Journal Home Page www.bbbulletin.org

BRITISH BIOMEDICAL BULLETIN

Review Article

Surface Modification of Titanium Endosseous Dental Implants and its Influence on Osseointegration: An Overview

SANDEEP ANANT LAWANDE*[1] and GAYATRI SANDEEP LAWANDE[2]

[1]*Department of Periodontics, Goa Dental College & Hospital, Bambolim, Goa, India*
[2]*Sai Multispecialty Dental Clinic & Research Centre, Porvorim, Goa, India*

ARTICLE INFO

Received 28 Feb. 2016
Received in revised form 22 April 2016
Accepted 22 May 2016

Keywords:
Osseointegration,
Dental implants,
Surface modification,
Titanium,
Surface roughness.

Corresponding author:
H.No. 874/5, 'Saideep', New Pundalik Nagar, Porvorim, Goa, India - 403521

E-mail address: drsanlaw@rediffmail.com

ABSTRACT

Endosseous dental implants have been well accepted for replacing missing teeth in today's dental practice. The success of dental implant therapy is essentially based on the process of osseointegration. In the recent years, surface composition, surface topography and surface roughness of titanium implant have been found to play a major role in osseointegration and success, which has resulted in commercial availability of many implants with different surface modifications. This article explores various methods of implant surface modifications and their role in osseointegration.

Introduction

Endosseous dental implants have revolutionized the approach to dental care for partially as well as completely edentulous patients. Osseointegration, defined as a direct structural and functional connection between ordered living bone and the surface of a load-carrying implant, is critical for implant stability, and is considered a prerequisite for implant loading and long-term clinical success of endosseous dental implants.[1, 2]

For dental implants, titanium is used in pure form (commercially pure titanium) or alloyed with aluminium and vanadium. Titanium is the material of choice for dental implant because of its properties such as excellent biocompatibility, corrosion resistance, high strength and relatively low modulus of elasticity, good formability and machinability.[3] Titanium is a highly reactive metal that would not become integrated with tissues. However, its instantaneous surface oxidation creates a passivation layer of titanium oxides, which have ceramic-like properties, making it very compatible with tissues. This oxide surface layer is very stable, capable of promoting osseointegration and highly resistant to crevice corrosion, pitting corrosion, stress cracking corrosion and galvanic corrosion.[4]

Osseointegration of titanium implant surfaces is dependent upon both physical and chemical properties. This structural and functional union of the implant with living bone is strongly influenced by the surface properties of the titanium implant. Dental implants with different surface modifications have been developed and currently used to improve the clinical performance of implants.[1, 5] On account of the influence of surface modifications of the titanium implants on osseointegration, such modifications have been successfully exploited to influence bone integration and long-term stability of the implant.

Surface roughness of dental implants

Implant surface roughness is one of the important parameters that play an important role in implant tissue interaction and osseointegration. Surface roughness of dental implants can be divided into three levels depending on the scale of features such as macro, micro, and nano-sized topographies. Macro level ranges from millimeters to tens of microns. The high roughness increases the mechanical interlocking between the implant surface and bone. However, a major risk with high surface roughness may be an increase in peri-implantitis as well as an increase in ionic leakage. Micro level surface roughness is in the range of 1-10 µm, which maximizes the interlocking between mineralized bone and the implant surface. Nano level surface roughness ranges between 1 and 100 nm and has been widely used in recent years.[6] According to Brett *et al*, nanometer roughness plays an important role in the adsorption of proteins and adhesion of osteoblasts, which ultimately affects the rate of osseointegration.[7]

The interaction between the physical, chemical, mechanical, and topographic characteristics of the surface determines the activity of the attached cells that are close to the dental implant surface. Osteogenesis at the implant surface is influenced by several mechanisms. A series of coordinated events, including cell proliferation, transformation of osteoblasts and bone tissue formation might be affected by different surface topographies.[1, 8]

