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The role of surface-modified titanium in tissue engineering for maxillofacial and reconstructive surgery; a narrative review study

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Abstract

Titanium and its alloys are widely used in maxillofacial and reconstructive surgery owing to their excellent biocompatibility, mechanical strength, and corrosion resistance. Despite these advantages, the inherent biological inertness of unmodified titanium limits its capacity for spontaneous osseointegration and increases susceptibility to peri-implant infections, thereby necessitating the development of surface modification strategies. This narrative review evaluates the necessity and clinical relevance of surface-modified titanium within the framework of tissue engineering, with a particular focus on applications in maxillofacial and reconstructive surgery. A targeted literature search was performed in the PubMed, Scopus, and Web of Science databases as well as the Google Scholar search engine using the keywords (titanium AND surface modification) combined with (maxillofacial OR craniofacial OR reconstructive surgery OR tissue engineering OR osseointegration OR bone healing). The search was restricted to peer-reviewed English-language articles, with emphasis on studies published between 2016 and 2026. Eligible studies included reviews, clinical investigations, and both in vitro and in vivo studies, while non-English publications and conference abstracts without full text were excluded. The findings demonstrate that surface modification significantly improves osseointegration, enhances bone regeneration, and imparts antimicrobial properties. Common approaches include sandblasting and acid-etching, anodization leading to nanotube formation, micro-arc oxidation (MAO), hydroxyapatite (HA) coatings, biomolecular functionalization using bone morphogenetic proteins such as bone morphogenetic proteins (BMP)-2 and BMP-7, and the application of three-dimensional printing to create porous architectures. These techniques operate across macro-, micro-, and nano-scale levels and target various stages of the bone–implant healing cascade. Overall, surface-modified titanium represents a clinically valuable and evidence-based strategy for improving outcomes in maxillofacial and reconstructive procedures. The incorporation of tissue engineering principles into implant surface design, particularly through the development of bioactive, antimicrobial, and structurally optimized surfaces, signifies a major advancement in craniofacial reconstruction. Further research focusing on multifunctional surface modifications and the translation of experimental findings into clinical practice remains essential.

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Introduction

Titanium (Ti) and its alloys, particularly Ti-6Al-4V, have long served as the gold standard biomaterial in maxillofacial and reconstructive surgery, such as orthopedics and dental implants (1-3). Their widespread adoption stems from an exceptional combination of physical and chemical properties: high strength-to-weight ratio, corrosion resistance conferred by a naturally forming passive titanium dioxide (TiO_2) oxide layer, low elastic modulus relative to other metals, and excellent biocompatibility (4). In the craniofacial and maxillofacial domain, titanium implants are employed in a broad spectrum of clinical scenarios, from the reconstruction of posttraumatic cranial defects and tumor-related bone ablations to mandibular reconstruction, zygomaticomaxillary repair, orbital floor restoration, and dental implantology (4,5).

Despite these favorable attributes, commercially pure titanium and its alloys are fundamentally bioinert materials (6). The native TiO_2 layer, while protective, cannot independently stimulate robust osseointegration, the direct structural and functional connection between living bone and the implant surface, particularly in compromised bony environments

Key point

Surface modification of titanium markedly improves implant performance by enhancing osseointegration, promoting bone regeneration, and providing antimicrobial effects. Techniques such as sandblasting and acid-etching, anodization with nanotube formation, micro-arc oxidation (MAO), hydroxyapatite (HA) coatings, and biomolecule functionalization with bone morphogenetic proteins (BMP)-2 and BMP-7, and porous architectures generated through three-dimensional printing act across macro-, micro-, and nano-scale levels to support different phases of bone healing. Collectively, these strategies demonstrate strong clinical value in maxillofacial and reconstructive surgery, with surface-modified titanium emerging as an evidence-based approach that integrates tissue-engineering principles to optimize implant bioactivity, structural design, and resistance to infection, while highlighting the need for further research on multifunctional surfaces and their translation into routine clinical practice.

such as irradiated tissue, osteoporotic bone, or large segmental defects (4). Implant failure due to insufficient osseointegration, fibrous encapsulation, and peri-implant infection remains a clinically significant concern, with premature failure rates reported at approximately 10% across orthopaedic and dental implant cohorts (4,6,7). In maxillofacial surgery, where anatomical complexity, aesthetic demands, and functional requirements are uniquely stringent, these failure rates carry profound consequences for patient quality of life (7).

