



Techniques for dental implant nanosurface modifications

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PURPOSE. Dental implant has gained clinical success over last decade with the major drawback related to osseointegration as properties of metal (Titanium) are different from human bone. Currently implant procedures include endosseous type of dental implants with nanoscale surface characteristics. The objective of this review article is to summarize the role of nanotopography on titanium dental implant surfaces in order to improve osseointegration and various techniques that can generate nanoscale topographic features to titanium implants.

MATERIALS AND METHODS. A systematic electronic search of English language peer reviewed dental literature was performed for articles published between December 1987 to January 2012. Search was conducted in Medline, PubMed and Google scholar supplemented by hand searching of selected journals. 101 articles were assigned to full text analysis. Articles were selected according to inclusion and exclusion criterion. All articles were screened according to inclusion standard. 39 articles were included in the analysis. **RESULTS.** Out of 39 studies, seven studies demonstrated that bone implant contact increases with increase in surface roughness. Five studies showed comparative evaluation of techniques producing microtopography and nanotopography. Eight studies concluded that osteoblasts preferably adhere to nano structure as compared to smooth surface. Six studies illustrated that nanotopography modify implant surface and their properties. Thirteen studies described techniques to produce nano roughness. **CONCLUSION.** Modification of dental osseous implants at nanoscale level produced by various techniques can alter biological responses that may improve osseointegration and dental implant procedures. [*J Adv Prosthodont 2014;6:498-504*]

KEY WORDS: Intelligent surfaces; Sputtering; Superhydrophilic; Chemical vapor deposition; Osseointegration; Engineered surface

INTRODUCTION

Nanotechnology has been around since ancient times. The inspiration for the field of nanotechnology was provided by American Physicist and Nobel Laureate Dr. Richard Phillips Feynmaan in 1959. The term “Nanotechnology” was first

coined by Norio Taniguchi in 1974. Substance which has at least one characteristic dimension between 1-100 nm is termed as Nanomaterial. Nanotechnology brings a wide-spread consideration in field of disease prevention, diagnosis and treatment. Nanotechnology can be defined as the science and engineering involved in design, synthesis, characterization and application of materials and devices whose smallest functional organization in at least one dimension is on nanometer scale (one billionth of meter).¹

Constituents of dental implant and its surface treatment determine electrical charge and chemical nature of implant surface which directly influence osteoblast adhesion and protein adsorption. Currently grade 4 commercially pure titanium (cpTi) is used for endosseous implants. Grade 4 cpTi has higher strength as compared to other unalloyed available grades. Grade 5 (Ti6Al4V) is an alloyed grade specially made for dental implant procedures because of its superior fatigue properties and yield strength. Hydrophilic

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Received 24 February, 2014 / Last Revision 10 August, 2014 / Accepted 29 August, 2014

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property is influenced by chemical composition of dental implant. In light of interactions with cells, tissues and biological fluids hydrophilic surfaces are preferred over hydrophobic surfaces.² After dental implantation two different types of reactions can occur. The first reaction includes the development of a soft tissue fibrous capsule around the metal implant termed as fibro osseous integration. The second reaction related to direct contact of bone to implant surface without interposing soft tissue between bone and dental implant. This type of reaction is named as osseointegration. Implant surface composition, topography, hydrophilicity, geometry and surface roughness determine rate and quality of osseointegration.³ Rapid and early osseointegration is significantly associated with long term success of oral implant.

Cochran *et al.*⁴ did a histometric analysis in foxhound dog's canine mandible and demonstrated that the surface roughness of oral implant is a determining factor for biomechanical fixation and osseointegration. Wennberg *et al.*⁵ performed evaluation of screw shaped implants histomorphometrically and concluded that bone implant contact (BIC) is dependent on the rough surface. Surface roughness increases specific surface area due to increase in thermodynamic reaction potential.⁶ Increase in specific surface area will increase surface active sites for interaction with cells, tissues and biological fluid. Depending on the scale features, surface roughness can be divided into three levels: a) Macro level topography b) Micro level topography c) Nano level topography.

