Patient-specific 3D-printed biodegradable scaffolds for regenerative endodontic therapy

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Abstract

Regenerative endodontic therapy has emerged as a promising biologically based approach for restoring the vitality and function of damaged pulp–dentin tissues. However, conventional scaffold materials often lack the ability to conform precisely to the complex anatomy of individual root canal systems, limiting their regenerative potential. Patient-specific three-dimensional (3D)-printed biodegradable scaffolds represent an innovative solution by integrating advanced imaging, digital design, and additive manufacturing to produce customized constructs that closely match patient-specific anatomical features. These scaffolds provide a favorable microenvironment for stem cell attachment, proliferation, differentiation, vascularization, and controlled tissue regeneration while gradually degrading as new tissue forms. Advances in biomaterials, bioactive molecule incorporation, and scaffold surface modification have further enhanced their biological performance and clinical applicability. Despite encouraging preclinical and early clinical findings, challenges remain regarding material optimization, manufacturing standardization, cost, regulatory approval, and long-term clinical validation. Continued integration of digital dentistry, tissue engineering, and regenerative medicine is expected to accelerate the translation of personalized scaffold technologies into routine endodontic practice. Patient-specific 3D-printed biodegradable scaffolds therefore represent a significant advancement toward predictable, minimally invasive, and biologically driven regenerative endodontic treatment.

Keywords: Regenerative endodontic therapy, three-dimensional printing, 3D printing, biodegradable scaffolds, patient-specific scaffolds, tissue engineering, dental pulp regeneration, biomaterials, additive manufacturing, personalized dentistry.

I. Introduction

Regenerative endodontic therapy (RET) has transformed the management of immature permanent teeth and pulpal diseases by shifting the focus from conventional root canal obturation to the biological restoration of the pulp–dentin complex. Unlike traditional endodontic procedures that primarily eliminate infection and seal the root canal system, regenerative approaches seek to promote the regeneration of functional pulp tissue, continued root development, dentin deposition, and restoration of the tooth's sensory and defensive functions. This paradigm shift is supported by advances in tissue engineering, stem cell biology, biomaterials, and digital technologies, all of

which have expanded the possibilities for biologically based dental treatments (Rasperini et al., 2015).

The foundation of regenerative endodontics relies on the interaction of three essential components: stem cells, signaling molecules, and scaffolds. Among these, the scaffold plays a pivotal role by providing a three-dimensional framework that supports cell migration, adhesion, proliferation, differentiation, and extracellular matrix formation. Conventional scaffold materials, including blood clots, platelet concentrates, collagen matrices, and synthetic biomaterials, have demonstrated encouraging regenerative potential; however, they frequently exhibit limitations related to inconsistent architecture, inadequate mechanical properties, unpredictable degradation rates, and poor adaptation to the highly variable anatomy of individual root canal systems. These shortcomings have stimulated growing interest in developing customized scaffold systems capable of overcoming anatomical and biological constraints.

The rapid evolution of additive manufacturing, commonly referred to as three-dimensional (3D) printing, has introduced unprecedented opportunities for fabricating patient-specific biodegradable scaffolds tailored to the unique morphology of each tooth. Unlike conventional manufacturing methods, 3D printing enables precise control over scaffold geometry, pore size, porosity, internal architecture, and degradation characteristics while allowing the incorporation of bioactive molecules and cells during fabrication. Such customization enhances scaffold adaptation within the root canal system and provides an optimized microenvironment for tissue regeneration, vascularization, and neural ingrowth. Early applications of 3D-printed bioresorbable scaffolds in periodontal regeneration have demonstrated promising regenerative outcomes, supporting their broader translation into endodontic tissue engineering (Rasperini et al., 2015).

The successful fabrication of patient-specific scaffolds depends heavily on accurate digital imaging and anatomical reconstruction. Cone-beam computed tomography (CBCT) has become an indispensable imaging modality in modern endodontics because it provides high-resolution three-dimensional visualization of root canal morphology, accessory canals, periapical lesions, and complex anatomical variations that are often difficult to identify using conventional radiography. The integration of CBCT imaging with computer-aided design and computer-aided manufacturing (CAD/CAM) technologies enables clinicians to generate precise digital models from which individualized scaffolds can be designed and printed with exceptional accuracy. This digital workflow significantly enhances treatment planning and facilitates personalized regenerative procedures (Singh, 2018).

Complementing CBCT, advances in digital surface scanning and three-dimensional facial imaging technologies have further strengthened the accuracy of patient-specific treatment planning. Contemporary optical scanning systems and structured light technologies provide detailed surface information that can be integrated with volumetric imaging to improve digital modeling and prosthetic design. Such technological convergence supports the development of comprehensive

digital workflows that extend beyond restorative dentistry and orthodontics into regenerative endodontics, where anatomical precision is fundamental for scaffold fabrication and successful tissue integration (Giorgio et al., 2022).

