Comparison of 3D Printing Technologies for Polymer-HA Bone Scaffolds: A Systematic Review Toward Hybrid Fabrication Strategies

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Abstract

Bone scaffold fabrication using 3D printing faces a fundamental dilemma: the trade-off between mechanical strength and biological functionality. To address this challenge, a systematic literature review (SLR) of 28 primary research articles was conducted to compare various hydroxyapatite-based scaffold fabrication technologies. The analysis confirms a clear trade-off: Fused Filament Fabrication (FFF) excels in mechanical strength, Digital Light Processing (DLP) in architectural precision (<100 µm), and Direct Ink Writing (DIW) in flexibility for bio-functionality, proving no single method is ideal. The main conclusion is that hybrid fabrication strategies—intelligently integrating the strengths of multiple technologies—offer the most promising approach to creating functional scaffolds with an optimal balance of strength and bioactivity for future clinical applications.

Keywords*: 3D Printing, Bone Scaffold, Hydroxyapatite, Hybrid Fabrication*

1. INTRODUCTION

Bone tissue engineering offers an innovative solution to overcome the clinical challenges in the repair of critical bone defects, which until now still rely on autografts and allografts with all their limitations, such as donor site morbidity and the risk of immune rejection [1], [2]. The main pillar of this approach is the use of a three-dimensional scaffold that serves as a framework to support tissue regeneration [3], [4], [5]. To mimic natural bone, composite materials that combine synthetic polymers such as polylactic acid (PLA) or polycaprolactone (PCL) with bioactive ceramic hydroxyapatite (HA) have become the main choice [6], [7]. This combination has proven to be very effective; the addition of HA not only provides essential osteoconductive signals [8], but also significantly improves mechanical performance, where the addition of 30% ceramic particles in PLA is able to increase the compressive strength from 27 MPa to 45 MPa [6], while the addition of 20% HA in PCL increases Young's modulus by 50% [7].

The realization of composite materials' full potential in functional scaffolds depends on additive manufacturing (3D printing) technologies, which allow precise control over scaffold architecture. These technologies enable the fabrication of scaffolds with precisely controllable internal architecture, including porosity and pore interconnectivity crucial for nutrient transport and cell infiltration [9], [10], [11]. However, a literature review indicates that the choice of fabrication technology—such as Fused Filament Fabrication (FFF), Direct Ink Writing (DIW), Digital Light Processing (DLP), and Selective Laser Sintering (SLS)—directly creates a fundamental dilemma between mechanical strength, architectural precision, and biological functionality. FFF technology, while affordable and capable of producing scaffolds with high mechanical strength (e.g., 25–45 MPa), suffers from lower resolution (>200 µm) [6], [9]. In contrast, DLP offers the highest architectural precision (<100 µm) and can produce very strong ceramic scaffolds after sintering (>80 MPa), but at a significantly higher cost and with challenges

in slurry formulation [2], [12]. Meanwhile, DIW offers unmatched material flexibility and the ability to print at room temperature, but with a very wide mechanical strength range (7-60 MPa) depending on ink composition and post-print processing [13].

The trade-offs between mechanical strength, architectural precision, and biological functionality raise critical questions about the optimal fabrication method for specific clinical applications, such as load-bearing or non-load-bearing bone defects. To date, the lack of systematic comparative analysis has hampered the development of evidence-based guidelines for technology selection. Therefore, this study aimed to conduct a systematic literature review to identify, evaluate, and synthesize the scientific evidence regarding various 3D printing technologies for the fabrication of HA-polymer composite-based bone scaffolds. Specifically, this study aimed to answer the following research questions (RQs):

1. What 3D printing technologies have been used for the fabrication of bone scaffolds from HA-based materials?
2. Scaffolds (such as resolution, porosity, and mechanical strength) produced by different 3D printing technologies are compared.
3. Which technology shows the most promising potential for clinical applications of HA-based bone scaffolds based on evidence from the literature?

