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REVIEW ARTICLE

Empowering Precision Medicine: The Impact of 3D Printing on Personalized Therapeutic

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Abstract

This review explores recent advancements and applications of 3D printing in healthcare, with a focus on personalized medicine, tissue engineering, and medical device production. It also assesses economic, environmental, and ethical considerations. In our review of the literature, we employed a comprehensive search strategy, utilizing well-known databases like PubMed and Google Scholar. Our chosen keywords encompassed essential topics, including 3D printing, personalized medicine, nanotechnology, and related areas. We first screened article titles and abstracts and then conducted a detailed examination of selected articles without imposing any date limitations. The articles selected for inclusion, comprising research studies, clinical investigations, and expert opinions, underwent a meticulous quality assessment. This methodology ensured the incorporation of high-quality sources, contributing to a robust exploration of the role of 3D printing in the realm of healthcare. The review highlights 3D printing's potential in healthcare, including customized drug delivery systems, patient-specific implants, prosthetics, and biofabrication of organs. These innovations have significantly improved patient outcomes. Integration of nanotechnology has enhanced drug delivery precision and biocompatibility. 3D printing also demonstrates cost-effectiveness and sustainability through optimized material usage and recycling. The healthcare sector has witnessed remarkable progress through 3D printing, promoting a patient-centric approach. From personalized implants to radiation shielding and drug delivery systems, 3D printing offers tailored solutions. Its transformative applications, coupled with economic viability and sustainability, have the potential to revolutionize healthcare. Addressing material biocompatibility, standardization, and ethical concerns is essential for responsible adoption.

Keywords 3D printing · cost-effectiveness · healthcare innovation · medical devices · nanotechnology · patient perspectives · personalized medicine · sustainability · therapeutic delivery · tissue engineering

Introduction

3D printing has initiated a revolution across various industries, and its impact on therapeutic delivery is undoubtedly no exception. Through its unique ability to fabricate intricate 3D structures with high precision and customization, 3D printing has garnered considerable attention as a promising approach for targeted and efficient therapeutic agent delivery. Within this review, we will delve into the noteworthy progress, utilizations, and forthcoming outlook of 3D printing concerning the domain of therapeutic delivery [1, 2]. 3D printing, also known as additive manufacturing, is an innovative technology that enables the creation of 3D objects through the layer-by-layer deposition of material. It has gained significant recognition in various fields, including engineering, manufacturing,

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and healthcare. Within the realm of therapeutic delivery, 3D printing is a versatile tool that has garnered attention due to its capacity to fabricate intricate structures with precision and customization [1, 3]. Advancements in 3D printing technology have undeniably reshaped therapeutic delivery as shown in Table I, offering unprecedented opportunities for personalized medicine and targeted drug release. The capability to fabricate intricate three-dimensional structures with precision has paved the way for developing delivery systems that can effectively surmount the limitations of traditional methods as shown in Fig. 1. Notably, researchers have achieved success in utilizing 3D printing to create personalized drug delivery systems tailored to individual patients, thereby enabling precise dosing, controlled release, and targeted drug delivery [4–6]. These noteworthy advancements possess the potential to revolutionize healthcare by optimizing therapeutic efficacy while simultaneously minimizing adverse side effects.

Table I Advantages and Disadvantages of Different Classes of 3D Printing

3D Printing Class	Advantages	Disadvantages
Stereolithography (SLA)	- High precision and resolution	- Limited build size
	- Wide range of compatible materials, including biocompatible resins for medical applications	- Post-processing steps often required to remove excess resin and improve surface finish
Fused Deposition Modeling (FDM)	- Relatively low cost and accessibility of FDM printers	- Limited resolution compared to other methods
	- Suitable for rapid prototyping and simple geometries	- Limited material options, especially for biocompatible materials
Selective Laser Sintering (SLS)	- Versatility in material selection, including biocompatible powders	- Limited resolution in comparison to some other methods
	- No need for support structures during printing, reducing post-processing	- High equipment costs, which may limit accessibility
Binder Jetting	- Fast printing speed due to the use of powdered materials	- Typically lower resolution compared to methods like SLA
	- Capability to produce full-color objects, beneficial for certain applications	- May require additional steps for post-processing and curing