Amount of bone-to-implant contact (BIC) is an important determinant in long-term success of dental implants. Factors influencing BIC include topography, chemistry, wettability and surface energy. Surface wettability, being most important is largely dependent on surface energy and relates to the degree of contact with the physiological environment by influencing protein adsorption and increasing adhesion of osteoblasts on the implant surface. Surface roughness also has a positive influence on cell migration and proliferation, which in turn leads to better BIC results, suggesting that the microstructure of the implant influences biomaterial–tissue interaction. Implant surface properties are likely to be of particular relevance to the chemical and biological interface processes in the early healing stages after implantation. It is generally accepted that these early stages are likely to have an effect on the host response to the implant and, therefore, the long-term outcome and success of the treatment.[1, 9]

The surface roughness of the implants can significantly alter the process of osseointegration because the cells react differently to smooth and rough surfaces. Fibroblasts and epithelial cells adhere more strongly to smooth surfaces, whereas osteoblastic proliferation and collagen synthesis are increased on rough surfaces. Several studies have demonstrated that implants with rough surfaces show better bone apposition and BIC than implants with smooth surfaces.[1,10,11]

Methods of Surface Modification of Implants

Different methods have been employed for titanium implant surface modifications to change the implant surface chemistry, morphology, and structure (Table No.1). The desired implant surface can be achieved by addition of material over the surface, removal of material from the surface or modification of the surface material. The main objective of these techniques is to improve the bio-mechanical properties of the implant such as stimulation of bone formation to enhance osseointegration, removal of surface contaminants, and improvement of wear and corrosion resistance.[1,12]

A) Mechanical Methods

Machining

Manufacturing an implant involves turning a long rod of titanium into a cylinder or screw with a resulting surface being referred to as a 'machined' surface. Machined titanium surfaces have ridges and grooves up to about 10 microns deep.[4] These surface defects provide mechanical resistance through bone interlocking. The disadvantage regarding the morphology of machined implants is the fact that osteoblastic cells are rugophilic – that is, they are prone to grow along the grooves existing on the surface. This characteristic requires a longer waiting time between surgery and implant loading. The use of these implants follows a protocol suggested by Branemark i.e., 3-6-month healing or waiting time prior to loading. These are the best documented implants with several reports suggesting good long-term clinical outcomes on all indications when used in sites with good bone quality using a two-stage procedure.[1] The surface modifications, through a variety of processes, have resulted in an increased bone to implant contact and biomechanical fixation at the earlier implantation times as compared to the machined implants.[13]

Polishing

Polishing of the implant surface involves use of a fine abrasive material that is applied to a flexible wheel or a belt and then the implant is brought into direct contact with the abrasive surface. Polishing is generally carried out using silicon carbide, alumina or diamond, in presence of lubricant, initially with coarse abrasive followed by a finer abrasive at a speed of 10-30 m/s to produce extremely smooth surface.[14,15]

Grinding

Grinding involves use of coarse particles as abrasive medium to remove the surface at a faster rate. Grinding creates relatively rough surface topographies. Grinding with an abrasive grade 60 leads to Ra values around 1µm and with the coarsest grade the surface roughnesses of up to 5-6 µm can be achieved.[16]

Blasting

This technique involves roughening the implant surface using hard ceramic particles delivered through a nozzle at high velocity by means of compressed air. Depending on the size of the ceramic particles, different surface roughness can be produced on titanium implants. The blasting material should be chemically stable, biocompatible and should not hamper the osseointegration of implants. Various ceramic particles have been used, such as alumina, titanium oxide and calcium phosphate particles. Alumina is often embedded into the implant surface and residue remains even after ultrasonic cleaning, acid passivation, and sterilization. In some cases, these particles have been released into the surrounding tissues and have interfered with the osseointegration of the implants.[2] Titanium oxide particles with an average size of 25 µm produce a moderately rough surface in the 1- 2 µm range on dental implants. Calcium phosphates such as hydroxyapatite, beta-tricalcium phosphate and mixtures have been used for blasting as they are resorbable, leading to a clean, textured, pure titanium surface. Research studies have demonstrated higher bone implant contact, positive success rates and higher marginal bone levels of Tio2 blasted implants as compared to machined surface.[9, 17- 19]

