MULTISCIA
JOURNALS PUBLISHERS

FRONTIERS IN CLINICAL TRIALS AND DRUG INTERACTIONS

ISSN: (3065- 3975)

https://multisciajournals.com/journals/index.php/fctdi

editor.fctdi@gmail.com

Frontiers in Clinical Trials and Drug Interactions
Volume1, Issue3, 2025

Dental Implant Surfaces using Nanostructure

R Hazra, A Saha

Department of Clinical Trials and Drug Interactions

Article Info

Received: 25-06-2025 ***Revised:22-07-2025*** ***Accepted:07-08-2025*** ***Published:17-08-2025***

Abstract: Osteointegration, or the structural and functional union of the dental implant's surface with the surrounding bone, is essential to the device's performance both now and in the future. In recent years, structural changes to the implant surface, especially at the nanoscale level, have allowed for the manipulation of osteoblast adhesion and spreading, which has improved bone formation at the bone-implant interface. To create the greatest dental implant technology, conventional chemical and physical processes are used in novel ways. The most popular manufacturing processes, together with the associated cell-surface interactions and regulation, are summarized in this article. To find research on implant surface nanostructuration and the biological interactions associated with it, a Medline and manual search were performed. The significance of the nanometric surface alterations on dental implants was emphasized in this article. Since the encouraging outcomes shown in animals and in vitro have not yet been verified in people, there is currently limited proof of the long-term advantages of nanofeatures. Nonetheless, there is no denying the growing interest in nanotechnology, and more studies will be released in the next years.

Keywords: adult stem cells; nanotechnologies; differentiation; osteogenesis; surfaces; dental implant

1. Introduction

Over the last 30 years, implant dentistry has grown gradually but steadily. Dental implants, such as dentures, are used to either support complicated prostheses or replace lost teeth due to caries, periodontal disease, or agenesis. The majority of the surgical process is standardized: the titanium screw is inserted into the recipient bone site using precision drills at a specific torque and speed, and as a result, at a consistent time. After then, it usually takes a few months to install a permanent repair. For osseointegration to occur, time is essential.

No one anticipated that dental implants would make significant progress over time when the concept of osseointegration initially surfaced in the late 1970s and early 1980s [1,2]. The structural and functional union of the implant surface with the surrounding bone is known as osseointegration. This is only connected to the device's geometry and surface topography, not to mention the surgical method of implantation, and is believed to be crucial for the dental implant's immediate and long-term effectiveness. This is the cause of the growing interest in dental implant technology. The gadgets are designed to replicate as closely as feasible the typical cell-to-cell interactions that occur during bone remodeling. To accelerate and enhance osseointegration, synthetic materials should have surface characteristics that are as close to the diameter and form of bone as feasible. At various sizes, the implant surface's characteristics may be described.

Macroscopically, the pitch spacing, thread shape, and screw design are essential for providing stability to implants. Dental implants should be made to optimize beneficial stresses and decrease unfavorable stresses at the bone-implant contact, as suggested by Abuhussein et al. [3]. To increase the surface area in contact with the surrounding bone, it may be beneficial to employ longer and bigger implants, deeper threads, and a narrower pitch.

The coating of the implant surface is involved at the microscopic level. Studies have been carried out both in vivo [5,6] and in vitro [4] to evaluate how these surface alterations affect the bone-implant interactions. It is commonly accepted that microscale characteristics provide a microenvironment that may alter the recruitment and function of cells [7]. Specifically, researchers demonstrated that surface roughness may affect osseointegration via cell attraction, enhancing cell adhesion [8–10]. Nonetheless, it is thought that the osteointegration process is indirectly influenced by the microscopic characteristics of the implant surface on bone growth at the implant site [11–13].

