REVIEW ARTICLE

3D Printing in Dentistry and Targeted Drug Delivery: A New Era of Personalized and Precision Medicine

Abhilasha Waghadkar[1], Vidya K. Lohe[2], Monica Mahajani[1], Manisha Waghadkar[3]

[1]Department of Oral Medicine and Radiology, DMIHER (Deemed to be University), Wardha, Maharashtra, India, [2]Department of Periodontics and Implantology, Dr. Hedgewar Smruti Rungna Seva Mandal's Dental College and Hospital, Hingle, Maharashtra, India, [3]Department of ???, Government Medical College and Hospital, Chandrapur, Maharashtra, India AQ2

Abstract

Three-dimensional (3D) printing, a transformative additive manufacturing technology, has ushered in a new era of personalized and precision medicine in both dentistry and drug delivery. This review explores the evolution and integration of 3D printing with digital workflows such as computer-aided design and computer-aided manufacturing, highlighting its application in fabricating custom dental prostheses, orthodontic aligners, surgical guides, and implant planning tools. It also examines the development of patient-specific drug delivery systems using 3D-printed devices with programmable release profiles, tailored for pediatric, geriatric, and chronic disease management. Core printing technologies such as stereolithography, digital light processing, selective laser sintering, fused deposition modeling, and photopolymer jetting are compared based on precision, material compatibility, and clinical use. The review further delves into recent advancements in regenerative dentistry, such as bioactive scaffolds and stem-cell-loaded constructs for tissue engineering. Challenges like biomaterial cytotoxicity, post-processing inaccuracies, regulatory gaps, and cost barriers are analyzed alongside emerging solutions. Future directions, including four-dimensional materials, artificial intelligence-driven predictive modeling, point-of-care manufacturing, and sustainable printing materials, are proposed. This synthesis bridges engineering and clinical practice, underlining the profound potential of 3D printing to transform oral healthcare and drug therapy delivery.

Key words: Additive manufacturing, dentistry dental, drug delivery systems, prostheses, three-dimensional printing

INTRODUCTION AND BACKGROUND

History of three-dimensional (3D) printing and its evolution to rapid prototyping and present-day clinical uses the history of 3D printing additive manufacturing goes back to the early 1980s, when rapid prototyping approaches were developed that allowed the creation of physical objects in response to a computer-based design.[1] Early innovators introduced methods such as stereolithography (SLA) and selective laser sintering (SLS) that formed the technical basis of the usage of the layer-by-layer deposition method to create complex structures.[2] In the decades that followed, innovations in printing resolution, the choice of materials, and the control of the process allowed shifting to more sophisticated production of extremely functional, patient-specific devices that are currently underbound into clinical use. The demise of important patents, such as that of fused deposition modeling (FDM), tended to democratize the 3D printing technology, thus decreasing its costs and encouraging mass spread into both non-industrial and medical realms.[2] In recent years, continual improvements in printer hardware, technology, and software, as well as in the biomaterials that these printers

Address for correspondence:
Abhilasha Waghadkar, Department of Oral Medicine and Radiology, DMIHER (Deemed to be University), Wardha, Maharashtra, India.
Phone: +91-9049167076; 9860608580.
Email: abhilashawaghadkar2@gmail.com

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use, and in this time 3D printing has become a consistent, replicable manufacturing solution that can tackle complex shapes or even individualized production in a way that subtractive manufacturing could not. This transition is not technological, it is conceptual: What was before an aid to speed up design loop has become an enabling technology allowing the support of a completely new paradigm of clinical practice in both tooth treatment as in drug delivery[3] [Figure 1].

Computer-aided design and computer-aided manufacturing (CAD/CAM) and Personalized Production Parallel to the evolution of 3D printing is the broader digital revolution in healthcare that has been catalyzed by the integration of CAD/CAM systems.[4] Due to the digital workflow, dentistry was changed, with the older methods of making impressions being swapped out with intraoral scans and digital imaging procedures, which create an extremely realistic 3D representation of the teeth and dental structures of a patient.[3] Those digital developments enable clinics to plan restorative operations virtually and develop restorations, crowns, bridges, implant abutments, and orthodontic apparatus, more precisely than before.[5] Simultaneously, the pharmacological sphere is a fortunate recipient of the digital transformation and the corresponding possibility to create custom drug supply channels. Computer aided design transforms patient specific information (including anatomic, physiologic and hereditary information) into individual dosage forms that have the ability to regulate drug release kinetics.[6] The meeting point of the CAD/CAM and 3D printing therefore illustrates how the digital-type of integration can beat the drawbacks of the one size scales on manufacturing processes, rolling down the age of personalized healthcare.[2]

The success of dental treatments relies on the precision and fit of restorations. Traditional fabrication methods are complex and prone to error, often resulting in suboptimal outcomes and the need for adjustments. 3D printing overcomes these challenges by converting digital designs directly into custom abutment, bridges, and implants that match each patient's unique anatomy. This not only enhances function and comfort but also reduces chairside time and the risk of complications like ill-fitting prostheses and periodontal issues. Digital workflows have been shown to improve long-term results, biomechanical stability, and patient satisfaction, highlighting the transformative impact of personalized dental restorations on treatment success and quality of life.

Patient-specific drug delivery is becoming more relevant with strengths of commercially available drug products that do not meet the differences in individuals which results in under/overdosing of side effects.[7] The 3D printing in the pharmaceutical industry allows the mapping out of personalized dosage forms of drugs. Such technology facilitates complicated drug release profiles and combined treatments with optimum bioavailability and therapeutic efficacy, and minimized toxicity. Personalization of this kind is particularly useful with chronic conditions and populations

