

## REVIEW

# Nano-scale surface modification of dental implants – An emerging boon for osseointegration and biofilm control

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Implant therapy is a commonly based method of replacing missing teeth. A range of physical, chemical, and biological modifications have been applied to the surface of titanium implants to improve their biological performance and osseointegration outcomes. Implant surface characteristics play an important function in several peri-implant cellular and molecular mechanisms. Clinicians are commonly placing dental implants with various surface roughness and modifications including plasma-sprayed, acid-etched, blasted, oxidized, hydroxyapatite-coated, or combinations of these procedures. Surface modifications are to facilitate early osseointegration and to ensure a long-term bone-to-implant contact without substantial marginal bone loss can be accomplished. It is apparent that different modifications have a range of beneficial effects, it is essential to consider at what time point and in what conditions these effects occur. This article reviews existing surface modification technologies of mainstream dental implants and the correlation between implant surface coatings and their performance of osseointegration or anti-bacterial ability it needs to be evaluated.

**Keywords:** dental implants, nano level implant modification, osseointegration, surface topography, coatings

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## Introduction

Implants are one of the best choices for replacing missing teeth in dentistry. Historically, grade 2 or 4 titanium alloys and their commercially pure forms materials are superior for endosseous implants [1]. But a range of problems are associated with titanium. The titanium dental implants can cause stress-shielding due to the high modulus of elasticity. This may lead to periodontal bone loss [2]. Hypersensitivity to titanium dental implants is also reported in a few cases [3,4]. Visibility of titanium dental implant through thin biotype gingiva can cause aesthetic complications [3].

An important aspect of implantology is attaining and maintaining osseointegration and the gingival epithelial junction. Bacterial colonization could be inhibited by emphasizing a close gingival tissue collar with a dental implant. A biomechanical anchoring of the artificial dental root may be ensured by direct bone bonding. Thus, various efforts are made towards faster and better osseointegration. The rate and extent of osseointegration are affected by various factors, implant surface character is one of the major factors [4, 5]. Faster osseointegration can be achieved by altering surface topography and surface chemistry. The surface biological properties of metal implants enhance the adsorption of proteins, cell adhesion and differentiation, and tissue integration. Cell behaviors can be directly affected by surface modifications.

The adhesion of a fibrin blood clot and the population of the implant surface by blood-derived cells and mesenchymal stem cells is orchestrated in a manner that results in osteoid formation and its subsequent mineralization [4]. A

modification of the tissue/implant interface results in due course results in bone-forming in direct contact with the implant surface. The nature of the implant surface influences the direct contact with bone, duration for the formation of this bone, and the mechanical nature of the bone/implant connection [8,9]. These biological properties are useful as they are linked to the wettability, chemical composition and roughness of metal implants surfaces. To achieve favorable outcomes of the biological properties at the cellular level is a great task for the researchers and dental implant manufacturers of today [3,5].

Nanotechnology has been defined as “the creation of functional materials, devices, and systems through control of matter on the nanometer length scale (1–100 nm), and exploitation of novel phenomena and properties (physical, chemical, and biological) at that length scale”. When implant surfaces are engineered to possess nanoscale surface features, implant surfaces will integrate between the implant and surrounding bone [5].

There are various methods to modify implant dental surfaces at the nanoscale level. Surface morphology significantly affects osteogenic cell activities and the rate of peri implant osteogenesis. This will finally determine the implant-bone integration. Dental implant surfaces can be modified by chemical methods and physical methods. In general, these treatments are utilized to change the surface properties of the implant, such as improving peri-implant osteogenesis, improving corrosion and wear resistance, and removing surface impurities. Chemical methods are commonly used to produce nanoscale surface modifications.

The surfaces of dental implants can be treated with numerous processing methods to develop controlled features at the nanometer scale range. The long-term goal is

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to substitute metal implants to a design synthetic ceramic or composite implants which will be superior to the present implant materials. The amalgamation of tissue engineering, biomimetics and nanoscience is essential for such achievement.