Material selection remains one of the most critical determinants of scaffold performance. Biodegradable polymers, bioactive ceramics, composite biomaterials, and hybrid constructs are increasingly engineered to mimic the extracellular matrix while maintaining adequate mechanical strength, biocompatibility, and controlled degradation profiles. In addition to the intrinsic properties of biomaterials, surface characteristics strongly influence cellular attachment, proliferation, and tissue integration. Research investigating surface conditioning of 3D-printed dental materials has demonstrated that modifications to scaffold surfaces can significantly influence adhesive performance and biological interactions, highlighting the importance of optimizing scaffold surface properties for future regenerative applications (Dederichs et al., 2025).

Beyond scaffold design, successful regenerative outcomes are influenced by numerous patient-related factors. Systemic health, oral hygiene, nutritional status, inflammatory conditions, and behavioral habits all contribute to the healing environment. The oral microbiome plays a particularly significant role in determining regenerative success because persistent microbial imbalance can impair tissue healing and stimulate chronic inflammation. Nutritional factors also modulate immune responses and microbial ecology, emphasizing the importance of maintaining a balanced oral environment during regenerative therapy (Santonocito et al., 2022). Likewise, digital health records and predictive analytics have demonstrated increasing value in identifying patient-specific risk factors, including smoking behavior and other variables that may influence healing potential and treatment outcomes, thereby facilitating more personalized clinical decision-making (Patel et al., 2018).

Artificial intelligence, predictive modeling, and data-driven clinical decision support are also emerging as valuable adjuncts in personalized dental care. Predictive algorithms capable of estimating postoperative complications and treatment prognosis illustrate how patient-specific clinical variables may be incorporated into individualized treatment planning. Although these predictive models have been primarily developed for implant dentistry, similar analytical approaches may eventually support regenerative endodontic therapy by optimizing patient selection, risk stratification, and long-term outcome prediction (Feher et al., 2020).

Collectively, patient-specific 3D-printed biodegradable scaffolds represent a major advancement in regenerative endodontic therapy by integrating digital imaging, biomaterial science, tissue engineering, and precision manufacturing into a personalized treatment paradigm. As research continues to refine scaffold materials, fabrication techniques, biological functionalization, and digital workflows, customized biodegradable scaffolds are expected to play an increasingly important role in achieving predictable regeneration of the pulp–dentin complex while supporting the broader evolution of personalized dentistry.

II. Foundations of Patient-Specific 3D-Printed Biodegradable Scaffolds

2.1 Regenerative Endodontic Therapy

Regenerative endodontic therapy (RET) is a biologically based treatment strategy that aims to restore the vitality and function of the pulp–dentin complex by promoting tissue regeneration rather than merely replacing lost tissue with inert filling materials. Unlike conventional root canal therapy, which focuses primarily on eliminating infection and obturating the canal space, RET seeks to regenerate functional pulp tissue through the coordinated interaction of stem cells, signaling molecules, and scaffold biomaterials. This tissue engineering paradigm has significantly transformed contemporary endodontics by offering the possibility of continued root development, reinforcement of dentinal walls, and restoration of pulpal immune and sensory functions.

The biological foundation of RET is based on the tissue engineering triad consisting of stem cells, bioactive signaling molecules, and a suitable scaffold. Stem cells derived from the apical papilla, dental pulp, periodontal ligament, and bone marrow possess remarkable regenerative potential when provided with an appropriate microenvironment. Growth factors released from dentin matrix or incorporated into scaffold materials stimulate cellular proliferation, migration, angiogenesis, and differentiation, while biodegradable scaffolds provide the three-dimensional structural framework required for tissue organization and extracellular matrix deposition (Rasperini et al., 2015).

Clinical regenerative procedures have traditionally relied on naturally formed blood clots, platelet-rich plasma, or platelet-rich fibrin as biological scaffolds. Although these approaches have demonstrated encouraging clinical outcomes, they present considerable variability in scaffold architecture, degradation behavior, and biological performance. The inability to control scaffold geometry, pore size, mechanical stability, and degradation kinetics has motivated the development of customized biomaterial-based scaffolds fabricated through additive manufacturing technologies.

Patient-specific scaffolds are designed to replicate the unique anatomical characteristics of each individual's root canal system. Such personalization improves scaffold adaptation within irregular canal spaces, enhances cell retention, facilitates vascular ingrowth, and supports more predictable tissue regeneration. Consequently, regenerative endodontics has increasingly embraced digital workflows integrating advanced imaging, computer-aided design (CAD), and three-dimensional (3D) printing technologies to fabricate individualized biodegradable scaffolds capable of overcoming many of the limitations associated with conventional regenerative materials (Singh, 2018; Rasperini et al., 2015).

2.2 Three-Dimensional Printing Technologies in Dentistry

Three-dimensional printing, also known as additive manufacturing, refers to the layer-by-layer fabrication of objects directly from digital models. Within dentistry, additive manufacturing has revolutionized prosthodontics, orthodontics, implantology, maxillofacial surgery, and increasingly, regenerative endodontics. The ability to produce customized structures with high dimensional accuracy has enabled clinicians and researchers to fabricate scaffolds that closely mimic the complex internal architecture of root canal systems.

