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Review

Surface treatments of titanium dental implants for rapid osseointegration

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ARTICLE INFO

Article history:

Received 9 November 2005

Received in revised form 9 June 2006

Accepted 20 June 2006

Keywords:

Osseointegration

Dental implants

Surface roughness

Nano-sized topography

Biomimetic calcium phosphate coating

ABSTRACT

The osseointegration rate of titanium dental implants is related to their composition and surface roughness. Rough-surfaced implants favor both bone anchoring and biomechanical stability. Osteoconductive calcium phosphate coatings promote bone healing and apposition, leading to the rapid biological fixation of implants. The different methods used for increasing surface roughness or applying osteoconductive coatings to titanium dental implants are reviewed. Surface treatments, such as titanium plasma-spraying, grit-blasting, acid-etching, anodization or calcium phosphate coatings, and their corresponding surface morphologies and properties are described. Most of these surfaces are commercially available and have proven clinical efficacy (>95% over 5 years). The precise role of surface chemistry and topography on the early events in dental implant osseointegration remain poorly understood. In addition, comparative clinical studies with different implant surfaces are rarely performed. The future of dental implantology should aim to develop surfaces with controlled and standardized topography or chemistry. This approach will be the only way to understand the interactions between proteins, cells and tissues, and implant surfaces. The local release of bone stimulating or resorptive drugs in the peri-implant region may also respond to difficult clinical situations with poor bone quality and quantity. These therapeutic strategies should ultimately enhance the osseointegration process of dental implants for their immediate loading and long-term success.

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1. Introduction

In the past 20 years, the number of dental implant procedures has increased steadily worldwide, reaching about one million dental implantations per year. The clinical success of oral implants is related to their early osseointegration. Geometry and surface topography are crucial for the short- and long-term success of dental implants. These parameters are associated with delicate surgical techniques, a prerequisite for a successful early clinical outcome [1]. After implantation, titanium implants interact with biological fluids and tissues. Direct bone apposition onto the surface of the titanium is critical for the rapid loading of dental implants. After the initial stages of osseointegration, both prosthetic biomechanical factors and patient hygiene are crucial for the long-term success of the implants. There are two types of response after implantation. The first type involves the formation of a fibrous soft tissue capsule around the implant. This fibrous tissue capsule does not ensure proper biomechanical fixation and leads to clinical failure of the dental implant. The second type of bone response is related to direct bone–implant contact without an intervening connective tissue layer. This is what is known as osseointegration. This biological fixation is considered to be a prerequisite for implant-supported prostheses and their long-term success. The rate and quality of osseointegration in titanium implants are related to their surface properties. Surface composition, hydrophilicity and roughness are parameters that may play a role in implant–tissue interaction and osseointegration.

This review focuses on the different surfaces and methods that aim to accelerate the osseointegration of dental implants. The physical and chemical properties of implant surfaces are discussed in relation to their biological and clinical behavior. Manufacturers of dental implants have developed a variety of surfaces with different compositions and degrees of roughness. However, there is controversy as to the optimal features for implant surfaces regarding osseointegration kinetics.

2. Chemical composition of the surface of dental implants

The chemical composition or charges on the surface of titanium implants differ, depending on their bulk composition and surface treatments. The composition and charges are critical for protein adsorption and cell attachment. Dental implants are usually made from commercially pure titanium or titanium alloys. Commercially pure titanium (cpTi) has various degrees of purity (graded from 1 to 4). This purity is

characterized by oxygen, carbon and iron content. Most dental implants are made from grade 4 cpTi as it is stronger than other grades. Titanium alloys are mainly composed of Ti6Al4V (grade 5 titanium alloy) with greater yield strength and fatigue properties than pure titanium [2].

