SURFACE TOPOGRAPHY OF DENTAL IMPLANTS

Vinaya Bhat¹ & S. Sriram Balaji²

¹Professor, Department of Prosthodontics & Implantology, A.B. Shetty Memorial Institute of Dental Sciences, Nitte University, Mangalore - 575018, Karnataka., ²Senior Lecturer, Department of Prosthodontics, Sri Ramakrishna Dental College & Hospital, Coimbatore - 641 006, India

Correspondence :

Vinaya Bhat

Professor, Department of Prosthodontics & Implantology,
A.B. Shetty Memorial Institute of Dental Sciences, Nitte University, Mangalore - 575 018, Karnataka, India.
Mobile : +91 94819 21180 E-mail : drvinayabhat@gmail.com

Abstract :

Surface treatment of titanium implants has been a new frontier in clinical dentistry. Usually it is based on additive and subtractive techniques that modify the surface topography of implants. It alters the roughness/smoothness of the implant surface which becomes more favourable to achieve osseointegration. This modified surface exhibits varied biological responses when the implant is placed in the oral cavity.

This article reviews the principles behind treating the surface of titanium, the numerous methods employed for treating the surface and the cellular response elicited. A complete electronic search and hand search has been conducted for the purpose.

Keywords : Dental Implants, Surface treatment, topography, osseointegration.

Introduction :

Early osseointegration determines the clinical success of dental implant therapy¹. In order to achieve such early osseointegration, delicate surgical technique during implant placement, geometry and surface topography of the implant are very crucial factors²⁻⁵. Immediately after fixture placement titanium reacts with body tissues and fluids. Two possible types of response observed would be formation of fibrous tissue capsule, which causes clinical failure of implant therapy and the direct contact of bone to implant, which is called as osseointegration¹. In the latter there is no intervening connective tissue layer and the fixation is usually biological. The surface properties of titanium have been found to have an influence on the rate and quality of biological fixation. Surface properties include composition, energy, topography, hydrophilicity and roughness. These are

interrelated and individually they determine the clinical outcome of implant therapy. Numerous in vivo and in vitro tests⁶⁻¹⁵ have been performed to

analyze the exact role of surface chemistry on osseointegration. But due to poor standardization techniques and lack of comparative studies between different surface treatment procedures, understanding this aspect of osseointegration is incomplete. This review focuses on the different surface treatment methods and a comparative evaluation of the different techniques and the cellular responses observed as a result of the treated surface.

Surface Chemical Composition And Roughness

Chemical composition and roughness of the implant surfaces have been known to play a crucial role in development of osseointegration. The titanium implants used presently have different surface compositions based on the type of metal used. For dental applications, Titanium is used in pure form (CpTi) or alloyed with aluminium and Vanadium (Ti6Al4V). Based on the content of oxygen, carbon and iron, CpTi has graded as 1-4 and alloy has been placed as grade 5¹⁶.

The reaction of water or body fluids on to the implant surface depends on the surface composition. A surface which will increase the hydrophilicity has found to be preferable. Numerous authors have attempted to

Access this article online

Quick Response Code

determine the ideal contact angle of the surface of the implant which could make the surface hydrophilic. It is suggested that shallow contact angle of 0° enhances hydrophilicity and contact angle of 140° results in hydrophobicity¹⁷⁻²².

Surface morphology enhances osseointegration by directing protein adsorption kinetics. Osteoblasts tend to attach more readily and their differentiation occurs more easily on a rough surface.

A turned/ machined implant has a smooth surface macroscopically and it has been in use for several decades after Prof PI Branemark invented implants. In machined implants bone contacted only the tip of the thread and not the root of the thread and also there is no connection between peri implant bony surface and implant surface. Since there is a delay in osseointegration and later loading of the implants by the prosthesis, the need for hastening the process is felt. Ever since, the implant surface has undergone tremendous metamorphosis in its roughness. The roughness of titanium implants has a direct effect on osseointegration and its bio mechanical fixation^{23, 24}. Three levels of surface roughness have been identified. They are macro, micro and nano size topography.

Macro level ranges from millimetres to tenth of microns. High surface roughness increases early osseointegration and stability. But increase in ionic leakage is a potential problem since it may lead to peri implantitis²⁵⁻²⁹.

Micro level ranges from 1 -10 micrometers. Maximum interlocking between bone and implant surface occurs at this level according to Wennerberg et al^{24, 27}. According to Hannson³⁰ ideal surface should be covered with hemispherical pits 1.5um in depth and 4 um in diameter³¹. Implants with surface roughness are mainly indicated where poor quality of bone is present. Rough surface increases bone to implant contact enhancing superior clinical results³².