Surface topography is often characteristically anisotropic. Isotropic features such as nano grooves or nanopits that are created largely by optical methods are not readily applied to complex screw-shaped objects. When endosseous implant surfaces, are subjected to these concepts the surface with nanometer-scale features lead to novel physicochemical behavior or biochemical events [4-7].

A thin nanolayer oxide(s) coating is unavoidable on all metallic implants thus cells never interact directly with the metallic implant surface [8]. Enhanced bone-to-implant contact and improved clinical performance has been shown by modifying surface roughness [8].

### **Nanoscale modification for dental implant surface-**

To develop an interfacial chemical bond between implant material as well as surrounding bone soft tissue a variety of bioactive coating can be used. This is due to the restricted interactions of bio-inert materials with the surrounding tissue [9].

Nanomaterials are promising delivery agents because they have a variety of biomedical features that influence interactions with biological surroundings. There are various ways in which nano-features can be created on titanium dental implants. The osseointegration, strong bone-implant contact, and bone osteogenesis can be achieved by Ti surface nano modifications [10]. 3D nanostructures developed invitro osteogenesis attachment, differentiation, along with growth. Physical approach like compaction of nanoparticles, ion beam deposition. Chemical method like anodization, acid etching, alkali treatment and peroxidation. Nanoparticle deposition Sol-gel, Discrete crystalline deposition and Lithography and contact printing technique.

### **Laser Ablation**

This is a technique used for designing nano-scale channels surrounding the implant collar region [11]. Modified techniques are advantageous compared to conventional surface as it has accurate surface geometry with high resolution which rapidly cleanse the surface [12]. In contrast to machined surface implants, laser-ablated implants have substantially more bone-to-implant contact and higher torque removal values [5]. Furthermore, the connective tissue fibers will flow perpendicular to the laser-ablated implant surface, as opposed to the usual parallel orientation of fibers around a surface. The collar of the implant appears to act as a biological seal by encouraging soft tissue and bone adhesion while inhibiting epithelial downgrowth. The cervical seal act as a barrier, by inhibiting apical migration of junctional epithelium [4]. In a vivo investigation,

laser-ablated titanium implants, as well as human enamel surfaces, has shown less plaque accumulation when compared with machining and grit-blasted implants [13]. In a desirable case of dental implants, laser ablation not only promotes rapid osseointegration as well as improves connective tissue attachment, reduces contamination. In a clinical study, shown biofilm deposition significantly lower when the surfaces blasted orthogonally with a laser beam [13]. Therefore, laser beam's orientation appears to influence biological interaction.

### **Nanocomposite**

To improve their compatibility with natural bone dental implants are coated with nanocomposite. Using chemical and physical methods, including cubic zirconia, ultrananocrystalline diamond, titanium dioxide (tio), pectins, silver (ag), hydroxyapatite (ha), and carbon nanotube. In a clinical study they concluded "Biocompatibility and osseointegration can be improved by using secondary nanoparticles." [12]. Nanoparticle compaction, physical vapor deposition, plasma spraying deposition and hot isostatic pressing are all physical processes and the introduction of secondary nanomaterials has the potential to improve biocompatibility and osseointegration. Titanium with a nano-composite coating demonstrated easy-to-clean surface qualities in oral environments, resulting in lower biofilm growth. By separating adsorbed salivary proteins and adhering microorganisms under shear stresses by providing a cleanable surface. In a study it was found that silver nanoparticles coated on titanium surfaces showed antibacterial properties, against *Staphylococcus aureus*, which prevents peri-implantitis. However, because of the cytotoxicity and possible danger associated with the use of silver nanoparticles, these particles must be firmly fixed to the surface [14]. Nanoscale modifications to implant surfaces have the potential to promote osteointegration and prevent biofilm formation. Although research in this field is still in its early stages. Additional research, including in vivo biosafety evaluations, are required [5,15].

