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Host-material interactions guided bioink formulation, structural design, and bioactive functionalization of 3D-printed and bioprinted biomaterials for oral tissue reconstruction

Running title: Host-guided design in oral 3D printing and bioprinting

Minglang Zou^{1†}, Yating Li^{1†}, Yusi Lu², Da Huang^{1*}, and Wen Zhou^{2,3*}

¹College of Biological Science and Engineering, Fuzhou University, Fuzhou, Fujian 350108, China

²Clinical Research Center for Oral Tissue Deficiency Diseases of Fujian Province & Fujian Key Laboratory of Oral Diseases & Fujian Provincial Engineering Research Center of Oral Biomaterial, School and Hospital of Stomatology, Fujian Medical University, Fuzhou, Fujian 350002, China

³Stomatological Key Laboratory of Fujian College and University & Institute of oral homeostasis & Research Center of Oral Tissue Engineering, Fujian Medical University, School and Hospital of Stomatology, Fujian Medical University, Fuzhou, Fujian 350002, China

[†]*These authors contributed equally to this work.*

***Corresponding author:**

Da Huang (huangda@fzu.edu.cn)

Wen Zhou (wenzhoudentist@fjmu.edu.cn)

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Abstract

Oral and maxillofacial tissue defects impair both anatomical integrity and essential oral functions. Three-dimensional (3D) bioprinting offers a promising strategy for fabricating patient-specific constructs with controlled architecture and biological composition. However, many current studies still focus primarily on fabrication performance, whereas the host responses that determine long-term regeneration remain insufficiently integrated into material design. In this review, we discuss 3D-printed and bioprinted biomaterials for oral tissue reconstruction from a host-material interaction-guided perspective. We first summarize the regenerative requirements of oral soft tissues, hard tissues, and soft-hard interfaces, together with the material systems and printing technologies for oral tissue reconstruction. We then examine how printed constructs interact with the oral microenvironment through physical, chemical, and biological mechanisms. These interactions shape regeneration by directing early host recognition, subsequent immune and vascular remodelling, and eventual microbial balance, matrix maturation, and tissue integration. Based on these mechanisms, we further discuss three major design strategies: bioink formulation for constructing a regenerative material microenvironment, structural design for guiding spatial organization and mechanical adaptation, and bioactive functionalization for directing host responses toward tissue-specific repair. Representative applications in soft tissue repair, hard tissue regeneration, and periodontal interface reconstruction are highlighted. Finally, current barriers and future opportunities for clinical translation are discussed. This review provides a an oral-specific host-material interaction-guided organizing perspective for developing host-instructive 3D-printed and bioprinted constructs for functional oral tissue regeneration.

Keywords: 3D-printing; Bioprinting; Oral tissue reconstruction; Host-material interactions; Immunomodulation; Pore architecture; Vascularization

1. Introduction

Oral and maxillofacial tissue defects arise from trauma, tumor resection, infection, congenital malformations, periodontal disease, and age-related degeneration^{1,2}. These defects may involve soft tissues, such as the gingiva and oral mucosa; hard tissues, including alveolar bone, dentin, cementum, and maxillofacial bone; or composite structures composed of multiple tissue components³. Unlike defects at many other anatomical sites, oral tissue defects are not merely esthetic problems⁴, but directly impair mastication, swallowing, speech, sensory perception, and barrier defense against microbial invasion. Moreover, oral tissues are continuously exposed to a complex local environment, making regeneration highly dependent on interactions between implanted materials and the host microenvironment⁵⁻⁷. Therefore, successful reconstruction requires not only restoration of anatomical contour, but also re-establishment of mechanical support, epithelial protection, vascular supply, immune homeostasis, antimicrobial defense, and functional integration.

Conventional reconstructive strategies, including autologous tissue grafting, allogeneic transplantation, xenogeneic grafts, and synthetic biomaterial implantation, have improved the treatment of oral and maxillofacial defects^{8,9}. Autologous grafts offer favorable biocompatibility and regenerative potential, but are limited by donor-site morbidity, restricted availability, prolonged surgery, and unpredictable remodeling¹⁰. Allogeneic and xenogeneic grafts alleviate tissue shortages but may introduce immunogenicity, disease-transmission risk, variable degradation, and inconsistent outcomes¹¹. Synthetic substitutes provide improved availability, structural stability, and processing flexibility; nevertheless, many still fail to match individualized defect geometry, reproduce native hierarchical architecture, or actively regulate host responses¹². Poor adaptation may consequently impair vascular and cellular infiltration, promote chronic inflammation and microbial colonization, and ultimately lead to fibrous encapsulation and compromised integration. These limitations highlight the need for biomaterials and biofabrication methods that combine anatomical accuracy, biological functionality, and host-adaptive regenerative capacity.

In this context, three-dimensional (3D) bioprinting has emerged as a promising biofabrication strategy for oral tissue engineering and regenerative dentistry. By integrating computer-aided design, patient-specific imaging data, printable biomaterials, living cells, and bioactive molecules, 3D bioprinting enables the fabrication of customized constructs with controllable geometry, internal architecture, and spatial biological composition¹³⁻¹⁵. These features are particularly relevant to oral reconstruction, where engineered constructs must fulfill two distinct yet complementary roles. First, they must ensure local survival by adapting to irregular defects, withstanding cyclic loading, and resisting microbial challenge^{16,17}. Second, they must promote tissue regeneration, specifically supporting the coordinated repair

of epithelial, connective, vascular¹⁸, and mineralized compartments¹⁹. Recent advances in natural hydrogel bioinks, synthetic polymer-based bioinks, ceramic-reinforced composites²⁰, bioactive ion-containing systems, and multimaterial or hybrid printing platforms have further expanded the structural and functional possibilities of oral tissue bioprinting. However, current studies remain largely fabrication-centered, with emphasis placed on printability, shape fidelity, mechanical reinforcement, and short-term cytocompatibility. Although these parameters are indispensable, they do not fully capture the decisive events that unfold after implantation²¹. These events follow a temporal cascade: (1) immediate host responses, including protein adsorption and inflammatory activation²²; (2) mid-term tissue remodeling, involving vascular ingrowth, extracellular matrix (ECM) reorganization, and microbial colonization²³; and (3) long-term outcomes, encompassing degradation-mediated signaling and tissue integration. The gap between precise construct fabrication and effective host-guided regeneration remains a major barrier to the clinical translation of 3D-printed and bioprinted oral constructs.

The oral cavity represents a uniquely dynamic and challenging regenerative environment. Once implanted, 3D-printed and bioprinted constructs are immediately challenged by a multifaceted oral milieu: (1) biological factors²⁴, including saliva-derived proteins, immune cells, oral microbiota, and their metabolites; (2) chemical factors²⁵, particularly pH fluctuations and enzymatic degradation; and (3) physical factors²⁶, namely mechanical forces from mastication, swallowing, and speech. These factors collectively shape the host response and determine whether the construct supports regeneration or instead induces persistent inflammation, infection, fibrotic encapsulation, premature degradation, or mechanical failure. Therefore, the success of 3D-printed and bioprinted oral constructs depends not only on how accurately they are fabricated, but also on how effectively they interact with and regulate the local host microenvironment. A host-material interaction-guided design paradigm is thus essential for advancing oral tissue bioprinting from structural replacement toward functional regeneration.

From this perspective, host-material interactions can be understood through physical, chemical, and biological dimensions that act in concert throughout immediate host responses, mid-term tissue remodeling, and long-term outcomes^{27–29}. Physical interactions arise from pore architecture, interconnectivity, surface topography, stiffness, viscoelasticity, and gradient organization, thereby regulating cell adhesion, migration, infiltration, mechanotransduction, and load transfer³⁰. Chemical interactions originate from material composition and interfacial properties, including functional groups, charge, hydrophilicity, ion release^{31,32}, degradation products, and mineral components, and influence protein adsorption, mineralization, antimicrobial activity, and microenvironmental homeostasis. Biological interactions involve active

communication mediated by cell-derived signals, immunomodulatory factors, angiogenic cues, antimicrobial components, and extracellular matrix-mimetic motifs, coordinating inflammation resolution, vascular network formation, matrix deposition, and tissue maturation³³. Together, these interactions provide a basis for designing bioinks, scaffold architectures, and delivery systems that actively guide host responses³⁴.

Previous reviews have established an important foundation for 3D bioprinting in regenerative dentistry and craniofacial tissue engineering^{35–37}. Early studies mainly summarized printing modalities, printable materials, and craniofacial fabrication strategies, whereas subsequent reviews addressed bioink formulations³⁸, printing technologies^{39,40}, and applications in pulp-dentin, periodontal, gingival, bone, cartilage, and other oral or craniofacial tissues⁴¹. More recent reviews have considered patient-specific reconstruction, clinical translation, vascularization, and regulatory challenges⁴². Collectively, these reviews provide valuable technology-, material-, application-, host-response-, and translation-oriented perspectives. However, comparatively fewer studies have organized these interactions specifically as design considerations linking the properties of 3D-printed and bioprinted constructs with tissue-specific host responses in oral reconstruction. Although immune modulation has emerged as a design variable in the broader bioprinting literature, an oral-specific framework integrating physical, chemical, and biological host-material interactions remains insufficiently developed. The relationships among architecture and mechanics, interfacial chemistry and degradation, and immune, vascular, microbial, and tissue-specific responses have not been systematically translated into unified design principles for oral reconstruction.

Accordingly, this review aims to determine how interactions between 3D-printed and bioprinted biomaterials and the oral host microenvironment can be translated into rational design strategies for oral tissue reconstruction. Specifically, it addresses three central questions: (1) How 3D-printed and bioprinted biomaterials interact with the oral host at physical, chemical, and biological? (2) How do these interactions regulate biological process and tissue-material integration? (3) How can this mechanistic understanding guide the design of 3D-printed and bioprinted biomaterials for tissue-specific oral regeneration?

As shown in **Figure 1**, we first establish the biological and technological foundation for this analysis by outlining the structural characteristics and regenerative requirements of oral soft tissues, hard tissues, and soft-hard tissue interfaces, together with representative material systems and printing technologies. We then examined how printed constructs interact with the oral host microenvironment through physical, chemical, and biological mechanisms, and how these interconnected interactions shape early host recognition, immune regulation, vascularization, microbial balance, matrix remodeling, and long-term tissue integration. On this mechanistic basis, the host-

material interactions guided three major design dimensions: bioink formulation, structural design, and bioactive functionalization. Representative applications are subsequently evaluated to illustrate how these interaction-guided principles are implemented in soft-tissue repair, hard-tissue regeneration, and periodontal interface reconstruction. Finally, current technical, biological, and translational limitations are critically discussed. Through this structure, the review provides an insight that links host-material interaction mechanisms to tissue-specific design decisions, rather than proposing an entirely new theory of host-biomaterial interactions.

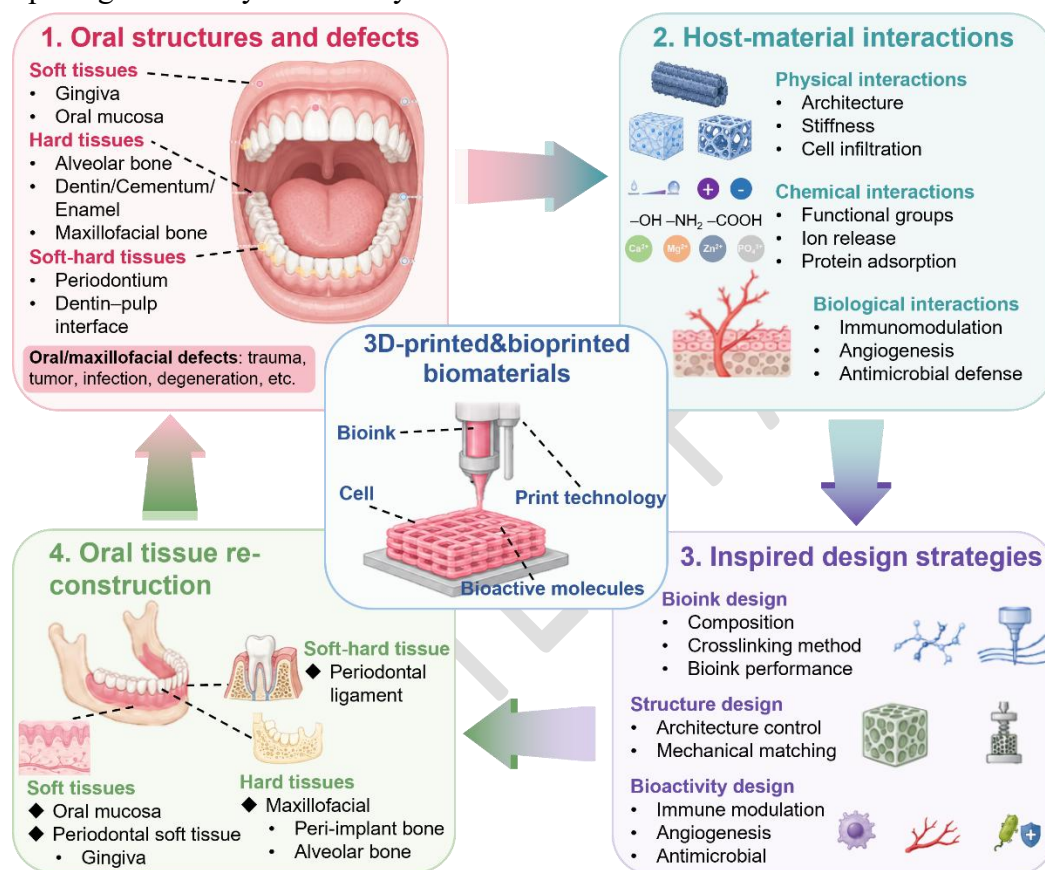


Figure 1. Schematic illustration of host-material interaction-guided design of 3D-printed and bioprinted biomaterials for oral tissue reconstruction.

1.1. Review Methodology

To address these questions, this narrative review was informed by a structured search of PubMed/MEDLINE, Web of Science Core Collection and Scopus for English-language publications available from 2015 to 2026. Search terms combined “3D printing,” “bioprinting,” “bioink,” and “additive manufacturing” with “oral,” “dental,” “periodontal,” “maxillofacial,” “host response,” “immune,” “vascularization,” and “microbiome.” Original studies and relevant reviews addressing printed biomaterials, host-material interactions, or oral tissue reconstruction were considered, whereas

studies unrelated to regenerative applications or lacking relevant biological outcomes were excluded. Representative studies were selected according to mechanistic relevance, oral specificity, and *in vivo* evidence.

2. Foundations of 3D Bioprinting for Oral Tissue Reconstruction

Oral tissue reconstruction poses distinctive challenges owing to the anatomical complexity, structural heterogeneity, and functional diversity of the oral and maxillofacial system^{43,44}. Defects may vary from superficial mucosal lesions to periodontal defects and large load-bearing maxillofacial bone defects^{45–47}, each imposing specific demands on material composition, mechanical competence, biological functionality, and fabrication accuracy. A comprehensive understanding of tissue-specific regenerative requirements, printable material systems, and appropriate bioprinting technologies is therefore fundamental to the rational design of 3D-printed and bioprinted constructs. This section establishes the conceptual basis for oral tissue bioprinting by summarizing the structural and functional characteristics of oral tissues, representative material platforms, and major printing strategies.

2.1. Structural Characteristics and Specific Requirements for Reconstruction in Oral Tissues

Oral and maxillofacial tissues are organized as mechanically coupled units rather than as isolated soft or hard tissue compartments^{48,49}. As illustrated in **Figure 2A**, the pulp-dentin complex, periodontium, and temporomandibular joint are dominated by mineralized structures but depend on compliant interfacial tissues to transmit and dissipate functional loads⁵⁰. Compression and fluid shear act across the pulp-dentin complex, whereas the aligned fibers of the periodontal ligament buffer tensile and torsional forces between cementum and alveolar bone. Within the temporomandibular joint, the fibrocartilaginous disc distributes compression and shear across the condylar cartilage and bone. These region-specific mechanical environments indicate that successful reconstruction must restore not only tissue stiffness and strength, but also hierarchical interfaces and physiologically appropriate load transfer.

The regenerative requirements nevertheless differ among individual hard tissues. Alveolar and maxillofacial bone are vascularized collagen-mineral composites that continuously remodel in response to masticatory loading and local biochemical signals⁵¹. Their reconstruction should therefore provide early mechanical support while permitting vascular invasion, bone remodeling, and stable integration with the host skeleton. Dentin and cementum exhibit more specialized microarchitectures and substantially lower remodeling capacities⁵². Strategies targeting these tissues should prioritize the reproduction of their characteristic structures and the re-establishment of functional connections with the dental pulp or periodontal ligament⁵³. In particular,

periodontal repair requires restoration of a compliant ligament with directionally organized collagen fibers that insert into both cementum and alveolar bone⁵⁴.

Soft oral tissues heal within an environment that differs markedly among anatomical sites. Tooth surfaces, keratinized gingiva, non-keratinized mucosa, the tongue, and buccal mucosa provide distinct substrates for microbial adhesion and biofilm development⁵⁵. Therefore, materials used for soft tissue reconstruction must function within a wet and microbe-rich environment while preserving epithelial renewal and a balanced host-microbial interface. Following injury, oral soft tissue repair proceeds through a coordinated sequence of overlapping biological stages (**Figure 2B**)⁵⁶. Hemostasis begins within minutes, when platelet aggregation and fibrin formation seal the defect and establish a provisional matrix. The subsequent inflammatory phase removes damaged tissue and microorganisms while recruiting macrophages and other reparative cells. As inflammation resolves, keratinocytes and fibroblasts repopulate the wound, and newly formed vessels restore local perfusion. During the final stage, re-epithelialization is completed and the provisional matrix is replaced by a more organized collagen network. Biomaterials designed for oral soft tissue repair should therefore support this temporal progression rather than provide a single static function. Early antibacterial and immunoregulatory activity should gradually give way to vascularization, epithelial closure, and controlled ECM remodeling.

Clinically, oral and maxillofacial defects rarely involve a single homogeneous tissue compartment, which often affect combinations of hard tissues, connective tissues, epithelial structures, and vascular networks. Successful reconstruction therefore depends on coordinated regeneration across multiple tissue compartments and interfaces^{57,58}. In this context, 3D bioprinting offers unique opportunities to spatially organize biomaterials, cells, and bioactive cues, enabling the fabrication of multilayered, multiphasic, and gradient constructs that better recapitulate the structural complexity and functional requirements of native oral tissues.