Brett³³ proposed that nano level roughness helps in protein adsorption and osteoblasts adhesion. The potential

drawbacks are, difficulty in achieving nano level roughness and quantifying the above mentioned protein adsorption and adhesion of osteoblasts. So far only fewer studies have been reported with nano surface modifications in a reproducible manner. The roughness formed in the nano meter level positively guides osteoblasts to attach Ti surface implant. Further, it also helps in primary healing.

Titanium Plasma Spraying (TPS)

This utilises a plasma torch through which titanium powders are injected at high temperatures. Then these titanium particles are sprayed on the surface of implants. A film of 30um thick is formed on the implant surface due to condensation and fusing. Ideal thickness must be 40-50 um with levels of roughness reaching 7 um. Buser et al²⁵ stated that this configuration increased tensile strength at bone implant surface. Rocuzzo³⁴ compared Sand Blasted Acid Etched (SLA) and TPS implant surfaces and found no significant difference between those two. Taba Junior et al³⁵ conducted a study in which TPS demonstrated inferior bone- to- implant contact when compared to plasma sprayed hydroxyapatite coated implants. Few authors^{25,36} suggested the use of micro level surface roughness while using TPS. The main drawbacks of this procedure are porosity of coating and residual stress development in the coated surface. Few cases of loosening of the coating and delamination has also been reported³⁵.

Sand Blasted Acid Etched (SLA) Treatment

In this method, surface is bombarded with aluminium oxide (Al₂O₃) particles and later followed by acid etching. This treatment results in formation of titanium hydride layer, which increases the mechanical properties of the implant. Uniform micro pits of 1-2 um diameter were formed which results in increased bone-to-implant-contact³⁷.

Grit Blasting:

In this procedure, hard ceramic particles are used to roughen the surface of dental implants. Alumina, titanium Oxide (TiO₂) and Calcium Phosphate particles have been used for this purpose, because they are chemically stable and biocompatible. These particles are delivered through a

nozzle at high velocity using compressed air. The size of these particles determines the surface roughness achieved.

Alumina is a commonly employed blasting material. However, main problem is that it gets embedded on the implant surface and cannot be removed by ultrasonic cleansing, acid passivation and sterilization. Since it is acid insoluble it is hard to remove thus leading to differential surface composition on titanium surface. Aparico et al³⁸ showed that this chemical heterogeneity decreases corrosion resistance of titanium in physiological environment.

Titanium oxide particles of size 25um produce roughness of 1-2 um. Ivanoff³⁹ demonstrated higher bone ti implant contact of Tio2 blasted implant surface when compared to machined surface. Researchers⁴⁰⁻⁴² showed higher bone implant contact, positive success rates and higher marginal bone levels of Tio2 blasted implants. Abron⁴³ et al showed that torque force increased with increase in surface roughness while positive bone apposition was observed. Roughening of implants increases the mechanical fixation and not biological fixation.

Calcium phosphates like hydroxyapatites and β tricalcium phosphates have also been used because they are bio compatible, osteoconductive and resorbable. Novaes et al⁴⁴ and Piatelli et al⁴⁵ separately demonstrated higher bone- to- implant contact of these surfaces when compared to machined surfaces.

Acid Etching :

Strong acids like HCl, H_2SO_4 , HNO_3 and Hf produces micro pits ranging from 0.5um to 2 um in diameter^{46,47}. Wong et al⁴⁸ showed increased osseo integration as a result of acid etching. Micro rough surface is produced by immersing titanium implants in concentrated solution of HCL and H_2SO_4 heated above 100°C. This is called as dual acid etching. Cho and Park⁴⁹ stated that the above processes increase osseointegration and help in long term success of implant therapy. Park and Davis⁵⁰ demonstrated that dual acid etching increases osseo conduction and causes bone

deposition directly on the implant surface. Several authors⁵¹⁻⁵⁴ reported increased bone to implant contact and reduced bone loss compared to TPS and machined surfaces. According to Novaes⁵⁵ and Papalexiou⁵⁶ homogenous micro porous surface with higher bone to implant contact results from high temperature acid etching as compared to TPS surfaces. Surface wettability provides fibrin adhesion which guides osteoblasts migration over the implant surface. Buser et al¹⁷ showed improved bone to implant contact of the hydrophilic surface. Qahash⁵⁷ conducted an animal model study in which he concluded surface dual acid etching accelerates osseo integration both in newly formed and native bone irrespective of differing bone densities. Sand blasted acid etched implants can be restored successfully after a 6-12 week healing period. According to Nelson et al.⁵⁸ acid etched titanium surfaces shows increased fibronectin absorption when compared to machined surfaces.

Fluoride treatment of titanium produces surface roughness favouring osseo integration. titanium forms soluble titanium fluoride which produces osteoblast differentiation⁵⁹. Ellingsen^{60,61} demonstrated greater resistance to push forces and increased torque for removal when implants are fluoride treated. This increases bio activity at the implant surface.

