Ramesh S. Chaughule
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# Advances in Dental Implantology using Nanomaterials and Allied Technology Applications

Springer

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Editors

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# Foreword

I am glad to write a foreword for this book "Advances in Dental Implantology using Nanomaterials and Allied Technology Applications" to be published by Springer, USA, that focuses on the use of nanotechnology in dentistry and particularly in the field of implants. This book, edited by Drs. Ramesh S. Chaughule and Rajesh Dashaputra, presents a collection of topics from eminent authors across the globe on the use of nanobiomaterials for implantology and their clinical applications.

Nanotechnology is a new field that has enormous scope in the dental science. One can make use of it in understanding and achieving cell-specific functions. Nanoscale surface morphology augments the surface area and thus provides an increased implant surface area that can react to the biologic environment. The composition of dental implants, surface energy, and roughness and topography can be improved for better osseointegration, and cellular activities and tissue responses occurring at the bone–implant interface can be altered by nanoscale modifications and can result in better treatment outcomes.

Nanosurface modification changes chemical as well as biological interactions of the implant, due to changed implant surface interaction with ions, biomolecules, and cells. This change in interactions in turn favorably influences molecular and cellular activities, leading to altered osseointegration. Numerous methods have been tried to enhance the osteointegration property by promoting the attachment, proliferation, and differentiation of bone-forming cells on the implant surface. Graphene and their products may provide excellent coating strategies for dental implants to improve osteointegration. Nanotechnology offers therapeutic methods for esthetic dentistry. Teeth that undergo treatment, such as fillings or crowns, will be restored with natural biological materials in a manner that is indistinguishable from natural dentition.

In recent years, there have been numerous publications appearing in the nanotechnology in dentistry. Developments in clinical applications are likely to accelerate in future. All the authors led by Dr. Chaughule should be congratulated to present a comprehensive and timely book to produce a useful and comprehensive text on nanobiomaterials and their clinical applications in dental implants.

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# Foreword

I am delighted to be asked to write a foreword for the second book in dentistry 'Advances in Dental Implantology Using Nanomaterials and Allied Technology Applications' to be published by Springer, USA.

Endo-osseous dental implants have revolutionised how clinicians manage patients with failing dentitions. Patient demand has driven the need for shorter treatment times necessitating quicker healing and rapid reconstructions leading to a search for newer technologies. Whilst a number of textbooks have been written, there are very few bringing together the application of nanotechnology across the field of implantology. This book builds on the concepts of nanotechnology, already covered in the first book 'Dental Applications of Nanotechnology' published by Springer, and its impact on the provision of dental implant treatment. The authors, led by Dr. Chaughule, have done an excellent job in succinctly putting together ways in which nanotechnology can influence and has influenced the provision of implant treatment from surgery to prosthetic reconstruction and post-treatment biological complications. The second section on 'Applications' of such new technologies in the field of implantology gives this book a unique feature by bringing science and technology into clinical application.

The book is aimed at experienced clinicians and those new to dental implantology as well as students, researchers and scientists. It is well written and structured making it easy for the reader to follow the difficult notions at the nano level as applied to implantology. In my 20 years of experience in implantology, this is a much needed book which provides useful and relevant content to readers and can serve as a general textbook or a reference book. I commend the efforts of the authors in producing this comprehensive book, which closes an important gap in an ever-changing field.

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# Foreword

As a clinician fascinated by scientific backgrounds and as a passionate reader from early childhood on, I always feel excited when I open a new book. This one over exceeded my expectations.

There are books that have more footnotes and references than text, which is great help for a small group of researchers, but the majority of clinicians would close the book as quickly as a flash. Then there are books in dentistry that look more like picture books: nice to turn pages, but nothing to underline. And finally, there are books like this one: valuable information, a good read, text parts to be underlined, literature references inviting for further study and images from clinical work excellently illustrating the topics at hand.

The editors of the book, "Advances in Dental Implantology using Nanomaterials and Allied Technology Applications", Professor Ramesh S. Chaughule and Dr. Rajesh Dashaputra, together with many prestigious contributors across the globe, collected research and clinic in the best way possible. This provides us with comprehensive information on the expanding fields of nanotechnology as well as the latest developments in materials science, engineering and technology applied in dentistry. This book is quite essential to valuable research and a natural sequel to their numerous published papers and the book: "Dental Applications of Nanotechnology".

It is the unique combination of clinician-researcher-teacher-mentor-author-speaker features with IT understanding, which enables one to write such a comprehensive work.

Nanotechnology and its application in dentistry are hot topics. This book covers aspects ranging from research to the clinic, providing a complete framework and knowledge base. Nanotechnologies are increasingly used for surface modifications of dental implants. This book explains why nanometer-controlled implant surfaces may ultimately direct the nature of peri-implant tissues and improve their clinical success rate.

Students, researchers and clinicians who want to learn more about nanomaterial utilization in bone regeneration, prosthetic rehabilitation, biofilm and peri-implantitis control, bone grafting and tissue engineering will benefit from the solid footing in this compilation.

