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Original Research Paper

Prosthodontics

DENTAL IMPLANT SURFACES – PHYSICOCHEMICAL PROPERTIES, BIOLOGICAL PERFORMANCE (OSTEOINTEGRATION) AND TRENDS

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KEYWORDS :

Pure titanium and titanium alloys are well established standard materials in dental implants because of their favorable combination of mechanical strength, chemical stability, and biocompatibility (Brunette et al., 2001)[1,2]. Integration of titanium implants with the surrounding bone is critical for successful bone regeneration and healing of dental implant. The concept of osseointegration was discovered by Brånemark and his co-worker and, has had a dramatic influence on clinical treatment of oral implants. The first generation of successfully used clinical titanium implants, which were machined with a smooth surface texture, now approach 50 years in clinical use.

Since then, implant surfaces have long been recognized to play an important role in molecular interactions, cellular response and osseointegration, and scientists all over the world have developed the second generation implants with surfaces which can accelerate and improve implant osseointegration. These second generation of clinically used implants underwent mechanical blasting coupled or not, with acid etch, bioactive coatings, anodized and, more recently, laser modified surfaces. (Cochran et al., 1998[3]; Jansen et al., 1993[4]; Palmquist et al., 2010 [5]; Brånemark et al., 2010[6 7 8]). The main objective for the development of implant surface modifications is to promote osseointegration, with faster and stronger bone formation. This will likely confer better stability during the healing process, which, preferentially, will improve the clinical performance in the area of poor bone quality and quantity. Furthermore, such promotion may, in turn, accelerate the bone healing and thereby allowing immediate or early loading protocols.

Recently growing micro and nano- technology is rapidly advancing surface engineering in implant dentistry. Such advances in surface engineering technologies have resulted in more complicated surface properties from micro- and nanometer scales, including the morphology, chemistry, crystal structure, physical, and mechanical properties. Such surfaces, intentionally modified with respect to microscale and nanoscale features, may represent a next generation of oral implant systems if possible to transfer to complex three-dimensional geometries. Hitherto, micro- and nano-fabricated surfaces have not reached the clinical evidence stage. However, it is not known whether the improved bone response is due to surface roughness or the surface composition. Furthermore, somewhat surprisingly, there is yet not enough hard evidence (randomized clinical trials) to tell whether the second generation of the implants has a better clinical performance than the machined implants used earlier. Nevertheless, experimental evidence from in vitro and in vivo studies strongly suggests that some types of surface modifications promote a more rapid bone formation than machined surfaces. It has been proposed that increasing osteoconductivity by these surface design strategies is related to the altered implant topography resulting in enhanced osteoblast and preosteoblast adhesion, thereby leading to accelerated bone formation (Chehroudi et al., 1992 [9]; Cooper et al., 1998 [10]). However, it is well known that titanium implantation in bone results in contact of the titanium surface with complex environment including blood components and other cells, not only the osteogenic ones. Recently, it has been shown that changes in the physicochemical properties of the titanium results in significant modulation of cell recruitment, adhesion, inflammation and bone remodelling activities in addition to regulation on bone formation response (Omar, 2010 [11]). These different methods for implant surface modification may lead to different and unique surface properties that might affect the host-to-implant response.

Surface roughness of titanium implants

Surface roughness has been identified as an important parameter for implants and its capacity for being anchored in bone tissue. There exist a variety of different manufacturing methods to increase the surface roughness of the implant, where the most commonly used are: Machining, Sandblasting, Acid etching, Anodic oxidation, Laser modification or a combination of these. Further, commercially available implants have been categorized according to the roughness value (Sa) into 4 groups (Albrektsson & Wennerberg, 2004 [12] a),1 smooth ($Sa < 0.5$ μm), 2 minimally rough ($Sa = 0.5\text{-}1.0$ μm),3 moderately rough ($Sa = 1.0\text{-}2.0$ μm) 4 rough ($Sa > 2.0$ μm).

Machined surface

The first generation of osseointegrated implants had a relatively smooth machined surface (Branemark et al. 1969 [6 7]). The machined implant surface is solely turned and considered to be minimally rough (Figure 1)

Sandblasted surface

Increased roughness of an implant could be achieved by blasting the surface by small particles, usually called sandblasting or grit blasting (Figure 2). When the particles hit the implant surface it will create a crater. The surface roughness is hence dependent on the bulk material, the particle material, the particle size, the particle shape, the particle speed and the density of particles. The resulting surface roughness is usually anisotropic consisting of craters and ridges and occasionally particles embedded in the surface. Significantly higher bone-implant contact was observed for the 25 μm blasted surface compared to machined surface while the bone area within the threads were significantly higher for the machined surface after 12 weeks (Wennerberg et al., 1995 [12]) and 1 year healing (Wennerberg et al., 2010[13]).

Acid etched surface

With acid etching the surface is pitted by removal of grains and grain boundaries of the implant surface, as certain phases and impurities are more sensitive to the etching a selective removal of material is obtained (Figure 3).