Yokoyama⁶² showed that acid etching causes hydrogen embrittlement of titanium causing microcracks leading to decreased fatigue resistance. He also explained formation of a brittle hybrid phase causing decreased ductility which causes fracture.

Anodization :

When strong acids are used at high density and potential of current (200A/m², 100V), it results in micro or nano surfaces. Anodization is employed to thicken the surface oxide layer upto 100nm^{63,64}. According to Sul^{65,66} modifications in microstructure and crystallinity are produced as a result of anodization. Anodization depends on density of current, acid concentration and electrolyte composition. Sul and Rocci⁶⁷⁻⁶⁹ postulated increased

biomechanical and histomorphometric values for anodization when compared to machined surfaces. Jungner⁷⁰ demonstrated higher clinical success of anodized dental implants. Both Mechanical interlocking and Biochemical bonding occurs due to anodization. Magnesium, sulphur, calcium and phosphorous was used by Sul^{65,66} to modify surface oxide layer of titanium. According to Sul^{65,66}, magnesium ions provide increased removal torque values when compared to other ions.

Ion Implantation⁷¹

It is a procedure where in sodium, calcium and phosphorous ions are implanted onto the surface of implants to modify their topography at a dose of 1 into 10¹⁷ ions/cm² utilizing a beam energy of 25KeV and a vacuum of 10⁻⁶ Pa. A novel technique of double implantation was also followed where Calcium ions were implanted followed by phosphorous ions. Care must be taken not to exceed the temperature above 40°C. This technique increased the corrosion resistance of titanium and also accelerated osseointegration. The highest corrosion resistance was seen in Ca+ P implanted titanium. Implants were treated initially with alkali to achieve heterogenous nucleation of Ca and P, since mechanical stability of this coating depends on rough surface of titanium. Presence of hydroxyl groups is a major necessity for calcium and phosphorous deposition since it provides sites for adsorption of ions from body fluids.

Alkali and Heat Treatment

Here, the implants are soaked in 10M NaOH at 60°C for 8 hours. Then it is washed with de ionised water and dried at 40°C for 24 hours. Further these were heated gradually from 500°C to 700°C at rate of 5°C/ min and then allowed to cool at room temperature. Krupa et al⁷² found out that increase in temperature increases corrosion resistance. This also increases bone bonding ability without causing roughening of the surface. According to Kim and Kokubo⁷³ alkali and heat treatment form a bone like apatite that binds to bone apatite chemically forming high bond strength. The above mentioned effect was demonstrated by applying fluorescent agent on the treated surface since it is difficult

to cut titanium to be visible in light microscope. When implants are alkali and heat treated it forms a foci over which bone matrix is deposited. The apatite formed due to this treatment is similar to inorganic component of bone. The apatite is formed by amorphous sodium titanate that is preformed on the metal after treatment. This is a complex process which occurs as a result of electrostatic interaction between surface of metal and fluids in the body. Ban proved that alkaline treatment is a simple and effective procedure for surface modification of titanium and it also increases adhesion to resin by formation of rutile particles.

Bio Mimetic Agents

Bio ceramics, bioactive proteins, ions and polymers constitute biomimetic agents. According to shin a bio mimetic agent is one that has been designed to elicit specified cellular responses, mediated by interactions with scaffold- tethered peptides from extra cellular matrix. According to glossary of implant dentistry bio mimetic material is one which is able to replicate/ imitate a body structure (anatomy) and/or function (physiology). The material must be easy to manufacture causing no allergic or immune response. Further it must have good differentiating capacity being chemically stable and economical. Biomimetic layer on the implant surface is a valuable alternative to other surface treatment modalities. Munisamy et al⁷⁴ developed a newer method to deposit cone like collagen mineral composite layer, which increased osseointegration in vitro. Higher percent of success is noticed when the mineral formed is similar to the one present in tissue itself. Recently biomimetic implants are available commercially and prove to have faster osseointegration. But further studies are required in this discipline to understand better the way of accelerated osseointegration and comparative studies with other surface treatment modalities.

Biologically Active Drugs

Tgf, Igf and Pdgf are employed with dental implant therapy these days. Care must be taken to ensure gradual release of the substance rather than a instant release. Bis phosphonates are drugs that prevent resorption of bone

and they can be coated on implants used in bone deficiency regions. According to Josse et al⁷⁵ bis phosphonates increase bone density at the vicinity of the implant. Other studies⁷⁶⁻⁷⁹ using these drugs also showed increase in bone contact area and absence of negative effects. But the optimal dose of these drugs to be coated onto the implant surface is yet to be determined.