The field of tissue engineering, defined by the application of scaffolds, cells, and signaling molecules to regenerate or replace damaged tissues, has introduced a paradigm shift in implant science (8). Surface modification of titanium implants serves as the primary vehicle for this biological activation (9). By engineering the implant surface at the macro-, micro-, and nanoscales through physical, chemical, and biochemical methods, clinicians and scientists can profoundly alter the osseointegration cascade, local inflammatory response, and long-term implant stability (4). This narrative review synthesizes current evidence from the literature on the role of surface-modified titanium in tissue engineering as applied to maxillofacial and reconstructive surgery. It addresses the biological rationale for surface modification, describes the principal modification strategies and their mechanisms of action, and discusses clinical translation and future directions.

Search Strategy

A comprehensive literature search was conducted using PubMed, Scopus, and Web of Science databases, supplemented by Google Scholar. The search strategy incorporated combinations of keywords (titanium AND surface modification) combined with (maxillofacial OR craniofacial OR reconstructive surgery OR tissue engineering OR osseointegration OR bone healing). Filters were applied to include English-language, peer-reviewed studies involving human and animal models with full-text availability. Studies were excluded if they were non-English, lacked full-text access, or presented incomplete or non-reproducible methodologies. The search covered publications from 1998 to 2026, with particular emphasis on studies published from 2016 onward. In total, more than 200 articles were identified and screened by title and abstract; approximately 60 were assessed in full text, and over 30 studies were ultimately included in the review.

Biological basis for surface modification

The bone-implant interface

Upon placement of a titanium implant, a cascade of biological events unfolds at the implant surface before osseointegration can be achieved. Within seconds, water molecules adsorb to the surface, followed by serum proteins including fibronectin, vitronectin, and fibrinogen; the conformation of these adsorbed proteins depends critically on the surface physicochemical properties, including roughness, charge, and chemistry (4). Platelets and immune cells subsequently migrate to the site, releasing cytokines and growth factors such as bone morphogenetic proteins (BMPs), insulin-like growth factors (IGF), fibroblast growth factor (FGF), and platelet-derived growth factor (PDGF) (10). Mesenchymal stem cells (MSCs) are subsequently recruited and must adhere, proliferate, and undergo osteogenic differentiation before mature lamellar bone can form directly at the implant interface (4,10).

Cell adhesion to the implant is mediated principally through integrins—glycoprotein transmembrane receptors that bind to specific amino acid motifs in adsorbed extracellular matrix proteins, such as the RGD (Arg-Gly-Asp) sequence of fibronectin. Integrin activation initiates downstream signaling cascades controlling cytoskeletal organization, focal adhesion formation, and ultimately osteoblastic differentiation. Surface topography at the nano- and microscale directly influences integrin clustering density, cell morphology, and the resultant signaling outcomes, making surface engineering a powerful tool for modulating cell fate at the bone-implant interface (4,6).

On smooth, machined titanium surfaces, initial protein adsorption and cell responses are limited; fibrous tissue rather than bone tends to form at the interface, predisposing to implant loosening. Conversely, moderately rough surfaces, particularly those with an average roughness (Ra) of 1–2 μm, are associated with increased bone-to-implant contact (BIC), enhanced mechanical interlocking, and superior osseointegration both in vitro and in vivo (4,6).

Surface wettability and hydrophilicity

Surface wettability, measured by contact angle, profoundly influences initial biological responses to titanium implants (6,11). Hydrophilic surfaces (contact angle < 90°) promote greater protein adsorption, accelerate fibrin adhesion, support osteoblast migration, and enhance

early-stage soft and hard tissue integration compared with hydrophobic surfaces (6). Studies have demonstrated that hydrophilic surface modifications increase BMP-2 and BMP-7 expression in peri-implant sulcular fluid, facilitate osteoblast proliferation, and activate beneficial innate immune responses, including macrophage polarization toward a pro-healing M2 phenotype. UV irradiation of sandblasting and acid-etching (SLA)-treated titanium surfaces, which converts the surface from hydrophobic to superhydrophilic without altering topography, has been shown to significantly increase BIC and accelerate osseointegration in animal models (4,6).