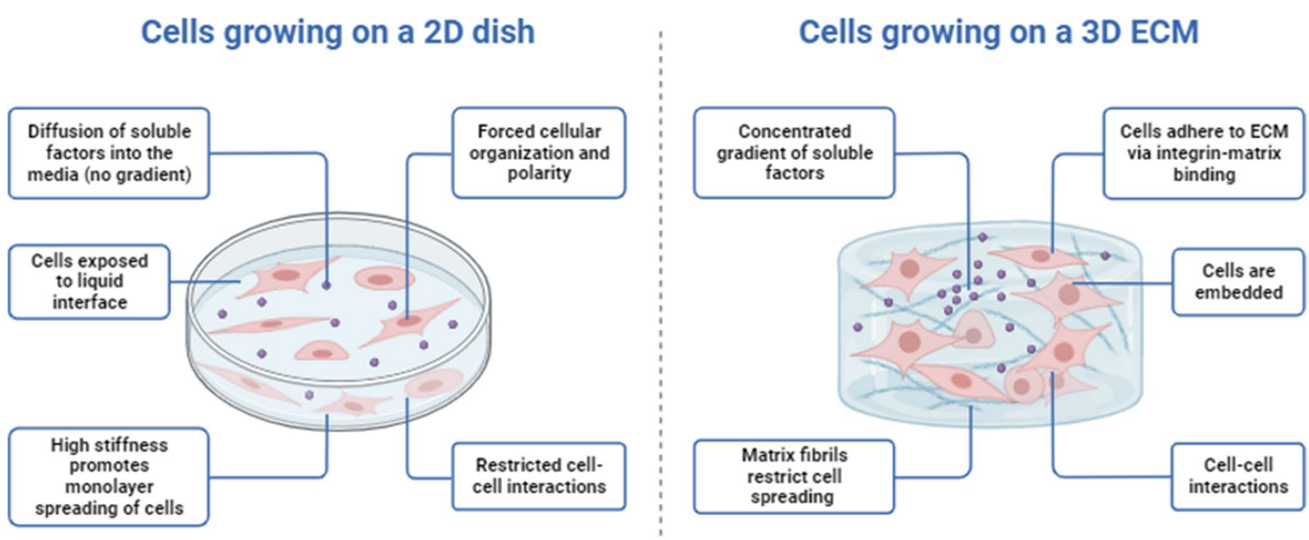

Fig. 1 Contrasting Cellular Environments—An Analytical Comparison of 2D Monolayer Culture Versus 3D ECM-Based Growth. This graphical representation delineates the inherent distinctions in cellular morphology, conduct, and interactions between conventional 2D cell culture and the progressive 3D cell culture grown upon an Extracellular Matrix (ECM) scaffold. While 2D cultivation lacks the intricacies found in the native tissue microenvironment, 3D ECM-based cultivation provides a more physiologically pertinent framework for the investigation of cellular behavior and responses. This comparative analysis delves into the ramifications of culture dimensionality on cellular physiology and their potential implications in the realms of biomedical research and tissue engineering. Image was generated by Biorender.com

Over the past decade, 3D printing, also recognized as additive manufacturing, has garnered significant attention across diverse fields, including engineering, manufacturing, and healthcare. The capacity to create complex structures layer by layer using various biocompatible materials has paved the way for fabricating personalized drug delivery systems adapted to suit individual patients [7, 8]. This transformative potential can redefine healthcare by facilitating precise dosing, controlled release, and targeted delivery of therapeutic agents. A fundamental benefit of employing 3D printing for therapeutic delivery is its capability to construct drug delivery systems featuring intricate geometries and internal structures. These achievements would pose exceptional challenges if pursued through traditional manufacturing methods. For instance, researchers have successfully printed scaffolds with intricate porosity and interconnected pore networks, thereby promoting tissue growth and regeneration [9, 10]. This, in turn, holds tremendous promise in the realm of regenerative medicine, where 3D-printed scaffolds can serve as vehicles to deliver bioactive molecules, stem cells, or growth factors to damaged tissues, thereby facilitating healing and tissue regeneration. Furthermore, 3D printing empowers the fabrication of drug delivery systems capable of controlled and sustained drug release. Through the incorporation of drug-loaded polymeric matrices or encapsulation of drugs within 3D-printed micro/nanoparticles, researchers have achieved precise release kinetics, leading to improved therapeutic efficacy and reduced side effects [10]. This capability holds remarkable value in the treatment of chronic diseases, wherein long-term drug release is often necessary.

