Surface Aspects of Titanium Dental Implants

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1. Introduction

This book chapter presents a brief description of a new emerging field of science, the biological surface science and stresses its importance in the field of alloplastic materials and dental implants. It is not intended to present a comprehensive review of the field, but rather to indentify some important trends and directions in the surface modifications of titanium (Ti) dental implants targeting the improvement of their bio/osseointegration (second subchapter). The third subchapter outlines the impact of fluoride on surfaces of titanium implants or other dental devices. The fourth one will give an overview of the effects of some chemical cleaning agents on titanium implant surfaces. The interaction between Ti and fluoride containing prophylactic agents or chemical cleaning agents can result in a beneficial or/and destructive alteration of the surface of Ti dental appliances. The objective of our studies was to characterize these specific modifications and alterations of Ti surfaces. The fifth subchapter focuses on the relation between biological surface science and dental implants related research.

2. Improving osseointegration of titanium implants by surface modifications - latest trends

These days much effort goes into the design, synthesis, and fabrication of Ti dental implants to obtain a long term (lifelong) secure anchoring in the bone. First of all, implants must carry and sustain the dynamic and static loads they are subjected to. The bulk structure of the material governs this ability. Evidently, it is important to achieve a proper function with the shortest possible healing time, with a very low failure rate, and with minimal discomfort for the patient. These factors are important for cost reasons, too.

The success and the long-term prognosis of dental implants depend mainly on three factors: 1) on the anchorage of the artificial root in the host bone, i.e. on the osseointegration; 2) on the peri-implant mucosal seal; 3) finally on the adequate loading of the implant, transmitted by the abutment, i.e. the biomechanical factor (Figure 1.) (Adell et al., 1981; Brånemark, 1983a; Davies, 1998).

During osseointegration, which is the formation of a direct connection between the living bone and the surface of the load-carrying implant, strong links must be formed between the biomaterial and the surrounding bone tissue (Binon et al., 1992; Cochran, 1999; Morra & Cassinelli, 1997; Olefjord & Hansson, 1993).
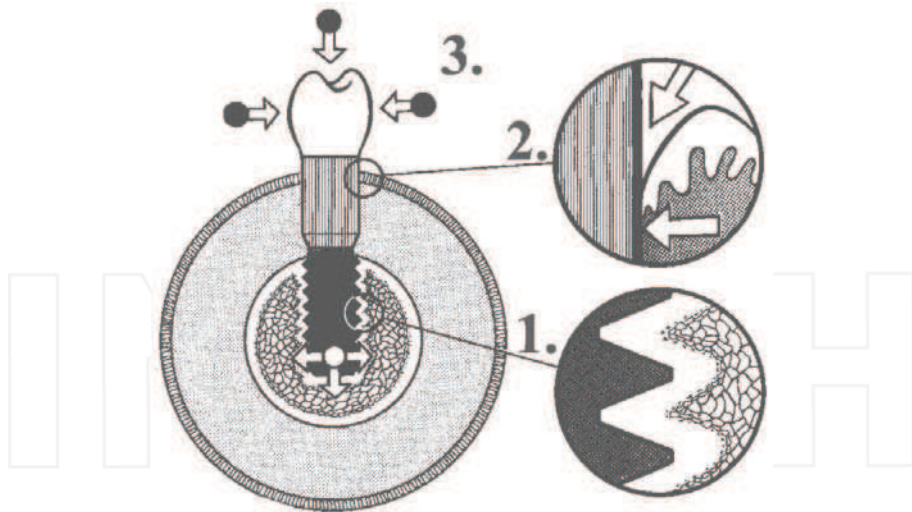
Fig. 1. Scheme of biointegration of a dental implant, representing osseointegration (1), mucosal seal (2) and biomechanical forces (3).

The family of Ti and its alloys represent a major class of materials successfully applied in prosthetic dentistry, dental implantology, and orthopaedics just because they meet the most important requirements of alloplastic materials (Brånemark et al., 1983b; Meffert et al., 1992).

Ti has been used in dentistry for over 30 years; its use in surgery was reported even earlier: in 1947 J. Cotton introduced Ti and its alloys as implants with medical applications. It is the sevenths most frequent metal in the earth's crust and it is a quite light material. Its density is 4.5 g/cm^3, considerably less than that of other metals used in dentistry, like gold (19.3 g/cm^3) or CoCrMo alloy (8.5 g/cm^3). In its unalloyed condition, Ti is as strong as steel, but it is 45% lighter (density of stainless steel is 7.9 g/cm^3). Its melting point is 1672-1727°C, and its other thermal properties (like thermal conductivity) are similar to those of the dental tissues. The Vickers Hardness Number (VHN) of Ti is 210, similar to gold alloys type III, IV (hard): 135-250. Ti6Al4V alloy has a VHN of 320 which is close to the value of CoCr alloys: 350-390 (Wang & Fenton, 1996; O'Brien, 2002).

Commercially pure (CP) Ti is available in four grades, which vary according to the oxygen (0.18 to 0.40 weight percent) and iron (0.20 to 0.50 weight percent) contents. These slight concentration differences have a substantial effect on the physical properties of the metal. Oxygen, in particular, has a great influence in the ductility and strength of Ti (Park & Kim, 2000; O'Brien, 2002).

To alter its properties, Ti can be alloyed with a wide variety of elements (Al, V, Nb, Zr), that can improve its strength, high temperature performance, creep resistance, weldability, response to ageing heat treatments, and formability.

Ti is a dimorphic allotrope: while at room temperature CP Ti has α-phase (HCP-hexagonally closed packed), above 883°C a body centred cubic (BCC), the β–phase will form (allotropic phase transformation). The β–form is stronger but more brittle than α–phase (Lautenschlager & Monaghan, 1993).

The two most useful properties of this metal are exceptional corrosion resistance and the highest strength-to-weight ratio of any metal (Lautenschlager & Monaghan, 1993; O'Brien, 2002; Park & Kim, 2000; Wang & Fenton, 1996).

Ti and its alloys are resistant to corrosion because of the formation of an insoluble and continuous titanium oxide layer on the surface (Figure 2) having one of the highest heats of reaction: $\Delta H = -912$ kJ/mol. In air, the oxide (usually TiO_2), begins to form within nanoseconds (10^{-9} s) and reaches a thickness of 20–100 Å already in 1 s. It is very adherent to the parent Ti, protects the metal from other impurities and it is impenetrable to oxygen. (Lautenschlager & Monaghan, 1993). TiO_2 may be catalytically active for a number of organic and inorganic chemical interactions influencing biological processes at the implant interface: the TiO_2 oxide film permits a compatible layer of biomolecules to attach. Explanations for that are still largely unidentified, but the high dielectric constant ($\varepsilon = 50\text{-}170$) of TiO_2 versus 4-10 for alumina and dental porcelain can outcome in considerably stronger van der Waals bonds between molecules and TiO_2 than other oxides. It is the nature of this surface layer that is thought to give titanium its excellent biocompatibility (Lautenschlager & Monaghan, 1993).
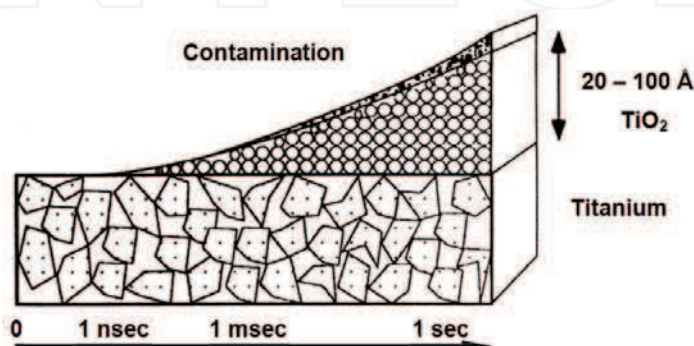

Fig. 2. Formation of an insoluble 20–100 Å thick TiO_2 layer on the surface of metal titanium.

Both CP Ti and Ti6Al4V own exceptional corrosion resistance for a wide range of oxide states and pH levels (Wang & Fenton, 1996). However, even in its passive condition, Ti is not totally inert. Its ions are released due to the chemical dissolution of titanium dioxide. Elevation of implant elements in blood can be observed for Ti6Al4V (measured in the fibrous membrane encapsulating implants), but they are non toxic: 21 ppm Ti, 10.5 ppm Al, 1 ppm V (Puleo & Nanci, 1999).

The strength of the material varies between a much lower value than that of 316 stainless steel or the CoCr alloys and a value about equal to that of annealed stainless steel of the cast CoCrMo alloy. But comparing its specific strength (yield strength per density) Ti alloys exceed any other implant materials. Ti, however, has poor shear strength making it less advantageous for bone screws, plates and similar applications (Park & Kim, 2000).

Ti also has the advantage that its mechanical properties (like elastic modulus) are closer to those of bone than are those of other metals, like stainless steel or CoCr alloys. Although its shear strength is too low for use in major load-bearing applications, it remains the material of choice for dental implants.

Although the bulk properties (mechanical and thermal characteristics) of biomaterials are important with respect to their biointegration, the biological responses of the surrounding

tissues to dental implants are controlled mostly by their surface characteristics (chemistry and structure) because biorecognition takes place at the interface of the implant and host tissue. Biological tissues interact mainly with the outermost atomic layers of an implant which is about 0.1-1 nm thick. The molecular and cellular events at the bone-implant interface are well described in Puleo & Nanci, 1999 and Kasemo, 2002 but many crucial aspects are still far from being understood (Kasemo, 2002; Puleo & Nanci, 1999). Although our knowledge regarding the molecular structure of the bone-implant interface has evolved much in the last decade there are still many uncertainties (Klinger et al., 1998).

Justification of the surface modification of implants is therefore straightforward: to retain the key physical properties of an implant while modifying only the outermost surface to control the bio-interaction. As a result, a lot of research work is devoted to elaborate methods of modifying surfaces of existing implants (biomaterials) to achieve the desired biological responses.