The second part of the book is the sum of accumulated knowledge about the newest developments in dentistry. And it is more than just an update. It provides an overview of the current state of knowledge, valuable clinical protocols for CAD/CAM technology, modelling and impressions in implants, printing in dentistry, maxillofacial reconstruction, 3D impressions in maxillofacial surgery and zygomatic implants. As an oral surgeon, periodontist and implantologist, I find this book to be a comprehensive professional reference that bridges the gap between fundamental materials science and medicine.

This book is laying the foundation for further publications that I am looking forward to read.

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# Preface

The term nanotechnology is widely attributed to the American Nobel Laureate Dr. Richard Feynman. It is mainly concerned for the creation of functional materials, devices, and systems through control of matter in 1–100 nm length scale exploiting physical, chemical, and biological properties. Nanotechnology is a relatively newer field of science that is finding enormous scope in dental and medical science. This field is useful in multitude of applications, including dental diagnosis, materials, surface treatments of dental implants, and improving orthopedic implant devices. The changes in chemistry or topography of implant surface can occur due to nanoscale modification which can alter the implant surface interaction with ions, biomolecules, and cells leading to create surfaces with controlled topography and chemistry. Nanobiomaterials used in dental applications have superior abrasion resistance, lower shrinkage, and enhanced optical and esthetic properties due to their enhanced surface-to-volume ratio as compared to their bulk materials. Thus, they are used in light polymerizable composites, impression materials, ceramics, and dental implant coatings. Nanotechnology offers engineers and biologists new ways of interacting with relevant biological processes. Moreover, it has provided means of understanding and achieving cell-specific functions. The elucidation of bone healing physiology has driven investigators to engineer implant surfaces that closely mimic natural bone characteristics. Thus, the field of nanotechnology has bright prospects as it offers the possibility of great advances and improvement in the field of dentistry with an extrapolation of current resources to a new scale.

In modern dentistry, dental implant plays most viable role in the replacement of missing teeth. Implant restores not only form and function but also esthetics of the patients. Dental implants are manufactured from materials such as pure titanium, surgical stainless steel, and titanium alloys. The long-term survival of implants primarily depends on seamless osseointegration with bone and can get compromised by the inflammatory condition that causes peri-implantitis and loss of supporting bone. Osseointegration at the bone–implant interface and the amount of bacterial colonization around the implants have to be looked into carefully. The enhancement of bone formation at the bone–implant interface has been achieved through the modulation of osteoblasts adhesion and spreading, induced by structural modifications of the implant surface, particularly at the nanoscale level. In this context, traditional chemical and physical processes find new applications to achieve the best dental implant technology.

The use of nanotechnology has been tested on a wide range of materials (such as metals, ceramics, polymers, and composites), either nanostructured surface features or constituent nanomaterials including grains, fibers, or particles with at least one dimension from 1 to 100 nm. The osteointegration of the orthopedic implants could improve the biocompatibility and the life span of the implants. The ideal implants should be made by materials easily colonized by bone-forming cells (osteoblasts), which can synthesize new bone matrix. The implant surfaces can alter cellular and tissue responses that may promote osseointegration. Some implant materials are not often compatible with osteoblasts, but rather promote the formation of soft connective tissue. Surface coatings using nanohydroxyapatite and calcium phosphate (CaP) particles make the new implants more acceptable as these materials enhance the integration of nanocoatings resembling biological materials to the periodontal tissues. Furthermore, osteoconductive nanoparticles induce a chemical bond with bone to attain good biological fixation for implants. Bioactive CaP nanocrystals deposited on titanium implants are resorbable and stimulate bone apposition and healing. Future nanometer-controlled surfaces may ultimately direct the nature of peri-implant tissues and improve their clinical success rate. Surface modification of implants using antibacterial properties can also decrease the potential for infection, and certainly improves clinical outcomes.

We are pleased to introduce this second book "Advances in Dental Implantology using Nanomaterials and Allied Technology Applications" to aspiring and working scientists, dental practitioners, and as a ready reference for the dental students to understand the principles of nanotechnology, its applications, and latest techniques. The first book "Dental Applications of Nanotechnology" was very well received by all the interested readers. The present second book covers primarily two sections. The first section covers **Nanobiomaterials** in implant applications, in bone regeneration, prosthetic rehabilitation, to control biofilm and peri-implantitis, bone grafting and tissue engineering. The second section covers implant stability, peri-implantitis, lasers, CAD/CAM technology, impressions, 3D printing, reconstruction with bone grafts, and zygomatic implants under **Applications**.