SLA Method

This type of surface (sandblasted-large grits-acid etched) is produced by a large grit 250-500 µm blasting process followed by etching with hydrochloric/sulfuric acid at elevated temperatures for 5 minutes. Sandblasting results in surface roughness and acid etching leads to microtexture and cleaning. These surfaces have demonstrated improved osseointegration.[1, 20, 21]

Shot peening

Shot peening is a modified method of grit blasting and is used primarily for introducing compressive stresses in the material's surface. It is most commonly used for producing specific surface topographies on various biomaterials. Surface topography achieved by shot peening depends greatly on the size of the particle used.[2, 14]

B) Chemical Methods

Acid Treatment

Acid etching of titanium removes the oxide layer and parts of the underlying material. The acids commonly used include hydrochloric acid, sulfuric acid, hydrofluoric acid, and nitric acid. Acid treatment of the surfaces of titanium implants results in uniform roughness with micro pits ranging in size from 0.5-2 µm, increase in surface area, and an improvement in bioadhesion. This yields low surface energy and reduces the possibility of contamination since no particles are encrusted in the surface. This type of surface not only facilitates retention of osteogenic cells, but also allows them to migrate towards the implant surface thus promoting rapid osseointegration and long term success. The manufacturers have their own acid etching method regarding concentration, time and temperature for treating implant surfaces.[1,22]

Dual acid-etching technique

This technique employs immersion of titanium implants for several minutes in a mixture of concentrated hydrochloric acid and sulphuric acid heated above 100°C (dual acid-etching) to produce a micro rough surface. The dual acid- etched surfaces enhance the osteoconductive process through the attachment of fibrin and osteogenic cells, resulting in bone formation directly on the surface of the implant.[1, 23]

Alkali Treatment

Alkali treatment involves immersion of titanium implant in sodium or potassium hydroxide followed by heat treatment by rinsing in distilled water to produce a bioactive, nanostructured sodium titanate layer on the implant surface with an irregular topography with high degree of porosity. Composition and structure of this layer can be further modified by proper heat treatment. Alkali and heat treatment form a bone-like apatite that binds to bone apatite chemically forming high bond strength.[12, 14]

Hydrogen peroxide Treatment

Chemical treatment of implant surfaces with hydrogen peroxide results in chemical dissolution and oxidation of the titanium surface. When titanium surfaces react with hydrogen peroxide, Ti-peroxy gels are formed. The thickness of titania layer formed can be controlled by adjusting the treatment time and it has been demonstrated that, when immersed in SBF, thicker layers of titania gel are more favorable for the deposition of apatite.[24]

Sol-gel Method

The sol-gel method represents a simple and low cost procedure to deposit thin hydroxyapatite (HA) coatings of less than 10 μm thickness on the implant surface. This process improves the biological activity of the titanium implants and contributes to enhanced bone formation during initial stages of osseointegration and thereby improving implant fixation. Materials such as TiO2, CaP, TiO2-CaP composite, and silica-based coatings can be deposited on the titanium surface by this technique.[1, 25]

Fluoride Treatment

Titanium implants can be treated with fluoride solution. Titanium being very reactive to fluoride ions forms soluble titanium fluoride which promotes osteoblast differentiation. The surface produced has microrough topography which favours osseointegration.[26] Ellingsen demonstrated greater resistance to push forces and increased torque for removal when implants are fluoride treated. This increases bio activity at the implant surface.[27]