The digital workflow generally begins with acquisition of high-resolution anatomical information using cone-beam computed tomography (CBCT) or other three-dimensional imaging modalities. CBCT provides accurate visualization of root canal morphology, accessory canals, apical anatomy, and surrounding periapical tissues, thereby facilitating precise scaffold design and individualized treatment planning (Singh, 2018). Digital reconstruction software converts imaging datasets into three-dimensional virtual models, allowing computer-aided design software to generate scaffold geometries that conform closely to patient anatomy.

Several additive manufacturing technologies have demonstrated applicability in regenerative dentistry.

Stereolithography (SLA) utilizes photopolymerization of liquid resins by ultraviolet lasers to fabricate highly accurate structures with smooth surface finishes. SLA provides excellent dimensional precision, making it suitable for producing intricate scaffold architectures required for dental applications.

Digital Light Processing (DLP) employs projected light patterns to polymerize entire resin layers simultaneously, resulting in faster production while maintaining high printing resolution. DLP has become increasingly popular in dentistry due to its efficiency and reproducibility.

Fused Deposition Modeling (FDM) fabricates objects through extrusion of thermoplastic polymers. Although FDM offers relatively lower resolution than resin-based technologies, it remains attractive because of its affordability and compatibility with several biodegradable polymers used in tissue engineering.

Extrusion-based bioprinting represents one of the most promising techniques for regenerative medicine. This technology enables simultaneous deposition of biomaterials, living cells, growth factors, and hydrogels, allowing fabrication of biologically active scaffolds that better replicate native tissue environments.

Advances in material processing have also improved the mechanical integrity and surface characteristics of printed dental biomaterials. Surface conditioning techniques have demonstrated the ability to enhance adhesion properties of printed resins, suggesting that similar modifications may improve cellular attachment and biological integration of regenerative scaffolds (Dederichs et al., 2025).

Beyond fabrication, digital dentistry increasingly incorporates advanced three-dimensional facial scanning technologies for comprehensive treatment planning. Although primarily applied in orthodontics and prosthodontics, modern structured-light scanning systems demonstrate the expanding role of digital acquisition technologies within personalized dental care and multidisciplinary treatment workflows (Giorgio et al., 2022).

2.3 Patient-Specific Design Concept

The defining characteristic of patient-specific biodegradable scaffolds is their customization according to individual anatomical and biological requirements. Rather than utilizing standardized scaffold designs, patient-specific fabrication creates constructs tailored to the dimensions, morphology, and regenerative needs of each root canal system.

The process begins with detailed anatomical assessment using CBCT imaging. Three-dimensional datasets enable accurate visualization of canal curvature, internal diameter, apical foramen dimensions, and areas of structural deficiency. These images are segmented using specialized software to generate digital models that accurately reproduce the patient's internal dental anatomy (Singh, 2018).

Computer-aided design software subsequently converts these anatomical reconstructions into scaffold models with predetermined architectural characteristics including pore size, pore interconnectivity, internal channels, wall thickness, and degradation profiles. These design parameters are optimized to promote nutrient diffusion, vascular infiltration, stem cell migration, and mechanical stability while ensuring gradual scaffold degradation as regenerated tissue develops.

The incorporation of patient-specific clinical information may further improve scaffold design. Digital health records containing demographic characteristics, systemic health conditions, smoking habits, and behavioral risk factors provide valuable data that can support individualized treatment planning. Integration of electronic dental records has demonstrated considerable potential for patient classification and personalized clinical decision-making, suggesting opportunities for future data-driven scaffold optimization (Patel et al., 2018).

Similarly, predictive modeling has become increasingly important in personalized dentistry. Machine learning algorithms and clinical prediction models have shown effectiveness in estimating treatment outcomes and identifying patients at increased risk of postoperative complications. Such predictive approaches may eventually assist clinicians in selecting scaffold materials, biological additives, and regenerative strategies tailored to individual patient profiles (Feher et al., 2020).

Personalized scaffold fabrication also allows optimization of biomechanical properties. Internal architecture may be adjusted according to root dimensions, expected functional loading, and

Table 1. Comparison of Major Three-Dimensional Printing Technologies Used for Fabricating Biodegradable Dental Scaffolds

Technology	Working Principle	Common Biomaterials	Major Advantages	Principal Limitations	Potential Application in Regenerative Endodontics
Stereolithography (SLA)	Ultraviolet laser polymerizes liquid resin layer-by-layer	Photopolymerizable biodegradable resins	Excellent dimensional accuracy, smooth surface finish, intricate scaffold architecture	Limited material selection and post-processing requirements	Customized root canal scaffolds with precise anatomical adaptation (Singh, 2018; Dederichs et al., 2025)
Digital Light Processing (DLP)	Entire resin layer polymerized using projected light	Light-curable biodegradable resins	Rapid fabrication, high resolution, reproducibility	Resin viscosity limitations and material cost	Patient-specific scaffold fabrication for complex canal morphology (Dederichs et al., 2025)
Fused Deposition Modeling (FDM)	Extrusion of thermoplastic filament through heated nozzle	Polycaprolactone (PCL), polylactic acid (PLA), PLGA	Cost-effective, simple operation, biodegradable polymer compatibility	Lower printing resolution and rougher surface finish	Fabrication of mechanically stable biodegradable scaffolds (Rasperini et al., 2015)
Extrusion-Based Bioprinting	Layered deposition of bioinks containing cells and biomaterials	Hydrogels, collagen, gelatin, alginate, cell-laden bioinks	Simultaneous incorporation of living cells and growth factors, highly biomimetic	Technical complexity, reduced mechanical strength, sterility challenges	Bioactive scaffolds supporting pulp tissue regeneration and vascularization (Rasperini et al., 2015)
Hybrid Additive Manufacturing	Combination of multiple printing technologies	Composite biomaterials integrating polymers and bioactive ceramics	Tailored mechanical and biological performance, multifunctional scaffold design	High equipment cost and workflow complexity	Next-generation personalized regenerative endodontic scaffolds integrating structural and biological functions (Rasperini et al., 2015; Dederichs et al., 2025)

