration processes. Initially, dental implants were developed for functional rehabilitation, therefore, at the initial stages, materials were determined that could be inserted into the bone without being rejected by the patient's immune system. In vitro and in vivo studies have shown that materials such as alloys of Ti, zirconium, tantalum, niobium and hafnium were biocompatible because they are bioinert and have pronounced osteoconductive properties.

Currently, the most common material for the manufacture of dental implants is titanium and its alloys. It is able to oxidize rapidly, forming a titanium dioxide film on the surface of the implant, which contributes to the formation of a bond between the implant surface and the bone. A promising material is zirconium and its alloys with titanium. However, the biocompatibility of bioinert materials did not provide enough tissue response, which slowed down the process of osseointegration.

Further research was aimed at studying the surface modification of implants. It was found that in addition to the implant materials, surface roughness promotes cell attachment and subsequent osseointegration. The roughness was further improved by reaching the nanoscale level to control the interaction of the protein with the surface. It was found that hydrophilic surfaces can positively affect protein adsorption, leading to increased bone positioning. Coatings with bioactive materials began to be used to direct bone regeneration through osteoconduction and osteoinduction processes.

Coating with calcium phosphate (such as hydroxyapatite), bioglass, and strontium improved osteoconduction and accelerated the rate of osseointegration in the early stages of bone healing, which is considered the most critical phase after implantation. Further research is needed on the characteristics of promising surfaces in order to assess their potential for clinical use.

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