Anodization

Anodization is a process by which oxide films are deposited on the surface of the titanium implants by means of an electrochemical reaction. Anodization increases the thickness of the TiO_2 surface layer (more than 1,000 nm) and also increases roughness making it more biocompatible.[5] In this process, titanium surface to be oxidized serves as the anode in an electrochemical cell with diluted solution of acids (sulphuric acid, phosphoric acid, nitric acid etc.) serving as the electrolyte. When a potential is applied, ionic transport of charge occurs through the cell and an electrolytic reaction takes place at the anode, resulting in the growth of an oxide film. This results in a surface with micropores which demonstrates increased cell attachment and proliferation.[28] Two mechanisms have been proposed to explain this osseointegration: Mechanical interlocking through bone growth in pores and biochemical bonding. The anodization process is rather complex and depends on various parameters such as current density, concentration of acids, composition and electrolyte temperature. The tissue healing process around anodized implants is quicker than in machined implants.[5] In a study performed on canine models to evaluate bone healing at oxidized and turned implant surfaces, a higher percentage of BIC and bone density was reported for anodized implants.[29] Modifications to the chemical composition of the titanium oxide layer have been tested with the incorporation of magnesium, calcium, sulfur or phosphorus. It has been found that incorporating magnesium into the titanium oxide layer leads to a higher removal torque value compared to other ions.[3,5]

C) Physical Methods

Plasma Spraying

Plasma spraying is a technique used for creating titanium and calcium phosphate (CaP) coatings on the surfaces of titanium implants. Titanium plasma spraying (TPS) method consists of injecting titanium powders into a plasma torch at high temperature. The titanium particles are projected onto the surface of the implants where they condense and fuse resulting in a substantial increase in the surface area. This is advantageous as the coating gives implant a porous surface that the bone can penetrate more readily achieving faster osseointegration. It has been shown that this three-dimensional topography increased the tensile strength at the implant-bone interface.[30] Al-Nawas *et al* have shown that the implant-bone interface formed faster with a TPS surface than with machined implants. TPS implants have been often recommended for regions with low bone density.[31]

Hydroxyapatite particles can be plasma-spayed resulting in the coating thickness of 20-50 µm. Hydroxyapatite is a calcium phosphate ceramic that is an osteophilic, osteoconductive, bioactive coating which is totally biocompatible and becomes an integral part of living bone tissue.[12] Plasma Sprayed Hydroxyapatite (PSHA) coatings normally rely on mechanical interlocking between a grit-blasted or etched metallic surfaces and the ceramic-like PSHA biomaterial for physical integrity during implant placement and function.[32] Fouda *et al* demonstrated that the osseointegration of the HA coated dental implant is faster than uncoated implants.[33] Bone maturation was reported to be more significant at the bone-implant interface and coating of titanium with HA lead to improved maturation of newly formed bone tissue.[34]

The plasma-spraying method has disadvantages, however, such as the porosity of the coating and residual stress at the substrate/coating interface, as well as drastic changes in the composition and crystallinity of the initial calcium phosphate. Plasma-sprayed HA–coated dental implants have also been associated with clinical problems. One of the major concerns with plasma-sprayed coatings is the possible separation of the coating from the titanium implant surface, a phenomenon known as delamination and failure at the implant-coating interface despite the fact that the coating is well-attached to the bone tissue. The discrepancy in dissoluton between the various phases that make up the coating has led to delamination, particle release and thus the clinical failure of implants. Loosening of the coating has also been reported, especially when the implants have been inserted into dense bone.[2, 4]

Sputtering

Sputtering is a process whereby atoms or molecules of a material are ejected in a vacuum chamber by bombardment of high-energy ions. The dislodged particles are deposited on a substrate also placed in a vacuum chamber. Sputtering has been used to deposit thin films on implant surfaces to improve their biocompatibility, biological activity, and mechanical properties such as wear resistance and corrosion resistance.[1, 35]