Another significant advantage of 3D printing lies in its potential to enable personalized medicine. Each patient possesses unique physiological characteristics, and their response to drugs can vary significantly. Through 3D printing, the creation of customized drug delivery systems becomes feasible, accounting for individual variations in anatomy, pathology, and drug metabolism. By integrating patient-specific data, such as medical imaging and pharmacokinetic profiles, into the design process, 3D-printed therapeutic delivery systems can be tailored to deliver precise drug doses to specific target sites, thereby maximizing therapeutic outcomes while minimizing systemic toxicity [11, 12].

Despite the remarkable potential of 3D printing for therapeutic delivery, several challenges and limitations necessitate attention as shown in Table I. The crucial factor of utmost significance revolves around the careful choice of materials possessing biocompatibility, mechanical attributes, and controlled degradation characteristics [13, 14]. Ongoing research is diligently focused on developing new biocompatible materials that can be printed with high resolution and exhibit optimal drug release profiles. Additionally, the regulatory landscape for 3D-printed therapeutic delivery systems is still evolving, demanding the standardization of manufacturing processes and quality control measures to ensure the safety and efficacy of these groundbreaking products [15]. In summary, 3D printing has emerged as a potent instrument for therapeutic delivery, facilitating the production of intricate structures while maintaining precise control over drug release. The capability to craft personalized drug delivery systems harbors the potential to transform healthcare, offering individualized treatments that optimize therapeutic effectiveness while minimizing adverse effects. Nevertheless, it is imperative to address challenges concerning material selection, manufacturing processes, and regulatory frameworks to fully unlock the potential of 3D printing in therapeutic delivery. In the upcoming sections of this review, we will delve deeper into the most recent scientific discoveries and explore the specific applications, advancements, and prospects of 3D printing in therapeutic delivery [16–18].

This comprehensive review holds a prominent position in contemporary research as it investigates the profound impact of 3D printing in healthcare, with a specific emphasis on therapeutic delivery. In addition to exploring recent advancements, it offers a thorough evaluation of the economic, environmental, and ethical dimensions associated with the widespread adoption of 3D printing in healthcare. What distinguishes this manuscript is its comprehensive examination of key elements, including the development of bioinks, the integration of nanotechnology, and the establishment of personalized drug delivery systems, all from diverse perspectives. Furthermore, it rigorously examines the intricate relationship between 3D printing technology and the continually evolving healthcare landscape, making it an invaluable resource for scholars, practitioners, and policymakers alike. In addition to its comprehensive analysis of the current state of 3D printing in healthcare, this review makes significant contributions to existing literature by bridging substantial gaps. It introduces novel perspectives on the multifaceted applications of 3D printing, illuminating innovative approaches to therapeutic delivery and personalized medicine. By emphasizing economic, environmental, and ethical considerations, it addresses evident gaps in the literature and provides a comprehensive framework for decision-makers. Moreover, the review's extensive analysis of bioink development, nanotechnology integration, and personalized drug delivery systems advances our understanding of these pivotal areas. It also serves as a model for scientific publications, adhering meticulously to the rigorous standards of academic research through its comprehensive research methodology, exhaustive analysis, and multifaceted perspectives.

Background on 3D Printing Technology

3D printing, often referred to as additive manufacturing, has emerged as a disruptive technology with far-reaching implications across a multitude of industries. Initially employed for rapid prototyping in the manufacturing sector, 3D printing has transformed the process of object design and production by meticulously constructing them layer by layer from digital blueprints. This construction is achieved using a wide range of materials, including polymers, metals, and even living cells. Over time, 3D printing has experienced substantial advancements in both technology and materials, making it progressively more accessible and versatile. As a result, it has found applications in a diverse array of fields, including architecture, fashion, art, and notably, healthcare [19]. The remarkable advancements in 3D printing technologies have extended to the field of therapeutic delivery, particularly in the fabrication of micro- and nano-robots. These developments have been driven by using smart materials, improved actuation techniques, and the integration of physical intelligence (PI) and artificial intelligence (AI) into the design process as shown in Table II. Consequently, 3D-printed microrobots hold immense potential as game-changers in minimally invasive medicine [20]. A key factor behind the success of 3D printing in therapeutic delivery lies in the layer-by-layer production process facilitated by computer-aided design (CAD). This approach allows for precise fabrication, overcoming challenges associated with conventional microrobot fabrication methods, such as lithography, deposition techniques, and assembly. When compared to conventional manufacturing techniques, 3D printing stands out for its cost-effectiveness, swift adaptability for design alterations, and its capacity to utilize an extensive array of materials, spanning from metals and polymers to bioinks and composites. The accessibility and consistency of 3D printing have firmly established it as the emerging method of choice for microrobot fabrication, even for individuals with limited expertise in micromanufacturing [21].

