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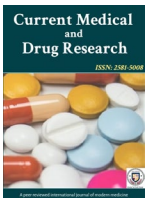

3D bioprinting of pulp tissue using dental pulp stem cells and bioactive hydrogels

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ABSTRACT

Three-dimensional (3d) bioprinting has emerged as a transformative strategy in regenerative endodontics by enabling the fabrication of biomimetic pulp tissue constructs that closely replicate the native dental pulp microenvironment. This approach combines dental pulp stem cells (dpscs), which possess high proliferative, angiogenic, neurogenic, and odontogenic potential, with bioactive hydrogels that serve as supportive bioinks for cell encapsulation and tissue development. Advances in hydrogel engineering have improved scaffold biocompatibility, printability, and biodegradability while promoting cell survival, proliferation, and differentiation into functional pulp-like tissues. Modern bioprinting technologies also allow precise spatial organization of cells and biomaterials, facilitating the formation of vascularized and structurally stable tissue constructs suitable for regenerative applications. Despite significant progress, challenges remain, including optimization of vascular integration, mechanical stability, long-term functionality, and translation from laboratory research to routine clinical practice. Continued innovations in biomaterials, biofabrication techniques, and personalized scaffold design are expected to accelerate the development of clinically applicable pulp regeneration therapies. Overall, 3d bioprinting using dental pulp stem cells and bioactive hydrogels represents a promising frontier for restoring pulp vitality, preserving natural tooth structure, and advancing minimally invasive regenerative dental treatments.

INTRODUCTION

Regenerative endodontics has evolved from conventional approaches focused primarily on infection control toward biologically driven therapies that aim to restore the structure and function of the pulp–dentin complex. Among emerging technologies, three-dimensional (3D) bioprinting has gained considerable attention because it enables the fabrication of patient-specific tissue constructs with precise spatial organization of cells, biomaterials, and bioactive molecules. By integrating dental pulp stem cells (DPSCs) with bioactive hydrogel-based bioinks, this technology offers a promising platform for regenerating functional pulp tissue while preserving the natural tooth structure (Athirasala et al., 2018).

Dental pulp stem cells possess remarkable proliferative capacity, multilineage differentiation potential, and immunomodulatory properties, making them ideal candidates for pulp tissue engineering. Bioactive hydrogels further enhance this regenerative process by providing a biomimetic extracellular matrix that supports cell adhesion, proliferation, migration, and differentiation. Dentin-derived hydrogel bioinks have demonstrated particular promise because they retain natural biochemical cues that facilitate odontogenic differentiation and vascularized tissue formation (Athirasala et al., 2018).

Table 1: missing

Component	*Biological Role*	*Contribution to Pulp Regeneration*
Dental pulp stem cells	Multipotent progenitor cells	Differentiate into odontoblasts, endothelial, and neural cells
Bioactive hydrogels	Extracellular matrix mimic	Support cell survival, proliferation, and differentiation
Dentin-derived bioink	Native dentin matrix proteins	Enhances odontogenic signaling and mineralization
Growth factors	Biological signaling molecules	Stimulate angiogenesis and tissue repair
3D bioprinting technology	Layer-by-layer fabrication	Produces patient-specific, structurally organized pulp constructs
Artificial intelligence	Digital workflow optimization	Improves scaffold design and regenerative treatment planning (Singh, 2022)

Table 2: missing

Aspect	*Current Status*	*Future Direction*
Bioinks	Natural and dentin-derived hydrogels	Smart, multifunctional hydrogels
Stem cells	DPSCs widely investigated	Gene-edited and personalized cell therapies
Bioprinting	High precision scaffold fabrication	Fully vascularized tissue constructs
Digital technologies	CBCT and AI-assisted planning	Real-time AI-guided bioprinting
Clinical translation	Limited human studies	Standardized multicenter clinical trials

Recent advances in digital dentistry, artificial intelligence, and imaging technologies have further strengthened regenerative workflows. Artificial intelligence supports treatment planning, scaffold optimization, and predictive analysis, while CBCT-based segmentation improves the accuracy of patient-specific scaffold design for tissue engineering applications (Singh, 2022; Polizzi et al., 2023). Similarly, computer vision and digital assessment methods are expanding precision diagnostics and treatment monitoring in dentistry (Feher et al., 2025). Progress in material science, including the characterization of dental biomaterials and 3D-printed restorative materials, continues to improve scaffold performance and clinical durability (Memè et al., 2021; Dederichs et al., 2025; Singh, 2025).

Despite these advances, important challenges remain, including achieving adequate vascularization, neural integration, long-term scaffold stability, and predictable clinical translation. Continued investigation into biomaterial design, cellular biology, diagnostic biomarkers, and advanced fabrication technologies is expected to accelerate the development of clinically viable pulp regeneration strategies (Taba Jr et al., 2005; Suh et al., 1996).

BIOLOGICAL BASIS AND 3D BIOPRINTING STRATEGIES

The biological success of 3D bioprinting for pulp tissue regeneration depends on the synergistic interaction between dental pulp stem cells (DPSCs), bioactive hydrogels, and advanced bioprinting technologies. DPSCs are mesenchymal stem cells isolated from the dental pulp that exhibit remarkable self-renewal capacity and the ability to differentiate into odontoblast-like, endothelial, neural, and connective tissue cells. These characteristics make DPSCs an ideal cellular source for reconstructing the pulp–dentin complex and restoring tooth vitality. Their regenerative potential is further enhanced by the secretion of angiogenic and immunomodulatory factors that promote tissue repair and vascularization (Athirasala et al., 2018).