These days, nanoscale characteristics that may trigger stem cell differentiation along the osteogenic pathway are responsible for improving the bone-forming activity at the bone-implant interface [7]. By manipulating matter on the nanoscale length scale (1–100 nm), nanotechnology creates useful materials, tools, and systems. The capacity of cells to interact with nanometric characteristics explains how nanotechnology is applied to biomedical surfaces. Integrins primarily mediate the biological action by attaching to the arginine-glycine-aspartate peptide sequences. When cells adhere to the extracellular matrix (ECM), intracellular signaling cascades are triggered and integrins cluster form focal adhesion complexes (FA) [14]. Nanofeatures are essential in this situation to control the activity of stem cells [15]. It has been shown that the surface pattern in particular is important because osteoblasts may "encode" the surface's three-dimensional properties (such as lines, pores, and dots) and adjust their development in accordance with the proposed structural features [4,10,11]. Nanoscale dimensional patterns are so important that a little change in the diameter of the nanotubes may result in the switch from growth decay (≥50 nm diameter) to cell adhesion and spreading augmentation (found for 15–30 nm TiO2 nanotubes) [16]. This finding was supported by Cavalcanti-Adam et al. [17], who showed that FA production was stimulated by 58 nm separation but not by 108 nm spacing.

We provide a review article on the most popular manufacturing processes and the associated cell-surface interactions because of the significance of the nanofeatures of dental implant surfaces in achieving osseointegration.

2. Cell and Surface

Stem cells (SCs) are generally defined as cells that are able to self-renew and to differentiate into various specialized tissues (e.g., fat, bone and cartilage, neural cells) [18]. Their main functions are tissue development, homeostasis and in the case of tissue damage, reparation. Multipotent mesenchymal stromal cells (MSCs) were found to be rare cells living in various mesenchymal tissues, for example in the bone marrow stroma, adipose tissue, dental pulp. Currently MSC represents an innovative tool in regenerative medicine and odontoiatric field stem cell biology is now is fulfilling tools for the development od biomedical devices for bone or tooth restoration [19]. Indeed, current dentistry resolves the problems related to those loose using autologous tissue grafts or metallic implants, but these treatments have some limitations such as an adjoining tooth damage, bone resorption *etc.*

Cell therapies represent the most challenging and, potentially, the most successful application of stem cells (SCs). Because of their ability to differentiate into different types of functional cells, SCs posses great potential in therapeutics to restore and regenerate native tissues. Atypical strategy based on SCs consists in engineering tissues by using cells coupled with suitable biomaterials to mimic the *in vivo* biochemical and biophysical microenvironment [19]; this approach has shown promising results in treating irreparable damage of native tissues caused by diseases or injuries [20]. However, before SC-based therapies are applied in clinics, a fundamental issue needs to be elucidated to gain a precise control over SCs response, in terms of self-renewal and differentiation, specifically, a broader understanding of the interplay between SCs, the surrounding microenvironment components (growth factors, cell-cell contacts, and cell-extracellular matrix interactions), and external forces [21], which is currently lacking [22].

In this view, the most applied stem cells are Human mesenchymal stem cells (hMSCs) that are self-renewing cells with multipotent differentiation potential.

They give rise to various anchorage-dependent cell types, including adipocytes, chondrocytes, myoblasts, and osteoblasts. Their differentiation potential is influenced by substrate elasticity, geometrical confinement, and substratetopography [23].

Cell-substrate or cell-extracellular matrix (ECM) adhesions are mediated by dynamic multiprotein structures called focal adhesions (FA). They are important for force transmission, cytoskeletal regulation and signaling. At these sites, the cell establishes a transmembrane connection between elements of the ECM and the actin cytoskeleton. The transmembrane integrin proteins orchestrate these events [24]. The integrins, heterodimers containingalfa and beta subunit, bind with their extracellular domain to the ECM proteins fibronectin, laminin, and vitronectin.

