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Review

Rapid bone healing induced by nanotechnology-modified titanium plates in orthognathic surgery; a narrative review study

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Abstract

Orthognathic surgery requires rigid skeletal fixation to maintain spatial relationships between osteotomized bone segments while new bone forms at the surgical interface. Titanium miniplates and screws have been the gold standard for this purpose for decades; however, conventional titanium hardware carries documented risks of infection, plate loosening, and the need for hardware removal, each of which compromises the speed and quality of bone healing. Advances in nanotechnology have yielded a range of surface modification strategies, including titanium dioxide (TiO2) nanotubes, nanoparticle coatings (silver, zinc, hydroxyapatite), graphene oxide, and functionalized nanostructured surfaces, that profoundly alter the biological interactions between titanium and the surrounding bone. These modifications operate through complementary mechanisms: enhancement of protein adsorption, stimulation of osteoblast adhesion and differentiation, suppression of osteoclastogenesis, promotion of vascularization, and targeted antibacterial activity. Collectively, they accelerate the cascade of bone healing and osseointegration. This narrative review synthesizes current evidence from in vitro, in vivo, and clinical studies on nanotechnology-modified titanium implants and evaluates their potential application to orthognathic surgery fixation plates. The available evidence suggests that nanotechnology-modified titanium surfaces offer a compelling strategy for reducing healing time, minimizing infection-related hardware complications, and improving the biological stability of osteotomy sites. Targeted clinical trials are needed to establish optimal surface modification protocols for the unique biomechanical and biological environment of orthognathic osteotomy fixation.

Keywords: Bone healing, Osseointegration, Orthognathic surgery, Titanium plates, Nanotechnology, Nanotubes, Surface modification, Osteogenesis, Fixation, Craniofacial surgery

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Introduction

Orthognathic surgery encompasses a spectrum of jaw osteotomy procedures, including bilateral sagittal split osteotomy (BSSO) of the mandible, Le Fort I osteotomy of the maxilla, and genioplasty, performed to correct dentofacial deformities and skeletal malocclusions that cannot be addressed by orthodontic treatment alone (1). The biological success of these procedures depends critically on the quality and speed of bone healing at the osteotomy site, which in turn is governed by the mechanical stability of the fixation construct, the local vascular and cellular environment, and the biocompatibility of the fixation material (1,2). Titanium miniplates and monocortical screws have been the standard of care for internal fixation in orthognathic surgery since the 1980s, largely replacing wire fixation because of titanium's favorable combination of mechanical strength, biocompatibility, and corrosion resistance (3).

Despite this established clinical track record, conventional titanium fixation systems are not without limitations. Postoperative complications including surgical site infection, plate loosening, hardware-associated cold sensitivity, and symptomatic hardware requiring plate removal remain significant clinical burdens (4). A systematic review and meta-analysis identified infection and plate exposure as the leading risk factors for symptomatic miniplate removal following orthognathic surgery, with reported removal rates varying depending on the patient population and osteotomy type (4). A 10-year retrospective audit from a United Kingdom center found an overall miniplate removal rate of 2.1%, with female sex and mandibular plate location

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Implication for health policy/practice/research/medical education

Nanotechnology-modified titanium surfaces, via titanium dioxide (TiO2) nanotubes, nanoparticle coatings (silver, zinc, hydroxyapatite), graphene oxide, and functionalized nanostructures, enhance protein adsorption, osteoblast adhesion and differentiation, vascularization, and antibacterial activity while suppressing osteoclastogenesis, thereby accelerating bone healing and osseointegration. Evidence from in vitro, in vivo, and clinical studies indicates these modifications can reduce healing time, lower infection-related hardware complications, and improve biological stability at osteotomy sites when applied to orthognathic fixation plates.

as the only independent predictors of removal (5). These complications, while individually infrequent, collectively reduce patient satisfaction, increase healthcare costs, and in some cases compromise the quality of bone healing at the osteotomy site (4,5).