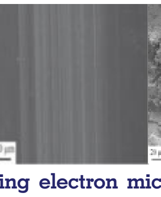
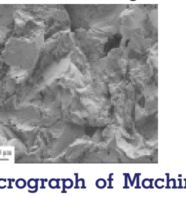

Fig. 1 Scanning electron micrograph of Machined implant surface Fig. 2. Scanning electron micrograph of sandblasted surface

The resulting roughness is dependent on the bulk material, the surface microstructure, the acid and the soaking time. The surfaces are generally considered minimally rough as the typical Sa values are 0.3-1.0 μm. The bone response to acid etched implants has been compared to machined implants in animal models. Significantly higher bone-implant contact was observed for acid etched implants compared to machined implants in a rabbit model after 1 and 2 months, while no difference was found after 14 days (Celletti et al., 2006 14). Significantly increased removal torque was needed to remove acid etched implants compared to the machined implant after 1, 2 and 3 months healing in rabbit while significantly lower removal torque was needed when comparing to titanium plasma sprayed implants (Klokkevold et al., 2001 [16]).

Sandblasted and acid etched surface (SLA)

Commercially available dental implants are usually both blasted by particles and then subsequent etched by acids. This is performed to obtain a dual surface roughness as well as removal of embedded blasting particles. The etching reduces the highest peaks while smaller pits will be created and the average surface roughness will be reduced (Figure 4). Several studies have shown that SLActive implants achieve a higher bone contact and stability at earlier time points (6 weeks) when compared with SLA implants, and dramatically reduced healing times from 12 to 6 weeks (Buser et al., 2004 [15]; Schwarz et al., 2007[17]).

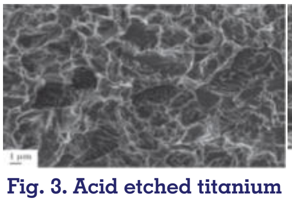

Fig. 3. Acid etched titanium surface

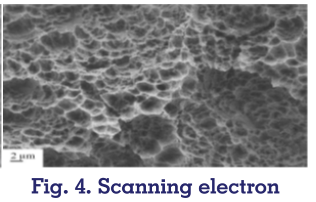

Fig. 4. Scanning electron micrograph of SLA.

Anodized surface

The anodized surface (TiUnite) is a partial crystalline and phosphate enriched titanium oxide characterized by a microstructured surface with open pores in the low micrometer range (Figure 5). Anodization or anodic oxidization as it's also called is an electrochemical process carried out in an electrolyte . The bone response to anodized implants has been evaluated in different species and healing times and most often compared to the original machined surface. Significant higher bone to implant contact has been reported as well as increased biomechanical removal torque values for phosphorous containing anodized surfaces compared to machined surfaces in dog and rabbit (Albrektsson et al., 2000 [18]; Henry et al., 2000 [19]). A higher clinical success rate was observed for the anodized titanium implants in comparison with turned titanium surfaces of similar shapes (Jungner et al., 2005 [20]). Two mechanisms have been proposed to explain this osseointegration: mechanical interlocking through bone growth in pores, and biochemical bonding.

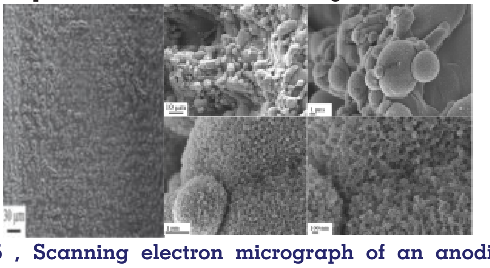

Fig. 5 , Scanning electron micrograph of an anodized TiUnite® implant surface

Fig. 6. Scanning electron micrograph of Brånemark BioHelix implant. The bottom portion of the threads is modified by laser processing, whereas the parts of the flanks and the tops are as machined.

Laser modified micro- and nano-structured surface

Laser is an emerging field for use as a micromachining tool to produce a 3-D structure at micrometer and nanometer level. The technique is a method of choice for complex surface geometries. The technique generates short pulses of light of single wavelength, providing energy focused on one spot. It is rapid, extremely clean, and suitable for the selective modification of surfaces and allows the generation of complex microstructures/ features with high resolution. These advantages make the technique interesting for geometrically complex biomedical implants.

The Brånemark BioHelix Implant (Figure6) has surface modified with laser micromachining process to create micro- and nano-structured surface roughness in only the inner part of the thread. The inner part of the thread is believed to be more suitable for bone formation than the outer part (Thomsson & Esposito, 2008 [21]). The laser technique has several advantages, add no chemicals and can be used in routine manufacturing. Only the valley and parts of the flank of the implant threads was laser treated while the remaining part was left as-machined. The idea behind this design is that the flack portion of the implant thread, which might have the higher risk to expose to the microorganism and plaque, is characterised by relatively smooth surface to minimize the incidence of peri-implantitis, whereas the valley part of the implant threads has the rougher surface. Of clinical importance is that nanostructured surfaces promoted long-term bone bonding and interface strength in vivo as determined by a coalescence between mineralized bone and the nanostructured surface and a substantial increase in removal torque (Palmquist et al., 2010 [22]). One 1-year retrospective case series showed excellent clinical results of Brånemark BioHelix dental implants placed according to conventional procedures (Thomsson & Esposito, 2008 [23]). However, randomized clinical trials with suitable controls are needed to confirm these preliminary results.