### **Discrete crystalline deposition (dcd)**

Dcd is a sol-gel method that employs discrete crystalline deposition that involves modifying a double acid-etched surface using 20–100 nm calcium phosphate particles dcd nanoscale surface has significantly better mechanical outcomes in animal research. Distal femurs were placed with titanium implants with the dcd coated in experimental research, after 9 days they observed disruption force at the bone-implant interface was substantially greater in dcd samples than non-dcd group [16]. Due to an improvement in surface nano topography, In animal model and human model dcd-coated titanium implants exhibited improved osteoconduction & bone-to-implant interface as commercially pure titanium cpTi & Ti6Al4V controls [17]. The dcd-modified implant surfaces demonstrated a substantial decrease in microbial colonization when com-

pared with machining and acid etching. Adherence of *S. sanguis*, *S. mutans*, *A. actinomycetemcomitans* and on dcd-modified surfaces was considerably decreased when compared to acid-etched surfaces, as measured by techniques such as viable bacterial number and confocal laser scanning microscopy have been used. A laser profilometer was also used to analyze the cell's reduction in surface roughness [3,18].

### Anodic Oxidation

A porous implant surface microstructure diameter of around 1.3–2.0mm<sup>2</sup>, a porosity of about “20%”, and a moderate degree of surface roughness of Sa = 1μm created in this method. This is achieved by treating the implant surface electrochemically and modifying it by anodic oxidation. This increases the thickness of the TiO<sub>2</sub> layer from 17–200 nm in conventional titanium implants to 600–1000nm [5]. This implant surface is known as titanium porous oxide (tpo) or anodized titanium surface implant (asi) [11]. The surface properties of Ti Unite implants have been proven at the nanoscale [13]. In experimental studies also revealed anodic oxidation could be easily transported to the implant's neck. This resulted in a good soft tissue seal. Anodic oxidation-generated nanostructured titanium surfaces have been found to promote the adhesion, proliferation, and extracellular matrix deposition of human gingival fibroblasts. Clinical trials confirmed the animal research findings of good biological responses to anodized titanium implant surfaces. The porous oxide surface does not allow for higher biofilm growth because of the anodized surface's roughness.

### Anodization

Anodic oxidation is an electrochemical alteration of the titanium implant surface that results in a denser TiO layer. It has been demonstrated that Ti implant surfaces can be anodized to produce nanotubes with diameters less than 100 nm and thicknesses between a few hundred nanometers and a few microns [4]. The anodization process is influenced by several factors, including current density, acid content, composition, and electrolyte temperature. In animal models compared to conventional surfaces, anodized surfaces have shown substantially greater bone contact and superior biomechanical torque removal values [4]. Anodized implants had a 10% superior success rate than machining implants after initial loading. Compared to “96.4 %” for turned titanium implants, anodized implants had a “100 %” survival rate and without any evidence of inflammatory process. In an animal model, they have evaluated at 6 and 12 weeks after implant implantation, TiUnite implants had more bone-to-implant contact than machined implants. In this experiment, the TiUnite surface was found to be equal to those evaluated for ha-coated implant surfaces [19,18]. When anodized titanium implant compared to conventional titanium, resulted in increased calcium deposition and production of osteocalcin by os-

teoblasts which initiate osteogenesis. The beneficial effect of nano topography on osteogenic gene up-regulation was observed when nanostructured titanium was compared to conventional titanium samples.

### Acid etching

These were designed to change the implant surfaces without the remnants found after blasting methods, to have a consistent implant surface topographical treatment, and to limit metallic material loss. Nitric acid, Hydrochloric acid, hydrofluoric acid, along with sulfuric acid are the most often utilized acids. Roughness is created by the acid treatment, which increases surface area and facilitates bone-to-implant contact [5,7]. Acid concentration, bath temperature process effect on acid-etching leads to “Contact osteogenesis”. Over the years numerous research has demonstrated the effectiveness of dual acid-etched (dae) surfaced implants in terms of increased bone-to-implant contact versus turned surfaced implants [7]. In minipig model resulted SLA implants in greater bone-anchoring than acid-etching alone or machined implants” [5]. Surface has homogeneous imperfections after the acid-etching phase, this leads to increases in the functional surface area which enhances bio adhesion [20]. Enhanced osseointegration, has been seen by improved micro-scaled roughness, but it also affects bacterial adherence and biofilm development. Sandblasting and H<sub>2</sub>O<sub>2</sub> treatment of micro/nanostructured Ti implants can produce reactive oxygen species on the surface, leading to high wettability and improved cell detachment and cell proliferation [21,22].