The emergence of nanotechnology as an engineering discipline has created new possibilities for redesigning the surface of titanium implants at the nanoscale, the length scale at which biological molecules, cells, and mineral crystals naturally operate, to direct and accelerate bone formation (6). Surface structures with features in the 1–100 nm range have been demonstrated to dramatically alter protein adsorption patterns, cell adhesion dynamics, osteoblast gene expression, immune cell polarization, and vascularization cascades compared with conventional machined or acid-etched titanium surfaces (7). These effects, well-documented in the context of endosseous dental implants and orthopedic implants, hold strong theoretical relevance for orthognathic fixation plates, where accelerated bone healing and reduced infection risk would translate directly into improved surgical outcomes. This narrative review examines the evidence base for nanotechnology-modified titanium surfaces, evaluates the mechanisms by which they accelerate bone healing, and discusses their potential application to titanium fixation plates used in orthognathic surgery.

Search strategy

A narrative literature search was conducted within PubMed/MEDLINE, Web of Science, and Scopus databases. Search terms included combinations of "orthognathic surgery," "titanium plates," "nanotechnology," "nanotubes," "nano surface modification," "bone healing," "osseointegration," "osteogenesis," "TiO2 nanotubes," "silver nanoparticles," "zinc nanoparticles," "hydroxyapatite nanoparticles," "graphene oxide," "titanium implant," "fixation," "osteotomy," "jaw surgery," and "craniofacial." Boolean operators (AND, OR) were used to combine terms. The search was limited to English-language, peer-reviewed articles. Articles were screened for relevance to the biological and clinical aspects of nanotechnology-enhanced bone healing in the context of titanium fixation systems. Review articles, randomized controlled trials, cohort studies, case-control studies, animal studies, and in vitro mechanistic studies were included.

Current role of titanium plates in orthognathic surgery

Titanium is the dominant material for craniofacial internal fixation hardware because of its well-established biocompatibility, fatigue resistance, and its capacity to permit direct bone-to-metal contact (osseointegration) rather than forming an encapsulating fibrous tissue capsule (3). Meta-analytic comparisons of titanium and biodegradable plate systems for orthognathic surgery have consistently demonstrated equivalent skeletal stability, while titanium fixation is associated with a lower incidence of screw breakage during placement; the mechanical rigidity of titanium plates in the immediate postoperative period is essential for preventing micromotion at the osteotomy interface, which would disrupt the early vascular in-growth and mesenchymal stem cell recruitment required to initiate bone regeneration (2).

Bone healing at an orthognathic osteotomy site follows the same fundamental sequence as fracture repair — initial hematoma formation, inflammatory cell recruitment, angiogenesis, intramembranous ossification depending on local mechanical strain, and finally bone remodeling (2). Cone-beam computed tomography (CBCT)-based fractal dimension analysis of BSSO osteotomy lines has demonstrated that trabecular bone density at the osteotomy site is markedly reduced in the immediate postoperative period and requires several months to recover to baseline levels, reflecting the biological demand placed on the local cellular environment (1). Digital surgical guides combined with pre-bent titanium plates have been employed to improve the accuracy of osteotomy cuts and plate adaptation, reducing operative time and promoting more precise fragment positioning, both of which support faster bone healing (8).

The limitations of conventional titanium surfaces, including susceptibility to bacterial biofilm formation, absence of direct osteoinductive activity, and limited stimulation of the angiogenic responses required for rapid bone healing, have motivated extensive research into surface modification strategies (6,9). In this context, nanotechnology offers a powerful platform for engineering surfaces that actively promote bone healing while simultaneously resisting infection, thereby addressing the two major drivers of hardware-related complications in orthognathic surgery.

Fundamentals of nanotechnology surface modification

Nanotechnology-based surface modification of titanium implants can be classified broadly into three categories: topographic modifications that create nanostructured surface features without altering chemical composition; chemical modifications that incorporate bioactive ions or molecules at the nanoscale; and composite modifications that combine topographic and chemical strategies to achieve multifunctional surfaces (6,7).