Calcium phosphate coatings on titanium implants

Some surface reactive materials have shown the ability to form an interfacial chemical bond with surrounding tissues through a series of biophysical and biochemical reactions, causing 'bioactive fixation' of the implant (Cao & Hench 1996 [24]). Bioactive materials can be biostable (i.e. synthetic hydroxyapatite) or bioresorbable (i.e. bioactive glasses and glass-ceramics). Some bioactive ceramics like bioactive glasses of certain compositions have been claimed to have a real chemical bonding ability with soft tissues (Wilson et al., 1981 [25]). Different types of methods have been introduced to prepare calcium phosphate coatings on dental implant (Table 1 & 2). These methods can be divided to two groups: physical and chemical methods. Sometimes they can also be called dry and wet methods. Typically physical techniques include plasma spraying deposition, physical vapour deposition, magnetron sputtering deposition, ion beam assisted deposition, pulsed laser deposition, and hot isostatic pressing. Chemical techniques include sol-gel method, biomimetic process, electrochemical deposition, micro-arc oxidation (MAO) and electrophoretic deposition.

Physical techniques are widely used for preparation of calcium phosphate coatings. The bonding strength between coatings and implants is higher than those prepared by chemical methods. However, most of these methods have difficulties in coating of complex 3D geometries such as rough screw-shaped dental implants.

Chemical methods can be used to treat the implants with complex geometries. The treating temperature of chemical methods is low. The most important thing is that bioactive molecules and drugs can be incorporate into calcium phosphate coatings via chemical methods, such as biomimetic process.

Table 1. Physical techniques for implant coatings

Technique	Characteristics	Properties
Plasma spraying deposition (PS) (most frequently used method for deposition of calcium phosphate coatings, such as HA, onto implant materials to improve their bioactivity)	(1). High temperature >1000°C (2). Reproducible (3). High deposition rate (4). Atmosphere: Air, vacuum (popular), low pressur 5) Thickness of hydroxyapatite coatings produced by plasma-spray varies from 100 to 300 m (Willmann, 1997).	(1). 2D (2). No homogeneity of crystallnity (3). Promote fast and strong fixation and bone growth in vivo and clinically (4). Bacteria adhesion
Magnetron sputtering (MS) (useful technique for the deposition of bioceramic thin films (based on Ca–P systems), due to the ability of the technique to provide greater control of the coating's properties and improved adhesion between the substrate and the coating)	(1). High deposition rate (2). Metallic and non-metallic substrates (3). DC and RF 4) time consuming	(1). 2D (2). Ion doped hydroxyapatite and composites coatings
Ion beam assisted deposition (IBAD)	(1). The coating is amorphous, and needed to be heat treated further (2) The final crystallinity is dependent on the time, temperature and amount of water vapour present during the coating. (3). Low deposition rate compared to PS	1). 2D (2). High adhesive strength (3). Graded crystallinity
pulsed laser deposition (PLD)	(1). Fast deposition rate (2).Multi-component and metastable materials	(1). 2D (2) HA, OCP, , -TCP
Hot isostatic pressing (HIP)	(1). High temperature and pressure	(1). 2D

Biological response to titanium implant surface modification

Osseointegration, defined as a direct structural and functional connection between ordered, living bone and the surface of a load-carrying implant, is critical for implant stability, and is considered a prerequisite for implant loading and long-term clinical success of endosseous dental implants. Osseointegration of titanium implant surfaces is dependent upon both physical and chemical properties (Sul et al., 2005 26). This structural and functional union of the implant with living bone is strongly influenced by the surface properties of the titanium implant. As titanium and its alloys cannot directly bond with living bone, modification of the implant surface has been proposed as a method for enhancing osseointegration.

Table 2. Chemical techniques for implant coatings

Technique	Characteristics	Properties
Sol-gel method	1). Combine with different coating process, such as dip and spinning coatings, following sintering (2).Substrates with complex geometry (3).Metallic and nonmetallic substrates (4). Thin film	(1). 3D (2). Easy to control the composition (3). High sintering temperature for HA coatings
Biomimetic process	(1). Low temperature (2). Different types of substrates which could induce HA formation, such as metallic implants, bioceramics, polymers	(1). 3D (2). Bone-like crystal structure (3). Ion doped HA (4). Low bonding strength (5) Porous structure (6). Incorporate biomolecules and drugs
Electrochemical deposition	(1). Conducting substrates (2). Chargeable particles (3). Low temperature	(1).3D (2). Low boding strength between coatings and substrates (3). Composite coatings (4). (4). Thick and cracked coatings
Electrophoretic deposition	(1). Conducting substrates (2). Chargeable particles (3). Low temperature	(1). 3D (2). Low boding strength between coatings and substrates (3). Composite coatings (4). Thick and cracked coatings
Micro-arc oxidation (MAO)	(1). Ambient temperature (2). Substrates with complex geometry (3). Electrolytic oxidation	(1).3D (2). HA and ion doped HA