On surface of micro/nanostructured media, reactive oxygen species could develop, Ti implants by sandblasting and H<sub>2</sub>O<sub>2</sub> processing, and this causes elevated wettability values and increases the segregation of cells and gene expression.

### Alkali Surface Treatment

In dentistry, alkali therapy is a common type of surface treatment. H<sub>2</sub>O<sub>2</sub> creates a Ti gel layer following NaOH treatment, and Ti nanostructures could be additional altered in conjunction with sodium titanate gel layer. In addition, ha accumulation led to creation of a coating on the dental implant's surface. Other metals, such as zirconium and aluminium, have shown similar traits [5]. On implant surfaces alkali treatment contributes to the formation of a nano level, bioactive sodium titanate coating. CaP crystals might nucleate when bioactive surface submerged in simulated physiological fluid. Electron transfer results in the production of Ti–oh by stimulating sodium titanate Na ions. Ti calcium is formed when negative Ti-OH combines with SBF CaC<sub>2</sub>. P and Ca ions could generate calcium titanate in apatite crystals, which could also help bone marrow cells differentiation. The creation of apatite is caused by Ti's neutral surface charge, which is mostly caused by pH variations. Alkaline therapy around the Ti implant, Ti surfaces have elicited significant bone growth. These find-

ings could be used to boost biomaterials research for bone implants in the future.

### Sol-Gel Technique

This is among the most used approaches for coating the implant surfaces with  $(\text{CaP}, \text{TiO}_2/\text{Ti})^2$ -Cap composite, including silicate-based coverings. Hydrolysis and condensation from a homogeneous sol suspension comprised of submicroscopic oxide particle. Various methods like spraying, spin coating, or dip-coating, can be used to mount the base on the surface of the substratum [7,18]. Precursor components adheres focus surface after drying then molded into a fine coating of a hydrogel. The calcium phosphate is coated on the implant's surface at a nanoscale level using a sol-gel approach. Because of the high electron density at the atomic level, the implant surface and nano surface coating form a high-level binding affinity.

### Chemical vapour deposition method (cvd)

In this technique, a layer of substratum can be deposited on the surface using chemical interactions. In vitro research, it was shown that this method was advantageous when graphene (Gp) employed as a substrate for dental implants. In a study, they reported the use of Gp coated copper foils coupled with cvd approach to induce dental pulp stem cells forms extracellular matrix components in lack of osteoblastic medium [5]. This approach can achieve a high level of enhanced strength, ultra-high hardness, as well as adhesion on Ti surfaces on dental implants coated in diamond nanoparticles [7]. The cvd process could be used to create bio-metal surfaces with nanoscale modifications. CaP-O bio-ceramic nano-coating could be created on Ti-based dental implants using this approach. Using the cvd technique with metal-ceramic surfaces to produce a distinctive from of a metallic nanocrystalline linkage to its tough-ceramic interaction on the metallic surface.

### Combination techniques

Certain combination techniques are also tried to develop a superior nano surface modification. The use of technological biomimetic methods for nanomodification of implants is an emerging field with significant potential for implant surface modification and localized drug delivery biomaterials. Laser-based, thermal oxidative, and electrochemical techniques have boosted the development of various novel enhanced nanostructured materials and drug carriers, including titanium-based nanotubes, peptides, polymer micelles, liposomes vesicle, multifunctional dendritic polymers, nanocapsules, nanospheres, and other bioactive ceramic material. The structural organization and chemical composition of nano-structured surfaces involving nano scale pores or irregularities (e.g., spike-like and nano arrays features) on titanium implant and biomaterials become a key factor to mimic the natural structure of bone and soft tissues and therefore to enhance the bone healing process [22]. The association of different emerging technological

methods such as titanium nanotube formation is an interesting strategy to produce hybrid implant and biomaterials involving a combined micro- and nanoscale structure composed of inorganic and organic bioactive materials.