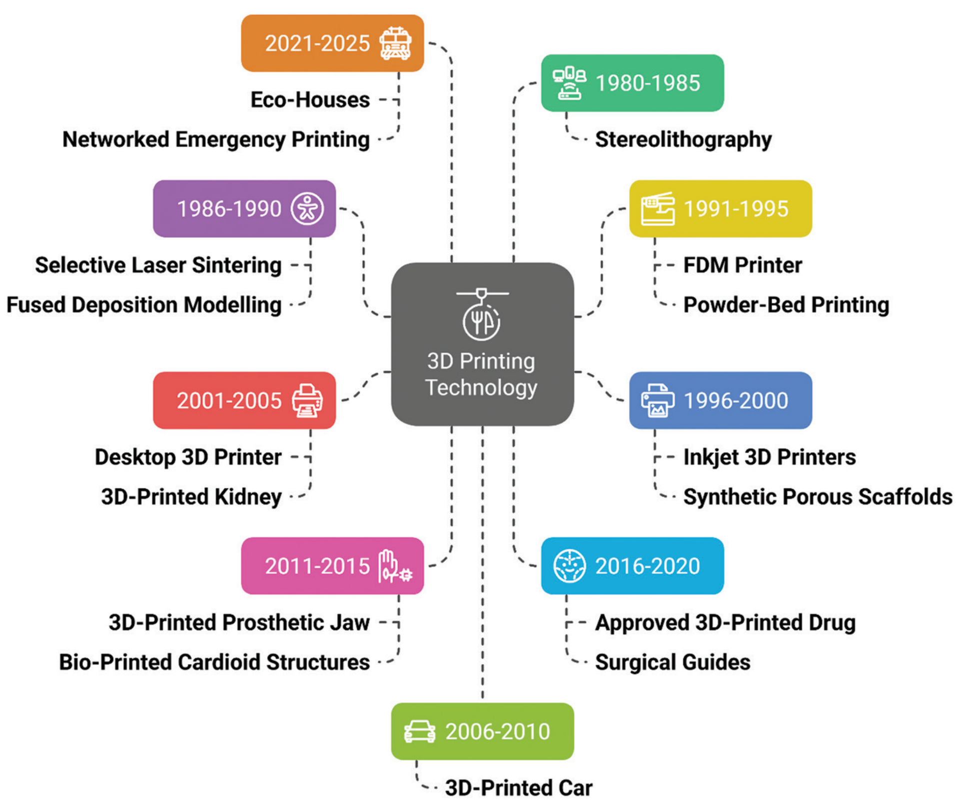

Figure 1: Timeline of key milestones in three-dimensional printing technology from its inception in the 1980s to its clinical applications in 2025

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and in instances where standard dosing can make little or no sense, as might be the case with children and/or the elderly.[6]

Customization has turned into a pillar of contemporary treatment, with treatments personalized in every case yielding improved results steadily.[4] In dentistry, 3D printing has made it possible to create custom restorations that perfectly match the affected areas and minimise mistakes, which improve the durability as well as aesthetics of prosthetics, causing greater patient satisfaction.[3,8] This precision reduces the necessity of corrections, reduces therapeutic length, reduces expenditures, and enhances clinical outcomes, particularly where mere slight discrepancies of a surgical operation may result to chronic repercussions.[9,10]

Drug delivery, some factors that influence patients, such as metabolism and genetics, can be mitigated by personalization in drug delivery, as mass-manufactured medicines do not tend to take the aspect of such factors into it.[6] 3D printing can be used to produce dosage forms of specific size, shape, and release profile to suit exact dosing and combination treatments. It increases compliance and decreases side effects, especially chronic, pediatric, and geriatric care.[7] In addition to technical advantages, an individually fitting solution has psychological improvement because the patients feel they get special attention, and psychological well-being is improved; patients turn out to be more satisfied and lead a qualitative life.[11] Customization of patient data into the production cycle is promoting 3D printing to the clinical sector, redesigning the notion of dentistry and medicine delivery.[12]

This review critically evaluates recent advances in 3D printing for dentistry and drug delivery, focusing on current trends, integration into digital healthcare, clinical benefits over traditional methods, and ongoing challenges such as biomaterial compatibility, regulatory issues, and scalability. It synthesizes findings from peer-reviewed research and clinical trials to clarify both technical and practical aspects, as well as the broader impact on patient-specific therapies in the dental and pharmaceutical fields. The review also explores future directions, including the integration of 3D printing with bioprinting, nanotechnology, and smart materials, the development of advanced bioinks and composites, and the use of real-time imaging for improved implant fit. It addresses strategies to overcome regulatory and technical barriers, aiming to accelerate the adoption of personalized healthcare solutions. AQ3 Serving as a resource for researchers, clinicians, and industry professionals, this article bridges engineering innovation and clinical practice by covering the history, recent developments, benefits, limitations, and future prospects of 3D printing in dentistry and drug delivery. It underscores the transformative potential of these technologies to enhance patient care and fundamentally change how dental restorations and drug therapies are designed and delivered. In summary, this review sets the stage for a detailed discussion of the evolution, impact, and future of 3D printing in personalized medicine, aiming to guide research and inspire new clinical applications worldwide.

PRINCIPLES OF 3D PRINTING

3D printing technology is based on additive manufacturing technology that constructs complicated structures digitally in a layer-by-layer sequence. It has helped to transform dentistry and drug delivery in the pharmaceutical field. Core technologies include SLA, which uses ultraviolet (UV) lasers to photopolymerize liquid resins into precise dental prosthetics and surgical guides with resolutions ≤50 µm;[13,14] FDM to extrude thermoplastic filaments (e.g., polylactic acid, polycaprolactone [PCL]) and print low-cost dental models as well as patient-specific drug tablets, with desired porosity;[15,16] SLS, fusing polymer powders (e.g., nylon) through laser to create robust, geometry-flexible implants and drug carriers;[15] and digital light processing (DLP), projecting UV patterns for rapid fabrication of dental restorations and microfluidic drug devices.[17]

In dentistry, these technologies enable customized solutions:

- SLA/DLP produce accurate surgical guides, crowns, and aligners, reducing chair time by >60% compared to traditional methods.[14,18]
- SLS/FDM facilitates anatomical models for preoperative planning and temporary prosthetics, enhancing osteointegration in dental implants[19,20] [Figure 2].

For targeted drug delivery, 3D printing allows:

- Dosage personalization: FDM/SLS-printed tablets with multi-drug compartments or modified release kinetics (e.g., Spritam®) improve bioavailability for pediatric and geriatric patients.[21]
- Stimuli-responsive systems: SLA-printed hydrogels or neutrophil exosome-coated carriers enable inflammation-triggered drug release at tumor sites.[22]
- Intestinal targeting: SLS-FDM hybrid systems with pH-sensitive polymers (e.g., Eudragit®) achieve site-specific delivery for inflammatory bowel disease therapy.[23]

There are still challenges, such as the lack of material biocompatibility, trade-offs of resolution in SLS/FDM, and regulatory barriers to the use of patient-specific pharmaceuticals.[13] In the future, it is possible to combine the artificial intelligence (AI) design to predictive release kinetics and multi-material bioprinting of the next-generation dental scaffold with embedded antimicrobial agents.[23]

TYPES OF 3D PRINTING TECHNOLOGIES IN DENTISTRY AND TARGETED DRUG DELIVERY

SLA

SLA is a vat photopolymerization technology that has attained the status of a pillar of additive manufacturing in the dentistry industry owing to its unrivalled fidelity, precision, and adaptability with even the most intricate dental components. Utilizing a laser to selectively cure liquid photopolymer resin layer-by-layer, SLA can be utilized to make anatomy precision dental models, surgical guides, splints, temporary crowns, and custom implants.[24-26] Its capacity to achieve sub-50 µm layer resolutions surpasses many other 3D printing methods, ensuring exceptional surface smoothness and dimensional fidelity critical for dental applications such as crown marginal fit and orthodontic aligners.[27] As summarized in Table 1, SLA offers a precision range of 20–50 µm, making it particularly suitable for applications requiring high accuracy, such as surgical guides and dental models.

The SLA workflow involves several integrated steps, from laser curing of resin to the production of customized appliances like surgical guides and dentures. The schematic in Figure 3a illustrates the sequential applications of SLA in dentistry, highlighting benefits such as precision, customization, and rapid production, as well as limitations like material brittleness and post-processing demands. Figure 3b shows a technical representation of the SLA printing process, where a focused laser beam selectively cures resin in a vat to form objects layer-by-layer. Figure 3c presents an example of a surgical guide fabricated using SLA and computer-aided design, showcasing the clinical relevance and high-resolution capabilities of this technique in producing implant placement aids.