Ultrasonic spray pyrolysis	(1). Ambient temperature (2). Continuous and pulse spray	(1). 2D (2). Cracks in coatings (3). The bonding strength of coatings prepared by pulse spray is better than that by continuous spray

Biology of wound healing following implant placement

Healing in bone occurs in four phases which include inflammation, soft and hard callusformation, and remodeling. Following a implant placement , blood coagulation and hematoma formation takes place. This is followed by inflammation. Various chemical mediators such as thrombin and growth factors released by activated leukocytes and platelets in the hematoma serve as chemotactic signals to many cell types which play an important role in bone healing. Unlike soft tissue healing, bone healing does not lead to scarring. Instead it leads to restoration of the bony tissue. During successful implantation, insertion of metal implants into cortical bone eventually leads to complete healing.

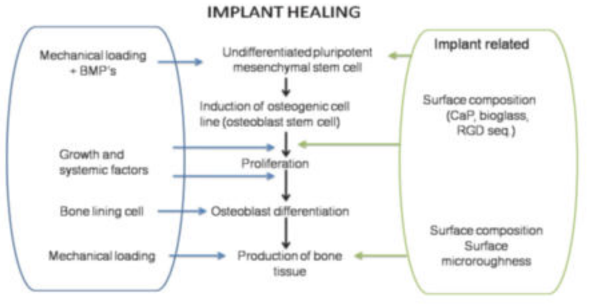

Fig. 7. The implant healing process - The surface composition, roughness and topography are interrelated surface characteristics that influence the biological response to an implant

Wound healing around a dental implant placed into a prepared osteotomy follows three stages of repair- Initial formation of a blood clot occurs through a biochemical activation followed by a cellular activation and finally a cellular response(Stanford and Schneider, 2004 [27]). During surgery, dental Implant surfaces interact with blood components from ruptured blood vessels. Within a short period of time, various plasma proteins such as fibrin get adsorbed on the material surface. Fibrinogen is converted to fibrin and the complement and kinin systems become activated. As in fracture healing, the migration of bone cells in peri-implant healing will occur through the fibrin of a blood clot. Since fibrin has the potential to adhere to almost all surfaces, it can be anticipated that the migration of osteogenic cell populations towards the implant surface will occur. However, as the migration of cells through fibrin will cause retraction of the fibrin scaffold, the ability of an implant surface to retain this fibrin scaffold during the phase of wound contraction is critical in determining whether the migrating cells will reach the implant surface.

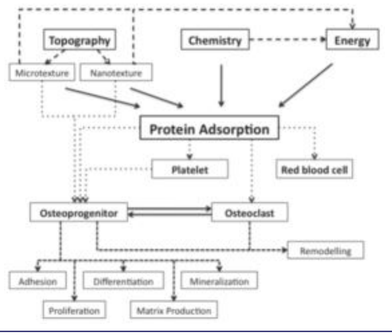

Fig. 8. Effect of submacron surface characteristics of the implant on the osteogenic response

Activation of platelets occurs as a result of interaction of platelets with the implant surface as well as the fibrin scaffold and this leads to thrombus formation and blood clotting. During the initial remodeling, a number of immune cells mediate early tissue response followed by migration of phagocyte macrophages. These cells initially remove the necrotic debris created by the drilling process and then undergo physiological changes which lead to expression of cell surface proteins and production of cytokines and pro-inflammatory mediators. This cytokine-regulated cellular recruitment, migration, proliferation and formation of an extracellular matrix on the implant surface can be influenced by the macrophages. These cells express growth factors such as fibroblast growth factor (FGF-1, FGF-2, FGF-4), transforming growth factors, epithelial growth factor as well as bone morphogenetic proteins (BMPs). The end result of this complex cascade is promotion of a wound healing process that includes angiogenesis.

Influence of implant surface topography on osseointegration

Dental implant quality depends on the chemical, physical, mechanical, and topographic characteristics of the surface (Grassi et al., 2006 [28]). These different properties interact and determine the activity of the attached cells that are close to the dental implant surface. Osteogenesis at the implant surface is influenced by several mechanisms. A series of coordinated events, including cell proliferation, transformation of osteoblasts and bone tissue formation might be affected by different surface topographies . Amount of bone-to-implant contact (BIC) is an important determinant in long-term success of dental implants. Albrektsson et al (1981 [18]) recognized that among the factors influencing BIC such as topography, chemistry, wettability and surface energy the most important is wettability. Surface wettability is largely dependent on surface energy and influences the degree of contact with the physiological environment . Several evaluations have demonstrated that implants with rough surfaces show better bone apposition and BIC than implants with smooth surfaces (Buser et al., 1999 [15])