These responses can be several: in case of a healthy patient a regular osseointegration process, but in case of elder or even ill patients a smaller bone quantity or not ideal bone quality means a handicap in biointegration. These cases are often avoided by patient selection. As the average human lifespan is growing, ever more people need tooth replacement using Ti dental implants. The demand is increasing to speed up the otherwise long osseointegration period (3-6 months) to rehabilitate the damaged chewing apparatus of the patients as soon as possible even for people in a worse than average health status.

The question of optimally functionalized Ti implant surface is very complex, not only for the above mentioned problems, but also because a dental implant has several different functional parts (root and neck), which are in contact with different biological tissues: alveolar bone, connective and epithelial tissue (Figure 3.). Usually a smooth surface is developed for epithelial attachment and to prevent plaque formation, a machined or rough oblique part for proper connective tissue attachment, and a rough surface for anchorage in the bone (Figure 3.).
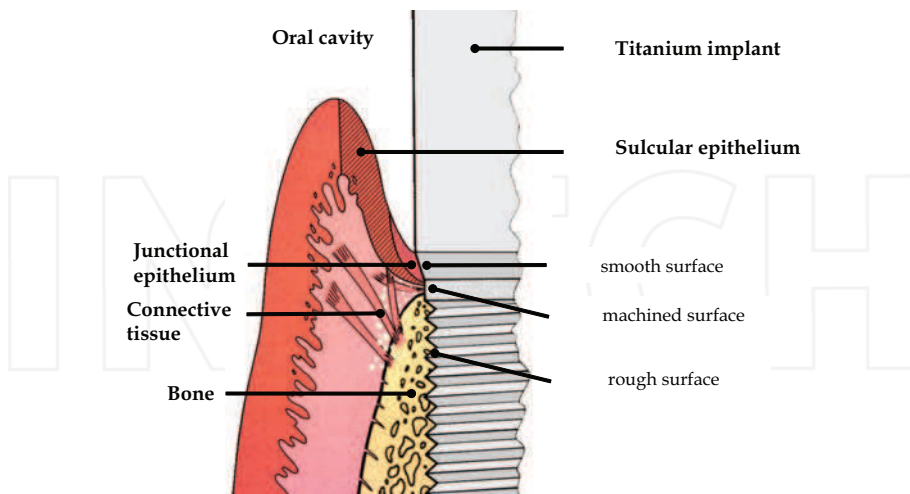

Fig. 3. The different types of biological tissues (epithelial, connective tissue, alveolar bone) in contact with the Ti implant will determine the ideal features of the surface of the implant at its given position.

The optimal implant surface is different for any given purposes, thus, when the goal is to develop an implant surface, then the targeted functional part and the purpose of the modification has to be specified.

For dental implants, likewise to biomaterials, bio- and osseointegration processes can be controlled at molecular and cellular level by the modification of the implant surface. There are several possible surface modifications, usually classified as **physicochemical and biochemical methods** (Puleo & Nanci, 1999).

Many of the surface modifications are in experimental stage and the *in vitro*, *in vivo* or clinical studies are still ahead. It is our belief that these surfaces will represent a huge positive contribution to clinical implant science, especially if we target the elder or ill patients.

2.1 Physicochemical methods

The most common physicochemical treatments are chemical surface reactions (e.g.: oxidation, acid-etching), sand blasting, ion implantation, laser ablation, coating the surface with inorganic calcium phosphate, etc. These methods are altering the energy, charge, and composition of the existing surface but they will provide surfaces with modified roughness and morphology as well (Ratner & Hoffman, 1996).

Surface energy/charge/composition/morphology is amongst the physicochemical characteristics, which can be altered in numerous ways. The surface energy (or surface wetting capability) plays an important role not only in protein adsorption, but also with respect to cell attachment and spreading (Baier & Meyer, 1988). This physical property can be determined by measuring the contact angles formed with the surface by different liquids. The surface charge influences both the molecular or cellular orientation and the cellular metabolic activity (Meyle, 1999).

One of the best examples demonstrating the importance of hydrophilic and hydrophobic properties of surfaces is the SLActive surface of Straumann implant. Neutralization of the implant in nitrogen atmosphere and storage in NaCl solution assures a hydrophilic surface with good clinical results. These implants present higher implant stability in the critical treatment period of 2 to 4 weeks (Eriksson et al. 2004; Buser et al. 2004).

Ion implantation methods are generally used to improve the mechanical quality of an implant. For example, iridium was ion implanted in Ti6Al4V alloy to improve its corrosion resistance and implanting nitrogen into Ti reduces wear significantly (Buchanan et al., 1990; Sioshansi, 1987).

The roughness (R_a) of the implant surface plays a significant role in anchoring cells and connecting the surrounding tissues, thereby leading to a shorter healing period. These surfaces display advantages over smooth ones as the area of contact with the bone is enlarged by micro-structuring the implant surface. Creation of mechanical interlocking accelerates bone ingrowths (Cochran et al., 1998; Joob-Fancsaly et al., 2004; Santis et al., 1996). The influence of R_a on growth of the different cells has been studied by many authors and it is known that epithelial cells do not attach so strongly to acid-etched or sand-blasted surfaces as to smooth (polished, $R_a < 0.5$ µm) surfaces, while fibroblasts adhere as well to

rough (as machined) and even smooth surfaces (Klinge & Meyle, 2006). Surfaces with a smooth topography promote epithelial cell growth, spreading, and the production of focal contacts on Ti surfaces (Baharloo et al., 2005).

Larsson et al. carried out implantation in rabbit bone, concluding that the surface roughness and the oxide thickness affect the rate of bone adhesion in the early stages of implantation (1-7 weeks) (Larsson et al., 1994; Larsson et al., 1996).

Other authors suggest that the metabolic activity (the production of osteocalcin, prostaglandin E2 (PGE2) and transforming growth factor-β1 (TGF-β1) or alkaline phosphatase activity) of osteoblast-like cells is significantly increased on rough (sand-blasted, etched or plasma-sprayed) surfaces. It has been concluded that the surface roughness may modulate the activity of cells interacting with an implant and thereby affect the bone-healing process (Boyan et al., 1998; Meyle, 1999)

Acid-etching, sand blasting and Ti plasma-spraying are typical methods for developing rough surfaces. These are well documented using *in vitro* and *in vivo* methods and are already applied in the production of dental implants (Buser et al. 1991; Wennerberg et al., 1997; Wong et al., 1995).

To increase the roughness of solid surfaces, a number of laser-based techniques have been applied in the last decade (Bauerle, 2000; Joob-Fancsaly et al., 2000). The advantages of using lasers for ablation of surfaces are the precise control of the frequency of the light, the wide range of frequencies available, the high energy density, the ability to focus and raster the light and the ability to pulse the source and control reaction time. Lasers commonly used for surface modification include ruby, Nd:YAG, argon, CO_2 and excimer. Recent studies on the laser machining of dental implants revealed that an appropriate structure with minimum contamination could be achieved by means of laser treatment (Gaggl et al., 2000; Pető et al., 2001). After multipulse irradiation with a focused Nd:YAG laser beam, a crown-like structure formation was observed on the Ti surface (György et al., 2002). An efficient oxidation of Ti by Nd:YAG laser irradiation was reported (Nánai et al. 1997; Perez del Pino et al. 2002). In addition to the prompt, intense heating of the surface, excimer laser illumination may also enhance the sterilizing effect as a consequence of the high dose of UV light (Bereznai et al., 2003).

Our group has developed two kinds of physicochemical surface modifications of Ti implants: laser surface modifications (ablation and polishing) and octacalcium phosphate layer deposition on the surface of implants (Bereznai et al., 2003; Szekeres et al., 2005). The properties of these modified surfaces were investigated by modern surface science techniques (atomic force microscopy (AFM), scanning electron microscopy (SEM), and X-ray photoelectron spectroscopy (XPS)). These experiments demonstrated that excimer laser ablation effectively increased the surface area available for the attachment of bone-cells and also raised the thickness of the TiO_2 layer (Figure 4.). In addition, XPS measurements showed that the UV light of the excimer laser effectively sterilized the surface. Amongst the most promising surface modifications that could enhance the osseointegration of dental implants are the laser modifications, as proven by our preliminary *in vitro* (cell culturing) results.
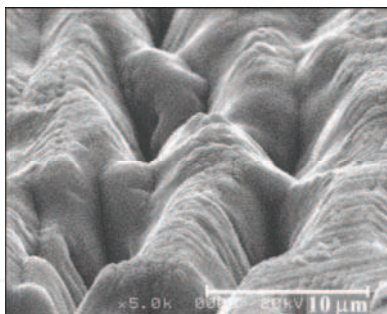
Fig. 4. SEM image of ablated holes formed on a titanium surface with 0.5 ps pulses of a KrF excimer laser. The laser fluence was 2.4 J/cm² and 1000 shots were applied (Bereznai et al., 2003).

The importance of these studies is further enhanced by the fact, that they involve laser technologies, which already have numerous industrial applications. However, even these techniques must still be refined, since medical applications require high accuracy in determination of both mechanical and chemical characteristics of the surface.

Despite of some positive indications from *in vitro* studies, the effectiveness of these two latter mentioned methods (ion implantation and laser-based methods) have not yet been investigated sufficiently under *in vivo* conditions.

Inorganic materials, such as bio-reactive calcium phosphate (or hydroxyl-apatite – HAP) coatings, have been applied extensively because of their chemical similarity to bone minerals. Several studies showed that these coatings achieve a very intimate contact between the implant and bone (Hench, 1996; Rohanizadeh et al., 2005; Sun et al., 2001; Szabo et al., 1995). Clinical investigations reported a high degree of success with HAP-coated implants, reducing the healing period (Block et al, 1996). However, in other studies HAP-coated implants showed signs of peeling off the covering material from the implant surface which may induce foreign body reactions (Buser et al. 1991; Matsui et al. 1994).

Furthermore, the long-term clinical study of Wheeler SL. (1996) on HAP-coated oral implants reported a significantly lower survival rate (77.8% after 8 years) for HAP-coated implants as compared to the Ti-plasma-sprayed (TPS)-coated implants (92.7%) (Wheeler, 1996). Biodegradation of these coatings may be the reason why HAP-coated implants are no longer the surface modifications of choice.