Sputtering techniques include diode sputtering, radiofrequency sputtering and magnetron sputtering. Radiofrequency sputtering involves deposition of thin films of CaP coatings on titanium substrates. The advantage of this technique is that the coating shows strong adhesion to the titanium and the Ca/P ratio and crystallinity of the deposited coating can be varied easily. Studies in animals have shown higher BIC percentages with sputter coated implants.[1, 36, 37] Studies have shown that these coatings were more retentive, with the chemical structure being precisely controlled.[38] Magnetron sputtering technique shows strong HA titanium bonding associated with outward diffusion of titanium into the HA layer, forming TiO2 at the interface.[39]

Ion implantation

In ion implantation method, surface of the implant is bombarded with high energy ions which will penetrate the implant surface to a depth of approximately 1 µm. Ion implantation is controlled by varying the concentration of ions and their energy. This technique increased the corrosion resistance of titanium and also accelerated osseointegration.[3,40] Braceras *et al* demonstrated that the ion implantation of cobalt onto titanium alloys significantly improved the osseointegration properties of the treated implant surface.[41]

Laser treatment

The process of laser ablation results in titanium surface microstructures with greatly increased hardness, corrosion resistance, and a high degree of purity with a standard roughness and thicker oxide layer.[49, 50] Biological studies evaluating the role of titanium ablation topography and chemical properties showed the potential of the grooved surface for the orientation of osteoblast cell attachment and control the direction of ingrowth.[51]

D) Biochemical Methods

Biomimetic and Bioactive Surface Modifications

Research developments directed towards improved and faster osseointegration have shown that implant surface properties can also be modified by incorporating bioactive factors or biomimetic agents into the implant surface. These include cell-adhesion molecules like fibronectin, vitronectin, type I collagen, osteogenin and bone sialoprotein; several growth and differentiation factors such as transforming growth factor (TGF), platelet-derived growth factor (PDGF), insulin-like growth factor (IGF), bone morphogenetic proteins (BMPs), which may act as bone-stimulating agents. Also, incorporation of bone antiresorptive drugs such as bisphonates, statins like simvastatin, antibacterial coatings including gentamycin or tetracycline have demonstrated impressive potential for improving the nature of osseointegration.[42 - 48].

Conclusion

Dental implants have gained wide recognition as a predictable and successful treatment modality for replacement of missing teeth. Studies have proved that surface roughness of an implant plays a major role in its stability and osseointegration. Although numerous methods of surface modification have been successfully developed and employed to produce dental implants with varying surface topographies, more research needs to be done with focus on increasing the scientific knowledge of cellular and molecular events leading to osseointegration. This will help achieve implant surfaces for faster, more predictable, improved and enhanced osseointegration enabling quicker, safer healing as well shortened treatment time and eventually, long-term success.

Conflict of interest

The authors have declared no conflict of interest.

References

1. Anil S, Anand PS, Alghamdi H, Jansen JA. Dental implant surface enhancement and osseointegration, Implant dentistry – a rapidly evolving practice (2011), Prof. Ilser Turkyilmaz (Ed.),ISBN:978-93-307-658-4,Intech,available from: http://www.intec-hopen.com/books/implant-dentistry-a-rapidly-evolving-practice/ dental-implant-surface-enhancement-and-osseointegration.
2. Guehennec L, Soueidan A, Layrolle P, Amouriq Y. Surface treatments of titanium dental implants for rapid osseointegration. *Dent Mater* 2007; 23:844-54.
3. Jemat A, Ghazali MJ, Razali M, Otsuka Y. Surface modifications and their effects on titanium dental implants. *Biomed Res International* 2015; 1-11.