The surface chemical composition of titanium implants also affects the hydrophilicity of the surface. Highly hydrophilic surfaces seem more desirable than hydrophobic ones in view of their interactions with biological fluids, cells and tissues [3,4]. Contact angle measurements give values ranging from 0° (hydrophilic) to 140° (hydrophobic) for titanium implant surfaces [3,5,6]. In a recent animal study, Buser et al. [3] found that a hydrophilic SLA surface gave higher bone-to-implant contact than regular SLA. Nevertheless, previous *in vivo* studies performed by Albrektsson and co-workers [7,8] failed to demonstrate higher osseointegration using hydrophilic surfaced dental implants.

3. Surface roughness of dental implants

There are numerous reports that demonstrate that the surface roughness of titanium implants affects the rate of osseointegration and biomechanical fixation [9,10]. Surface roughness can be divided into three levels depending on the scale of the features: macro-, micro- and nano-sized topologies.

The macro level is defined for topographical features as being in the range of millimetres to tens of microns. This scale is directly related to implant geometry, with threaded screw and macroporous surface treatments giving surface roughness of more than 10 μm . Numerous reports have shown that both the early fixation and long-term mechanical stability of the prosthesis can be improved by a high roughness profile compared to smooth surfaces [11–13]. The high roughness resulted in mechanical interlocking between the implant surface and bone ongrowth. However, a major risk with high surface roughness may be an increase in peri-implantitis as well as an increase in ionic leakage [14]. A moderate roughness of 1–2 μm may limit these two parameters [15].

The microtopographic profile of dental implants is defined for surface roughness as being in the range of 1–10 μm . This range of roughness maximizes the interlocking between mineralized bone and the surface of the implant [10,13]. A theoretical approach suggested that the ideal surface should be covered with hemispherical pits approximately 1.5 μm in depth and 4 μm in diameter [16].

The main clinical indication for using an implant with a rough surface is the poor quality or volume of the host bone. In these unfavorable clinical situations, early and high

Table 1 – Surface properties of titanium dental implants

Type of implant	Surface roughness (μm)	Contact angle ($^\circ$)	References
cpTi	$R_a = 0.22 \pm 0.01^a$	55.4 ± 4.1	[5,107]
Ti6Al4V	$R_a = 0.23 \pm 0.01^a$	56.3 ± 2.7	[5,107]
TPS	$R_a = 7.01 \pm 2.09$	n.d.	[5]
SLA	$S_a = 1.15 \pm 0.05$	138.3 ± 4.2	[3]
Modified SLA	$S_a = 1.16 \pm 0.04$	0	[3]
Plasma-sprayed HA coating	$R_a = 1.06 \pm 0.21$	57.4 ± 3.2	[6,108]
Biomimetic CaP coating	$R_a = 1.83 \pm 0.64$	13.4 ± 0.17	This work

^a Machined and polished surfaces.

bone-to-implant contact would be beneficial for allowing high levels of loading. In the cases of insufficient bone quantity or anatomical limitations, short designed implants with a rough surface have demonstrated superior clinical outcomes than smooth surfaces [17,18]. Numerous studies have shown that surface roughness in this range resulted in greater bone-to-implant contact and higher resistance to torque removal than other types of surface topography [10,13]. These reports have demonstrated that titanium implants with roughened surfaces have greater contact with bone than titanium implants with smoother surfaces [9,10]. However, the Cochrane collaboration has not found any clinical evidence demonstrating the superiority of any particular implant surface [19].

Surface profiles in the nanometer range play an important role in the adsorption of proteins, adhesion of osteoblastic cells and thus the rate of osseointegration [20]. However, reproducible surface roughness in the nanometer range is difficult to produce with chemical treatments. In addition, the optimal surface nano topography for selective adsorption of proteins leading to the adhesion of osteoblastic cells and rapid bone apposition is unknown.

Various methods have been developed in order to create a rough surface and improve the osseointegration of titanium dental implants (Table 1). These methods use titanium plasma-spraying, blasting with ceramic particles, acid-etching and anodization.

