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REVIEW ARTICLE

Implant Surface Modification and Osseointegration-Past, Present and Future

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ABSTRACT

Biological fixation between the dental implant surfaces and jaw bones should be considered a prerequisite for the long-term success of implant-supported prostheses. The implant surface modifications gained an important and decisive place in implant research over the last years. Nowadays, a large number of implant types with a great variety of surface properties and other features are commercially available and have to be treated with caution. Although surface modifications have been shown to enhance osseointegration at early implantation times, for example, the clinician should look for research evidence before selecting a dental implant for a specific use.

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INTRODUCTION

Dental implant success has evolved from modest results of the middle of the past century. Beginning in the late 1960s the focused efforts of PI Branemark led to the detailed microscopic characterization of interfacial bone formation at machined titanium endosseous implants (1,2). Titanium dental implants are widely employed due to their good performance and predictable lifetime. The long-term benefits of such implants are caused by the responses of different surrounding tissues. These concepts of osseointegration focused the profession on a proscribed surgical technique and the biocompatible nature of the machined titanium surface. Bone formation at the endosseous implant surface was considered a positive outcome that was contrasted to fibrous encapsulation, a negative and undesired result (3). The main clinical advantage of osseointegration was the predictable clinical result that occurred when an osseous interface was reproducibly formed and maintained at the titanium surface of load bearing dental implants.

Osseointegrated implants are used widely in the dental, maxillofacial, and ear nose throat fields and, although not as frequently, also in orthopaedic surgery. Osseointegration, the direct structure-function adhesion between bone and implant surface, is a prerequisite for the long-term success of dental implants. Albrektsson *et al* (1) suggested the following as the six most important factors for establishing reliable osseointegration: implant material, implant design, surface quality, bone status, surgical technique and loading conditions. Many techniques have been developed during the last 30 years with the aim of improving osseointegration from a physical or chemical stand point. The first osseointegrated surfaces were produced by industrial machining of a bulk titanium implant, which led to minimally rough surfaces with some residual periodic microgrooves.

Implant surface character is one implant design factor affecting the rate and extent of osseointegration (4). The process of osseointegration is now well described both histologically and at the cellular level. The adhesion of a fibrin blood clot and the population of the implant surface by blood-derived cells and mesenchymal stem cells is orchestrated in a manner that results in osteoid formation and its subsequent mineralization (5). A seamless progression of changing cell populations and elaboration and modification of the tissue/implant interface eventually results in bone forming in direct contact with the implant surface.

Lee *et al* reported that the surface characteristics and biocompatibility of oxidized titanium surfaces increased as the temperature increased. This indicates that surface modification by thermal treatment could be another useful method for medical and dental implants. Chien *et al* reported that deposition of dopamine/ Hydroxyapatite greatly enhanced the adhesion, proliferation, and mineralization of osteoblasts. Furthermore, enhanced cell adhesion and osteogenic differentiation were noted.

Surface quality of an implant depends on the chemical, physical, mechanical and topographical properties of its surface. Several implant surface modifications have been used to improve the quantity and quality of the bone-to-implant interface. Surface composition and roughness are parameters that may play a role in implant tissue interaction and osseointegration.

Zhang *et al* used a surface modification strategy encompassing the use of bioactive trace elements together with surface micron/nano-topographical modifications in a study in an attempt to enhance the osseointegration of Titanium alloy, a commonly used implant. The results suggested that developed Sr-HT coatings have the potential for future use as coatings for orthopedic/dental and maxillofacial devices. Furthermore, Yoneyama *et al* have developed a simple surface modification of titanium alloy that improves its bio-functional activity. The surface of a titanium alloy disk was modified by applying 3% hydrogen peroxide hydrothermal treatment using an autoclave. Treated surfaces exhibited higher hydrophilicity, protein adsorption, and cell proliferation than untreated surfaces. 3% hydrogen peroxide hydrothermal treatment is thought to provide biofunctional activity for aged titanium surface. Della Valle *et al* introduced an innovative osteointegrative and antibacterial biomimetic coating on titanium and performed a chemical physical and in vitro biological characterization of the coating using the SAOS-2 cell line.

Still, there has been a growing demand for implants with better surface features and consequently better osseointegration, therefore the topography of the implant surfaces can now be manipulated at a wide range of length scales, down to the nanolevel. In the light of the continuing development of new dental implants, this review focuses on the different surfaces and methods that aim to accelerate the osseointegration of dental implants.