Surface roughness also has a positive influence on cell migration and proliferation, which in turn leads to better BIC results, suggesting that the microstructure of the implant influences biomaterial–tissue interaction.. the use of alterations in surface chemistry to modify osseointegration events. Specifically, an investigation utilizing sandblasted, large-grit, acidetched (SLA) surfaces that were chemically different but had the same physical properties was conducted to assess BIC as a measure of osseointegration. The chemically enhanced SLA surface demonstrated significantly enhanced BIC during the first 4 weeks of bone healing, with 60% more bone than the standard SLA surface after 2 weeks (Buser et al., 2004[15]). The chemical modifications for the test SLA surface resulted in increased wettability (ie, in a hydrophilic surface rather than a hydrophobic one). Water contact angles of zero degrees were seen with the chemically enhanced surface compared to 139.9 degrees for a standard SLA surface, and the hydrophilicity was maintained after drying. The chemical composition of the surface was also altered, including a 50% reduction in carbon concentration compared with the control implant surface .

Surface roughness Implant surface roughness is divided, depending on the dimension of the measured surface features into macro, micro, and nano-roughness.

Macro roughness comprises features in the range of millimeters to tens of microns. This scale directly relates to implant geometry, with threaded screw and macro porous surface treatments.

Micro roughness is defined as being in the range of 1–10 μm. This range of roughness maximizes the interlocking between mineralized bone and implant surface.

Nanoscale topographies are widely used in recent years. Nanotechnology involves materials that have a nano-sized topography or are composed of nano-sized materials with a size range between 1 and 100 nm.

The micro- and nanoscale surface properties of metal implant, including chemistry, roughness, and wettability, could affect bone formation. It has been shown that grit-blasting with biphasic calcium phosphate (BCP) ceramic particles gave a high average surface roughness and particle-free surfaces after acid etching of titanium implants.

Biological influence of Surface treatment of titanium implants

1 Turned surface (machined dental implants)

The first generation of dental implants, termed the turned implants, had a relatively smooth surface. After being manufactured, these implants are submitted to cleaning, decontamination and sterilization procedures. Scanning electron microscopy analysis showed that the surfaces of machined implants have grooves, ridges and marks of the tools used for their manufacturing. These surface defects provide mechanical resistance through bone interlocking. The disadvantage regarding the morphology of non-treated implants (machined) is the fact that osteoblastic cells are rugophilic – that is, they are prone to grow along the grooves existing on the surface. This characteristic requires a longer waiting time between surgery and implant loading. The use of these implants follows a protocol suggested by Brånemark i.e., 3-6-month healing or waiting time prior to loading. These are the best documented implants with several reports suggesting good long-term clinical outcomes on all indications when used in sites with good bone quality using a two stage procedure. The success rates of turned implants in challenging situations such as low bone density has been reported to be lesser than when placed in areas with good bone quality.

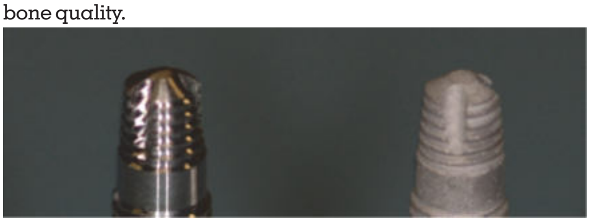

Fig. 9. The machined and nano etched implant surface

2 Etched surface dental Implants

Etching with strong acids is another method for roughening titanium dental implants. Acid etching of titanium removes the oxide layer and parts of the underlying material. The extent of material removed depends on the acid concentration, temperature and treatment time. The most commonly used solutions for acid etching of titanium includes either a mixture of HNO_3 and HF or a mixture of HCl and H_2SO_4 (MacDonald et al., 2004 [29]). Acid treatment provides homogeneous roughness, increased active surface area and improved bioadhesion (Braceras et al., 2009 [15]). This yields low surface energy and reduces the possibility of contamination since no particles are encrusted in the surface. This type of surface not only facilitates retention of osteogenic cells, but also allows them to migrate towards the implant surface. The manufacturers have their own acid etching method regarding concentration, time and temperature for treating implant surfaces. Roughening of implants by acid-etching produces micro pits on titanium surfaces and has been shown to promote rapid osseointegration with long term success

3 Dual acid-etched technique

Immersion of titanium implants for several minutes in a mixture of concentrated HCl and H_2SO_4 heated above 100 °C (dual acid-etching) is employed to produce a micro rough surface. The 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 (Park and Davies, 2000 [30]). The dual acid-etched surface produces a microtexture rather than a macrotexture. 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 . Advantage of the dual acid-etched technique is in higher adhesion and expression of platelet and extracellular genes, which help in colonization of osteoblasts at the site and promote osseointegration. It has been hypothesized that implants treated by dual acid-etching have a specific topography which enables them to attach to the fibrin scaffold, to promote the adhesion of osteogenic cells, and thus to promote bone apposition . High temperature acid-etching methods produced a homogeneous micro-porous surface which showed increased cell adhesion and higher BIC than TPS surfaces. The wettability of the surface has also been proposed to promote fibrin adhesion. This fibrin adhesion provides contact guidance for the osteoblasts migrating along the surface (Buser et al., 2004 [15]).