However, SLA faces significant challenges, including material limitations. The majority of dental resins used are methacrylate-based based which are inherently brittle, have poor mechanical properties (e.g., flexural strength ≤100 MPa), and as low as possible cytotoxicity due to the release of unreacted monomers, which creates concern regarding the biocompatibility of these materials in oral environments over long time periods.[28] Additional post-processing needs, such as washing and UV curing, also complexify workflows and add dimensional errors to the part associated with resin shrinking, especially in sub-mm features, as observed in cavity preparations where deviations of 50–200 µm compromise clinical fit.[29]

Material innovation remains pivotal. Recent advances include nanocomposite resins infused with beta-tricalcium phosphate or titanium dioxide (TiO_2) nanoparticles, enhancing mechanical properties and enabling antimicrobial photodynamic activity.[30] For instance, urethane dimethacrylate-based resins (BioM1)

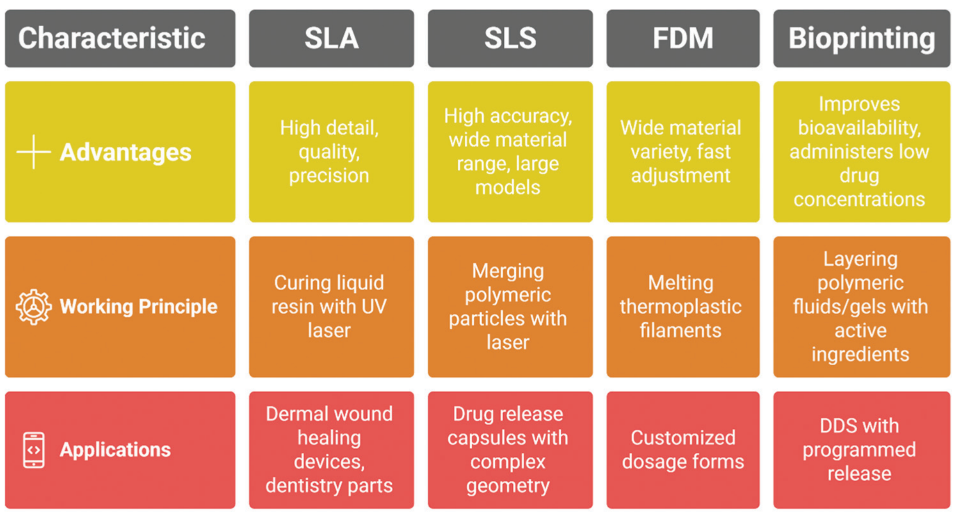

Figure 2: Comparative overview of four principal 3D printing technologies – Stereolithography (SLA), Selective Laser Sintering (SLS), Fused Deposition Modeling (FDM), and Bioprinting. The figure illustrates their respective advantages, working principles, and specific applications, such as customized drug dosage forms, dermal wound healing devices, drug release capsules with complex geometries, and drug delivery systems (DDS) with controlled release properties

Table 1: Comparison of 3D printing technologies in dentistry based on precision, speed, materials, and applications

Technology	Precision (µm)	Speed	Materials	best suited applications
SLA	20–50	Medium	Resins	Surgical guides, high-accuracy models
DLP	25–100	High	Ceramics	Crowns, implants, bioprinting
FFF	100–200	Medium	Thermoplastics	Denture bases, training models
PolyJet	16–30	Medium	Multi-resins	Simulators, soft-tissue replicas
Binder Jetting	50–150	High	Metals/ceramics	Frameworks, porous implants

3D: Three-dimensional, SLA: Stereolithography, DLP: Digital light processing, FFF: Fused filament fabrication, PolyJet: Photopolymer jetting

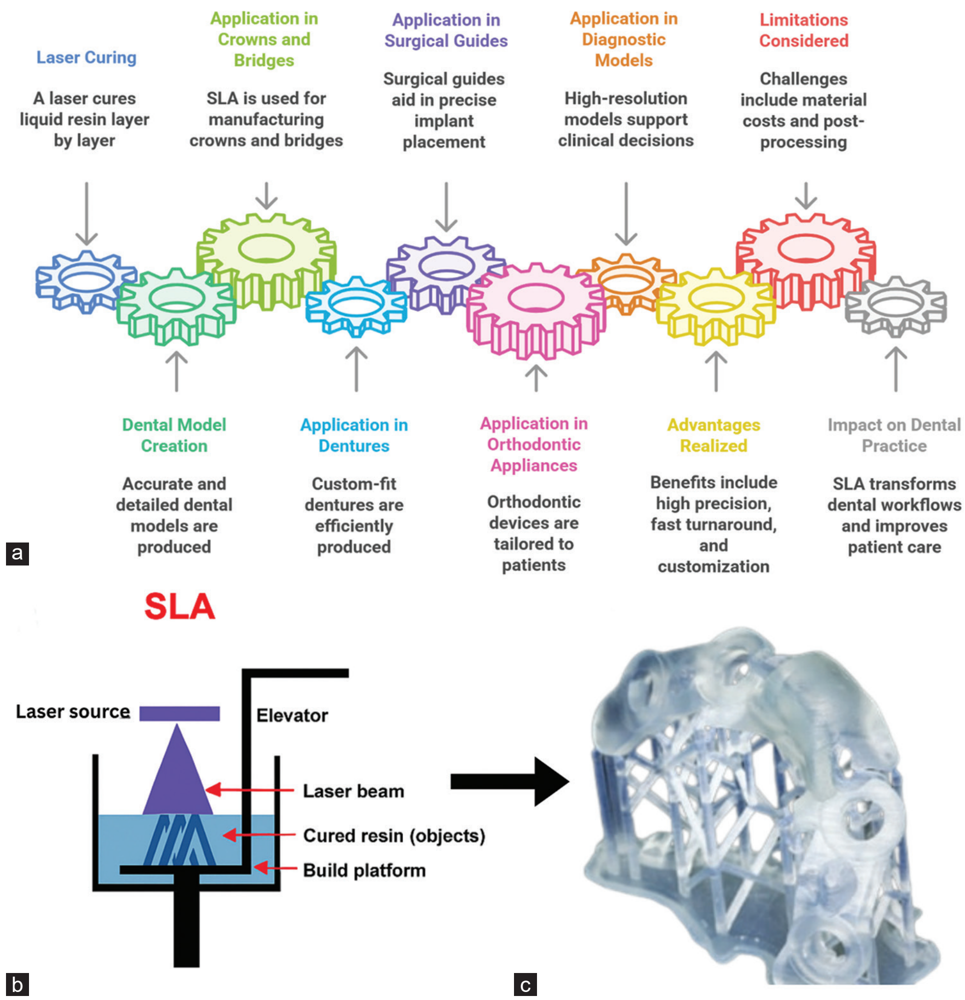

Figure 3: Applications and process of stereolithography (SLA) 3D printing in dentistry (a) Overview of the SLA 3D printing workflow and its diverse dental applications, including dental model creation, crowns and bridges, dentures, surgical guides, orthodontic appliances, and diagnostic models, alongside associated benefits and limitations. (b) Schematic representation of the SLA printing process, where a laser beam selectively cures photopolymer resin layer-by-layer in a vat to create 3D structures, image adopted from Sultana *et al*.[21] (c) Example of a surgical guide fabricated using computer-aided design (CAD) and produced via SLA 3D printing technology for precise implant placement, image adopted from Patel *et al*.[34]