Lasers⁸⁰

Lasers are used in dentistry for decades for cutting hard tissues. Co₂ lasers were the first lasers to be used. Now lasers occupy a prime position in every field of medicine including dentistry. Bacterial infiltration of peri implant tissue reduces success rate of implant therapy. Hence, an adequate maintenance of peri implant tissues is a must for successful osseointegration. Other than plastic curettes and bactericidal chemicals, lasers also are an adjunct for peri implant sterilization. Lasers are mainly used while exposure of cover screws (stage II surgery). The most commonly used lasers are Co₂ laser and NdYag laser. They are used in surface treatment of implants. However, higher doses of Co₂ laser (3.5- 5v) cause destruction of micro machined groove. When focussed, Co₂ lasers are employed no discolouration of titanium is seen. In contrast, NdYag laser treatment surface melting, porosity loss and other damages were observed. The damage observed was proportional to the dose applied. NdYag lasers are also used for decontaminating the surface of failing and diseased implants. Also laser treatment did not sterilize plasma sprayed titanium and plasma sprayed Hydroxyapatite (HA) coated titanium. Park et al⁸⁰ contraindicates use of lasers as they cause peri implant soft tissue damage while used near endosseous implants. Co₂ lasers get reflected from the implant surface, so they do not cause temperature rise and more useful in surface implant treatment.

Critical Evaluation of Different Surface Treatment Procedures

TPS increases tensile strength at the bone implant surface and surface is similar to SLA treated surface, but it causes porosity, delamination and loosening of the coating. Grit

blasted implant surface demonstrated higher bone-to-implant contact and good marginal bone levels. Grit blasted implants have 31% contact with bone and is much higher when compared to porous (17%) and polished (15%) implants. But grit blasting produces differential surface composition and chemical heterogeneity, which decreases corrosion resistance of titanium. Acid etching results in increased bone-to-implant contact and reduced marginal bone loss when compared to TPS and machined surfaces. Irrespective of differing bone densities acid etching accelerates osseointegration and also demonstrated increased fibronectin absorption. But this procedure causes micro cracks on titanium surface which decreases the fatigue resistance. Anodization increases removal torque values, because it causes both mechanical interlocking and bio chemical bonding. Implantation of calcium, sodium and phosphorous ions increases corrosion resistance and hastens osseointegration. SLA treatment has shown higher clinical success rates and forms uniform diameter pores. But acid etching decreases surface roughness after sand blasting. Alkaline treatment is a simple procedure for surface modification. It forms an apatite similar to inorganic component of bone. This increases bonding to bone without roughening of the surface. Bio mimetic agents increase osseointegration but further studies are required in this discipline. Implantation of biologically active drugs onto the implant surface is being practiced off late. But optimal dose of these drugs is yet to be determined. Co₂ lasers are reflected back so they are used in surface treatment. They are also used on diseased and failing implants. But studies showed that they cause peri implant soft tissue damage. Electron beam radiation decreases surface roughness and causes polishing of the surface, so it cannot accelerate osseointegration. None of the surface treatment procedures have been proved optimal. Every manufacturer has their own theory for the treatment procedure they follow. So the search for ideal surface treatment method is not complete.

Cellular Responses To The Surface Treatment Procedures
Cell attachment on the implant surface takes by direct and

indirect methods. Physico chemical links are responsible for direct attachment and proteins such as fibronectin and vibronectin helps in indirect attachment. Fibronectin is the earliest protein produced by the tooth and bone forming cells.

Wang et al⁸¹ stated that carbonate apatite globules is necessary for adequate cell attachment. Ti OH groups which is seen on the titanium surface is the major driving factor for the formation of calcium and phosphate precipitates. Fibroblast growth and adhesion depends on the intrinsic chemical composition of the material rather than roughness of the surface. Osteoblasts attach more on the blasted surface when compared to acid etched and TPS surfaces. Also TPS and smooth surfaced implants showed lesser levels of alkaline phosphatase activity. Major emphasis is placed on ALP because it is the earliest marker for osteoblast differentiation. Micro rough surfaces ranging from 7 -10um give the optimum environment for osteoblast differentiation. Since sand blasting gives such optimum surface, osteoblasts adhere more readily over these surfaces.

Recombinant human bone morphogenic protein 2 (rh BMP2) forms fine trabecular woven bone along the surface of the implant. It also increases osteogenic activity without any obvious compression of tissues.

A machined implant treated subsequently with acid and alkali demonstrated higher attachment and growth of bone forming cells. Ban⁸² showed that acid etching reduces bone marrow cell proliferation.

NaOH and heat treatment results in uniform formation of the sodium titanate layer on the metal. This treatment modality results in bone growth into the porous surface created by it. This results in reducing immobilization time prior to loading. The stability obtained is long lasting since a bone like apatite layer is formed. But few studies have shown the bio activity obtained as a result of alkaline and heat treatment is limited and not satisfactory.

Amorphous surface is formed as a result of implantation of ions, which is not advocated for apatite layer formation.

Higher calcium phosphate ratio is seen on fluoridated implant surface when compared to anodized, alkali treated and heat treated implants and hydroxyapatite coated implants. But the above studies have been done on simulated body fluid which lacks many components contained in human plasma.