3.1. Roughening of implants by titanium plasma-spraying

A titanium plasma-spraying (TPS) method has been used for producing rough implant surfaces (Fig. 1). This method consists in 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 $30\mu\text{m}$ thick. The thickness must reach $40\text{--}50\mu\text{m}$ to be uniform. The resulting TPS coating has an average roughness of around $7\mu\text{m}$, which increases the surface area of the implant. It has been shown that this three-dimensional topography increased the tensile strength at the bone/implant interface [11]. In this pre-clinical study using minipigs, the bone/implant interface formed faster with a TPS surface than with smooth surface implants presenting an average roughness of $0.2\mu\text{m}$. However, particles of titanium have sometimes been found in the bone adjacent to these implants [21]. The presence of metallic wear particles from endosseous implants in the liver, spleen, small aggregates of macrophages and even in the para-aortic lymph nodes have also been reported [21]. Metal ions released from implants may be the product of dissolution, fretting and wear, and may be a source of concern due to their potentially harmful local and systemic carcinogenic effects [22,23]. However, the local and systemic adverse effects of the release of titanium ions have not been universally recognized. In a clinical study comparing SLA and TPS implant surfaces, no clinical difference was observed between these two surfaces [24]. In a pre-clinical model, the percentage of bone/implant contact was found to be inferior for the TPS surface than for plasma-sprayed hydroxyapatite-coated implants [25]. Nowadays, there is a consensus on the clinical advantages of implanting moderately rough surfaced implants (in the micrometric range) rather than using rough plasma-sprayed implant surfaces [11,26].

3.2. Roughening of implants by grit-blasting

Another approach for roughening the titanium surface consists in blasting the implants with hard ceramic particles. The

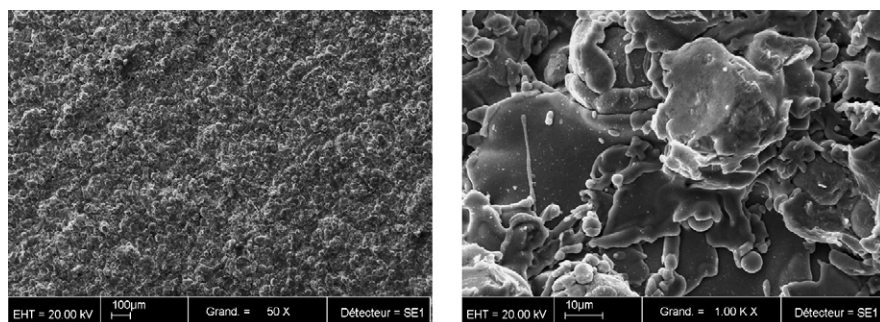


Fig. 1 – SEM micrographs of a titanium plasma-sprayed (TPS) surface (Courtesy of Cam Implants BV, The Netherlands).

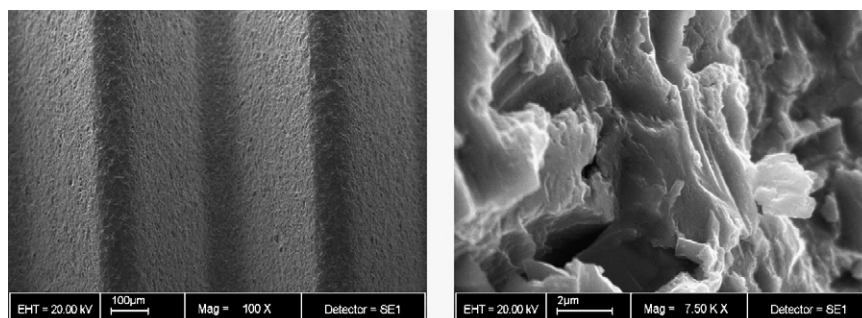


Fig. 2 – SEM micrographs of a TiO blasted surface (Courtesy of Astratech TiOblast™, France).

ceramic particles are projected through a nozzle at high velocity by means of compressed air. Depending on the size of the ceramic particles, different surface roughnesses can be produced on titanium implants. The blasting material should be chemically stable, biocompatible and should not hamper the osseointegration of the titanium implants. Various ceramic particles have been used, such as alumina, titanium oxide and calcium phosphate particles.