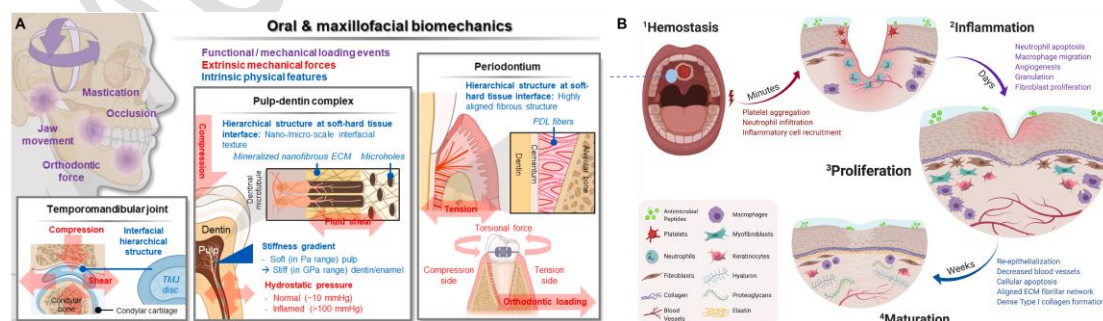


Figure 2. Structural and regenerative characteristics of oral tissues. (A) Tissue-specific biomechanical environments of the pulp-dentin complex, periodontium, and temporomandibular joint⁵⁰. (B) Sequential phases of oral mucosal wound healing⁵⁶.

2.2. Material Systems for Oral Tissue Bioprinting

The development of suitable material systems is central to oral tissue bioprinting. An ideal material platform should first enable reliable printing while preserving cell viability during fabrication⁵⁹. After implantation, it should provide sufficient structural support, degrade in coordination with new tissue formation, and actively deliver bioactive signals that guide regeneration. As shown in **Table 1**, current material strategies therefore combine several classes of components that serve distinct but complementary functions^{38,60}. In this review, bioinks and structural inks are distinguished according to their primary role during fabrication. Bioinks refer to printable biomaterial formulations designed to provide a biologically permissive microenvironment and, in conventional cell-laden bioprinting, incorporate living cells during deposition⁶¹. In contrast, structural inks are generally cell-free printable materials used primarily to provide mechanical reinforcement, dimensional stability, or long-term structural support⁶². Natural hydrogels are widely used as bioinks because they partially mimic the ECM and provide cell-interactive microenvironments. Collagen and gelatin provide abundant cell-interactive motifs, making them favorable for cell attachment and matrix deposition, but their weak networks generally cannot maintain load-bearing structures^{63,64}. Gelatin methacryloyl (GelMA) partially overcomes this limitation by introducing photocrosslinkable groups into gelatin⁶⁵. It therefore retains many of gelatin's biological features while allowing stiffness and post-printing stability to be adjusted through light-induced crosslinking. Alginate approaches the problem from the opposite direction: its rapid and mild ionic gelation provides excellent printability and shape preservation, but the polymer itself offers few binding sites for mammalian cells. It is consequently combined with collagen, gelatin, GelMA, or adhesive peptides to restore biological activity⁶⁶⁻⁶⁸. Hyaluronic acid and fibrin are especially useful when cell migration, tissue remodeling, or vascular ingrowth is required, although both usually need chemical modification or reinforcement to prevent rapid deformation or degradation⁶⁹. Thus, natural hydrogel bioinks are selected not simply according to their source, but according to the balance they provide between cell support and structural persistence.

Table 1. Representative material systems for 3D bioprinting and 3D-printed oral tissue reconstruction.

Category	Material	Key Characteristics	References
Bioink	Collagen	Excellent biocompatibility; supports cell adhesion, spreading, and ECM remodeling; limited mechanical strength and shape fidelity	52,70–73
	Gelatin	Contains cell-interactive motifs; improves cell attachment and matrix remodeling; usually requires crosslinking or blending to enhance stability	42,74–77
	Gelatin methacryloyl (GelMA)	Photocrosslinkable gelatin derivative; retains cell-binding motifs; tunable stiffness, degradation, and print fidelity; widely used in cell-laden bioprinting	78–81
	Alginate	Good printability; mild ionic gelation; protects encapsulated cells; lacks intrinsic mammalian cell-adhesion motifs and often requires blending with GelMA, gelatin, collagen, or RGD modification	82–86
	Hyaluronic acid	ECM-like component; promotes hydration, cell migration, and tissue repair; weak mechanical stability unless chemically modified or combined with other polymers	26,87–91
	Fibrin	Highly bioactive; supports cell infiltration and angiogenesis; rapid degradation and poor long-term structural stability	15,42,70,92,93
Structural synthetic polymers	Polyethylene glycol-based hydrogels	Chemically defined and tunable; suitable for photo-crosslinking; bioinert without functionalization; often modified with peptides or combined with natural polymers	94–97

Category	Material	Key Characteristics	References
Inorganic bioactive additives	Polycaprolactone (PCL)	Good mechanical stability and slow degradation; widely used in extrusion or melt-based 3D printing; generally serves as a structural scaffold rather than a cell-laden bioink	98–102
	Poly(lactic-co-glycolic acid) (PLGA)	Biodegradable and clinically relevant; tunable degradation; useful for structural or delivery functions; acidic degradation products should be considered	103–106
	Polylactic acid (PLA)	Printable and biodegradable; provides structural support; limited intrinsic bioactivity and often requires surface modification or composite design	107–109
	Hydroxyapatite (HA/HAp)	Major mineral component of bone and dental hard tissues; improves osteoconductivity, mineral deposition, and mechanical reinforcement	110–113
	β -tricalcium phosphate (β -TCP)	More resorbable than hydroxyapatite; supports dynamic balance between scaffold degradation and new bone formation; enhances osteogenic potential	114–116
	Bioactive glass	Releases calcium, phosphate, and silicon species; promotes osteogenesis and angiogenesis; some formulations show antibacterial activity	81,100,117,118
	Silica-, zirconia-, magnesium-, or other oxide-containing particles	Improve mechanical stability, print fidelity, or biological activity; excessive loading may impair printability, cell viability, or cause nozzle clogging	116,119,120

Category	Material	Key Characteristics	References
Metallic materials	Titanium and titanium alloys	High strength, corrosion resistance, and osseointegration; fabricated by metal additive manufacturing; not conventional bioinks because they do not encapsulate living cells during printing	28,121–123

Synthetic polymers provide complementary advantages because their mechanical properties, degradation kinetics, and chemical functionalities can be more precisely controlled. Polyethylene glycol (PEG)-based hydrogels, including PEG diacrylate and related derivatives, are widely used as tunable platforms for photocrosslinkable bioinks⁹⁷. However, their intrinsic bio-inertness necessitates functionalization with cell-adhesive peptides or incorporation of natural polymers to support cellular activities. Thermoplastic and biodegradable polymers, such as polycaprolactone (PCL), poly(lactic-co-glycolic acid) (PLGA), and polylactic acid (PLA), have also been extensively applied in oral and bone-related 3D printing¹²⁴. These materials, however, are more appropriately classified as cell-free structural inks used to fabricate supporting scaffolds rather than conventional cell-laden bioinks¹²⁵, because they are commonly processed under conditions that are unsuitable for direct cell encapsulation. Their primary contribution lies in providing mechanical reinforcement, dimensional stability, and long-term structural support, particularly when integrated with cell-laden hydrogels. This division of labor allows structural stability and cellular function to be optimized separately.

For hard oral tissues regeneration, structural support alone is insufficient as the construct must also provide cues that encourage mineral deposition and integration with host bone. Inorganic additives are therefore introduced into hydrogel bioinks or polymeric scaffolds as a mineral-like phase¹²⁶. Hydroxyapatite closely resembles the stable mineral component of bone and dental tissues and primarily enhances osteoconduction and mineralized matrix formation¹²⁷. β -Tricalcium phosphate is more readily resorbed and is useful when scaffold dissolution is intended to proceed alongside new bone deposition¹²⁸. Bioactive glass provides a more dynamic form of stimulation by releasing calcium, phosphate, and silicon species that can promote osteogenesis and angiogenesis; depending on its composition, it may also contribute antibacterial activity. Other silica-, zirconia-, magnesium-, or metal-oxide-containing particles are generally incorporated to provide more specific functions, such as mechanical reinforcement, ion-mediated signaling, or improved printing fidelity¹²⁹. These inorganic components should nevertheless be regarded as functional modifiers rather than as universally beneficial fillers. Increasing particle content may strengthen the construct or enhance mineral bioactivity, but it can also increase viscosity, disturb extrusion, reduce cell viability, or block the printing nozzle¹³⁰. Their effectiveness therefore depends on controlling particle size, concentration, surface chemistry, and dispersion within the surrounding polymer network.

For large-volume defects or load-bearing oral and maxillofacial reconstruction, hydrogel-based or ceramic-reinforced hydrogel systems alone are generally insufficient to provide immediate mechanical stability. Metallic materials, particularly titanium and titanium alloys, are therefore widely used as additively manufactured structural frameworks¹²¹. Their high strength, fatigue resistance, corrosion resistance, and capacity for osseointegration allow them to maintain defect space and withstand functional loading during the early stages of reconstruction¹³¹. Like thermoplastic polymers, metals are not bioinks as living cells are not incorporated during their high-energy fabrication processes. Instead, they are typically fabricated into porous or patient-specific frameworks through metal additive manufacturing and subsequently combined with

bioprinted hydrogels, bioactive coatings, or cell-seeded constructs. Such hybrid approaches integrate the mechanical reliability of metallic scaffolds with the biological functionality of bioprinted materials, making them particularly relevant for maxillofacial, and implant-associated reconstruction.

Overall, material systems for oral tissue bioprinting are evolving from single-component formulations toward composite, multimaterial, and hybrid platforms. The central design principle is to align material composition and function with tissue-specific regenerative demands¹³²: cell-permissive hydrogels for soft tissue repair, mineral-reinforced composites for hard tissue regeneration, structurally supportive polymers or metals for load-bearing defects, and spatially organized multimaterial systems for soft-hard tissue interfaces. This materials-oriented foundation provides the basis for selecting appropriate printing technologies and developing host-responsive 3D-printed and bioprinted constructs for functional oral tissue reconstruction.

2.3. 3D Bioprinting Technologies for Oral Tissue Reconstruction

3D printing is a broad additive-manufacturing approach in which materials are deposited or solidified layer by layer to fabricate three-dimensional constructs with predefined geometries. In contrast, 3D bioprinting represents a biofabrication-oriented subset of these technologies that enables the spatial deposition of biologically active materials, particularly cell-laden bioinks, to generate tissue-mimetic constructs. Accordingly, cell-free polymeric, ceramic, or metallic scaffolds fabricated for structural support are referred to as 3D-printed constructs in this review, whereas constructs fabricated through the controlled deposition of cell-containing or biologically active bioinks are described as bioprinted constructs¹³⁻¹⁵. For oral tissue reconstruction, printing technology should be selected according to the biological and structural requirements of the target tissue. Soft and cell-rich tissues generally require gentle processing conditions that preserve cell viability, whereas hard or load-bearing tissues demand greater geometric precision and mechanical support¹⁵. In this context, extrusion-based bioprinting is widely used as depositing cell-laden hydrogels and relatively viscous composite bioinks into customized three-dimensional structures¹³³. Vat photopolymerization-based techniques provide higher resolution and better shape fidelity, making them suitable for fine architectures and tissue interfaces, although their application depends on photocrosslinkable materials¹³⁴. Multimodal bioprinting combines two or more fabrication methods to integrate soft, cell-permissive regions with mechanically reinforced compartments. For defects requiring immediate load-bearing stability, metal additive manufacturing can further provide patient-specific structural frameworks that are subsequently combined with bioprinted hydrogels, cells, or bioactive coatings.

Specifically, extrusion-based bioprinting is particularly suitable for fabricating porous scaffolds, soft-tissue grafts, and hydrogel-based constructs with tunable shapes¹³⁵. However, this method requires careful optimization of bioink viscosity, nozzle diameter, extrusion pressure, printing speed, and crosslinking conditions, since excessive shear stress may impair cell viability, whereas insufficient viscosity can reduce shape fidelity. Yi et al.⁴² developed an injectable platelet-rich fibrin/alginate/gelatin bioink for oral soft tissue regeneration (**Figure 3A**). The bioink was processed by extrusion-based 3D bioprinting into customized constructs, prolonged the release of

multiple growth factors, supported gingival fibroblast viability, and promoted angiogenic activity *in vivo*.

Microextrusion-based cell bioprinting is particularly suitable for PDL regeneration¹³⁶. By adjusting the printing path, filament spacing, and deposition direction, this technique enables spatial control over cell distribution and matrix orientation. These features are important for reproducing the aligned fibrous architecture of the native PDL and for guiding functional attachment between cementum and alveolar bone. Microextrusion is also compatible with hydrogel bioinks that can encapsulate periodontal ligament cells under relatively mild processing conditions. After deposition, photo-crosslinking can stabilize the printed geometry without eliminating the hydrated environment required for cell survival and matrix remodeling. Raveendran et al.¹³⁷ demonstrated this advantage by optimizing the bioprinting of human periodontal ligament cells in GelMA hydrogels (**Figure 3B**). The authors separately tuned the GelMA formulation, light-crosslinking conditions, extrusion pressure, and nozzle dimensions. This optimization preserved high cell viability while improving printing resolution and construct stability.

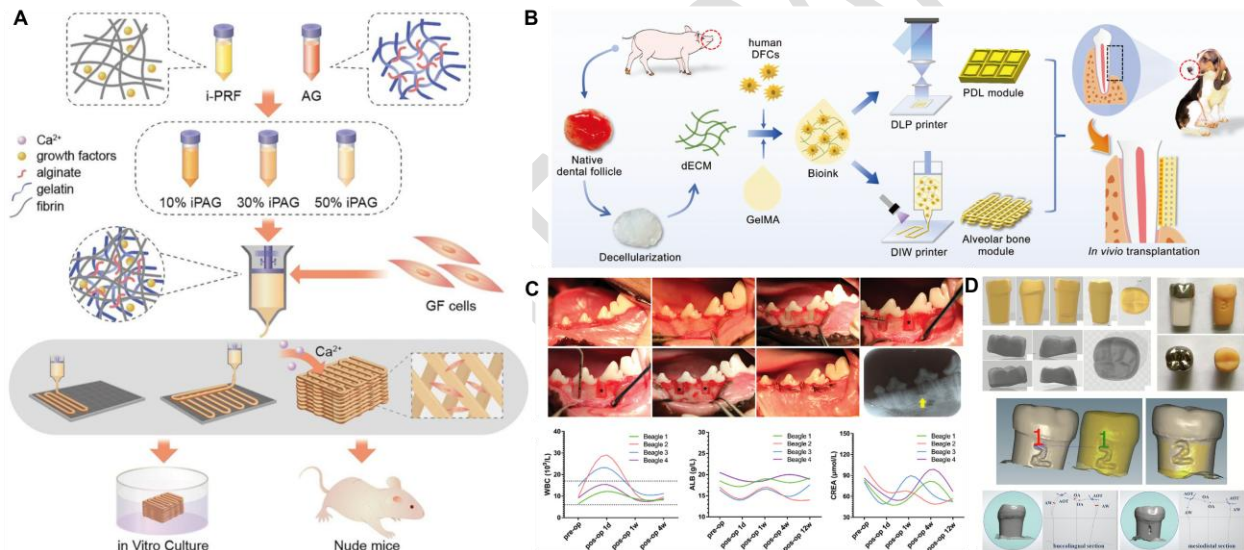


Figure 3. Representative 3D printing and bioprinting technologies for oral tissue reconstruction. (A) Extrusion-based bioprinting of injectable platelet-rich fibrin/alginate/gelatin bioinks for oral soft tissue regeneration⁴². (B) Multimodal bioprinting for periodontal soft-hard tissue interface regeneration and (C) its evaluation of the osteoinduction activities and immune rejection of the bioprinted periodontal module¹³⁸. (D) Metal additive manufacturing-assisted fabrication of patient-specific oral restorations¹³⁹.

Vat photopolymerization-based bioprinting, including stereolithography and digital light processing, uses light-induced polymerization to fabricate constructs with high resolution and good shape fidelity¹⁴⁰. This technology is especially useful for photocrosslinkable bioinks and fine architectural designs, such as aligned structures or tissue-interface modules. High-resolution bioprinting has its advantages for complex soft-hard periodontal interfaces. Yang et al.¹³⁸ used a GelMA/decellularized ECM bioink and digital light projection printing to fabricate a PDL module

with topographical guidance (**Figure 3B**). In combination with direct ink writing for the alveolar bone module, the printed construct promoted aligned periodontal fibers, bone, and functional bone-ligament interface regeneration in a beagle periodontal defect model (**Figure 3C**). It highlights the advantage of high-resolution bioprinting for complex soft-hard periodontal interfaces.

Metal additive manufacturing-assisted hybrid fabrication is important for load-bearing oral and maxillofacial applications¹⁴¹, which it even should be distinguished from conventional cell-laden bioprinting. Metallic materials are not bioinks, but they can provide patient-specific mechanical support and may be combined with bioprinted hydrogels, bioactive coatings, or cell-seeded constructs. By providing customized structural components, metal additive manufacturing can complement bioprinting for oral restoration and reconstruction. Xu et al.¹³⁹ fabricated Cu-bearing Ti-6Al-4V-6Cu alloy pediatric crowns using laser powder-bed fusion (**Figure 3D**). The printed crowns showed favorable mechanical properties, corrosion resistance, biocompatibility with human gingival fibroblasts, antibacterial activity against *Streptococcus mutans*, and improved internal fit compared with prefabricated stainless-steel crowns.

Taken together, the technologies mentioned above play complementary roles in oral tissue reconstruction. Rather than relying on a single printing method, future oral tissue reconstruction likely depends on the integration of appropriate printing technologies with tissue-specific bioinks, structural design, and host-responsive biological cues.