Macro and Micro level surface features demonstrated to be efficient in enhancing *in vitro* and *in vivo*⁷ biological events. A variety of techniques has been employed to create micron scale surface characteristics on the surface of biocompatible metals but macro and micron scale features can only have an indirect influence on cellular activity so these features have limited actions and performances. Now it is documented that interaction between material and body tissue is principally governed by nanometric implant surface modifications.⁸ Various approaches have been devised and implemented to create nano rough surfaces that can directly influence the biological performance of oral implant.⁹

This systematic review aimed to summarize the role of nanoscale surface modifications of titanium dental implants for the purpose of improving osseointegration and various techniques that can impart nanoscale topographic features to dental implants.

MATERIALS AND METHODS

A search of online studies was conducted using PubMed, Medline and Google Scholar databases. A systematic search of English language dental literature was performed for articles published between December 1987 to January 2012. The search was conducted to identify studies related to response of nanotopography on the bone implant contact (BIC), osteoblast response, changes occurring on the titanium implant surface. Full text of all relevant articles was

obtained. The aim was to identify different techniques used to generate nano topography on dental implants up to and including January 2012.

The systematic search was further enhanced by hand search through following journals: Nanostructured Materials, Journal of Biomedical Materials Research Part A, Dental Material, Journal of Biomedical Materials Research, Clinical Oral Implants Research, Trends in Biomaterials & Artificial Organs, Journal of Long-Term Effects of Medical Implants, Biomaterials, Materials and technology, Journal of Materials Science: Materials in Medicine, Small, Nano Letters, Acta Biomaterialia, Advanced Engineering Materials, International Journal of Nanomedicine, Nanotechnology, Progress in Materials Science, Journal of Biomedical Materials Research Part B: Applied Biomaterials, Materials Science and Engineering: C, European Journal of Oral Implantology.

Electronic search was conducted by applying the following free text and Medical Subject Headings (MeSH)

Search 1: Dental Implant, Dental Implants, Dental Implantation, Endosseous Implant, Endosseous dental Implantation, Titanium implants. Titanium Implant surfaces.

Search 2: Nanotechnology, Nano surface, Nanotopography, Nano surface characteristics, nano roughness, nano surface modification.

Search 3: Combination of #1 and #2 (not including case reports).

All studies were screened according to inclusion criteria:

- 1) Physicochemical studies of novel dental implant surfaces.
- 2) *In vitro* studies illustrating cellular responses in different implant surfaces such as smooth or rough surfaces.
- 3) *In vivo* action of various implant surfaces.
- 4) Studies related to osseointegration and clinical performance from different implant surface modification techniques.
- 5) Studies of which complete text could be assessed
- 6) Published in English language.

Exclusion criteria:

- 1) Case reports
- 2) Case studies
- 3) Book chapters
- 4) Conference proceedings
- 5) *In vivo* studies including sample size less than 5 were excluded
- 6) *In vitro* studies include agents that do not use bone related cells
- 7) Studies including evaluation of currently commercially available surfaces
- 8) Studies whose title did not meet aim of present review

After applying search strategy, total of 101 studies displaying the used terms were found. All studies were assigned to full text analysis. The extracted data were assigned for comparison. By applying inclusion and exclusion criteria total 39 studies were selected.

We restricted our search to publications in English language. Selection of relevant studies was conducted as fol-

lows: Initial assessment of each publication for relevance using information presented in abstract. When the abstract failed to provide sufficient information, a print of full paper was obtained. Data extraction was done by one reviewer. After checking studies that did not fulfill selection criteria, the final outcome of the search was combined.

RESULTS

Using search strategy in PubMed, Medline and Google Scholar databases yielded 101 titles using search terms like dental implants and surface modifications Or Surface modifications on Dental implant surfaces. 20 publication journals were selected using screening of titles and abstract. 101 articles were screened by analyzing the text. The articles in which nanotechnology and dental implants were described along with the illustration of techniques to produce nano-surface were selected and they were 39 in number.