The cytosolic domain of integrins binds to a large number of proteins such as paxillin and zyxin either directly or via scaffolding proteins. Some of these proteins are implicated in strengthening the linkage between the extracellular matrix and the cytoskeleton, others play a role in adhesion-mediated signaling. Cellular adhesions can be classified into three categories: Focal complexes (FX), FA and fibrillar adhesions. The FX along the leading lamella of migrating cells are early adhesions, which transform into focal adhesion upon RhoA activation [25,26] or as a result of external mechanical perturbation [27,28]. Fibrillar adhesions develop from FAs following actomyosin contraction. Recruitment of zyxin protein has been proposed as a molecular marker for mature Fas. Zyxin facilitates actin polymerization in response to mechanical forces and dissociates from focal adhesions upon force dissipation [29]. Focal adhesions are closely linked to cellular migration, which is driven by repeated cycles of protrusion of the leading edge, formation of new matrix adhesions and retraction of the trailing edge. FA play a dual role in motility. On one hand, they provide a robust anchor to the ECM, necessary for the actomyosin system to exert the force to pull the cell body and the trailing edge forward, but on the other hand they may also restrain the migration process. The mechanical connections between the matrix and the cytoskeleton allow cells to exert traction forces that are transmitted to the cell nucleus through intracellular pathways; the resulting force triggers signaling transduction into biochemical signals that affect SC response, for example, the synthesis of specific transcription factors in the nucleus. Various mechanotransduction pathways have been proposed, including the Ras/MAPK, the PI3K/Akt, RhoA /ROCK, Wnt/catenin, and the TGF-*beta* pathways, which are generally integrin-based, and mechano-sensitive ion channels.

Recent studies have shown that mechanical cues, including the stiffness of the substrate, the nanotopography of the adhesion surface, and extracellular forces, are able to direct stem cell fate *in vitro*, even in the absence of biochemical factors [30].

3. Stem Cells and Bone Commitment

Osteogenesis is an active process tightly regulated to ultimately generate a normal vascularized bone structure. Bone formation depends on the cooperation of several factors, namely: (i) the genesis of specific cell types such as progenitor cells and osteoblasts; (ii) a mineralized extracellular matrix scaffold; (iii) soluble bioactive molecules (cytokines, growth factors, hormones, ions, vitamins); and (iv) mechanical stimuli. In the adult, the osteoblast is derived from a bone marrow stromal fibroblastic stem cell termed the mesenchymal stem cell (MSC), a non-hematopoietic multipotent stem-like cell vital for the osteogenic process and capable of differentiating into both osteoblastic and non-osteoblastic lineages [31].

The commitment and differentiation of MSCs towards osteogenic lineage is regulated by a certain group of factors. Among these factors, the initial and most specific marker is Runx2. Runx2 activates and regulates osteogenic differentiation by two independent signaling pathways via transforming growth factor-beta 1 (TGF β1) and bone morphogenetic protein 2 (BMP2) [32].

Along with Runx2, BMP2 and distal-less homeobox 5 (Dlx5) commit MSCs towards the osteogenic lineage. Commitment is the process that restricts MSCs to respond and undergo differentiation towards a specific lineage. In addition to the induction of osteogenic differentiation, Runx2 inhibits the differentiation of MSCs towards the adipogenic lineage. BMP2 induces the expression of Osx independent of Runx2 [33].

Following commitment, MSCs are differentiated into preosteoblasts. Preosteoblast are elliptical in shape with an elongated nucleus and are capable of proliferation. They express Runx2, D1x5, msh homeobox homologue 2 (Msx2), P2Y4 and P2Y14 [34], and few markers of osteoblasts such as ALP, type I collagen, and osteopontin (OPN), but their expression is weaker than immature osteoblasts. Alkaline phosphatase is one of the early proteins and regulates bone mineralization.

β-Catenin, Runx2, and Osx differentiate preosteoblasts into immature osteoblasts. These cells are spindle shape. They express bone matrix protein, bone sialoprotein, and OPN [35].

At later stages, Runx2 inhibits the maturation of osteoblasts. Osx causes the terminal maturation of osteoblasts and induces osteocalcin expression. When osteoblasts are completely differentiated, they become cuboidal and produce a self-mineralized organic matrix. The expression of OPN is reduced in mature osteoblasts; while the expression of other proteins such as P2X5, alkaline phosphatase, collagen type I, and osteocalcin [36] is increased.