2.2 Biochemical methods

In addition to the physicochemical methods, biochemical techniques have currently generated a great deal of interest. Today we struggle to produce biomaterials that interact with specific targets within the body or mimic tissue architecture. It is well known that biological systems have a highly developed ability to recognize special features of the surface on the molecular scale. We look to nature when we design "biomimetic" materials to understand how cells interact with other cells, extracellular proteins, and tissues. This knowledge is then utilized to develop bio-mimetic strategies for functional, interactive biomaterials. These strategies include biodegradable and "smart" materials used in targeted

drug delivery systems and tissue engineering, as well as biochemical modifications of biomaterial surfaces for implant or wound-healing applications (Dillow & Lowman, 2002; de Jonge et al., 2008).

In case of implants the goal of biochemical methods is to immobilize peptides, proteins, enzymes on the surface in order to induce specific cell and tissue responses (adhesion, signaling, stimulation) and to control the tissue-implant interface with molecules delivered directly there (Hoffman, 1996; Ito et al., 1991; Puleo & Nanci, 1999).

A lot of different, biologically functional molecules can be immobilized onto Ti surfaces to enhance bone regeneration at the interface of implant devices. An essential aspect is to maintain the bioactivity (or the recognizable binding site) of these molecules while incorporating them into a biomimetic coating (Dillow & Lowman, 2002).

Immobilization of bio-molecules can be achieved by physical absorption (van der Waals or electrostatic interactions), physical entrapment (use of barrier systems) and covalent attachment. The selection of the immobilization method depends on the working mechanism of the specific bio-molecules which dictates, for instance, a short-term, transient immobilization for growth factors and a long-term immobilization for adhesion molecules and enzymes.

Anchoring of proteins to Ti surfaces was previously achieved by direct adsorption onto the surface, but such physical adsorption frequently induces denaturation and loss of the functional activity of the protein (Hoffman, 1996). To eliminate these problems, our group developed a self-assembled polyelectrolyte (PE) multilayer film (Pelsőczi et al, 2005). The film is made by alternating adsorption of poly-cations (poly-L-lysine (PLL)) and poly-anions (poly-L-glutamic acid (PGA)) from aqueous solution onto a charged, solid surface (in our case, Ti surface, Figure 5.). PE film coatings modify the solid/liquid interface in such a way as to ensure a proper environment for the adsorption of proteins. The alternating adsorption technique has been successfully applied in different fields of science, as a consequence of its numerous practical applications. It can be automated, it involves the use of aqueous solutions, it is environment-friendly, and various substrates can be covered with films of readily variable thickness.
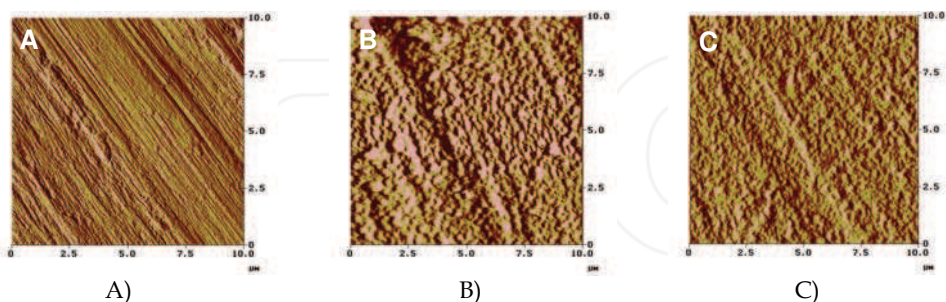

A)   B)   C)

Fig. 5. Typical AFM deflection images of Ti substrate and PE layers on Ti (*in situ* measurements). A) Bare Ti, $z = 500$ nm; B) (PLL/PGA)$_6$ multilayer, $z = 800$ nm; and C) (PLL/PGA)$_8$ film, $z = 1.5$ μm (Pelsőczi et al, 2005).

The inorganic calcium phosphate coatings as well as the purely organic components of bone can serve as carrier systems for osteogenic drugs, rendering them osteoinductive as well as

osteoconductive. The most promising candidates for osteogenic agents are the members of the transforming growth factor β (TGF-β) superfamily, such as bone morphogenic proteins (BMPs). BMP-2 has been successfully coprecipitated with the inorganic components and, thus incorporated, retains its biological activity *in vitro* (Liu et al, 2004).

At present four major strategies exist for organic coating approaches: immobilization of extra cellular matrix (ECM) proteins (collagen, etc.) or peptide sequences as modulators for bone cell adhesion, deposition of cell signaling agents (bone growth factors) to trigger new bone formation, immobilization of DNA for structural reinforcement and enzyme-modified Ti surfaces for enhanced bone mineralization (de Jonge et al., 2008).

The cell membrane receptor family of integrins is involved in cell adhesion to ECM proteins. These integrins bind to specific amino acid sequences within ECM molecules, in particular to RGD (arginine-glycine-aspartic) sequence. For this reason the most commonly used peptide sequence for surface modification is the above mentioned cell adhesion motive (Ferris et al, 1999; Schliephake et al, 2005).

The structural properties of DNA show high potential for application as biomaterial coating, regardless of its genetic information. Additionally, DNA can be used as a drug delivery system since its functional groups allow incorporation of growth factors. The studies of Beucken et al., 2007 proved that DNA-based coatings improved the deposition of CaP (van der Beucken et al., 2007).

A relatively new approach for surface modification is the enzyme-modified titanium surface to enhance bone mineralization along the implant surface. Especially, the enzyme alkaline phosphatase (AP) is known to increase the local concentration of inorganic phosphate, and to decrease the concentration of extracellular pyrophosphate, a potent inhibitor of mineralization (Golub & Boesze-Battaglia, 2007).

In the last decade another viable bio-mimetic strategy appeared, the organic-inorganic composite coatings. These mimic the bone structure, which is composed of an organic matrix (90% of which are collagenous proteins) and an inorganic CaP phase. Collagen-CaP (Morra et al., 2003), growth-factor-CaP (Liu et al., 2007) and polyelectrolyte multilayers-CaP (Sikirić et al., 2008) composite coatings were developed until now with promising *in vitro* and *in vivo* experimental results.

As in the case of physicochemical surface modifications, many of the biochemical methods described above are in experimental stage yet and their *in vivo* or clinical studies are still ahead.

3. Impact of fluoride on surfaces of titanium implants or other dental devices

Endosseous dental implants and surgical implants for fixating or replacing hard tissue are made from ''commercially pure'' Ti (CP Ti) and the most common Ti alloy, Ti6Al4V (Mändl et al., 2005; Park & Kim, 2000). Ti is also used in prosthetic dentistry to manufacture crowns and multiple-unit fixed restorations (Huget, 2002; Wang & Fenton, 1996), and in orthodontic dentistry to produce Ti brackets (Harzer et al., 2001).

Dental arch wires and orthopedic braces are usually made from the special TiNi shape memory alloy (Mändl et al., 2005; Park & Kim, 2000).

Ti and its alloys are resistant to corrosion because of the formation of an insoluble TiO_2 layer on the surface, as described earlier. Oxidative agents are well known to exert a corrosive effect on the alloys used in dentistry, with the exceptions of Ti and other bioinert materials. Indeed, oxidative processes can thicken and condense the TiO_2 layer on the surface, improving the corrosion stability of the underlying Ti. On the other hand, reductive agents, such as fluoride (F^-), may have the opposite effect and attack this layer. Strietzel et al., demonstrated that Ti ion release was enhanced in the presence of F^-, and this effect was even further accelerated at low pH (Strietzel et al., 1998). High F^- concentrations and an acidic pH are known to impair the corrosion resistance of Ti (Toumelin-Chemla et al., 1996), and as a result crevice and pitting corrosion occur (Reclaru & Meyer, 1998; Schiff, et al., 2002).

Patients regularly use different oral care products containing F^-, such as toothpastes, rinsing solutions, or prophylactic gels. The Ti alloys applied in the form of orthodontic wire (Huang, 2007; Walker et al., 2005) or as the framework of a prosthesis, therefore come into contact with a wide range of preventive agents and these F^--containing materials can attack the surface of Ti (Boere, 1995; Siirilä & Könönen, 1991).

SEM investigations have revealed that topical F^- solutions can cause stress corrosion cracking on CP Ti (Könönen et al., 1995) Galvanic corrosion has been reported to occur between orthodontic wires and brackets (NiTi and CuNiTi) immersed in fluoride mouthwashes (Schiff et al., 2006).

Such corrosion has two undesirable consequences: the mechanical performance of the wire-bracket system deteriorates, and the risk of local Ni^{2+} release is increased.

Moreover, such F^--containing agents may come into contact with the neck part of dental Ti implants, which may extend into the oral cavity (Fig. 3). The long-term success of dental implants depends to a large extent on the gingival attachment to the neck of an implant. This mucosal seal ensures protection against bacterial attack and other injurious effects exerted by the oral environment. The epithelial attachment (junctional epithelium) may be anchored onto a rough or a smooth surface by hemidesmosomes through a preformed glycoprotein layer. A rough surface is more favorable for the plaque accumulation in the peri-implant crevices of the gingiva, which is an undesired effect in this very sensitive region of the implant. Accordingly, to avoid pathogenic plaque accumulation, the neck of an implant must be polished (Bollen et al., 1996; Vogel, 1999). From this respect, it is easy to realize the great importance of the maintenance of the continuity of these surfaces.