desired degradation rate. The resulting constructs exhibit improved adaptation within root canal spaces while minimizing dead space and maximizing regenerative efficiency.

The convergence of advanced imaging, digital modeling, biomaterial science, and additive manufacturing has therefore established a comprehensive digital workflow capable of producing individualized biodegradable scaffolds specifically designed for regenerative endodontic therapy. This patient-centered approach represents a significant advancement over conventional scaffold systems by combining anatomical precision with biological functionality.

Overall, the foundation of patient-specific 3D-printed biodegradable scaffolds lies in the integration of regenerative biology, advanced diagnostic imaging, digital design, and additive manufacturing. Collectively, these technologies enable the production of anatomically accurate, biologically compatible, and functionally optimized scaffolds that have the potential to enhance the predictability and long-term success of regenerative endodontic therapy while supporting the broader transition toward precision and personalized dental care.

III. Biomaterials and Biological Considerations

3.1 Biodegradable Materials for Endodontic Scaffolds

The success of regenerative endodontic therapy (RET) relies heavily on the selection of an appropriate scaffold material capable of supporting cell attachment, proliferation, differentiation, and extracellular matrix formation while gradually degrading as new tissue develops. Patient-specific three-dimensional (3D)-printed biodegradable scaffolds have expanded the possibilities of regenerative dentistry by enabling customized constructs that conform precisely to the anatomical complexity of individual root canal systems. Unlike conventional scaffolds, these personalized biomaterials are designed to provide temporary structural support while promoting biological healing and minimizing the need for secondary surgical removal.

Biodegradable scaffold materials used in regenerative endodontics are generally categorized into natural polymers, synthetic polymers, composite biomaterials, and bioactive ceramic-based materials. Each category possesses unique biological and mechanical characteristics that influence tissue regeneration, degradation kinetics, and clinical performance.

Natural polymers, including collagen, gelatin, fibrin, hyaluronic acid, alginate, chitosan, and silk fibroin, closely resemble the extracellular matrix (ECM), making them highly favorable for supporting stem cell adhesion and proliferation. Their excellent biocompatibility facilitates angiogenesis and odontogenic differentiation, although their relatively poor mechanical stability and rapid degradation often necessitate reinforcement with synthetic materials. Natural polymers

also serve as effective carriers for growth factors and signaling molecules involved in pulp regeneration (Rasperini et al., 2015).

Synthetic biodegradable polymers such as polycaprolactone (PCL), polylactic acid (PLA), polyglycolic acid (PGA), poly(lactic-co-glycolic acid) (PLGA), and polyethylene glycol (PEG)-based hydrogels offer superior mechanical strength, predictable degradation profiles, and excellent printability. These materials are particularly suitable for additive manufacturing because they maintain dimensional accuracy during fabrication while allowing customization of scaffold porosity and architecture. Their degradation rates can be modified according to the expected pace of tissue regeneration, making them highly adaptable for patient-specific regenerative applications (Rasperini et al., 2015).

Composite biomaterials combine natural and synthetic polymers to exploit the advantages of both material classes. Incorporation of hydroxyapatite, β-tricalcium phosphate, bioactive glass, or calcium phosphate nanoparticles improves osteoconductivity, mechanical stability, and mineralization potential. Composite scaffolds also exhibit enhanced resistance to deformation while maintaining favorable biological properties, thereby supporting dentin-pulp complex regeneration.

Bioactive ceramics contribute additional regenerative capabilities by releasing calcium and phosphate ions that stimulate mineralized tissue formation. Although ceramics alone are brittle and difficult to fabricate into complex anatomical structures, their integration with biodegradable polymers produces mechanically stable scaffolds capable of supporting both hard and soft tissue regeneration.

Recent advances in additive manufacturing have also enabled the fabrication of multi-material scaffolds possessing spatially controlled mechanical properties and biological functionality. These hybrid constructs allow different regions of the scaffold to mimic native tissue characteristics more accurately, thereby improving regenerative outcomes.

3.2 Biological Properties Required for Regenerative Endodontic Therapy

The biological success of patient-specific biodegradable scaffolds depends not only on their material composition but also on several critical biological characteristics that influence tissue regeneration.