Alumina (Al_2O_3) is frequently used as a blasting material and produces surface roughness varying with the granulometry of the blasting media. 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. Moreover, this chemical heterogeneity of the implant surface may decrease the excellent corrosion resistance of titanium in a physiological environment [27].

Titanium oxide is also used for blasting titanium dental implants. Titanium oxide particles with an average size of $25\text{ }\mu\text{m}$ produce a moderately rough surface in the $1\text{--}2\text{ }\mu\text{m}$ range on dental implants. An example of a titanium oxide-blasted surface is shown in Fig. 2. An experimental study using microimplants in humans has shown a significant improvement for bone-to-implant contact (BIC) for the TiO_2 blasted implants in comparison with machined surfaces [28]. Other experimental studies confirmed the increase in BIC for titanium grit-blasted surfaces [12,29]. Other studies have reported high clinical success rates for titanium grit-blasted implants, up to 10 years after implantation [30,31]. Comparative clinical

studies gave higher marginal bone levels and survival rates for TiO_2 grit-blasted implants than for machined turned implants [32,33].

Wennerberg et al. [13] demonstrated with a rabbit model that grit-blasting with TiO_2 or Al_2O_3 particles gave similar values of bone-implant contact, but drastically increased the biomechanical fixation of the implants when compared to smooth titanium. These studies have shown that the torque force increased with the surface roughness of the implants while comparable values in bone apposition were observed [34]. These studies corroborate that roughening titanium dental implants increases their mechanical fixation to bone but not their biological fixation.

A third possibility for roughening titanium dental implants consists in 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. Experimental studies have demonstrated a higher bone-to-implant contact with these surfaces when compared to machined surfaces [35,36]. Experimental studies have demonstrated a bone-to-implant contact similar to that observed with other blasting surfaces when osseointegration is achieved [37].

3.3. Roughening of implants by acid-etching

Etching with strong acids such as HCl , H_2SO_4 , HNO_3 and HF is another method for roughening titanium dental implants. Acid-etching produces micro pits on titanium surfaces with sizes ranging from 0.5 to $2\text{ }\mu\text{m}$ in diameter [38,39]. Acid-

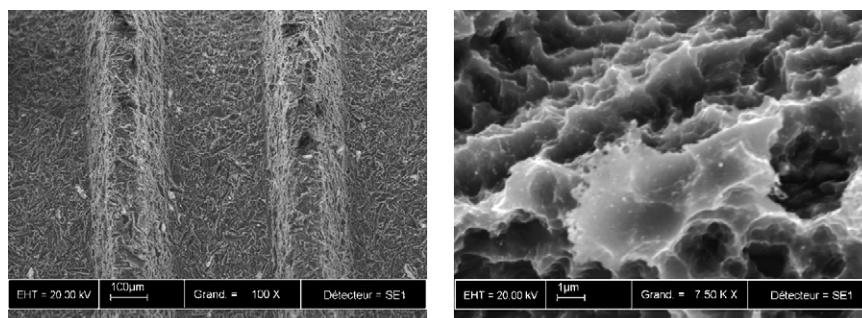


Fig. 3 – SEM micrographs of an SLA surface on a titanium dental implant (Courtesy of Straumann AG, Switzerland).