3. Host Responses to 3D-printed and bioprinted biomaterials

The oral cavity presents a distinctive anatomical and environmental context for implanted or surface-contacting biomaterials¹⁴². Host responses in this setting extend beyond conventional assessments of biocompatibility. Instead, they emerge from the combined effects of construct architecture, interfacial chemistry, degradation behavior, and biologically active signals released from the material. Immediately after contact with saliva, blood, or tissue fluid, proteins adsorb onto the material surface and form the first biological interface²⁸. This provisional layer influences subsequent immune activation and cell recruitment. It also affects vascular invasion, extracellular matrix remodeling, and eventual tissue integration¹⁴³. These processes are further modified by conditions unique to the oral cavity. Resident microorganisms may colonize the material surface, while local pH and enzymatic activity alter material degradation and molecular release. At the same time, repeated mechanical loading can reshape both cellular responses and interfacial stability. Host responses should therefore be regarded not only as outcomes used to evaluate material performance, but also as mechanistic information for designing 3D-printed and bioprinted constructs that function effectively within the oral microenvironment.

3.1. Physical Interactions

Physical interactions refer to host responses regulated by the geometric, topographical, and mechanical features of 3D-printed or bioprinted constructs. At the surface level, topography and roughness act as early regulators of host recognition¹⁴⁴. Printing-induced filament morphology, layer-by-layer deposition, post-printing surface modification, and incorporation of micro- or nanoscale fillers can all alter the surface microenvironment. Moderate micro- or nanoscale roughness may enhance osteoblast adhesion, stem cell osteogenic differentiation, and mineral

deposition, thereby benefiting alveolar bone and periodontal regeneration. However, this effect is not simply proportional to roughness. Excessive roughness, poorly dispersed particles, or irregular filament surfaces may impair print fidelity, increase stress concentration, enhance nonspecific protein adsorption, or facilitate bacterial retention. Therefore, surface topography should be optimized within a tissue-specific window rather than maximized indiscriminately. A representative example is the 3D-printed PEEK implant modified with a biomimetic PDL fiber-like hydrogel. Xu et al.¹⁴⁵ fabricated customizable PEEK implants by fused deposition modeling, followed by sulfonation and surface grafting of a simvastatin-cefepime-loaded acrylic acid-acrylamide hydrogel (**Figure 4A**). This modification improved hydrophilicity, reduced surface roughness and friction coefficient, enhanced antibacterial activity and biocompatibility, and significantly promoted osseointegration *in vivo*. Importantly, the hydrogel layer was designed to mimic PDL-like fibers and contributed to stress dissipation around the implant interface.

At the architectural level, pore size, porosity, and interconnectivity determine whether a printed scaffold can support host cell migration, vascular ingrowth, nutrient diffusion, and waste removal¹⁴⁶. Highly interconnected pores provide transport pathways for cells and fluids, which is essential for large or mineralized constructs. Nevertheless, increasing porosity often reduces compressive strength and structural stability, creating a trade-off between biological integration and mechanical competence¹⁴⁷. For oral hard tissue reconstruction, pore architecture should support vascularized bone formation while maintaining resistance to functional loading. For soft tissue and periodontal applications, pore and fiber organization should additionally guide fibroblast migration, epithelial integration, and oriented ECM deposition. This architecture-dependent host response has been demonstrated in 3D-printed titanium meshes for alveolar bone augmentation. Ma et al.¹⁴⁸ compared personalized titanium meshes with porosities of 55%, 62%, and 68% in a beagle mandibular defect model (**Figure 4B**). Micro-CT and histological analyses showed that the high-porosity group (porosity = 68%) exhibited higher trabecular thickness, trabecular number, and bone volume fraction, together with lower trabecular separation, indicating that an optimized high-porosity architecture favored bone regeneration in large oral bone defects. Mechanical properties provide another major class of physical cues. Scaffold stiffness, viscoelasticity, and degradation-dependent mechanical evolution regulate cell behavior through mechanotransduction pathways¹⁴⁹. In hard tissue regeneration, sufficient stiffness is required for space maintenance and load-bearing support, whereas excessive stiffness or mechanical mismatch may cause stress shielding, impaired bone remodeling, or interfacial failure. In contrast, oral soft tissues require compliant and deformable materials that can accommodate stretching, compression, and shear during mastication, swallowing, and speech. The PDL represents a particularly demanding interface, as it requires aligned fibrous organization and appropriate compliance to mediate load buffering, proprioception, and tooth support¹⁵⁰.

At soft-hard tissue interfaces, mechanical gradients are essential for stable integration. Native oral tissues often display gradual transitions in stiffness, composition, and architecture, such as the cementum-PDL-alveolar bone complex¹⁵¹. Sharp mechanical discontinuities in printed constructs may concentrate stress and lead to delamination, fibrous encapsulation, or failure under cyclic

loading. Gradient printing, multimaterial deposition, and spatially controlled crosslinking provide opportunities to reproduce these transitions. In this sense, physical interactions directly inform the design of pore architecture, filament organization, stiffness distribution, and multiphasic scaffold structures.

3.2. Chemical Interactions

Whereas physical interactions determine how host tissues perceive construct geometry and mechanics, chemical interactions define how the local microenvironment responds to the material's intrinsic properties-namely, its composition, surface chemistry, ionic release, and degradation profile. Surface chemistry plays a central role in forming the initial protein adsorption layer, which subsequently mediates cell-material interactions¹⁵². Upon contact with saliva, blood, or tissue fluids, proteins rapidly adsorb onto material surfaces¹⁵³. The composition, density, orientation, and conformation of this interfacial protein layer are influenced by surface hydrophilicity, charge, and functional groups. Functional groups such as hydroxyl, carboxyl, amine, catechol, and phosphate groups can regulate protein binding, mineral nucleation, and cell adhesion. For hard oral tissues regeneration, calcium- and phosphate-rich surfaces are particularly relevant because they support osteoblast attachment and matrix mineralization¹⁵⁴. Polydopamine coating represents a widely used chemical modification strategy for improving the bioactivity of 3D-printed scaffolds. Sun et al.¹⁵⁵ coated 3D-printed β -tricalcium phosphate scaffolds with polydopamine (PDA). They showed that the coating increased surface roughness, promoted bone marrow mesenchymal stem cells (BMSCs) adhesion and osteogenic differentiation, and enhanced new bone formation in a rat critical-size calvarial defect model (**Figure 4C**). However, the calvarial defect is a non-oral bone model and does not reproduce saliva exposure, oral microbial communities, or cyclic masticatory loading. Therefore, these findings should be interpreted as mechanistic evidence of osteogenic activity rather than direct evidence of therapeutic performance in the oral cavity, and further validation in alveolar or mandibular defect models is required.

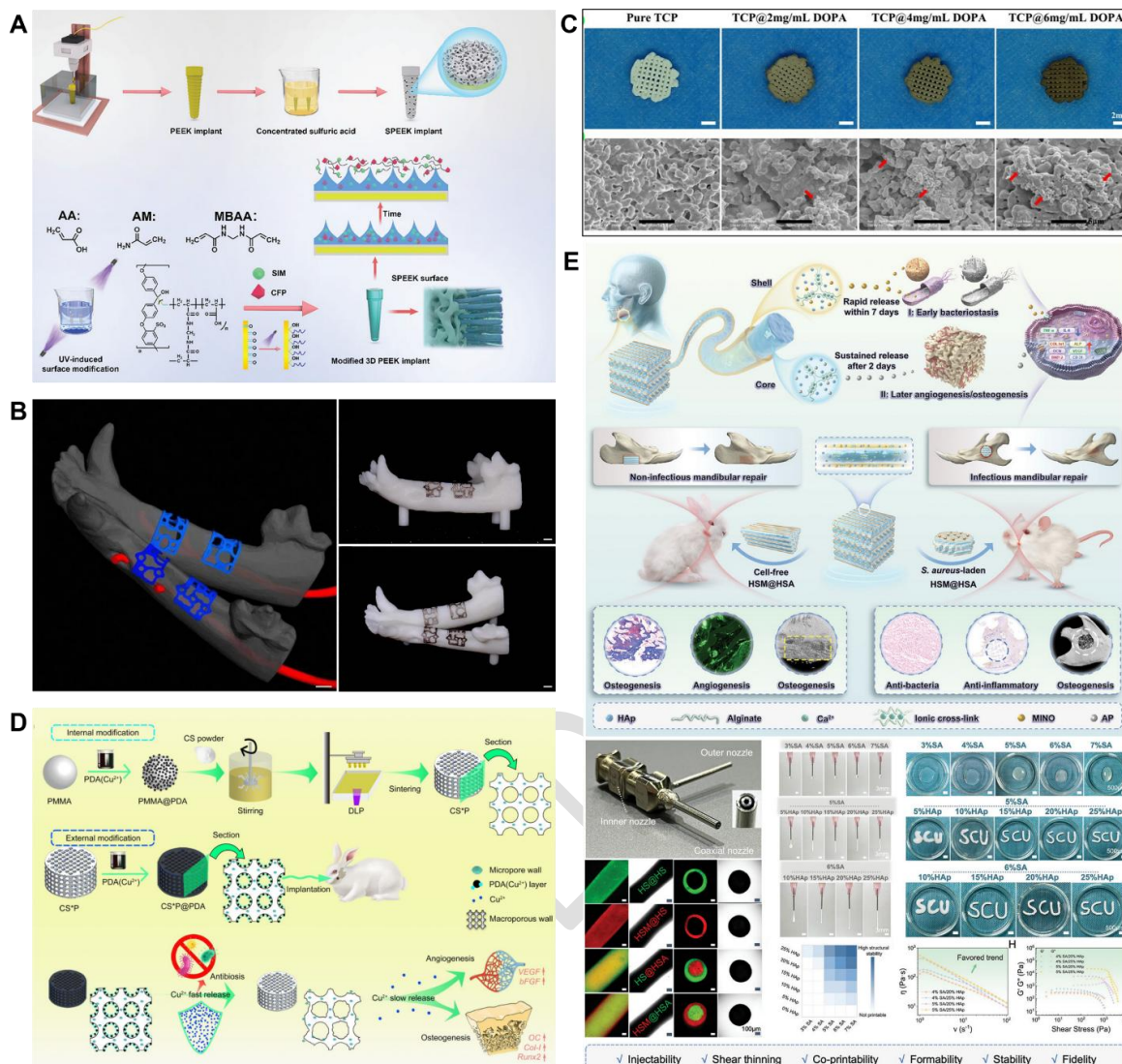


Figure 4. Representative examples of host-material interactions in 3D-printed and bioprinted biomaterials for oral tissue reconstruction. (A) Surface and interfacial structural regulation of 3D-printed PEEK implants through sulfonation and biomimetic hydrogel modification. Modified and reprinted with permission from Xu *et al.*¹⁴⁵. Copyright © 2023 Wiley-VCH GmbH. (B) Personalized 3D-printed titanium meshes with different porosities¹⁴⁸. (C) Polydopamine-coated 3D-printed β -tricalcium phosphate scaffolds with surface functionalization modifies physicochemical properties. Modified and reprinted with permission from Sun *et al.*¹⁵⁵. Copyright © 2023 Royal Society of Chemistry. (D) Copper-containing polydopamine-modified magnesium-doped calcium silicate scaffolds with surface chemistry and controlled Cu^{2+} release to the host microenvironment. Modified and reprinted with permission from Jiang *et al.*¹⁵⁶. Copyright © 2024 Zhejiang University Press. (E) Coaxial 3D-printed scaffolds with sequential antibacterial and osteogenic functions for infected mandibular defect repair. Modified and reprinted with permission from Zhang *et al.*¹⁵⁷. Copyright © 2024 Wiley-VCH GmbH.

Bioactive ion release represents a dynamic form of chemical signaling, especially in hard oral tissues reconstruction. Inorganic components such as hydroxyapatite, β -tricalcium phosphate, calcium silicate, and bioactive glass can release calcium, phosphate, silicate species, and other

functional ions into the local microenvironment. Calcium and phosphate contribute to mineral deposition, whereas silicate-, magnesium-, zinc-, strontium-, or copper-containing systems may further regulate osteogenesis, angiogenesis, immunomodulation, or antibacterial activity¹⁵⁸. However, ion release must be carefully controlled, because excessive local ion concentrations may disturb osmotic balance, impair cell viability, or induce cytotoxicity. Jiang et al.¹⁵⁶ provided a representative example of controlled chemical functionalization using copper-containing polydopamine (**Figure 4D**). In their study, digital light processing-printed magnesium-doped calcium silicate (CS) scaffolds were modified through a two-step internal/external PDA(Cu^{2+}) strategy. External PDA(Cu^{2+}) modification enabled rapid early copper release for antibacterial activity, whereas internal modification using PDA(Cu^{2+})-modified polymethyl methacrylate microspheres allowed sustained copper release during scaffold degradation, thereby supporting osteogenesis and angiogenesis. Cylindrical defects measuring 8 mm in diameter and 4 mm in thickness were created in the mandible, and the animals were evaluated 4 weeks after implantation. Micro-CT showed that the internally and externally modified CSP@PDA scaffolds produced significantly higher BV/TV and trabecular number than unmodified CS scaffolds ($p < 0.01$), with new bone extending further from the scaffold periphery toward the center.

Material degradation and the resulting chemical microenvironment also strongly affect host responses. Degradable polymers and hydrogel networks may break down through hydrolysis, enzymatic cleavage, oxidation, or cell-mediated remodeling. Their degradation products can alter local pH, osmotic pressure, and inflammatory status¹⁵⁸. For instance, acidic degradation products from aliphatic polyesters may aggravate local inflammation or impair mineralization if not properly buffered, whereas calcium phosphate ceramics and silicate-based ceramics may release buffering ions that help stabilize the local microenvironment¹⁵⁹. In oral tissue reconstruction, degradation should be synchronized with tissue formation: overly rapid degradation may compromise structural support, whereas excessive stability may hinder matrix remodeling and tissue integration. Chemical interactions are therefore not passive consequences of material composition. Instead, they can be deliberately engineered to regulate host recognition, antimicrobial activity, mineralization, vascularization, and matrix remodeling. For 3D-printed or bioprinted oral constructs, the optimization of surface chemistry, ion-release kinetics, degradation behavior, and bioactive molecule delivery should be considered together with printability and mechanical performance.

3.3. Biological Interactions

Biological interactions encompass the host- and microenvironment-mediated processes that determine how printed biomaterials are recognized, remodeled, and ultimately integrated after implantation¹⁶⁰. These processes evolve over time and collectively regulate the transition from early defense responses to vascularized tissue formation and functional maturation. Their balance determines whether the construct supports regenerative integration or progresses toward persistent inflammation, fibrosis, infection, or structural failure.

The early biological response is dominated by innate immune activation. Neutrophils are rapidly recruited to the implantation site and contribute to acute inflammation, pathogen defense, and

debris clearance. Subsequently, monocytes and macrophages become central regulators of host response. Macrophage responses should not be interpreted as a fixed transition between discrete M1 and M2 phenotypes⁸¹. Instead, macrophages exhibit dynamic and overlapping functional states that vary with implantation stage, tissue context, microbial exposure, and material-derived signals. Material properties, including surface topography, stiffness, degradation products, and released ions, can influence macrophage activation and the transition from inflammatory to pro-regenerative responses²². Persistent inflammatory activation may lead to foreign body giant cell formation, fibrous encapsulation, and impaired tissue integration.

Vascularization is another essential biological interaction, particularly for large-volume or metabolically active constructs. Endothelial cells and progenitor cells respond to material architecture, matrix stiffness, oxygen gradients, and angiogenic cues by migrating, proliferating, forming lumens, and maturing into vascular networks¹⁶¹. For hard tissues, vascular ingrowth is required not only for oxygen and nutrient delivery, but also for coupling angiogenesis with osteogenesis. Scaffold pore architecture, degradation kinetics, and released bioactive ions can all influence this process¹⁶². For example, magnesium- or copper-containing systems may promote angiogenic responses when released within appropriate concentration windows, whereas excessive ion release may impair cellular viability¹⁶³.

Microbiological interactions are particularly important in the oral cavity. Unlike many sterile implantation sites, oral defects are constantly exposed to resident microbiota and opportunistic pathogens¹⁶⁴. Bacterial adhesion and biofilm formation compete with host cells for surface adhesion and produce acidic metabolites. These local perturbations prolong inflammation and, ultimately, compromise bone regeneration. Therefore, oral biomaterials should not only support host cell colonization but also prevent early microbial occupation. Antibacterial strategies may include antibiotic delivery, metal-ion release, antimicrobial peptides, photothermal effects, surface charge regulation, and anti-adhesive surface design¹⁶⁵. However, the oral microbiota should not be regarded solely as a collection of pathogens to be eliminated. Commensal microorganisms contribute to ecological homeostasis and colonization resistance, whereas dysbiosis and pathogenic biofilm development can prolong inflammation and compromise tissue regeneration. Therefore, microbiome-oriented material design should balance infection control with preservation of beneficial host–microbial relationships. Zhang et al.¹⁵⁷ developed a coaxial 3D-printed scaffold with a shell loaded with minocycline hydrochloride and a core containing deproteinized antler powder (**Figure 4E**). *In vivo* performance was examined using two mandibular models: a 5-mm-diameter *S. aureus*-infected mandibular defect in rats and a noninfected 5 × 4 × 10 mm mandibular defect in rabbits. In the infected rat model, micro-CT evaluation at 1, 2, and 8 weeks showed that the dual-functional HSM@HSA scaffold increased BV/TV relative to the infected untreated control, supporting an early antibacterial-to-regenerative transition. In the larger rabbit model, scaffolds remained partially detectable at 8 weeks but were almost completely degraded by 12 weeks; at 12 weeks, the HSM@HSA group showed significantly higher BV, BV/TV, bone surface density, trabecular thickness, trabecular number, and connectivity density than the comparison groups.

Cellular interactions ultimately determine whether host cells can repopulate the printed construct and generate functional tissue. For hard tissue reconstruction, the recruitment, adhesion, proliferation, and osteogenic differentiation of osteoprogenitor cells are essential. For soft tissue repair, epithelialization, fibroblast migration, collagen deposition, and vascularization dominate the regenerative process¹⁶⁶. For periodontal regeneration, successful repair requires coordinated formation of cementum, PDL, and alveolar bone, together with oriented collagen fiber insertion across the soft-hard interface¹⁶⁷. Overall, biological interactions in oral tissue reconstruction should be understood as an integrated process involving inflammation, angiogenesis, osteogenesis, soft tissue repair, and microbial regulation. The most effective 3D-printed and bioprinted biomaterials are therefore not merely inert scaffolds, but host-instructive platforms capable of temporally coordinating antibacterial defense, immune resolution, vascular formation, and tissue-specific regeneration.