Nanotechnology assists in understanding and achieving cell-specific functions and thus critical steps in osseointegration can be modulated by nanoscale modification of the implant surface. It is possible to mimic bone formation process occurring at nanoscale level to achieve better osseointegration and higher implant surface ratio. Praveena et al. discuss in their chapter about the role of nanotechnology in the various methods and techniques of imparting nanoparticle-coated implants for the improvement of osseointegration using nanosurface features of dental implants and their antimicrobial activity. The application of nanomaterials in craniofacial bone regeneration is a newly advancing field which holds great capabilities for enhancing conventional therapeutic methods. Chapter by Hosseinpour et al. highlights the applications of nanobiomaterials as bone scaffolds, delivery systems, and barrier membranes for craniofacial bone regeneration. Maxillofacial reconstruction is complicated due to the etiology and nature of the tissue injury. Nanobiomaterials in prosthetic rehabilitation of maxillofacial defects play an important role. Sybil et al. have shown in their chapter that the restoration of soft tissues like skin, cartilage, and mucosa without the support of the underlying bony architecture is possible with prosthesis. Graphene-based materials have gained extensive attention in the field of dentistry. Rokaya et al. have summarized the basic properties of graphene and the latest progress based on current knowledge. Minimizing biofilm formation and peri-implantitis is a great concern. Petrini et al. have discussed the novel materials and surfaces that could decrease early failure and improve long-term success in implantology. Reconstruction of craniofacial defects poses a challenging task for craniofacial surgeons. Bone grafting is the standard technique employed for bone reconstruction. However, with the advent of novel biomaterials as bone substitutes for grafting procedures, attractive alternatives have unlocked for surgeons. Kalluri and Duan have focused on the various biomaterials that are currently used as bone substitutes in craniofacial bone regeneration along with an update of the active research among each class of biomaterials going on in this area. For damaged tissues and organs affected by trauma, a regenerative medicine is required. Advanced nano-functional biomaterials can promote cellular adhesion, proliferation, differentiation, and morphogenesis in a controlled spatiotemporal manner. Midha et al. discuss about the importance of nanobiomaterials in tissue engineering and biological interaction with stem cells. In implants, a direct relationship seems to exist between the primary stability and bone density. Polyurethane foam has been proposed for in vitro tests to simulate the consistency and the density of the bone. Chapter by Tumedei et al. emphasizes the role of polyurethane foam as a model to study primary implant stability.

Peri-implant diseases, such as peri-implant mucositis and peri-implantitis, correspond to former periodontal conditions—gingivitis and periodontitis, and, analogically, are considered serious and chronic conditions jeopardizing the undertaken rehabilitation treatment using implant. Peri-implantitis, which is defined as a pathologic condition of all tissues supporting dental implant, can lead to its loss, if not recognized and treated on time. Porenczuk and Gorski in their chapter discuss to bring closer prevalence and risk factors of peri-implantitis along with prevention and treatment methods. The use of laser has increased rapidly in the last couple of decades. Their use in implant dentistry has seen an upsurge in the past years. At present, wide varieties of procedures are carried out using lasers. Laser can be classified based on the wavelengths and tissue on which it acts. The chapter by Miglani and Patro highlights the various types of lasers and their various applications at different stages of dental implantology. Proper diagnosis and appropriate treatmesnt planning is paramount to achieve the best long-term prognosis in implant dentistry. Computer-aided implant surgery has dramatically improved the quality of surgical procedures used for dental implant bed preparation and implant placement. The three-dimensional assessment of the restorative goal using cone beam computerized tomography (CBCT), radiographic template, and implant design programs allows realistic planning and optimized positioning of implants using surgical guides. D'Souza and Aras in their chapter explain the applications of CAD/CAM technology in dental implant planning and implant surgery. Accurate replication of the clinical situations in a physical or virtual mode is required before and during the treatment for the planning or execution of the prosthetic phase by the laboratories. Impression making and modelling tools form a vital segment in the armamentarium of implantologists and so also the techniques need high level of skill development. Chapter by Dashaputra et al. explores all the techniques and critical steps essential in both the forms of modelling and impression making for accurate replications and success. The dental field is embracing the trend of digital dentistry. 3D printers and 3D scanners designed for dental applications can now help dentists offer a better and more personalized service to patients while offering substantial cost reductions and simplifying complex dental appliances production workflows. Implant dentistry was one of the first disciplines to experience 3D printed guides for predictable surgeries. A revolution in materials and technologies has resulted in further evolution, including the printing of prosthodontic frameworks, dentures, and implant components. Kalman discusses the exciting advancement of 3D printing and its applications to industry and medicine, with an in-depth presentation of its application to dentistry. Maxillofacial reconstruction using bone grafts, dental implants, and bone tissue engineering approach is a complex and exciting topic and poses significant challenges to oral and maxillofacial surgeons. Advances in the field of bone tissue engineering over the past few decades offer promising new treatment alternatives using biocompatible scaffold materials, autologous mesenchymal stem cells, and growth factors. Guastaldi et al., in their chapter, focus on the reconstruction of the maxilla and the mandible. The prime objective of the 3D impression-taking process in oral surgeries is obtaining a high-quality copy of one or several implants. This requires structures, healthy adjacent and antagonist teeth and other maxillofacial regions, establishing a proper interocclusal relationship and then converting this information into accurate replicas of the missing or abnormal implanted structures. Chapter by Irfan addresses the technical aspects and applications of digital impressions in maxillofacial surgeries. On severely resorbed maxilla the limitations for the installation of conventional implants require alveolar reconstructive procedures with the use of autogenous bone grafts harvested from iliac intraoral donor sites or autologous bone graft, increasing morbidity and cost of the treatment. As an alternative to the use of large bone reconstruction, zygoma bone can be used as anchorage for long implants supporting prosthetic rehabilitation. Chapter by Soares et al. discusses the importance of technology and virtual planning to correctly disseminate the masticatory forces on these implants.