Biocompatibility remains the most essential requirement. Scaffold materials should not elicit significant inflammatory or immunological reactions while providing a favorable environment for stem cells from the apical papilla (SCAP), dental pulp stem cells (DPSCs), periodontal ligament

stem cells, and endothelial progenitor cells. High biocompatibility promotes rapid cellular colonization and supports long-term tissue integration.

Controlled biodegradation is equally important. The degradation rate should closely correspond with the rate of new tissue formation so that the scaffold gradually transfers mechanical function to regenerating tissues without leaving harmful degradation products. Excessively rapid degradation may compromise structural integrity, whereas delayed degradation could interfere with normal tissue remodeling.

Mechanical stability allows scaffolds to maintain their three-dimensional architecture during the early stages of healing. Although root canals are not subjected to heavy functional loading, scaffolds should possess sufficient compressive strength to preserve their internal pore structure and resist collapse during implantation.

Interconnected porosity plays a fundamental role in nutrient diffusion, oxygen transport, vascular ingrowth, and waste removal. Large interconnected pores facilitate angiogenesis and allow migration of progenitor cells throughout the scaffold. Advances in 3D printing enable precise control of pore size, orientation, and distribution, producing scaffolds that closely mimic the natural extracellular matrix.

Surface chemistry and topography significantly influence cellular behavior. Surface roughness, wettability, and chemical composition regulate protein adsorption, cell attachment, proliferation, and differentiation. Surface modification techniques have therefore become increasingly important for improving scaffold performance. Investigations into surface conditioning of 3D-printed dental materials have demonstrated that optimized surface treatments substantially improve adhesive interactions and biological compatibility, supporting broader applications of additive manufacturing within regenerative dentistry (Dederichs et al., 2025).

In addition, patient-specific scaffold design benefits from high-resolution digital imaging technologies such as cone-beam computed tomography (CBCT), which provide detailed anatomical information for precise scaffold fabrication. Accurate imaging minimizes dimensional discrepancies and improves adaptation of customized scaffolds within irregular root canal systems (Singh, 2018).

3.3 Biofunctionalization Strategies

Modern regenerative scaffolds are no longer viewed as passive structural supports but rather as biologically active platforms capable of directing tissue regeneration.

Growth factor incorporation represents one of the most widely investigated biofunctionalization strategies. Bioactive molecules including vascular endothelial growth factor (VEGF), bone morphogenetic proteins (BMPs), transforming growth factor-beta (TGF-β), platelet-derived

growth factor (PDGF), and fibroblast growth factors (FGFs) stimulate angiogenesis, stem cell recruitment, odontoblastic differentiation, and extracellular matrix deposition. Controlled-release systems incorporated within biodegradable scaffolds enable sustained delivery of these signaling molecules during healing.

Table 2. Biodegradable Biomaterials Used for Patient-Specific Regenerative Endodontic Scaffolds and Their Biological Characteristics

Material Category	Representative Materials	Major Biological Advantages	Limitations	Potential Applications in RET
Natural polymers	Collagen, gelatin, fibrin, chitosan, alginate, hyaluronic acid	Excellent biocompatibility, promotes cell adhesion, angiogenesis, ECM mimicry	Low mechanical strength, rapid degradation	Dental pulp regeneration, growth factor delivery
Synthetic polymers	PCL, PLA, PGA, PLGA, PEG hydrogels	Controlled degradation, excellent printability, mechanical stability	Lower intrinsic bioactivity	Customized patient-specific scaffold fabrication
Composite biomaterials	Polymer-ceramic composites, polymer-hydroxyapatite composites	Combines mechanical strength with biological activity	More complex manufacturing	Dentin-pulp complex regeneration
Bioactive ceramics	Hydroxyapatite, β-TCP, bioactive glass, calcium phosphate	Mineralization, osteoconductivity, ion release	Brittleness, limited flexibility	Hard tissue regeneration and mineralized barrier formation
Hybrid multi-material scaffolds	Polymer–ceramic–hydrogel combinations	Personalized architecture, optimized biological and mechanical performance	Higher fabrication cost and complexity	Advanced patient-specific regenerative endodontic therapy

3.4 Interaction Between Scaffold, Oral Microbiome and Host Tissue

Stem cell loading further enhances regenerative potential. Autologous dental pulp stem cells, stem cells from the apical papilla, bone marrow-derived mesenchymal stem cells, and induced

pluripotent stem cells have all demonstrated promising regenerative capabilities when seeded onto biodegradable scaffolds. Customized scaffold architecture promotes uniform cell distribution while supporting long-term cell survival.

Antimicrobial modification has become increasingly important due to the polymicrobial nature of endodontic infections. Incorporation of silver nanoparticles, antimicrobial peptides, chlorhexidine, calcium hydroxide, bioactive glass particles, and antibiotic-loaded microspheres provides localized antimicrobial activity without significantly impairing host cell viability.

