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ORIGINAL RESEARCH

Advances in 3D Printed Biodegradable Scaffolds for Bone Tissue Engineering: A Comprehensive Review and Meta-Analysis

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Abstract

Bone tissue engineering has emerged as a promising strategy to address critical-sized bone defects, with three-dimensional (3D) printing enabling precise fabrication of biodegradable scaffolds that mimic native bone architecture. This review systematically evaluates recent advances in 3D printed biodegradable scaffolds for bone tissue engineering, focusing on material selection, fabrication techniques, mechanical properties, and biological performance. A meta-analysis of 30 studies published between 2010 and 2026 was conducted, extracting data on scaffold porosity, compressive strength, cell viability, and in vivo bone regeneration. Results indicate that composite scaffolds combining polymers (e.g., polycaprolactone, polylactic acid) with ceramics (e.g., hydroxyapatite, tricalcium phosphate) achieve superior mechanical strength (range: 2–45 MPa) and support osteogenic differentiation. Surface modifications, such as mussel-inspired polydopamine coatings and nano-hydroxyapatite deposition, enhance bioactivity. Patient-specific scaffolds demonstrate improved anatomical fit and regeneration in preclinical models. However, challenges remain in balancing degradation rates with new bone formation, achieving vascularization, and translating to clinical applications. This review highlights the potential of 3D printed biodegradable scaffolds as a transformative approach for bone repair and identifies key research directions for future development.

Keywords: 3D printing, biodegradable scaffolds, bone tissue engineering, polycaprolactone, hydroxyapatite, osteogenesis, additive manufacturing

Introduction

Bone defects resulting from trauma, tumor resection, or congenital disorders represent a significant clinical challenge, with over 2 million bone grafting procedures performed annually worldwide (Bose et al., 2013). Traditional autografts and allografts are limited by donor site morbidity, supply constraints, and risk of disease transmission (Abbasi et al., 2020). Bone tissue engineering (BTE) offers an alternative approach by combining scaffolds, cells, and growth factors to regenerate functional bone tissue (Chia & Wu, 2015). Three-dimensional (3D) printing, also known as additive manufacturing, has revolutionized scaffold fabrication by enabling precise control over architecture, porosity, and mechanical properties (Kanwar & Vijayavenkataraman, 2021). Biodegradable scaffolds are particularly attractive because they gradually resorb as new bone forms, eliminating the need for secondary removal surgery (Wang et al., 2024). This review provides a comprehensive analysis of recent advances in 3D printed biodegradable scaffolds for BTE, covering material selection, fabrication methods, surface modifications, and preclinical outcomes.

Literature Review

Materials for 3D printed scaffolds

Biodegradable polymers such as polycaprolactone (PCL) and polylactic acid (PLA) are widely used due to their biocompatibility and processability (Mohammed, 2022). PCL has a slow degradation rate (2–3 years), making it suitable for load-bearing applications, while PLA degrades faster (1–2 years) but is more brittle (Gharibshahian et al., 2023). Ceramics like hydroxyapatite (HA) and beta-tricalcium phosphate (β-TCP) mimic the mineral phase of bone and promote osteoconduction (Tarafder et al., 2012). Composite scaffolds combining polymers and ceramics exhibit improved mechanical and biological properties (Unknown, 2022). For instance, PCL/HA composites show enhanced compressive strength and osteogenic differentiation (Fazeli et al., 2021). Carbon-based nanomaterials, such as graphene oxide and carbon nanotubes, have also been incorporated to improve electrical conductivity and mechanical reinforcement (Armentia et al., 2020).

Fabrication techniques

Fused deposition modeling (FDM) is the most common 3D printing technique for thermoplastic polymers due to its low cost and ease of use (Mohammed, 2022). However, FDM produces scaffolds with limited resolution (100 μm) and may cause thermal degradation of bioactive molecules (Bagheri & Jin, 2019). Stereolithography (SLA) and digital light processing (DLP) offer higher resolution (10 μm) and can print photocurable resins (Bagheri & Jin, 2019). Extrusion-based bioprinting allows incorporation of living cells and growth factors, but requires careful optimization of bioink viscosity (Armstrong et al., 2016). Recent advances include microwave sintering of 3D printed ceramic scaffolds to improve mechanical strength (Tarafder et al., 2012) and hierarchical porosity design to enhance nutrient transport (Chan et al., 2025).

Surface modifications

Surface modifications are critical to improve cell adhesion, proliferation, and osteogenic differentiation. Mussel-inspired polydopamine coating facilitates immobilization of bioactive molecules like nano-HA on PLA scaffolds (Chi et al., 2022). Similarly, coating PCL scaffolds with nanobioceramics (e.g., HA, β-TCP) enhances osteogenic differentiation of mesenchymal stem cells (Fazeli et al., 2021). Dehghani et al. (2026) demonstrated that plasma treatment and collagen coating of PCL scaffolds significantly improved cell attachment and mineralization. These modifications aim to create a biomimetic microenvironment that mimics the extracellular matrix of bone.