The editors wish to thank all the distinguished and expert contributors for their enthusiastic participation in this endeavor and also some contributors who did the job at last hour. We are confident that the book will serve as a valuable guide for researchers and students of dentistry, materials engineering, bioengineering, and medicine. Dr. Chaughule wishes to thank Dr. Suhas Pednekar, Vice Chancellor, Mumbai University, Dr. Anushree Lokur, Principal, Ramnarain Ruia Autonomous College, and his family members for all the supports. Dr. Dashaputra wishes to thank his mentor Dr. Chaughule first to give the opportunity to be a coeditor. He too wishes to thank his wife and family for the support during this book preparation.

Special thanks are also due to Dr. Snigdha Patki-Chitnis, oral and maxillofacial surgeon, who did a very difficult but meticulous job of moderating a difficult chapter on zygoma implants originally written by non-English authors. Last but not least, the editors sincerely thank Springer staff for their support from time to time.

Mumbai, India

Ramesh S. Chaughule
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# Nanotechnology in Implant Dentistry

**Channamsetty Praveena, Ramesh S. Chaughule, and K. V. Satyanarayana**

**Abstract** Recent advancements in engineering tools and techniques coupled with the extrapolation of nanotechnology in the field of dentistry have rendered dental implant therapy as the most reliable treatment option for replacement of missing natural dentition. Nanotechnology has driven dental implants to a newer level. It assists in understanding and achieving cell-specific functions, and thus critical steps in osseointegration can be modulated by nanoscale modification of the implant surface. It is possible to mimic bone formation process occurring at nanoscale level to achieve better osseointegration and higher implant surface ratio. This review chapter also discusses the various methods and techniques of imparting nanoparticle-coated implants for the improvement of osseointegration using nanosurfaced features of the dental implants and their antimicrobial activity.

**Keywords** Nanotechnology · Osseointegration · Nanoscale · Implant surface ratio · Surface treatment · Nanotopography

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# 1 Introduction

Dental implants have been in the market place for a long period of time for restoring or replacing teeth. The challenges faced by dental surgeons during dental implantation are controlling the high chances of infections and achieving osseointegration. Many studies have been attempted to enhance the osseointegration of implants by various surface modifications. The aim of dental manufacturers is to provide dental implants with surface biological properties for the adsorption of proteins, the adhesion and differentiation of cells, and tissue integration. These biological properties are allied to chemical composition, wettability, and roughness of metal implants surfaces. However, the control of these surface properties at the protein and cell levels, thus in the nanometer range, remains a potential challenge for researchers and dental implants manufacturers [1].

Modern science and technology has undergone a major revolution with the evolution of nanotechnology and hence has been assimilated into various medical disciplines including dentistry. Bulk material when reduced to nanoscale, there is significant change in the optical, thermal, and antimicrobial properties [2]. This alteration of the desired physicochemical properties of nanomaterials has led to the conceptual development of "**nanodentistry.**" The continuous ongoing quest for the introduction of newer materials for promoting better oral health has led to the discovery of various nanobiomaterials, advanced clinical tools, and better treatment modalities.

With the advent of hybrid science named nanobiotechnology, nanomaterials have noteworthy applications in implant dentistry [3]. The application of "nano" to implants, abutments, and bone substitutes drastically changed their biologic response. Nanotechnologies generate surfaces with controlled topography and chemistry that would aid in understanding biological interactions and developing novel implant surfaces with predictable tissue-integrative properties [4].

In this chapter, the biomedical applications of nanoparticles and nanopatterned surfaces in implant dentistry, including the recent nanocoated implant materials and technologies which are responsible for tuning the cell-specific interactions and promoting osseointegration, are discussed. The sequence of biological events in relation to the surface is related. Mechanisms of interaction with blood, platelets, and mesenchymal stem cells on the surface of implants are described.

## *1.1 Nanotechnology Definition*

While many definitions of nanotechnology exist, the most widely used is from the US Government's National Nanotechnology Initiative (NNI). According to the NNI, nanotechnology is defined as: "Research and technology development at the atomic, molecular and macromolecular levels in the length scale of approximately 1–100 nm range, to provide a fundamental understanding of phenomena and materials at the nanoscale and to create and use structures, devices and systems that have novel properties and functions because of their small and/or intermediate size" [5].

Nanotechnology or molecular engineering is the production of functional materials and structures in the range of 0.1–100 nm-nanoscale by various physical or chemical methods [6]. The term "nano" is derived from "***nanos***," the Greek word for "***dwarf***." A nanometer is $10^{-9}$ a meter or one-billionth of a meter [7]. In simple terms, it is engineering at the atomic and molecular scale. It is a highly multidisciplinary field and cuts across many disciplines, including colloidal science, chemistry, applied physics, and biology.

## *1.2 Historical Review*

Nanotechnology is not a new term. Although nanotechnology has been around since the beginning of time, the discovery of nanotechnology is widely attributed to the American Physicist and Nobel Laureate, Dr. Richard Phillips Feynman [7]. The first use of the word "nanotechnology" has been attributed to Taniguchi in 1974. In 1986, Eric Drexler introduced and popularized the term "nanotechnology" in his book "Engines of Creation" [5]. Dr. Robert A. Fretias Jr. is one among the pioneer scientists who has written about nanomedicine, nanodentistry, and their future changes [5]. It was introduced into dentistry as nanocomposites in the year 2002 by Filtek Supreme [8].