Surface engineering techniques including plasma treatment, ultraviolet irradiation, laser modification, chemical etching, and bioactive peptide coating improve scaffold hydrophilicity and increase protein adsorption, thereby enhancing cell attachment and differentiation. Research evaluating surface conditioning of 3D-printed dental materials has highlighted the importance of optimizing scaffold surfaces to improve biological interactions and mechanical performance (Dederichs et al., 2025).

Successful regeneration requires continuous interaction among the scaffold, host tissues, immune system, and resident oral microbiota. Persistent microbial contamination within the root canal system remains one of the principal obstacles to regenerative success because bacterial biofilms can induce chronic inflammation, inhibit stem cell differentiation, and impair vascularization.

Biodegradable scaffolds influence local immune responses by regulating macrophage polarization, cytokine release, and inflammatory resolution. An ideal scaffold promotes a transition from a pro-inflammatory environment toward a regenerative phenotype characterized by increased angiogenesis, collagen synthesis, and odontoblast differentiation.

Emerging evidence indicates that nutritional status and the composition of the oral microbiome also influence regenerative outcomes. Dietary factors modulate microbial ecology, host immune responses, and inflammatory pathways, all of which affect tissue healing. Maintenance of microbial homeostasis through appropriate infection control and nutritional support may therefore enhance scaffold-mediated regeneration and improve long-term treatment outcomes (Santonocito et al., 2022).

Patient-related systemic factors likewise contribute to regenerative success. Electronic dental records have facilitated identification of behavioral risk factors such as smoking, which negatively influences tissue vascularization and healing capacity. Integration of patient-specific health information into treatment planning may improve case selection and regenerative outcomes (Patel et al., 2018). Furthermore, predictive clinical models developed for dental implant therapy illustrate how individualized risk assessment can assist clinicians in anticipating postoperative complications and optimizing personalized regenerative protocols (Feher et al., 2020).

Overall, the convergence of advanced biomaterials, biofunctionalization strategies, patient-specific digital imaging, and individualized biological assessment has positioned 3D-printed biodegradable scaffolds as one of the most promising technologies for achieving predictable and biologically driven regenerative endodontic therapy (Singh, 2018; Rasperini et al., 2015; Dederichs et al., 2025).

Clinical Applications, Advantages, Challenges and Future Perspectives

4.1 Clinical Workflow for Patient-Specific Scaffold Fabrication

The clinical translation of patient-specific three-dimensional (3D)-printed biodegradable scaffolds for regenerative endodontic therapy (RET) relies on an integrated digital workflow that combines advanced imaging, computer-aided design (CAD), additive manufacturing, and biological principles of tissue regeneration. The process begins with comprehensive clinical and radiographic examination, followed by cone-beam computed tomography (CBCT), which provides detailed three-dimensional visualization of the pulp space, root canal morphology, dentinal thickness, and periapical tissues. Compared with conventional radiography, CBCT significantly improves diagnostic accuracy and facilitates precise treatment planning for complex endodontic cases (Singh, 2018).

Following image acquisition, digital segmentation software is used to reconstruct the patient's root canal anatomy into a virtual three-dimensional model. Computer-aided design enables clinicians and engineers to customize scaffold dimensions, internal pore architecture, porosity, and degradation characteristics according to the anatomical and biological requirements of individual teeth. This personalized approach minimizes dimensional discrepancies commonly associated with prefabricated scaffolds and maximizes contact between the scaffold and host tissues.

The finalized digital model is transferred to an appropriate 3D-printing platform, where biodegradable biomaterials are fabricated into patient-specific scaffolds. Depending on material composition and intended application, post-processing procedures such as cleaning, curing, sterilization, and surface conditioning may be required before clinical use. Surface modification techniques have demonstrated improvements in bonding characteristics and biological performance of printed materials, providing valuable insights into optimizing scaffold integration within dental tissues (Dederichs et al., 2025).

During regenerative treatment, following canal disinfection and induction of intracanal bleeding or incorporation of stem cells and bioactive molecules, the customized scaffold is positioned within the root canal space to provide structural support for cell migration, vascular ingrowth, and

extracellular matrix deposition. As tissue regeneration progresses, the biodegradable scaffold gradually resorbs while being replaced by newly formed pulp-like tissue and dentin.

4.2 Current and Potential Clinical Applications

Patient-specific biodegradable scaffolds have broadened the therapeutic possibilities of regenerative endodontics by providing customized biological templates that accommodate anatomical variations and optimize tissue regeneration. Their applications extend beyond conventional regenerative procedures and include several challenging clinical scenarios.

One of the primary indications is the treatment of immature permanent teeth with necrotic pulps. In these teeth, continued root maturation is essential to improve dentinal wall thickness, root length, and apical closure. Customized scaffolds can precisely occupy the enlarged canal space while providing an environment conducive to stem cell recruitment, angiogenesis, and continued tissue development.

Scaffold technology also offers significant advantages for dental pulp regeneration following traumatic injuries or extensive carious lesions. By supporting stem cell proliferation and differentiation, these constructs facilitate regeneration of pulp-like connective tissue rather than merely forming calcified repair tissue.

Complex canal morphologies, including teeth with internal resorption, developmental anomalies, or irregular canal anatomy, may particularly benefit from patient-specific scaffold fabrication. Digital customization enables scaffolds to conform closely to intricate canal geometries that would be difficult to manage using conventional biomaterials.