In 1999, Nakagawa et al. found a relation between the F^- concentration and the pH at which the corrosion of CP Ti occurred (Nakagawa et al., 1999). The results of their anodic polarization and immersion tests indicated that the corrosion of Ti in a F^--containing solution depends on the concentration of hydrofluoric acid (HF). The passivation film on Ti was destroyed when the HF concentration in the solution was > 30 ppm. In 1995, Boere had demonstrated that the corrosion of Ti is enhanced in an acidic environment, because F^- in solution combines with H^+ to form HF, even if the NaF concentration is low (Boere, 1995). Nakagawa et al. investigated the corrosion behaviour of Ti alloys: Ti6Al4V, Ti6Al7Nb, and the new alloy Ti-0.2Pd (Nakagawa et al., 2001). Their experimental results demonstrated that even a low F^- concentration causes corrosion in an acidic environment. If Ti alloy contains at least 0.2% Pd, this process does not take place. The high corrosion resistance of this alloy is because of the surface enrichment of Pd promoting the repassivation of Ti.

The studies by Huang (Huang, 2002) indicated that, when the NaF concentration was >0.1%, the protectiveness of TiO_2 on Ti was destroyed by F^-, leading to the severe corrosion of Ti. In 2003, Huang investigated the effects of F^- and albumin concentrations on the corrosion resistance of Ti6Al4V in acidic (pH 5) artificial saliva (Huang, 2003). The XPS results showed that when the NaF concentration was >0.1%, a hexafluorotitanate complex (Na_2TiF_6) was formed on the Ti surface, which destroyed the stable TiO_2 layer.

As the pH of the rinses and gels used for caries prevention in dentistry ranges from 3.5 up to neutral, and the F^- concentration in these materials is between 1000 and 10,000 ppm (Nakagawa et al., 1999), it is essential for the dental practitioner to know whether a F^--containing material can attack the Ti surface or can modify the corrosion resistance of the Ti surface of a dental implant, a prosthesis, or the wires of orthodontic braces. Besides 0.1–0.15% (1000–1500 ppm) F^-, toothpastes contain other constituents, such as rubbing, cleaning, foaming materials, and calcium complexes, which reduce the effectiveness of toothpastes by 25–50% (Neubert & Eggert, 2001).

Although all the above-mentioned studies point to the deleterious effect of F^--containing prophylactic gels, there are a huge number of data documenting that F^- exerts a bone-promoting activity. Ellingsen et al. proved that, when F^- is incorporated in the TiO_2 layer, the retention of implants is significantly increased, even as compared with rough surface implants (Ellingsen, 1995; Ellingsen et al., 2004). The success of a TiO_2-blasted surface with a F^--modified TiO_2 layer (OsseoSpeed implants, Astratech) is because of the ability of the F^- coating to stimulate the bone response, leading to binding between Ti and the phosphate from tissue fluids. The free F^- catalyzes this reaction and induces the formation of fluoridated hydroxyapatite and fluorapatite in the surrounding bone (Ellingsen, 1995). The studies by Cooper et al., demonstrated that the F^- modification of TiO_2 grit-blasted CP Ti surfaces enhanced osteoblastic differentiation and interfacial bone formation (Cooper et al., 2006).
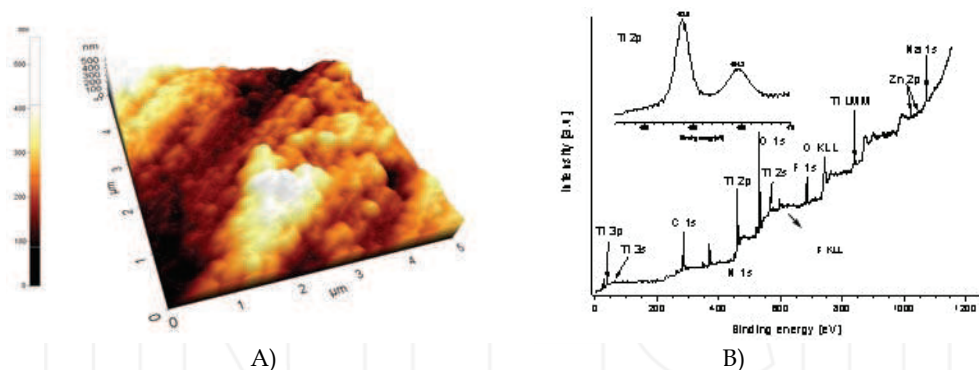

Fig. 6. 3D AFM picture (A) of a Ti disc treated with gel (12,500 ppm F^-, pH 4.8), reveals deep corrosive regions and granular forms. Image size: 5 x 5 µm. Typical XPS spectra of gel-treated Ti discs (B). Three new peaks can be observed on the spectra originating from Na_2TiF_6, which modifies the TiO_2 layer of the surface (Stájer et al., 2008).

In our study (Stájer et al., 2008), the effects of different F-containing caries-preventive prophylactic rinses and gels on the surface structure and roughness of CP Ti were investigated, through the use of XPS and AFM. A further aim was to survey the attachment

and proliferation of human epithelial cells after treatment of the Ti surface with an acidic NaF solution, a widely used F^--containing mouthwash or a gel. The epithelial cell attachment and proliferation were examined by means of dimethylthiazol-diphenyl tetrazolium bromide (MTT) and protein content assays. For the visualization of cells, SEM was applied. The results of this study proved that aqueous 1% NaF solution (3800 ppm F^-, pH 4.5) or high (12,500 ppm) F^- content gel (pH 4.8) strongly corroded the surface and modified its composition (Figure 6.). XPS revealed formation of a strongly bound F^--containing complex (Na_2TiF_6). AFM indicated an increase in roughness (R_a) of the surfaces: 7-fold for the NaF solution and smaller for the gel or a mouthwash (250 ppm F^-, pH 4.4). MTT revealed that cell attachment was significantly increased by the gel, but was not disturbed by either the mouthwash or the NaF. Cell proliferation determined by MTT decreased significantly only for the NaF treated samples; protein content assay experiments showed no such effect. This study indicates that epithelial cell culturing results can depend on the method used, and the adverse effects of a high F^- concentration and low pH should be considered when prophylactic gels are applied by patients with Ti implants or other dental devices.

4. Effects of chemical cleaning agents on titanium implant surfaces

The failure of dental implants is caused mainly by the inflammatory processes affecting the soft and hard tissues of the oral cavity, as the lifetime of such implants rely on the responses of the various surrounding tissues (the alveolar bone, or the conjunctive and epithelial parts of the mucosa, Figure 3.) (Norowski & Bumgardner, 2009).

Peri-implant infections involve peri-implant mucositis, defined as a reversible inflammatory change of the peri-implant soft tissues without bone loss, and peri-implantitis, an inflammatory process resulting in loss of supporting bone and associated with bleeding and suppuration (Norowski & Bumgardner, 2009; Renvert et al., 2008b; Zitzmann & Berglundh, 2008).

Several studies have evaluated peri-implant infections, but only a few were cross-sectional and provide information on the prevalence of peri-implant diseases among patients with implants functioning for approx. 10 years. The incidence of peri-implant mucositis has been reported to be in the range of 60% of implant recipients and in 48% of implants (Renvert et al., 2007; Roos-Jansaker et al., 2006a). The prevalence of peri-implantitis was found to be around 15, 16 and 28% with respect to the recipients (Fransson et al., 2005; Renvert et al., 2007; Roos-Jansaker et al., 2006a), and 7 and 12% regarding implant sites (Fransson et al., 2005; Roos-Jansaker et al., 2006a). The differences in the prevalence of peri-implantitis may be explained by differing criteria used for the diagnosis of peri-implantitis, as well as variations in maintenance procedures (Fransson et al., 2008; Zitzmann & Berglundh, 2008).

The etiology of marginal peri-implantitis is based mainly on an infectious factor and a biomechanical factor (Uribe et al., 2004). Although the causes may differ in both cases, microbial colonization occurs on the surface of the implant (Renvert et al., 2008b; Kotsovilis et al., 2008). If the conditions become pathogenic, bacteria start to proliferate, leading to inflammation around the implant. Peri-implant diseases have been primarily linked to Gram-negative anaerobic microflora (Leonhardt et al. 1999). The process is aggravated by microorganism colonization and their toxins, and extensive bone destruction will occur. The inflammation spreads apically thus, in very severe cases, therefore, the patient may lose the implant. Methods which remove the bacteria and the toxins from the surface of challenged implants would prevent or terminate the development of peri-implant bony defects.

The therapy of peri-implantitis in the surgical phase is a complex process, starting with surgical debridement of devitalized peri-implant tissue and continuing with decontamination of the exposed implant surface. The implant surface can be cleaned by mechanical (an air-powder abrasive) or chemical (citric acid, H_2O_2, chlorhexidine digluconate (CHX) or EDTA) procedures or with laser irradiation (CO_2, diode, Er:YAG or Nd:YAG) (Roos-Jansaker et al., 2003; Schwarz et al., 2006). To support antimicrobial treatment, topical and/or systemic antibiotics may be administered (Roos-Jansaker et al., 2003). After removal of damaged tissues from the peri-implant pocket, surgical treatment (guided tissue regeneration with or without the use of bone grafts and barrier membranes) promotes regeneration of any bone defect (Khoury & Buchmann, 2001; Roos-Jansaker et al., 2003).

For the chemical detoxification of implants, various cleaning solutions are used: CHX, H_2O_2, citric acid, phosphoric acid gel, delmopinol, ListerineR, iodine, saline irrigation, beta-isodona, chloramine-T, etc. Besides these chemical agents, a number of systemic antibiotics can be applied to support the therapy: e.g. tetracycline, amoxicillin, augmentin, metronidazol, penicillin, etc. (Roos-Jansaker et al., 2003; Zitzmann & Berglundh, 2008).

CHX is a commonly administered antimicrobial agent with a wide range of medical applications. It is used in dentistry as a mouthwash and topical antimicrobial. In the treatment of peri-implantitis it can serve as a rinsing solution (Abu-Ta'a et al., 2008; Roos-Jansaker et al., 2006b) or more often as an implant irrigation solution, in combination with systemic antibiotics (Khoury & Buchmann, 2001; Roos-Jansaker et al., 2003). Renvert et al. investigated the difference in effectiveness of minocycline microspheres and CHX gel, and concluded that the adjunctive use of these microspheres led to improved probing depths and bleeding scores, CHX alone resulting in only a limited reduction of the bleeding scores (Renvert et al., 2006; Renvert et al. 2008a). CHX is also effective in the surgical treatment of late peri-implant defects using guided tissue regeneration (Hämmerle et al., 1995; Schou et al., 2003a).

