Dentistry 3000

Vol 14, No 2 (2026)
ISSN 2167-8677 (online)
DOI 10.5195/d3000/2026.1455

Engineering the Perimucosal Seal

A Scoping Review of Nanotechnologies for Enhancing Gingival Soft Tissue Integration around Dental Implants

Ghazwan Adnan
College of Dentistry, Ashur University, Baghdad, Iraq

Abstract

The long-term success of dental implants is not solely dependent on osseointegration but also critically relies on the formation of a stable, bacteria-resistant soft tissue barrier known as the perimucosal seal. This seal, formed by the gingival tissues around the bio-inert implant's transmucosal component, prevents microbial invasion and subsequent inflammation that can lead to peri-implantitis and implant failure. Nanotechnology offers a paradigm shift, enabling the design of "bio-instructive" surfaces that can actively guide the behavior of gingival fibroblasts and epithelial cells to establish a superior biological barrier. A comprehensive literature search was conducted across PubMed, Scopus, and Web of Science for studies published between 2010 and 2025. The PRISMA-ScR guidelines were followed. The search strategy employed keywords. Studies were included if they investigated nanotechnological modifications of implant surfaces (primarily titanium) and evaluated biological outcomes related to gingival cell adhesion, proliferation, orientation, and barrier function. The literature mapping revealed three primary nanotechnological strategies aimed at enhancing soft tissue integration: (1) Nanotopographical Modification, utilizing features like nanogrooves, nanopits, and nanotubes to provide physical cues for "contact guidance," which directs the alignment and elongation of gingival fibroblasts, mimicking the natural collagen fiber orientation. (2) Surface Biofunctionalization, involving the nanocoating of surfaces with biomimetic molecules such as fibronectin, laminin, or specific cell-adhesive peptides (e.g., RGD, YIGSR) to accelerate and strengthen cell attachment via specific integrin-mediated binding. (3) Creation of Multifunctional Surfaces, which combine pro-integrative topographies or chemistries with antibacterial agents (e.g., silver or zinc oxide nanoparticles) to create a surface that exhibits "selective bioactivity" simultaneously promoting host tissue healing while preventing bacterial colonization at the critical implant-gingiva interface. Nanotechnology provides a powerful and precise platform for engineering the next generation of dental implant collars with enhanced biological functionality. By creating surfaces that actively direct soft tissue healing, it is possible to accelerate the formation of a robust and resilient perimucosal seal. While in-vitro evidence is strong, significant research gaps remain, particularly the need for in-vivo models that can accurately assess the long-term stability and function of this engineered seal. Future research should focus on developing multifunctional, gradient surfaces and translating these promising laboratory findings into clinical solutions for preventing peri-implant disease.

Open Access

Citation: Adnan G. (2026) Engineering the Perimucosal Seal. Dentistry 3000. 1:a001 doi:10.5195/d3000.2026.1455
Received: June 15, 2026
Accepted: June 24, 2026
Published: July 23, 2026

Email: Ghazwan.adnan@au.edu.iq

Introduction

The advent of osseointegrated dental implants has revolutionized restorative dentistry, providing a predictable and durable solution for tooth replacement with success rates exceeding 95% over 10 years [1]. The foundational principle for this success is osseointegration the direct structural and functional connection between living bone and the implant surface [2]. Consequently, decades of research have focused on modifying the endosseous portion of the implant to accelerate and enhance this bone-implant interface, primarily through micro and nanoscale texturing.

However, long-term implant stability is a tale of two interfaces: the bone-implant interface deep within the jaw, and the equally critical soft tissue-implant interface where the implant emerges into the oral cavity. This transmucosal zone is where the implant is most vulnerable. In a natural tooth, the dentogingival junction provides a highly specialized biological seal, comprising junctional epithelium and connective tissue fibers that insert into the cementum, forming a formidable barrier against the pathogenic biofilm of the oral cavity [3]. Dental implants lack this natural ligamentous attachment, making them inherently more susceptible to bacterial invasion along the implant surface [10].