BONE IMPLANT INTERFACE CONTROL

Various approaches are employed to obtain desired outcomes at the bone implant interface. As a general rule, an ideal implant biomaterial should present a surface that will not disrupt, and that may even enhance, the general processes of bone healing, regardless of implantation site, bone quantity and bone quality (6) Ito *et al* described the approaches to alter implant surfaces can be classified as physicochemical, morphologic or biochemical (7).

Physicochemical Method mainly involves the alteration of surface energy, surface charge, and surface composition with the aim of improving the bone-implant interface. The method employed is the Glow discharge treatment, in which materials are exposed to ionized inert gas, such as argon. During collisions with substrate, high energy species "scrub" contaminants from the surface, thereby unsaturating surface bonds and increasing surface energy. This higher surface energy will then influence adsorption of biomolecules, which in turn affects subsequent cell and tissue behavior (8).

Morphological Methods mainly deals with alteration of surface morphology and roughness to influence cell and tissue response to implants. Many animal studies support that bone in growth into macro rough surfaces enhances the interfacial and shear strengths. In addition; surfaces with specially contoured grooves can induce contact guidance, whereby direction of cell movement is affected by morphology of substrate. The added advantage is that this method prevents the epithelial down growth on dental implants (9). Implant surfaces have been classified on different criteria, such as roughness, texture and orientation irregularities.

Wennerberg and coworkers (10) have classified implant surfaces based on the surface roughness as: Minimally rough (0.5-1 m), intermediately rough (1-2 m), rough (2-3 m). Based on texture obtained, the implant surface can be divided as: concave texture (mainly by additive treatments like hydroxyapatite (HA) coating and titanium plasma spraying), convex texture (mainly by subtractive treatment like etching and blasting). Based on the orientation of surface irregularities (11), implant surfaces are divided as: isotropic surfaces: have the same topography independent of measuring direction and anisotropic surfaces: have clear directionality and differ considerably in roughness.

DIFFERENT METHODS THAT INCREASE THE SURFACE ROUGHNESS ARE

Blasting implant surface with particles of various diameters is one of the frequently used methods of surface alteration. Depending on the size of the ceramic particles, different surface roughness can be produced on titanium implants. The blasting material should be chemically stable, biocompatible and should not hamper the osseointegration of implants. Various ceramic particles have been used, such as alumina, titanium oxide and calcium phosphate particles.

Alumina (AlO) is frequently used as a blasting material and produces surface roughness. However, the blasting material is often embedded into the implant surface and residue remains even after ultrasonic cleaning, acid passivation and sterilization. Alumina is insoluble in acid and is thus hard to remove from the titanium surface. In some cases, these particles have been released into the surrounding tissues and have interfered with the osseointegration of the implants (12).

Titanium oxide is also used for blasting titanium dental implants. Titanium oxide particles with an average size of 25 μm produce a moderately rough surface in the 1- 2 μm range on dental implants (13,14). A third possibility for roughening dental implants consists of using a biocompatible, osteoconductive and resorbable blasting material. Calcium phosphates such as hydroxyapatite, beta-tricalcium phosphate and mixtures have been considered useful blasting materials. These materials are resorbable, leading to a clean, textured, pure titanium surface (15).

Chemical etching with strong acids such as HCl, H2 SO 4, HNO3 and HF is another method for roughening dental implants. Acid-etching produces micro pits on implant surfaces with sizes ranging from 0.5 to 2 μm in diameter. Acid- etching has been shown to greatly enhance osseointegration. Immersion of titanium implants for several minutes in a mixture of concentrated HCl and H2 SO4 heated above 100°C (dual acid- etching) is employed to produce a microrough surface. This type of surface promotes rapid osseointegration while maintaining long-term success over 3 years. It has been found that dual acid etched surfaces enhance the osteoconductive process through the attachment of fibrin and osteogenic cells, resulting in bone formation directly on the surface of the implant. Another approach involves treating titanium dental implants in fluoride solutions. Titanium is very reactive to fluoride ions, forming soluble TiF species. The surface produced has microrough topography. This chemical treatment of the titanium created both a surface roughness and fluoride incorporation favorable to the osseointegration of implants (12)

Porous surfaces are produced when spherical powder of the metallic/ ceramic material becomes a coherent mass within the metallic core of the implant body. These are characterized by pore size, shape, volume and depth, which are affected by the size of the spherical particles and the temperature and pressure of the sintering chamber. Pore depth depends on the size of the particles (44 to 150 m) and their concentration per unit area, as well as on the thickness of the applied coating (usually 3,000 m). A pore depth of 150 to 300 m appears to be the optimal size for bone ingrowth and maximum contact with the walls of the pore (16,17). In the future, porous-coated implants could be impregnated with growth factors and act as delivery vehicles because of increased surface volume.