Techniques for surface modification of titanium implants

Sandblasting and acid-etching

Sandblasting followed by acid-etching, commonly referred to as SLA, is among the most extensively validated and clinically adopted surface modification strategies (4, 12). In the SLA process, large-grit aluminum oxide (Al_2O_3) particles are blasted onto the titanium surface to create macroscale roughness, followed by immersion in a mixture of hydrochloric (HCl) and sulfuric (H_2SO_4) acids to superimpose a micropit texture (4,12). The resultant surface demonstrates a combination of macro- and micro-roughness that promotes osteoblast adhesion, proliferation, and osteogenic gene expression. In vitro studies using human fetal osteoblast cell lines have shown that the grain size used during blasting significantly influences cell growth, with smaller Al_2O_3 grains producing enhanced biomineralization at later time points. In vivo, SLA surfaces consistently exhibit higher removal torque values and BIC compared with machined surfaces, confirming superior biomechanical anchorage in rabbit and sheep animal models. The further development of SLActive surfaces, SLA-treated implants stored in isotonic NaCl solution to preserve their hydrophilicity, has demonstrated reduced inflammatory response and increased osteogenic activity in early healing phases compared with standard SLA (4,12,13).

Anodization and titanium dioxide nanotubes

Electrochemical anodization converts the native TiO_2 oxide layer on titanium into a highly ordered nanotube array (TiO_2 nanotube arrays), whose diameter and length can be precisely tuned by modifying voltage, electrolyte composition, and oxidation time. Nanotubes typically range from 20 to 200 nm in diameter and create a biomimetic nano-topography that closely resembles the collagen fibril architecture of native bone extracellular matrix. This nanotopography amplifies surface area, improves wettability, enhances protein adsorption, and provides a potent stimulus for MSC adhesion and osteogenic differentiation. In vivo studies show that nano-tubular surfaces promote superior peri-implant bone formation and BIC compared with machined controls (14,15).

Micro-arc oxidation and plasma electrolytic oxidation

Micro-arc oxidation (MAO), also known as plasma electrolytic oxidation (PEO), is an advanced electrochemical technique that generates a thick, porous, and firmly adherent oxide ceramic coating directly on the titanium surface (10). Unlike simple anodization, MAO employs high-voltage arc discharges that create instantaneous localized temperatures and pressures, allowing the incorporation of bioactive electrolyte constituents, principally calcium and phosphate ions, into the surface oxide (4,10). The resulting calcium phosphate-containing TiO_2 coating exhibits a hierarchical micro/nano-porous morphology with enhanced wettability, roughness, and biological activity. MAO coatings have been shown to promote osteoblast proliferation, increase BIC, and accelerate bone formation around both dental and orthopedic implants in multiple animal model studies (4,10,16).

In the context of maxillofacial reconstruction, a study on osseointegration of 3D-printed titanium implants demonstrated that microarc oxidation applied to 3D-printed titanium scaffolds induced significant cell proliferation and increased osteogenic gene expression for some markers in human MSCs. MAO can further be combined with hydrothermal treatment, alkali treatment, laser texturing, or ion incorporation (strontium, zinc, silver) to achieve synergistic osteoinductive and antimicrobial effects (10,16,17).

Hydroxyapatite and calcium phosphate coatings

Hydroxyapatite (HA), the principal inorganic component of bone mineral, represents one of the most biologically relevant coating materials for titanium implants; the HA coatings may be applied by plasma spraying, electrochemical deposition, pulsed laser deposition, sol-gel methods, and MAO, each yielding different coating thickness, crystallinity, and adhesive strength (18-20). A systematic review by Neto et al identified favorable osseointegration outcomes for HA-coated surfaces in 12 of 15 included studies, concluding that HA treatment enhances protein absorption, promotes bone cell adhesion, and increases peri-implant mineralization (19). HA-coated implants have been shown to achieve a bone integration rate of 75.9% at three months compared with 45.7% for uncoated titanium controls (18).