Looking ahead, the integration of AI and PI holds immense potential in enhancing the capabilities of 3D-printed microrobots for therapeutic delivery. AI can optimize parameters like dimensions and material selection based on the specific chemical properties of the target site, accelerating the design process. Furthermore, AI can predict the printability of designs and fine-tune 3D printing parameters for optimal outcomes. Once produced, AI can enable precise control of microrobots *in vitro* and *in vivo*, adjusting actuation parameters to navigate unpredictable changes in the surrounding environment, such as variations in blood flow rates within vessels [20]. PI empowers microrobots to autonomously sense and adapt to their operating environment. By utilizing stimuli-responsive materials, microrobots can navigate biological fluids with improved efficiency and precision, releasing drugs at specific pH levels, for instance. The convergence of AI and PI opens new avenues for developing intelligent microrobots capable of performing complex tasks with minimal external guidance [22]. While the potential of 3D-printed microrobots for therapeutic delivery is indeed promising, it is vital to acknowledge the challenges and limitations that may hinder their widespread adoption. For instance, ensuring the safety and biocompatibility of these microrobots remains a paramount concern. Rigorous testing and evaluation in preclinical and clinical settings will be essential to establish their efficacy and safety profiles [23]. Moreover, the complexity of integrating AI and PI into microrobot designs necessitates interdisciplinary collaboration among experts in robotics, materials science, biology, and medicine. Such cross-disciplinary efforts will be crucial in advancing the development of intelligent and efficient microrobots that can truly revolutionize therapeutic delivery [23, 24]. In conclusion, the transformative potential of 3D printing in therapeutic delivery is evident through the fabrication of micro- and nano-robots. The marriage of AI and PI in this context offers exciting prospects for enhanced microrobot capabilities and performance. However, comprehensive research, rigorous testing, and interdisciplinary collaboration are imperative to overcome existing challenges and fully

Table II Comparative Analysis of Traditional Manufacturing vs. 3D Printing in Healthcare

Aspect	Traditional Manufacturing Methods	3D Printing
Customization	Limited options for customization	Highly customizable; Examples: Patient-specific medical devices
Complexity of Structures	Limited complexity of designs	Allows intricate designs and complex geometries
Time to Prototype	Lengthy prototyping process	Rapid prototyping for faster development and testing
Material Selection	Few material options	Wide range of materials, including biocompatible polymers, metals, ceramics
Manufacturing Efficiency	Batch production	On-demand and decentralized manufacturing
Resource Consumption	Higher material waste	Minimizes material waste through optimized designs
Tooling and Molds	Requires expensive tooling and molds	Eliminates the need for costly tooling and molds
Cost-effectiveness	Expensive for small-scale runs	Cost-effective for prototypes and small-batch production
Quality Control	Standardized quality control processes	Variable quality control; requires consistent printing parameters
Sustainability Indicators	Energy-intensive and higher waste	Potential for reduced energy consumption and material waste
Regulatory Approval	Well-established processes	Evolving regulatory landscape for 3D-printed products

exploit the benefits of 3D-printed microrobots in revolutionizing targeted therapeutic delivery. In the subsequent sections of this review, we will delve deeper into the latest scientific findings, explore specific applications, and discuss the future directions of 3D printing in therapeutic delivery [25].