etching has been shown to greatly enhance osseointegration [40]. Immersion of titanium implants for several minutes in a mixture of concentrated HCl and H₂SO₄ heated above 100°C (dual acid-etching) is employed to produce a microrough surface (Fig. 3). This type of surface promotes rapid osseointegration while maintaining long-term success over 3 years [41]. 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 [42]. In the peri-implant area, woven bone with thin trabeculae projecting into the implants, has been described [43]. These studies hypothesized that implants treated by dual acid-etching have a specific topography able to attach to the fibrin scaffold, to promote the adhesion of osteogenic cells, and thus to promote bone apposition [44,45]. Several experimental studies have reported higher bone-to-implant contact and less bone resorption with dual acid-etched surfaces compared to machined or TPS surfaces [9,46,47]. Recently, acid-etching methods have been improved in order to increase cell adhesion and bone neoformation. High temperature acid-etching produces a homogeneous microporous surface with higher bone-to-implant contact than TPS surfaces in experimental studies [48,49]. 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. An experimental study has demonstrated that a hydrophilic surface greatly improved the bone/implant contact compared to standard sand-blasted and acid-etched implants in minipigs [3].

Another approach involves treating titanium dental implants in fluoride solutions. Titanium is very reactive to fluoride ions, forming soluble TiF₄ species. The surface produced has a microrough topography as shown in Fig. 4. This chemical treatment of the titanium created both a surface roughness and fluoride incorporation favorable to the osseointegration of dental implants [50,51]. It has been shown that this chemical surface treatment enhanced osteoblastic differentiation in comparison with control samples [52]. Fluoridated rough implants also withstood greater push-out forces and showed a significantly higher torque removal than the control implants [50,51]. This chemical treatment may have the potential to further improve implant anchorage in bone by rendering the implant surface bioactive.

Nevertheless, chemical treatments might reduce the mechanical properties of titanium. For instance, acid-etching can lead to hydrogen embrittlement of the titanium, creating micro cracks on its surface that could reduce the fatigue resistance of the implants [53]. Indeed, experimental studies have reported the absorption of hydrogen by titanium in a biological environment. This hydrogen embrittlement of titanium is also associated with the formation of a brittle hybrid phase, leading to a reduction in the ductility of the titanium. This phenomenon is related to the occurrence of fracture mechanisms in dental implants [53].

3.4. Roughening of implants by anodization

Micro- or nano-porous surfaces may also be produced by potentiostatic or galvanostatic anodization of titanium in strong acids (H₂SO₄, H₃PO₄, HNO₃, HF) at high current density (200 A/m²) or potential (100 V). The result of the anodization is to thicken the oxide layer to more than 1000 nm on titanium. 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 nano-pores on the titanium surface [54–57]. Anodization produces modifications in the microstructure and the crystallinity of the titanium oxide layer [58]. 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 [59,60]. A higher clinical success rate was observed for the anodized titanium implants in comparison with turned titanium surfaces of similar shapes [61]. Two mechanisms have been proposed to explain this osseointegration: mechanical interlocking through bone growth in pores, and biochemical bonding [55,62]. Modifications to the chemical composition of the titanium oxide layer have been tested with the incorporation of magnesium, calcium, sulfur or phosphorus [63,64]. It has been found that incorporating magnesium into the titanium oxide layer leads to a higher removal torque value compared to other ions [55].

In summary, surface roughness plays a major role in both the quality and rate of osseointegration of titanium dental

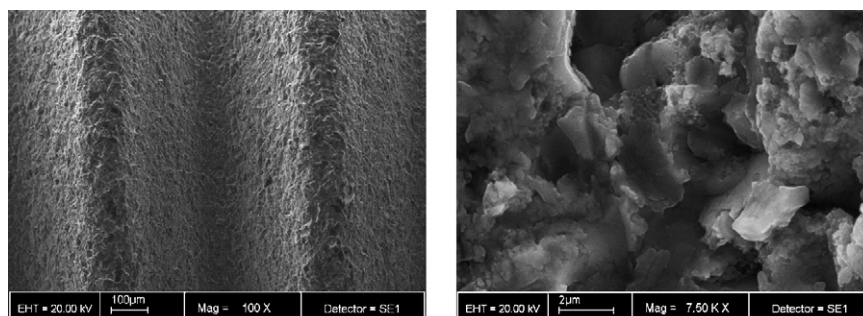


Fig. 4 – SEM micrographs of treatment of titanium dental implants in a fluoride solution surface (Courtesy of Astratech OsseoSpeed™, France).

implants. Highly roughened implants such as TPS or grit-blasted have been shown to favor mechanical anchorage and primary fixation to bone. Topographies in the nanometer range have been used to promote protein adsorption, osteoblastic cell adhesion and the rate of bone tissue healing in the peri-implant region.