4. Osseointegration of Dental Implants

Biomaterials are never truly inert, being at best biotolerable. The cell-substratum interface functions as more than a simple boundary of definition between the host and an implanted device, rather it presents primary cues for cellular adhesion and subsequent induction and tissue neogenesis. Indeed, the function and cytocompatibility of a construct can be assessed *in vitro* by observing the viability and adhesion of cells at the substratum interface [37]. The range of materials currently in use within biomedical applications and their lack of biofunctionality reflects an increasing need for biomimetic constructs but also indicates the challenges present within the field, *i.e.*, to ultimately control the interactions that occur at the cell-substratum interface [38].

A key tenet of medical device technology is to use the exquisite ability of biological systems to respond to the material surface or chemical stimuli in order to help develop next-generation biomaterials [39]. In order to investigate the reaction elicited by a material *in vivo* an understanding is required of the roles played by the cytoskeleton, cellular membranes, and the extracellular matrix

(ECM) following implantation of a foreign material [40]. An increased knowledge of the extracellular environment, topographical and chemical cues present at the cellular level and how cells react to these stimuli has resulted in the development of advanced orthopedic materials with an aim to regulate cell attachment and subsequent cellular function [38].

In recent years it has become self-evident that cells can use features such as filopodia (or microspikes), which have a tip diameter in the range of 50–100 nm, to gather and use spatial information. The cells can use filopodia to produce contact guidance with features as small as 10 nm high—around the size of a typical protein [40]. In addition, it has also been observed that MSCs have an increased interaction with topography compared with differentiated cells like fibroblasts. This evidence that stem cells are exquisitely sensitive to their nanoenvironment adds further evidence that the topographical environment is important for tissue-specific differentiation [41]. The recruitment of immunological cells to a site of implant involves a complex cascade of immune mediators, including various cell types, soluble signaling molecules, and cell-cell interactions. Previous studies have made it clear that the macrophage is the dominant cell in the foreign body response. Once adhered to an implanted material single macrophage cells fuse through a complex series of events to form multinucleated giant cells; this response is accompanied by the recruitment of fibroblasts and fibrous tissue formation. The adherence of giant cells to a biomaterial surface is correlated to the release of enzymes (e.g., esterases, lipases) and other bioreactive intermediates that can degrade and cause a loss of implant function [37]. It follows that the regulation of cellular adhesion or selective adhesion of specific cellular phenotypes is crucial to regulate optimal tissue-specific integration while preventing inflammatory cell recruitment and scar tissue formation.

Conversely, inert materials may be successfully employed for applications in which protein and/or cellular interaction may reduce device functionality. *In vitro* studies indicate that endogenous proteins become rapidly adsorped to a material surface providing a structural framework on which cellular adhesion may initiate. Modern implants make use of chemical and topographical modification to regulate cellular adhesion [38], differentiation, and *de novo* tissue deposition.

Therefore, it should to put in evidence that that more cues for the cell destiny come from additional parameters, such as the stiffness of the substrate [42], its chemical composition [43], its availability to mineralization [44,45] presence of proper extracellular matrix [46,47] and many other parameters.

In particular, recent developments in small technologies encompassing the generation of micro- and nanoscale structures have been successfully translated into the development of second generation implantable materials. Strategies adopted are described in the following sections.

5. Surface Modifications

The application of nanotechnology to dental implant surfaces deals with many different arrangements. In particular, surfaces could potentially assume an organized (isotropic) or unorganized (anisotropic) pattern. Due to the difficulties of application of standardized sequences to complex designs, the pattern for dental implants is generally anisotropic [48].