2. RESEARCH METHODS

This study is a systematic literature review (SLR) designed following the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) protocol to identify, evaluate, and synthesize scientific evidence in a transparent and replicable manner. The literature search was conducted in the Scopus and Google Scholar databases using a comprehensive query to ensure broader coverage of relevant studies (Figure 1).

The selection process began with 221 potential articles identified from the initial search. After screening duplicates and assessing eligibility based on title, abstract, and full-text reading per the inclusion/exclusion criteria in Table 1 (e.g., excluding studies focused on metallic materials or non-primary research), 28 articles were selected for in-depth analysis. Conference proceedings were excluded to focus on peer-reviewed journal articles, though this may limit emerging findings. This structured selection process is illustrated in Figure 1.

Table 1. Article Inclusion and Exclusion Criteria

Criteria	Inclusion	Exclusion
Type of Study	Primary research, journal articles.	Review articles, conference proceedings, editorials, letters to the editor, and book chapters.
Material Focus	Ceramic-polymer composite scaffold (HA/TCP/BCP) or pure ceramic.	Scaffolds with metal as the main material (e.g., titanium, magnesium).
Technology Focus	Discusses specifically the 3D printing fabrication method used (e.g., FFF, DLP, SLS, DIW).	Does not mention or explain the 3D printing technology used.
Language & Year	Publications in English, published between 2020 and 2025.	Publications in languages other than English, published outside the specified timeframe.

Data were systematically extracted using a standard tabulation form. Collected information included fabrication details (technology, materials), physical-mechanical characteristics (scaffolds such as porosity, pore size, and compressive strength), and biological evaluation results (in vitro and in vivo). Data analysis was conducted using a qualitative synthesis approach, where data were grouped and narratively compared based on fabrication technology

type. This synthesis aimed to identify patterns, trends, and trade-offs between technologies to answer research questions and ultimately formulate significant insights and research gaps.

3. RESULTS AND DISCUSSION

An analysis of 28 selected primary research articles reveals a diversity of additive manufacturing technologies that have been explored for the fabrication of hydroxyapatite (HA)-based bone scaffolds and their derivatives. Each technology has its own unique working principles, advantages, and challenges, which fundamentally influence the architectural, mechanical, and biological characteristics of the resulting scaffolds. In general, these technologies can be classified into three main categories: material extrusion-based technologies, vat photopolymerization-based technologies, and other technologies such as powder bed fusion and hybrid approaches.