Topographic modifications include anodization to produce TiO2 nanotube arrays, acid-etching to create nano-roughness, sandblasting at the nano-micro scale, laser surface texturing, and micro-arc oxidation (7,10). These methods alter the surface energy, wettability, and topographic curvature at the nanoscale, which in turn determines the conformation of adsorbed proteins, the morphology of adherent osteoblasts, and the activation state of macrophages and immune cells in the peri-implant environment (6). Chemical modification strategies include the incorporation of nanoparticles of silver, zinc oxide, hydroxyapatite, strontium, or graphene oxide into or onto the titanium surface through techniques such as ion implantation, plasma immersion, electrodeposition, and dip-coating (9,11,12). These nanoparticle-based approaches confer specific biological functions, antibacterial activity for silver and zinc, osteoconductivity for hydroxyapatite, and osteostimulatory activity for strontium and graphene that are not available on standard titanium surfaces.

Crucially, the biological effects of nanotopographic features are size- and geometry-dependent. TiO2 nanotube diameters between 15 and 100 nm differentially regulate osteoblast adhesion, spreading, and differentiation, with smaller diameters favoring early adhesion and larger diameters promoting greater differentiation (13). These diameter-dependent effects are mediated through integrin clustering and focal adhesion kinase (FAK) activation at the cell-surface interface, which propagate downstream osteogenic signaling through the Runx2 and bone morphogenetic protein (BMP)-2/SMAD pathways (14). Understanding the optimal nanotube dimensions for a given biological target is therefore a prerequisite for rational surface design in orthognathic fixation applications.

TiO_2 nanotube arrays and osseointegration

The fabrication of TiO2 nanotube arrays through electrochemical anodization of titanium surfaces is among the most extensively studied surface modification strategies in the implant literature; in an in vivo rat model, TiO2 nanotube-coated titanium implants demonstrated significantly superior biomechanical pull-out resistance and enhanced bone-implant contact compared with machined titanium surfaces, confirming the functional relevance of nanotube topography for accelerating osseointegration (15). This improvement in mechanical integration reflects the enhanced osteoblast spreading, cytoskeletal reorganization, and early mineralization nodule formation that nanotube surfaces promote relative to smooth titanium controls (10, 15).

Modification of TiO2 nanotubes to achieve superhydrophilic surfaces through hydrogen reduction treatment has been shown to further accelerate early osseointegration events. Hydrogenated TiO2 nanotube surfaces induced more rapid osteoblast adhesion, promoted alkaline phosphatase (ALP) expression at earlier time points, and stimulated greater mineral deposition in vitro compared with unmodified nanotube surfaces, consistent with the well-established role of surface wettability in governing initial protein adsorption and cell attachment (16). In the orthognathic surgery context, faster early osseointegration at fixation plate surfaces would reduce the window of mechanical vulnerability during which interfragmentary micromotion could compromise bone union.

Electric fields applied through TiO2 nanotube surfaces have been demonstrated to further amplify osteogenic differentiation of mesenchymal stem cells, inducing upregulation of osteocalcin, osteopontin, and collagen type I expression through voltage-sensitive calcium channel activation (13). While direct clinical application of electrostimulation via nanotube-coated plates remains a future frontier, these findings establish the principle that nanotube surfaces can serve as conductive scaffolds capable of integrating bioelectrical signals with mechanical fixation functions.

Nanoporous titanium surfaces, a related topographic modification, have been shown to promote osteogenesis through a distinct and clinically relevant mechanism: suppression of osteoclastogenesis. He et al demonstrated that nanoporous titanium implant surfaces inhibited osteoclast differentiation through the integrin beta1/FAKpY397/MAPK signaling pathway, thereby shifting the local bone remodeling balance toward net bone deposition rather than bone resorption (14). This immunomodulatory osteogenic effect is of direct clinical relevance at orthognathic osteotomy sites, where postoperative bone resorption at fixation screw holes and plate contact areas is a recognized cause of delayed union and plate failure.