## *1.3 Classification of Nanomaterials*

Siegel has classified nanomaterials [6, 9] based on dimensions as shown in Table 1.

## *1.4 Approaches in Nanotechnology*

The fabrication techniques of the nanoscale materials can be divided into the following three approaches [7, 8]:

(a) Larger to smaller (top-down approach)

**Table 1** Classification of nanomaterials based on dimensions

| Dimension | Characteristics | Examples |
|---|---|---|
| Zero | Clusters/powders | Atomic clusters, filaments, and cluster assemblies |
| One | Multilayers | Nano thin film |
| Two | Ultrafine grained over-layers | Nanotubes, Nanofibers, and Nanowires |
| Three | Nanophase materials consisting of equiaxed nanometer-sized grains | Nanoparticles, Nanopowders, Dendrimers, Fullerences, Quantum dots, Nanostructures, Nanocapsules, and Nanopores |

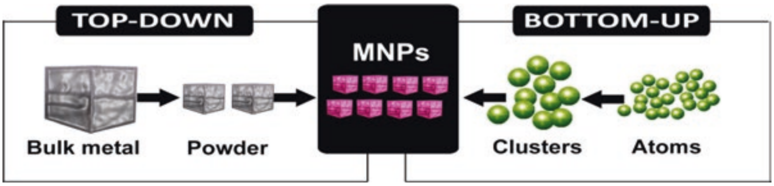


**Fig. 1** Top-down and bottom-up approaches

**Table 2** Examples of top-down and bottom-up approach

| Top-down approach examples | Bottom-up approach examples |
|---|---|
| 1. Salivary diagnostics | 1. Inducing local anesthesia |
| 2. Laser plasma application for periodontia | 2. Hypersensitivity cure |
| 3. Nanotechnology-based root-end sealant | 3. Tooth repair |
| 4. Nano needles | 4. Nanorobotic dentifrice (dentifrobots) |
| 5. Nano bone fibers | 5. Orthodontic nanorobots |
| 6. Nanocomposites | 6. Dental durability and cosmetics |
| 7. Nanotechnology for GIC | 7. Nanotech floss |
| 8. Nanoceramic technology | 8. Photosensitizers and carriers |
| 9. Nanobond | 9. Diagnosis and treatment of oral cancer |
| 10. Nanosolutions | |
| 11. Coating agents | |
| 12. Nanotechnology for impression materials | |
| 13. Nanocomposite denture teeth | |
| 14. Nanoparticles as antimicrobial agents | |
| 15. Implants surface coatings | |
| 16. Nano bone replacement materials | |

Top-down fabrication reduces large pieces of materials all the way down to the nanoscale (Fig. 1). This approach requires larger amounts of materials and can lead to waste if excess material is discarded. Here, larger materials are patterned and carved down to make nanoscale structures in precise patterns. Materials reduced to the nanoscale can suddenly show very different properties, enabling unique applications (Table 2).

(b) Simple to complex (bottom-up approach)
The bottom-up approach to nano-manufacturing creates products by building them up from atomic and molecular-scale components, which can be time-consuming (Fig. 1). This begins by designing and synthesizing custom-made molecules that have the ability to self-assemble or self-organize into higher-order structures.

(c) Functional approach
In this approach, components of the desired functionality are developed without regard to how they might be assembled.

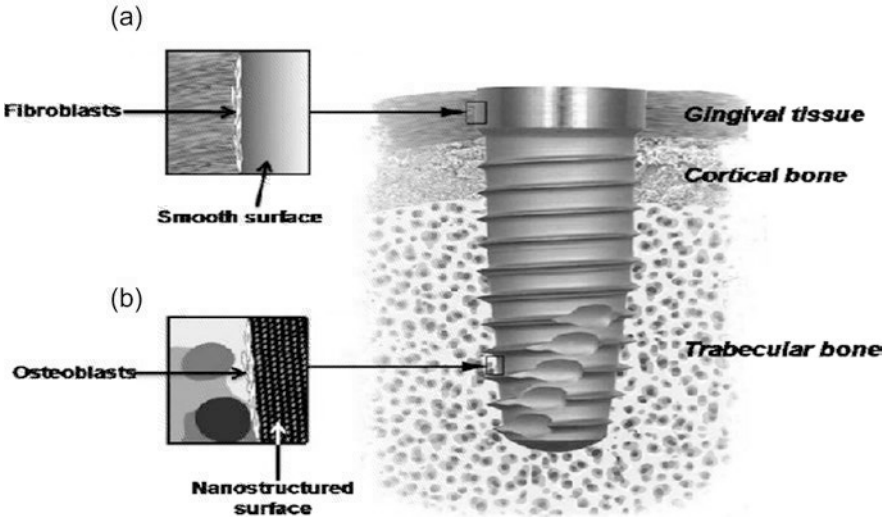


**Fig. 2** Osseointegration. (**a**) Intimate contact with gingival tissue. (**b**) Contact osteogenesis

## 2 Concept of Osseointegration

Modification of dental osseous implants at nanoscale level produced by various techniques can alter biological responses that may improve osseointegration and dental implant procedures. The high success rates for endosseous implants have resulted from many research approaches with the aim of enhancing and accelerating bone anchorage to the implant, thereby providing optimal support for the intraoral prosthetic devices. This innovatory breakthrough has first emerged from the research efforts of the Branemark group in the late 1960s by pioneering the placement of machined screw-type commercially pure titanium (cpTi) implants with minimum surgical trauma. The bone bonding ability, termed as "osseointegration" by Brånemark et al. (1977), of this machined implant was principally the result of the proper surgical technique providing macrostability to the implant and the biocompatible nature of the bulk titanium [10].