Anodization of dental implant surface produces osteoblasts which has higher alkaline phosphatase activity. Since anodization results in higher surface roughness it causes increased Calcium and phosphorous deposition. Anodization followed by hydrothermal treatment demonstrated best bio activity. Also ALP production increases with increased B glycerophosphate production. But the validity of the above mentioned responses must be further evaluated.

Future Trends

Researchers have developed a novel method of spraying mesenchymal stem cells on the surface of titanium and making it to differentiate into osteoblasts or bone building cells.

A titanium foam is prepared by mixing titanium powder with foaming agents. These foaming agents cause swelling of polymer when heated. Later this polymer is removed and titanium is condensed to provide strength to the porous structure. This enhances bone growth into the pores created and makes it less invasive.

When zinc and titanium are made in nano topography, it increases the surface area providing more space for bone forming cells to adhere. They also have shown to possess anti bacterial effect.

When SLA treated surface is coated with Arg-Gly-Asp (RGD), peptide-modified polymer (PLL-g-PEG/PEG-RGD) higher bone-to-implant contact is seen. These peptides act on integrins which leads to increased bonding of osteoblasts onto the implant surface.

Recombinant human Bone Morphogenic Protein (rhBMP-2) when coated on the implant surface causes regeneration of the lost surface.

Off late high energy sputter deposition, adhesive coatings, bio pore structuring, titanium zirconium alloying and nano pore structuring have been evolved by various manufacturers. They are still in infancy and further long term clinical studies are required to validate their clinical application

Conclusion :

From the earlier days when titanium was used for implants, it has undergone a sea of changes to improve

osseointegration. Modifying the surface topography is one of the aspects in this regard. Surface of titanium has been subjected to various treatment procedures to improve its chemical composition and roughness which is favourable for bone formation. Certain procedures are additive in nature and certain procedures are subtractive in nature. This review article evaluated, critically, the different surface treatment procedures that are in vogue to modify the dental implants. The future of this concept has also been discussed.

References :