Plasma-spraying is a technique in which hydroxyapatite (HA) ceramic particles are injected into a plasma torch at high temperature approximately 15,000-20,000 K and projected on to the surface of the titanium where they condense and fuse together, forming a film. Plasma-sprayed coatings can be deposited with a thickness ranging from a few micrometers to a few millimetres. In order to obtain mechanical retention of the coating, the surface of the metallic implant must be roughened, e.g. by means of gritblasting, when using this method. The plasma-spraying method has disadvantages, however, such as the porosity of the coating and residual stress at the substrate/coating interface, as well as drastic changes in the composition and crystallinity of the initial calcium phosphate Plasma-sprayed HA -coated dental implants have also been associated with clinical problems. One of the major concerns with plasma-sprayed coatings is the possible delamination of the coating from the surface of the titanium implant and failure at the implant-coating interface despite the fact that the coating is well-attached to the bone tissue. The discrepancy in dissolution between the various phases that make up the coating has led to delamination, particle release and thus the clinical failure of implants. Loosening of the coating has also been reported, especially when the implants have been inserted into dense bone (12).

Ion-sputtering coating is the process by which a thin layer of HA can be coated onto an implant substrate. This is performed by directing a beam of ion onto an HA block that is vaporized to create plasma and then recondensing this plasma onto the implant.

Anodized surface- micro- or nano-porous surfaces may also be produced by potentiostatic or galvanostatic anodization of titanium in strong acids (H2 SO4 , H3 PO4 , HNO3 , HF) at high current density (200A/m2) or potential (100 V). When strong acids are used in an electrolyte solution, the oxide layer will be dissolved along current convection lines and thickened in other regions. The dissolution of the oxide layer along the current convection lines creates micro or nanopores on the titanium surface. Anodization reduces modifications in the microstructure and the crystallinity of the titanium oxide layer. The anodization process is rather complex and depends on various parameters such as current density, concentration of acids, composition and electrolyte temperature. Anodized surfaces result in a strong reinforcement of the bone response with higher values for biomechanical and histomorphometric tests in comparison to machined surfaces (18).

Hydroxyapatite coating

HA coating was brought to dental profession by De Groot (19)

Various methods of coating are:

- **Functionally graded coating:** Delamination is the main disadvantage of plasma coating. But this disadvantage is overcome by the use of HA along with Ti6Al4V (20). The coating becomes mechanically strong, bioinert and biocompatible.
- **Laser ablation technique (21):** This technique is best suited to control the morphology of coating of HA i.e. either crystalline or amorphous.
- **Pulsed laser deposition (22):** Latest method of coating HA on to an implant surface. HA is deposited on to pure Ti substrates at 400degree C in water vapour and oxygen atmosphere, the pressure valve in the range of 3.5 .10 -10 torr.
- **Antibiotic coating:** Gentamycin along with the layer of HA can be coated onto the implant surface. Gentamycin acts as a local prophylactic agent along with the systemic antibiotics in dental implant surgery.

Sputtering is a process whereby, in a vacuum chamber, atoms or molecules of a material are ejected from a target by bombardment of high energy ions (23). The dislodged particles are deposited on a substrate also placed in a vacuum chamber. There are various sputtering techniques like diode sputtering ion sputtering, radiofrequent/ direct current sputtering, magnetron sputtering and reactive sputtering. All these techniques are variant of above mentioned physical phenomenon.

Ratio frequency sputtering (RF) Technique (24) involves the deposition of HA in thin films. Studies have shown that these coating are more retentive and chemical structure is precisely controlled. The other major advantage of this technique is that the design of implant particularly threaded implant is maintained.

Magnetron sputtering (23) technique shows strong HA titanium bonding associated with outward diffusion of Ti in to HA layer forming TiO2 at an interface.

Surface chemistry/ chemical topography: Ti-6Al-4V and commercially pure titanium are commonly used dental implant materials, although new alloys containing niobium, iron, molybdenum, manganese and zirconia are developed. Biomaterial surface interacts with water, ions and numerous biomolecules after implantation. The nature of these interaction such as hydroxylation of the oxide surface by dissociative adsorption of water, formation of an electrical double layer and protein adsorption and denaturation, determine how cells and tissues respond to the implant (25).