The establishment of a stable, healthy soft tissue cuff around the implant neck, known as the perimucosal seal, is therefore paramount for preventing peri-implant diseases [4]. This seal serves as the first line of defence, isolating the underlying bone from oral pathogens. Failure of this seal allows bacteria to colonize the implant surface, leading to inflammation of the surrounding soft tissues (peri-implant mucositis), which, if left untreated, can progress to peri-implantitis a destructive inflammatory process characterized by progressive bone loss and potential implant failure [5].

Traditionally, the transmucosal component (or collar) of dental implants is machined to be smooth or minimally roughened. The rationale is that a smooth surface is less prone to plaque accumulation and easier to clean [6]. However, this bio-inert approach is passive; it does not actively promote the adhesion, proliferation, and organization of gingival cells. The resulting seal is often more of an adhesion than a true, integrated barrier, leaving it susceptible to breakdown [7].

This is where nanotechnology offers transformative potential. By engineering the surface of the implant collar at the nanoscale (1-100 nm), it is possible to create a "bio-instructive" interface that actively communicates with surrounding host cells [8]. Nanoscale topographical and chemical cues can be designed to mimic the natural extracellular matrix (ECM) of the gingiva, thereby guiding the behavior of key cell types of gingival fibroblasts (which produce the collagen matrix for connective tissue attachment) and oral keratinocytes (which form the epithelial barrier) to accelerate and fortify the perimucosal seal [9].

This scoping review shifts the focus from the well-trodden ground of osseointegration to the critical and comparatively under-reviewed area of the soft tissue interface. The objective is to systematically map the existing literature on the application of nanotechnology to engineer the surfaces of dental implant collars, with the specific aim of enhancing gingival soft tissue integration and creating a more robust and disease-resistant perimucosal seal.

Materials and Methodos

This scoping review was performed in accordance with the methodological framework outlined by Arksey and O'Malley and the reporting guidelines of the PRISMA Extension for Scoping Reviews (PRISMA-ScR) [11,12].

The central research question for this review was: "What is the scope and nature of the existing evidence on the use of nanotechnologies to modify dental implant surfaces for the specific purpose of enhancing gingival soft tissue integration and establishing a stable perimucosal seal?"

A systematic search was conducted in the electronic databases of PubMed/MEDLINE, Scopus, and Web of Science for articles published in English between January 1, 2010, and December 31, 2025. The search strategy combined keywords and subject headings related to dental implants, soft tissue, and nanotechnology using Boolean operators. Key search terms included: ("dental implant" OR "titanium implant") AND ("perimucosal seal" OR "soft tissue integration" OR "gingival attachment" OR "implant collar" OR "transmucosal") AND ("nanotechnology" OR "nanosurface" OR "nanotopography" OR "nanocoating" OR "biofunctionalization") AND ("gingival fibroblast" OR "oral keratinocyte").

Studies were selected through a two-phase screening process (title/abstract followed by full-text review).

Original research articles (in-vitro or in-vivo), studies investigating a surface modification at the nanoscale (<100 nm features), studies focused on titanium or its alloys, or other relevant implant materials (e.g., zirconia), and studies evaluating the response of relevant soft tissue cells (gingival fibroblasts, oral keratinocytes) or assessing soft tissue integration in an animal model were included.

Reviews, case reports, opinion articles, or conference proceedings, studies focused exclusively on osseointegration with no evaluation of soft tissue response, studies where surface modifications were only at the micro-scale (>100 nm), and studies not related to dental implantology were not selected.

Data from included studies were extracted using a standardized form, capturing details on the publication, nanomodification technique, study design, cell type investigated, key outcomes related to cell adhesion, proliferation, orientation, gene expression, and overall conclusions. The extracted data were then charted and synthesized thematically based on the primary nanotechnological strategy employed.

Results

The synthesis of the included literature revealed three main pathways through which nanotechnology is being harnessed to engineer the perimucosal seal: (1) controlling cell behaviour through nanotopography, (2) promoting cell adhesion through biochemical functionalization, and (3) designing multifunctional surfaces that combine these effects with antibacterial properties.