Biomolecule functionalization; BMP and growth factor delivery

The immobilization of osteoinductive biomolecules on titanium surfaces represents a sophisticated tissue engineering approach that seeks to transform an osteoconductive scaffold into an osteoinductive one. Bone morphogenetic proteins, particularly BMP-2 and BMP-7, are members of the TGF-β superfamily and serve as potent inducers of osteogenic differentiation in MSCs. A systematic review of BMP-coated titanium

implant surfaces demonstrated that BMP-2 coating consistently accelerates bone formation and enhances osseointegration across animal models, with BMP-2/7 heterodimers showing stronger inductive potential than either homodimer at lower doses. In oral and maxillofacial surgery, BMP-2 applied via collagen sponge delivery to titanium-containing reconstruction sites has been shown to increase bone volume at the peri-implant defect, though high doses are associated with adverse effects including hematoma formation, ectopic bone, and soft tissue edema (21).

The osteoinductive function of BMP-2 is not solely determined by concentration but also by the nature of the titanium surface onto which it is adsorbed or incorporated. Surfaces treated with acid-alkali show the highest BMP-2 adsorption amounts but sustain activity for shorter durations, while anodized oxidized surfaces show lower adsorption but superior long-term retention and osteogenic function, suggesting that gradual release from an incorporated three-dimensional reservoir is superior to rapid burst release from surface-adsorbed depots. Beyond BMP, other growth factor functionalization strategies, including vascular endothelial growth factor for angiogenesis and FGF for soft tissue healing, have been evaluated on titanium surfaces with promising results for accelerated osseointegration in craniofacial models (6,21).

Three-dimensional printing and porous titanium scaffolds

The advent of additive manufacturing has fundamentally altered the landscape of craniofacial reconstruction by enabling the fabrication of patient-specific, anatomically precise titanium implants with controlled porous architectures; selective laser melting and electron beam melting allow creation of Ti-6Al-4V implants with pore sizes, porosity gradients, and trabecular geometries tailored to specific defect sites and based on current evidence, pore diameters of 300–600 μm and porosities of 60–90% are considered optimal to balance bone ingrowth, vascularization, and mechanical integrity (10,17,22,23).

A key study investigated the osseointegration of 3D-printed titanium implants for the reconstruction of maxillofacial segmental bone defects, comparing various mesh structures with and without microarc oxidation surface modification. The results showed that solid non-mesh 3D-printed structures achieved superior osteogenic differentiation in vitro and osseointegration in vivo compared with mesh variants, while surface MAO modification enhanced cell proliferation and partially improved osteogenic gene expression (17). A separate study of a titanium grid scaffold printed in 3D demonstrated successful bone fusion at critical maxillofacial segmental defect sites in an animal model, establishing the feasibility of complex scaffold designs for mandibular reconstruction (22,23). High-porosity 3D-printed titanium meshes have also been shown to generate superior bone regeneration compared with lower-porosity controls when used for alveolar bone augmentation (24). The long-term clinical outcomes of patient-specific titanium implants in maxillofacial surgery are well documented. A cohort study reported successful reconstruction of maxillary, mandibular, and zygomatic defects using patient-specific titanium implants with satisfactory functional and aesthetic results at long-term follow-up (22). A systematic review of 3D-printed patient-specific implants in maxillofacial reconstruction documented a pooled implant success rate of 94.7% (95% CI: 91.4–98.0%), with minimal heterogeneity, confirming excellent clinical outcomes in properly selected patients (25).

Antimicrobial surface modifications

Infection is the most serious complication following titanium implantation, particularly in maxillofacial surgery, due to persistent oral microbiome colonization, where rapid biofilm formation on implant surfaces, driven by pathogens such as *Staphylococcus aureus, Staphylococcus epidermidis, Porphyromonas gingivalis,* and *Prevotella intermedia*, serves as the primary cause of peri-implantitis and exhibits strong resistance to systemic antibiotics because of the protective extracellular polymeric matrix (6,26,27).