1. Uehennec, A. Soueidan, P. Layrolle, Y. Amouriq. Surface Treatments Of titanium dental implants for rapid osseointegration. *Dental Materials* 23(2007)844-54.
2. Albrektsson T, Branemark PI, Hansson HA, Lindstrom J. Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. *Acta Orthop Scand*. 1981;52(2):155-170
3. Buser D, Nydegger T, Hirt HP. Removal torque values of titanium implants in the maxilla of miniature pigs. *Int J Oral Maxillofac Implants*. 1998;13:611-19.
4. Klokkevd PR, Johnson P, Dadgostari S. Early endosseous integration enhanced by dual acid etching of titanium: A torque removal Study in the rabbit. *Clin Oral Implants Res*. 2001;12:350-57.
5. Buser D, Schenk RK, Steinemann S. Influence of surface characteristics on bone integration of titanium implants. A histomorphometric study in miniature pigs. *J Biomed Mater Res*. 1991;25:889-902.
6. Filiaggi MJ, Coombs NA, Pilliar RM. Characterization of the interface in the plasma-sprayed HA coating/Ti-Al6-4V implant system. *J Biomed Mater Res*. 1991;25:1211-1230
7. Radin S, Ducheyne P. Plasma spraying induced changes of calcium phosphate ceramic characteristics and the effect on in vitro stability. *Mater Med*. 1992;3:33-42
8. De Groot K, Wolke JCG, Jansen JA. State of the art: hydroxylapatite coatings for dental implants. *J Oral Implant*. 1994;20:232-234 v
9. Kim Y, LeGeros J, LeGeros RZ. Characterization of commercial HA-coated implants. *J Dent Res*. 1994;73:137:[abstract no. 287]
10. LeGeros RZ, LeGeros JP, Kim Y, Kijkowska R, Zheng R, Bautista C. Calcium phosphates in plasma-sprayed HA coatings. *Ceram Trans*. 1995;48:173-189
11. Wheeler S. Eight-year clinical retrospective study of titanium plasma-sprayed and hydroxyapatite-coated cylinder implants. *Int J Oral Maxillofac Implants*. 1996;11:340-350
12. Chang YL, Lew D, Park JB, Keller JC. Biomechanical and morphometric analysis of hydroxyapatite-coated implants with varying crystallinity. *J Oral Maxillofac Surg*. 1999;57:1096-1108
13. Lee J, Rouhfar L, Beirne O. Survival of hydroxyapatite-coated implants: a meta-analytic review. *J Oral Maxillofac Surg*. 2000;58:1372-1379 [discussion 1379-80]
14. Tinsley D, Watson C, Russell J. A comparison of hydroxyapatite coated implant retained fixed and removable mandibular prostheses over 4 to 6 years. *Clin Oral Implant Res*. 2001;12:159-166
15. Anselme K, Bigerelle M, Noel B, Iost A, Hardouin P. Effect of grooved titanium substratum on human osteoblastic cell growth. *J Biomed Mater Res*. 2002;60:529-540
16. Steinemann S. Titanium-the material of choice?. *Periodontology* 2000. 1998;17:7-21
17. Buser D, Broggnini N, Wieland M, Schenk RK, Denzer AJ, Cochran DL. Enhanced bone apposition to a chemically modified SLA titanium surface. *J Dent Res*. 2004;83:529-533
18. Zhao G, Schwartz Z, Wieland M, Rupp F, Geis-Gerstorf J, Cochran DL. High surface energy enhances cell response to titanium substrate microstructure. *J Biomed Mater Res A*. 2005;74:49-58
19. Bagno A, Di Bello C. Surface treatments and roughness properties of Ti-based biomaterials. *J Mater Sci Mater Med*. 2004;15:935-949
20. Giavaresi G, Fini M, Cigada A, Chiesa R, Rondelli G, Rimondini L. Mechanical and histomorphometric evaluations of titanium implants with different surface treatments inserted in sheep cortical bone. *Biomaterials*. 2003;24:1583-1594
21. Carlsson L, Albrektsson T, Berman C. Bone response to plasma-cleaned titanium implants. *Int J Oral Maxillofac Implants*. 1989;4:199-204
22. Wennerberg A, Bolind P, Albrektsson T. Glow discharge pre-treated implants combined with temporary bone ischaemia. *Swed Dent J*. 1991;15:95-101
23. Cochran DL, Schenk RK, Lussi A, Higginbottom FL, Buser D. 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*. 1998;40:1-11
24. Wennerberg A, Hallgren C, Johansson C, Danelli S. A histomorphometric evaluation of screw-shaped implants each prepared with two surface roughnesses. *Clin Oral Implants Res*. 1998;9:11-19
25. Buser D, Schenk R, Steinemann S, Fiorellini J, Fox C, Stich H. Influence of surface characteristics on bone integration of titanium implants. A histomorphometric study in miniature pigs. *J Biomed Mater Res*. 1991;25:889-902
26. Gotfredsen K, Wennerberg A, Johansson C, Skovgaard LT, Hjorting-Hansen E. Anchorage of TiO2-blasted, HA-coated, and machined implants: an experimental study with rabbits. *J Biomed Mater Res*. 1995;29:1223-1231
27. Wennerberg A, Albrektsson T, Albrektsson B, Krol JJ. Histomorphometric and removal torque study of screw-shaped titanium implants with three different surface topographies. *Clin Oral Implant Res*. 1996;6:24-30
28. Becker W, Becker BE, Ricci A, Bahat O, Rosenberg E, Rose LF. A prospective multicenter clinical trial comparing one- and two-stage titanium screw-shaped fixtures with one-stage plasma-sprayed solid-screw fixtures. *Clin Implant Dent Relat Res*. 2000;2:159-165
29. Albrektsson T, Wennerberg A. The impact of oral implants—past and future, 1966–2042. *J Can Dent Assoc*. 2005;71:327
30. Hansson S, Norton M. The relation between surface roughness and interfacial shear strength for bone-anchored implants. A mathematical model. *J Biomech*. 1999;32:829-836
31. Testori T, Wiseman L, Woolfe S, Porter S. A prospective multicenter clinical study of the Osseotite implant: four-year interim report. *Int J*