Collectively, host responses to 3D-printed and bioprinted oral biomaterials are governed by interconnected physical, chemical, and biological interactions. Physical cues regulate surface recognition, cell adhesion, tissue infiltration, and mechanical integration. Chemical cues control protein adsorption, ion-mediated signaling, antimicrobial activity, and degradation-related microenvironmental changes. Biological cues determine inflammation resolution, vascularization, cellular repopulation, microbiological balance, and long-term tissue integration. These interactions provide the mechanistic basis for developing next-generation oral biofabrication strategies, in which printed constructs are designed not only to match defect geometry, but also to actively guide host responses toward functional tissue reconstruction.

4. Material and Structural Design Strategies for 3D-printed and bioprinted Oral Constructs

The host-material interactions discussed above provide mechanistic guidance for the rational design of 3D-printed and bioprinted constructs. Rather than serving as passive space-filling matrices, next-generation bioinks and scaffolds are expected to actively regulate how printed constructs are recognized, colonized, remodeled, and integrated by host tissues. This requirement is particularly important in oral tissue reconstruction, where implanted materials must operate within a complex microenvironment. Accordingly, effective design strategies should integrate three interconnected dimensions (**Figure 5**): bioink composition, which defines the chemical and biological signaling capacity of the construct; structural architecture, which regulates physical interactions, tissue ingrowth, and mechanical adaptation; and bioactive functionalization, which modulates immune, vascular, cellular, and microbial responses.

4.1. Bioink formulation

Bioink formulation constitutes the material foundation for constructing a regenerative microenvironment. An ideal bioink for oral tissue reconstruction should integrate printability, cytocompatibility, structural stability, degradation behavior, and tissue-specific bioactivity. Achieving these properties simultaneously remains challenging because oral tissues differ markedly in composition, mechanical properties, vascularity, microbial exposure, and regenerative potential. Therefore, bioink development should be guided not only by printing performance, but

also by the anticipated host response after implantation. Based on the material characteristics summarized in Section 2.2, bioink formulation should focus on balancing cell permissiveness, structural persistence, degradation, and host-instructive signaling according to tissue-specific requirements.

From a processing perspective, rheological behavior and crosslinking strategy determine whether a bioink can be printed with sufficient fidelity while preserving biological function. Shear-thinning behavior allows viscosity to decrease during extrusion, thereby reducing shear-induced cell damage, whereas rapid recovery after deposition helps maintain the printed architecture¹⁶⁸. Crosslinking strategies, including photo-crosslinking, ionic gelation, thermo responsive gelation, enzymatic crosslinking, and dual-crosslinking systems, regulate the initial network structure, stiffness, swelling, and degradation kinetics¹⁶⁹. Importantly, crosslinking should not be viewed only as a printing aid; by controlling matrix density and degradability, it also influences nutrient diffusion, cell infiltration, enzymatic remodeling, and long-term tissue integration⁷¹. Thus, bioink formulation should generate constructs that are both manufacturable and biologically instructive, enabling controlled host-mediated remodeling rather than merely preserving printed shape.

4.2. Structural Design

Structural design translates physical host-material interactions into controllable architectural parameters. Compared with conventional scaffold fabrication methods, 3D bioprinting enables precise regulation of pore geometry, filament arrangement, fiber orientation, material distribution, and mechanical gradients¹⁷⁰. These architectural features influence protein adsorption, cell migration, nutrient transport, vascularization, load transfer, and tissue maturation. Therefore, structure should be regarded as an active regulator of host response rather than a passive geometric feature.

Pore architecture is one of the most important structural determinants of tissue ingrowth. In bone-oriented scaffolds, pore sizes of approximately 200-500 μm are commonly considered favorable for vascularized bone ingrowth¹⁷¹, although the biological effects of pore size depend on total porosity, interconnectivity, pore geometry, material composition, surface properties, degradation behavior, defect location, and loading conditions. High porosity improves mass transport and biological integration, but excessive porosity may compromise compressive strength and spatial stability³⁰. Therefore, pore design requires a balance between biological accessibility and mechanical reliability, particularly in alveolar and mandibular reconstruction.

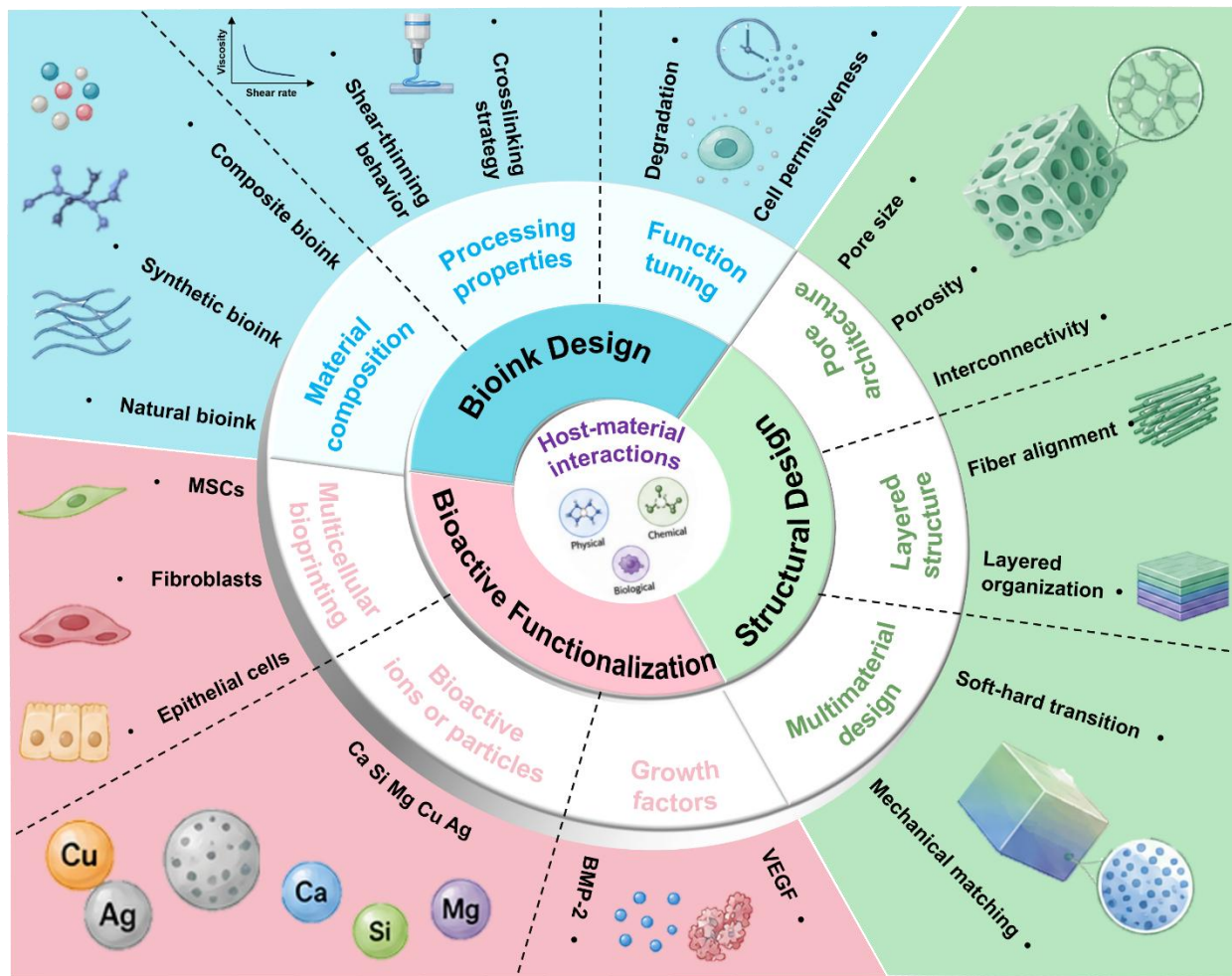


Figure 5. The schematic of host-material interaction-guided design strategies for 3D-printed and bioprinted oral constructs. Bioink formulation focuses on material composition, processing properties, and functional tuning, including natural bioinks, synthetic bioinks, composite bioinks, shear-thinning behavior, crosslinking strategies, degradation, and cell permissiveness. Structural design regulates physical host-material interactions through pore architecture, layered structures, and multimaterial or gradient organization, thereby controlling pore size, porosity, interconnectivity, fiber alignment, soft-hard transition, and mechanical matching. Bioactive functionalization introduces biological cues, such as growth factors, bioactive ions or particles, and multiple cell types, including MSCs, fibroblasts, and epithelial cells, to modulate osteogenesis, vascularization, antimicrobial activity, immune response, and tissue integration.

For soft tissue and periodontal applications, structural design should also account for compliance, anisotropy, and tissue-specific organization. Fiber alignment, filament orientation, and layered architecture can guide cell elongation, collagen deposition, and ECM alignment¹⁷². These features are especially important for PDL regeneration, where oriented fibrous structures are required for load transmission and functional insertion between cementum and alveolar bone¹⁷³. Similarly, epithelial and mucosal reconstruction may benefit from layered constructs that distinguish barrier-forming epithelial regions from underlying vascularized connective tissue compartments.

Gradient and multimaterial structures are particularly valuable for soft-hard tissue interfaces. Native oral tissues often exhibit gradual transitions in composition, stiffness, porosity, and cellular organization¹⁷⁴, as exemplified by the cementum-PDL-alveolar bone complex. Abrupt transitions within printed constructs may cause stress concentration, delamination, fibrous encapsulation, or mechanical failure under cyclic loading. By spatially varying material composition, pore architecture, and mechanical properties, gradient scaffolds can better recapitulate native tissue transitions and facilitate coordinated regeneration across multiple compartments¹⁷⁵. Multimaterial bioprinting further enables the integration of mechanically reinforced hard tissue regions with cell-permissive soft tissue regions within a single construct.

Spatial patterning of cells and bioactive cues can also be incorporated into structural design¹⁷⁶. Region-specific deposition of osteogenic cells, fibroblasts, endothelial cells, epithelial cells, or stem cells may help reconstruct tissue-specific microenvironments¹⁷⁷. Likewise, localized delivery of angiogenic, osteogenic, immunomodulatory, or antimicrobial cues can guide vascular invasion, mineralization, immune regulation, and matrix remodeling in a spatially controlled manner. In this sense, structural design determines not only the external geometry of a construct, but also the spatial and temporal sequence of host-material interactions.

4.3. Bioactive Functionalization

Bioactive functionalization provides a direct strategy for regulating biological host responses. While bioink composition and structural architecture mainly define the physical and chemical context of regeneration, bioactive components introduce specific signals that modulate inflammation, vascularization, cell differentiation, antimicrobial defense, and tissue remodeling²⁴. The central challenge is to deliver these signals at appropriate concentrations, locations, and time scales without compromising printability, cytocompatibility, or safety.

Growth factors and signaling molecules are widely used to guide tissue-specific regeneration. Bone morphogenetic protein-2 promotes osteogenic differentiation and mineralized tissue formation, whereas vascular endothelial growth factor supports endothelial cell migration and vascular network formation¹⁷⁸. Fibroblast growth factors may contribute to soft tissue repair, angiogenesis, and fibroblast activity, depending on the isoform and local context. However, direct incorporation of soluble growth factors often leads to burst release, short biological half-life, and potential off-target effects. Controlled delivery strategies, including microsphere encapsulation, nanoparticle immobilization, affinity binding, and hydrogel-based release systems, can provide more localized and sustained signaling¹⁷⁹. For soft-hard tissue interfaces, spatial gradient delivery may further help coordinate angiogenesis, osteogenesis, and connective tissue remodeling.

Functional ions and particles can act as stable and multifunctional bioactive cues. Calcium phosphate ceramics and bioactive glasses release calcium, phosphate, silicate species, and other ions that support osteogenesis, mineralization, and vascularization. Zinc, magnesium, strontium, copper, and silver-containing systems may further provide antibacterial, immunomodulatory, osteogenic, or angiogenic effects, depending on their dose and release kinetics^{180,181}. Nevertheless, excessive ion release or nanoparticle loading may induce cytotoxicity, inflammatory activation, or

impaired printability. Therefore, bioactive particles should be designed as controlled signaling reservoirs rather than inert fillers.

Given the microbe-rich oral environment, antimicrobial and immunomodulatory functions are indispensable. Antimicrobial peptides, antibacterial ions, antibiotics, functional nanoparticles, anti-biofilm surfaces, and stimuli-responsive systems can reduce bacterial colonization and biofilm formation on printed constructs¹⁸². However, strong antimicrobial activity may also damage host cells or disturb the local microbial balance. Similarly, immunomodulatory cues should not simply suppress inflammation, because early inflammatory responses are necessary for pathogen defense and tissue repair initiation. The desired outcome is a balanced microenvironment that allows effective host defense, timely inflammation resolution, and subsequent regenerative remodeling.

Cell-laden and multicellular bioprinting further expands the biological functionality of printed constructs. Mesenchymal stem or stromal cells can contribute to osteogenic, chondrogenic, or fibroblastic differentiation depending on matrix and biochemical cues¹⁵. Fibroblasts and epithelial cells are important for gingival and mucosal reconstruction, whereas endothelial cells and endothelial progenitor cells support vascular network formation. Co-culture strategies, such as combining mesenchymal stem cells with endothelial cells, may promote angiogenesis-osteogenesis coupling through paracrine signaling and direct cell-cell interactions. However, cell source, density, viability, differentiation status, and spatial distribution must be carefully controlled to ensure reproducible regenerative outcomes¹⁸³.

Overall, bioactive functionalization should be guided by the biological processes identified in host-material interactions. Instead of adding bioactive signals indiscriminately, design strategies should match the target tissue and regeneration stage: immunomodulatory cues for inflammation resolution, angiogenic cues for vascular ingrowth, osteogenic cues for mineralized tissue formation, antimicrobial cues for microbial control, and multicellular organization for complex tissue reconstruction. Through such host-instructive design, 3D-printed and bioprinted constructs can evolve from passive frameworks into dynamic regenerative systems capable of coordinating the sequential events required for functional oral tissue repair.

5. Applications in Oral Tissue Reconstruction

The application of 3D bioprinting and 3D-printed biomaterials in oral and maxillofacial reconstruction is progressing from proof-of-concept fabrication toward tissue-specific functional repair. The central challenge is no longer limited to whether a construct can reproduce an anatomically matched shape; rather, it lies in whether material selection, structural organization, and bioactive functionalization can be coordinated to regulate host-material interactions after implantation¹⁸⁴. In this context, the physical, chemical, and biological interactions discussed above provide a useful framework for understanding current applications. For soft tissue repair, the required material properties depend on the anatomical site and intended function. Mucosal constructs may prioritize rapid epithelial closure and barrier restoration, whereas connective tissue-oriented strategies may place greater emphasis on matrix remodeling, vascularization, or integration with adjacent tissues. Hard tissue reconstruction shares the general requirements of

biocompatibility, tissue integration, and controlled remodeling, but additionally demands tissue-specific functions associated with mineralized regeneration¹⁸⁵. These include the maintenance of defect space, the support of vascularized mineral deposition, and the restoration of mechanical competence under functional loading. Soft-hard interfaces, exemplified by the periodontal complex, impose an additional requirement¹⁸⁶: the regenerated tissues must be spatially organized and mechanically coupled across regions with distinct compositions and functions.

5.1. Soft Tissue Repair

For gingival and oral mucosal reconstruction, 3D bioprinting primarily aims to recreate a site-appropriate ECM-like environment that restores epithelial continuity and supports regeneration of the underlying connective tissue¹⁷². Printed constructs should therefore balance compliance, biological permissiveness, and remodeling capacity so that they remain stable within the oral environment and integrate with adjacent tissues. Natural hydrogel-based bioinks are particularly relevant to this goal because they provide hydrated networks and cell-interactive motifs. Yi et al.⁴² developed an i-PRF/alginate/gelatin bioink for oral soft tissue regeneration (**Figure 6A**). In this system, alginate and gelatin provided the printable and shape-retentive matrix, while i-PRF supplied a biologically active fibrin-rich component containing multiple growth factors. This design addressed two major limitations of i-PRF alone: poor intraoperative shaping and burst-like growth factor release. The printed constructs supported gingival fibroblast viability and proliferation and enhanced angiogenic activity *in vivo*. This work illustrates how soft tissue bioink formulation can be informed by all three host-material interactions.

Surface functionalization provides another route to improve oral soft tissue repair, especially when synthetic polymers are used. Dang and Kim fabricated 3D-printed PLGA scaffolds and introduced amine groups by plasma polymerization, followed by FGF immobilization for periodontal soft tissue repair¹⁸⁷. The amine-functionalized surface enhanced the chemical reactivity and wettability of PLGA, while immobilized FGF provided a localized biological signal for gingival fibroblasts. As a result, cell adhesion, migration, and proliferation were markedly improved compared with unmodified PLGA scaffolds. This study suggests that chemically inert or hydrophobic printed polymers can be converted into bioactive soft tissue scaffolds by engineering the host-material interface at the molecular level.