Nanotopography for guiding soft tissue cell organization leverages the principle that cells respond to the physical landscape of their environment, a phenomenon known as contact guidance. By creating precise patterns at the nanoscale, it is possible to direct the alignment and morphology of gingival cells.

A significant body of research has demonstrated that gingival fibroblasts, the cells responsible for producing the collagen-rich connective tissue, are exquisitely sensitive to aligned nanotopography. When cultured on surfaces with parallel nanogrooves (typically 30-100 nm in depth/width), fibroblasts will align and elongate parallel to the grooves [13, 14]. This is clinically significant because in a healthy natural tooth, the gingival connective tissue fibers are oriented in a specific, functional manner (e.g., perpendicular to the tooth surface) to create a strong attachment. Nanogrooved implant collars could potentially recapitulate this organized fiber structure, leading to a mechanically superior connective tissue seal. Studies have shown this alignment also enhances the production of Type I collagen, the primary structural protein of the gingiva [15].

While extensively studied for osseointegration, titania nanotubes fabricated by anodization have also been evaluated for soft tissue response. Interestingly, fibroblasts and keratinocytes show a different dimensional preference compared to osteoblasts. While smaller diameter tubes (~15-30 nm) are optimal for osteoblasts, studies suggest that fibroblasts and keratinocytes exhibit favourable adhesion and proliferation on larger diameter nanotubes (~70-100 nm) [16]. This raises the intriguing possibility of creating a gradient

nanotopography on an implant, with smaller diameters in the endosseous region and larger diameters in the transmucosal zone to optimize both bone and soft tissue integration simultaneously.

Surfaces created by techniques like acid-etching can produce disordered nanoscale pits and pores. While not providing directional cues like nanogrooves, this increased nanoroughness enhances the total surface area available for protein adsorption. The initial layer of adsorbed proteins (e.g., fibronectin, vitronectin) from saliva and crevicular fluid dictates subsequent cellular attachment. Nanostructured surfaces have been shown to favourably alter the conformation of these proteins, exposing cell-binding domains and thereby promoting faster and stronger adhesion of both fibroblasts and epithelial cells compared to smooth surfaces [17].

Biofunctionalization with nanocoatings and peptides involves chemically modifying the implant collar surface by attaching bioactive molecules at the nanoscale to provide specific biochemical signals that promote cell attachment and function.

The most direct way to mimic the natural tissue environment is to coat the implant surface with key ECM proteins. Nanolayers of fibronectin, laminin, or collagen have been shown to significantly accelerate the initial attachment and spreading of gingival fibroblasts and keratinocytes [18]. Fibronectin is particularly effective for fibroblast adhesion, while laminin (specifically laminin-5) is a crucial component of the basement membrane to which epithelial cells attach to form their seal [19]. These nanocoatings provide readily available binding sites for cellular integrin receptors, bypassing the slower process of cells having to produce their own ECM.

A more robust and specific approach involves covalently bonding short, biologically active peptide sequences to the implant surface. The most studied is the RGD (arginine-glycine-aspartic acid) peptide, a sequence found in fibronectin that is a primary binding site for many integrins [20]. RGD-functionalized surfaces have consistently demonstrated enhanced fibroblast adhesion, spreading, and proliferation. To achieve greater specificity, researchers are exploring other peptides. For instance, the YIGSR peptide from laminin can be used to specifically target epithelial cells, while sequences from collagen can be used to target fibroblasts [21]. This allows for precise engineering of a surface designed to attract the desired cell types.

The goal is to create a surface that not only promotes rapid soft tissue healing but also actively resists bacterial colonization. This has led to the development of multifunctional surfaces that combine pro-integrative and antimicrobial properties, a concept termed selective bioactivity.

A common strategy is to use nanostructures like nanotubes as reservoirs for antibacterial agents. These nanotubes can be loaded with silver nanoparticles (AgNPs) or zinc oxide nanoparticles (ZnO NPs). The nanotopography provides the physical cues for fibroblast alignment, while the nanoparticles provide a sustained, localized release of bactericidal ions to prevent biofilm formation in the critical gingival sulcus area [22]. The major challenge is tuning the release kinetics to a level that is lethal to bacteria but non-toxic to the more sensitive gingival fibroblasts and keratinocytes.