Recognizing the increasing interest in the functionalization of dental implant surfaces with antimicrobial agents prior to implantation, Barbour et al. investigated the adsorption of CHX to TiO_2 crystals of anatase and rutile (Barbour et al., 2007). Their results proved that CHX in 4-morpholinoethanesulphonic acid (MES) and phosphate-buffered saline (PBS) buffers adsorbed rapidly to anatase and rutile TiO_2, equilibrium being attained in less than 60 sec, with gradual desorption over a period of several days. More CHX adsorbed to anatase than to rutile, and the CHX desorbed more rapidly from anatase than from rutile, depending on the buffer used.

The study by Burchard et al. revealed that fibroblasts adhere more readily to surfaces exposed to CHX or saline than to those exposed to stannous fluoride (Burchard et al., 1991).

Saturated citric acid can also be applied for the decontamination of Ti surfaces in the surgical treatment of peri-implantitis with bone grafts and membranes (Deporter & Todescan, 2001; Schou et al., 2003b). In a comparison of the effects of citric acid and 10% H_2O_2, Alhag et al. demonstrated that rough surfaces (with an enhanced TiO_2 layer and textured surface; Nobel Biocare AB®, Gothenburg, Sweden) which were plaque-contaminated and cleaned with either solution, can re-osseointegrate (Alhag et al., 2008). H_2O_2 can be used successfully at a concentration of 3% in the surgical treatment of peri-implantitis, employing bone substitutes with, or without, resorbable membranes (Roos-Jansaker et al. 2007a; Roos-Jansaker et al., 2007b).

Some authors, including Khoury & Buchmann have even used a combination of these three different cleaning solutions in the surgical therapy of peri-implantitis (Khoury & Buchmann, 2001). After removal of the granulomatous tissue, the surgical site was repeatedly rinsed with CHX, after which citric acid (pH = 1) was applied for 1 min to decontaminate the implant surface, this then being rinsed with H_2O_2 and 0.9% saline.

Dennison et al. found that machined implants (without a surface coating) are decontaminated by a variety of methods (air-powder abrasive, citric acid solution, or CHX) more readily than hydroxyapatite-coated surfaces (Dennison et al., 1994).

The above-mentioned chemical agents are commonly applied in the therapy of peri-implantitis, but only investigations relating to the adsorption of CHX on different TiO_2 crystals (anatase and rutile) appear to have been conducted. When used for implant surface decontamination, these materials may alter the morphology and chemical structure of the surface. The aim of our investigation (Ungvári et al., 2010), therefore, was to study the effects of three cleaning solutions in clinical use for peri-implantitis therapy (H_2O_2, citric acid and CHX gel) on Ti.

In vitro studies are essential in the development of such treatments, as these are the basic steps with which to reveal the action of cleaning solutions on the implant surface. Additionally, fewer animal experiments would be required.

Commercially pure (grade 4) machined Ti discs (CAMLOG Biotechnologies AG, Switzerland) were treated with 3% H_2O_2 (5 min), saturated citric acid (pH = 1) (1 min) or CHX gel (5 min), and their surface properties were examined by AFM and XPS. A further aim was to survey the response of the biological environment to these changes, by examining the attachment and proliferation of human epithelial cells after treatment of the Ti surfaces with these solutions. The epithelial cell attachment and proliferation was examined by means of MTT and protein-content assays (the latter with bicinchoninic acid).

Our results revealed no significant difference in the roughness (AFM measurements) of the three treated surfaces. XPS confirmed the constant presence of typical surface elements and an intact TiO_2 layer on each surface. The XPS peaks after CHX gel treatment demonstrated C-O and/or C=O bond formation, due to CHX infiltrating the surface. MTT and BCA assays indicated similar epithelial cell attachments in the three groups; epithelial cell proliferation being significantly higher after H_2O_2 than after CHX gel treatment (not shown by BCA assays). In conclusion these agents do not harm the Ti surface. Cleaning with H_2O_2 slightly enhances human epithelial cell growth, in contrast to CHX gel.

5. Biological surface science in dental implants research

Biological surface science was defined in 2002 by Bengt Kasemo from Göteborg University, Sweden, as a broad interdisciplinary area in which the properties and processes at interfaces between alloplastic materials (biomaterials) and biological environments are studied and also biofunctional surfaces are fabricated (Kasemo, 2002).

Alloplastic or biomaterials are synthetic materials used in devices replacing parts of living systems or to function in intimate contact with the living tissues for any period of time. Beside this, alloplastic materials must not have any adverse or damaging effect on the body as a whole. The successful biointegration of biomaterials may depend on several factors

related to the material, like the bulk and surface characteristics of the material, the design (construction) and the biocompatibility of the material. Naturally, the applied surgical technique and the general health condition and life-quality of the patient are also important features. Biocompatibility is defined as the acceptance of an artificial implant by the surrounding tissues and by the body as a whole (Park, 2000).

Achievement of biointegration of alloplastic materials is one of the most important targets of research in the medical, dental, and biological sciences. For developing a viable biomaterial, the knowledge of several disciplines have to be integrated, like science and engineering (e.g. materials science: structure-property relationship of synthetic and biological materials), biology and physiology (e.g. cell and molecular biology, anatomy, animal and human physiology, histopathology, experimental surgery, immunology) and clinical sciences (e.g. dental and maxillofacial implantology, orthopedics, neurosurgery, obstetrics, plastic, reconstructive, cardiovascular surgeries, etc.) (Park, 2000). Medical implants in the human body, biomimetic materials, tissue engineering, biosensors and biochips for diagnostics, bioelectronics and artificial photosynthesis are research areas constituting a strong driving force for the current rapid development of biological surface science (Kasemo, 2002).

The development of different surface modifications with the ultimate goal of improving the biointegration process of alloplastic materials is stimulating the progress in surface specific biotechnologies, like fabrication of high-tech, sophisticated surfaces (e.g. self-organizing monolayers) and in nano- and microfabrication (Kasemo, 2002).

The importance of bio- and alloplastic materials' knowledge in dentistry is evident as one of the goal of dentistry is to maintain and improve the health of the human teeth (oral cavity) in order to improve the quality of life of the dental patient. All of these activities require the replacement or alteration of the existing tooth structure and also the development of auxiliary dental appliances using alloplastic materials. As healthcare improves and people tend to live longer, materials with specific biomedical applications become more and more important. The most frequently used medical implants are dental implants that serve to substitute human teeth. In dentistry the main challenges for centuries have been the development and selection of biocompatible prosthetic materials that can withstand the adverse conditions of the oral environment. Oral cavity represents a multivariate external environment with a wide range of circumstances, like foods, abrasion, acidic pH, temperatures from 5 to 55^0C, high masticator forces, bacteria, etc. (Lemons, 1996).

There is an increasing need to develop materials that can be implanted into the maxillofacial area in order to rehabilitate the damaged chewing apparatus due to loss of natural teeth. Multiplicity of dental applications requires more than one type or class of material because no material has yet been developed that can fulfil the varying requirements.

The main research topics are investigations of the biointegration of alloplastic materials and studies of how the chemical and surface microstructural modifications of the titanium dental implants influence their biointegration. These studies relate to replacements of body structures in case the biological function requires a significant load-bearing capability. Examples for this are dental implants and artificial hip-joint replacements. These devices have several common aspects: in general they are made of Ti, and their biological integration depends strongly on the surface structure of the metal. These studies have general interest in basic research but are highly applicable for biomedical and industrial uses as well. As experienced by many groups, including ours, the practical/clinical

applications of the findings of studies in cooperation with representatives of other basic sciences, are welcomed on both sides. The multi -or interdisciplinary aspects of these topics are obvious, and without the results of basic science the field of alloplastic materials and biological surface science could not have developed so extensively. Nevertheless, without the experience and observations of clinical scientists, these studies would be purposeless.

6. Conclusion

Since the interactions between medical implants and their biological surroundings are controlled mostly by their surface characteristics (chemistry and structure), characterization of these properties is of main importance. Biorecognition takes place at the interface of the implant and host tissue and the most relevant molecular and cellular events are also localized at this bone-implant interface. The osseointegration of dental implants is relatively long (3-6 months); therefore the surface modifications that can shorten this process will achieve a decreased healing time, a lower failure rate and minimal discomfort for the patients. These improved/modified surfaces will open the possibility of implantation for people in relatively poor health status. A lower bone quantity and/or quality of elder or even ill patients is frequently a handicap in biointegration, therefore these cases are often rejected at patient selection.

The surface modifications outlined above retain the key physical properties of the implants and modify only their outermost surfaces with the ultimate goal of achieving the desired biological responses. The advantages and disadvantages of different physicochemical and biochemical surface modifications were presented in this chapter. Most of these modifications are still in experimental stage, their *in vivo* or clinical studies are still ahead. However, the tools offered by the biological surface science will certainly provide a huge contribution to the development of this field. These methods will help us in understanding the biological events occurring at the bone-implant interfaces and in the development of optimally functionalized implant surfaces as well.

Studies of the impact of fluoride on Ti implant surfaces are becoming more and more important because the chance for such interactions potentially degrading artificial surfaces is quickly growing with the increasing use of biomaterials in the oral cavity. The oral hygiene is enhanced considerably by the use of prophylactic rinses and gels. For both the dental practitioner and the patient it is essential to know whether or not a F^--containing material has the potential to destruct the Ti surface of a dental implant, prosthesis, or the wires of orthodontic braces or at least to decrease its corrosion resistance.

Failure of dental implants is mostly caused by the inflammatory processes affecting the soft and hard tissues. Peri-implant infections involve peri-implant mucositis, defined as a reversible inflammatory change of the periimplant soft tissues without bone loss, and peri-implantitis, an inflammatory process resulting in a loss of supporting bones and associated with bleeding and suppuration. The treatment of peri-implantitis, that causes tissue deterioration surrounding the osseointegrated implants, involves surface decontamination and cleaning. However, chemical cleaning agents may alter the structure of implant surfaces. This sub-chapter presented an overview of the current literature and pointed out the importance of further *in vitro* and *in vivo* studies for the safe application of these decontaminating agents on titanium implants.

