Next-Generation Surface Engineering for Optimal Osseointegration a Synthesis of Emerging Methods and Mechanistic Insights

Dr. Harshad. B[1], Dr. Kaarunyan. M[2], Dr. Ananda Deeban. K. B. S[3]
[1,2.] *Undergraduate, BDS Meenakshi Ammal Dental College and Hospital, Chennai, Tamil Nadu, India.*
[3]. *Assistant Professor, MDS, Meenakshi Ammal Dental College and Hospital, Chennai, Tamil Nadu, India.*

***Abstract*—Long-term dental implant stability relies on successful osseointegration, critical for clinical predictability and patient outcomes. Recent advances in surface modification have moved beyond traditional macro- and micro-roughening to nanoscale engineering techniques such as anodization, plasma immersion ion implantation, and laser texturing, which enhance topography, wettability, and protein adsorption at the bone–implant interface. Chemical functionalization with trace element doped hydroxyapatite (e.g., Mg, Si, Sr) improves osteo conductivity and bone bonding, while biologically active coatings deliver osteo inductive growth factors and peptides to promote targeted osteogenesis.**

To combat peri-implantitis, antimicrobial strategies using silver nanoparticles, antimicrobial peptides, and multifunctional polymers help prevent microbial colonization, a leading cause of implant failure. Surface chemistry and nano topography also modulate immune responses, particularly macrophage polarization, fostering a regenerative peri-implant environment. Modified surfaces demonstrate superior bone-to-implant contact, biomechanical stability, and faster healing compared to machined implants. However, challenges remain, such as coating durability, immune compatibility, release kinetics, and patient variability, limiting broader clinical use. Future trends focus on integrating nanotechnology, bio functional coatings, and additive manufacturing to create patient-specific, smart implants with enhanced therapeutic precision and durability. This interdisciplinary approach promises more biologically responsive and precise implantology.

I. INTRODUCTION

The long-term success of dental implants, a vital solution for global tooth loss, hinges on a critical biological process called osseointegration. This process is defined as the direct structural and functional connection between the implant's surface and living bone tissue, with no intervening fibrous tissue. Stable osseointegration is the cornerstone of modern implantology, as it ensures the integrity of the bone-implant interface, minimizes adverse outcomes like marginal bone resorption, prevents inflammation, and guarantees the successful transfer of occlusal forces, ultimately defining the longevity and clinical predictability of the prosthetic restoration.[1,2]

The modern era of implantology was pioneered by Dr. Per-Ingvar Brandmark's 1965 discovery of the intimate bond formed between bone and root-form titanium implants. Titanium (Ti) and its alloys quickly became the gold standard due to their excellent biocompatibility, corrosion resistance, and mechanical strength. Despite these favourable properties, pure titanium is biologically inert, posing challenges for achieving rapid and predictable osseointegration, especially in areas of compromised bone. Early efforts to enhance integration focused on increasing the physical roughness of the titanium surface. Techniques like machining, grit blasting, and acid etching successfully created macro- and micro-scale modifications, increasing surface area for bone ingrowth and improving primary mechanical stability. While these foundational approaches significantly improved clinical outcomes over smooth surfaces, they were limited to mechanical enhancements and did not directly influence the molecular and cellular signalling pathways essential for new bone matrix deposition.[3]

The field has since undergone a significant paradigm shift from passive integration to the development of biofunctional platforms. The implant surface is now recognized as the primary interface that controls the host tissue's initial response and subsequent healing. The last two decades have leveraged nanotechnology (features measuring 1−100 nanometres) and precise

chemical functionalization to orchestrate specific cellular behaviours, including crucial steps like protein adsorption, osteoblast adhesion, proliferation, and differentiation. This advanced surface engineering aims to promote regenerative outcomes, moving beyond mere structural enhancement. Current research emphasizes multifunctionality: the capacity of the implant surface not only to accelerate osseointegration but also to provide a robust defence against bacterial colonization and the onset of peri-implantitis. This transition toward sophisticated physical, chemical, and biological surface modification strategies paves the way for the future of patient-specific implantology.[4,5]

II. PHYSICAL SURFACE MODIFICATIONS: MACRO-, MICRO-, AND NANO-SCALE ENGINEERING

The topographical features of a dental implant surface, spanning macro, micro, and nano scales, are fundamental determinants of successful osseointegration. Each scale operates distinctly, contributing synergistically to mechanical stability and biological activity.