4. Osteoconductive calcium phosphate coatings on dental implants

Metal implants have been coated with layers of calcium phosphates mainly composed of hydroxyapatite. Following implantation, the release of calcium phosphate into the peri-implant region increases the saturation of body fluids and precipitates a biological apatite onto the surface of the implant [65,66]. This layer of biological apatite might contain endogenous proteins and serve as a matrix for osteogenic cell attachment and growth [67]. The bone healing process around the implant is therefore enhanced by this biological apatite layer. The biological fixation of titanium implants to bone tissue is faster with a calcium phosphate coating than without [68,69]. It is well-recognized that calcium phosphate coatings have led to better clinical success rates in the long-term than uncoated titanium implants [68,70]. These long-term success rates are due to a superior initial rate of osseointegration [70]. Different methods have been developed to coat metal implants: plasma-spraying, sputter-deposition, sol-gel coating, electrophoretic deposition or biomimetic precipitation. However, only the plasma-spraying coating method has been used for titanium dental implants in clinical practice.

Plasma-spraying is a technique in which hydroxyapatite (HA) ceramic particles are injected into a plasma torch at high temperature and projected on to the surface of the titanium where they condense and fuse together, forming a film (Fig. 5). Plasma-sprayed coatings can be deposited with a thickness ranging from a few micrometers to a few millimeters. In order to obtain mechanical retention of the coating, the surface of the metallic implant must be roughened, e.g. by means of grit-blasting, 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 powder [71,72]. Several calcium phosphate phases have been observed in plasma-sprayed HA coatings such as

tricalcium phosphates (β - and α -TCP), tetracalcium phosphate, calcium oxide and amorphous calcium phosphate (ACP) [73–75]. Plasma-sprayed HA coatings are usually composed of large crystalline HA particles embedded into a highly soluble amorphous calcium phosphate phase. Moreover, the plasma-spraying technique is not very effective for coating tiny dental implants with a complex shape.

Plasma-sprayed HA-coated dental implants have also been associated with clinical problems [6,76–79]. 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 [76–79]. Coating delamination has been reported in dental situations where the efficacy of plasma-spraying is not optimal due to the size of the dental implants [6]. Loosening of the coating has also been reported, especially when the implants have been inserted into dense bone.

For all of the above reasons, the clinical use of plasma-sprayed HA-coated dental implants is limited. Plasma-sprayed HA-coated prostheses are nevertheless highly successful in orthopedics. Despite their negative reputation in dental practice, a meta-analytic review did not show that long-term survival rates were inferior for plasma-sprayed HA-coated dental implants compared to other types of dental implant [78].

5. Future trends in dental implant surfaces

A few strategies should be considered in order to improve both the short and long-term osseointegration of titanium dental implants. These future trends concern the modifications of surface roughness at the nanoscale 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.

5.1. Surface roughness at the nanoscale level

The chemistry and roughness of implant surfaces play a major role in the biological events that follow implantation. Nevertheless, surfaces are often developed using an empirical

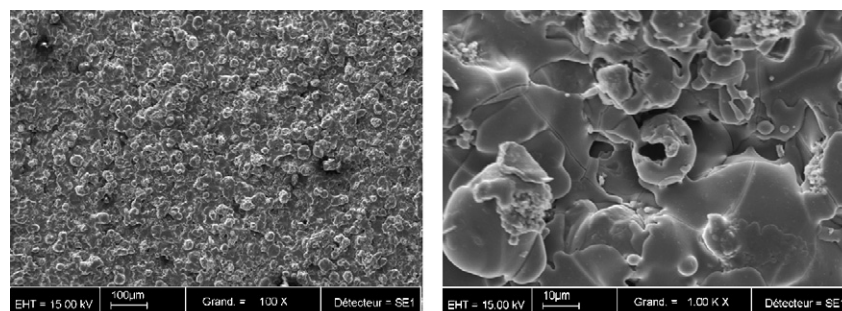


Fig. 5 – SEM micrographs of a plasma-sprayed hydroxyapatite (HA) coating surface (Courtesy of Cam Implants BV, The Netherlands).