4 Hydroxyapatite coated implants

Hydroxyapatite is one of the materials that may form a direct and strong binding between the implant and bone tissue. The coating with hydroxyapatite ($Ca_{10}(PO_4)_6(OH)_2$) can be considered as bioactive because of the sequence of events that results in precipitation of a CaP rich layer on the implant material through a solid solution ion exchange at the implantbone interface . The CaP incorporated layer will gradually be developed, via octacalcium phosphate , in a biologically equivalent hydroxyapatite that will be incorporated in the developing bone . Several methods have been described for applying hydroxyapatite coatings onto metals and different material properties may result from each method. Plasma-spraying is the most important commercially used technique for coating metals, especially titanium. In a so called plasma gun, an electric arc current of high energy is struck between a cathode and an anode. Plasma spraying technique results in a coating thickness of 40-50 μm.

5 Sol-gel coated implants

The sol-gel method represents a simple and low cost procedure to deposit thin coatings with homogenous chemical composition onto substrates with large dimensions and complex design. The high mechanical strength and toughness of titanium alloys are the most important advantages over bioactive HA ceramics. A system that join both materials has the mechanical advantages of the underlying (metallic) substrate and biological affinity of the HA. Coating metallic implants with bioactive materials, like HA, may accelerate bone formation during initial stages of osseointegration and thereby improving implant fixation. Thin HA film on titanium substrates can be prepared using sol–gel or electrophoresis techniques . The sol-gel and electrophoresis methods are capable of improving chemical homogeneity in the resulting HA coating to a significant extent, when compared to conventional methods such as solid state reactions, wet precipitation and hydrothermal synthesis

(Milev et al., 2003). These methods are also simple and less expensive than the plasma spraying method that is widely used for biomedical applications. Sol-gel titania films may be prepared using a dip coating or spin coating process . In vivo bone tissue evaluations of surfaces modified using the sol-gel method have shown better osseointegration with no adverse reaction . However, the behavior of sol-gel modifications of loaded osseointegrated implants in the long term remains unknown.

6 Sandblasted and acid-etched (SLA) implants

This type of surface is produced by a large grit 250-500 m blasting process followed by etching with hydrochloric/sulfuric acid. Sandblasting results in surface roughness and acid etching leads to microtexture and cleaning . These surfaces are known to have better bone integration as compared to the above-stated methods .

7 Grit-blasted surface

The grit blasting technique usually is performed with titania or alumina particles. The final surface roughness may be controlled by varying the particle size selected. Titanium implants blasted with alumina and titania particles with sizes of 25 μm and 75 μm demonstrated enhanced bone formation compared to turned implants. TioBlast implants (AstraTech) surface modification included grit blasting with titania particles. The success rate of TioBlast implants reported in a prospective study after 7 years was 96.9% with the same survival rate at 10 years. Compared to turned implants, TioBlast implants demonstrated lower bone loss and higher overall success rates . Grit blasting represented the first clinically applied surface modification of titanium implants; the technique has then been further modified with acid etching, such as: SLA (Straumann) and Osseospeed (AstraTech).

8 Oxidized surface

Alteration of the topography and composition of the surface oxide layer of the implants can be achieved by a process of anodization. Anodic oxidation is an electrochemical process that increases the TiO_2 surface layer and roughness. The oxidation process changes the characteristic of the oxide layer and makes it more biocompatible (Gupta et al., 2010 [37]). The implant is immersed in a suitable electrolyte and becomes an anode in an electrochemical cell.

When a potential is applied to the sample, ionic transport of charge occurs through the cell, and an electrolytic reaction takes place at the anode, resulting in the growth of an oxide film. This results in a surface with micropores which demonstrates increased cell attachment and proliferation (Gupta et al., 2010[37]). The anodization process is rather complex and depends on various parameters such as current density, concentration of acids, composition and electrolyte temperature. The tissue healing process around anodized implants is quicker than in machined implants

9 Plasma-spray coating

Plasma Sprayed (PS) Titanium coating is an optimized way to achieve a surface topography and morphology. The advantage of plasma coating is that these coatings give implants a porous surface that bone can penetrate more readily. Osseointegration was shown to be fastest and most effective for rough surfaces with open structure that varied between 50 to 400 μm. Titanium plasma spraying (TPS) method consists of injecting titanium powders into a plasma torch at high temperature. The titanium particles are projected on to the surface of the implants where they condense and fuse together, forming a film about 30 μm thick. This processing results in a substantial surface area increase compared to the other commercially available surfaces. It has been shown that this three-dimensional topography increased the tensile strength at the implant-bone interface. Based on that, TPS implants have been often recommended for regions with low bone density. Studies have shown that the implant-bone interface formed faster with a TPS surface than with machined implants . Rough surfaces, obtained by TPS and gritblasted/acid-etched have shown torque to failure values significantly higher than implants with machined profiles .