Multiple surface modification strategies demonstrate antimicrobial efficacy while preserving or enhancing osseointegration, including silver nanoparticle coatings that release Ag^+ ions to disrupt bacterial membranes and inhibit DNA replication, zinc- and copper-incorporated MAO coatings that combine antimicrobial activity with osteogenic potential, and iodine-coated titanium surfaces that show significant bactericidal effects against *S. aureus* compared with unmodified titanium (6,10,26-28). Critically, a comprehensive review by Damiati et al concluded that surface modifications could be designed to confer both osteoinductive and antimicrobial properties simultaneously, representing a dual-functional approach that addresses two of the most clinically significant sources of implant failure. This is particularly important in the maxillofacial context, where implants are routinely in proximity to the oral cavity (6).

Surface modification in the context of maxillofacial reconstruction

Craniofacial bone biology and specific considerations

Maxillofacial bone exhibits distinct biological characteristics compared with long bones, including intramembranous origin, reduced bone mass and cortical thickness in certain regions, and unique biomechanical loading patterns, while frequently presenting in compromised conditions such as prior radiotherapy, infection, or congenital dysplasia that impair vascularity and regenerative capacity, thereby necessitating surface modifications that enhance angiogenesis, modulate inflammation, and provide antimicrobial activity to

improve osseointegration outcomes (3,6,7,21).

Biomaterials used in craniofacial reconstruction must meet stringent cosmetic and contour demands by accurately replicating the complex three-dimensional geometry of native bone in regions such as the calvarium, orbit, midface, and mandible, underscoring the importance of combining patient-specific additive manufacturing with bioactive surface modification (3-5,22). A study by Mistry et al directly compared bioactive glass-coated and HA-coated titanium implants placed in anterior maxillary and mandibular regions of human patients over one year, demonstrating superior osseointegration for the bioactive glass-coated surface in the maxillary region, `illustrating that the optimal surface strategy may differ across regions within the maxillofacial skeleton (29).

Mandibular and maxillary reconstruction

Mandibular reconstruction represents one of the most demanding challenges in reconstructive surgery (30). Surface-modified titanium implants, particularly those with SLA or hydrophilic SLA-active surfaces, have demonstrated improved osseointegration rates in irradiated bone compared with machined surfaces in both animal models and clinical series, making surface modification a potentially significant adjunct to standard reconstructive approaches (31). 3D printing combined with surface treatment enables the fabrication of maxillary and mandibular reconstruction plates and scaffolds precisely customized to patient anatomy, reducing operative time and improving functional and aesthetic outcomes (17).

Conclusion

Surface modification of titanium implants is not merely an adjunct but a biological necessity in maximizing osseointegration and healing outcomes in maxillofacial and reconstructive surgery. The inherent bioinertia of bare titanium is insufficient to meet the demands of complex craniofacial reconstructive environments, where compromised tissue beds, polymicrobial exposure, and aesthetic imperatives converge. Techniques spanning SLA roughening, anodization-derived nanotubes, MAO, HA and calcium phosphate coatings, growth factor functionalization, and three-dimensional porous scaffold architectures have each demonstrated the capacity to enhance specific aspects of the bone-implant healing cascade. When strategically combined and tailored to the site-specific biology of maxillofacial bone, these modifications collectively transform a passive structural implant into an active participant in tissue regeneration. Continued multidisciplinary collaboration between surgeons, materials scientists, and tissue engineers is essential to close the remaining gap between experimental promise and universal clinical benefit.

Authors' contribution

Conceptualization: Abbas Jasim Mohammed and Qais Mussa.
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Visualization: Abbas Jasim Mohammed.
Supervision: All authors.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Ethical issues

Ethical issues (including plagiarism, data fabrication, and double publication) have been completely observed by the authors.

Conflicts of interest

The authors declare that they have no competing interests.

Declaration of generative artificial intelligence (AI) and AI-assisted technologies in the writing process

During the preparation of this work, the authors utilized AI tools (Perplexity and Grammarly) to refine grammar points and language style in writing. Subsequently, the authors thoroughly reviewed and edited the content as necessary, assuming full responsibility for the publication's content.

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