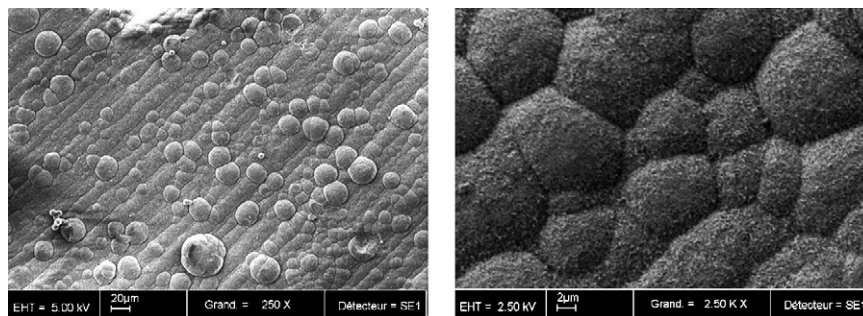


Fig. 6 – SEM micrographs of a biomimetic calcium phosphate coating.

approach with *in vitro* and *in vivo* tests. Most of the surfaces currently available have random topography with a wide range of thicknesses, from nanometers to millimeters. The exact biological role of these features is unknown because of the absence of standardized surfaces with repetitive topography at the nano-sized level (e.g. pits with fixed diameters and depth, lanes with controlled profiles). Such controlled or standardized surfaces might help to understand the interactions between specific proteins and cells. These standardized surfaces might also promote early bone apposition on the implants.

Only a few studies have reported modifications to the roughness as well as the chemistry at the nanometer scale in a reproducible manner. Most of these attempts have used processing methods from the electronic industry such as lithography and surface laser-pitting. *In vitro* experimental studies [80–82] have demonstrated that the attachment of osteoblastic cells was enhanced on submicron scale structures but not on smooth surfaces. Well-developed filopodia directly entered nanometer-sized pores for the initial attachment of the osteoblastic cells. These nanometer structures may also give the cells positive guidance by means of the selective attachment of osteoblasts to the implant surface. This selective attachment process might result in the improvement of initial healing around dental implants.

5.2. Biomimetic calcium phosphate coatings on titanium dental implants

In order to avoid the drawbacks of plasma-sprayed HA coatings (see Section 4), scientists have developed a new coating method inspired by the natural process of biomineralization. In this biomimetic method, the precipitation of calcium phosphate apatite crystals onto the titanium surface from simulated body fluids (SBF) formed a coating at room temperature (Fig. 6). In order to accelerate the deposition of coatings from aqueous solutions, several methods have been developed.

The first method involves the electrodeposition of calcium phosphate by using a current, a titanium cathode and a platinum anode [83,84]. This electrochemical method is usually conducted in acidic calcium phosphate solutions and leads to the formation of brushite coatings which are subsequently converted into apatite by hydrothermal processing. The electrochemical deposition performed in simulated body fluid buffered at neutral pH can produce a carbonated apatite coating directly on the titanium surfaces [85]. This method makes

possible perfect control of the thickness of the deposit on all kinds of complicated surfaces. The time required for coating is very short and the process presents high reproducibility and efficacy [86,87].