Nanoparticle-based coatings for osteogenesis and infection prevention

Silver nanoparticles

Peri-implant infection is the most important cause of hardware failure and plate removal following orthognathic surgery (4,5). Silver nanoparticles (AgNPs) incorporated into or onto titanium surfaces provide a broad-spectrum antibacterial effect through multiple mechanisms: direct membrane disruption by released silver ions, reactive oxygen species generation, and interference with bacterial enzyme function (9). A comprehensive review of AgNP-titanium surface combinations confirmed that silver nanoparticles embedded in surface coatings or nanotube arrays exhibit strong antibacterial activity against both gram-positive and gram-negative pathogens commonly encountered in oral and maxillofacial surgical sites, including Staphylococcus aureus and Streptococcus species (9). A critical design parameter for AgNP-functionalized implants is the balance between silver ion release kinetics and cytotoxicity. Studies have consistently

demonstrated that low, sustained silver ion release rates promote osteoblast proliferation and differentiation while preserving antibacterial activity, whereas high concentrations of silver are cytotoxic (9,11). A novel silver-incorporated sparsely distributed TiO2 nanotube surface fabricated using plasma immersion ion implantation demonstrated robust antibacterial properties against Staphylococcus aureus alongside significant enhancement of osteogenic differentiation and mitigation of peri-implant inflammatory encapsulation in a rat model, without overt cytotoxicity (11). These findings establish a proof-of-concept for dual-function antibacterial and osteogenic titanium surfaces directly applicable to orthognathic fixation hardware.

Zinc-incorporated TiO_2 nanotube surfaces

Zinc incorporation into TiO2 nanotube arrays represents an alternative dual-function strategy that leverages zinc's role as both an antibacterial agent and a trace element essential for osteoblast metabolism. Zn-incorporated TiO2 nanotube surfaces were shown to promote osteogenesis in vitro and in vivo not only through direct stimulation of osteoblast differentiation but also through immunomodulatory polarization of macrophages toward an M2 anti-inflammatory phenotype, which is associated with a favorable peri-implant healing environment (17). This immunomodulatory osteogenic mechanism suggests that zinc incorporation provides an additional regulatory axis for accelerating bone healing at fixation sites in inflammatory-prone environments such as the oral and perioral tissues.

Graphene oxide coatings

Reduced graphene oxide (rGO) applied as a coating to titanium implant surfaces has emerged as a promising nanotechnology strategy for enhancing osseointegration while simultaneously suppressing bacterial colonization. rGO-coated titanium implants demonstrated significantly increased osteoblast proliferation, ALP activity, and mineralized nodule formation in vitro, alongside enhanced new bone formation in vivo, compared with uncoated titanium controls (12).

The mechanisms underlying the osteogenic activity of rGO coatings include mechanical stimulation through the high elastic modulus of graphene layers, which promotes mechanotransduction in adherent osteoblasts, and the intrinsic antibacterial activity of graphene sheets through physical disruption of bacterial membranes by their sharp nanoedges (12). For orthognathic fixation plates that must simultaneously maintain structural integrity and promote bone union in a bacterial-rich oral environment, rGO coatings represent a compelling candidate technology.

Nanostructured hydroxyapatite

Hydroxyapatite (HA), the principal mineral phase of bone, is inherently osteoconductive and biocompatible (6). At the nanoscale, HA coatings on titanium surfaces more closely replicate the crystallographic dimensions of natural bone apatite crystals (20–80 nm in length), which significantly enhances their interaction with osteoblast surface receptors compared with micron-scale HA coatings; nanostructured HA coatings on titanium implants have been demonstrated to accelerate early osteoblast attachment, enhance ALP activity, and promote collagen type I synthesis, collectively accelerating the transition from fibrous repair to lamellar bone deposition at the implant surface (6). Hybrid coatings incorporating both silver nanoparticles and nano-HA have been developed to provide combined antibacterial and osteogenic functionality, addressing both principal causes of fixation hardware complications simultaneously (9).