Macro-roughness refers to features on the millimetre to several micron scale, relating primarily to the implant's overall geometry, such as thread shape, pitch, and depth. These macroscopic characteristics are essential for achieving high primary mechanical stability, which is vital for initial fixation and effective load transfer. For instance, sophisticated thread designs optimize stress distribution pathways and maximize the initial bone-implant contact area. Techniques like Titanium Plasma Spray (TPS) create robust macro-roughness up to 240 μm, enhancing mechanical interlocking and friction upon insertion.[6]

Micro-roughness involves surface irregularities ranging from approximately 1 to 10 microns (typically defined by an average roughness Ra between 0.5 and 2μm). This scale is crucial for biochemical activity. Grit blasting, which propels abrasive particles like alumina (Al_2O_3) or titanium dioxide (TiO_2) (25–75 μm) at high velocity, and acid etching, using strong acids such as hydrochloric acid (HCl) or sulfuric acid (H_2SO_4) to create micro-pits (0.5–2 μm in diameter), are standard methods. These modifications increase the effective surface area for cellular and protein interactions, enhance surface wettability, and stabilize the fibrin matrix, providing an initial scaffold for cellular migration and osteogenesis. Modern systems frequently adopt dual-scale treatments, such as Sandblasted, Large-grit, Acid-etched (SLA) surfaces, achieving a hierarchical roughness that leverages macro-features for initial fixation and micro-features for directing early bone apposition.[6,7]

Nano-scale roughness, encompassing features from 1 to 100 nanometres (nm), represents the evolution of surface engineering, progressing beyond micro-features to influence biological responses at the molecular level. The fundamental biological rationale for nanoscale modification is that it closely replicates the natural extracellular matrix (ECM) environment, providing physical and chemical cues that regulate early cellular interactions.[7]

Nanostructured surfaces significantly modulate the initial adsorption and conformation of adhesive proteins like fibronectin and vitronectin, setting the stage for downstream osteogenic activities. Furthermore, nano topography directly influences osteoblast morphology, orientation, and particularly differentiation by regulating integrin receptors and subsequent cytoskeletal organization. Advanced methods used to create nanoscale features on implant surfaces include anodization, laser surface texturing, and chemical deposition techniques. Anodization is an electrochemical process that generates highly ordered TiO_2 nanotubes or nanoporous layers with customizable dimensions, which improve osteoblast adhesion and can act as nanoscale reservoirs for localized delivery of growth factors or drugs. Laser surface texturing employs femtosecond or nanosecond pulses to produce precisely controlled nanostructures that increase surface energy and may reduce bacterial adhesion. Chemical vapor deposition (CVD) and sol-gel techniques enable the accurate deposition of thin, nanostructured bioactive ceramic coatings such as hydroxyapatite or calcium phosphate, which mimic the mineral composition of bone.[8,9]

III. THE CRITICAL BALANCE: DIFFERENTIATION VERSUS PROLIFERATION

While nanoscale features are effective in guiding cell fate, they introduce a critical engineering compromise. Experimental observations of osteoblasts on nanorough surfaces reveal a phenomenon described as "dichotomy kinetics". Specifically, while nanoscale roughness strongly stimulates osteogenic

differentiation (the specialization of cells into bone-forming cells), it may concurrently inhibit cell proliferation (the rapid multiplication of cells).[10]
Successful, rapid osseointegration requires a synergistic sequence: first, rapid cell proliferation to populate the entire implant surface, followed by effective differentiation to deposit new bone matrix. If nanoscale topography maximizes differentiation at the expense of early proliferation, the overall rate of new bone volume formation may be suboptimal. This recognition validates the current clinical trend of incorporating hybrid micro-nano titanium model surfaces. These hybrid designs intentionally leverage micro-features to promote cell number while using superimposed nano-features to guide specialized cell function, ensuring a synergistic enhancement of both phases of tissue regeneration. Optimizing this delicate balance between proliferative capacity and differentiation commitment is a key objective in rational implant design.[11,12]