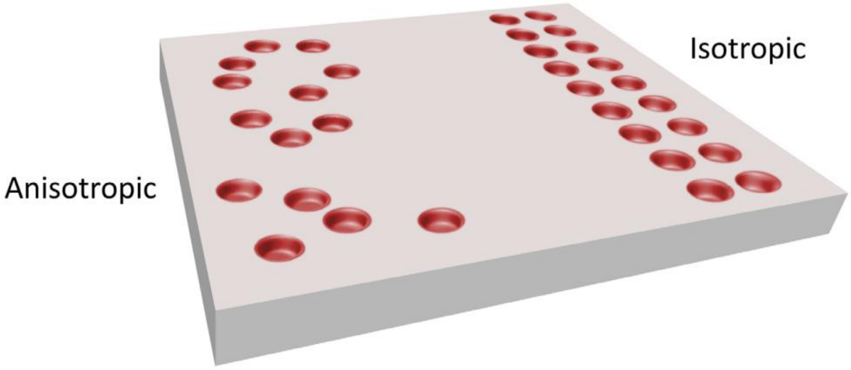
A great variety of techniques are used to create nanofeatures on dental implants surface. These can be divided into chemical and physical processes.

5.1. Chemical Modifications

5.1.1. Anodic Oxidation

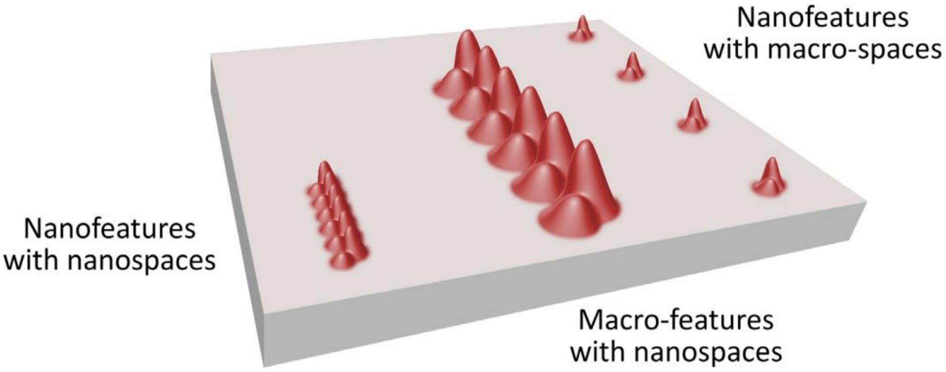
Anodization is one of the most commonly used techniques to create nanostructures with diameters of less than 100 nm on titanium implants [49]. Voltage and direct current (galvanic current) are used to thicken the oxide layer among the implant surface. The titanium substrates serves as the anode in the process, while an inert platinum sheet provides the cathode. The anode and cathode are then connected by copper wires and linked to a positive and negative port of a 30 V/3 A power supply, respectively. During the process, the anode and cathode are kept separated (about 1 cm distance) and they are submerged into an electrolyte solution in a Teflon beaker. Diluted hydrogen fluoride (either at 0.5 wt% or 1.5 wt%) is used as electrolyte. Subsequently, a strong acid dissolves the oxide layer creating a pattern that follows the convective lines of the galvanic current. Therefore, through the regulation of voltage and density it is possible to control the diameters of nanotubes and the gap between them (Figure 1).

Figure 1. Difference between isotropic (uniform in all direction) and anisotropic distribution of surface nanofeatures. Due to the complexity of dental implants design these are usually anistropic.



As an example, the outcome of the anodization of titanium in diluted hydrofluoric acid at 20 V for 20 min is the creation of surface nanotubes, while the anodization at 10 V for the same time produces nanoparticles. In addition, the distance between nanotubes/nanoparticles can be very different among different surfaces. Nanoscale features can be separated alternatively by microscale or nanoscale spaces (Figure 2).

Figure 2. Characterization on nano-surfaces: nanoscale features separated by nanoscale spaces; microscale features separated by nanoscale spaces; nanoscale features separated by microscale spaces.