Biochemical method offer an alternative to physiochemical and morphological methods. This method mainly endeavors to utilize current understanding of biology and biochemistry of cellular function and differentiation. The goal of biochemical surface modification is to immobilize proteins, enzymes/ peptides on biomaterial for the purpose of inducing specific cells and tissue response or in other words to control the tissue implant interface with molecules delivered directly to the interface (26).

Future trends concern the modifications of surface roughness at the nano-scale level for promoting protein adsorption and cell adhesion, biomimetic calcium phosphate coatings for enhancing osteoconduction and the incorporation of biological drugs for accelerating the bone healing process in the peri-implant area.

The new nanotechnology has opened new opportunities for the manipulation of implant surfaces. It is believed that implant surfaces could be improved by mimicking the surface topography formed by the extracellular matrix (ECM) components of natural tissue. These ECM components are of nanometre scale with typical dimensions of 10-100 nm. Cell attachment, proliferation, and differentiation are responsive to nano-scale features such as pillars or grooves prepared, for example, using nanolithography. Nanopatterned surfaces may also provide better adhesion of the fibrin clot that forms right after implantation, facilitating the migration of osteogenic cells to the material surface.

Alumina/zirconia nanocomposites offer an example of how nanotechnology offers an attractive path to the development of new implant materials but ceramics, even nanocomposite ceramics, will not replicate the unique combinations of mechanical properties of tooth tissues as they are, for example, much stiffer and wear-resistant (12). Recently, it has been shown that a possible path to combining high strength and toughness in a ceramic material is to take advantage of the transformation toughening mechanisms in nanozirconia-alumina materials. These materials consist of a dispersion of a small amount of tetragonal ZrO particles (typically around 200 nm in size) in an Al2 O3 matrix. Despite conflicting reports regarding the effect of ceramic coatings and micro- and/or nano-topography on the osseointegration of dental implants, the prevailing philosophy is that they may significantly influence the bone growth and attachment to implant surfaces and ultimately improve the success of dental implants and the rapid return to function (i.e. mastication) (27,28).

DRUGS AND DENTAL IMPLANTS

The surface of titanium dental implants may be coated with bone-stimulating agents such as growth factors in order to enhance the bone healing process locally. Members of the transforming growth factor (TGF-a) superfamily, and in particular bone morphogenetic proteins (BMPs), TGF- 1, platelet-derived growth factor (PDGF) and insulin-like growth factors (IGF-1 and 2) are some of the most promising candidates for this purpose. Another possibility may be the adjunction of a plasmid containing the gene coding for a BMP. This possibility is limited due to the poor efficacy of inserting plasmids into the cells and the expression of the protein. In addition, overproduction of BMPs by cells might not be desirable after the bone healing process.

The implants surface could also be loaded with molecules controlling the bone remodeling process. Incorporation of bone anti-resorptive drugs, such as biphosphonates, might be very relevant in clinical cases lacking bone support, e.g. resorbed alveolar ridges. Biphosphonate incorporation on to titanium implants increased bone density locally in the periimplant region. Plasma-sprayed HA-coated dental implants immersed in pamidronate or zoledronate demonstrated a significant increase in bone contact area. The main problem lies in the grafting and sustained release of antiresorptive drugs on the titanium implant surface. Due to the high chemical affinity of biphosphonates for calcium phosphate surfaces, incorporation of the antiresorptive drug on to dental implants could be achieved by using the biomimetic coating method at room temperatures (29,30).

CONCLUSION

Titanium dental implant needs to be osseointegrated with the host bone in order to achieve enough resistance against torsion caused by masticating. Surface conditions, such as surface roughness, surface charge, surface energy and composition have important influences on the osseointegration process. Therefore, modifying titanium implant surface seems to be a promising way to achieve stronger and faster osseointegration of the implants. Currently, surface roughening (e.g., SLA) and coating (e.g., with HA) are commonly used techniques in clinical practice. In addition, the surface charge of the titanium dental implant has been found to be directly related to the latter's osseointegration. In conclusion, negatively charged surfaces are beneficial to the implant's osseointegration. Accordingly, the development of new methods that negatively charge the surface of a titanium dental implant seems to be a promising direction to improve osseointegration.

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