IV. CHEMICALLY DRIVEN SURFACE ACTIVATION

Chemical methods for optimizing titanium implant surfaces focus on enhancing wettability and hydrophilicity, which are essential for rapid protein adsorption and early cell attachment. Acid etching chemically activates the surface by removing contaminants and significantly increasing surface free energy and hydrophilicity. Similarly, alkali heat treatment creates a porous sodium titanate hydrogel layer that promotes apatite nucleation in body fluids, thereby enhancing bioactivity and providing a scaffold for bone mineralization. Plasma immersion ion implantation (PIII) introduces reactive species like oxygen, nitrogen, or argon to boost surface energy and incorporate functional groups that improve cell adhesion. Additionally, PIII can incorporate antibacterial ions such as silver or copper to offer infection resistance without compromising biocompatibility. Fluoride treatment alters the titanium surface charge and energy profile, accelerating osteoblast proliferation and differentiation; this method is used in commercial products like OsseoSpeed™ to promote faster implant integration.[13]
Osteoconductive mineral coatings and advanced doping strategies involve immobilizing biologically active molecules to regulate cellular processes, enhance bone regeneration, and reduce healing times. Hydroxyapatite (HA) and calcium phosphate coatings are widely used because they closely mimic bone's natural mineral composition, supporting rapid osteo conduction and osseointegration. However, traditional plasma-sprayed HA coatings face challenges in mechanical stability, with risks of delamination and degradation under oral mechanical loading. To improve durability and bioactivity, research has focused on doping HA with trace elements naturally present in bone, such as magnesium, silicon, and strontium. These dopants enhance HA crystallinity, mechanical strength, and osteogenic potential. Strontium is especially effective due to its similarity to calcium, enabling it to promote bone formation by stimulating osteoblast activity and reducing osteoclast-mediated bone resorption. This approach improves biological potency while reducing the risk of coating failure.[14]

V. OPTIMIZING STABILITY AND BIOACTIVITY

The evolution of bioactive coatings demonstrates a clear engineering principle: the necessity of balancing biological potency with long-term mechanical demands. Early reliance on thick, bulk HA coatings often prioritized maximal bioactivity but risked material failure, such as delamination and degradation, under continuous mechanical stress. The shift toward integrating trace elements, such as strontium, chemically reinforces the HA structure while maintaining or boosting osteogenic potential. Furthermore, utilizing precision methods like PIII, sol-gel, and advanced doping allows for the creation of ultra-thin, highly adherent, and stable films. This strategy reflects a design philosophy centred on achieving an optimal bioactive surface that prioritizes long-term functional stability and durability over mere transient biological effect.[15,16]

IV. MULTIFUNCTIONAL STRATEGIES: DUAL ACTION AGAINST INFECTION AND FAILURE

A primary biological complication and significant cause of long-term implant loss is peri-implantitis, a chronic inflammatory condition driven by bacterial colonization and subsequent biofilm formation on the implant surface. Consequently, advanced implant surface design must move beyond osteogenic

promotion and provide crucial dual functionality: fostering osseointegration while actively suppressing microbial adhesion and biofilm persistence. Antimicrobial coatings function by inhibiting bacterial adhesion, killing pathogens upon contact, or releasing antibacterial agents locally in a controlled manner.