Large periapical lesions requiring regenerative management also represent promising applications. Customized biodegradable scaffolds may assist in directing tissue healing while supporting vascular and neural regeneration within the canal system. Although most current evidence originates from laboratory and animal studies, experiences from periodontal tissue engineering demonstrate the feasibility of customized bioresorbable scaffolds in promoting organized regeneration of mineralized and soft tissues, providing an encouraging translational foundation for endodontic applications (Rasperini et al., 2015).

Beyond regenerative endodontics, advances in three-dimensional facial scanning and digital anatomical reconstruction continue to improve personalization across dentistry. These developments complement CBCT-based planning by facilitating accurate digital workflows that enhance individualized treatment design (Giorgio et al., 2022).

4.3 Advantages Over Conventional Scaffolds

Patient-specific 3D-printed biodegradable scaffolds provide numerous advantages compared with conventional scaffold materials currently used in regenerative endodontic therapy.

The most important advantage is anatomical customization. Traditional scaffolds, including blood clots, platelet concentrates, collagen matrices, and synthetic plugs, often fail to conform precisely to irregular canal configurations. Customized scaffolds eliminate this limitation by reproducing patient-specific canal morphology obtained through digital imaging, thereby maximizing scaffold adaptation and tissue contact.

Another major advantage is the ability to control scaffold architecture. Parameters such as pore size, pore interconnectivity, mechanical strength, degradation rate, and overall geometry can be optimized according to biological requirements. Such customization promotes nutrient diffusion, vascular infiltration, and stem cell migration, thereby improving the regenerative microenvironment.

Biodegradable scaffolds also eliminate the need for surgical retrieval after tissue healing. As degradation occurs in a controlled manner, the scaffold is gradually replaced by newly regenerated tissues, reducing long-term foreign body reactions.

The incorporation of bioactive molecules, stem cells, antimicrobial agents, and growth factors further enhances regenerative efficiency. Surface engineering techniques improve cellular attachment and biomaterial performance, increasing the biological effectiveness of printed scaffolds (Dederichs et al., 2025).

Digital workflows additionally improve treatment predictability by reducing operator variability and facilitating standardized fabrication processes. High-resolution CBCT imaging significantly contributes to precise scaffold design and treatment planning (Singh, 2018).

4.4 Challenges and Limitations

Despite encouraging progress, several biological, technological, and clinical challenges continue to limit widespread clinical implementation.

Material selection remains one of the greatest obstacles. An ideal scaffold should simultaneously possess adequate mechanical stability, controlled biodegradation, excellent biocompatibility, suitable porosity, antimicrobial activity, and the capacity to support vascularization. Few currently available biomaterials satisfy all these requirements simultaneously.

Printing resolution and manufacturing precision may also influence scaffold performance. Minor inaccuracies during image segmentation or printing may compromise scaffold adaptation within narrow and complex canal systems. Maintaining structural integrity while preserving interconnected porosity remains technically demanding.

Surface characteristics significantly influence cellular attachment and tissue integration. Studies evaluating surface conditioning of printed dental materials indicate that appropriate post-processing protocols substantially improve material performance, suggesting that similar optimization strategies may benefit biodegradable endodontic scaffolds (Dederichs et al., 2025).

Clinical translation is additionally constrained by high production costs, limited availability of specialized equipment, lengthy fabrication times, and the absence of standardized manufacturing guidelines. Sterilization methods capable of preserving scaffold architecture and incorporated biological agents also require further optimization.

Another important limitation is the relatively limited number of long-term clinical investigations. Although laboratory and preclinical studies demonstrate favorable regenerative outcomes, robust randomized clinical trials with extended follow-up periods remain scarce.

Patient-related variables further influence regenerative success. Smoking status, systemic health, nutritional status, microbial composition, and inflammatory burden all affect tissue healing and regenerative outcomes. Electronic dental record analytics may facilitate improved patient stratification and individualized treatment planning by identifying risk factors associated with regenerative failure (Patel et al., 2018). Similarly, predictive models developed for implant dentistry demonstrate how digital risk assessment tools may contribute to personalized decision-making and improved treatment prognosis (Feher et al., 2020).

Moreover, host inflammatory responses and oral microbial ecology remain critical determinants of regenerative success. Emerging evidence indicates that dietary habits influence oral microbiome composition and immune regulation, potentially affecting scaffold integration and tissue healing (Santonocito et al., 2022).

4.5 Role of Artificial Intelligence and Digital Dentistry

Artificial intelligence (AI) and digital dentistry are expected to play increasingly important roles in advancing patient-specific regenerative endodontics. Machine learning algorithms integrated with CBCT imaging may automate segmentation of root canal anatomy, reducing design time while improving consistency. Automated optimization of scaffold architecture based on anatomical characteristics could further personalize regenerative treatment.

AI-assisted predictive analytics may identify patients who are most likely to benefit from regenerative procedures by integrating demographic, clinical, radiographic, and behavioral variables. Large-scale electronic dental records provide valuable datasets for developing predictive models that support evidence-based clinical decision-making (Patel et al., 2018).