Bioactive hydrogels serve as printable bioinks that encapsulate DPSCs while mimicking the extracellular matrix. Natural hydrogels, including collagen, gelatin methacrylate (GelMA), fibrin, alginate, and dentin-derived extracellular matrix hydrogels, provide favorable environments for cell adhesion, proliferation, and differentiation. Dentin-derived hydrogel bioinks are particularly valuable because they contain native biochemical cues that support odontogenic differentiation and extracellular matrix deposition, resulting in improved regenerative outcomes (Athirasala et al., 2018). The integration of digital technologies and artificial intelligence further enhances scaffold design, optimization, and personalized treatment planning for regenerative endodontics (Singh, 2022). Emerging additive manufacturing advances have also improved the precision and reproducibility of dental biomaterials used in tissue engineering, supporting the development of clinically relevant printed constructs (Dederichs et al., 2025).

APPLICATIONS, CHALLENGES, AND FUTURE PERSPECTIVES

Three-dimensional (3D) bioprinting of pulp tissue using dental pulp stem cells (DPSCs) and bioactive hydrogels has expanded the possibilities of regenerative endodontics by enabling the fabrication of living constructs that closely resemble the native pulp–dentin complex. Clinically, these constructs have potential applications in revitalizing necrotic immature teeth, regenerating damaged pulp tissue after trauma or deep caries, and creating patient-specific tissue substitutes for personalized dental care. Dentin-derived hydrogel bioinks have demonstrated excellent cytocompatibility and bioactivity, supporting DPSC proliferation and differentiation while promoting extracellular matrix deposition and tissue maturation (Athirasala et al., 2018). Artificial intelligence

is also expected to optimize scaffold architecture, printing precision, and treatment planning, thereby improving regenerative outcomes and workflow efficiency (Singh, 2022). Advanced digital imaging, including CBCT-based tooth segmentation, further facilitates individualized scaffold design (Polizzi et al., 2023).

Despite encouraging progress, several challenges remain before widespread clinical implementation can be achieved. Maintaining high cell viability during printing, ensuring rapid vascularization and innervation, achieving appropriate mechanical stability, and establishing standardized manufacturing protocols remain significant obstacles. Biomarker-guided monitoring may improve assessment of tissue regeneration and inflammatory responses following implantation (Taba Jr. et al., 2005). In addition, lessons from material durability studies of dental polymers and 3D-printed restorative materials may support the long-term optimization of scaffold performance (Memè et al., 2021; Dederichs et al., 2025).

Future developments may integrate computer vision for treatment monitoring, intelligent biomaterial design, and predictive analytics to improve regenerative success (Feher et al., 2025; Singh, 2022). Although unrelated to regenerative dentistry, advances in material engineering reported by Suh et al. (1996) illustrate how interdisciplinary innovations may inspire future biofabrication technologies. Likewise, continuing improvements in restorative biomaterials provide complementary insights into dental material performance and clinical durability (Singh, 2025).

CONCLUSION

Three-dimensional bioprinting of pulp tissue using dental pulp stem cells (DPSCs) and bioactive hydrogels represents a major advancement in regenerative endodontics, offering the potential to restore the biological function of the pulp–dentin complex rather than merely replacing lost tissue. The combination of highly regenerative DPSCs with biomimetic hydrogel bioinks has demonstrated encouraging outcomes in supporting cell viability, proliferation, differentiation, and extracellular matrix deposition, thereby creating an environment conducive to functional tissue regeneration (Athirasala et al., 2018). Continued improvements in bioink composition, scaffold architecture, and printing precision are expected to further enhance the structural and biological performance of engineered pulp tissues.

The integration of emerging digital technologies, including artificial intelligence and advanced imaging, is expected to improve patient-specific scaffold design, treatment planning, and prediction of regenerative outcomes, thereby increasing the precision and efficiency of clinical applications (Singh, 2022; Polizzi et al., 2023; Feher et al., 2025). Moreover, developments in additive manufacturing and material engineering continue to strengthen the reliability and durability of printed dental constructs, supporting broader applications of three-dimensional fabrication in dentistry (Dederichs et al., 2025; Memè et al., 2021). Biomarker-based assessment may also facilitate monitoring of tissue healing and regenerative success during clinical follow-up (Taba Jr et al., 2005).

Despite these advances, important challenges remain, including achieving adequate vascularization, neural integration, long-term functional stability, and compliance with regulatory standards before widespread clinical translation can occur. Future investigations should prioritize multidisciplinary collaboration to optimize biomaterials, printing strategies, and biological signaling mechanisms while validating long-term safety and efficacy through well-designed clinical trials. Although studies outside regenerative dentistry, such as those by Suh et al. (1996), contribute broadly to material science and engineering concepts, clinical progress in pulp bioprinting will depend primarily on advances in dental biomaterials and regenerative biology. Collectively, current evidence indicates that 3D bioprinting of pulp tissue holds substantial promise for transforming regenerative endodontic therapy and improving long-term tooth preservation (Singh, 2025).

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