Osseointegration of dental implants was earlier characterized as a structural and functional connection between newly formed bone and the implant surface, which became a synonym for the biomechanical concept of secondary stability [11]. Osseointegration comprises a cascade of complex physiological mechanisms similar to direct fracture healing (Fig. 2). The drilling of an implant cavity resembles a traumatic insult to bony tissue leading to distinct phases of wound healing [12]. New bone generates from the borders of the drill hole (distance osteogenesis) or by osteogenic cells on the surface of the implant (contact osteogenesis). In distance osteogenesis, osteoblasts migrate to the surface of the implant cavity, differentiate, and lead to the formation of new bone. Thus, bone grows in an appositional manner towards the implant. In contact osteogenesis, osteogenic cells migrate directly onto the implant surface and generate *de novo* bone [13].

After decades of research, better designs and materials have evolved, with increase in survival rate and low failure rate. The most frequent cause for failure is insufficient bone formation around the implant surface. In this, the implant surface and tissue interface play a critical role [14]. Implant surface composition, surface energy, surface roughness, and topography are the four material-related factors which can influence biological events at the bone–implant interface. Macro, micro, and nano are the three types of surface structures. Current surface structures are controlled, at best, at the micron level, but tissue response is mainly dictated by processes controlled at the nanoscale. Surface profiles of implants in the nanometer range play an important role in the adsorption of proteins and adhesion of osteoblastic cells, promote osteogenic differentiation, and may improve the osseointegration of the implants [15]. Hence, we need strategies to improve the current metallic dental implants, through surface modifications of the implant either by applying novel ceramic coatings or by patterning the implant's surfaces.

## 3 Interactions of Surface Dental Implants with Blood

The first biological event after the implantation is blood–implant contact [16]. Immediate response is adsorption of platelets and interaction of plasma proteins with the implant surface (Fig. 3). Plasma proteins with other substances such as glucose, amino acids, and various ions influence the wettability of implant surface

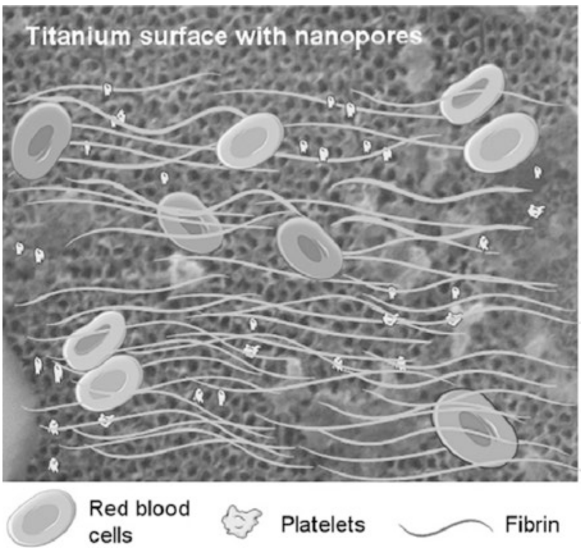


**Fig. 3** Interactions of the surface of implant with blood

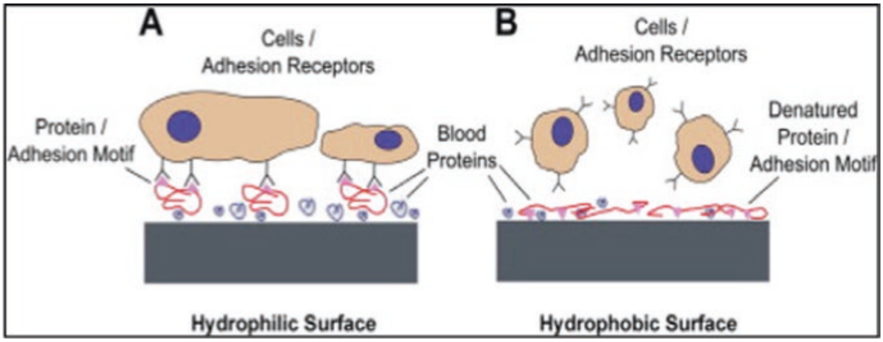


**Fig. 4** Cellular interactions of hydrophilic surface (**a**) and hydrophobic surface (**b**)

which can be altered by its surface modifications [17]. It is assumed that Vroman effect will be observed around the implant surface in which the highest mobility proteins generally arrive first and are later replaced by less mobile proteins that have a higher affinity for the surface which enhance osseointegration [18]. As it has been proven that hydrophilic surface exhibits better blood coagulation and osseointegration than a hydrophobic surface, modern implants are emerging with high hydrophilic and rough implant surfaces (Fig. 4) [19].

Fibronectin and vitronectin help in cell attachment by cell-binding RGD domain (arg-gly-asp tripeptide). RGD chain interacts with cell membrane [20] integrins, which in turn play a vital role in adhesion of many cell lineages.