demonstrate superior osseointegration *in vivo* compared to conventional materials,[30] while TiO_2-doped nanocomposites improve flexural strength (≈120 MPa) in denture bases.[28,31] Nevertheless, SLA resins do not show the fatigue properties and toughness of milled ceramics or metal alloys, and SLA resins are therefore unsuitable in high-stress applications such as definitive prostheses.[31] Economic and logistical constraints also persist, as SLA printers require costly proprietary resins and rigorous calibration, while support structures during printing increase material waste and post-processing time.[26]

Significantly, SLA is best suited in fabricating individual devices. The surgical guides and anatomical models created by printing with the help of SLA technology to be utilized in implantology and oncologic reconstructions decrease the percentage of operative mistakes by 30–40% in contrast to the standard implantology approach.[32] Its integration with digital workflows (e.g., intraoral scanning, CAD/CAM) streamlines production, enabling same-day delivery of devices like aligners or occlusal splints.[18] The anisotropic material behavior should be implemented in future work because it can come through the grayscale photopolymerization to attain the functionally graded properties,[33] develop biodegradable resins for temporary implants, and standardize validation protocols for clinical safety. While SLA's precision and efficiency will continue driving its adoption in dentistry, overcoming material deficiencies and process-induced inaccuracies remains critical to expanding its applications beyond provisional and auxiliary devices.

DLP

DLP has become the transformative additive manufacturing technology in dentistry, which takes advantage of the high-resolution projection using vat photopolymerizations to create remarkably precise and smooth surface dental prostheses, surgical guides, and anatomical models with exceptional accuracy (±30–50 μm trueness) and smooth surface finishes critical for clinical applications.[35] Based on the use of digital masks, this method is used to project pulses of UV (or visible) light through geometries, allowing photopolymer resins, including biocompatible resins such AQ4 as methacrylated gelatin (GelMA) and ceramic-reinforced composites, to be rapidly cured strategically, building up the complex shape.[36,37] Recent advances in DLP-optimized resins, such as those incorporating aluminum oxide nanoparticles or carbon nanotubes, enhance mechanical properties (e.g., flexural strength >120 MPa) and oral rinsing stability, addressing durability challenges in long-term dental restorations.[38] In addition, DLP use in CAD/CAM procedures simplifies the development of patient-specific devices, for example, root-analog implants and temporary crowns, whereas developments in multi-material 3D printing and four-dimensional (4D) printing paradigms might lead to smart materials, that is, stimuli-responsive materials, to create dynamic tissue engineering scaffolds.[39] Despite these advantages, challenges persist in standardizing post-processing protocols – such as optimal UV-curing durations and support structure removal – to mitigate residual stress and ensure dimensional fidelity across diverse clinical designs.[40,41]

Targeted drug delivery via DLP 3D printing

DLP 3D printing allows revolutionizing targeted drug delivery by allowing the precise manufacture of patient-specific devices whose release kinetics can easily be programmed. The technology makes use of photopolymerizable resins to produce complex geometries (e.g. microneedles, hollow implants, and gradient-porosity tablets) that spatially and temporally control drug release. Key advancements include.

Microneedle arrays for transdermal delivery

The hollow microneedles produced using DLP are most useful when it comes to optimizing the drug bioavailability, as due to their design, they avoid enzymatic degradation in the GoT. As one example, Gelatin methacryloyl (GelMA) microneedles loaded with antibiotics (e.g., amoxicillin) provide localized release with >90% release after 6 h. These probes can advance easily through the skin layer because of tunable sharpness (15–25 mm) and the density of array probes, resulting in low systemic side effects.[42,43]

Dental Implants with Localized Therapeutics

DLP-dental crowns and scaffolds include drug-loaded hydrogels (e.g., Polyethylene Glycol Diacrylate resins) that provide location-specific anti-inflammatory or antimicrobial effect. Capillary and arteriolar arteriogenesis in oral ischemic tissue is synergistically regenerated by devices that elute VEGF and Delta-like 4 to enhance periodontal healing.[44,45] Resin formulations with zinc oxide nanoparticles further provide sustained antibacterial activity (≈99% reduction in *Staphylococcus aureus* growth over 72 h).[46]

Programmable release tablets

Hydrophilic excipients (e.g., PEG 400) in DLP-printed tablets modulate dissolution rates, achieving zero-order kinetics for drugs like theophylline. Geometric designs (lattice structures, internal channels) control surface area-to-volume ratios, enabling 12–48 h delayed release profiles tailored to circadian rhythms or disease states.[47,48]

Fused filament fabrication (FFF)

FFF 3D printing is increasingly adopted in dentistry for its cost-efficiency, customization capabilities, and rapid prototyping, yet it faces critical challenges in material performance, accuracy, and clinical integration. The technology can be used to make surgical guides, dental models, and provisional prosthetics through layer-by-layer deposition of thermoplastics such as PLA, ABS, or even specially formulated biocompatible composite materials. Nevertheless, it can only be used to a limited extent because of the anisotropic mechanical characteristics of low interlayer bond strength that impairs structural stability with masticatory forces.[49,50] This is further worsened by material constraints in that majority of FFF polymers (e.g., PLA) are not biocompatible, show poor wear resistance and stability over the long term in comparison to conventional polymethylmethacrylate (PMMA) and ceramics.[51] Surface roughness of FFF-printed parts often exceeds clinically acceptable thresholds (Ra>5 μm Ra>5 μm), necessitating AQ5 post-processing like laser polishing, which introduces thermal distortion risks.[52]

In clinical practice, FFF has potential in custom products such as wrist braces or prosthodontic parts that can be reproduced anatomically reproducibly in a digital content-controlled workflow, using cone beam computed tomography (CBCT) and intraoral dimension scans.[53,54] Nonetheless, dimensional error remains at the curvature and seams because of the limitations of path-planning, and results in visible artifacts and lower fracture resistance – particularly in fiber-reinforced composites where misaligned fibers divide up load transfer packaging.[55,56] Hybrid strategies integrating FFF with SLA or PBF improve surface quality but escalate costs and complexity, undermining FFF's core affordability advantage.[54]

The next step will be innovation in material and streamlining the process. There is an emerging use of bioactive composites containing antimicrobial agents (e.g., chlorhexidine-infused resins) to counter infection risks,[57] while *in situ* debinding-sintering methods for ceramic-filled filaments could enhance density and biocompatibility.[58] Machine learning-assisted defect detection during printing may mitigate structural flaws, though real-time quality control remains underdeveloped.[59] Regulatory gaps for 3D-printed medical devices further impede standardization, demanding rigorous validation of FFF outputs against International Organization for Standardization 13485 benchmarks. Ultimately, while

FFF democratizes customized dental solutions, its transition from provisional to permanent applications requires resolution of material deficiencies and precision barriers through interdisciplinary collaboration.