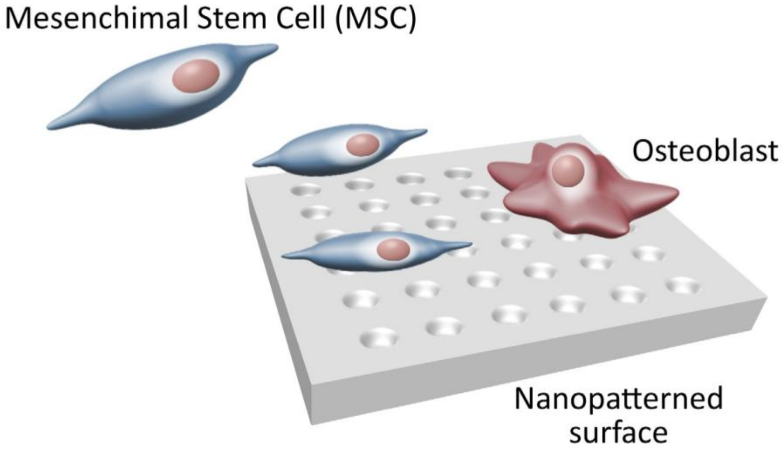
Oxidative nanopatterning confers Ti-based metals the exciting capacity to selectively influence cellular behavior by enhancing the growth of osteoblastic cells while limiting the proliferation of fibroblasts. The physic-chemical cueing impacts on gene and protein expression, in a way that is strongly determined by slight modifications of the dimensions of the nanofeatures, as mentioned above [48]. Von Wilmowsky *et al.* provided the confirmation that implant surface with interface features of 30 nm TiO_2 nanotubes positively influence bone-to-implant contact (BIC) and peri-implant bone formation [50].

5.1.2. Combinations of Acids (Bases) and Oxidants

The combination of strong acids is effective in creating a thin grid of nanopits on a titanium surface (diameter 20–100 nm) [48]. The titanium sample etched with a solution of strong acids, e.g., H_2SO_4 and H_2O_2, at a constant temperature and for a specific duration. Etching is then stopped by adding distilled water. The recovered disks are washed further with ethanol in an ultrasonic bath for 20 min and dried [51].

As for anodic oxidation, some reaction parameters such as temperature, duration, and solutes, can be adjusted in order to modify the number and depth of nanopits, therefore modulating cell function. Specifically, the treatment with H_2SO_4-H_2O_2 on titanium screw-shaped implants creates a nanopattern that has been demonstrated *in vivo* to be associated with an enhanced osteogenesis [48]. Vetrone *et al.* [52] confirmed the observation, stating the promotion of stem cells growth provided by oxidative nanopattering. Ferreira *et al.* [15] further characterized the most suitable nanoarrangement of TiO_2 nanotubes, noting that a diameter of 15 nm with a vertical alignment was associated with a high spreading and differentiation of rat mesenchymal stem cells into the osteogenic lineage. Notably, 15 nm roughly correspond to the predicted lateral spacing of integrin receptors in the FA complexes [53] (Figure 3).

Figure 3. Mesenchimal Stem Cells (MSCs) Differentiation Process. Nanostructured Surfaces promote MSCs osteogenic differentiation while limiting fibroblast differentiation.



5.2. Physical Modifications

5.2.1. Plasma Spray

The plasma deposition process is able to create an engineered-surface nanostructure, with features usually standing below 100 nm. First, a vacuum is used to remove all contaminants. Then, kinetic energy guides the charged metallic ions or plasma to the device surface. The process enables a wide range of materials (e.g., Ag, Au, Ti, *etc.*) to be coated onto a wide range of underlying materials (e.g., metals, polymers, and ceramics) [54]. In dental implants, titanium particles deposit on the implant surface with a uniform pattern.

The nanoparticulate coating with titanium particles achieved through the plasma spray technique has been demonstrated to increase the osteoblast density on the implant surface both in *in vitro* and in *in vivo* studies. Particularly, Reising *et al.* [54] detected a greater deposition of calcium on the nano Ti-coated surfaces when compared to uncoated surfaces.