The second method is based on the biomimetic precipitation of calcium phosphate on titanium surfaces by immersion in SBF. This method involves the heterogeneous nucleation and growth of bone-like crystals on the surface of the implant at physiological temperatures and under pH conditions. In general, two subsequent steps have been used to enhance the heterogeneous nucleation of the Ca–P. First, the implants are treated with an alkaline in order to form titanium hydroxyl groups on the titanium surface, to serve as nucleating points [88]. Others have used high concentrations of calcium and phosphate in an increasing pH solution to form a thin layer on the titanium surface. In the second step, the coating develops under crystal growth conditions [89]. The heterogeneous nucleation and growth of the Ca–P on the titanium surface is initiated by the chemical bonding of nano-sized clusters, forming an interfacial unstructured matrix, stabilized by the presence of magnesium ions [90]. The mechanical stability of the Ca–P coating requires a rough titanium surface to ensure the mechanical stability of the coating. In addition, this physiological method broadens the variety of calcium phosphate phases that can be deposited, such as octacalcium phosphate or bone-like carbonate apatite [88,91]. It has been shown that such biomimetic coatings are more soluble in physiological fluids and resorbable by osteoclastic cells like dentin materials than high temperature coatings such as plasma-sprayed HA [91,92]. The osseointegration of titanium implants coated with biomimetic calcium phosphate has been investigated in pre-clinical comparative models. These studies have demonstrated a higher bone-to-implant contact for biomimetic calcium phosphate coatings than for uncoated titanium implants [69,93]. However, the osseointegration of titanium dental implants coated biomimetically has not yet been compared with other surface treatments in pre-clinical models.

5.3. Incorporation of biologically active drugs into titanium 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- β) superfamily, and

in particular bone morphogenetic proteins (BMPs), TGF- β 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. Experimental data, in which BMPs have been incorporated into dental implants, have been obtained from a variety of methodologies [94–99]. The limiting factor is that the active product has to be released progressively and not in a single burst. Another possibility may be the adjunction of a plasmid containing the gene coding for a BMP [100]. 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 surface of implants could also be loaded with molecules controlling the bone remodeling process. Incorporation of bone antiresorptive drugs, such as biphosphonates, might be very relevant in clinical cases lacking bone support, e.g. resorbed alveolar ridges. It has been shown recently that a biphosphonate incorporated on to titanium implants increased bone density locally in the peri-implant region [101]. The effect of the antiresorptive drug seems to be limited to the vicinity of the implant. Experimental *in vivo* studies have demonstrated the absence of negative effects but only a slight increase in dental implant osseointegration [102,103]. Other experimental studies using plasma-sprayed HA-coated dental implants immersed in pamidronate or zoledronate demonstrated a significant increase in bone contact area [104–106]. 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. However, the ideal dose of antiresorptive drug will have to be determined because the increase in peri-implant bone density is biphosphonate concentration-dependent [106].

6. Conclusion

There are a number of surfaces commercially available for dental implants. Most of these surfaces have proven clinical efficacy (>95% over 5 years). However, the development of these surfaces has been empirical, requiring numerous *in vitro* and *in vivo* tests. Most of these tests were not standardized, using different surfaces, cell populations or animal models. The exact role of surface chemistry and topography on the early events of the osseointegration of dental implants remain poorly understood. Furthermore, comparative clinical studies with different implant surfaces are rarely performed. The future of dental implantology should aim at developing surfaces with controlled and standardized topography or chemistry. This approach is the only way to understand protein, cell and tissue interactions with implant surfaces. The local release of bone-stimulating or resorptive drugs in the peri-implant region may also respond to difficult clinical situations with poor bone quality and quantity. These therapeutic strategies should ultimately enhance the osseointegration process of dental implants for their immediate loading and long-term success.

Acknowledgements

The authors acknowledge Straumann AG (Bern, Switzerland) for providing the SLA samples, Astra Tech (Astra Zeneca, Rueil-Malmaison, France) for providing the TiOblast™ and OsseoSpeed™ samples. Cam Implants BV (Leiden, The Netherlands) is also acknowledged for providing the TPS and HA plasma-sprayed samples. We also thank Paul Pilet from the Microscopy Centre for SEM pictures and Kirsty Snaith for grammar corrections of the manuscript.

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