Mechanisms of accelerated bone healing by nano-modified titanium surfaces

The acceleration of bone healing by nanotechnology-modified titanium surfaces operates through a cascade of sequential and overlapping biological events. The initial event, protein adsorption from blood and interstitial fluid, is fundamentally governed by surface energy, wettability, and nanoscale topographic curvature (6). Nanotextured titanium surfaces adsorb fibronectin, vitronectin, and BMPs in conformations that expose their integrin-binding domains more effectively than smooth titanium surfaces, thereby promoting stronger and more specific cell attachment (7,10).

This enhanced early protein adsorption translates into more robust osteoblast adhesion, involving more numerous and larger focal adhesion complexes, and more extensive cytoskeletal spreading, which together provide the mechanical substrate for the downstream activation of osteogenic transcription factors, including Runx2 and osterix (10,14). Nanosurface features also influence the differentiation trajectory of mesenchymal stem cells (MSCs), with nanorough surfaces consistently shown to favor osteogenic over adipogenic or chondrogenic differentiation in vitro (7). In addition to direct cellular stimulation, nanotopographic and nanocomposite surfaces modulate macrophage polarization toward the M2 anti-inflammatory phenotype, which releases pro-osteogenic cytokines including IL-10, TGF-beta, and VEGF, promoting angiogenesis and the creation of a permissive healing microenvironment (14,17).

Osteoclast suppression represents an additional mechanism by which nanosurfaces accelerate net bone formation. Studies on nanoporous titanium surfaces have demonstrated that the altered integrin signaling at the cell-nanomaterial interface inhibits receptor activator of nuclear factor-kappa B ligand (RANKL)-induced osteoclastogenesis, shifting the RANK/OPG ratio toward net bone formation at the fixation plate surface (14). This is of particular clinical relevance in orthognathic surgery, where systemic inflammatory conditions, hormonal

factors, and mechanical loading at the osteotomy fixation site may otherwise tilt the remodeling balance toward bone loss and delayed union.

Surface modification effects on titanium biocompatibility and cell behavior

The behavior of bone-forming cells on titanium is intimately determined by the physicochemical properties of the surface (7). In vitro comparisons of different titanium surface treatments, including sandblasting, acid-etching, nanostructuring, and combined micro-nano texturing, have demonstrated that nanotextured surfaces consistently outperform smoother titanium surfaces in promoting osteoblast adhesion, proliferation, and mineralization (10).

Stoilov et al demonstrated that different sandblasting and acid-etching protocols produced measurable differences in osteoblast cell behavior on Ti6Al4V surfaces, establishing the sensitivity of bone cell responses to even subtle surface modifications at the nano-micro level (10). Micro/nano hierarchical titanium surfaces treated with NH4OH/H2O2 were further shown to significantly enhance human mesenchymal stem cell adhesion, proliferation, and osteogenic differentiation through increased surface hydroxyl group density and nano-roughness (18).

The effects of surface modification on cellular function extend beyond osteoblasts to include endothelial cells, fibroblasts, and immune cells, all of which play important roles in wound healing and bone regeneration at orthognathic osteotomy sites (6). Titanium surfaces with selective laser melting-generated micro-/nano-tube or micro-/nano-net topographies demonstrated superior osseointegration in *in vivo* studies, with different architectures favoring distinct phases of the bone healing cascade, net architectures promoting early cell adhesion, and tube architectures favoring later mineralization (19). Titanium surfaces with combined micro/nano structures have also been shown to enhance osteoblast resistance to oxidative stress, which is of clinical significance in the pro-oxidant microenvironment generated by tissue disruption during orthognathic surgical procedures (20).