Out of 39 studies seven^{4,7,10,11,12} studies demonstrated that bone implant contact increases with increase in surface roughness. Four^{4,5,7,12} *in vivo* studies, two^{10,11} *in vitro* and one⁶ review article concluded that amount of bone contact to implant is dependent on surface roughness.

Five studies^{7,10,13-15} showed comparative evaluation of techniques producing micro roughness and nanotopography. Three^{7,13,15} *in vivo* studies and two^{10,13} *in vitro* studies showed difference in bone implant contact between acid-etched and machined surfaces, influence of electrical stimulation on anodized surfaces, Calcium ion coated on titanium showed better bone response than titanium alone (uncoated).

Eight studies^{9,16-22} concluded that osteoblasts preferably adhere to nano structure as compared to smooth surface. Seven^{9,16,17,19-22} *in vitro* studies and one¹⁸ *in vivo* study concluded that nano topography influence cell adhesion and osteoblastic differentiation.

Six^{2,23-27} studies illustrated that nanotopography modifies implant surface and their properties. Four^{16,25-27} *in vitro* studies, one² *in vivo* study and one review²⁴ described role of nano topography in influencing dental implant surface. Thirteen²⁸⁻⁴⁰ studies described techniques to produce nano roughness on surface of implant. Nine^{28,29,31,33,34-36,38,40} *in vitro* studies and four^{30,32,37,39} *in vivo* studies described various techniques such as electrochemical method, ion implantation, fluoride modification, non lithographic method, chemical oxidation, sol-gel technique, plasma spray, magnetron sputtering and ultra violet treatment.

DISCUSSION

A nanostructure is an object described between 1 and 100 nm. Nanotopography can determine various cellular processes like cell orientation, alignment, differentiation, migration and proliferation by regulating cell behavior. These surfaces hasten the recovery process thus enhancing the process of osseointegration. Nano topographic modifications are described as surface nano roughness produced by add-

ing nano features to the implant surface. Dalby *et al.*¹⁶ concluded that nanoscale topography controls osteoblastic differentiation and cell adhesion. Oh *et al.*²³ illustrated that nanoscale technology can alter oral implant surface at an atomic level and may influence the chemical composition of these implant surfaces.

There are various methodologies to modify implant dental surfaces at nanoscale level. Surface morphology appreciably affects osteogenic cell activities and rate of peri-implant osteogenesis. This will finally determine the implant-bone integration. Dental implant surface structure, morphology and chemistry can be changed by two ways: Chemical methods, Physical methods. Principal function of these techniques is to modify the implant surface characteristics such as increasing bone formation to improve peri-implant osteogenesis, improvement of corrosion and wear resistance and removal of surface contaminants.¹⁰

Chemical method is the most commonly used method to modify titanium surface at nanoscale. Chemical method includes i) Anodic oxidation (Anodization) ii) Acid Treatment iii) Alkali Treatment iv) Combination of Anodization and Chemical etching v) hydrogen peroxide treatment vi) sol-gel treatment vii) Chemical vapor deposition viii) Combination of Chemical vapor deposition and Sol-Gel method.¹³ According to Bagno and Di Bello⁴¹ surface roughness, composition and surface wettability are altered by chemical surface modification of titanium.