Nano-roughness, chemical composition, and hydrophilicity of implant surfaces can determine the adhesion of osteogenic cells and therefore to avoid the bacterial accumulation during the healing process and maintenance of the soft and bone tissues surrounding the implant. Few techniques are shown to be more beneficial than the single methods, but more studies are needed in this direction.

### Future research

Chronic inflammation and infections surrounding implants, as well as osseointegration complications, are the causative factors of dental implant failure. Non-metallic substitutes, excluding metal implants, could be used as the tooth's root. (e.g., bioceramics, bio-glasses, "polyether ether ketone (pekk)" [10,18,23]. Nanotechnology encourages the creation of bioactive and anti-bacterial implant materials with high efficiency and relatively low cost, as well as multifunctional characteristics and effective host response management.

In recent study by Feridoun concluded Coating of Ti surfaces with nanoparticles can improve soft tissue integration and osseointegration that leads to improved fixation of implants. Furthermore, osteoconductive nanoparticles induce a chemical bond with bone to attain good biological fixation for implants [24]. Surface modification of implants using antibacterial properties can also decrease the potential for infection, and certainly, present improve clinical outcomes.

PEEK can be modified in numerous ways at a nanometer level to overcome its restricted bioactivity. Various nanometer level modifications are done to overcome limited bioactivity in peek [7]. Melt-blending can be used to combine nanoparticles like haf, and HAp,  $\text{TiO}_2$  with peek to create bioactive nanocomposites. When compared to pure peek, composites have much better tensile qualities. Haf also has antimicrobial abilities that may help to early implant failures also reduce peri-implantitis. Gas plasma etching, Spin-coating, electron beam deposition, also plasma-ion immersion these methods could be utilized to cover surface of peek implant on nanoscale scale. Spin-coating nanocoating of materials like HAp and  $\text{TiO}_2$  could impart bioactive characteristics to the substrate. Anodized electron beam-coated  $\text{TiO}_2$  nanolayer on peek can also carry immobilized bmp-2 growth factor, boost cellular activity beyond. However, there are limited in vitro testing the use of peek implants, which have not been subjected to significant animal and human trials, provides a possibility of early failure [19]. The implant showed a micro-nano-textured surface supporting the formation of a biocompatible apatite when immersed in HBSS [25]. These properties may likely favour bone anchorage and healing by stimulation of mineralizing cells.



As a result, further *in vivo* research is needed before nano modified peek implants might well be widely used in clinical settings [5,7,18].

## Conclusion

The introduction of nanotechnology in the dental implant manufacturing industry has opened a new avenue of nanoscale characterization of dental implant enabling the implant surface to mimic the surface topography of extracellular matrix components of the natural tissue. This has provided new insight into the science of osseointegration and has set a new trend in implant surface modification techniques. Comparative studies performed *in vitro*, and *in vivo*, pre-clinical models have shown the superiority of the nanomodified surfaces to their predecessors. The 3D printing, bioactive nanoparticles and stimulus-dependent variable materials have been research hotspots in recent years, and their combination with surface modification is expected to produce more new orthopedic implants. In addition, it is a trend of surface modification to produce composite surfaces structures with multiple morphologies and sizes [26].

However, such comparative long clinical trials have been lacking from the literature. In absence of such randomized controlled trials (rct), it cannot be ascertained whether these nanoscale modifications have a significant clinical impact. Thus, more research work and long-term clinical trials are warranted in this field to fully acknowledge its true potential. Nanotechnology has contributed to the development of new and innovative implants, and the synthesis of nanomaterials seems to be an important pathway in restorative dentistry research along with microbial innovations that attempt to mimic anatomy and design. Many studies need long-term *in vivo* tests.

## Authors' contribution

PGS - Conceptualization, data curation, Writing – original draft, Writing – review & editing.

ASU - Conceptualization, data curation, Review & editing. Visualization, formal analysis of the manuscript

SUN - Conceptualization, data curation, Writing – original draft, Writing – review & editing

## Conflict of interest

None to declare.

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