- Oral Maxillofac Implants. 2001;16:193–200
32. Conner K, Sabatini R, Mealey B, Takacks V, Mills M, Cochran D. Guided bone regeneration around titanium plasma-sprayed, acid-etched and hydroxyapatite-coated implants in the canine model. *J Periodontol*. 2003;74:658–668
33. Brett PM, Harle J, Salih V, Mihoc R, Olsen I, Jones FH. Roughness response genes in osteoblasts. *Bone*. 2004;35:124–133
34. Rocuzzo M, Bunino M, Prioglio F, Bianchi SD. Early loading of sandblasted and acid-etched (SLA) implants: a prospective split-mouth comparative study. *Clin Oral Implants Res*. 2001;12:572–578
35. Taba Junior M, Novaes Junior AB, Souza SL, Grisi MF, Palioto DB, Pardini LC. Radiographic evaluation of dental implants with different surface treatments: an experimental study in dogs. *Implant Dent*. 2003;12:252–258
36. Ong JL, Carnes DL, Bessho K. Evaluation of titanium plasma-sprayed and plasma-sprayed hydroxyapatite implants in vivo. *Biomaterials*. 2004;25:4601–4606
37. Stefano Guizzardi, Carlo Galli, Deisree Martini, Silvana Bellati, Anna Tinti, Mario Raspanti, Paola Taddei, Alessandro Ruggeri. Different titanium surface treatment influences on human mandibular osteoblast response. *J Periodontol* 2004; 75:273–82.
38. 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. *Biomaterials*. 2003;24:263–273
39. Ivanoff CJ, Hallgren C, Widmark G, Sennerby L, Wennerberg A. Histologic evaluation of the bone integration of TiO₂ blasted and turned titanium microimplants in humans. *Clin Oral Implants Res*. 2001;12:128–134
40. Rasmusson L, Kahnberg KE, Tan A. Effects of implant design and surface on bone regeneration and implant stability: an experimental study in the dog mandible. *Clin Implant Dent Relat Res*. 2001;3:2–8
41. Gotfredsen K, Karlsson U. A prospective 5-year study of fixed partial prostheses supported by implants with machined and TiO₂-blasted surface. *J Prosthodont*. 2001;10:2–7
42. Rasmusson L, Roos J, Bystedt H. A 10-year follow-up study of titanium dioxide-blasted implants. *Clin Implant Dent Relat Res*. 2005;7:36–42
43. Abron A, Hopfensperger M, Thompson J, Cooper L. Evaluation of a predictive model for implant surface topography effects on early osseointegration in the rat tibia model. *J Prost Dent*. 2001;85:40–46
44. Novaes A, Souza S, de Oliveira P, Souza A. Histomorphometric analysis of the bone-implant contact obtained with 4 different implant surface treatments placed side by side in the dog mandible. *Int J Oral Maxillofac Implants*. 2002;17:377–383
45. Piatelli M, Scarano A, Paolantonio M, Iezzi 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
46. Massaro C, Rotolo F, De Riccardis F, Milella E, Napoli A, Wieland M. Comparative investigation of the surface of commercial titanium dental implants. Part 1: chemical composition. *J Mater Sci Mater Med*. 2002;13:535–548
47. Zinger O, Anselme K, Denzer A, Habersetzer P, Wieland M, Jeanfils J. Time-dependent morphology and adhesion of osteoblastic cells on titanium model surfaces featuring scale-resolved topography. *Biomaterials*. 2004;25:2695–2711
48. Wong M, Eulenberger J, Schenk R, Hunziker E. Effect of surface topology on the osseointegration of implant materials in trabecular bone. *J Biomed Mater Res*. 1995;29:1567–1575
49. Cho SA, Park KT. The removal torque of titanium screw inserted in rabbit tibia treated by dual acid etching. *Biomaterials*. 2003;24:3611–3617
50. Park JY, Davies JE. Red blood cell and platelet interactions with titanium implant surfaces. *Clin Oral Implants Res*. 2000;11:530–539
51. Davies JE. Mechanisms of endosseous integration. *Int J Prosthodont*. 1998;11:391–401
52. Trisi P, Lazzara R, Rao W, Rebaudi A. Bone-implant contact and bone quality: evaluation of expected and actual bone contact on machined and osseointegrated implant surfaces. *Int J Periodontics Restorative Dent*. 2002;22:535–545
53. Trisi P, Marcato C, Todisco M. Bone-to-implant apposition with machined and MTX microtextured implant surfaces in human sinus grafts. *Int J Periodontics Restorative Dent*. 2003;23:427–437
54. Cochran DL, Buser D, ten Bruggenkate CM, Weingart D, Taylor TM, Bernard JP, et al. 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;13:144–153
55. Novaes AB, Papalexiou V, Grisi MF, Souza SS, Taba M, Kajiwara JK. Influence of implant microstructure on the osseointegration of immediate implants placed in periodontally infected sites. A histomorphometric study in dogs. *Clin Oral Implants Res*. 2004;15:34–43
56. Papalexiou V, Novaes AB, Grisi MF, Souza SS, Taba M, Kajiwara JK. Influence of implant microstructure on the dynamics of bone healing around immediate implants placed into periodontally infected sites. A confocal laser scanning microscopic study. *Clin Oral Implants Res*. 2004;15:44–53
57. Mohammad Qahash, Ross Hardwick, Micheal D Rohrer, John M Wozney, Ulf M. Wikesjö. Surface etching enhances titanium implant osseointegration in newly formed(rhBMP-2-induced) and native bone. *Int J Oral Maxillofac Implants* 2007; 22:472–477.
58. Nelson K, Semper W, Hidelbrand D, Ozyuvaci H. A retrospective analysis of sandblasted acid etched implants with reduced healing times with an observation period up to 5 years. *Int J Oral Maxillofac Implants* 2008;23:726–732.
59. Cooper LF, Takabe J, Guo J, Abron A, Holmen A, Ellingsen JE. Fluoride modification effects on osteoblast behavior and bone formation at TiO₂ grit-blasted c.p. titanium endosseous implants. *Biomaterials*. 2006;27:926–936
60. Ellingsen JE. Pre-treatment of titanium implants with fluoride improves their retention in bone. *J Mater Sci Mater Med*. 1995;6:749–758
61. 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;19:659–666
62. Yokoyama K, Ichikawa T, Murakami H, Miyamoto Y, Asaoka K. Fracture mechanisms of retrieved titanium screw thread in dental implants. *Biomaterials*. 2002;23:2459–2465
63. Xiropaidis AV, Qahash M, Lim WH, Shanaman RH, Rohrer MD, Wikesjö UM. Bone-implant contact at calcium phosphate-coated and porous titanium oxide (TiUnite)-modified oral implants. *Clin Oral Implants Res*. 2005;16:532–539
64. Huang YH, Xiropaidis AV, Sorensen RG, Albandar JM, Hall J, Wikesjö UM. Bone formation at titanium porous oxide (TiUnite) oral implants in type IV bone. *Clin Oral Implants Res*. 2005;16:105–111
65. Sul YT, Johansson CB, Jeong Y, Roser K, Wennerberg A, Albrektsson T. Oxidized implants and their influence on the bone response. *J Mater Sci Mater Med*. 2001;12:1025–1031
66. Sul YT, Johansson C, Wennerberg A, Cho LR, Chang BS, Albrektsson T. 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;20:349–359
67. Sul YT, Johansson CB, Roser K, Albrektsson T. Qualitative and quantitative observations of bone tissue reactions to anodized implants. *Biomaterials*. 2002;23:1809–1817
68. Sul YT, Johansson CB, Jeong Y, Wennerberg A, Albrektsson T. Resonance frequency and removal torque analysis of implants with turned and anodized surface oxides. *Clin Oral Implants Res*. 2002;13:252–259
69. Rocci A, Martignoni M, Gottlow J. Immediate loading of Branemark System TiUnite and machined-surface implants in the posterior mandible: a randomized open-ended clinical trial. *Clin Implant Dent Relat Res*. 2003;5:S57–S63