10 Plasma sprayed hydroxyapatite

The addition of calcium and phosphorous based materials as coatings have received significant attention due to the fact that these elements are the same basic components of natural bone and coatings can be applied along the implant surfaces by various industrial processing methods (Kirsch, 1986 [38]). Most commercially available bio-ceramic coatings are processed as a 20–50 μm thick Plasma Sprayed Hydroxyapatite (PSHA) coatings. PSHA coatings normally rely on mechanical interlocking between a grit-blasted or etched metallic surfaces and the ceramic-like PSHA biomaterial for physical integrity during implant placement and function . The osseointegration of the dental implant with plasma-sprayed HA is faster than uncoated implants.

11 Fluoride treatment

Titanium is very reactive to fluoride ions, forming soluble TiF_4 by treating titanium dental implants in fluoride solutions. This chemical treatment of titanium enhances the osseointegration of dental implants. An in vitro analysis of fluoride modified implants on human mesenchymal cells revealed no difference in cell attachment between the fluoride modified and control (grit-blasted) implants.

12 Laser deposition

The surface characteristics of titanium implants have been modified by additive methods, such as titanium and hydroxyapatite plasma spray, as well as by subtractive methods, such as acid etching and laser ablation. The laser ablation technology for surface preparation already has numerous industrial applications. This process results in titanium surface microstructures with greatly increased hardness, corrosion resistance, and a high degree of purity with a standard roughness and thicker oxide layer. Biological studies evaluating the role of titanium ablation topography and chemical properties showed the potential of the grooved surface to orientate osteoblast cell attachment and control the direction of ingrowth .

13 Sputter deposition

Sputtering is a process whereby atoms or molecules of a material are ejected in a vacuum chamber by bombardment of high-energy ions. There are several sputter techniques and a common drawback inherent in all these methods is that the deposition rate is very low and the process itself is very slow . The deposition rate is improved by using a magnetically enhanced variant of diode sputtering, known as radio frequency magnetron sputtering.

Radio frequency sputtering (RF) : Radiofrequency (RF) magnetron sputtering is largely used to deposit thin films of CaP coatings on titanium implants. RF magnetron sputtering is a very suitable technique to deposit standardized CaP coatings on titanium substrates. The advantage of this technique is that the coating shows strong adhesion to the titanium and the Ca/P ratio and crystallinity of the deposited coating can be varied easily. Studies in animals have shown higher BIC percentages with sputter coated implants. Studies have shown that these coatings were more retentive, with the chemical structure being precisely controlled .

Magnetron sputtering:

Magnetron sputtering is a viable thin-film technique as it allows the mechanical properties of titanium to be preserved while maintaining the bioactivity of the coated HA. Films were deposited in a custom-built sputter deposition chamber at room temperature. This technique shows strong HA titanium bonding associated with outward diffusion of titanium into the HA layer, forming TiO2 at the interface .

Biologically active drugs incorporated dental implants

Several attempts have been made to improve and accelerate osseointegration by modification of surface properties, such as introducing bioactive factors to titanium surfaces. Of these, some osteogenic drugs have been applied to implant surfaces. Incorporation of bone antiresorptive drugs, such as bisphosphonate, might be very relevant in clinical cases lacking bone support.

1 Bisphosphonates

Bisphosphate-loaded implant surfaces have been reported to improve implant osseointegration. Bisphosphates are antiresorptive agents that have beneficial effects for the patients on preventing further bone loss, and their effects on increasing the bone mass is modest . It has been shown that bisphosphonate incorporated on to titanium implants increased bone density locally in the peri-implant region with the effect of the antiresorptive drug limited to the vicinity of the implant.

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 bisphosphonates for CaP surfaces, incorporation of the antiresorptive drug on to dental implants could be achieved by using the biomimetic coating method at room temperatures. However, the ideal dose of antiresorptive drug will have to be determined because the increase in peri-implant bone density is bisphosphonate concentration-dependent .

2 Simvastatin

Statins are commonly prescribed drugs that inhibit 3-hydroxy-3-methylglutaryl coenzyme reductase to decrease cholesterol biosynthesis by the liver, thereby reducing serum cholesterol concentrations and lowering the risk of heart attack .

Simvastatin, could induce the expression of bone morphogenetic protein (BMP) 2 mRNA that might promote bone formation . Simvastatin given per-orally to adult rats increased cancellous bone mass and increased cancellous bone compressive strength . Ayukawa et al (2009 [21]) confirmed that topical application of statins to alveolar bone increased bone formation and concurrently suppressed osteoclast activity at the bone-healing site. In addition, clinical studies reported that statin use is associated with increased bone mineral density.