Metallic nanoparticles and ions, particularly silver nanoparticles (AgNPs), are widely studied for their strong, broad-spectrum antibacterial properties. Their antibacterial activity arises from disrupting bacterial cell membranes and generating reactive oxygen species (ROS). In addition to silver, ions such as copper (Cu) and zinc (Zn) can be incorporated into implant surfaces using techniques like plasma immersion ion implantation (PIII) or sputtering. Strontium (Sr), well known for its osteogenic effects, also provides dual benefits by offering antimicrobial activity while enhancing bone mineralization. Antimicrobial peptides (AMPs), which can be natural or synthetic, exhibit selective toxicity against bacterial pathogens through mechanisms such as physical pore formation in bacterial membranes or intracellular targeting. These peptides are often immobilized on implant surfaces through covalent bonding or layer-by-layer (LbL) assembly, minimizing the risk of bacterial resistance while also supporting beneficial host immune responses. Some dipeptides, like Fmoc-FF (derived from Fmoc-protected amino acids), have shown potent antibacterial and antibiofilm effects against pathogens like Staphylococcus aureus.[15]

Beyond chemical agents, nanoscale physical surface features themselves can provide antimicrobial effects. Bionic nanostructures, such as sharp nanopillars created by sequential anodizing and hydrothermal treatments, physically damage bacterial membranes or prevent bacterial adhesion. This physical mechanism achieves bactericidal effects without the need for releasing chemical agents, offering a unique strategy to reduce implant-associated infections.

Designing Synergy: Coordinated Osteogenesis and Antibacterial Action

The forefront of implant technology involves the development of multifunctional coatings designed to leverage synergistic effects between bone regeneration and infection control. Techniques such as Layer-by-Layer (LbL) self-assembly allow for the creation of layered architectures. This enables spatiotemporal control, whereby an outer layer releases antimicrobial agents (AgNPs or AMPs) early to prevent acute infection, while a sublayer releases osteogenic factors (BMP−2 or collagen peptides) subsequently to promote sustained bone regeneration.[16]

Preclinical data provides strong support for these synergistic designs. For instance, surface modification achieved through Plasma Electrolytic Oxidation (PEO) incorporating Strontium (Sr) and Silver (Ag) nanoparticles demonstrated a 100% antibacterial rate against Methicillin-resistant S. aureus (MRSA) within 24 hours. Critically, this combined action simultaneously enhanced Alkaline Phosphatase (ALP) activity (a key marker of osteogenic differentiation) in precursor cells (MC3T3−E1 cells), illustrating successful dual functionality.[16,17]

V. NAVIGATING THE THERAPEUTIC WINDOW

The design of dual-functionality surfaces requires navigating a critical "therapeutic window" where antibacterial potency is maximized, yet cytotoxicity toward essential host cells (osteoblasts and pro-regenerative macrophages) is strictly minimized. High concentrations of broad-spectrum antimicrobials, such as silver, are known to impair osteoblast function, potentially compromising osseointegration. Similarly, mechanical killing mechanisms using sharp nanostructures must be rigorously tested for host cell compatibility before clinical translation.[17]

The success of synergistic implants, such as the PEO/Sr/Ag surfaces, hinges on precisely engineered release kinetics and optimal agent concentrations. Strontium actively promotes bone formation, creating a microenvironment conducive to osteogenesis, while the controlled release of silver effectively manages the microbial load. This critical engineering requirement ensures that neither the antimicrobial function nor the osteogenic function compromises the other, elevating the challenge from simple material modification to precise biochemical engineering.[17,18]

VI. THE NANO-BIO INTERFACE: GOVERNING PROTEIN ADSORPTION AND CELLULAR ADHESION

The initial and arguably most critical stage of osseointegration begins immediately upon implant placement with the rapid adsorption of host blood proteins (e.g., fibronectin, vitronectin, albumin) onto

the implant surface. This adsorbed protein layer forms the provisional matrix that dictates all subsequent cellular responses. Surface characteristics, including oxide layer composition, charge, and notably wettability (hydrophilicity), govern the type, orientation, and conformation of these adsorbed proteins. Hydrophilic and high-energy surfaces selectively favour the adsorption of adhesive proteins that promote osteoblast attachment and spreading through integrin receptors. Nanostructured surfaces enhance this process by increasing the surface area and providing nanoscale topographies that better mimic the native extracellular matrix (ECM) architecture, further optimizing protein binding. This optimally configured protein layer initiates cytoskeletal organization and intracellular signalling cascades essential for osteogenic differentiation, including focal adhesion kinase (FAK), MAPK, PI3K/Akt, and Wnt/β-catenin pathways.[19]