4. Koshy E, Philip SR. Dental implant surfaces: An overview. *Int J Clin Implant Dent* 2015; 1(1): 14 – 22.
5. Sul YT, Johansson C, Wennerberg A, Cho LR, Chang BS. Optimum surface properties of oxidized implants for reinforcement of osseointegration: Surface chemistry, oxide thickness, porosity, roughness and crystal structure. *Int J Oral Maxillofac Implants* 2005; 20(3): 349-59.
6. Shalabi MM, Gortemaker A, Van't Hof MA, Jansen JA, Creugers NH. Implant surface roughness and bone healing: a systematic review. *J Dent Res* 2006; 85: 496-500.
7. Brett PM, Harle J, Salih V, Mihoc R, Olsen I, Jones FH, Tonetti M. Roughness response genes in osteoblasts. *Bone* 2004; 35: 124-33.
8. Shibli JA, Grassi S, de Figueiredo LC, Feres M, Marcantonio E Jr, Iezzi G, Piattelli A. Influence of implant surface topography on early osseointegration: a histological study in human jaws. *J Biomed Mater Res* 2007; 80: 377-85.
9. Novaes A, Souza S, de Oliviera P, Souza A. Histomorphmetric analysis of the bone to implant contact obtained with 4 different implant surface treatment placed side by sides in the dog mandible. *Int J Oral Maxillofac Implants* 2002; 17:377-83.
10. Buser D, Nydegger T, Oxland T, Cochran DL, Schenk RK, Hirt HP, Snetivy D, Nolte LP. Interface shear strength of titanium implants with a sandblasted and acid-etched surface: a biomechanical study in the maxilla of miniature pigs. *J Biomed Mater Res* 1999; 45: 75-83.
11. Cochran DL, Buser D, Bruggenkate CM, Weingart D, Taylor TM, Bernard JP, Peters F, Simpson JP. The use of reduced healing times on ITI implants with a sandblasted and acid-etched (SLA) surface: early results from clinical trials on ITI SLA implants. *Clin Oral Implants Res* 2002; 13: 144-53.
12. Sharma S, Rahul GR, Poduval S, Sharma R. Implant surface micro-design. *Global J Med Res* 2014; 14(4): 1-19.
13. Coelho PG, Cardaropoli G, Suzuki M, Lemons JE. Histomorphometric evaluation of a nanothickness of bioceramic deposition on endosseous implants: A study in dogs. *Clin Implant Dent Rel Res* 2009; 11(4):292-302.
14. Ellingsen JE, Thomsen P, Lyngstadaas SP. Advances in dental materials and tissue regeneration. *Periodontol 2000* 2006; 41: 136-156.
15. Wennerberg A, Albrektsson T, Lausmaa J, – Torque and Histomorphometric evaluation of c.p. titanium screws blasted with 25-and 75-microns- sized particles of Al_2O_3. *J Biomed Mater Res* 1996; 30(2): 251 - 60.
16. Bowers KT, Keller JC, Randolph BA, Wick DG, Michaels CM. Optimization of surface micromorphology for enhanced osteoblast responses in vitro. *Int J Oral Maxillofac Implants* 1992; 7: 302-10.
17. Aparicio C, Gil FJ, Fonseca C, Barbosa M, Planell JA. Corrosion behavior of commercially pure titanium shot blasted with different materials and size of shot particles for dental implant applications. *Biomater* 2003; 24: 263-73.
18. Piatelli M, Scarano A, Paoloanntonio M, lezzi G, Petrone G, Piatelli A. Bone response to machined and resorbable blast material titanium implants: An experimental study in rabbits. *J Oral Implantol* 2002; 28:2-8.
19. Ivanoff CJ, Hallgren C, Widmark G, Sennerby L, Wennerberg A. Histologic evaluation of the bone integration of TiO(2) blasted and turned titanium microimplants in humans. *Clin Oral Implants Res* 2001; 12:128–134.
20. Galli C, Guizzardi S, Passeri G, Martini D, Tinti A, Mauro G, Macaluso GM. Comparison of human mandibular osteoblasts grown on two commercially

available titanium implant surfaces. *J Periodontol* 2005; 76: 364-372.