3 Antibiotic coating

Antibacterial coatings on the surface of implants that provide antibacterial activity to the implants themselves have been studied as a possible way to prevent surgical site infections associated with implants. Gentamycin along with the layer of HA can be coated onto the implant surface which may act as a local prophylactic agent along with the systemic antibiotics in dental implant surgery. Tetracycline-HCl treatment has been regarded as a practical and effective chemical modality for decontamination and detoxification of contaminated implant surface . Tetracycline-HCl functions as an antimicrobial agent capable of killing microorganisms that may be present on the contaminated implant surface. It also effectively removes the smear layer as well as endotoxins from the implant surface. Further, it inhibits collagenase activity, increases cell proliferation as well as attachment and bone healing . Tetracycline also enhances blood clot attachment and retention on the implant surface during the initial phase of the healing process and thus promotes osseointegration .

Future directions in implant surface modifications

Several growth factors and cytokines have also been suggested to stimulate a deposition of cells with the capacity of regenerating the desired tissue. An enhanced proliferation and differentiation of undifferentiated mesenchymal cells, osteoprogenitor cells, and preosteoblasts into osteoblasts may improve bone response and subsequently osseointegration of titanium implants . The adhesion of plasma proteins on the surface of titanium implants has been reported to play an essential role in the process of osseointegration .Polypeptide growth and differentiation factors and cytokines have been suggested as potential candidates in this regard to stimulate a deposition of cells with the capacity of regenerating the desired tissue. Biologically active implants surfaces may have the potential to enhance the proliferation and differentiation of undifferentiated mesenchymal cells and osteoblasts which can improve bone response and subsequent osseointegration of titanium implants. Researchers have shown that growth factors released during the inflammatory phase have the potential of attracting undifferentiated mesenchymal stem cells to the injured site. These growth factors include PDGF, EGF, VEGF, TGF-, and BMP-2 and BMP-4. These factors are released in the injured sites by cells involved in tissue healing. 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-) 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. Among these, bone morphogenetic protein (BMP), has shown considerable potential to stimulate bone formation both in extra skeletal sites and in defect models in different species . investigated the effect of local application of autologous platelet-rich plasma (PRP) on bone healing in combination with the use of titanium implants with 2 different surface configurations - CaP coated and non-coated implants. PRP fractions were obtained from venous blood sample of 6 goats and applied via gel preparation and subsequent installation in the implant site or via dipping of the implant in PRP liquid before insertion,

CONCLUSION

The endosseous dental implant has become a scientifically accepted and well documented treatment for fully and partially edentulous patients. Titanium and its alloys are the materials of choice clinically, because of their excellent biocompatibility and superior mechanical properties. The composite effect of surface energy, composition, roughness, andtopography on implant determines its ultimate ability to integrate into the surrounding tissue. Surface modification technologies involve preparation with either an additive coating or subtractive method. Cell migration, adhesion, and proliferation on implant surfaces are important prerequisites to initiate the process of tissue regeneration, while modifications of the implant surface by incorporation of biologic mediators of growth and differentiation may be potentially beneficial in enhancing wound healing following implant placement. These topographical modifications have boosted the success rate of the implant therapy, especially in patients with poor bone quality sites, and have significantly reduced the healing period. The cellular mechanisms involved in this faster and improved osseointegration are yet to be fully determined. Further research should be directed to explore the biologic basis underlying the clinical improvement with altered implant surfaces.

Nowadays, patients can be treated dental implants with a success rate above 97 %. Although novel approaches were able to accelerate and enhance the osseointegration, the healing limits of the body, which make the immediate loading challenging, should not be neglected. Osseointegrated or ankylotic titanium implants don't behave like natural teeth. Since they lack a periodontal ligament, they only had tenth of the mobility of the natural teeth. Axial and horizontal loads bellow a subjective tolerance limit can be compensated by the natural periodontium, but such loads on osseointegrated implants would lead to local disruption of the bony interface. Additionally, it has been reported that the defensive capacity of the peri-implant tissue against bacterial invasion is inferior to that of the natural tooth, that make them more prone to bone loss . A third disadvantage of the osseointegrated implant is the absence of a periodontal neurophysiological mechanoreceptive system for the biocybernetic control of the stomatognatic system . Considering these drawbacks, establishment of a periodontal ligament surrounding an implant, termed as bio-root, would provide the ideal condition for implant-supported treatments in future. To overcome the above mentioned disadvantages of the dental implants, several in vivo experiments attempted to create a periodontal ligament around these implants by placing them adjacent to retained tooth roots . Although they were able to partially regenerate the periodontal ligament consisting of cementum, periodontal ligament and alveolar bone, the application of these methods in patients seems to be impossible due to technical and physical factors. Furthermore, several studies have reported that periodontal ligament cells cultured on titanium implants can produce a periodontal ligament-like tissue when placed in the jaws of animals . Although it has been shown that generating a periodontallike tissue around implants may be experimentally possible, also in human trials approaches until now were not able to innovate a predictable and feasible method for producing dental implants with periodontal-like ligament.

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