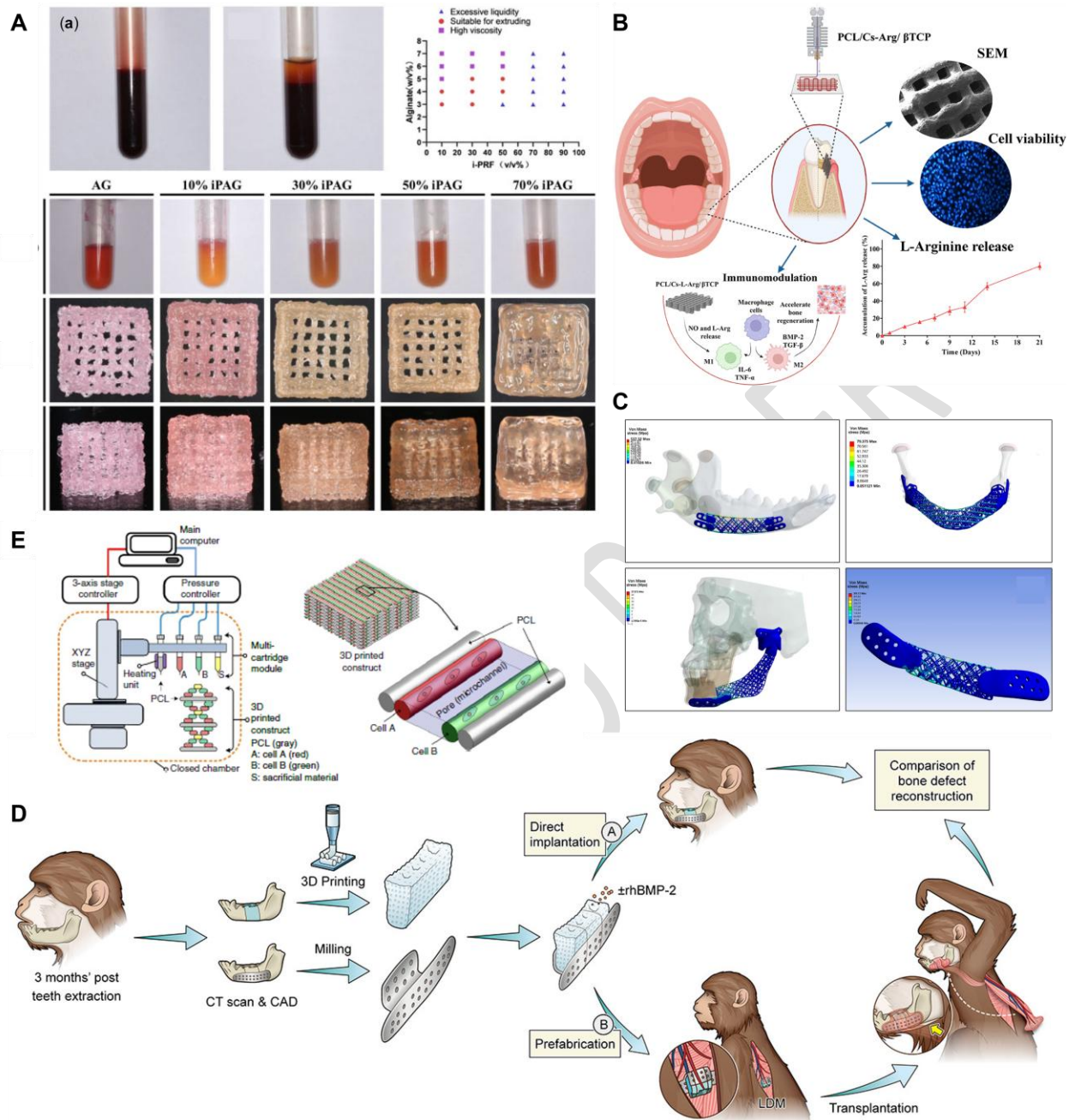


Figure 6. Representative applications of 3D-printed and bioprinted biomaterials in oral soft and hard tissue reconstruction. (A) 3D-printed and bioprinted injectable platelet-rich fibrin/alginate/gelatin biinks for oral soft tissue regeneration⁴². (B) 3D-printed PCL/chitosan/L-arginine/β-TCP scaffolds for guided bone regeneration. Modified and reprinted with permission from Hooshiair *et al.*¹⁸⁸. Copyright © 2025 Royal Society of Chemistry. (C) 3D-printed titanium grid scaffolds for mandibular segmental defects reconstruction¹⁸⁹. (D) Prefabricated tissue-engineered bone for mandibular reconstruction in a primate model¹⁹⁰. (E) Integrated tissue-organ printing platform for human-scale tissue constructs. Modified and reprinted with permission from Kang *et al.*¹⁹¹. Copyright © 2016 Springer Nature.

5.2. Hard Tissue Repair

In hard tissue repair, 3D-printed constructs must provide mechanical support, osteoconductive guidance, vascularized bone formation, and stable integration with host bone or implants¹⁹². Compared with soft tissue repair, hard tissue reconstruction relies more strongly on structural architecture and inorganic chemical signaling. Successful hard tissue regeneration depends first on whether the scaffold permits host cells and newly formed vessels to penetrate the defect. Once this regenerative space is established, mineral-related chemical cues can support matrix mineralization and new bone formation. Bioactive or immunomodulatory signals may further facilitate the transition from early inflammation to a pro-regenerative bone-healing response.

Mineral-reinforced composite systems represent a major strategy for translating chemical interactions into bone regeneration. Hooshier et al.¹⁸⁸ designed multifunctional 3D-printed PCL/chitosan/L-arginine/ β -TCP scaffolds for guided bone regeneration (**Figure 6B**). In this system, PCL and chitosan contributed to structural integrity and degradation control, β -TCP supplied osteoconductive calcium phosphate cues, and L-arginine served as a bioactive regulator with both osteogenic and immunomodulatory functions. The sustained release of L-arginine reduced pro-inflammatory cytokines such as IL-6 and TNF- α , increased anti-inflammatory and osteogenic factors such as BMP-2 and TGF- β , and suggested a shift toward a pro-regenerative macrophage profile. These results demonstrate that hard tissue scaffold design should not only promote mineralization, but also regulate immune-bone coupling through coordinated physical, chemical, and biological cues.

For large mandibular and maxillofacial defects, physical interactions become especially important because the construct must maintain defect space and resist functional loading. Li et al.¹⁸⁹ fabricated 3D-printed titanium grid scaffolds by selective laser melting for mandibular segmental defects (**Figure 6C**). *In vivo*, 20 adult beagle dogs received 4-cm segmental mandibular defects; ten defects were treated with the titanium grid alone, whereas the other ten were additionally filled with autologous bone chips and a bone substitute. After 18 months, continuous mineralized tissue and trabecular bone had formed within the scaffold pores in both groups. Micro-CT showed a significantly greater mineralized bone volume fraction in the graft-filled group than in the scaffold-only group (29.31 (9.74)% vs 22.2 (7.44)%, $p < 0.05$). Importantly, the animal study also reported scaffold exposure in five animals and excluded three animals because of anesthesia-related loss or scaffold fracture caused by unanticipated overloaded biting, illustrating that mechanical and soft-tissue complications remain relevant even when long-term osteogenesis is achieved. The same study reported three clinical cases with follow-up ranging from 6 months to 3 years, with no scaffold fracture, loosening, or exposure observed in these patients. Given the very small and heterogeneous clinical sample, these observations should be regarded as preliminary feasibility evidence rather than established clinical efficacy.

Prefabricated tissue-engineered bone provides another strategy for overcoming insufficient vascularization in large-volume mandibular reconstruction. Cao et al.¹⁹⁰ compared 3D-printed PLGA/TCP and TCP scaffolds, with or without rhBMP-2 coating, in a primate mandibular defect model (**Figure 6D**). The PLGA/TCP-BMP scaffolds lost their original 3D architecture during

prefabrication, whereas TCP-BMP scaffolds better maintained their porous structure, mechanical stability, and mineralization capacity. Notably, prefabricated TCP-BMP bone flaps showed improved vascularization, osseointegration, and mandibular defect recovery compared with direct implantation. This study highlights that hard tissue repair is governed by the coupling of physical stability, chemical degradation behavior, and biological vascularization. It also indicates that scaffold degradation should be synchronized with tissue formation, particularly in large defects exposed to masticatory loading.

Bioprinting platforms can further expand the scale and complexity of hard tissue fabrication. Kang et al.¹⁹¹ developed an integrated tissue-organ printing system that combines cell-laden hydrogels with biodegradable polymers to fabricate human-scale tissue constructs with improved structural integrity (**Figure 6E**). The system incorporated microchannels to support nutrient and oxygen diffusion and was used to fabricate mandible-like bone constructs. Although this work is not limited to oral applications, it provides a useful platform concept for craniofacial reconstruction: physical reinforcement is needed for large-scale structural integrity, chemical composition must support osteogenesis, and biological design should address diffusion, vascularization, and cell survival.

Beyond osteogenesis alone, hard tissue repair increasingly emphasizes neuro-vascularized regeneration. Fitzpatrick et al.¹⁹³ fabricated 3D-printed silk-hydroxyapatite scaffolds functionalized with BMP2, VEGF, and neural growth factor. The silk-hydroxyapatite matrix provided a printable and osteoconductive scaffold, while the combined morphogens supported osteogenic differentiation, endothelial cell activity, and neural-associated cell responses. Although further *in vivo* validation is required, this study broadens the biological design concept of bone scaffolds from simple mineralization toward coordinated osteogenesis, angiogenesis, and innervation.

5.3. Soft-hard Tissue Interface Reconstruction

Soft-hard tissue interfaces represent one of the most challenging targets in oral tissue reconstruction¹⁹⁴. Periodontal tissues, for example, require coordinated regeneration of gingiva, PDL, cementum, and alveolar bone. Unlike isolated soft or hard tissue repair, interface reconstruction depends on spatially organized physical architecture, tissue-specific chemical composition, and multicellular biological regulation. A single homogeneous scaffold is therefore unlikely to recapitulate the graded structure and function of native periodontal tissues. PDL regeneration provides a representative example of this challenge. de Souza Araujo et al.¹⁹⁵ developed PDLSC-laden collagen bioinks for PDL regeneration (**Figure 7A**). The collagen-based bioink mimicked native ECM conditions and exhibited shear-thinning behavior, porous microstructure, and stable swelling and degradation characteristics. When bioprinted onto root fragments, the constructs supported PDLSC viability, proliferation, differentiation, alignment, and migration toward the root surface. This work highlights that successful interface-oriented bioprinting depends on a combination of physical, chemical, and biological cues. Physically, the system must ensure proper printability and matrix architecture. Chemically, it should present ECM-like signals, such as collagen-mediated adhesion. Biologically, it must guide cell behavior,

mm and were assigned to saline, optimized GelMA/PEGDA hydrogel, or PDLSC-laden hydrogel groups. Micro-CT evaluation at 3 and 6 weeks showed that BV/TV increased from $28.7 \pm 1.6\%$ and $33.4 \pm 4.1\%$ in the saline controls to $31.2 \pm 1.5\%$ and $40.5 \pm 4.4\%$ with hydrogel alone, and further to $36.1 \pm 3.3\%$ and $60.1 \pm 3.6\%$ with the PDLSC-laden hydrogel, respectively. At 6 weeks, histological analysis showed continuous newly formed bone filling almost the entire defect in the PDLSC/hydrogel group, whereas bone formation remained partial with hydrogel alone and limited after saline treatment. This example suggests that host-material interactions can be investigated and optimized systematically before implantation: matrix composition determines chemical and mechanical cues, printability controls spatial presentation, and encapsulated PDLSCs provide biological regenerative potential.

Overall, the success of 3D-printed and bioprinted oral constructs depends on how effectively material design is translated into favorable host responses. To further integrate these relationships, **Table 2** summarizes how major host responses can be linked to controllable design variables, target oral tissues, and representative regenerative outcomes. Soft tissue applications require a tripartite coordination⁶: (1) a biomimetic scaffold, primarily ECM-like hydrogels, (2) dynamic cellular remodeling, involving fibroblast activity and vascularization, and (3) durable barrier integrity, comprising epithelial sealing and balanced antimicrobial defense. Hard tissue applications require a threefold design strategy: (1) physical scaffold properties, primarily pore architecture and mechanical stability; (2) osteoconductive chemistry; and (3) biological functionality, encompassing angiogenesis, matrix mineralization, and subsequent osseointegration. Interface applications demand a hierarchical coordination: (1) microenvironmental cues, particularly spatial gradients and cell alignment; (2) multicellular organization, involving diverse cell types and their interactions; and (3) cross-compartment regeneration, ensuring coordinated tissue repair across multiple boundaries. Thus, the application of 3D bioprinting in oral reconstruction should not be evaluated only by printing resolution or anatomical fidelity. More importantly, each construct should be assessed according to whether it can regulate physical, chemical, and biological interactions in a tissue-specific manner. This host-material interaction-guided perspective provides a more rational basis for selecting materials, designing architectures, incorporating bioactive signals, and translating 3D-printed and bioprinted constructs toward functional oral tissue regeneration.

Table 2. Summary of host responses, corresponding design variables, target oral tissues, and representative regenerative outcomes in 3D-printed and bioprinted oral constructs.

Host response	Design variables	Material strategies	Target oral tissues	Regenerative outcomes	Reference
Cell adhesion and tissue infiltration	Surface topography; wettability; pore size; porosity; interconnectivity	Surface modification; interconnected porous scaffolds; ECM-like hydrogel bioinks	Gingiva; oral mucosa; alveolar and maxillofacial bone	Improved cell adhesion and migration; enhanced host-cell infiltration; establishment of a permissive environment for subsequent tissue regeneration	145,146,148
Mechanical adaptation and tissue integration	Scaffold stiffness; viscoelasticity; pore architecture; mechanical gradients; degradation-dependent mechanical changes	PCL, PEEK, or titanium structural frameworks; multimaterial and gradient constructs	Alveolar/maxillofacial bone; PDL; soft–hard tissue interfaces	Maintenance of defect space and load transfer; reduced mechanical mismatch; improved osseointegration and structural integration	121,145,149,189,198
Matrix mineralization and osteogenesis	Surface functional groups; calcium/phosphate content; ion release; mineral phase; degradation kinetics	Hydroxyapatite, β -TCP, calcium silicate, bioactive glass, and mineral-reinforced composites	Alveolar bone; maxillofacial bone; cementum	Enhanced osteogenic differentiation and mineral deposition; increased bone formation and integration with surrounding mineralized tissues	155,156,158,188,196
Immune regulation and inflammation resolution	Surface chemistry; stiffness; degradation products; bioactive ions;	Immunomodulatory bioinks; ion-containing scaffolds;	Periodontal tissues; alveolar bone; mandibular defects	Modulation of inflammatory responses toward regenerative remodeling; reduced persistent	22,157,188

Host response	Design variables	Material strategies	Target oral tissues	Regenerative outcomes	Reference
Vascularization	immunomodulatory molecules	controlled bioactive molecule delivery	Oral soft tissues; alveolar/maxillofacial bone	inflammation and improved tissue-repair environment	156,161,162,178,193
	Pore interconnectivity; matrix degradability; angiogenic cues; bioactive ion release	VEGF-containing systems; endothelial-cell-containing bioinks; Mg- or Cu-containing materials; highly interconnected scaffolds		Increased endothelial activity and vascular ingrowth; improved nutrient supply and support for subsequent tissue maturation	
Microbial balance and infection control	Surface adhesion; surface charge; antimicrobial release kinetics; anti-adhesive properties	Antibiotic delivery; antimicrobial peptides; Cu-, Zn-, or Ag-containing systems; anti-biofilm surfaces	Oral mucosa; periodontal tissues; infected mandibular defects	Reduced bacterial adhesion and biofilm formation; early infection control while maintaining host-cell compatibility and regenerative potential	55,157,164,165
Soft-tissue remodeling and barrier restoration	Bioink compliance; cell-adhesive motifs; degradation rate; growth-factor delivery	Collagen-, gelatin-, GelMA-, fibrin-, and i-PRF-containing bioinks; FGF-functionalized scaffolds	Gingiva; oral mucosa; periodontal soft tissues	Enhanced fibroblast adhesion, migration, and proliferation; improved angiogenic activity; support of epithelial and connective-tissue repair	42,187
Spatially organized soft–hard tissue regeneration	Fiber alignment; layered architecture; compositional gradients; regional	Multimaterial printing; aligned collagen/GelMA constructs; dECM-containing bioinks;	Cementum–PDL–alveolar bone complex	Guided PDL-cell alignment and matrix organization; enhanced osteogenic/cementogenic differentiation; improved	138,151,195,196

Host response	Design variables	Material strategies	Target oral tissues	Regenerative outcomes	Reference
	stiffness; spatial cell distribution	cell-patterned constructs		coordination of soft- and hard-tissue regeneration	

6. Challenges and Future Perspectives

Despite the growing promise of 3D bioprinting for oral tissue reconstruction, its translation from experimental fabrication to routine clinical application remains constrained by technical, biological, and regulatory challenges⁴¹. These limitations are particularly evident in the oral cavity, where printed constructs must withstand complex microenvironment while maintaining cell viability, structural integrity, and regenerative functionality. A major technical challenge lies in balancing printability, resolution, mechanical stability, and biological performance. In extrusion-based bioprinting¹⁹⁹, highly viscous bioinks improve shape fidelity but may generate shear stress that compromises cell survival, whereas low-viscosity bioinks are more cell-friendly but often lack post-printing stability. Similarly, stronger crosslinking can enhance mechanical robustness, yet excessive network density may restrict cell migration, nutrient diffusion, and matrix remodeling. These trade-offs are especially problematic for large bone defects and soft-hard interfaces, where constructs must simultaneously provide mechanical support, spatially organized cellular components, and tissue-specific bioactivity. Biological integration remains another critical barrier. Large 3D-printed and bioprinted constructs²⁰⁰ frequently suffer from insufficient vascularization, which limits nutrient transport, cell survival, and tissue maturation. Although angiogenic factors and vascular cell incorporation have shown potential, the coordinated regulation of vascularization, osteogenesis, innervation, and matrix remodeling remains insufficiently understood. Soft-hard tissue interfaces, such as the PDL-bone-mucosa complex^{54,201}, are even more demanding because they require region-specific mechanical, biochemical, and cellular cues to achieve stable integration under functional loading. The oral microenvironment further complicates regeneration. Persistent microbial challenge may lead to biofilm formation, chronic inflammation, and implant failure, while saliva, enzymes, and fluctuating pH can alter degradation behavior and bioactive molecule release. Mechanical stress during mastication may additionally cause material fatigue, interfacial micromotion, or structural failure. Therefore, future oral bioprinting systems should not only reproduce defect geometry, but also be designed to actively adapt to host responses and environmental stimuli.

Future development is likely to focus on multimaterial and multicellular printing^{202,203}, immune-instructive bioinks, and in situ bioprinting. Multimaterial fabrication can integrate stiff mineralized regions with softer cell-permissive hydrogel domains, thereby better mimicking the structural transitions between alveolar bone, PDL, gingiva, and oral mucosa¹⁸⁶. Multicellular printing may further enable spatial organization of stem cells, endothelial cells, fibroblasts, epithelial cells, and immune-regulatory components to promote vascularized and functionally integrated tissue formation. Immune-instructive and antimicrobial bioinks represent another important direction. Instead of merely avoiding inflammation, future materials should guide immune responses toward regeneration by promoting inflammation resolution, macrophage-mediated tissue remodeling, and balanced antimicrobial defense. In situ bioprinting may also improve anatomical adaptation by directly depositing bioactive or cell-laden materials into irregular oral and maxillofacial defects during surgery²⁰⁴. At the translational level, personalized oral bioprinting will require closer integration of medical imaging, computational design, robotic fabrication, and real-time quality

monitoring²⁰⁵. However, clinical implementation will depend on standardized manufacturing protocols, sterility control, potency testing, long-term safety evaluation, cost-effectiveness, and regulatory frameworks for personalized bioprinted products. Future studies should therefore prioritize clinically relevant large-animal models, long-term functional assessment, reproducible quality-control standards, and interdisciplinary collaboration among biomaterials scientists, clinicians, engineers, cell biologists, and regulatory specialists.