i) *Anodic oxidation*: Smooth titanium surfaces can be successfully transformed into nano tubular structures with diameter less than 100 nm with the help of anodization.⁴² By modifying parameters like voltage, current density and chemistry of electrolyte one can control physicochemical properties of surfaces,²⁴ spacing and diameter of nano tubes.¹⁷ On titanium surfaces, anodization also form pillar like nanostructures with tunable size as well as deposition of long nano tube arrays (10 μm).¹⁸ For example, multi walled nano tubes and nano hydroxyapatite coatings (15-25 nm) have been deposited on titanium that results in improved bioactivity.²⁸

ii) *Acid treatment*: Acid treatment serves to produce uniform and clean implant surface by removing contamination and oxide layer formed on implant surface. The acids commonly used are hydrochloric acid, hydrofluoric acid, nitric acid and sulfuric acid. Roughness produced by acid treatment increases surface area and enhances bone to implant contact. Takeuchi *et al.*²⁵ evaluated the efficiency of three acids H_2SO_4 , $\text{Na}_2\text{S}_2\text{O}_8$, HCl decontamination to Ti surfaces as pretreatment for implant surface modifications and concluded that decontamination done by hydrochloric acid was an excellent treatment. By combining strong acids or bases and oxidants nano pits networks (pit diameter 20-100 nm) can effectively be generated on Titanium, Ti6Al4V, CrCoMo alloys and Tantalum.¹⁹ Various parameters such as nano roughness, wettability, surface topography as well as thickness of protective oxide layer can be controlled by modu-

lating temperature, length of exposure and composition of etching solution.²⁶ Moreover by making variation in nature of etching solution it is possible to incorporate selected elements (Fluorine, which has antibacterial effects²⁹ and also contributes to bone formation³⁰ on nano surface of Titanium.

iii) *Alkali treatment*: It is the method in which the titanium implant is immersed in either sodium or potassium hydroxide followed by heat treatment at 800°C for 20 minutes that is followed by rinsing in distilled water. This method results in the growth of a nano structured and bioactive sodium titanate layer on dental implant surface. On immersion in simulated body fluid (SBF) this bioactive surface acts as a site for nucleation of calcium phosphate. Through ion exchange there is release of sodium ion from sodium titanate results in formation of Ti-OH. When negatively charged Ti-OH reacts with positively charged calcium ion from SBF leads to the formation of calcium titanate. In calcium titanate, phosphate and calcium ion are present which develop into apatite crystal that can provide favorable conditions for bone marrow cell differentiation.

iv) *Combination of Anodization and Chemical etching*: These two methods are combined to create metal or polymer composites with improved biological properties. Anodized nano tubular titanium has been coated with sodium hydroxide treated nano porous poly (lactic-co-glycolic acid) (PLGA) that results in stimulation of cell activity but when compared with anodized titanium no significant difference was seen.¹¹ A combination of hydrothermal treatments (tuning concentration, temperature, reaction medium composition and time duration) and sodium hydroxide has been employed to titanium to create wide variety of unique nano structures such as octahedral bipyramids, nano flowers, nano needles, nano rods and mesoporous nanoscaffolds.³¹

v) *Hydrogen peroxide treatment*: This method leads to oxidation and chemical dissolution of the titanium dental implant surface. Reaction takes place between hydrogen peroxide and titanium dental surfaces leads to formation of Titanium peroxy gels. Control on treatment time determines the thickness of titania layer. Tavares *et al.*³² concluded that immersion in simulated body fluid lead to development of thicker layers of titania gel which is beneficial for deposition of apatite crystals.

vi) *Sol-gel method*: It is one of the widely used methods for depositing CaP, TiO₂, TiO₂-CaP composite and silica-based coatings on implant surface materials. This method leads to the formation of sol which is a uniform suspension of submicroscopic oxide particles in liquid by the procedure of controlled hydrolysis and condensation. Factors such as surface roughness, chemical pretreatment and sintering temperature determines the degree of adhesion of TiO₂ sol gel coatings on substrate (implant surface). Bajgai *et al.*³³ studied bioactivity of titanium coating and concluded that when substrate immersed in simulated body fluid for 1

to 15 days results in faster growth of apatite crystals in gel containing titania. Nishimura *et al.*²⁰ illustrated a process of dual acid-etching on titanium dental implant surfaces in a rat model in order to deposit CaPO₄ nano scale features. By the deposition of discrete 20-40 nm nanoparticles on a dual acid-etched implant surface led to early bone healing and enhanced mechanical interlocking with bone. Gutwein and Webster²¹ investigated osteoblast viability and its proliferation in presence of nano phase titania and alumina particle and concluded that nanoparticles impose positive impact on osteoblast viability and its proliferation. Sol-gel coating process improves dental implant surfaces by nanoscale surface modifications. High bond strength between implant surface and nanoscale coating is due to high electron density at atomic level.