7. Acknowledgment

8. References

Abu-Ta'a, M., Quirynen, M., Teughels, W. & van Steenberghe, D. (2008). Asepsis during periodontal surgery involving oral implants and the usefulness of peri-operative antibiotics: a prospective, randomized, controlled clinical trial. *J Clin Periodontol*, Vol.35, pp.58-63

Adell, R., Leckholm. U., Rockler. B. & Brånemark, P.I. (1981). A 15-year study of osseointegrated implants in the treatment of the edentulous jaw. *Int J Oral Surg*, Vol.10, pp. 387-416

Alhag, M., Renvert, S., Polyzois, I. & Claffey, N. (2008). Re-osseointegration on rough implant surfaces previously coated with bacterial biofilm: an experimental study in the dog. *Clin Oral Impl*, Vol.19, pp.182-187

Anusavice, K.J. (1996). Dental Implants, In: *Phillips' Science of Dental Materials*, K.J. Anusavice, (Ed.), 655-662, W.B. Saunders Company, Tenth Edition, ISBN 0-7216-5741-9, Philadelphia, Pennsylvania, USA

Baharloo, B., Textor, M. & Brunette, D.M. (2005). Substratum roughness alters the growth, area, and focal adhesions of epithelial cells, and their proximity to titanium surfaces. *J Biomed Mater Res A*, Vol.74, pp.12–22

Baier, R.E. & Meyer, A.E. (1988). Implant surface preparation. *Int J Oral Maxillofac Implants*, Vol.3, pp.9-20

Barbour, M.E., O'Sullivan, D.J. & Jagger, D.C. (2007). Chlorhexidine adsorption to anatase and rutile titanium dioxide. *Colloids and Surfaces A: Physicochem Eng Aspects*, Vol.307, pp.116-120

Bauerle, D. (2000). *Laser processing and chemistry*. Springer, Berlin, Heidelberg, New York, Tokyo ISBN 978-3-540-66891-6

Bereznai, M., Pelsőczi, I., Tóth, Z., Turzó, K., Radnai, M., Bor, Z. & Fazekas, A. (2003). Surface modifications induced by ns and sub-ps excimer laser pulses on titanium implant material. *Biomaterials*, Vol.24, pp.4197-4203

van den Beucken, J.J., Walboomers, X.F., Leeuwenburgh, S.C., Vos, M.R., Sommerdijk, N.A., Nolte, R.J. & Jansen, J.A. (2007). Multilayered DNA coatings: *in vitro* bioactivity studies and effects on osteoblast-like cell behavior. *Acta Biomater*, Vol.3, pp.587-596

Binon, P.P., Weir, D.J. & Marshall, S.J. (1992). Surface analysis of an original Brånemark implant and three related clones. *Int J Oral Max Imp*, Vol.7, pp.168-175

Block, M., Gardiner, D., Kent, J., Misiek, D., Finger, I. & Guerra, L. (1996). Hydroxyapatite-coated cylinder implants in the posterior mandible: 10 years observations. *Int J Oral Maxillofac Implants*, Vol.11, pp.626-633

Boere, G. (1995). Influence of fluoride on titanium in an acidic environment measured by polarization resistance technique. *J Appl Biomater* , Vol.6, pp.283–288

Boyan, B.D., Batzer, R., Kieswetter, K., Liu, Y., Cochran, D.L., Szmuckler-Moncler, S.S., Dean, D.D. & Schwartz, Z. (1998). Titanium surface roughness alters responsiveness of MG63 osteoblast-like cells to 1 alpha,25-(OH)(2)D-3. *J Biomed Mater Res*, Vol.39, pp.77–85

Brånemark, P.I. (1983a). Osseointegration and its experimental background. *J Prosthet Dent*, Vol.50, pp. 399-410

Brånemark, P.I., Adell, R., Albrektsson, T., Lekholm, U., Lundkvist, S. & Rockler, B. (1983b). Osseointegrated titanium fixtures in the treatment of edentulousness. *Biomaterials*, Vol.4. pp. 25–28

Buchanan, R.A., Lee, I.S. & Williams, J.M. (1990). Surface modification of biomaterials through noble metal ion implantation. *J Biomed Mater Res*, Vol.24, pp.309–318

Burchard, W.B., Cobb, C.M., Drisko, C.L. & Killoy, W.J. (1991). Effects of chlorhexidine and stannous fluoride on fibroblast attachment to different implant surfaces. *Int J Oral Maxillofac Implants*, Vol.6, pp.418-426

Buser, D., Schenk, R.K., Steinmann, S., Fiorellini, J.P., Fox, C.H. & Stich, H. (1991). Influence of surface characteristics on bone integration of titanium implants—a histomorphometric study in miniature pigs. *J Biomed Mater Res*, Vol.25, pp.889–902

Buser, D., Broggini, N., Wieland M., Schenk, R., Denzer, A., Cochran, D., Hoffman, B., Lussi, A. & Steinemann, S.G. (2004). Enhanced bone apposition to a chemically modified SLA titanium surface. *J Dent Res*, Vol.83, No.7, pp.529-533.

Bollen, C.M.L., Papaioannou, W., van Eldere, J., Schepers, E., Quirinen, M. & van Steenberghe, D. (1996). The influence of abutment surface roughness on plaque accumulation and peri-implant mucositis. *Clin Oral Implants Res*, Vol.7, pp.201–211

Cochran, D.L. (1999). A comparison of endosseous dental implant surfaces. *J Periodontology*, Vol.70, pp.1523-1539

Cochran, D.L., Schenk, R.K., Lussi, A., Higginbottom, F.L. & Buser, D. (1998). Bone response to unloaded and loaded titanium implants with a sandblasted and acid-etched surface: a histometric study in the canine mandible. *J Biomed Mater Res,* Vol.40, pp.1-11

Cooper, L.F., Zhou, Y., Takebe, J., Guo, J., Abron, A., Holmén, A. & Ellingsen, J.E. (2006). Fluoride modification effects on osteoblast behaviour and bone formation at TiO_2 grit-blasted c.p. titanium endosseous implants. *Biomaterials*, Vol.27, pp.926–936

Davies, J.E. (1998). Mechanisms of endosseous integration. *Int J Prosthodont,* Vol.11, pp. 391-401

Dennison, D.K., Huerzeler, M.B., Quinones, C.R.G. (1994). Contaminated implant surfaces: an *in vitro* comparison of implant surface coating and treatment modalities for decontamination. *J Periodontol*, Vol.65, pp.942-948

Deporter, A.D. & Todescan, R. Jr. (2001). A possible "rescue" procedure for dental implants with a textured surface geometry: a case report. *J Periodontol*, Vol.72, pp.1420-1423

Dillow, A.K. & Lowman, A.M. (2002). *Biomimetic Materials and Design,* Dillow, A.K. & Lowman, A.M. (Eds.), Marcel Dekker, ISBN 0-8247-0791-5, New York, USA

Ellingsen, J.E. (1995). Pre-treatment of titanium implants with fluoride improves their retention in bone. *J Mater Sci: Mater Med*, Vol.6, pp.749–753

Ellingsen, J.E., Johansson, C.B., Wennerberg, A. & Holmen, A. (2004). Improved retention and bone-to-implant contact with fluoride modified titanium implants. *Int J Oral Maxillofac Implants*, Vol.19, pp.659–666

Eriksson, C., Nygren, H. & Ohlson K. (2004). Implantation of hydrophilic and hydrophobic titanium discs in rat tibia: cellular reactions on the surfaces during the first 3 weeks in bone. *Biomaterials*, Vol.25, No.19, pp.4759-4766.

Ferris, D.M., Moodie, G.D., Dimond, P.M., Gioranni, C.W., Ehrlich, G.M. & Valentini, R.F. (1999). RGD-coated titanium implants stimulate increased bone formation *in vivo*. *Biomaterials*, Vol.20, pp.2323-2331

Fransson, C., Lekholm, U., Jemt, T. & Berglundh, T. (2005). Prevalence of subjects with progressive bone loss at implants. *Clin Oral Impl Res*, Vol.16, pp.440-446

Fransson, C., Wennström, J. & Berglundh, T. (2008). Clinical characteristics at implants with a history of progressive bone loss. *Clin Oral Impl Res* , Vol.19, pp.142-147

Gaggl, A., Schultes, G., Müller, W.D. & Kärcher, H. (2000). Scanning electron microscopical analysis of laser-treated titanium implant surfaces - a comparative study. *Biomaterials,* Vol.21, pp.1067–1073

Golub, E.E. & Boesze-Battaglia, K. (2007). The role of alkaline phosphatase in mineralization. *Curr. Opin. Orthop*, Vol.18, pp.444-448

György, E., Mihailescu, I.N., Serra, P., Pérez del Pino, A. & Morenza, J.L. (2002). Crown-like structure development on titanium exposed to multipulse Nd:YAG laser irradiation. *Appl Phys A*, Vol.74, pp.755–759

Harzer, W., Schroter, A., Gedrange, T., Muschter, F. (2001). Sensitivity of titanium brackets to the corrosive influence of fluoride-containing toothpaste and tea. *Angle Orthod*, Vol.71, pp.314–323

Hämmerle, C., Fourmousis, I., Winkler, J.R., Weigel, C., Brägger, U. & Lang, N.P. (1995). Successful bone fill in late peri-implant defects using guided tissue regeneration. A short communication. *J Periodontol*, Vol.66, pp.303-308

Hench, L.L. (1996). Ceramics, glasses and glass-cements. In: *Biomaterials Science: An Introduction to Materials in Medicine,* B.D. Ratner, A.S. Hoffman, F.J. Schoen, J.E. Lemons (Eds.). 309-312, Academic Press, ISBN 0-12-582461-0, San Diego, California, USA