5.2.2. Blasting

Blasting is a technique that leads to the creation of a porous layer on the implant surface achieved through the collision with microscopic particles. The thickness of the porous layer can be modulated by the granulometry of the particles. For example, the surface of commercial endosseous titanium implants is a rough porous layer ranging between 50 and 200 nm created through the combination of particles blasting and hydrogen fluoride treatment [48]. The rough surface has been demonstrated to stimulate osteoblastic gene expression, as well as to enhance bone formation and bone-implant fixation, in a word osseointegration [55,56]. While an associated inflammatory response was reported [57], the overall success rate was satisfactory, with the majority of implants yielding good osseointegration and stability at one year after surgery [48].

Among the range of available materials, aluminia is one of the most used for blasting. Nevertheless, Aparicio *et al.* [58] highlighted some features related to alumina blasting for dental implants that could compromise osseointegration, like particles detachment during the healing process and absorption by the surrounding tissues.

TiO_2 is also used as a blasting material showing interesting results in experimental studies. Particularly, TiO_2 blasted implants were associated in humans to a significant enhancement of BIC when compared with machined surfaces [59]. This result was confirmed by Rasmusson *et al.* [60] who investigated the osteogenic properties of titanium grit-blasted surfaces.

A further enhancement in the blasting technology was achieved through the integration of bioceramic grit-blasting and acid etching (BGB/AE), to produce submicrometric topographies on titanium implants. The evaluations made two months after implantation showed a significantly higher BIC and osteocyte density around modified implants when compared to simple dual-acid etching implants [48]. Clinically, the combination of blasting and etching on the surfaces has been associated to a 10-year cumulative survival rate of 96.2% [61]. Not surprisingly, Masaki *et al.* [62] further demonstrated that around this surface human mesenchymal stem cells increased the expression of type I collagen and of alkaline phosphatase, which is a key enzyme in the biomineralization along the bone-implant interface.

6. Conclusions

The significance of the nanometric surface alterations on dental implants was emphasized in this article. Since the encouraging outcomes shown in animals and in vitro have not yet been verified in people, there is currently limited proof of the long-term advantages of nanofeatures. Furthermore, nothing is known regarding the potential systemic consequences and the release of metal ions in the surrounding tissues. Additionally, one aspect of nanoscale manipulation that makes it more difficult is that there are

Numerous chemical changes occur on the surface of bulk materials, and it may be challenging to examine whether they have beneficial or negative impacts [63]. Nonetheless, there is no denying the growing interest in nanotechnology, and more studies will be released in the next years. In order to provide patients with the most biocompatible and long-lasting material to replace their teeth, dental implant manufacturers are likely to spend more resources.

References

1. Breine, U.; Lindström, J.; Hallén, O.; Öhman, A.; Hansson, B.O.; Adell, R.; Brenemark, P.I. Osseointegrated titanium implants are used to treat edentulous jaws. experience spanning ten years. Reconstr. Surg. Scand. J. Plast. 1977, 16, 1–132.
2. Osseointegrated titanium implants Albrektsson, T.; Lindström, J.; Hansson, H.A.; Brånemark, P.I. conditions necessary to provide a direct, long-lasting bone anchoring in humans. Acta Orthop. Scand. 52, 155–170 (1981).
3. Abuhussein, H.; Pagni, G.; Rebaudi, A.; Wang, H.L. Thread pattern's impact on implant osseointegration. 129–136 in Clin. Oral Implants Res. 2010, 21.