FFF has also become a disruptive technology in making personalized drug delivery systems, especially targeted ones. Nevertheless, there are some major issues that should be solved to make it clinically achievable. Material limitations are paramount: drug-polymer compatibility during hot-melt extrusion often compromises filament integrity and drug stability. For instance, high processing temperatures (>150°C) can degrade thermolabile antibiotics like chlorhexidine, reducing bioactivity by up to 30%.[60,61] Structural heterogeneity in printed devices further undermines controlled release kinetics. The effects of layer-by-layer deposition result in microporosity differences (±15% deviation from designed infill density), leading to inconsistent drug elution rates – critical for time-sensitive applications like jet lag therapy, where delayed caffeine release must synchronize with melatonin pharmacokinetics.[62,63]

Physiological constraints are also seen in programmable release mechanisms. Intestinal targeting coatings (e.g., Kollicoat MAE 100P) are subject to pH-dependent erosion, and GI differences inter-patient destabilize the spatiality of the targeting.[64] Although hybrid systems (e.g., hydrogel-nanoparticles composites) facilitate more effective targeting, the resolution capabilities of FFF (~100–200 m) do not permit the precise incorporation of functional moieties such as folic acid ligands to tumor-homing the nanoparticle-containing hybrid.[65] Moreover, scalability barriers persist, as current good manufacturing practice adaptations lack real-time quality monitoring, risking dose inaccuracies exceeding ±10% in multi-drug implants.[66,67]

Although multi-material printing advancements are being made (e.g., PLA-PVA matrices of antimicrobial agents), taking place through post-processing, including but not limited to lack of standardization of hydrothermal processing (e.g. gamma irradiation) in sterilization, degrades polymeric crystallinity and expedites burst release.[61] Future advancements demand machine learning-driven parameter optimization and stimuli-responsive bio-inks to dynamically modulate release profiles *in vivo*. Failure to address these technical-economic gaps may confine FFF to niche preclinical applications rather than mainstream therapeutics.

Photopolymer jetting (PolyJet) (Material Jetting)

PolyJet (Material Jetting) 3D printing transforms the area of dentistry with high-resolution (<30 μm), multi-material dental applications such as surgical guides, splints, and anatomic models using high-resolution photopolymer jetting and instant UV curing.[13,68] Key strengths encompass exceptional dimensional accuracy (validated at ±50 μm for dental models),[69] the ability to simulate gingiva-tooth interfaces via simultaneous rigid/flexible material deposition,[69] and reduced lead times for complex geometries.[70] However, critical limitations persist: resin-based outputs exhibit lower fracture resistance versus milled PMMA or ceramics (e.g., 15–30% reduced flexural strength in occlusal splints);[13,71] the selection of material is still limited to proprietary photopolymers with no known long-term oral stability data;[72] and operational costs exceed mainstream methods like FDM (Material Jetting constitutes <5% market share).[14] Defect susceptibility – from nozzle clogging to incomplete curing – further challenges clinical reliability.[68] Although PolyJet facilitates the introduction of individualized care through anatomic precision and biomimetic surfaces, its use is limited by the material science limitations, poor mechanical characteristics in situations where strength and loading are critical, and it has great economic inefficiencies that require future developments of nano-reinforced resins as well as environment-friendly processes.[73]

These performance traits are quantitatively highlighted in Table 2, which compares key parameters of PolyJet 3D printing versus conventional PMMA or ceramic-based dental fabrication. For instance, while PolyJet offers superior dimensional accuracy (±50 μm vs. ±100–200 μm) and faster production times (<24 h vs. 24–72 h), it underperforms in load-bearing durability (flexural strength: 80–100 MPa vs. 120–150 MPa) and remains costly, limiting its adoption in smaller clinical setups.

The potential of the PolyJet (Material Jetting) technology as an approach to additive manufacturing makes a breakthrough

Table 2: Comparative performance of polyjet versus conventional dental manufacturing

Parameter	PolyJet 3D Printing	Conventional (PMMA/Ceramic)	Clinical Implications	Ref
Dimensional accuracy	±50 μm	±100–200 μm	Superior fit for surgical guides/splints	[69,80]
Flexural strength	80–100 MPa	120–150 MPa (PMMA)	Limited load-bearing durability in occlusal devices	[81,82]
Production time	<24 h (complex geometries)	24–72 h (milling)	Faster chairside solutions	[70]
Material versatility	Multi-material (rigid/flexible)	Single-material dominance	Biomimetic gingiva-tooth simulations	[68]
Relative cost	High (2% market share)	Medium (milling dominant)	Barrier for small clinics	[68,83]

in the targeted drug delivery using additive manufacturing and allows the unprecedented levels of precision when considering the fabrication of the multi-material structures with the local drug-release characteristics. By jetting photopolymer droplets cured layer-by-layer with UV light, PolyJet achieves micro-scale resolution (<100 µm), critical for engineering drug-loaded geometries with controlled porosity and compartmentalization to modulate release kinetics, such as pulsatile or sustained profiles.[74,75] The process enables patient-specific individualization of implants and ingestible devices based on patient-specific anatomies and their treatment needs, for example, colon-specific systems, having pH-responsive segments that degrade selectively in intestinal environments.[76,77] The therapeutic agents are functionalized to the biocompatible photopolymers (e.g., acrylic-based resins), and multi-jetting has the capability to co-deposit the drug loaded and the barrier materials, spatially controlling drug diffusion paths and minimizing burst release.[78] Recent innovations include stimuli-responsive hydrogels for on-demand antibiotic delivery in gastrointestinal applications, demonstrating PolyJet's potential to integrate sensing and release mechanisms within a single printed structure.[79] Although the scaling of sterile production is still complicated, and polymer stability is a long-time issue, the PolyJet technology takes personalized medicine to a new level as anatomical specifications are combined with spatiotemporal drug targeting.