Risk prediction systems already employed successfully in implant dentistry illustrate the potential for individualized prognostic assessment in regenerative endodontics. Similar predictive

algorithms could estimate treatment success, identify complications, and guide patient selection (Feher et al., 2020).

Table 3. Advantages, Challenges, and Future Perspectives of Patient-Specific 3D-Printed Biodegradable Scaffolds for Regenerative Endodontic Therapy

Aspect	Current Status	Clinical Significance	Future Perspective
Anatomical customization	Patient-specific scaffold geometry based on CBCT imaging	Improved adaptation to complex canal anatomy	Fully automated AI-assisted design workflows
Tissue regeneration	Supports stem cell migration, angiogenesis, and dentin-pulp regeneration	Enhanced biological healing	Integration with advanced stem cell therapies and bioactive molecules
Biodegradability	Scaffold gradually resorbs during tissue regeneration	Eliminates need for scaffold removal	Development of programmable degradation profiles
Digital workflow	CAD/CAM and additive manufacturing improve precision	Greater treatment predictability	Complete chairside digital manufacturing systems
Surface modification	Surface conditioning improves material performance	Enhanced cell attachment and scaffold integration	Nanoengineered multifunctional scaffold surfaces
Clinical limitations	Limited long-term human evidence, high production costs, regulatory challenges	Restricts routine clinical application	Standardized manufacturing protocols and multicenter clinical trials
Patient-specific treatment planning	Digital imaging and predictive analytics improve case selection	More personalized regenerative therapy	AI-driven clinical decision support using electronic dental records and predictive models
Biological considerations	Host immunity, nutrition, and oral microbiome influence healing	Variable regenerative outcomes among patients	Personalized regenerative strategies integrating microbiome profiling and precision medicine

Future integration of CBCT imaging, intraoral scanning, three-dimensional facial imaging, CAD software, AI-assisted planning, and high-resolution bioprinting may establish a fully digital

workflow capable of delivering highly personalized regenerative therapies. Such interdisciplinary collaboration between biomaterials science, regenerative medicine, computer engineering, and clinical dentistry is expected to accelerate the routine clinical adoption of customized biodegradable scaffolds.

Conclusion

Patient-specific three-dimensional (3D)-printed biodegradable scaffolds have emerged as one of the most promising innovations in regenerative endodontic therapy by combining advances in digital imaging, tissue engineering, biomaterials, and additive manufacturing. Unlike conventional scaffold systems, personalized scaffolds are designed to replicate the unique anatomy of individual root canal systems, thereby providing an optimized environment for stem cell attachment, proliferation, vascularization, and pulp–dentin complex regeneration. The integration of cone-beam computed tomography (CBCT) and other three-dimensional imaging modalities has significantly improved the precision of scaffold design and treatment planning, facilitating more predictable regenerative outcomes (Singh, 2018; Giorgio et al., 2022).

The evolution of biodegradable biomaterials has further strengthened the clinical potential of customized scaffolds by offering controlled degradation, favorable mechanical properties, and excellent biocompatibility. Surface modification strategies and improvements in the fabrication of 3D-printed dental materials continue to enhance scaffold performance, supporting stronger biological interactions and improved clinical durability (Dederichs et al., 2025). Previous successes achieved with bioresorbable scaffolds in periodontal tissue regeneration provide encouraging evidence that similar principles can be successfully translated to regenerative endodontics, where the restoration of pulp vitality and continued root development remain primary therapeutic objectives (Rasperini et al., 2015).

The increasing integration of digital dentistry with artificial intelligence and electronic health data also presents new opportunities for personalized treatment planning and outcome prediction. Predictive analytical models and patient-specific risk assessment using electronic dental records may enable clinicians to identify factors influencing regenerative success, optimize case selection, and improve long-term prognosis (Patel et al., 2018; Feher et al., 2020). Such data-driven approaches complement advances in scaffold fabrication by supporting individualized clinical decision-making throughout the regenerative treatment process.

Nevertheless, several challenges continue to limit widespread clinical implementation. Standardization of printing protocols, optimization of biodegradable materials, regulatory approval pathways, manufacturing costs, and the availability of long-term clinical evidence remain important considerations before routine adoption can be fully realized. In addition, successful

regeneration depends not only on scaffold design but also on the biological environment of the oral cavity, where host immune responses, nutritional status, and interactions with the oral microbiome play important roles in tissue healing and regenerative outcomes (Santonocito et al., 2022).

Overall, patient-specific 3D-printed biodegradable scaffolds represent a significant advancement toward precision regenerative endodontics. Continued collaboration among biomaterial scientists, engineers, clinicians, and digital technology specialists is expected to further refine scaffold fabrication techniques, improve biological performance, and expand clinical applications. As evidence continues to accumulate, these personalized regenerative strategies are well positioned to transform future endodontic care by promoting more predictable, biologically driven, and patient-centered treatment outcomes (Rasperini et al., 2015; Singh, 2018; Dederichs et al., 2025).

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