Hoffman, A.S. (1996). Biologically functional materials. In: *Biomaterials Science: An Introduction to Materials in Medicine,* B.D. Ratner, A.S. Hoffman, F.J. Schoen, J.E. Lemons (Eds.). 309-312, Academic Press, ISBN 0-12-582461-0, San Diego, California, USA

Huang, H. (2002). Effects of fluoride concentration and elastic tensile strain on the corrosion resistance of commercially pure titanium. *Biomaterials*, Vol.23, pp.59–63

Huang H. (2003). Effect of fluoride and albumin concentration on the corrosion behavior of Ti-6Al-4V alloy. *Biomaterials*, Vol.24, pp.275–282

Huang, H.H. (2007). Variation in surface topography of different NiTi orthodontic archwires in various commercial fluoride-containing environments. *Dent Mater*, Vol.23, pp.24–33

Huget, E.F. (2002). Base metal casting alloys. In: *Dental Materials and Their Selection* O'Brien, W.J. (Ed.), 3. ed. Quintessence, ISBN 0-86715-406-3

Ito, Y., Kajihara, M. & Imanishi, Y. (1991). Materials for enhancing cell adhesion by immobilization of cell-adhesive peptide. *J Biomed Mater Res*, Vol.25, pp.1325-1337

de Jonge, L.T., Leeuwenburgh, S.C.G., Wolke, J.G.C. & Jansen, J.A. (2008). Organic-inorganic surface modifications for titanium implant surfaces. *Pharmaceutical Research* Vol.25, No.10, pp.2357-2369

Joob-Fancsaly, A., Divinyi, T., Fazekas, A., Peto, G. & Karacs, A. (2000). Surface treatment of dental implants with high-energy laser beam. *Fogorv Sz*, Vol.93, pp.169-180

Joob-Fancsaly, A., Huszar, T., Divinyi, T., Rosivall, L. & Szabo, G. (2004). The effect of the surface morphology of Ti-implants on the proliferation activity of fibroblasts and osteoblasts. *Fogorv Sz*, Vol.97, pp.251-255

Kasemo, B. (2002). Biological surface science. *Surface Science*, Vol.500, pp. 656-677

Khoury F. & Buchmann, R. (2001). Surgical therapy of peri-implant disease: a 3-year follow-up study of cases treated with 3 different techniques of bone regeneration. *J Periodontol*, Vol.72, pp.1498-1508

Klinge, B. & Meyle, J. (2006). Soft-tissue integration of implants. Consensus report of Working Group 2. *Clin Oral Impl Res*, Vol.17, pp.93–96

Klinger, M.M., Rahemtulla, F., Prince, C.W., Lucas, L.C. & Lemons, J.E. (1998). Proteoglycans at the bone-implant interface. *Crit Rev Oral Biol Med*, Vol.9, No.4, pp.449-463

Kotsovilis, S., Karoussis, I.K., Trianti, M. & Fourmousis, I. (2008). Therapy of peri-implantitis: a systematic review. *J Clin Periodontol*, Vol.35, No.7, pp.621-629

Könönen, M.H.O., Lavonius, E.T. & Kivilahti, J.K. (1995). SEM observations on stress corrosion cracking of commercially pure titanium in a topical fluoride solution. *Dent Mater*, Vol.11, pp.269–272

Larsson, C., Thomsen, P., Lausmaa, J., Rodahl, M., Kasemo, B. & Ericson, L.E. (1994). Bone response to surface modified titanium implants: studies on electropolished implants with different oxide thickness and morphology. *Biomaterials,* Vol.15, pp.1062-1074

Larsson, C., Thomsen, P., Aronsson, B.O., Rodahl, M., Lausmaa, J., Kasemo, B. & Ericson L.E. (1996). Bone response to surface modified titanium implants: studies on the early tissue response to machined and electropolished implants with different oxide thicknesses. *Biomaterials*, Vol.17, pp.605-616

Lautenschlager, E.P. & Monaghan, P. (1993). Titanium and titanium alloys as dental materials. *Int Dent J,* Vol.43, pp. 245–253

Lemons, J.E. (1996). Dental Implants, In: *Biomaterials Science: An Introduction to Materials in Medicine,* B.D. Ratner, A.S. Hoffman, F.J. Schoen, J.E. Lemons (Eds.). 309-312, Academic Press, ISBN 0-12-582461-0, San Diego, California, USA

Leonhardt, A., Renvert, S. & Dahlén, G. (1999). Microbial findings at failing implants. *Clin Oral Impl Res*, Vol.10, pp.339-345

Liu, Y., Hunziker, E.B. & de Groot, K. (2004). BMP-2 incorporated into biomimetic coatings retain its biological activity. *Tissue Eng*, Vol.10, pp.101-108

Liu, Y., Huse, R.O., de Groot, K., Buser, D. & Hunziker, E.B. (2007). Delivery mode and efficacy of BMP-2 in association with implants. *J Dent Res*, Vol.86, pp.84-89

Matsui, Y., Ohno, K., Michi, K. & Yamagata, K. (1994). Experimental study of high velocity flame-sprayed hydroxyapatite coated and noncoated titanium implants. *Int J Oral Maxillofac Implants*, Vol.9, pp.397-404

Mändl, S., Gerlach, J.W. & Rauscenbach, B. (2005). Surface modification of NiTi for orthopaedic braces by plasma immersion ion implantation. *Surf Coat Technol*, Vol.196, pp.293–297

Meffert, R.M., Langer, B. & Fritz, M.E. (1992). Dental implants: a review. *J Periodontol*, Vol.63, pp. 859–870

Meyle, J. (1999). Cell adhesion and spreading on different implant surfaces. *Proceedings of the 3rd European Workshop on Periodontology,* Lang, N., Karrig. T. & Lindhe, J. (Eds.), ISBN 3-87652-306-0 Quintessenz Verlags-GmbH, Berlin, Germany

Morra, M. & Cassinelli, C. (1997). Organic surface chemistry on titanium surfaces via thin film deposition. *J Biomed Mater Res*, Vol.37, pp.198-206

Morra, M., Cassinelli, C., Cascardo, G., Cahalan, P., Cahalan, L., Fini, M. & Giardino R. (2003). Surface engineering of titanium by collagen immobilization. Surface characterization and *in vitro* and *in vivo* studies. *Biomaterials*, Vol.24, pp.4639-4654

Nakagawa, M., Matsuya, S., Shiraishi, T. & Ohta, M. (1999). Effect of fluoride concentration and pH on corrosion behavior of titanium for dental use. *J Dent Res*, Vol.78, pp.1568–1572

Nakagawa, M., Matsuya, S. & Udoh, K. (2001). Corrosion behavior of pure titanium and titanium alloys in fluoride-containing solutions. *Dent Mater J* , Vol.20, pp.305–314

Nánai, L., Vajtai, R. & George, T.F. (1997). Laser-induced oxidation of metals: state of art. *Thin Solid Films*, Vol.298, pp.160-164

Neubert, R. & Eggert, F. (2001). Fluoridhaltige Zahnpasten. *Dtsch Apoth Ztg*, Vol.141, pp.42–45

Norowski, P.A., Jr. & Bumgardner, J.D. (2009). Review. Biomaterial and Antibiotic Strategies for peri-implantitis. *J Biomed Mater Res Part B: Appl Biomater*; Vol.88B, pp.530-543

Olefjord, I. & Hansson, S. (1993). Surface analysis of four dental implant systems. *Int J Oral Max Imp*, Vol.8, pp.32-40

O'Brien, W.J. (2002). *Dental Materials and Their Selection*, 3. ed. Quintessence, ISBN 0-86715-406-3

Park, J.B. (2000). Biomaterials, In: *The Biomedical Engineering Handbook*, 2nd ed., Vol. I, Bronzino, J.D., (Ed.), IV-1-IV-5, CRC Press and IEEE Press, ISBN 0-8493-0461-X, Boca Raton, Florida, USA

Park, J.B. & Kim, Y.K. (2000). Metallic biomaterials. In: *The Biomedical Engineering Handbook* 2nd ed., Vol. I, Bronzino, J.D., (Ed.), 37-1–37-20, CRC Press and IEEE Press, ISBN 0-8493-0461-X, Boca Raton, Florida, USA

Pelsőczi, I., Turzó, K., Gergely, Cs., Fazekas, A., Dékány, I. & Cuisinier, F.: Structural characterization of self-assembled polypeptide films on titanium and glass surfaces by atomic force microscopy. *Biomacromolecules*, Vol.6, No.6, pp.3345-3350

Perez del Pino, A., Serra, P. & Morenza, J.L. (2002). Oxidation of titanium through Nd:YAG laser irradiation. *Appl Surf Sci*, Vol.197-198, pp.887-890

Pető, G., Karacs, A., Pászti, Z., Guczi, L., Divinyi, T. & Joób, A. (2001). Surface treatment of screw shaped titanium dental implants by high intensity laser pulses. *Appl Surf Sci*, Vol.7524, pp.1-7.

Puleo, D.A. & Nanci, A. (1999). Understanding and controlling the bone-implant interface. *Biomaterials.* Vol.20, No.23-24, (December), pp.2311-2321

Ratner, B.D. & Hoffman, A.S. (1996). Thin films, Grafts, and Coatings, In: *Biomaterials Science: An Introduction to Materials in Medicine,* B.D. Ratner, A.S. Hoffman, F.J.