Clinical implications and future directions for orthognathic surgery

The translation of nanotechnology-modified titanium surfaces from the well-studied dental and orthopedic implant fields to orthognathic fixation plates presents both compelling opportunities and important challenges. The fundamental biological mechanisms by which nanosurfaces accelerate osseointegration and resist infection are not specific to any particular implant geometry or anatomical location; they are properties of the titanium-bone interface that would be expected to operate at orthognathic osteotomy fixation sites as effectively as at endosseous implant surfaces (6,7,11). The clinical implications of faster and more robust bone healing at orthognathic osteotomy sites include shortened healing periods before completion of postsurgical orthodontic treatment, reduced risk of relapse due to more rapid bone consolidation, and potentially lower rates of hardware-associated infection requiring plate removal (4,8).

At present, the orthognathic surgery-specific evidence base for nanotechnology-modified fixation hardware remains limited to in vitro and animal model data, with no published randomized controlled trials evaluating nanotechnology-enhanced titanium plates in human patients undergoing orthognathic surgery. The broader evidence base from dental implantology and orthopedics, however, provides substantial mechanistic and preclinical justification for such studies. Nanofeatured titanium surfaces have been shown to improve early osseointegration outcomes in clinical implant studies, though their long-term advantage over modern microrough surfaces remains less certain (7). The unique demands of orthognathic fixation, including the need for precision plate adaptation, maintenance of skeletal stability during jaw movement, and operation in the bacterial-rich oral environment, may require specific optimization of nanosurface parameters beyond those established for endosseous dental implants.

Future research priorities include (1) head-to-head in vivo comparisons of nanotechnology-modified versus standard titanium fixation plates in animal models of jaw osteotomy; (2) characterization of the optimal nanotube diameter, nanoparticle concentration, and coating thickness for orthognathic applications; (3) evaluation of the effect of nano-modified plates on the biomechanics of osteotomy segment fixation and micromotion; and (4) adequately powered, prospective randomized clinical trials with healing time, infection rate, and patient-reported outcomes as primary endpoints. Drug delivery approaches, such as BMP-2- or vitamin D3-loaded nanotube arrays, represent a particularly promising avenue, given emerging preclinical evidence that they can accelerate early osseointegration in vivo (21,22).

Conclusion

Nanotechnology-modified titanium surfaces represent a promising evolution in the engineering of fixation hardware for orthognathic surgery. Through mechanisms including enhanced protein adsorption, accelerated osteoblast adhesion and differentiation, immunomodulatory polarization toward a pro-osteogenic environment, osteoclast suppression, and targeted antibacterial activity, nano-modified titanium surfaces address the principal biological limitations of conventional orthognathic fixation plates. TiO2 nanotube arrays, silver and zinc nanoparticle coatings, graphene oxide layers, and nano-hydroxyapatite coatings each offer distinct and complementary biological advantages that, alone or in combination, could substantially accelerate bone healing and reduce infection-related hardware complications at osteotomy fixation

sites. While the evidence base for direct application in orthognathic surgery remains preclinical, the translational rationale is well-grounded in established implant biology. Collaboration between materials scientists, oral and maxillofacial surgeons, and clinical trial investigators is needed to develop and validate nanotechnology-enhanced orthognathic fixation plates that deliver faster, safer, and more biologically optimized bone healing for patients undergoing corrective jaw surgery.

Authors' contributions

Conceptualization: Abbas Jasim Mohammed and Shaikhaliev Astemir Ikramovich
Data curation: Abbas Jasim Mohammed and Shaikhaliev Astemir Ikramovich.
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Supervision: All authors
Validation: Qais Mussa.
Visualization: Qais Mussa and Abbas Jasim Mohammed.
Writing–original draft: All authors.
Writing–review and editing: All authors.

Ethical issues

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

Declaration of generative AI and AI-assisted technologies in the writing process

During the preparation of this manuscript, the authors used generative artificial intelligence (Perplexity) and AI-assisted writing tools (Grammarly) to assist with drafting, language editing, and refinement of grammar and style. All content generated by these tools was subsequently critically reviewed, revised, and validated by the authors, who take full responsibility for the accuracy, integrity, and originality of the work.

Conflicts of interest

The authors declare that they have no competing interests.

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