Despite the impressive advancements in creating and controlling 3D-printed microrobots, the transition from laboratory experimentation to clinical deployment is met with substantial challenges. Foremost among these challenges is the economical large-scale production of microscale robotic devices, a hurdle that currently looms large. Additionally, microrobots face a series of obstacles, commencing with their introduction into the human body and the subsequent navigation to reach the intended destination. These hurdles encompass potential immune system reactions and clearance issues, demanding meticulous deliberation and the implementation of strategic mitigation measures. Furthermore, the current standard test procedures for ensuring safety and functionality impose cumbersome and costly barriers, resulting in delays that hinder the rapid translation of these groundbreaking technologies into commercially viable clinical applications. To facilitate the successful integration of 3D-printed microrobots into real-world medical practice, it is essential to address these challenges head-on [20]. Addressing these challenges requires a multifaceted approach involving the development of new materials, fabrication methods, and actuation modalities. Additionally, there is a pressing need for streamlined and efficient test procedures that maintain safety without incurring unnecessary delays. A collaborative, multidisciplinary effort involving engineers, clinicians, and regulatory bodies is necessary to establish comprehensive guidelines and standards. By fostering seamless communication and cooperation among these stakeholders, we can expedite the translation process from the laboratory bench to the patient's bedside. Besides, the field of 3D printing for therapeutic delivery has witnessed significant advancements, holding immense promise for revolutionizing minimally invasive medicine as shown in the SWOT analysis in Table III. The precision fabrication capabilities of 3D printing, combined with the integration of AI, PI, and smart materials, have propelled the development of intelligent microrobots capable of targeted drug delivery, microsurgeries, imaging, and other transformative biomedical applications [20, 26]. Nevertheless, to fully harness the potential of 3D-printed microrobots, it is imperative to address challenges associated with mass production, immune system responses, and test procedures. Through proactive engagement in future research initiatives and the cultivation of collaborative partnerships, we have the potential to surmount these challenges. This collective effort will enable a smooth transition from laboratory settings to the realization of commercially viable and broadly accessible clinical applications. With unwavering commitment and persistence, the fusion of state-of-the-art technology and medical expertise holds the promise of genuinely transforming the landscape of therapeutic delivery and patient care [16].

Importance of Therapeutic Delivery in Healthcare

Therapeutic delivery assumes a pivotal role in modern healthcare, aiming to administer medications, therapies, and medical interventions with unparalleled precision and efficacy. As the healthcare landscape shifts towards personalized medicine and patient-centered care, innovative solutions are imperative for tailored therapeutic delivery, accounting for each patient's unique characteristics and medical history. By customizing drug formulations and precisely delivering therapies to the affected site, therapeutic delivery optimizes treatment outcomes, enhances efficacy, reduces toxicity, and improves patient compliance [17]. In healthcare, the delivery of therapeutic agents plays a critical role in achieving desired treatment outcomes as depicted in Fig. 2. The primary challenge in drug delivery revolves around the precise targeting of specific sites within the body while simultaneously minimizing systemic side effects. Conventional drug delivery approaches like oral ingestion or intravenous infusion inherently possess limitations concerning accuracy, effectiveness, and patient adherence. Nonetheless, the emergence of 3D printing technology has ushered in a paradigm shift within the realm of therapeutic delivery, offering innovative solutions to tackle these challenges. This section delves into the significance of therapeutic delivery in healthcare and elucidates the advantages of 3D printing over traditional drug delivery methods [18]. One of the key advantages of 3D printing in therapeutic delivery resides in its capacity to fabricate complex structures with remarkable precision and customization. Traditional drug delivery methods often lack the ability to precisely target specific sites within the body, leading to broader distribution of therapeutic agents and potential off-target effects. In contrast, 3D printing empowers the design and production of drug delivery systems with intricate geometries, facilitating site-specific delivery and localized drug release. This heightened level of precision not only enhances therapeutic efficacy but also mitigates the risk of adverse effects associated with systemic drug distribution [8, 18, 27]. Another significant advantage of 3D printing in therapeutic delivery is the ability to create drug delivery systems with tailored release profiles. Conventional drug delivery methods frequently result in rapid drug release, leading to suboptimal drug concentrations at the target site or a short duration of action. With 3D printing, it becomes feasible to engineer drug delivery systems with controlled release kinetics, facilitating sustained and controlled drug release over an extended period. This capability proves particularly valuable in the treatment of chronic conditions where maintaining therapeutic drug levels is pivotal for long-term efficacy [28].