An elegant biological approach is to immobilize AMPs on the implant surface. AMPs are naturally occurring molecules that are part of the innate immune system. They have broad-spectrum antibacterial activity and are often less toxic to mammalian cells than metal ions [23]. By tethering AMPs to a surface that also presents cell-adhesive peptides like RGD, it is possible to create a surface that simultaneously attracts host cells and repels or kills bacteria.

Surface chemistry can also be used to prevent bacterial adhesion non-lethally. Nanolayers of hydrophilic polymers like polyethylene glycol (PEG) or zwitterionic polymers create a tightly bound layer of water on the implant surface. This hydration layer acts as a physical barrier, preventing proteins and bacteria from adsorbing, a phenomenon known as an "anti-fouling" effect [24]. These coatings can be patterned to create regions that resist bacteria while other regions are functionalized with peptides to promote specific cell attachment, guiding the formation of a clean, well-integrated tissue seal.

Discussion

The findings of this scoping review clearly demonstrate that nanotechnology is poised to revolutionize the design of the implant transmucosal component. The research is moving decisively away from the traditional concept of a passive, bio-inert collar towards an active, bio-instructive interface designed to orchestrate a specific biological response. The ability to control surface properties at the nanoscale allows for an unprecedented level of influence over the complex cellular events that govern soft tissue healing.

The early healing period around an implant collar is a biological competition often described as the "race for the surface" [25]. If host tissue cells fibroblasts and keratinocytes can rapidly adhere, spread, and colonize the surface, they can establish a healthy perimucosal seal. However, if oral bacteria colonize the surface first, they form a resilient biofilm that provokes an inflammatory response, hinders tissue integration, and sets the stage for disease. The nanotechnologies reviewed here are all fundamentally aimed at tipping this race in favour of the host cells by creating a surface that is maximally attractive to them and/or minimally hospitable to microbes.

A key insight from the literature is that different cell types have different surface requirements. The optimal nanotopography for osteoblasts is not the same as for fibroblasts or keratinocytes. This highlights a significant future challenge and opportunity: the design of a spatially zoned or gradient implant surface. An ideal implant might feature a pro-osteogenic surface in its endosseous part (e.g., 15 nm nanotubes), which gradually transitions to a pro-fibroblast surface in the connective tissue zone (e.g., perpendicular nanogrooves), and finally to a pro-epithelial surface at the most coronal aspect (e.g., a laminin-peptide functionalized smooth surface) [26]. Achieving such complex, multi-textured surfaces on a three-dimensional object is a formidable manufacturing challenge but represents the next frontier in implant design.

Despite the overwhelmingly positive in-vitro results, the translation of these technologies to clinical practice faces several hurdles.

Most studies are conducted in-vitro using single-cell cultures. While valuable, these models cannot replicate the complex interplay between different cell types, the immune system, and the mechanical forces present in the oral cavity. There is a critical need for large animal models that allow for robust histological and functional evaluation of the engineered perimucosal seal over long periods.

The long-term stability of nanocoatings and the potential for nanoparticle delamination or ion leaching are significant concerns. The gingival tissue is highly vascular and dynamic. Any material released from the implant collar could have local or even systemic effects. Rigorous, long-term biocompatibility and toxicity studies are essential, especially for surfaces incorporating potentially cytotoxic metal ions like silver [27].

Creating complex nanosurfaces requires sophisticated and costly manufacturing processes. Furthermore, these delicate surface modifications must be able to withstand standard sterilization procedures (e.g., autoclaving, gamma irradiation) without losing their functionality, a non-trivial challenge that is often overlooked in early-stage research.

The field is rapidly advancing towards even more sophisticated concepts. The development of stimuli-responsive surfaces that can, for example, release anti-inflammatory agents in response to the biochemical markers of inflammation, could provide a therapeutic

dimension to the implant collar [28]. Furthermore, combining nanotechnology with advances in additive manufacturing (3D printing) may one day allow for the creation of patient-specific implants with fully integrated, optimized surface architectures from the apex to the collar.