Immunomodulation: Controlling Macrophage Polarization

The immune response mounted at the peri-implant site is a pivotal determinant of osseointegration success. An adverse, chronic inflammatory response, typically mediated by pro-inflammatory M1 macrophages, results in the release of destructive cytokines that can lead to fibrous encapsulation rather than direct bone apposition.[19]

Next-generation implant surfaces are actively engineered to reduce M1 macrophage activation and instead favour the polarization toward the pro-healing M2 phenotype. M2 macrophages release anti-inflammatory cytokines and growth factors that actively support angiogenesis and bone remodelling. Surface modifications such as specific nano topographies or bioactive coatings incorporating anti-inflammatory molecules help regulate this immune response by controlling cytokine profiles and mitigating the chronic inflammation that impedes proper healing. This development illustrates that modern implant design actively reprograms the host immune response to accelerate healing, establishing immunomodulation as a core design parameter alongside osteo induction and stability.[19]

Adequate blood supply is fundamental for delivering essential nutrients, oxygen, and osteoprogenitor cells to the healing site. Therefore, surface modifications increasingly incorporate angiogenic factors, such as Vascular Endothelial Growth Factor (VEGF), to promote capillary sprouting and vascular maturation adjacent to the implant. Nanoporous and nano-channel structures are specifically utilized as reservoirs for the sustained local release of these angiogenic proteins, integrating vascularization promotion with osteo conduction in multifunctional designs. The final stage of osseointegration involves matrix mineralization, where mature osteoblasts deposit and mineralize the bone extracellular matrix (collagen type I, osteocalcin, osteo pontin). Surface roughness and chemistry promote osteoblast proliferation and increase Alkaline Phosphatase (ALP) activity. Bioactive surfaces, particularly hydroxyapatite or calcium phosphate coatings, actively encourage calcium phosphate nucleation and crystal growth, leading to the formation of a strong, integrated interfacial bond with the host bone.[19]

VII. CLINICAL OUTCOMES AND TRANSLATIONAL CHALLENGES

The primary objective of advanced implant surface modifications is to translate enhanced biological responses into measurable clinical benefits, including improved implant survival, faster functional recovery, and reduced complication rates.

Clinical and histological studies confirm the efficacy of surface modification. Hydrophilic surface treatments (e.g., SLActive®) have been shown to significantly reduce the time required to establish secondary implant stability. This acceleration allows for earlier functional loading protocols, often within 3 to 6 weeks, compared to the traditional 3 to 6 months required for conventional surfaces. Furthermore, long-term clinical evidence demonstrates higher overall implant survival and success rates, often exceeding 95% after 5 to 10 years for micro-roughened and bioactive-coated implants compared to machined controls. These modifications also crucially contribute to enhanced marginal bone preservation, a critical metric for long-term implant success.[5,19]

Surface-modified implants provide a significant clinical advantage in challenging clinical situations where endogenous healing capacity is reduced. This includes treating patients with poor bone quality (types III and IV bone), individuals who smoke, and those with systemic health conditions, such as uncontrolled diabetes or osteoporosis. In these scenarios, the

increased surface bioactivity and targeted delivery of osteogenic agents help compensate for the reduced regenerative potential of the host tissues, ultimately leading to more predictable osseointegration outcomes than would be possible with inert surfaces.[5,19]