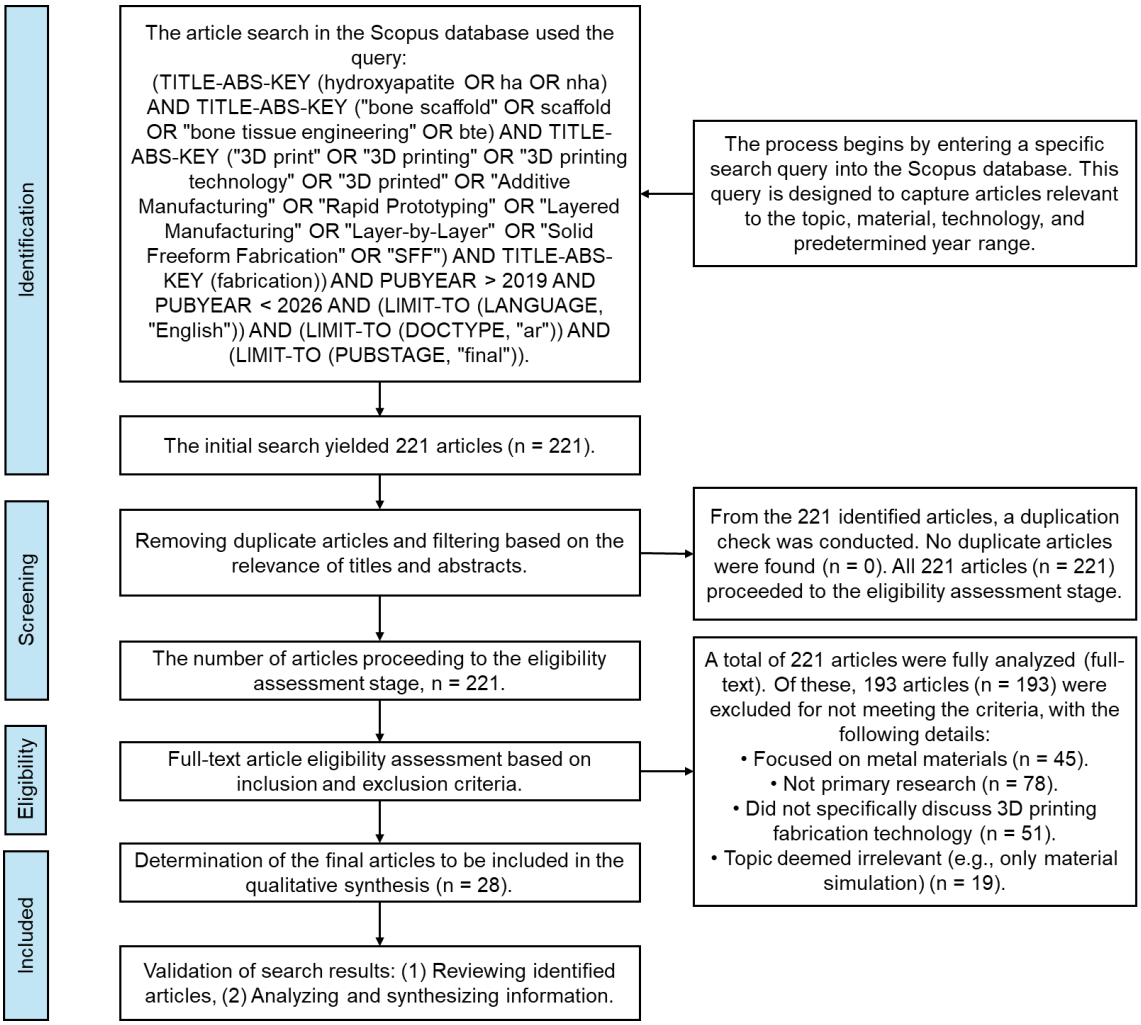

Figure 1. PRISMA flowchart illustrating the research article selection process, including initial identification (n=221), screening, eligibility assessment, and final inclusion (n=28) of studies.

3.1 Various 3D Printing Technologies for HA Scaffold Fabrication (Answer to RQ1)

Based on literature studies, HA scaffold fabrication is dominated by extrusion-based technologies, which are divided into two main variants: Fused Filament Fabrication (FFF) and

Direct Ink Writing (DIW). FFF, which works by melting thermoplastic composite filaments (e.g., PLA-HA), excels in producing scaffolds with high mechanical strength, where the addition of 30% ceramics can increase the compressive strength from 27 to 45 MPa [6]and the addition of 20% HA increases Young's modulus by up to 50% [7]. The main challenge lies in fabricating filaments with a homogeneous dispersion of HA particles [7]. In contrast, DIW, which extrudes pastes at room temperature, offers superior material flexibility, allows the direct incorporation of heat-sensitive biological components such as drugs or proteins [6], and supports multi-material fabrication [14]. However, the success of DIW is highly dependent on the optimization of complex ink rheology [15].

On the other hand, Vat Photopolymerization-based -based technologies (such as DLP and SLA) offer unmatched architectural precision. Based on the principle of polymerizing a liquid resin containing ceramic particles [16], this method can achieve feature resolutions below 100 µm, thus enabling the fabrication of highly complex internal architectures such as gyroids or TPMS [2], [3], [17]. This precision is balanced by technical challenges in slurry formulation so that HA particles do not block light penetration [16]. Beyond these dominant approaches, several studies explore advanced fabrication methods, such as the adaptation of Selective Laser Melting (SLM, defined as a powder bed fusion technique using a laser to melt and fuse materials) to create bioactive ceramic composites in situ [18]. In addition, hybrid strategies that combine the advantages of several techniques, such as FDM for external molding and DLP for internal networks, have been proven successful in creating high-strength HA [4]scaffolds with complex architectures that are difficult to achieve by single methods. The emergence of these innovative approaches indicates a shift in research focus from optimizing single methods to engineering smarter and more multifunctional fabrication systems.