CLINICAL APPLICATIONS IN DENTISTRY

Prosthodontics and restorative dentistry

SLA, DLP, and SLS are used in prosthodontics and restorative dentistry to make crowns, bridges, dentures or fixed partial prostheses.[84] These additive manufacturing methods offer customized solutions that can improve marginal fit and mechanical performance.[85]

Additive manufacturing, especially the 3D printing, has changed the field of prosthodontics by allowing the production of patient-specific devices. These technologies allow for precise customization based on the unique anatomy of each patient's jaw and facial structures.[84] SLA, DLP, and SLS are prominent techniques in this field. SLA involves solidifying a liquid photopolymer resin with a UV laser, offering high resolution. DLP, similar to SLA, uses a shaped light projection to solidify the resin, providing a cost-effective alternative. SLS selectively melts powder materials using a laser, suitable for both metal and polymer powders.[85] As an example, a new two-step process to make mobile dentures after extraction applies such materials as dental polymers, metals, ceramics, and composite materials to increase functionality, durability, and look. The process includes capturing occlusal registration immediately following tooth extraction to ensure precise adaptation.[86]

Studies have shown that the mechanical properties of the self-etching adhesives would not be affected adversely when bioactive glasses such as 45S5 and niobophosphate bioactive glass (NbG) are added to the self-etching adhesives. Deposition of hydroxyapatite and calcium carbonate can be promoted by adding 20% 45S5 bioactive glass, and this leads to improved bioactivity.[87] Moreover, the use of nanozirconia in bioceramics and implantology provides high strength, biocompatibility, and wear resistance, making it ideal for long-lasting dental implants.[88]

The integration of digital workflows in prosthodontics allows for improved design and manufacturing of dental prostheses.[89] Digital models, as depicted in Figure 4 from Todaro *et al*., offer detailed 3D representations of the dental arch, aiding in precise planning for implant surgeries and prosthodontic applications.[90]

The single crowns or fixed dental prostheses are improved in fit and precision by application of CAD/CAM systems.[91] A method for measuring and correcting the fit of fixed dental prostheses has been developed to improve the efficiency and accuracy of prosthodontic treatments.[92] Studies comparing milled and 3D-printed PMMA prostheses have shown variations in marginal fit, emphasizing the importance of selecting appropriate materials and manufacturing techniques.[93]

Orthodontics and alignment devices

The incorporation of 3D printing in the orthodontic field has transformed the manufacturing process of the alignment device, and specifically, clear aligners, due to its accuracy, comfort, and effectiveness in treatment. The case studies confirm that direct-printed aligners, which are created using resins such as Tera Harz TC-85, produce the controlled

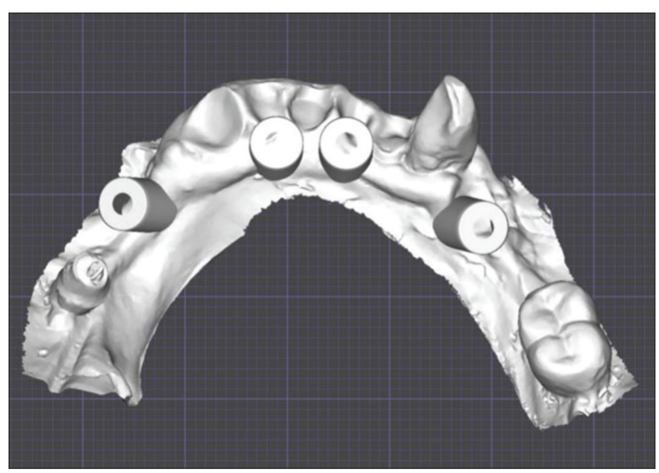

Figure 4: Scan abutments transferred from the surgical planning phase on Implant3D® to the prosthetic design phase on Exocad®. (adapted from Todaro *et al*.,[90] under the terms and conditions of the Creative Commons Attribution [CC-BY] license [CC-BY 4.0])

force (0.3–0.5 N for rotation; 1.3–2.3 N for translation),[94] overcoming limitations of traditional thermoformed aligners, such as force decay and reduced stiffness due to thinning during thermoforming.[95,96] For example, Yu *et al*. reported a 97% patient satisfaction rate using 3D-printed polyurethane aligners molded on personalized dental models, which reduced treatment duration by 20% compared to conventional methods.[97] These devices leveraged optimized photocurable resins with <0.2% residual monomers, ensuring biocompatibility.[97]

Clinical workflows now integrate AI-powered digital model that is used to simulate a tooth motion, and mistakes are minimized. Tartaglia *et al*. confirmed that direct printing eradicates the effects of thermoforming on the material properties, and aligned geometry accuracy is within 0.05 mm precision standards.[98] Nevertheless, difficulties are still present, such as resin fatigue after 14 days of the use and occlusal interference in complex malocclusions.[95,98] Future advancements focus on shape-memory polymers for active force adjustment and bioactive resins that reduce enamel demineralization risks.[99] Current research underscores 3D printing's potential to enable fully digital, patient-specific orthodontics, though long-term clinical validation remains essential for widespread adoption.[96] An overview of the 3D printing workflow and comparison of orthodontic devices is illustrated in Figure 5.

Implantology and surgical planning

The use of 3D printing in dental implantology and surgical planning has allowed great progress in terms of precision, customization, and efficiency of the working process. It allows the production of a very precise surgical guides and models of implants based on patient-specific data, including cone-beam CT and intraoral scans, which greatly improves implant placement accuracy and outcomes.[100] Customized drill guides created with 3D printing allow clinicians to perform minimally invasive surgeries with reduced chair time and improved predictability.[101] The technology can also be utilized in the production of implant-supported prosthetics since they precisely recreate the structures of anatomies structures, which helps in planning and simulating complex implant cases.[102] Furthermore, the integration of CAD/CAM with 3D printing offers high design accuracy, reducing the risk of surgical errors and enhancing patient-specific treatments.[103] Overall, 3D printing has become an indispensable tool in modern dental implantology and surgical planning, driving better outcomes through precise, individualized care.

Several research studies and case applications have validated the clinical advantages of 3D printing in implantology and surgical planning. As an example, Zaharia *et al*. showed with the production of surgical remodeled guides provided by collected cone-beam CT data and printed by SLA that the accuracy of implant placement has been enhanced, reducing both intraoperative maladaptive and post-operative morbidity.[100] Similarly, Dawood *et al*. described multiple clinical cases where patient-specific 3D printed guides facilitated flapless implant surgeries with higher precision and shorter operative times, leading to faster healing and improved aesthetic outcomes.[101] In another study, Alqutaibi *et al*. reviewed clinical implementations and reported that