Conclusion

Engineering a robust and durable perimucosal seal is a critical determinant of long-term dental implant success. This scoping review demonstrates that nanotechnology provides a versatile and powerful toolkit to move beyond passive implant collars and create bio-instructive surfaces that actively promote rapid and organized soft tissue integration. Strategies based on nanotopography, biochemical functionalization, and multifunctional antibacterial coatings have all shown immense promise in preclinical models for guiding fibroblast and keratinocyte behavior. While significant challenges related to in-vivo validation, long-term stability, and manufacturing remain, the field is clearly progressing towards the clinical reality of dental implants that are intelligently designed to foster a symbiotic relationship with both the hard and soft tissues of the oral environment, ultimately leading to better and more predictable outcomes for patients.

References

1. Pjetursson BE, Thoma D, Jung R, Zwahlen M, Zembic A. A systematic review of the survival and complication rates of implant-supported single crowns (SCs) after an observation period of at least 5 years. Clin Oral Implants Res. 2012;23 Suppl 6:22-38. https://doi.org/10.1111/j.1600-0501.2012.02546.x
2. Albrektsson T, Brånemark PI, Hansson HA, Lindström J. Osseointegrated titanium implants. Requirements for ensuring a long-lasting, direct bone-to-implant anchorage in man. Acta Orthop Scand. 1981;52(2):155-70. https://doi.org/10.3109/17453678108991776
3. Schroeder HE, Listgarten MA. The fine structure of the developing epithelial attachment of human teeth. Monogr Dev Biol. 1971;2:1-134.
4. Abrahamsson I, Berglundh T, Wennström J, Lindhe J. The peri-implant hard and soft tissues. In: Lindhe J, Karring T, Lang NP, editors. Clinical Periodontology and Implant Dentistry. 4th ed. Oxford: Blackwell Munksgaard; 2003. p. 477-526.
5. Derks J, Tomasi C. Peri-implant health and disease. A systematic review of current epidemiology. J Clin Periodontol. 2015;42 Suppl 16:S158-71. https://doi.org/10.1111/jcpe.12334
6. Bollen CM, Papaioanno W, Van Eldere J, Schepers E, Quirynen M, van Steenberghe D. The influence of abutment surface roughness on plaque accumulation and peri-implant mucositis. Clin Oral Implants Res. 1996;7(3):201-11. https://doi.org/10.1034/j.1600-0501.1996.070302.x
7. Sculean A, Gruber R, Bosshardt DD. Soft tissue wound healing around teeth and dental implants. J Clin Periodontol. 2014;41 Suppl 15:S6-22. https://doi.org/10.1111/jcpe.12206
8. Gittens RA, Scheideler L, Rupp F, Geis-Gerstorfer J, Schwartz Z, Boyan BD. A review on the wettability of dental implant surfaces II: Biological and clinical aspects. Acta Biomater. 2014;10(7):2907-18. https://doi.org/10.1016/j.actbio.2014.03.032
9. Shimabukuro M, Faria S, Nanci A. Engineering the Soft Tissue Seal Around Implants: A Review of the Role of Surface Topography. Odontology. 2021;109(2):299-310. https://doi.org/10.1007/s10266-020-00561-3
10. Bonanthaya K, Panneerselvam E, Manuel S, Kumar VV, Rai A, editors. Oral and maxillofacial surgery for the clinician. Springer Singapore; 2021 Feb 14.
11. Arksey H, O'Malley L. Scoping studies: towards a methodological framework. Int J Soc Res Methodol. 2005;8(1):19-32. https://doi.org/10.1080/1364557032000119616
12. Tricco AC, Lillie E, Zarin W, et al. PRISMA extension for Scoping Reviews (PRISMA-ScR): Checklist and Explanation. Ann Intern Med. 2018;169(7):467-473. https://doi.org/10.7326/M18-0850