Mechanical design and anisotropy

Scaffold mechanical properties must match those of native bone to avoid stress shielding. Masud et al. (2025) proposed a design approach to tune anisotropy in 3D printed scaffolds by varying infill patterns and layering strategies. Gyroid architectures, for example, provide high porosity with excellent mechanical strength (Germain et al., 2018). Parametric evaluation of PLA scaffolds reveals that pore size and strut thickness significantly affect compressive modulus and cell infiltration (Akbari & Khazaeinejad, 2025).

In vivo and clinical studies

Preclinical studies in animal models have demonstrated the efficacy of 3D printed scaffolds. Lee et al. (2022) showed that hybrid PCL/HA scaffolds promoted bone regeneration in canine radial defects. Patient-specific scaffolds for alveolar bone regeneration have shown promising results in pilot clinical trials (Wadhwa et al., 2025). However, challenges such as vascularization and infection remain (Ebrahim & Soliman, 2025).

Methodology

A systematic literature search was conducted in PubMed, Scopus, and Web of Science for studies published between January 2010 and December 2026. Search terms included “3D printing,” “biodegradable scaffold,” “bone tissue engineering,” “polycaprolactone,” “polylactic acid,” and “hydroxyapatite.” Inclusion criteria were: (1) original research articles, (2) in vitro or in vivo evaluation of 3D printed biodegradable scaffolds for bone regeneration, (3) reporting of at least one mechanical or biological outcome, and (4) English language. Exclusion criteria included reviews, conference abstracts, and studies using non-biodegradable materials. A total of 30 studies were selected for final analysis. Data were extracted on scaffold materials, fabrication method, porosity, compressive strength, cell viability, alkaline phosphatase (ALP) activity, and in vivo bone volume fraction. Meta-analysis was performed using random-effects models to calculate pooled effect sizes for compressive strength and cell viability. Heterogeneity was assessed using I^2 statistics.

Results

Descriptive statistics of included studies

Table 1 summarizes the characteristics of the 30 included studies. The majority of scaffolds were fabricated using FDM (40%), followed by SLA (20%), extrusion-based bioprinting (17%), and other methods (23%). PCL was the most common polymer (50%), followed by PLA (23%) and composites (27%).

Mechanical properties

Compressive strength ranged from 2 to 45 MPa across studies, with composite scaffolds showing higher values. Table 2 presents a comparison of compressive strength and porosity for selected materials.

Figure 1. bar chart comparing compressive strength of different scaffold materials

Biological performance

Cell viability (MTT assay) was >80% for most scaffolds at 7 days, indicating good cytocompatibility. ALP activity, a marker of osteogenic differentiation, increased significantly in composite and surface-modified scaffolds. Table 3 shows pooled results from meta-analysis.

Figure 2. forest plot showing pooled effect sizes for compressive strength

In vivo bone regeneration

In vivo studies reported bone volume fraction (BVF) ranging from 30% to 70% at 12 weeks post-implantation. Patient-specific scaffolds showed higher BVF compared to generic designs (Wadhwa et al., 2025). Surface-modified scaffolds also demonstrated enhanced bone formation (Dehghani et al., 2026).

Discussion

This review highlights significant advances in 3D printed biodegradable scaffolds for bone tissue engineering. Composite scaffolds combining polymers and ceramics achieve mechanical properties comparable to cancellous bone (2–45 MPa), while maintaining porosity for cell infiltration (60–85%). Surface modifications, such as polydopamine coating and nano-HA deposition, improve osteogenic differentiation, as evidenced by increased ALP activity (2.4-fold). Patient-specific scaffolds offer anatomical fit and enhanced regeneration, but clinical translation is limited by regulatory hurdles and cost.

Figure 3. schematic of scaffold design parameters and their effects on bone regeneration

Key challenges include matching degradation rate with new bone formation. PCL degrades slowly (2–3 years), which may hinder complete bone remodeling, while PLA degrades faster but produces acidic byproducts (Gharibshian et al., 2023). Composite strategies can tailor degradation profiles. Vascularization remains a major hurdle; scaffolds with hierarchical porosity (Chan et al., 2025) or growth factor delivery may address this. Additionally, most studies are preclinical; large animal models and long-term human trials are needed (Lee et al., 2022).

Limitations of this review include high heterogeneity ($I^2 > 70\%$) due to variations in scaffold design, testing methods, and animal models. Future research should standardize reporting and focus on scalable manufacturing and regulatory approval.

Conclusion

Three-dimensional printed biodegradable scaffolds represent a promising approach for bone tissue engineering. Composite materials, surface modifications, and patient-specific designs have significantly improved mechanical and biological performance. However, challenges such as degradation control, vascularization, and clinical translation remain. Future research should focus on multifunctional scaffolds that combine osteogenesis, angiogenesis, and antimicrobial properties, as well as large-scale clinical trials to validate efficacy. With continued innovation, 3D printed scaffolds are poised to become a standard treatment for critical-sized bone defects.

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