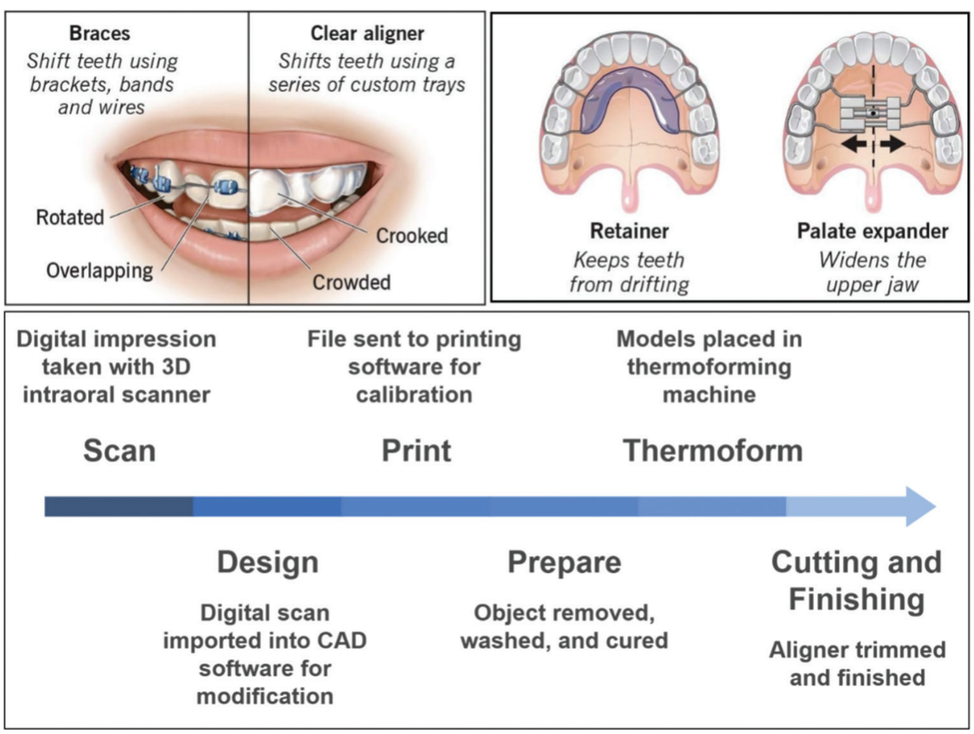

Figure 5: Workflow of three-dimensional-printed orthodontic aligners and comparison with traditional appliances

additive manufacturing not only improved implant fit and stability but also reduced the need for bone grafting in complex anatomical zones due to more accurate pre-surgical planning.[102] These studies collectively emphasize that 3D printing enhances both surgical precision and patient-specific customization, leading to more predictable and efficient outcomes in implantology (Table 3). This comparison of digital planning and actual implant placement is well illustrated in a recent *in vitro* study by Adams *et al*., which used CBCT superimposition to assess surgical accuracy for guides with and without metal sleeves [Figure 6].

Tissue engineering and regenerative therapies

The concept of 3D printing has revolutionized the aspects of tissue engineering and regenerative therapies in the dental field since it has allowed the production of personalized scaffolds with high structural and biological complexity that is reminiscent of the native oral tissues. 3D printing can be used to create accurate constructs to facilitate the regeneration of periodontal ligament, Alveolar bone, dental pulp, and soft gingival tissue, by incorporating digital imaging, computer-aided designing, and biocompatible materials. This has been shown by the ability of the use of bioinks consisting of hydrogels, stem cells, and growth factors to engineer living tissues to reproduce the promise of regenerative dental therapies in a truly regenerative dental treatment.[105] For example, 3D-printed polycaprolactone scaffolds embedded with microspheres have been successfully used to regenerate complex craniofacial tissues, including bone and cartilage.[106] While printed soft-tissue constructs have shown promise in replacing gingival tissues with both functional and aesthetic integration.[2] New studies are also pointing to the incorporation of stem cells in the bioprinting process, which will have potential down the road to grow replacement tissues entirely *in vitro* that could be transplanted into people.[107] These advances collectively point toward a new era in dentistry where biological

Table 3: Clinical outcomes and performance metrics of 3D printing in dental implantology

Study/Author	Sample size	Application	Accuracy (mm)	Surgery time reduction	Complications	Notes
Zaharia *et al.*[100]	30 implants	Guided surgery using 3D-printed guides	<0.9 mm deviation	~40% reduction	Minimal	Improved flapless procedure and esthetics
Dawood *et al.*[101]	Case series	Patient-specific surgical guides	0.5–1.2 mm	30–45% reduction	None reported	High precision in limited bone areas
Alqutaibi *et al.*[102]	Literature review	Surgical a prosthetic stages	~0.8 mm (avg)	25–60%	Reduced need for grafts	Enhanced anatomical conformity
Borisov *et al.*[103]	Controlled test	Implant guide accuracy vs. method	0.3–1.5 mm	N/A	N/A	SLA printing yielded highest design fidelity

3D: Three-dimensional, SLA: Stereolithography

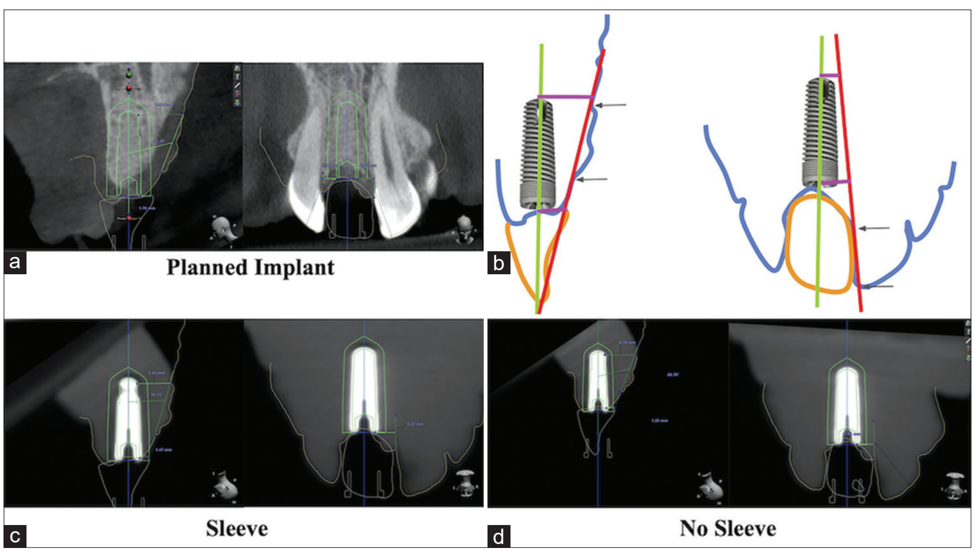

Figure 6: Assessment of planned versus actual implant placement using guided surgical templates. (a) Displays the digital pre-surgical implant positioning. (b) Illustrates the reference planes and alignment axes – green indicating implant trajectory, red marking anatomical reference lines, and magenta showing deviation measurements in both buccolingual and mesiodistal views. (c and d) show comparative evaluations of implant positions using guides with and without metal sleeves, respectively, based on cone beam computed tomography overlays with the digital plan (adapted from Adams *et al.*[104] under the terms and conditions of the Creative Commons Attribution[CC-BY] license [CC-BY 4.0])

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reconstruction becomes a personalized and predictable component of clinical care.