Schoen, J.E. Lemons (Eds.). 309-312, Academic Press, ISBN 0-12-582461-0, San Diego, California, USA

Reclaru, L. & Meyer, J.M (1998). Effects of fluorides on titanium and other dental alloys in dentistry. *Biomaterials*, Vol.19, pp.85–92

Renvert, S., Lessem, J., Dahlén, G., Lindahl, C. & Svensson, M. (2006). Topical minocycline microspheres versus topical chlorhexidine gel as an adjunct to mechanical debridement of incipient peri-implant infections: a randomized clinical trial. *J Clin Periodontol*, Vol.33, pp.362-369

Renvert, S., Roos-Jansaker, A.M., Lindahl, C., Renvert, H. & Persson, G.R. (2007). Infection at titanium implants with or without a clinical diagnosis of inflammation. *Clin Oral Impl Res*, Vol.18, pp.509-516

Renvert, S., Lessem, J., Dahlén, G., Renvert, H. & Lindahl, C. (2008a). Mechanical and repeated antimicrobal therapy using a local drug delivery system in the treatment of peri-implantitis: A Randomized Clinical Trial. *J Periodontol*, Vol.79, pp.836-844

Renvert, S., Roos-Jansaker, A-M. & Claffey N. (2008b). Non-surgical treatment of peri-implant mucositis and peri-implantitis: a literature review. *J Clin Periodontol*, Vol.35, pp.305-315

Rohanizadeh, R., LeGeros, R.Z., Harsono, M. & Bendavid, A. (2005). Adherent apatite coating on titanium substrate using chemical deposition. *J Biomed Mater Res* A, Vol.72, pp.428-438

Roos-Jansaker, A-M., Renvert, S. & Egelberg, J. (2003). Treatment of peri-implant infections: a literature review. *J Clin Periodontol*, Vol.30, pp.467-485

Roos-Jansaker, A-M., Lindahl, C., Renvert, H. & Renvert, S. (2006a). Nine- to fourteen year follow-up of implant treatment. Part II: presence of peri-implant lesions. *J Clin Periodontol*, Vol.33, pp.290-295

Roos-Jansaker, A-M., Renvert, H., Lindahl, C. & Renvert S. (2006b). Nine- to fourteen year follow-up of implant treatment. Part III: factors associated with periimplant lesions. *J Clin Periodontol*, Vol.33, pp.296-301

Roos-Jansaker, A-M., Renvert, H., Lindahl, C. & Renvert, S. (2007a). Surgical treatment of periimplantitis using a bone substitute with or without a resorbable membrane: a prospective cohort study. *J Clin Periodontol*, Vol.34, pp.625-632

Roos-Jansaker, A-M., Renvert, H., Lindahl, C. & Renvert S. (2007b). Submerged healing following surgical treatment of peri-implantitis: a case series. *J Clin Periodontol*, Vol.34, pp.723-727

Santis, D., Guerriero, C., Nocini, P.F., Ungersbock, A., Richards, G., Gotte, P. & Armato, U. (1996). Adult human bone cells from jaw bones cultured on plasma-sprayed or polished surfaces of titanium or hydroxyapatite discs. *J Mater Sci Mater Med*, Vol.7, pp.21-28

Schiff, N., Grosgogeat, B., Lissac, M. & Dalard, F. (2002). Influence of fluoride content and pH on the corrosion resistance of titanium and its alloys. *Biomaterials*, Vol.23, pp.1995–2002

Schiff, N., Boinet, M., Morgon, L., Lissac, M., Dalard, F. & Grosgogeat, B. (2006). Galvanic corrosion between orthodontic wires and brackets in fluoride mouthwashes. *Eur J Orthod*, Vol.28, pp.298–304

Schliephake, H., Scharnweber, D., Dard, M., Sewing, A., Aref, A. & Roessler, S. (2005). Functionalization of dental implant surfaces using adhesion molecules. *J Biomed Mater Res B Appl. Biomater*, Vol.73, pp.88-96

Schou, S., Holmstrup, P., Jorgensen, T., Stoltze, K., Hjorting-Hansen, E. & Wenzel, A. (2003a). Autogenous bone graft and ePTFE membrane in the treatment of peri-implantitis. I. Clinical and radiographic observation in cynomolgus monkeys. *Clin Oral Impl Res*, Vol.14, pp.391-403

Schou, S., Holmstrup, P., Jorgensen, T., Skovgaard, L.T., Stoltze, K., Hjorting-Hansen, E. & Wenzel, A. (2003b). Implant surface preparation in the surgical treatment of experimental peri-implantitis with autogenous bone graft and ePTFE membrane in cynomolgus monkeys. *Clin Oral Impl Res*, Vol.14, pp.412-422

Schwarz, F., Bieling, K. & Bonsmann, M. (2006). Nonsurgical treatment of moderate and advanced periimplantitis lesions: a controlled clinical study. *Clin Oral Invest* Vol.10, pp.279-288

Sikirić, M.D., Gergely, C., Elkaim, R., Wachtel, E., Cuisinier, F.J. & Füredi-Milhofer. H. (2008). Biomimetic organic-inorganic nanocomposite coatings for titanium implants. *J Biomed Mater Res A* Vol.89, No.3, pp.759-771

Sioshansi, P. (1987). Surface modification of industrial components by ion implantation. *Mater Sci Eng*, Vol.90, pp.373-383

Siirilä, H.S. & Könönen, M. (1991). The effect of oral topical fluorides on the surface of commercially pure titanium. *Int J Oral Maxillofac Implants*, Vol.6, pp.50–54

Stájer, A., Ungvári, K., Pelsőczi, K.I., Polyánka, H., Oszkó, A., Mihalik, E., Rakonczay, Z., Radnai, M., Kemény, L., Fazekas, A., Turzó, K. (2008). Corrosive effects of fluoride on titanium: investigation by X-ray photoelectron spectroscopy, atomic force microscopy and human epithelial cell culturing. *J Biomed Mater Res A*. Vol.87, No.2, pp.450-458

Strietzel, R., Hösch, A., Kalbfleish, H. & Buch, D. (1998). *In vitro* corrosion of titanium. *Biomaterials*, Vol.19, pp.1495–1499

Sun, L., Berndt, C.C., Gross, K.A. & Kucuk, A. (2001). Material fundamentals and clinical performance of plasma-sprayed hydroxyapatite coatings: a review. *J Biomed Mater Res*, Vol.58, pp.570-592.

Szabo, G., Kovacs, L. & Vargha, K. (1995). Possibilities for improvement of the surface properties of dental implants (2). The use of ceramic oxides in surface coating for titanium and tantalum implants. *Fogorv Sz*, Vol.88, pp.73-77

Toumelin-Chemla, F., Rouelle, F. & Burdairon, G. (1996). Corrosive properties of fluoride-containing odontologic gels against titanium. *J Dent*, Vol.24, pp.109–115

Ungvári, K., Pelsőczi, K.I., Kormos, B., Oszkó, A., Rakonczay, Z., Kemény, L., Radnai, M., Nagy, K., Fazekas, A., Turzó, K. (2010). Effects on titanium implant surfaces of chemical agents used for the treatment of peri-implantitis. *J Biomed Mater Res B Appl Biomater*, Vol.94, No.1, pp.222-229

Uribe, R., Penarrocha, M., Sanchis, J.M. & Garcia, O. (2004). Marginal peri-implantitis due to occlusal overload. A case report. *Med Oral*, Vol.9, pp.159-162

Vogel, G. (1999). Biological aspects of a soft tissue seal. In: *Proceedings of the, 3rd European Workshop on Periodontology*, Lang, N.P., Karring, T., Lindhe, J. (Eds.). ISBN: 3-87652-306-0 Quintessenz Verlags- GmbH, Berlin, Germany

Wang R.R. & Fenton A. (1996). Titanium for prosthodontic applications: A review of the literature. *Quintessence Int*, Vol.27, pp. 401–408

Walker, M.P., White, R.J. & Kula, K.S. (2005). Effect of fluoride prophylactic agents on the mechanical properties of nickel-titanium-based orthodontic wires. *Am J Orthod Dentofacial Orthop*, Vol.127, pp.662–669

Wennerberg, A., Ektessabi, A., Albrektsson, T., Johansson, L. & Andersson, B. (1997). A 1-year follow-up of implants of differing surface roughness placed in rabbit bone. *Int J Oral Max Implants*, Vol.12, pp.486–494

Wheeler, S.L. (1996). Eight-year clinical retrospective study of titanium plasma-sprayed and hydroxyapatite-coated cylinder implants. *Int J Oral Maxillofac Implants*, Vol.1, pp.340-350

Wong, M., Eulenberger, J., Schenk, R. & Hunziker E. (1995). Effect of surface topology on the osseointegration of implant materials in trabecular bone. *J Biomed Mater Res*, Vol.29, pp.1567–1575

Zitzmann, N.U. & Berglundh, T. (2008). Definition and prevalence of peri-implant diseases. *J Clin Periodontol*, Vol.35, Suppl.8, pp.286-291
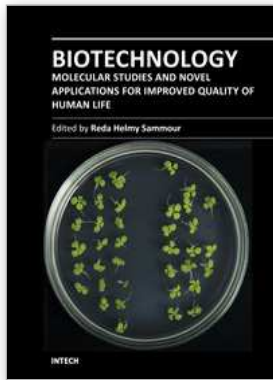
Biotechnology - Molecular Studies and Novel Applications for Improved Quality of Human Life
Edited by Prof. Reda Sammour

ISBN 978-953-51-0151-2
Hard cover, 250 pages
Publisher InTech
Published online 14, March, 2012
Published in print edition March, 2012

This book deals with the importance of application of molecular biology as an approach of biotechnology for improvement of the quality of human life. One of the interesting topics in this field, is the identification of the organisms that produce bioactive secondary metabolites. It also discusses how to structure a plan for use and preservation of those species that represent a potential source for new drug development, especially those obtained from bacteria. The book also introduces some novel applications of biotechnology, such as therapeutic applications of electroporation, improving quality and microbial safety of fresh-cut vegetables, producing synthetic PEG hydro gels to be used as an extra cellular matrix mimics for tissue engineering applications, and other interesting applications.

How to reference
In order to correctly reference this scholarly work, feel free to copy and paste the following:

Kinga Turzo (2012). Surface Aspects of Titanium Dental Implants, Biotechnology - Molecular Studies and Novel Applications for Improved Quality of Human Life, Prof. Reda Sammour (Ed.), ISBN: 978-953-51-0151-2, InTech, Available from: http://www.intechopen.com/books/biotechnology-molecular-studies-and-novel-applications-for-improved-quality-of-human-life/surface-aspects-of-titanium-dental-implants

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