70. Jungner M, Lundqvist P, Lundgren S. Oxidized titanium implants (Nobel Biocare TiUnite) compared with turned titanium implants (Nobel Biocare mark III) with respect to implant failure in a group of consecutive patients treated with early functional loading and two-stage protocol. *Clin Oral Implants Res*. 2005;16:308–312
71. Krupa D, Baszkiewicz j, Kozubowski JA, Mizera J, Barcz A, Sobczak JW, Bilinski A, Rajchel B. Corrosion resistance and bioactivity of titanium after surface treatment by three different methods: ion implantation, alkaline treatment and anodic oxidation. *Anal Bioanal Chem* 2005;381:617-625.
72. Krupa D, Baszkiewicz j, Kozubowski JA, Mizera J, Barcz A, Sobczak JW, Bilinski A, Rajchel B. 2001 *Biomaterials* 22:2139-2151.
73. Kim H-M, Miyaji F, Kokubo T, Nakamura T (1996) *J Biomed Mater Res* 32:409-417.
74. Munisamy S, Vaidyathan TK, Vaidhyathan TK. A bone like precoating strategy for implants: Collagen immobilization and its mineralization on pure titanium implant surface. 2008. 34:2:67-75.
75. Josse S, Faucheux C, Soueidan A, Grimandi G, Massiot D, Aïonso B. Chemically modified calcium phosphates as novel materials for bisphosphonate delivery. *Adv Mater*. 2004;16:1423–1427
76. Meraw SJ, Reeve CM. Qualitative analysis of peripheral peri-implant bone and influence of alendronate sodium on early bone regeneration. *J Periodontol*. 1999;70:1228–1233
77. Meraw SJ, Reeve CM, Wollan PC. Use of alendronate in peri-implant defect regeneration. *J Periodontol*. 1999;70:151–158
78. Yoshinari M, Oda Y, Ueki H, Yokose S. Immobilization of bisphosphonates on surface modified titanium. *Biomaterials*. 2001; 22: 709–715
79. Kajiwaru H, Yamaza T, Yoshinari M, Goto T, Iyama S, Atsuta I. The bisphosphonate pamidronate on the surface of titanium stimulates bone formation around tibial implants in rats. *Biomaterials*. 2005;26:581–587
80. Park CY, Kim Su Gwan, Kim MD, Eom TG, Yoon JH, Surface properties of endosseous dental implants after NDYag and CO2 laser treatment at various energies. *J Oral Maxillofac Surg* 2005;63:1522-27.
81. Lu X, Wang Y, Yang X, Zhang Q, Zhao Z, Weng LT, Leng Y. Spectroscopic analysis of titanium surface functional groups under various surface modification and their behaviours in vivo and in vitro. *J Biomed Mater Res* 84A:523-534, 2008.
82. Ban S. Effect of alkaline treatment of pure titanium and its alloys on the bonding strength of dental veneering resins. *J Biomed Mater Res*. 66A:138-145, 2003.