Incorporation of 3D printing in dental tissue engineering has triggered groundbreaking improvements to recreate complex tissues such as dental pulp, dentin, periodontal ligaments, alveolar bone, and so on. There are case studies that show innovative biomaterials and stem-cell synergies. As an example, Raveendran *et al*. have optimized gelling of Gelatinmethacryloyl (GelMA) to then bioprint periodontal ligament cells (PDLCs) >90% viability in which they observed an osteogenic differentiation within microextrusion-based constructs. The scaffold retains native tissue elasticity, which makes this scaffold design more suitable to promote PDLC proliferation and ligament regeneration.[108,109] In
AQ6 alveolar bone repair, Ostrovidov *et al*. combined bioceramic scaffolds with dental follicle progenitor cells (DFPCs) to stimulate osteogenesis, leveraging DFPCs' innate role in periodontal development. Preclinical models showed significant bone volume increase (~40%) within 8 weeks, attributed to the scaffolds' pore architecture facilitating vascular ingrowth.[58,110]

In dental pulp-dentin complexes, cell-homing techniques (e.g. injectable hydrogels loaded with stromal-derived factor-1) were used to recruit endogenous stem cells in necrotic teeth, leading to pulp-like tissue regeneration without transplantation of exogenous cells. Revascularization and apical closure of immature teeth in the course of 6 months were seen in clinical cases.[111,112] Similarly, Zhao *et al*. engineered bioprinted enamel-dentin layers using CAD-designed scaffolds infused with dental pulp stem cells (DPSCs) and hydroxyapatite nanoparticles, though functional enamel hardness remains challenging due to its non-regenerative nature.[113]

CHALLENGES AND LIMITATIONS

The implementation of 3D printing in dentistry and drug delivery confronts substantial material limitations, where current printable biomaterials exhibit challenges in achieving long-term biocompatibility and mechanical stability, particularly due to unresolved cytotoxicity issues in photopolymers and bioinks that necessitate further formulation refinements to ensure biological safety and durability.[114]

Table 4: Challenges and proposed solutions in the application of 3D printing for dental and drug delivery systems

Category	Challenge/Limitation	Solution/Innovation	Ref
Material limitations	Biocompatibility and cytotoxicity: Synthetic polymers may induce immune responses.	Natural hydrogels (e.g., chitosan, gelatin) with optimized crosslinking. Hybrid systems (e.g., ROS-scavenging hydrogels) reduce inflammation.	[120-122]
	Mechanical instability: Soft hydrogels lack structural integrity for load-bearing tissues.	Nanocomposite reinforcement (e.g., silica nanoparticles, calcium phosphate). Multi-layered designs for gradient stiffness.	[123-125]
Drug delivery	Unpredictable release profiles: Burst release reduces therapeutic efficacy.	Stimuli-responsive systems (e.g., pH/magnetic-field-triggered release. Core-shell nanoparticles for sustained delivery.	[126,127]
	Limited drug-loading capacity: Low payload efficiency in microneedles/hydrogels.	High-volume designs (e.g., funnel structures), hydrogel-forming materials. Micro-nanoliter droplet technology for precision dosing.	[125,128]
Manufacturing hurdles	Printing resolution: Inaccurate reproduction of microvascular features (<50 µm).	PBP for sub-10 µm resolution. Optimized laser parameters in powder-bed fusion.	[120,129]
	Skin elasticity barriers: Incomplete microneedle penetration.	LMNs with moisture-resistant packaging and stiff tip design. Applicator-integrated arrays for uniform insertion.	[125,128]
Biological integration	Cell viability reduction: Shear stress during extrusion damages cells.	Low viscosity bioinks with rapid photo crosslinking. Bacterial EVs to enhance CNS delivery.	[120,130]
	Lack of vascularization: Poor nutrient/waste exchange in thick tissues.	Sacrificial bioinks for perfusable channels. Co-bioprinting endothelial cells with growth factors.	[131]
Regulatory compliance	Standardization gaps: Absence of cGMP for bioprinted implants/drugs.	Digital-twin-assisted quality control. Blockchain-tracked manufacturing for audit trails.	[132]
	Long-term safety data: Unclear metabolic pathways of biodegradable materials.	AI-powered toxicity prediction models. Accelerated aging studies aligned with ISO 10993.	[133,134]

3D: Three-dimensional, AI: Artificial intelligence, cGMP: Current good manufacturing practice, CNS: Central nervous system, EVs: Extracellular vesicles, ISO: International Organization for Standardization, LMNs: Layered microneedles, PBP: Projection-based 3D printing, ROS: Reactive oxygen species

These difficulties are reinforced by technical factors with printing resolution, speed, and build size restricting the decisions to be made between layer accuracy and production speed and metallic biomaterials further complicating trade-offs between mechanical characteristics and biocompatibility, while metallic biomaterials face additional complexities in balancing mechanical properties with biocompatibility during fabrication;[115] moreover, post-processing requirements like curing and surface finishing often compromise dimensional accuracy and functional performance in hydrogel-based systems, especially for drug-loaded constructs requiring precise release kinetics.[116,117] Regulatory landscapes present formidable barriers due to the absence of standardized protocols for material biocompatibility testing and quality control, particularly for personalized drug delivery devices, where evolving compliance frameworks delay clinical adoption despite promising technological capabilities.[118] Economically, the cost of equipment and specialized maintenance of more advanced procedures such as the SLS makes it inaccessible and, the introduction of 3D printing in the environment of a dental technician and a pharmacist involves re-educating the professional and learning the digital design tools as well as biomaterial handling procedures, which adds a layer of delay to the implementation of the technology despite the benefits it can bring in terms of customization [Table 4].[119]

FUTURE DIRECTIONS

The future directions of 3D printing in dentistry and targeted drug delivery herald transformative advancements in personalized and precision medicine, with several key trajectories emerging. First, smart material innovation will drive the development of stimuli-responsive "4D" polymers that enable on-demand drug release in response to physiological cues like pH or temperature shifts, particularly for site-specific antimicrobial delivery in periodontal therapies and implant coatings.[135,136] Second, multi-material bioprinting will advance as a technique to print vascularized dental tissues and hybrid scaffolds composed of structural polymers (ex: PCL to regenerate bones) and bioactive hydrogels in which growth factors can be encapsulated that enhance the pace of osseointegration and reduce the probability of infection.[137] Third, point-of-care manufacturing will grow using miniaturized AI-compatible printers to create chairside polypharmacy formulations, for example, polypharmacy polypills using FDM-based printers and compartmentalized drug combinations for geriatric polypharmacy management or SLA-fabricated mucoadhesive films for localized oral chemotherapy,[138] though this necessitates streamlined regulatory frameworks for real-time quality validation.[21] Fourth, machine learning-optimized design will permit predictive modeling of drug release kinetics and biomechanical implant behavior using patient-specific genomic and radiomic data, thus advancing from anatomical customization to biologically driven personalization.[139] Finally, sustainable material circularity must be addressed through recycled PLA filaments and bio-sourced resins to reduce environmental impact while maintaining clinical-grade sterility and biocompatibility.[140] All these directions point in the direction of closed-loop systems in which diagnostic information alone sets off the production of therapeutic devices, the most significant new frontier of precision medicine.

CONCLUSION

3D printing has redefined the landscape of personalized care in dentistry and drug delivery by enabling patient-specific solutions that were previously unattainable through conventional manufacturing. Its integration into digital workflows enhances precision, efficiency, and clinical outcomes, while innovations in bioinks, drug release systems, and scaffold engineering are expanding its utility in regenerative therapies. Despite its transformative potential, widespread clinical adoption faces hurdles including material limitations, regulatory ambiguity, and economic constraints. Addressing these through interdisciplinary innovation, robust safety validation, and user-centered technologies will be crucial. As Artificial Intelligence AI and smart materials further evolve, 3D printing is poised to become a cornerstone of precision medicine – customizing treatments down to the biological and molecular level.

ETHICS APPROVAL AND CONSENT TO PARTICIPATE

Not applicable.

CONSENT FOR PUBLICATION

Not applicable.

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