Current Roadblocks: Durability, Standardization, and Cost-Effectiveness

Despite promising clinical outcomes, the widespread adoption of advanced implant surface technologies faces several significant challenges. One major issue is the durability and mechanical integrity of bioactive and multifunctional coatings. These coatings are prone to delamination or degradation when subjected to continuous cyclic mechanical loading and exposure to the corrosive biofluids found in the oral environment, which can compromise the long-term stability of the bone–implant interface. Another barrier is the lack of standardization in clinical research. Considerable heterogeneity exists among clinical trial designs, varying by implant systems, surface treatment methods, patient demographics, and outcome measures. This variability complicates comparative analyses and makes it difficult to establish unified, evidence-based guidelines for emerging surface modification technologies.

In the Indian clinical context, cost, and clinical adoption present additional hurdles. Manufacturing advanced implant systems that use technologies like plasma electrolytic oxidation (PEO) or layer-by-layer (LbL) assembly of multifunctional agents is complex and expensive. While basic single-tooth implants typically start around ₹20,000, premium implants with sophisticated surface features can cost ₹50,000 or more. This cost increase, along with the complexity of managing such implants, often leads to reluctance among general dental practitioners to adopt these technologies. Concerns over high costs and unclear long-term care pathways may result in inadequate patient follow-up, highlighting the need to improve accessibility and cost-effectiveness to encourage broader clinical use. Despite encouraging clinical outcomes, several challenges limit the widespread adoption of advanced implant surfaces. Maintaining the durability and mechanical integrity of bioactive and multifunctional coatings is difficult, as these may delaminate or degrade under continuous cyclic loading and exposure to the corrosive oral environment, threatening long-term interface stability.[18]

In the Indian context, cost and clinical adoption pose significant barriers. The complex manufacturing processes of next-generation surfaces, such as Plasma Electrolytic Oxidation (PEO) or Layer-by-Layer (LbL) assembly, drive up production costs. Basic single-tooth implants start near ₹20,000, but premium systems with advanced surfaces can exceed ₹50,000. High costs and management complexity contribute to hesitation among general practitioners, who may avoid specialized implants due to unclear long-term care pathways and patient follow-up challenges. Improving affordability and accessibility is essential to facilitate broader clinical acceptance.[18]

VIII. CHALLENGES AND FUTURE DIRECTIONS

The continued development of implant surface technology is guided by the need to overcome the challenges of coating instability, patient variability, and the complexity of controlled drug delivery. One of the most promising future directions is the development of smart and responsive surfaces. The difficulty in controlling the release kinetics of therapeutic agents to match the dynamic stages of bone healing is a major technical difficulty. Responsive surfaces aim to solve this by integrating stimuli-sensitive materials capable of detecting local environmental cues, such as shifts in pH (indicating inflammation or bacterial activity) or the presence of bacterial enzymes.[16]

These surfaces can then trigger the localized, "on-demand" release of therapeutic agent's antimicrobials, anti-inflammatories, or growth factors only when and where they are needed. This dynamic, self-regulating mechanism minimizes systemic drug exposure, reduces potential adverse side effects, and provides superior temporal control over healing and infection prevention compared to static release systems. Patient-specific variability, including differences in local bone quality, systemic health status (e.g., diabetic healing response), and genetic predispositions, strongly influences the outcome of osseointegration. Since current implant designs largely utilize uniform surface modifications, their effectiveness is limited in compromised clinical scenarios.[19]

The future trajectory points decisively toward personalized implant engineering. Advances in high-resolution imaging (micro-CT), combined with machine learning algorithms and precision additive