vii) *Chemical vapor deposition*: In this procedure chemical reaction takes place between implant surface and chemicals present in the gas phase that will lead to deposition of compound (non-volatile) on the oral implant substrate. Popescu *et al.*³⁴ did comparative study and concluded that by the process of chemical vapor deposition, metallic surface properties can be modified at the nanoscale level.

viii) *Combination of Chemical vapor deposition and Sol-Gel method*: Metallic surface properties can also be improved by these methods.³⁴ With the help of these techniques Niobium oxide and diamond like carbon nano topographies has been deposited on titanium and other substrates which improve the bioactivity of implantable metals.³⁵

Various physical techniques had been employed to create bioactive nanosurface on biocompatible metal surface. These methods include i) *Plasma spraying* ii) *Sputtering* iii) *Ion implantation*.

i) *Plasma spraying*: This method is able to create a nano engineered surface with less than 100 nm in dimensions. This process includes elimination of surface contaminants with the help of vacuum followed by deposition of charged metallic ions or plasma guided by kinetic energy on dental implant surface. This process allows coating of various materials like Au, Ti, Ag on wide range of materials such as polymers, metals or ceramics. This process is widely used for deposition of calcium phosphate coatings (HA) onto dental implant surfaces to modify its bioactivity. Osteoblast density increases on the implant nano scale surface. According to De Groot *et al.*³⁶ hydroxyapatite coated implants leads to high percentage of bone-implant contact. Regardless of clinical success there are disadvantages of plasma-spraying method such as variation in composition of coatings, non-uniform thickness of deposited layer and lack of long-term adherence of the coating to the substrate material that can pose health hazards and affect the long term stability of dental implants.⁴³

ii) *Sputtering*: This process involves ejection of atoms or

molecules by bombardment of high-energy ions that results in deposition of bio ceramic thin films. This method provides greater adhesion between the coating and substrate along with greater control on properties of coating. This method also improves mechanical properties like wear and corrosion resistance, biological activity and bio compatibility. Vercaigne *et al.*¹⁴ did histological evaluation on trabecular bone of goat using TiO₂ grit blasted and sputtered CaP implants. Improved healing response and initial fixation were found with sputtered CaP coatings. The main drawback of this technique is that this process is very slow as well as deposition rate is also very low. The slow deposition rate is improved by radio frequency magnetron sputtering.³⁷

- a) Magnetron sputtering: This is a method of depositing viable thin-film coating. This process maintains the bioactivity of hydroxyapatite coating along with the preservation of mechanical properties of metal. Custom-built sputter deposition chamber is used for deposition of coatings at room temperature. Wolke *et al.*³⁸ concluded that hydroxyapatite coating deposited by magnetron sputtering was dense and uniform.
- b) Radio frequency sputtering: This method involves deposition of thin films of calcium phosphate on substrate metal surface. The main advantage of this method is strong adhesion of coating to metal surface, crystalline nature of coating and Ca:P ratio can be altered easily.
- iii) *Ion implantation*: This method includes atomic rearrangements. Ion implantation method enables to inject any element on the near-surface region of any substrate like hydroxyapatite layer on the titanium surface is synthesized by implantation of calcium and phosphorous ion. This method includes using beam of high energy (10 KeV) ions to fall on metal surface under vacuum chamber. Due to the collision between incident ions and substrate ions, incident ions loses energy and come to rest on near-surface region of metal. Following are advantages of this technique:

- a) It is an ultra clean process so synthesis of high purity layers is possible.
- b) Depth and concentration of impurities are easily controlled and determined.
- c) Adhesion between implanted surface and substrate is excellent.
- d) Process is performed at low substrate level so no effect on bulk properties of substrate.
- e) Method is easily reproducible and controllable.³⁹

When using ion implantation method, modification of preexisting nanometric features and creation of superficial stresses must be carefully considered.^{15,44} This approach offers possible insertion of biologically effective ions such as calcium ion (Ca²⁺), fluoride ion (F⁻), sodium ion (Na⁺).