3.2 Comparison of Scaffold Characteristics (Answer to RQ2)

The choice of 3D printing technology shapes the scaffold's final profile, balancing mechanical strength (e.g., compressive strength ranging from 7–80 MPa), architectural precision (e.g., feature resolution as low as 20 µm), and microstructural functionality (e.g., microporosity for cell attachment). On the one hand, technologies involving high-temperature processing, such as FFF and DLP (after sintering), excel in producing superior mechanical strength, achieving compressive strengths between 45 MPa and over 80 MPa, making them prime candidates for load-bearing applications [6], [12], [13]. However, the highest architectural precision belongs to DLP, which can create complex features such as gyroids with a resolution below 100 µm [2], [10], a capability that is difficult to achieve with FFF, whose resolution is limited by the nozzle diameter. [9].

Fundamental differences are also found at the microstructural level. Ink- or slurry-based methods such as DIW and DLP are intrinsically capable of creating microporosity on the scaffold wall surface originating from the gaps between compacted ceramic particles [19]. This hierarchical structure has proven to be very useful for increasing surface area and facilitating cell attachment and spreading [15], a functional advantage that FFF filament surfaces, which tend to be dense and smooth, lack.

In summary, these findings demonstrate that no single technology is universally superior. The selection of the most effective method is a strategic decision that depends on the priorities of the clinical application: FFF is preferred when mechanical strength and cost-effective production are the goals; DLP is the preferred choice for scaffolds with unmatched microarchitectural precision; and DIW offers the highest material flexibility, particularly in incorporating bioactive components at room temperature.

3.3 Clinical Potential Analysis (Answer to RQ3)

The success of a 3D printing technology in clinical applications depends on biocompatibility, osteogenic potential, and fabrication practicality, including considerations like

regulatory approval (e.g., FDA/ISO standards) and scalability for clinical use. A literature review shows that while composite materials such as PCL/HA and PLA/HA consistently demonstrate excellent biocompatibility, both in vitro by supporting cell attachment and proliferation [7], [20] and in vivo by inducing only a minimal inflammatory response, [21], the ability to actively stimulate new bone formation (osteogenesis) is the main differentiating factor.

In this regard, technologies capable of creating hierarchical biomimetic architectures (macro and micro), such as DLP and DIW, show the most promising in vivo results. The ability of these two technologies to produce scaffolds with complex surface topographies has been shown to significantly accelerate bone regeneration in animal defect models [2], [10], a success attributed to an optimal pore architecture for vascularization and intercellular communication [22]. However, these biological advantages must be weighed against the practicality of fabrication. FFF is recognized as the most affordable and rapid method for prototyping [9], but with lower precision. Conversely, the superior precision of DLP and SLM comes at a significantly higher cost of equipment and material investment [16], [18], while the flexibility of DIW materials is offset by the complexity in ink rheology optimization [23].

Overall, this analysis demonstrates that no single technology is superior across the board. This suggests that the future of functional and accessible scaffold fabrication likely depends not on a single technology, but rather on the intelligent integration of multiple approaches to balance strength, precision, and biological functionality.

4. DISCUSSION

4.1. Insight: The Mechanical-Biological Dilemma and the Emergence of Hybrid Fabrication Strategies

A comparative analysis of the reviewed literature strongly illustrates a fundamental dilemma in bone scaffold fabrication: a strong trade-off between mechanical performance and biological functionality. High-temperature-based technologies such as FFF can produce scaffolds with mechanical strengths approaching those of cortical bone [6], [24], but their processing temperatures preclude the inclusion of sensitive biological components and produce less-than-ideal surfaces for initial cell interactions [25]. In contrast, hydrogel ink-based technologies such as DIW excel in biological functionality by enabling cell or drug encapsulation at room temperature [19], [26], but at the cost of very low mechanical strength, making them unsuitable for load-bearing applications [15].