manufacturing (3D printing), now offer the technical capability to design patient-specific implants. Surfaces can be customized in terms of topography, thread geometry, and biochemical functionalities (e.g., tailored Sr-doping levels) to precisely address individual anatomical and biological constraints. Furthermore, the integration of omics technologies (genomics, proteomics) is providing deeper insights into patient-specific peri-implant tissue responses, which can guide the rational design of biomaterials that interact optimally with individual host biology, ushering in an era of precision implant medicine.[9,19]
Future coatings will heavily rely on biomimetic strategies, drawing inspiration from natural antimicrobial surfaces, such as the micro- and nano-patterns found on insect wings, to simultaneously deter bacterial adhesion and support host cell colonization. Hierarchical coatings will combine optimized micro- and nano-scale roughness with multilayer bioactive components, providing sequential or synergistic delivery of multiple agents osteogenic, angiogenic, and immunomodulatory to maximize the regenerative capacity of the peri-implant microenvironment. The goal is to create surfaces that are not just tolerated, but which actively engage with and guide host tissue regeneration throughout the implant lifespan.[20]

IX. CONCLUSION

Dental implant surface engineering is a rapidly advancing field in restorative dentistry, evolving implants from inert structures to sophisticated biofunctional platforms through nanoengineering, chemical modifications like trace element–doped hydroxyapatite, and targeted biological strategies such as growth factor and peptide delivery. This progress has effectively accelerated osseointegration and enhanced protection against peri-implantitis. Research shows that optimizing micro- and nanoscale surface features modulates critical molecular processes including protein adsorption and osteoblast signaling, resulting in faster secondary stability and improved long-term implant survival, especially in medically compromised patients. Despite these advances, key challenges remain, such as ensuring the long-term mechanical durability and stability of complex multilayer coatings in the dynamic oral environment, achieving standardized protocols across varied technologies, and addressing manufacturing complexity and cost barriers—particularly in markets like India. The future of implant surface technology is geared toward personalized, stimuli-responsive smart implants. By combining biomimetic design with advanced digital manufacturing and –omics technologies, these next-generation implants will be tailored to individual biological and anatomical needs, promising improved predictability, durability, and patient-centered outcomes that will set new standards in implant dentistry.[21]

REFERENCES

[1] Kapoor N, Nagpal A, Verma R, Thakur J, Singla A. A review on surface treatment of titanium implant. IP Ann. Prosthodont. Restor. Dent. 2020; 6:194-200.How implant surfaces shape osseointegration. International Journal of Periodontology and Implantology, 2025-07-19.

[2] Zhang H, Wu Z, Wang Z, Yan X, Duan X, Sun H. Advanced surface modification techniques for titanium implants: a review of osteogenic and antibacterial strategies. Frontiers in Bioengineering and Biotechnology. 2025 Mar 19; 13:1549439. The Effect of Antibacterial-Osteogenic Surface Modification on the Osseointegration of Titanium Implants: A Static and Dynamic Strategy. ACS Biomaterials Science & Engineering, 2024-06-03.

[3] Jackson J, Samarah H, Palmer W, Kaplan Z, Nicodem M, Kumar P Jr., Short S, Bridgham K, Harshyne L, Curry J. The impact of biomaterial characteristics on macrophage phenotypes in tissue engineering: a review. Plast Aesthet Res. 2025; 12:12.

[4] Li Y, Li X, Guo D, Meng L, Feng X, Zhang Y, Pan S. Immune dysregulation and macrophage polarization in peri-implantitis. Frontiers in bioengineering and biotechnology. 2024 Jan 29; 12:1291880.

[5] Nascimento MD, Brito TO, Lima AM, Elias CN. Protein interactions with Osseo integrable titanium implants. Brazilian Journal of Oral Sciences. 2023 Nov 3;22: e238749. Chen S, Saeed AF, Liu Q, Jiang Q, Xu H, Xiao GG, Rao L, Duo Y. Macrophages in immunoregulation and therapeutics. Signal transduction and targeted therapy. 2023 May 22;8(1):207.

[6] Matos GR. Surface roughness of dental implant and osseointegration. Journal of maxillofacial and oral surgery. 2021 Mar;20(1):1-4.

[7] Thirumalaivasan N, Nangan S, Verma D, Shellaiah M, Ali S, Rajendran S, Kanagaraj K, Pothu R, Boddula R, Radwan AB, Al-Qahtani N. Exploring the diverse nanomaterials employed in dental prosthesis and implant techniques: An overview.