7. Conclusion

3D bioprinting provides a versatile platform for oral tissue reconstruction by enabling the spatial organization of biomaterials, cells, and bioactive cues within patient-specific constructs. Compared with conventional scaffold-based approaches, it offers greater potential to reproduce the anatomical complexity, structural heterogeneity, and biological requirements of oral soft tissues, hard tissues, and soft-hard interfaces. This review emphasizes that the performance of 3D-printed and bioprinted oral constructs should be understood from the perspective of host-material interactions, including physical, chemical and biological cues. These interactions provide a rational basis for bioink formulation, structural optimization, and bioactive functionalization. Although several technical and translational barriers remain, the field is moving toward host-instructive, multimaterial, multicellular systems. By integrating precise biofabrication with a deeper understanding of the oral microenvironment, next-generation 3D-printed and bioprinted constructs may advance oral tissue engineering from anatomical repair toward functional regeneration. Nevertheless, their clinical translation remains a future expectation rather than a currently established outcome and will require substantial additional experimental and clinical validation.

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Conflict of interest

The authors declare they have no competing interests.

Author contributions

Conceptualization: Minglang Zou, Da Huang, Wen Zhou

Methodology: Minglang Zou, Yusi Lu

Funding acquisition: Wen Zhou

Supervision: Da Huang, Wen Zhou

Visualization: Minglang Zou, Yating Li

Writing—original draft: Minglang Zou, Yating Li

Writing—review & editing: Da Huang, Wen Zhou

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Further disclosure

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References

1. Jiang Y, Li X, Li Z, Jiang H, Wang B, Xiang L. Smart stimuli-responsive biomaterials for oral and maxillofacial tissue repair and regeneration. *Chem Eng J.* 2025;524:168339. doi:10.1016/j.cej.2025.168339
2. Wu Y, Li X, Liu H, et al. Organoids in the oral and maxillofacial region: present and future. *Int J Oral Sci.* 2024;16(1):61. doi:10.1038/s41368-024-00324-w
3. Li N, Wang J, Feng G, et al. Advances in biomaterials for oral-maxillofacial bone regeneration: spotlight on periodontal and alveolar bone strategies. *Regen Biomater.* 2024;11:rbac078. doi:10.1093/rb/rbac078
4. Yu Y, Liu Z, Qin X, Song K, Xu L. Smart materials: innovative strategies for oral-maxillofacial bone defects repair. *Front Bioeng Biotechnol.* 2025;13:1629292. doi:10.3389/fbioe.2025.1629292
5. Wang P, Ye Y, Mei K, Chen B, Kankala R, Tong F. Nanoscale approaches to oro-dental tissue engineering: a review of strategies, composites, and translational challenges. *Int J Nanomedicine.* 2026;Volume 21:1-21. doi:10.2147/IJN.S575296
6. Zhao D, Xiong C, Xie L, Xiao Y. Current progress of 3D bioprinting in oral and craniomaxillofacial tissue regeneration: a systematic review. *Int J Biol Macromol.* 2026;351:151060. doi:10.1016/j.ijbiomac.2026.151060
7. Wang F, Cai X, Shen Y, Meng L. Cell–scaffold interactions in tissue engineering for oral and craniofacial reconstruction. *Bioact Mater.* 2023;23:16-44.

doi:10.1016/j.bioactmat.2022.10.029

8. Sun Z, Ma L, Sun X, Sloan AJ, O'Brien-Simpson NM, Li W. The overview of antimicrobial peptide-coated implants against oral bacterial infections. *Aggregate*. 2023;4(3):e309. doi:10.1002/agt2.309
9. Liu H, Tang Y, Zhang S, et al. Anti-infection mechanism of a novel dental implant made of titanium-copper (TiCu) alloy and its mechanism associated with oral microbiology. *Bioact Mater*. 2022;8:381-395. doi:10.1016/j.bioactmat.2021.05.053
10. Zhang S, Zhang X, Li Y, et al. Clinical reference strategy for the selection of treatment materials for maxillofacial bone transplantation: a systematic review and network meta-analysis. *Tissue Eng Regen Med*. 2022;19(3):437-450. doi:10.1007/s13770-022-00445-5
11. Stavropoulos A, Marcantonio CC, De Oliveira VXR, Marcantonio É, De Oliveira GJPL. Fresh-frozen allogeneic bone blocks grafts for alveolar ridge augmentation: biological and clinical aspects. *Periodontol 2000*. 2023;93(1):139-152. doi:10.1111/prd.12543
12. Zhan H, Shi R, Ni H, et al. Functional requirements for guided bone regeneration/guided tissue regeneration membrane design: progress and challenges. *Periodontol 2000*. Published online November 12, 2025:prd.70019. doi:10.1111/prd.70019
13. Wadhwa P, Lim HK, Jang HS, Lee ES. 3D printed patient-specific resorbable bone scaffolds for alveolar bone regeneration. *Tissue Eng Regen Med*. 2026;23(1):85-106. doi:10.1007/s13770-025-00773-2
14. Davidopoulou S, Karakostas P, Batas L, et al. Multidimensional 3D-printed scaffolds and regeneration of intrabony periodontal defects: a systematic review. *J Funct Biomater*. 2024;15(2):44. doi:10.3390/jfb15020044
15. Dai Y, Wang P, Mishra A, et al. 3D bioprinting and artificial intelligence-assisted biofabrication of personalized oral soft tissue constructs. *Adv Healthc Mater*. 2025;14(13):2402727. doi:10.1002/adhm.202402727
16. Van Hede D, Liang B, Anania S, et al. 3D-printed synthetic hydroxyapatite scaffold with In silico optimized macrostructure enhances bone formation In vivo. *Adv Funct Mater*. 2022;32(6):2105002. doi:10.1002/adfm.202105002
17. Bu L, Wei X, Zhang Y, et al. Gradient 3D printed PEEK with nano-coating facilitates rapid manufacturing with dual enhanced osteogenic and anti-bacterial property. *Mater Today Bio*. 2025;35:102432. doi:10.1016/j.mtbio.2025.102432
18. Smirani R, Médina C, Becker J, et al. In vivo vessel connection of pre-vascularised 3D-bioprinted gingival connective tissue substitutes. *Biofabrication*. 2025;17(2):025009. doi:10.1088/1758-5090/adac90
19. Yu GT, Zhu WX, Zhao YY, et al. 3D-printed bioink loading with stem cells and cellular vesicles for periodontitis-derived bone defect repair. *Biofabrication*. 2024;16(2):025007.

doi:10.1088/1758-5090/ad2081

20. Mostafavi Moghaddam SA, Mojtahedi H, Bahador A, Kamali Hakim L, Tebyaniyan H. Three-dimensional printing and personalized bioceramic scaffolds for dental and maxillofacial applications: a narrative review. *Dent J.* 2026;14(4):237. doi:10.3390/dj14040237
21. Woo HN, Cho YJ, Tarafder S, Lee CH. The recent advances in scaffolds for integrated periodontal regeneration. *Bioact Mater.* 2021;6(10):3328-3342. doi:10.1016/j.bioactmat.2021.03.012
22. Cunha DM, Santana AP, Pereira MMA, et al. Immunoinflammatory mechanisms and biocompatibility of bioactive dental biomaterials: from fundamental insights to clinical translation. *Adv Healthc Mater.* 2026;15(27):e71335. doi:10.1002/adhm.71335
23. Obregon F, Vaquette C, Ivanovski S, Hutmacher DW, Bertassoni LE. Three-dimensional bioprinting for regenerative dentistry and craniofacial tissue engineering. *J Dent Res.* 2015;94(9_suppl):143S-152S. doi:10.1177/0022034515588885
24. Sun J, Feng T, Jiang J, et al. Functional bioinks for dental tissue engineering: design principles, mechanisms, and applications. *Adv Eng Mater.* Published online May 5, 2026:e202600013. doi:10.1002/adem.202600013
25. Cui C, Yan J, Zhou L, et al. The next generation of dental treatments: leveraging smart-responsive nanomaterials for unique oral environments. *Mater Today Bio.* 2025;33:102057. doi:10.1016/j.mtbio.2025.102057
26. Almeida ND, Carneiro CA, De Marco AC, Porto VC, França R. 3D bioprinting techniques and bioinks for periodontal tissues regeneration—a literature review. *Biomimetics.* 2024;9(8):480. doi:10.3390/biomimetics9080480
27. Leelaponglit S, Klaisiri A, Angkananuwat C, Krajangta N. Effect of pH and temperature on the surface roughness of 3D-printed and milled dental hybrid resin–ceramic. *Polymers.* 2025;17(24):3308. doi:10.3390/polym17243308
28. Kim JH, Kim MY, Knowles JC, et al. Mechanophysical and biological properties of a 3D-printed titanium alloy for dental applications. *Dent Mater.* 2020;36(7):945-958. doi:10.1016/j.dental.2020.04.027
29. Aati S, Shrestha B, Fawzy A. Cytotoxicity and antimicrobial efficiency of ZrO₂ nanoparticles reinforced 3D printed resins. *Dent Mater.* 2022;38(8):1432-1442. doi:10.1016/j.dental.2022.06.030
30. Choi DJ, Park SJ, Gu BK, Kim YJ, Chung S, Kim CH. Effect of the pore size in a 3D bioprinted gelatin scaffold on fibroblast proliferation. *J Ind Eng Chem.* 2018;67:388-395. doi:10.1016/j.jiec.2018.07.013
31. Kwon JS, Kim JY, Mangal U, et al. Durable oral biofilm resistance of 3D-printed dental base

- polymers containing zwitterionic materials. *Int J Mol Sci.* 2021;22(1):417. doi:10.3390/ijms22010417
32. Loganathan S, Sharma G, Daskalakis E, Strafford S, Kumi Barimah E, Jha A. Ultrashort pulsed laser-assisted direct restoration of human enamel using 3D printable biocomposite. *Adv Mater Technol.* 2025;10(9):2401362. doi:10.1002/admt.202401362
 33. Ghezzi B, Artesani L, Giovati L, et al. Biological behavior of human gingival fibroblasts and formation of microbial biofilm on 3D-printed dental resin restorations. *Dent Mater.* 2025;41(10):1266-1276. doi:10.1016/j.dental.2025.07.012
 34. Shang L, Deng D, Krom BP, Gibbs S. Oral host-microbe interactions investigated in 3D organotypic models. *Crit Rev Microbiol.* 2024;50(4):397-416. doi:10.1080/1040841X.2023.2211665
 35. Atala A, ed. Introduction: 3D printing for biomaterials. *Chem Rev.* 2020;120(19):10545-10546. doi:10.1021/acs.chemrev.0c00139
 36. GhavamiNejad A, Ashammakhi N, Wu XY, Khademhosseini A. 3D bioprinting: crosslinking strategies for 3D bioprinting of polymeric hydrogels (small 35/2020). *Small.* 2020;16(35):2070195. doi:10.1002/smll.202070195
 37. Pati F, Gantelius J, Svahn HA. 3D bioprinting of tissue/organ models. *Angew Chem Int Ed.* 2016;55(15):4650-4665. doi:10.1002/anie.201505062
 38. Cai Y, Chang SY, Gan SW, Ma S, Lu WF, Yen CC. Nanocomposite bioinks for 3D bioprinting. *Acta Biomater.* 2022;151:45-69. doi:10.1016/j.actbio.2022.08.014
 39. Sfetsas T, Patsatzis S, Chioti A. A review of 3D printing techniques for bio-carrier fabrication. *J Clean Prod.* 2021;318:128469. doi:10.1016/j.jclepro.2021.128469
 40. Prados-Martin L, Tran HA, Mota C, et al. Advances in light-based 3D bioprinting. *Biofabrication.* 2026;18(3):033001. doi:10.1088/1758-5090/ae7208
 41. Zhu H, Ma H, Chen Y, Wei Y, Tang Z, Li Q. From 3D printing to 3D bioprinting: principles and applications in dentistry. *Mater Today Sustain.* 2026;34:101372. doi:10.1016/j.mtsust.2026.101372
 42. Yi K, Li Q, Lian X, Wang Y, Tang Z. Utilizing 3D bioprinted platelet-rich fibrin-based materials to promote the regeneration of oral soft tissue. *Regen Biomater.* 2022;9:rbac021. doi:10.1093/rb/rbac021
 43. Huang Y, Huang Z, Wang Q, et al. Revolutionizing oral and maxillofacial region: the promise of multiscale composite materials. *Mater Des.* 2026;268:116380. doi:10.1016/j.matdes.2026.116380
 44. Gu J, Ke Z, Pan H, et al. Hierarchical engineering scaffolds for oral and craniofacial tissue regeneration: recent advances and challenges. *Appl Mater Today.* 2025;42:102546.

doi:10.1016/j.apmt.2024.102546

45. Chen E, Wang T, Sun Z, Gu Z, Xiao S, Ding Y. Polyphenols-based intelligent oral barrier membranes for periodontal bone defect reconstruction. *Regen Biomater.* 2024;11:rbae058. doi:10.1093/rb/rbae058
46. Parisi L, Mavrogonatou E, Sculean A, Kletsas D, Degen M. Reviewing the benefits and clinical outcomes of oral fibroblasts over mesenchymal stem cells for repairing periodontal defects during or after orthodontic tooth movement. *Periodontol 2000*. Published online August 20, 2024:prd.12602. doi:10.1111/prd.12602
47. Allen BN, Wang Q, Filali Y, Worthington KS, Kacmarynski DSF. Full-thickness oral mucoperiosteal defects: challenges and opportunities. *Tissue Eng Part B Rev.* 2022;28(4):813-829. doi:10.1089/ten.teb.2021.0044
48. Wu H, Li Y, Shi L, Liu Y, Shen J. New advances in periodontal functional materials based on antibacterial, anti-inflammatory, and tissue regeneration strategies. *Adv Healthc Mater.* 2025;14(9):2403206. doi:10.1002/adhm.202403206
49. Cheng QS, Xu PY, Luo SC, Chen AZ. Advances in adhesive materials for oral and maxillofacial soft tissue diseases. *Macromol Biosci.* 2025;25(3):2400494. doi:10.1002/mabi.202400494
50. Park JH, Sagar V, Leong KW, Kim HW, Kim HS. Mechanobiological engineering strategies for oral and maxillofacial tissue regeneration. *Biomaterials.* 2026;332:124158. doi:10.1016/j.biomaterials.2026.124158
51. Hu L, Cheng D, Yuan X, et al. Engineered pre-dentin with well-aligned hierarchical mineralized collagen fibril bundles promote bio-root regeneration. *J Tissue Eng.* 2024;15:20417314241280961. doi:10.1177/20417314241280961
52. Thirumalaivasan N. Collagen-composite scaffolds for alveolar bone and dental tissue regeneration: advances in material development and clinical applications—a narrative review. *Dent J.* 2025;13(9):396. doi:10.3390/dj13090396
53. Wang H, Yang L, Huang X, et al. Cementum regeneration strategies: insights from development and periodontal microenvironment. *Front Cell Dev Biol.* 2025;13:1685609. doi:10.3389/fcell.2025.1685609
54. Liu J, Ruan J, Weir MD, et al. Periodontal bone-ligament-cementum regeneration via scaffolds and stem cells. *Cells.* 2019;8(6):537. doi:10.3390/cells8060537
55. Mark Welch JL, Ramírez-Puebla ST, Borisy GG. Oral microbiome geography: micron-scale habitat and niche. *Cell Host Microbe.* 2020;28(2):160-168. doi:10.1016/j.chom.2020.07.009
56. Toma AI, Fuller JM, Willett NJ, Goudy SL. Oral wound healing models and emerging regenerative therapies. *Transl Res.* 2021;236:17-34. doi:10.1016/j.trsl.2021.06.003

57. Tripathi S, Dash M, Chakraborty R, et al. Engineering considerations in the design of tissue specific bioink for 3D bioprinting applications. *Biomater Sci.* 2025;13(1):93-129. doi:10.1039/D4BM01192A
58. Mierzejewska ŻA, Veselinović V, Trtić N, Marin S, Borys J, Antonowicz B. Advanced biomaterials for craniofacial tissue regeneration: from fundamental mechanism to translational applications—a scoping review. *J Funct Biomater.* 2026;17(1):44. doi:10.3390/jfb17010044
59. Mohd N, Razali M, Ghazali MJ, Abu Kasim NH. Current advances of three-dimensional bioprinting application in dentistry: a scoping review. *Materials.* 2022;15(18):6398. doi:10.3390/ma15186398
60. Valot L, Martinez J, Mehdi A, Subra G. Chemical insights into bioinks for 3D printing. *Chem Soc Rev.* 2019;48(15):4049-4086. doi:10.1039/C7CS00718C
61. Adhikari J, Roy A, Das A, et al. Effects of processing parameters of 3D bioprinting on the cellular activity of bioinks. *Macromol Biosci.* 2021;21(1):2000179. doi:10.1002/mabi.202000179
62. Heid S, Boccaccini AR. Advancing bioinks for 3D bioprinting using reactive fillers: a review. *Acta Biomater.* 2020;113:1-22. doi:10.1016/j.actbio.2020.06.040
63. Yang J, He H, Li D, Zhang Q, Xu L, Ruan C. Advanced strategies in the application of gelatin-based bioink for extrusion bioprinting. *Bio-Des Manuf.* 2023;6(5):586-608. doi:10.1007/s42242-023-00236-4
64. Sawyer SW, Takeda K, Alayoubi A, et al. 3D bioprinting optimization of human mesenchymal stromal cell laden gelatin-alginate-collagen bioink. *Biomed Mater.* 2023;18(1):015016. doi:10.1088/1748-605X/aca3e7
65. Shi H, Li Y, Xu K, Yin J. Advantages of photo-curable collagen-based cell-laden bioinks compared to methacrylated gelatin (GelMA) in digital light processing (DLP) and extrusion bioprinting. *Mater Today Bio.* 2023;23:100799. doi:10.1016/j.mtbio.2023.100799
66. Diamantides N, Dugopolski C, Blahut E, Kennedy S, Bonassar LJ. High density cell seeding affects the rheology and printability of collagen bioinks. *Biofabrication.* 2019;11(4):045016. doi:10.1088/1758-5090/ab3524
67. Mitra S, Chrungoo S, Dutta R, Bharadwaj T, Verma D. Eggshell membrane incorporated gelatin-tannic acid-alginate composite bioink with tissue adhesive and antibacterial properties for skin tissue engineering. *Adv Mater Technol.* 2026;11(6):e02158. doi:10.1002/admt.202502158
68. Guo K, Wang H, Li S, et al. Collagen-based thiol–norbornene photoclick bio-ink with excellent bioactivity and printability. *ACS Appl Mater Interfaces.* 2021;13(6):7037-7050. doi:10.1021/acsami.0c16714