21. Kim H, Choi SH, Ryu JJ, Koh SY, Park JH, Lee IS. The biocompatibility of SLA-treated titanium implants. *Biomed Mater* 2008; 3(2): 25011- 24.
22. Cho SA, Park KT. The removal torque of titanium screw inserted in rabbit tibia treated by dual acid etching. *Biomater* 2003; 24: 3611-7.
23. Park JY, Davies JE. Red blood cell and platelet interactions with titanium implant surfaces. *Clin Oral Implant Res* 2000; 12: 530-9.
24. Tavares MG, de Oliveira PT, Nanci A, Hawthorne AC, Rosa AL, Xavier SP. Treatment of a commercial, machined surface titanium implant with H2SO4/H2O2 enhances contact osteogenesis. *Clin Oral Implant Res* 2007; 18: 452-8.
25. Vidigal GM, Aragones LC, Campos A, Groisman M. Histomorphometric analysis of hydroxyapatite-coated and uncoated titanium dental implants in rabbit cortical bone. *Implant Dent* 1999; 8: 295-302.
26. Cooper LF, Zhou Y, Takebe J, Guo, J, Abron A, Holmen A, Ellingsen JE. Fluoride modification effects on osteoblast behavior and bone formation at TiO2 grit-blasted commercially pure titanium endosseous implants. *Biomater* 2006; 27: 926-36.
27. Ellingsen JE, Johansson CB, Wennerberg A, Holmen A. Improved retention and bone-to-implant contact with fluoride-modified titanium implants. *Int J Oral Maxillofac Implants* 2004; 19: 659-66.
28. Gupta A, Dhanraj M, Sivagami G. Status of surface treatment in endosseous implant: a literary overview. *Indian Journal Dent Res* 2010; 21: 433-8.
29. Gurgel BC, Goncalves PF, Pimentel SP, Nociti FH, Sallum EA, Sallum AW, Casati MZ. An oxidized implant surface may improve bone-to-implant contact in pristine bone and bone defects treated with guided bone regeneration: an experimental study in dogs. *J Periodontol* 2008; 79: 1225-31.
30. Novaes AB Jr, Souza SL, Barros RR, Pereira KK, Jezzi G, Piatelli A. Influence of implant surfaces on osseointegration. *Braz Dent J* 2010; 21(6):471-81.
31. Al-Nawas B, Groetz KA, Goetz H, Duschner H, Wagner W. Comparative histomorphometry and resonance frequency analysis of implants with moderately rough surfaces in a loaded animal model. *Clin Oral Implants Res* 2008; 19: 1-8.
32. Knabe C, Klar F, Fitzner R, Radlanski RJ, Gross U. In vitro investigation of titanium and hydroxyapatite dental implant surfaces using a rat bone marrow stromal cell culture system. *Biomater* 2002; 23: 3235-45.
33. Fouda MFA, Nemat A, Gawish A, Baiuomy AR. “Does the coating of titanium implants by hydroxyapatite affect the elaboration of free radicals: An experimental study.” *Aus J Bas Appl Sci* 2009; 3:1122-9.
34. Clark PA, Rodriguez A, Sumner DR, Hussain MA, Mao JJ. Modulation of bone ingrowth of rabbit femur titanium implants by in vivo axial micromechanical loading. *J Appl Physio* 2005; 98: 1922-9.
35. Jansen JA, Wolke JG, Swann S, Van der Waerden JP, de Groot K. Application of magnetron sputtering for producing ceramic coatings on implant materials. *Clin Oral Implant Res* 1993; 4: 28-34.
36. Vercaigne S, Wolke JG, Naert I, Jansen JA. A histological evaluation of TiO2-gritblasted and Ca-P magnetron sputter coated implants placed into the trabecular bone of the goat: Part 2. *Clin Oral Implants Res* 2000a; 11: 314-24.
37. Vercaigne S, Wolke JG, Naert I, Jansen JA. A mechanical evaluation of TiO2-gritblasted and Ca-P magnetron sputter coated implants placed into the trabecular bone of the goat:

Part 1. *Clin Oral Implants Res* 2000b; 11: 305-13.