Facing this dilemma, key insights from recent literature suggest that breakthroughs are no longer focused on optimizing a single technology, but rather on developing hybrid fabrication strategies that integrate the advantages of multiple approaches. These strategies manifest in two main forms. First, process and structure hybridization, such as combining fast FDM for printing external molds with precise DLP for fabricating internal tissues [4], or coating a robust PCL-FFF framework with bioactive ceramics to enhance cell responsiveness [25]. Second, material hybridization, where multifunctional resins for DLP are engineered by combining HA particles and bioactive glass to produce scaffolds that are both robust and capable of releasing therapeutic ions [16]. The emergence of these strategies signals a paradigm shift from single-component optimization to holistic system integration, paving the way for the fabrication of a new generation of robust and biologically functional bone scaffolds.

4.2. Research Gap and Future Research Directions

Despite the promise of hybrid fabrication strategies, this review identifies a key research gap: the lack of a systematic framework to guide the selection of optimal hybrid strategies for specific clinical applications, such as cranial defects requiring high precision or long bone

fractures needing robust mechanical support. Currently, the choice of approach—whether through post-impression coating [25], the use of multifunctional composite resins [16], [22], or the integration of multiple technologies [4]—tends to be case-specific and not based on robust evidence-based comparisons. Consequently, it is difficult to objectively determine which approach is most effective for a given clinical scenario, such as load-bearing versus non-load-bearing bone defects. To fill this knowledge gap and accelerate the translation of hybrid scaffold technology into the clinical setting, several future research directions should be prioritized:

1. Head-to-Head Comparative Studies: Studies are needed that directly compare the performance of different hybrid strategies (e.g., coating vs. internal composite vs. hydrogel infiltration) under identical in vivo testing conditions. Such studies would provide invaluable comparative data to build an evidence base for a rational strategy selection framework.
2. Development of Integrated Fabrication Systems: Engineering innovation needs to be directed toward the creation of a single manufacturing platform capable of processing multiple material types (e.g., thermoplastic filaments and bio-inks) simultaneously in a single, continuous process [4]. This will simplify current complex fabrication processes, increase standardization, and improve the quality of the interfaces between materials within the scaffold.
3. In Vivo Studies: Future research should invest in longer-term studies (e.g., 6–12 months) in clinically relevant large animal models. This is crucial to comprehensively evaluate degradation profiles, tissue integration, and long-term mechanical stability, going beyond the currently prevalent short-term studies (typically 4–12 weeks) [2], [10].

4.3. Study Limitations

It is important to acknowledge that this study has several methodological limitations that define its scope. Limitations include the use of only Scopus and Google Scholar databases, potentially missing studies in other repositories, restriction to English-language publications, and exclusion of grey literature (e.g., conference proceedings), which may contain emerging findings in 3D printing technologies. This combination of factors potentially introduces selection and publication bias, where studies with negative results or those not published in English-language journals may be underrepresented. Furthermore, the analysis was a qualitative synthesis. Due to the high heterogeneity in experimental designs and evaluation methods across studies, a quantitative meta-analysis was not possible, and conclusions were drawn based on identifying narrative trends. However, with a transparent protocol, these limitations do not diminish the validity of the findings but rather clarify their context and provide a strong foundation for future, broader systematic reviews.

5. CONCLUSION

This systematic review concludes that although extrusion-based 3D printing (FFF, DIW) and vat photopolymerization (DLP) technologies dominate the bone scaffold fabrication landscape, no single method is universally superior. Each technology exhibits fundamental trade-offs between mechanical strength, architectural precision, and biological functionality. Therefore, the key insight is not the crowning of a single technology as superior, but rather the affirmation that the most promising approach to future bone tissue engineering lies in the implementation of hybrid fabrication strategies.