[8] Tripathi S, Raheem A, Dash M, Kumar P, Elsebahy A, Singh H, Manivasagam G, Nanda HS. Surface engineering of orthopedic implants for better clinical adoption. Journal of Materials Chemistry B. 2024;12(44):11302-35.

[9] Cheraghiyan M. Nanotechnology in dentistry: Potential applications and future perspectives. Journal of Oral and Dental Health Nexus. 2025 Jan 1;2(1):1-3.

[10] Mohammed RF. The Clinical Evaluation of Dental Implants with Nano Surface. Clinical Medicine And Health Research Journal. 2023 Apr 27;3(2):355-63.

[11] López-Valverde N, Aragoneses J, López-Valverde A, Quispe-López N, Rodríguez C, Aragoneses JM. Effectiveness of biomolecule-based bioactive surfaces, on os-seointegration of titanium dental implants: A systematic review and meta-analysis of in vivo studies. Frontiers in Bioengineering and Biotechnology. 2022 Sep 26; 10:986112.

[12] Khabadze Z, Dolzhikov N, Aude R, Abdul K, Savitskaya D, Dorofeev I, Kikhov M, Shikhaliev R, Akhmedov A, Bakaev Y, Dashtieva M. The Effect of Dental Implant Nanotopography on its Osseointegration. Journal of International Dental and Medical Research. 2025;18(1):410-20.

[13] Zhang H, Wu Z, Wang Z, Yan X, Duan X, Sun H. Advanced surface modification techniques for titanium implants: a review of osteogenic and antibacterial strategies. Frontiers in Bioengineering and Biotechnology. 2025 Mar 19; 13:1549439. Strontium-Doped Nano-Hydroxyapatite (Sr-Nano-HA). MDPI Materials, 2024.

[14] López-Valverde A, Quispe-López N, Rodríguez C, Aragoneses JM. surfaces, on os-seointegration of titanium dental implants: A systematic review and meta-analysis of in vivo studies. Functional surfaces and biomaterials. 2023 Feb 17; 16648714:202.

[15] Hou C, A J, Zhao D, Ma X, Zhang W, Zhao W, Wu M, Zhang Z, Yuan F. Surface modification techniques to produce micro/nano-scale topographies on Ti-based implant surfaces for improved osseointegration. Frontiers in Bioengineering and Biotechnology. 2022 Mar 25; 10:835008.

[16] Wei H, Cui J, Lin K, Xie J, Wang X. Recent advances in smart stimuli-responsive biomaterials for bone therapeutics and regeneration. Bone research. 2022 Feb 23;10(1):17.

[17] Jahanmard F, Dijkmans FM, Majed A, Vogely HC, Van Der Wal BC, Stapels DA, Ahmadi SM, Vermonden T, Amin Yavari S. Toward antibacterial coatings for personalized implants. ACS Biomaterials Science & Engineering. 2020 Sep 7;6(10):5486-92.

[18] Das A, Rajkumar P. Metal 3D printing of biometals for prostheses and implants: a review. Exploration of BioMat-X. 2025 May 13; 2:101338.

[19] Nanotechnology Reviews. 2025 May 2;14(1): 20250140.Nanofeatured surfaces in dental implants. International Journal of Implant Dentistry, 2024-07-03.

[20] Rayannavar S, Kumar S, Kamath V, Bembalgi M, Nayak N, Jodalli P. Osseointegrative and antimicrobial properties of graphene oxide nano coated dental implants: A systematic review. F1000Research. 2024 Aug 9; 13:281.

[21] Maekawa S, Cho YD, Kauffmann F, Yao Y, Sugai JV, Zhong X, Schmiedeler C, Kinra N, Moy A, Larsson L, Lahann J. BMP Gene-Immobilization to Dental Implants Enhances Bone Regeneration (Adv. Mater. Interfaces 22/2022). Advanced Materials Interfaces. 2022 Aug 3;9(22).