4. Bone-implant contact in the human maxilla after two months of healing on machined and dual acid-etched surfaces (Trisi, P.; Lazzara, R.; Rebaudi, A.; Rao, W.; Testori, T.; Porter, S.S.).
74, 945–956; J. Periodontol. 2003.
5.Buser, D.; Fox, C.H.; Stich, H.; Fiorellini, J.P.; Steinemann, S.; Schenk, R.K.; Steinemann, S. surface properties' impact on titanium implant bone integration. A research using histomorphometry on little pigs. J. Biomed. Mater. Res. 25, 889-902, 1991.
6. Bio-adhesive surfaces to encourage osteoblast development and bone formation (Garcúa, A.J.; Reyes, C.D.). 2005, J. Dent. Res. 84, 407–413.
7. Variola, F.; Yi, J.H.; Richert, L.; Wuest, J.D.; Rosei, F.; Nanci, A. Using controlled chemical oxidation to modify the surface characteristics of Ti6Al4V. Biomaterials 29, 1285–1298, 2008.
Amouriq, Y.; Layrolle, P.; Soueidan, A.; Le Guèhennec, L. Surface treatments of titanium dental implants for quick osseointegration. 23, 844–854; Dent. Mater. 2007, 23.
9. Cochran, D.L.; Schenk, R.K.; Lussi, A.; Higginbottom, F.L.; Buser, D. Bone response to loaded and unloaded titanium implants with a surface that has been acid-etched and sandblasted: A histometric investigation in the canine mandible. In 1998, J. Biomed. Mater. Res. 40, 1–11. 10. Mazzoleni, S.; Lith, A.; Tomasi, C.; Bressan, E.; Corazza, B.; Stellini, E. dependability and repeatability of linear mandible measurements using two object inclinations and cone-beam computed tomography. Radiol. Dentomaxillofac. 2011, 4, 244–250.

11. Mendonça, G.; Mendonça, D.B.S.; Aragão, F.J.L.; Cooper, L.F. Developing Nanotopography from Microns in Dental Implant Surface Technology. Biomaterials 2008, 29, 3822–3835.
12. Liu, H.; Webster, T.J. Nanomedicine for implants: An overview of research and essential experimental resources. Biomaterials, 28, 354-369, 2006.
13. Whitesides, G.M. Nanobiotechnology's "right" size. 21 1161–1165, Nat. Biotechnol. 2003.
14. Sniadecki, N.J.; Desai, R.A.; Ruiz, S.A.; Chen, C.S. Nanotechnology for interactions with cell substrates. 59–74 in Ann. Biomed. Eng. 2006, 34.
15. Ferreira, L.; Karp, J.M.; Nobre, L.; Langer, R. New Opportunities: Manipulating and tracking stem cells using nanotechnologies. Cell Stem Cell 3, 136–146 (2008).
16. Size-selective behavior of mesenchimal stem cells on ZrO2 and TiO2 nanotube arrays: Bauer, S.;

Park, J.; Faltenbacher, J.; Berger, S.; von Der Mark, K.; Schmuki, P. Cambridge: Integr. Biol. 2009, 1, 525–532.
17.Cavalcanti-Adam, E.A.; Volberg, T.; Micoulet, A.; Kessler, H.; Geiger, B.; Spatz, J.P. Integrin ligand spacing controls focal adhesion dynamics and cell spreading. 2007, 92, 2964–2974; Biophys. J.
18. Dental pulp stem cells and their characterisation by Suchaneka, J.; Soukupb, T.; Visekb, B.; Ivancakovaa, R.; Kucerovac, L.; Mokryb, J. 2009, 153, 31–36; Biomed. Pap. Med. Fac. Univ. Palacky Olomouc Czech Repub.
19. Elsevier, Burlington, Massachusetts, USA, 2008; Volume 1448; Atala, A.; Lanza, R.; Thomson, J.A.; Nerem, R.M. Principles of Regenerative Medicine.
20. Asnaghi, M.A.; Rees, L.E.; Cogan, T.A.; Dodson A.; Martorell, J.; Bellini, S.; Parnigotto, P.P.; Macchiarini, P.; Jungebluth, P.; Go, T.; Asnaghi, M.A.; et al. Tissue-engineered airway transplantation in a clinical setting. 2008, Lancet, 372, 2023–2030.