### *3.1 Role of Macrophage Cells*

Macrophage lineage depends on its phenotype, i.e., if the stimulus is for proregenerative (M2) macrophage phenotype, more number of M2 will be in that vicinity compared to proinflammatory (M1) phenotype [16]. Dominant proregenerative (M2) macrophage phenotype which aids in tissue regeneration forms the bone around the implant, by stimulating the osteogenic differentiation of osteoprogenitor cells and suppressing the inflammatory response [16].

### *3.2 Interactions Between Surfaces and Mesenchymal Stem Cells*

Blood coagulation is followed by various cell interactions. After migration of mesenchymal stem cells (MSCs) to the implant site by chemokine stimulus from surrounding tissues, it invades the three-dimensional microporous structure that allows diffusion of regulatory factors [21, 22] and helps in the migration, proliferation, and

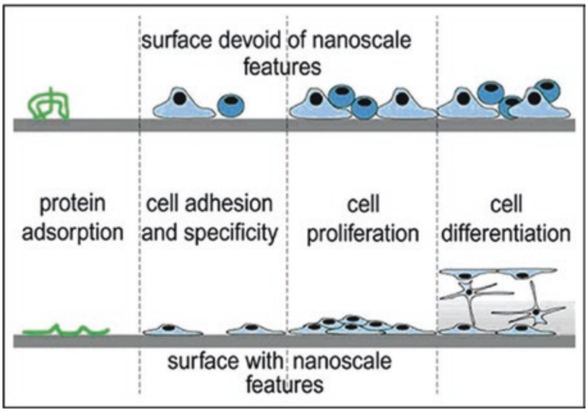


**Fig. 5** Depiction of cell interactions on surfaces with and without nanoscale features

differentiation of MSCs. Once the MSC recruitment in the injured site is completed, it adheres on the local extracellular matrix as well as on the implant surface beginning an extensive proliferation in order to build up new tissue. Surface modification of implant surface at nano level helps in the adhesion of MSCs (Fig. 5).

Here MSCs can be differentiated into either fibroblastic or osteoblastic based on the stimulus. If the stimulus is for fibroblast cells, it initiates fibrous capsule formation obstructing the bond between implant and bone by forming collagen and thus results in an implant failure [23]. At the same time, it is desired to have more fibroblastic proliferation near gingival part of implant. Studies have revealed less fibroblast proliferation at nanosurface than conventional surface which facilitates better osseointegration [24].

Increased levels of alkaline phosphatase and calcium are observed in cell layers on nanosized materials after 21 and 28 days [25, 26]. Nanorough Ti and nanostructured Ti showed better results compared to nanosmooth surfaces [27, 28] and greatly enhanced osseointegration has been observed with micro- and nanopore surfaces [29, 30]. Adhesion, proliferation, and differentiation of MSCs depend on local chemical environment, surface topography of implant, and its surface tension for predictable regeneration.

## 3.3 *Nanosurface and Bacterial Proliferation*

It is noted that a profound decrease in bacterial colonization on nanostructured $TiO_2$ and ZnO regardless of the surface [31]. These observations need further research on biofilm formation and peri-implantitis around implants.

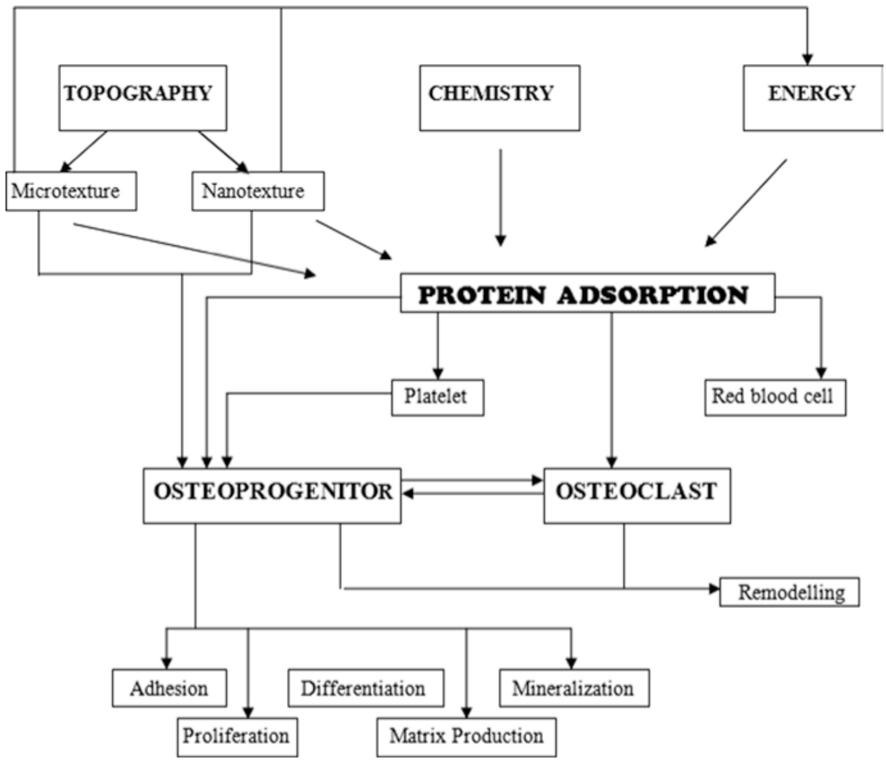


**Fig. 6** Effect of surface characteristics of the implant on the osteogenic response

## 4 Surface Functionalization for Enhanced Osseointegration

The surface of a titanium implant plays a central role in determining the biological response of the host bone for several reasons (Fig. 6).