38. Ong JL, Bessho K, Cavin R, Carnes DL. Bone response to radio frequency sputtered calcium phosphate implants and titanium implants in vivo. *J Biomed Mater Res* 2002; 59:184-90.
39. Wolke JG, van Dijk K, Schaeken HG, de Groot K, Jansen JA. Study of the surface characteristics of magnetron-sputter calcium phosphate coatings. *J Biomed Mater Res* 1994; 28: 1477-84.
40. Lacefield WR. Materials characteristics of uncoated/ceramic-coated implant materials. *Adv Dent Res* 2007; 13:21-26.
41. Braceras I, Alava JI, Onate JI. Improved osseointegration in ion implantation-treated dental implants. *Surf Coatings Tech* 2002; 158:28-32.
42. Kwak HB, Kim JY, Kim KJ, Choi MK, Kim JJ, Kim KM, Shin YI, Lee MS, Kim HS, Kim JW, Chun CH, Cho HJ, Hong GY, Juhng SK, Yoon KH, Park BH, Bae JM, Han JK, Oh J. Risedronate directly inhibits osteoclast differentiation and inflammatory bone loss. *Biol Pharma Bull* 2009; 32: 1193-8.
43. Yoshinari M, Oda Y, Inoue T, Matsuzaka K, Shimono M. Bone response to calcium phosphate-coated and bisphosphonate-immobilized titanium implants. *Biomater* 2002; 23: 2879-85.
44. Du Z, Chen J, Yan F, Xiao Y. Effects of simvastatin on bone healing around titanium implants in osteoporotic rats. *Clin Oral Implants Res* 2009; 20: 145-50.
45. Alt V, Bitschnau A, Osterling J, Sewing A, Meyer C, Kraus R, Meissner SA, Wenisch S, Domann E, Schnettler R. The effects of combined gentamicin-hydroxyapatite coating for cementless joint prostheses on the reduction of infection rates in a rabbit infection prophylaxis model. *Biomater* 2006; 27: 4627-34.
46. Herr Y, Woo J, Kwon Y, Park J, Heo S, Chung J. Implant surface conditioning with tetracycline-HCl: A SEM study. *Key Engineering Mat* 2008; 361: 849-52.
47. Chappard D, Aguado E, Hure G, Grizon F, Basle MF. The early remodeling phases around titanium implants: a histomorphometric assessment of bone quality in a 3- and 6-month study in sheep. *Int Journal Oral Maxillofac Implants* 1999; 14: 189-96.
48. Becker J, Kirsch A, Schwarz F, Chatzinikolaidou M, Rothamel D, Lekovic V, Laub, M, Jennissen HP. Bone apposition to titanium implants biocoated with recombinant human bone morphogenetic protein-2 (rhBMP-2): A pilot study in dogs. *Clin Oral Invest* 2006; 10: 217-24.
49. Gaggl A, Schultes G, Muller WD, Karcher H. Scanning electron microscopical analysis of laser-treated titanium implant surfaces--a comparative study. *Biomater* 2000; 21: 1067-73.
50. Hallgren C, Reimers H, Chakarov D, Gold J, Wennerberg A. An in vivo study of bone response to implants topographically modified by laser micromachining. *Biomater* 2003; 24: 701-10.
51. Frenkel SR, Simon J, Alexander H, Dennis M, Ricci JL. Osseointegration on metallic implant surfaces: effects of microgeometry and growth factor treatment. *J Biomed Mater Res* 2002; 63: 706-13.

Table 1. Methods of Implant Surface Modifications

Mechanical	Chemical	Physical	Biochemical
Machining Polishing Grinding Blasting	Acid treatment Alkali heat treatment Hydrogen peroxide treatment Sol-gel method Fluoride treatment Anodization	Plasma spraying Sputtering Ion implantation Laser treatment	Bioactive factors Biomimetic agents