69. Yang X, Yao L, Sun X, Wang L, Xiao J. Low-temperature DLP 3D printing of low-concentration collagen methacryloyl for the fabrication of durable and bioactive personalized scaffolds. *Chem Eng J.* 2024;497:155650. doi:10.1016/j.cej.2024.155650
70. Yang B, Liu H, Jiang L, et al. 3D bioprinting of collagen-based materials for oral medicine. *Collagen Leather.* 2023;5(1):23. doi:10.1186/s42825-023-00129-3
71. Heo G, Noh H, Yoon D, et al. Mechanotransduction-enhanced bioconstructs fabricated using a bioink comprising collagen and omega-3 fatty acids for gingival tissue regeneration. *Theranostics.* 2025;15(13):6476-6496. doi:10.7150/thno.114503
72. Wang CY, Chiu YC, Lee AKX, Lin YA, Lin PY, Shie MY. Biofabrication of gingival fibroblast cell-laden collagen/strontium-doped calcium silicate 3D-printed Bi-layered scaffold for osteoporotic periodontal regeneration. *Biomedicines.* 2021;9(4):431. doi:10.3390/biomedicines9040431
73. Zhang Q, Nguyen PD, Shi S, Burrell JC, Cullen DK, Le AD. 3D bio-printed scaffold-free nerve constructs with human gingiva-derived mesenchymal stem cells promote rat facial nerve regeneration. *Sci Rep.* 2018;8(1):6634. doi:10.1038/s41598-018-24888-w
74. Déchelette C, Smirani R, Médina C, Naveau A. Cellularized biomaterials used as gingival connective tissue substitutes *In Vivo*: a systematic review. *Tissue Eng Part B Rev.* 2025;31(2):109-125. doi:10.1089/ten.teb.2024.0031
75. Liu P, Li Q, Yang Q, et al. Three-dimensional cell printing of gingival fibroblast/acellular dermal matrix/gelatin–sodium alginate scaffolds and their biocompatibility evaluation *in vitro*. *RSC Adv.* 2020;10(27):15926-15935. doi:10.1039/D0RA02082F
76. Asim S, Tabish TA, Liaqat U, Ozbolat IT, Rizwan M. Advances in gelatin bioinks to optimize bioprinted cell functions. *Adv Healthc Mater.* 2023;12(17):2203148. doi:10.1002/adhm.202203148
77. Dallos Ortega M, Aveyard J, Magdy Abdelgawad R, et al. Antimicrobial 3D printed gelatin scaffolds for root canal disinfection in regenerative endodontics procedures. *Biomater Sci.* 2025;13(14):3795-3813. doi:10.1039/D5BM00440C
78. Xie M, Gao Q, Zhao H, et al. Electro-assisted bioprinting of low-concentration GelMA microdroplets. *Small.* 2019;15(4):1804216. doi:10.1002/smll.201804216
79. Ying G, Jiang N, Yu C, Zhang YS. Three-dimensional bioprinting of gelatin methacryloyl (GelMA). *Bio-Des Manuf.* 2018;1(4):215-224. doi:10.1007/s42242-018-0028-8
80. Han P, Raveendran N, Liu C, et al. 3D bioprinted small extracellular vesicles from periodontal cells enhance mesenchymal stromal cell function. *Biomater Adv.* 2024;158:213770. doi:10.1016/j.bioadv.2024.213770
81. Miao G, Liang L, Li W, et al. 3D bioprinting of a bioactive composite scaffold for cell delivery in periodontal tissue regeneration. *Biomolecules.* 2023;13(7):1062.

doi:10.3390/biom13071062

82. Gomes Neto JDF, Lima TDPDL, Brand LM, et al. Recent advances in natural polymers-based hydrogels for periodontal regeneration. *Macromol Biosci.* 2026;26(5):e70194. doi:10.1002/mabi.70194
83. Denizhan D, Buke AN, Kilicarslan M, Orhan K, Erol HB, Kaskatepe B. Effect of chitosan-alginate polyelectrolyte complex formation and multilayer polymer configuration on the characteristics of 3D -printed metronidazole-loaded periodontal films. *Biopolymers.* 2026;117(4):e70107. doi:10.1002/bip.70107
84. Renn TY, Ma YR, Hsu CC, et al. Biofunctionalized 3D-printed gelatin-alginate scaffolds with arginine-glycine-aspartic acid (RGD) peptides for enhanced in vitro osteogenesis. *J Dent Sci.* 2026;21(1):484-493. doi:10.1016/j.jds.2025.10.030
85. Anderson M, Dubey N, Bogie K, et al. Three-dimensional printing of clinical scale and personalized calcium phosphate scaffolds for alveolar bone reconstruction. *Dent Mater.* 2022;38(3):529-539. doi:10.1016/j.dental.2021.12.141
86. Athirasala A, Tahayeri A, Thrivikraman G, et al. A dentin-derived hydrogel bioink for 3D bioprinting of cell laden scaffolds for regenerative dentistry. *Biofabrication.* 2018;10(2):024101. doi:10.1088/1758-5090/aa9b4e
87. Tavakoli S, Krishnan N, Mokhtari H, Oommen OP, Varghese OP. Fine-tuning dynamic cross-linking for enhanced 3D bioprinting of hyaluronic acid hydrogels. *Adv Funct Mater.* 2024;34(4):2307040. doi:10.1002/adfm.202307040
88. Zhao N, Wang Y, Qin L, Guo Z, Li D. Effect of composition and macropore percentage on mechanical and in vitro cell proliferation and differentiation properties of 3D printed HA/ β -TCP scaffolds. *RSC Adv.* 2017;7(68):43186-43196. doi:10.1039/C7RA07204J
89. Iaconisi GN, Lunetti P, Gallo N, et al. Hyaluronic acid: a powerful biomolecule with wide-ranging applications—a comprehensive review. *Int J Mol Sci.* 2023;24(12):10296. doi:10.3390/ijms241210296
90. Möro A, Samanta S, Honkamäki L, et al. Hyaluronic acid based next generation bioink for 3D bioprinting of human stem cell derived corneal stromal model with innervation. *Biofabrication.* 2023;15(1):015020. doi:10.1088/1758-5090/acab34
91. Feng Q, Li D, Li Q, et al. Assembling microgels via dynamic cross-linking reaction improves printability, microporosity, tissue-adhesion, and self-healing of microgel bioink for extrusion bioprinting. *ACS Appl Mater Interfaces.* 2022;14(13):15653-15666. doi:10.1021/acsami.2c01295
92. Bıçakçioğlu HA, Çolak G. Platelet-rich fibrin-derived extracellular vesicles: emerging biological mediators in periodontal regeneration. *Odontology.* 2026;114(3):1086-1098. doi:10.1007/s10266-025-01275-2

93. Lin HH, Chao PHG, Tai WC, Chang PC. 3D-printed collagen-based waveform microfibrinous scaffold for periodontal ligament reconstruction. *Int J Mol Sci.* 2021;22(14):7725. doi:10.3390/ijms22147725
94. Li M, Lv J, Yang Y, et al. Advances of hydrogel therapy in periodontal regeneration—a materials perspective review. *Gels.* 2022;8(10):624. doi:10.3390/gels8100624
95. Kim S, Hwangbo H, Chae S, Lee H. Biopolymers and their application in bioprinting processes for dental tissue engineering. *Pharmaceutics.* 2023;15(8):2118. doi:10.3390/pharmaceutics15082118
96. Gao B, Yao J, Wang Y, et al. Periodontal ligament stem cells-loaded photocrosslinking GelMA/PEGDA scaffolds for periodontal bone regeneration. *BMC Biotechnol.* 2026;26(1):56. doi:10.1186/s12896-026-01127-z
97. Piluso S, Skvortsov GA, Altunbek M, et al. 3D bioprinting of molecularly engineered PEG-based hydrogels utilizing gelatin fragments. *Biofabrication.* 2021;13(4):045008. doi:10.1088/1758-5090/ac0ff0
98. Pant S, Loganathan S, Valapa RB. Dual amine functionalized 3D printed polycaprolactone/mesoporous bioactive glass based composite scaffolds with improved osteogenesis characteristics. *Appl Surf Sci.* 2026;717:164798. doi:10.1016/j.apsusc.2025.164798
99. Bae KB, Kim HM, Son JW, et al. Effect of 3D-printed polycaprolactone/osteolectin scaffolds on the odontogenic differentiation of human dental pulp cells. *Biomed Mater.* 2024;19(4):045027. doi:10.1088/1748-605X/ad4ad9
100. Mousavi Nejad Z, Zamanian A, Saeidifar M, Vanaei HR, Salar Amoli M. 3D bioprinting of polycaprolactone-based scaffolds for pulp-dentin regeneration: investigation of physicochemical and biological behavior. *Polymers.* 2021;13(24):4442. doi:10.3390/polym13244442
101. Wei X, Shen J, Dai H, et al. 3D-printed PCL scaffolds functionalized with GelMA for sustained delivery of human dental follicle stem cell-derived conditioned medium in bone regeneration. *Colloids Surf B Biointerfaces.* 2026;262:115486. doi:10.1016/j.colsurfb.2026.115486
102. Stafin K, Śliwa P, Piątkowski M. Towards polycaprolactone-based scaffolds for alveolar bone tissue engineering: a biomimetic approach in a 3D printing technique. *Int J Mol Sci.* 2023;24(22):16180. doi:10.3390/ijms242216180
103. Sowmya S, Mony U, Jayachandran P, et al. Tri-layered nanocomposite hydrogel scaffold for the concurrent regeneration of cementum, periodontal ligament, and alveolar bone. *Adv Healthc Mater.* 2017;6(7):1601251. doi:10.1002/adhm.201601251
104. Zhang C, Chen Z, Liu J, et al. 3D-printed pre-tapped-hole scaffolds facilitate one-step surgery of predictable alveolar bone augmentation and simultaneous dental implantation. *Compos*

105. Jia L, Yang Z, Sun L, et al. A three-dimensional-printed SPION/PLGA scaffold for enhanced palate-bone regeneration and concurrent alteration of the oral microbiota in rats. *Mater Sci Eng C*. 2021;126:112173. doi:10.1016/j.msec.2021.112173
106. Xu CY, Zhao Y, Zhan JF, et al. Reparative effects of 3D -printed PLGA / CHA / NMZNO composite scaffolds on inflammatory periodontal bone defects in rats. *J Biomed Mater Res A*. 2026;114(1):e70001. doi:10.1002/jbma.70001
107. Chou PY, Lee D, Chen SH, Liao CT, Lo LJ, Liu SJ. 3D-printed/electrospun bioresorbable nanofibrous drug-eluting cuboid frames for repair of alveolar bone defects. *Int J Pharm*. 2022;615:121497. doi:10.1016/j.ijpharm.2022.121497
108. Feng KC, Li J, Wang L, et al. Combination of 3D printing and ALD for dentin fabrication from dental pulp stem cell culture. *ACS Appl Bio Mater*. 2021;4(10):7422-7430. doi:10.1021/acsabm.1c00577
109. Karimipour A, Mouli KVVC, Karimipour A. PCL/nano-hardystonite electrospun nanofiber coating on cellulose nanocrystal-reinforced PLA 3D-printed dental implants. *Carbohydr Polym Technol Appl*. 2026;14:101157. doi:10.1016/j.carpta.2026.101157
110. Zhang L, Dong Y, Liu Y, et al. Multifunctional hydrogel/platelet-rich fibrin/nanofibers scaffolds with cell barrier and osteogenesis for guided tissue regeneration/guided bone regeneration applications. *Int J Biol Macromol*. 2023;253:126960. doi:10.1016/j.ijbiomac.2023.126960
111. Zhao M, Geng Y, Fan S, et al. 3D printing of biological tooth with multiple ordered hierarchical structures. *Mater Today Bio*. 2025;30:101454. doi:10.1016/j.mtbio.2025.101454
112. Zhao M, Yang D, Fan S, et al. 3D-printed strong dental crown with multi-scale ordered architecture, high-precision, and bioactivity. *Adv Sci*. 2022;9(5):2104001. doi:10.1002/advs.202104001
113. Chen J, Gui X, Qiu T, et al. DLP 3D printing of high-resolution root scaffold with bionic bioactivity and biomechanics for personalized bio-root regeneration. *Biomater Adv*. 2023;151:213475. doi:10.1016/j.bioadv.2023.213475
114. He M, Zhang F, Li C, et al. Mechanical properties and oral restoration applications of 3D printed aliphatic polyester-calcium composite materials. *Alex Eng J*. 2024;88:245-252. doi:10.1016/j.aej.2024.01.042
115. Cao S, Han J, Sharma N, et al. In vitro mechanical and biological properties of 3D printed polymer composite and β -tricalcium phosphate scaffold on human dental pulp stem cells. *Materials*. 2020;13(14):3057. doi:10.3390/ma13143057
116. Jaramillo N, Moreno A, Ospina V, et al. Effect of synthesis on the antimicrobial response of β -TCP/Mg with potential applications in the regeneration of dental tissue: 3D printing of

- ceramic paste in a β -TCP/Mg/bioglass system. *Mater Lett.* 2023;350:134907. doi:10.1016/j.matlet.2023.134907
117. Zhang J, Chen Y, Xu J, Wang J, Li C, Wang L. Tissue engineering using 3D printed nano-bioactive glass loaded with NELL1 gene for repairing alveolar bone defects. *Regen Biomater.* 2018;5(4):213-220. doi:10.1093/rb/rby015
 118. Deng L, Ai L, Li R, et al. Animal experimental study on delayed implantation in a severely atrophic alveolar ridge reconstructed using a 3D-printed bioactive glass scaffold: a pilot study. *J Funct Biomater.* 2025;16(5):176. doi:10.3390/jfb16050176
 119. Zhang F, Spies BC, Willems E, et al. 3D printed zirconia dental implants with integrated directional surface pores combine mechanical strength with favorable osteoblast response. *Acta Biomater.* 2022;150:427-441. doi:10.1016/j.actbio.2022.07.030
 120. Alghauli M, Alqutaibi AY, Wille S, Kern M. 3D-printed versus conventionally milled zirconia for dental clinical applications: trueness, precision, accuracy, biological and esthetic aspects. *J Dent.* 2024;144:104925. doi:10.1016/j.jdent.2024.104925
 121. Li Z, Lu Y, Liu Q, et al. Applicative assessment of a selective laser melting 3D-printed Ti–6Al–4 V plate with a honeycomb structure in the reconstruction of a mandibular defect of a beagle dog. *ACS Biomater Sci Eng.* 2023;9(11):6472-6480. doi:10.1021/acsbiomaterials.3c00457
 122. Lee UL, Yun S, Cao HL, et al. Bioprinting on 3D printed titanium scaffolds for periodontal ligament regeneration. *Cells.* 2021;10(6):1337. doi:10.3390/cells10061337
 123. Zhao D, Dong H, Niu Y, et al. Electrophoretic deposition of novel semi-permeable coatings on 3D-printed Ti-Nb alloy meshes for guided alveolar bone regeneration. *Dent Mater.* 2022;38(2):431-443. doi:10.1016/j.dental.2021.12.026
 124. Ma Z, Wang Q, Xie W, et al. Performance of 3D printed PCL / PLGA / HA biological bone tissue engineering scaffold. *Polym Compos.* 2021;42(7):3593-3602. doi:10.1002/pc.26081
 125. Peng C, Zheng J, Chen D, et al. Response of hPDLSCs on 3D printed PCL/PLGA composite scaffolds in vitro. *Mol Med Rep.* 2018;18(2):1335-1344. doi:10.3892/mmr.2018.9076
 126. Chen RS, Hsu SH, Chang HH, Chen MH. Challenge tooth regeneration in adult dogs with dental pulp stem cells on 3D-printed hydroxyapatite/polylactic acid scaffolds. *Cells.* 2021;10(12):3277. doi:10.3390/cells10123277
 127. Mohd N, Razali M, Ghazali MJ, Abu Kasim NH. 3D-printed hydroxyapatite and tricalcium phosphates-based scaffolds for alveolar bone regeneration in animal models: a scoping review. *Materials.* 2022;15(7):2621. doi:10.3390/ma15072621
 128. Li X, Yuan Y, Liu L, et al. 3D printing of hydroxyapatite/tricalcium phosphate scaffold with hierarchical porous structure for bone regeneration. *Bio-Des Manuf.* 2020;3(1):15-29. doi:10.1007/s42242-019-00056-5

129. Jiaxiao S, Xie B, Zhu Z. Extrusion-based 3D printing of fully dense zirconia ceramics for dental restorations. *J Eur Ceram Soc.* 2023;43(3):1168-1177. doi:10.1016/j.jeurceramsoc.2022.10.076
130. Rashad A, Gomez A, Gangrade A, et al. Effect of viscosity of gelatin methacryloyl-based bioinks on bone cells. *Biofabrication.* 2024;16(4):045036. doi:10.1088/1758-5090/ad6d91
131. Zhang G, Huang L, Gao Y, Cai X. Tooth-supported 3D -printed surgical guide for titanium mesh placement in bone augmentation of the esthetic zone. *J Esthet Restor Dent.* 2026;38(2):228-237. doi:10.1111/jerd.70063
132. Xu H, Zhang Y, Zhang Y, et al. 3D bioprinting advanced biomaterials for craniofacial and dental tissue engineering – a review. *Mater Des.* 2024;241:112886. doi:10.1016/j.matdes.2024.112886
133. Wang D, Zeng J, Zhu H, et al. Extrusion bioprinting of elastin-containing bioactive double-network tough hydrogels for complex elastic tissue regeneration. *Aggregate.* 2024;5(3):e477. doi:10.1002/agt2.477
134. Lu Z, Gao W, Liu F, et al. Vat photopolymerization based digital light processing 3D printing hydrogels in biomedical fields: key parameters and perspective. *Addit Manuf.* 2024;94:104443. doi:10.1016/j.addma.2024.104443
135. Chen XB, Fazel Anvari-Yazdi A, Duan X, et al. Biomaterials / bioinks and extrusion bioprinting. *Bioact Mater.* 2023;28:511-536. doi:10.1016/j.bioactmat.2023.06.006
136. Mahadik B, Margolis R, McLoughlin S, et al. An open-source bioink database for microextrusion 3D printing. *Biofabrication.* 2023;15(1):015008. doi:10.1088/1758-5090/ac933a
137. Thattaruparambil Raveendran N, Vaquette C, Meinert C, Samuel Ipe D, Ivanovski S. Optimization of 3D bioprinting of periodontal ligament cells. *Dent Mater.* 2019;35(12):1683-1694. doi:10.1016/j.dental.2019.08.114
138. Yang X, Ma Y, Wang X, et al. A 3D-bioprinted functional module based on decellularized extracellular matrix bioink for periodontal regeneration. *Adv Sci.* 2023;10(5):2205041. doi:10.1002/advs.202205041
139. Xu D, Chen W, Lu Y, et al. 3D-printed Cu-bearing titanium alloy crowns for pediatric oral health: biocompatibility, antibacterial activity, and internal fit. *J Adv Res.* Published online December 2025. doi:10.1016/j.jare.2025.12.024
140. Levato R, Dudaryeva O, Garciamendez-Mijares CE, et al. Light-based vat-polymerization bioprinting. *Nat Rev Methods Primer.* 2023;3(1):47. doi:10.1038/s43586-023-00231-0
141. Monalisa S, Alipuor M, Paul D, et al. Transforming dental care, practice and education with additive manufacturing and 3D printing: innovations in materials, technologies, and future pathways. *Dent J.* 2025;13(12):555. doi:10.3390/dj13120555