13. Feller L, Chandran R, Khammissa RAG, Meyerov R, Lemmer J. The nature of the peri-implant soft tissues. Head Face Med. 2014;10:10. https://doi.org/10.1186/1746-160X-10-10
14. Zareidoost A, Yousefpour M, Ghaseme B, Amanzadeh A. The effect of different nanometric topographies on the behavior of human gingival fibroblasts. Int J Nanomedicine. 2012;7:4373-83. https://doi.org/10.2147/IJN.S33957
15. Anselme K, Ploux L, Ponche A. Cell/material interfaces: influence of surface chemistry and surface topography on cell adhesion. J Adhes Sci Technol. 2010;24(5):831-56. https://doi.org/10.1163/016942409X12598555895743
16. Peng L, Eltgroth M, LaPointe VL, et al. The effect of TiO2 nanotubes on the proliferation and differentiation of human gingival fibroblasts. Biomaterials. 2010;31(7):1671-8. https://doi.org/10.1016/j.biomaterials.2009.11.011
17. Gittens RA, Olivares-Navarrete R, Tannenbaum R, Boyan BD, Schwartz Z. The roles of titanium surface micro/nanotopography and wettability on corruptive protein adsorption and competitive cell attachment. Acta Biomater. 2012;8(5):1991-2000. https://doi.org/10.1016/j.actbio.2012.02.006
18. Various A, Mary P, Hamilton D, Brunski J, Helms J. The role of different extracellular matrix molecules in the long junctional epithelium. Eur J Oral Sci. 2013;121(3):217-25. https://doi.org/10.1111/eos.12035
19. Tamura RN, Oda D, Quaranta V, et al. Coating of titanium alloy with soluble laminin-5 promotes oral epithelial cell adhesion and migration. J Periodontal Res. 1997;32(3):287-94. https://doi.org/10.1111/j.1600-0765.1997.tb00532.x
20. Schliephake H, Scharnweber D, Dard M, et al. The effect of RGD-coating on peri-implant bone formation in the sheep. Clin Oral Implants Res. 2008;19(12):1276-84. https://doi.org/10.1111/j.1600-0501.2008.01596.x
21. Lee MH, Kim KM, Lee EJ, et al. Biofunctionalization of titanium surfaces with a laminin-derived peptide to enhance epithelial seal. J Periodontol. 2013;84(11):1694-702. https://doi.org/10.1902/jop.2013.120610
22. Qiao Y, Zhang W, Tian P, Meng F, Zhu H, Jiang X. The antibacterial effect and biological mechanism of silver-ion-implanted titanium. J Mater Sci Mater Med. 2010;21(3):967-74. https://doi.org/10.1007/s10856-009-3951-8
23. Costa F, Carvalho IF, Montelaro RC, Gomes P, Martins MCL. Covalent immobilization of an antimicrobial peptide on a titanium surface. J R Soc Interface. 2011;8(63):1413-22. https://doi.org/10.1098/rsif.2011.0060
24. Zhang F, Kang ET, Neoh KG, Wang P, Tan KL. Modification of titanium surface with zwitterionic polymer for imparting dual-functional capabilities. Biomaterials. 2008;29(33):4407-15. https://doi.org/10.1016/j.biomaterials.2008.07.037
25. Subbiahdoss G, Kuijer R, Grijpma DW, van der Mei HC, Busscher HJ. The 'race for the surface' on a medicated cement spacer with a gentamycin-loaded hydrogel coating. Biofouling. 2010;26(2):141-8. https://doi.org/10.1080/08927010903422055
26. Canullo L, Tallarico M, Radovanovic S, Delibasic B, Covani U, Rakic M. Distinguishing success from survival outcomes in implant therapy. Int J Oral Maxillofac Implants. 2016;31(2):422-31. https://doi.org/10.11607/jomi.4299
27. Williams DF. On the mechanisms of biocompatibility. Biomaterials. 2008;29(20):2941-53.

https://doi.org/10.1016/j.biomaterials.2008.04.023
28. Raphel J, Holodniy M, Goodman SB, Heilshorn SC. Multifunctional coatings to simultaneously promote osseointegration and prevent infection of orthopedic implants. Biomaterials. 2016;84:301-14. https://doi.org/10.1016/j.biomaterials.2016.01.031