- iv) Bioactivity can also be increased by *thermal oxidation*

on biocompatible metal surface. Thermal oxidation method act by changing crystalline structure of nanometric oxide layer.^{12,45}

Recent advancements that will modify surface chemistry of dental implant surface without altering bioactive surface topography includes effect of laser procedure, pico to nanometer thin TiO₂ coatings and synergistic effect of micro-nano hybrid topography on titanium surface with ultraviolet (UV) photo functionalization.

Nano-structured dental implant surface can be altered through Laser technology.

Laser is used as a micromachining device to produce a three dimensional structure at micrometer and nanometer scale level. This technique enables the energy to focus on one spot by generation of short pulses of single wavelength. Advantages of laser technology: (i) Allows generation of complex feature with high resolution (ii) Extremely clean (iii) Rapid (iv) Suitable for the selective changes in implant surfaces (v) Precise, targeted and guided surface roughening.²² Thomsson and Esposito⁴⁰ performed retrospective case series and developed laser micromachining procedure to create micro and nano scale surface roughness only in the inner part of the thread of dental implant as inner part is considered suitable for osteogenesis.

Secondly, Nanosurface modification is possible through Picometer to Nanometer thin TiO₂ coatings.

Sugita *et al.*²⁷ directed the possibility of pico to nanometer thin TiO₂ coatings on micro roughened metal surfaces. Using slow rate sputter deposition method a thin titanium oxide coating (300 pm - 6.3 nm) was effectively deposited on implant surface. This technique augmented the surface oxygen components without changing surface topography. These biological activities were exponentially correlated with the thickness of TiO₂ coating and oxygen saturation on the surface. This suggests that biological response of titanium can effectively be enhanced by even picometer super thin coatings.

Another surface modification is through synergistic effect of nanotopography with ultraviolet (UV) photofunctionalization.

The effect of micro-nano hybrid surface topography with UV photofunctionalization on implant surface is synergistic. UV Photofunctionalization is a new method of surface modification. This method involves removal of surface contaminants of hydrocarbon with the help of titanium oxide mediated by photo catalysis and decomposition by ultra violet light.⁴⁶ Tsukimura *et al.*⁴⁷ addressed the synergistic effects of UV photofunctionalization and surface factors responsible for synergistic effect. They concluded that high biological activity occurred with the micro pits having 300 nm nodules after ultra violet treatment.

Advantages of nanoroughness on titanium implants

1. Increase surface area of implant adjacent to bone.
2. Improved cell attachment to the implant surface.

3. Increase bone present at the implant surface.
4. Improve biomechanical interaction of implant with bone.

CONCLUSION

Several techniques have been widely studied and developed to modify dental implant surfaces to promote rapid osseointegration and faster bone healing. Several *in vivo* and *in vitro* studies demonstrated various novel dental implant surfaces mostly consisting in modifications of commercial available ones. Nano surface modification methods are likely to enhance surface properties of titanium dental implant that increase peri-implant osteogenesis. The main shortcoming in dental implant surfaces is empirical nature of manufacturing process as it lacks generalized consensus to make one standard for obtaining controlled topographies. In order to overcome this matter, several *in vitro* and *in vivo* studies are still required. Nanotechnology is still advancing and need much more testing before appreciating its maximum potential.

ACKNOWLEDGEMENTS

The authors would like to thank to Mr. Ajay Saha for his most support and encouragement. He kindly read paper and offered invaluable detailed advice on grammar, organization and editing English of the paper.

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