142. Huang S, Guo F, Liu N, Hu K, Liu C. Cellular experimental study and mechanism of surface modification of 3D printed titanium materials to modulate the sealing and antimicrobial properties of oral implants. *Eur J Inflamm.* 2024;22:1721727X241252959. doi:10.1177/1721727X241252959
143. Xuan Y, Guo Y, Li L, et al. 3D-printed bredigite scaffolds with ordered arrangement structures promote bone regeneration by inducing macrophage polarization in onlay grafts. *J Nanobiotechnology.* 2024;22(1):102. doi:10.1186/s12951-024-02362-2
144. De Stefano M, Singh K, Raina A, Mohan S, Ul Haq MI, Ruggiero A. Tribocorrosion of 3D printed dental implants: an overview. *J Taibah Univ Med Sci.* 2024;19(3):644-663. doi:10.1016/j.jtumed.2024.05.004
145. Xu X, Zuo J, Zeng H, Zhao Y, Fan Z. Improving osseointegration potential of 3D printed PEEK implants with biomimetic periodontal ligament fiber hydrogel surface modifications. *Adv Funct Mater.* 2024;34(14):2308811. doi:10.1002/adfm.202308811
146. Wang X, Zhang D, Peng H, Yang J, Li Y, Xu J. Optimize the pore size-pore distribution-pore geometry-porosity of 3D-printed porous tantalum to obtain optimal critical bone defect repair capability. *Biomater Adv.* 2023;154:213638. doi:10.1016/j.bioadv.2023.213638
147. Zhang Y, Sun N, Zhu M, et al. The contribution of pore size and porosity of 3D printed porous titanium scaffolds to osteogenesis. *Biomater Adv.* 2022;133:112651. doi:10.1016/j.msec.2022.112651
148. Ma R, Liu Q, Zhou L, Wang L. High porosity 3D printed titanium mesh allows better bone regeneration. *BMC Oral Health.* 2023;23(1):6. doi:10.1186/s12903-023-02717-5
149. Steffen C, Sellenschloh K, Willsch M, et al. Patient-specific miniplates versus patient-specific reconstruction plate: a biomechanical comparison with 3D-printed plates in mandibular reconstruction. *J Mech Behav Biomed Mater.* 2023;140:105742. doi:10.1016/j.jmbbm.2023.105742
150. Snarski-Adamski A, Pieniak D, Krzysiak Z, Firlej M, Brumerčik F. Evaluation of the tribological behavior of materials used for the production of orthodontic devices in 3D DLP printing technology, due to oral cavity environmental factors. *Materials.* 2025;18(2):301. doi:10.3390/ma18020301
151. Hu X, Qiu T, Xiao Y, Wang Y, Guo W, Chen Y. DLP 3D-printed biomimetic periodontium composite with xenogenic treated dentin matrix modulates periodontal regeneration and inflammatory response. *Biomater Adv.* 2026;182:214668. doi:10.1016/j.bioadv.2025.214668
152. Batool F, Özçelik H, Stutz C, et al. Modulation of immune-inflammatory responses through surface modifications of biomaterials to promote bone healing and regeneration. *J Tissue Eng.* 2021;12:20417314211041428. doi:10.1177/20417314211041428
153. Kunrath MF, Dahlin C. The impact of early saliva interaction on dental implants and biomaterials for oral regeneration: an overview. *Int J Mol Sci.* 2022;23(4):2024.

doi:10.3390/ijms23042024

154. Kim YS, Shin YS. Surface functionalization of 3D-printed bio-inspired scaffolds for biomedical applications: a review. *Biomimetics*. 2024;9(11):703. doi:10.3390/biomimetics9110703
155. Sun X, Jiao X, Wang Z, et al. Polydopamine-coated 3D-printed β -tricalcium phosphate scaffolds to promote the adhesion and osteogenesis of BMSCs for bone-defect repair: mRNA transcriptomic sequencing analysis. *J Mater Chem B*. 2023;11(8):1725-1738. doi:10.1039/D2TB02280J
156. Jiang X, Lei L, Sun W, et al. Bioceramic scaffolds with two-step internal/external modification of copper-containing polydopamine enhance antibacterial and alveolar bone regeneration capability. *J Zhejiang Univ-Sci B*. 2024;25(1):65-82. doi:10.1631/jzus.B23d0004
157. Zhang H, Sun H, Zhang L, et al. Coaxial 3D printing scaffolds with sequential antibacterial and osteogenic functions to effectively repair infected mandibular defects. *Adv Funct Mater*. 2024;34(44):2407483. doi:10.1002/adfm.202407483
158. Ho CC, Hsu TT, Chiu YC, Lin YH, Xie PC, Wang CY. 3D-printed magnesium/strontium-co-doped calcium silicate scaffolds promote angiogenesis and bone regeneration through synergistic bioactive ion stimulation. *J Biol Eng*. 2025;19(1):58. doi:10.1186/s13036-025-00528-6
159. Santos MS, Silva JC, Carvalho MS. Hierarchical biomaterial scaffolds for periodontal tissue engineering: recent progress and current challenges. *Int J Mol Sci*. 2024;25(16):8562. doi:10.3390/ijms25168562
160. Zhou Y, Xu T, Han P, Wang C, Bartold M, Ivanovski S. Biological responses to biomaterials: mechanisms and opportunities for enhanced oral tissue regeneration. *J Periodontal Res*. Published online February 11, 2026. doi:10.1111/jre.70078
161. Hsu YJ, Wei SY, Lin TY, Fang L, Hsieh YT, Chen YC. A strategy to engineer vascularized tissue constructs by optimizing and maintaining the geometry. *Acta Biomater*. 2022;138:254-272. doi:10.1016/j.actbio.2021.11.003
162. Song Y, Hu Q, Liu S, et al. 3D printed biomimetic composite scaffolds with sequential releasing of copper ions and dexamethasone for cascade regulation of angiogenesis and osteogenesis. *Chem Eng J*. 2024;496:153662. doi:10.1016/j.cej.2024.153662
163. Chen K, Wang Y, Tang H, et al. Fabrication of a nanoscale magnesium/copper metal–organic framework on Zn-based guided bone generation membranes for enhancing osteogenesis, angiogenesis, and bacteriostasis properties. *ACS Appl Mater Interfaces*. 2024;16(5):5648-5665. doi:10.1021/acsami.3c16970
164. Sedghi L, DiMassa V, Harrington A, Lynch SV, Kapila YL. The oral microbiome: role of key organisms and complex networks in oral health and disease. *Periodontol 2000*.

2021;87(1):107-131. doi:10.1111/prd.12393

165. Chen Z, Chu Z, Jiang Y, et al. Recent advances on nanomaterials for antibacterial treatment of oral diseases. *Mater Today Bio*. 2023;20:100635. doi:10.1016/j.mtbio.2023.100635
166. Iezzi G, Zavan B, Petrini M, et al. 3D printed dental implants with a porous structure: the in vitro response of osteoblasts, fibroblasts, mesenchymal stem cells, and monocytes. *J Dent*. 2024;140:104778. doi:10.1016/j.jdent.2023.104778
167. Chen H, Wang Y, Lai Y, et al. Advances of 3D bioprinting technology for periodontal tissue regeneration. *iScience*. 2025;28(6):112532. doi:10.1016/j.isci.2025.112532
168. Geevarghese R, Żur-Pińska J, Parisi D, Włodarczyk-Biegun MK. A comprehensive protocol for hydrogel-based bioink design: balancing printability, stability, and biocompatibility. *J Mater Chem B*. 2025;13(42):13750-13768. doi:10.1039/D5TB00737B
169. Zhang W, Ye W, Yan Y. Advances in photocrosslinkable materials for 3D bioprinting. *Adv Eng Mater*. 2022;24(1):2100663. doi:10.1002/adem.202100663
170. Liu Q, Chen L, Liu H, et al. Promotion of bone defect repairs using multiscale 3D printed silk porous hydrogel scaffolds. *Acta Biomater*. 2025;198:24-36. doi:10.1016/j.actbio.2025.04.027
171. Liu H, Liu LL, Tan JH, Yan YG, Xue JB. Definition of pore size in 3D-printed porous implants: a review. *ChemBioEng Rev*. 2023;10(2):167-173. doi:10.1002/cben.202200043
172. Liu P, Li Q, Yang Q, et al. Evaluation of the effect of 3D -bioprinted gingival fibroblast-encapsulated ADM scaffolds on keratinized gingival augmentation. *J Periodontal Res*. 2023;58(3):564-574. doi:10.1111/jre.13126
173. Vahdatinia F, Hooshyarfard A, Jamshidi S, et al. 3D-printed soft membrane for periodontal guided tissue regeneration. *Materials*. 2023;16(4):1364. doi:10.3390/ma16041364
174. Chen T, Jiang Y, Huang J, et al. Integrating disease mechanisms and design strategies in gradient biomaterials for soft-hard tissue interfaces. *Adv Healthc Mater*. 2026;15(10):e04432. doi:10.1002/adhm.202504432
175. Golafshan N, Castilho M, Daghrery A, et al. Composite graded melt electrowritten scaffolds for regeneration of the periodontal ligament-to-bone interface. *ACS Appl Mater Interfaces*. 2023;15(10):12735-12749. doi:10.1021/acsami.2c21256
176. Staples R, Ivanovski S, Vaquette C. Fibre-guiding biphasic scaffold for perpendicular periodontal ligament attachment. *Acta Biomater*. 2022;150:221-237. doi:10.1016/j.actbio.2022.07.023
177. Daghrery A, Ferreira JA, De Souza Araújo IJ, et al. A highly ordered, nanostructured fluorinated CaP-coated melt electrowritten scaffold for periodontal tissue regeneration. *Adv Healthc Mater*. 2021;10(21):2101152. doi:10.1002/adhm.202101152

178. Synofzik J, Heene S, Jonczyk R, Blume C. Ink-structuring the future of vascular tissue engineering: a review of the physiological bioink design. *Bio-Des Manuf.* 2024;7(2):181-205. doi:10.1007/s42242-024-00270-w
179. Zhuang Y, Cui W. Biomaterial-based delivery of nucleic acids for tissue regeneration. *Adv Drug Deliv Rev.* 2021;176:113885. doi:10.1016/j.addr.2021.113885
180. Loukelis K, Kontogianni GI, Arango-Ospina M, et al. 3D bioprinted constructs enriched with zinc-doped bioactive glass promote antibacterial activity and osteochondral tissue regeneration. *Adv Healthc Mater.* 2026;15(10):e03186. doi:10.1002/adhm.202503186
181. Luo Y, Zhang H, Wang Z, et al. Strategic incorporation of metal ions in bone regenerative scaffolds: multifunctional platforms for advancing osteogenesis. *Regen Biomater.* 2025;12:rba068. doi:10.1093/rb/rba068
182. Zhang Q, Chen Y, Jiang Q, et al. Antimicrobial effects and mechanistic exploration of micronized mgh2 particles against common oral pathogenic bacteria. *Appl Mater Today.* 2025;42:102567. doi:10.1016/j.apmt.2024.102567
183. Jiao Y, Tay FR, Niu LN, Chen JH. Advancing antimicrobial strategies for managing oral biofilm infections. *Int J Oral Sci.* 2019;11(3):28. doi:10.1038/s41368-019-0062-1
184. Zhao F, Zhang Z, Guo W. The 3-dimensional printing for dental tissue regeneration: the state of the art and future challenges. *Front Bioeng Biotechnol.* 2024;12:1356580. doi:10.3389/fbioe.2024.1356580
185. Liu T, Li Z, Zhao L, et al. Customized design 3D printed PLGA/calcium sulfate scaffold enhances mechanical and biological properties for bone regeneration. *Front Bioeng Biotechnol.* 2022;10:874931. doi:10.3389/fbioe.2022.874931
186. Jeong HJ, Hoang LAP, Chen N, et al. Engineering soft-hard tissue interfaces in dental and craniofacial system by spatially controlled bioactivities. *Bioact Mater.* 2025;45:246-256. doi:10.1016/j.bioactmat.2024.11.030
187. Dang H, Kim BH. Effectiveness of amine plasma-functionalized 3D PLGA scaffolds immobilized with fibroblast growth factor in periodontal tissue regeneration. *Appl Surf Sci.* 2025;684:161905. doi:10.1016/j.apsusc.2024.161905
188. Hooshier MH, Ostadsharifmemar N, Javaheri T, et al. Functionalized 3D-printed scaffolds for enhanced osteogenesis and guided bone regeneration. *J Mater Chem B.* 2025;13(22):6493-6507. doi:10.1039/D4TB02788D
189. Li Y, Liu H, Wang C, et al. 3D printing titanium grid scaffold facilitates osteogenesis in mandibular segmental defects. *Npj Regen Med.* 2023;8(1):38. doi:10.1038/s41536-023-00308-0
190. Cao SS, Li SY, Geng YM, et al. Prefabricated 3D-printed tissue-engineered bone for mandibular reconstruction: a preclinical translational study in primate. *ACS Biomater Sci Eng.*

2021;7(12):5727-5738. doi:10.1021/acsbiomaterials.1c00509

191. Kang HW, Lee SJ, Ko IK, Kengla C, Yoo JJ, Atala A. A 3D bioprinting system to produce human-scale tissue constructs with structural integrity. *Nat Biotechnol.* 2016;34(3):312-319. doi:10.1038/nbt.3413
192. Wu T, Du Y, Yang B, Wang J. Three-dimensionally printed mesoporous bioactive glass for craniomaxillofacial bone regeneration: material evolution, functional mechanisms, and clinical translation. *Cell Transplant.* 2026;35:09636897261445514. doi:10.1177/09636897261445514
193. Fitzpatrick V, Martín-Moldes Z, Deck A, et al. Functionalized 3D-printed silk-hydroxyapatite scaffolds for enhanced bone regeneration with innervation and vascularization. *Biomaterials.* 2021;276:120995. doi:10.1016/j.biomaterials.2021.120995
194. Janmohammadi M, Nourbakhsh MS. Recent advances on 3D printing in hard and soft tissue engineering. *Int J Polym Mater Polym Biomater.* 2020;69(7):449-466. doi:10.1080/00914037.2019.1581196
195. De Souza Araújo IJ, Perkins RS, Ibrahim MM, Huang GTJ, Zhang W. Bioprinting PDLSC-laden collagen scaffolds for periodontal ligament regeneration. *ACS Appl Mater Interfaces.* 2024;16(44):59979-59990. doi:10.1021/acsami.4c13830
196. Mei N, Wu Y, Chen B, et al. 3D-printed mesoporous bioactive glass/GelMA biomimetic scaffolds for osteogenic/cementogenic differentiation of periodontal ligament cells. *Front Bioeng Biotechnol.* 2022;10:950970. doi:10.3389/fbioe.2022.950970
197. Ma Y, Ji Y, Zhong T, et al. Bioprinting-based PDLSC-ECM screening for in vivo repair of alveolar bone defect using cell-laden, injectable and photocrosslinkable hydrogels. *ACS Biomater Sci Eng.* 2017;3(12):3534-3545. doi:10.1021/acsbiomaterials.7b00601
198. Zhao D, Xie W, Li T, et al. New-designed 3D printed surgical guide promotes the accuracy of endodontic microsurgery: a study of 14 upper anterior teeth. *Sci Rep.* 2023;13(1):15512. doi:10.1038/s41598-023-42767-x
199. Zhang YS, Haghighiastiani G, Hübscher T, et al. 3D extrusion bioprinting. *Nat Rev Methods Primer.* 2021;1(1):75. doi:10.1038/s43586-021-00073-8
200. Pitacco P, Sadowska JM, O'Brien FJ, Kelly DJ. 3D bioprinting of cartilaginous templates for large bone defect healing. *Acta Biomater.* 2023;156:61-74. doi:10.1016/j.actbio.2022.07.037
201. Hirashima S, Ohta K, Togo A, Nakamura K ichiro. 3D mesoscopic architecture of a heterogeneous cellular network in the cementum–periodontal ligament–alveolar bone complex. *Microscopy.* 2022;71(1):22-33. doi:10.1093/jmicro/dfab051
202. Ruiz-Cantu L, Gleadall A, Faris C, Segal J, Shakesheff K, Yang J. Multi-material 3D bioprinting of porous constructs for cartilage regeneration. *Mater Sci Eng C.* 2020;109:110578. doi:10.1016/j.msec.2019.110578

203. Qin C, Ma J, Chen L, et al. 3D bioprinting of multicellular scaffolds for osteochondral regeneration. *Mater Today*. 2021;49:68-84. doi:10.1016/j.mattod.2021.04.016
204. Norahan MH, Sivarasu S, Fayzullin A, et al. Bioengineering of periodontal tissues: cell therapy and biomaterials application. *Bioengineering*. 2025;12(11):1213. doi:10.3390/bioengineering12111213
205. Nesic D, Schaefer BM, Sun Y, Saulacic N, Sailer I. 3D printing approach in dentistry: the future for personalized oral soft tissue regeneration. *J Clin Med*. 2020;9(7):2238. doi:10.3390/jcm9072238

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