By combining the advantages of different techniques, materials, or processes—such as combining a robust mechanical framework with bioactive surface functionality—hybrid approaches have proven capable of overcoming the limitations of single methods. This strategy enables the design of scaffolds that balance the demands for reliable mechanical support with the need for a biologically functional microarchitectural environment to support cell regeneration.

This paradigm shift from single-method optimization to the integration of hybrid systems opens significant opportunities for engineering next-generation bone scaffolds that are not only anatomically precise but also functional, accelerating the pace of innovation translation from the laboratory to clinical applications and delivering more effective regenerative solutions to patients.

Table 2. Comparison of *Scaffold Characteristics* Based on Fabrication Technology

Technology Name	Main Material	Porosity Range (%)	Compressive Strength Range (MPa)	Resolution & Key Features	Main Weaknesses	Source
Hydrogel 3D Printing	Gelatin/HA/rGO	Smaller pores with powder (no numerical range)	Increases with HA (0.3 g) & graphene (0.0045 g), no specific value	Expands & retains water, biocompatible, biodegradable, good cell adhesion	Low mechanical strength, high degradation for hard bone	[27]
Material Extrusion (FFF/FDM)	CDHA, HA/Gelatin/GO, PLGA/nHA, PCL/HA, CS/HA, PLA/HA, PVDF/HA/CS	CDHA: 61.9–74.37%; HA/GO: 60–95% (300–900 µm); PLGA: 0.122 mm^2; PCL: ~60% (400–550 µm); PLA: 70%	CDHA: 25; HA/GO: +15% compression, +22% flex; PCL: 30–70; PVDF: 33.92	Precision porous structure, low cost, porosity control, mechanical integrity, environmentally friendly	Low reproducibility, defects reduce strength, high viscosity, shrinkage	[4], [5], [6], [7], [9], [15], [21], [24], [28], [29]
Vat Photopolymerization - DLP/SLA	TCP, GelMA/HAp, BNT/HA, HA bioceramic, HA-coated, PLA/HA/BBG: PLLA/HA/GO	TCP: 59.375–60%; HA: 49.32–54.52%; GelMA: 9.12% shrinkage; PLA: 46.3–52.8% (458–844 µm); 43–50% (300–500 µm)	TCP: 48–82; HA: 1.45–1.92; GelMA: 0.68–0.9; HA-coated: > 4; +54% with optimization (unspecified)	High precision (20–100 µm), fast, good cell viability, complex geometry, material compatibility; Automated multimaterial, high resolution, strong cell adhesion	Residutoxic if not removed, shrinkage, ceramic sedimentation, Bubbles, shrinkage, post-heat strength reduction	[2], [4], [10], [12], [16], [22], [25], [30]
Robocasting	BEN/HAP, HAp, calcium phosphate	HAp: 74.05 ± 0.38%; BEN/HAP: pores shrink with sintering	BEN/HAP: 52 (1000°C); HAp: not specific	Complex structures via CAD, low cost, controlled porosity, good cell adhesion	Breakage during printing, low dimensional accuracy, slurry expansion	[1], [20]
Selective Laser Melting (SLM)	HAp (50–70 wt%)/silicon	The pore is designed to be 400 µm, smaller with high laser power	2–18 (highest ~18)	Rapid prototyping, complex scaffolding, personalization	Oxidation phase, mechanical strength is inconsistent	[18]
Hybrid (FDM+DLP +Slurry Casting)	HA bioceramics/PF-127, PLA resin, DLP resin	32–37% (481–811 µm channel)	40–238.9; hardness 1.43–1.87 GPa	Fast mass production, high precision, good density, high cell viability	Low FDM precision, toxic DLP residue if not removed,	[4]
3D Printing (General)	CS/HA, template candle	86.7% (honeycomb)	Increases with coating (unspecified)	Internal geometry & structure control, high mechanical strength	Shrinkage after process	[31]

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