The surface characteristics of an implant regulate the healing mechanisms at the bone–implant interface since it is the only region contacting the bone. Surface functionalization had gained the interest of many manufacturers for enhancing the biomechanical anchorage and osseointegration of the implant at the histological level. Commonly used techniques [14] to alter surface properties of titanium are as follows (Table 3).

All these modifications regulate the morphology, physicochemical composition, and surface energy of the implant surface. Two categories of surface properties are commonly suggested for affecting the tissue response to the implant: surface topography and physicochemical composition.

## 4.1 Topographical Features of Titanium Surfaces

The fate of an implant after implantation is decided by the adsorption of biomolecules and the consequent interactions of cells on the implant surface. Rough topography increases the surface area of the implant and cell adhesion, thereby achieving higher bone-to-implant contact and better biomechanical integrity [32]. It has been shown that moderate roughness (Ra, between 1 and 2 μm) and complex microtopographies are important for the enhanced osseointegration of titanium implants [33]. Implants with rough surfaces exhibited greater bone–implant interface compared to smooth surfaces [34].

**Table 3** Methods for creating nano-features on dental implants

| S. no. | Method | Characteristics |
|---|---|---|
| I. | **Ceramic coatings** | Thin layer of bioactive ceramics is applied on the implant surface and form a carbonated apatite layer on the implant surface through dissolution and precipitation.<br>**Advantages:**<br>– Faster healing time<br>– Enhanced bone formation<br>– Firmer implant-bone attachment<br>– Reduction of metallic ion release |
| II. | **Self-assembly of monolayer** | These are ordered organic films in supramolecular chemistry formed by chemisorptions of an active organic coating on a solid surface |
| III. | **Physical approaches** | |
| | (a) Plasma spraying | Charged metallic ions or plasma are deposited on the surface by kinetic energy. Widely used for calcium phosphate coatings (HA) deposition.<br>**Advantages:**<br>– Increased osteoblastic density.<br>– Greater bone-implant contact<br>**Drawbacks:**<br>– Long-term stability of implants affected<br>– Lack of adherence of the coating can result in health hazards |
| | (b) Sputtering | Thin films of bioceramics are deposited by high-energy bombardment of high-energy ions.<br>**Advantages:**<br>Improved healing response and initial fixation.<br>**Drawbacks:**<br>Very slow deposition rate |
| | (c) Ion deposition | This method enables injection of elements on the near-surface region of the substrate using a beam of high-energy (10 keV) ions. |

(continued)

**Table 3** (continued)

| S. no. | Method | Characteristics |
|---|---|---|
| IV. | **Chemical methods** | |
| | (a) Anodic oxidation | With the help of this technique, the smooth surface of titanium implants can be transformed into nano tubular structures of less than 100 nm diameter. |
| | (b) Acid treatment | By combining strong acids or bases and oxidants nano pits networks (pit diameter 20–100 nm) can effectively be generated on Titanium, Ti6Al4V, CrCoMoalloys, and Tantalum. |
| | (c) Alkali treatment | In this method, the titanium implant is immersed in either sodium or potassium hydroxide followed by heat treatment at 800 °C for 20 min that is followed by rinsing in distilled water.<br>**Advantages:**<br>Results in the growth of a nanostructured and bioactive sodium titanate layer on the dental implant surface. |
| | (d) Combination of anodization and chemical treatment | A combination of hydrothermal treatments and sodium hydroxide has been employed to titanium to create a wide variety of unique nanostructures.<br>**Advantages:**<br>Improved biological properties |
| | (e) Hydrogen peroxide treatment | $H_2O_2$ leads to oxidation and chemical dissolution of the titanium surface. The reaction between hydrogen peroxide and titanium dental surfaces leads to the formation of Titanium peroxy gels.<br>**Advantages:**<br>Immersion of treated dental implants in simulated body fluid leads to the development of thicker layers of titania gel which is beneficial for deposition of apatite crystals |
| | (f) Sol-gel treatment | This method leads to the formation of a uniform suspension of submicroscopic oxide particles in liquid (sol) by the procedure of controlled hydrolysis and condensation.<br>**Advantages**:<br>Leads to early bone healing and enhanced mechanical interlocking with bone. Sol-gel coating process improves dental implant surfaces by nanoscale surface modifications |
| | (g) Chemical vapor deposition | Nonvolatile compounds are deposited on the implant surface by a chemical reaction between implant surface and chemicals present in the gas.<br>**Advantages:**<br>By the process of chemical vapor deposition, metallic surface properties can be modified at the nanoscale level. |
| | (h) Combination of chemical vapor and sol-gel method | With the help of these techniques Niobium oxide and diamond-like carbon nano topographies have been deposited on titanium and other substrates which improve the bioactivity of implantable metals.<br>**Advantages:**<br>Metallic surface properties can be improved |

(continued)