Table III Comparative Analysis of 3D Printing Technologies: including Fused Deposition Modeling (FDM), Stereolithography (SLA), Selective Laser Sintering (SLS), and Digital Light Processing (DLP)

3D Printing Technology	Printing Mechanism	Materials Used	Printing Speed	Resolution	Application Areas	Advantages	Disadvantages
Fused Deposition	Extrusion of thermoplastic	PLA, ABS, PETG, TPU, etc	Moderate to Fast	Medium to High	Prototyping, Hobbyist, Functional Parts, Education	Low-cost, User-friendly, Wide material selection	Layer lines visible, Limited resolution for intricate details
Modeling (FDM)	filament through a nozzle						
Stereolithography	Photopolymerization	Photopolymer resins (UV-curable)	Moderate to Slow	High	Dentistry, Jewelry, Prototyping, Medical, Engineering	High-detail printing, Smooth surface finish, Wide range of resins	Post-processing required, Limited build volume
(SLA)	using UV light						
Selective Laser	Scanning of laser on	Nylon, TPU, Metal powders, Ceramics, etc	Fast	High	Aerospace, Automotive, Medical, Prototyping, Tooling	Diverse material compatibility, Complex geometries	Expensive machines, Post-processing required
Sintering (SLS)	powdered material						
Digital Light	Photopolymerization using	Photopolymer resins (UV-curable)	Fast	High	Dentistry, Jewelry, Prototyping, Education, Animation	High-speed printing, High-resolution, Multiple parts at once	Limited build volume, Cost of resins
Processing (DLP)	a digital light projector						

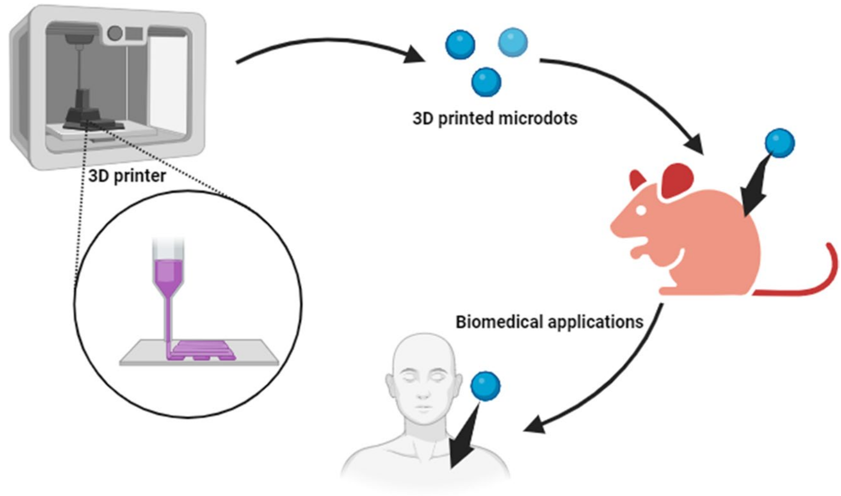

Fig. 2 The Evolution from 3D Printing to Clinical Utility: This caption highlights the ongoing advancement of 3D printing technology, showcasing its crucial contribution to the restructuring of clinical methodologies and the initiation of a novel era characterized by tailored healthcare solutions. Image was generated by Biorender.com

3D printing introduces a distinctive advantage when it comes to the advancement of combination therapies. This approach allows for the integration of multiple drugs or therapeutic agents into a single delivery system. In contrast, traditional drug delivery methods frequently necessitate the separate administration of individual drugs, which can pose challenges in terms of coordinating drug schedules, realizing synergistic effects, and ensuring patient adherence to complex treatment regimens. By harnessing 3D printing, it is possible to create sophisticated drug delivery systems that combine multiple therapeutic agents, enabling simultaneous and targeted delivery of different drugs. This approach augments treatment efficacy and unlocks new possibilities in personalized medicine [29]. Every patient possesses unique attributes, and their responses to therapeutic treatments can vary significantly. Conventional drug delivery techniques often employ a standardized approach, overlooking individual patient distinctions and requirements. Conversely, 3D printing enables the creation of patient-tailored drug delivery systems designed to precisely match the distinct needs of each individual. By integrating patient-specific data, such as anatomical scans or genetic information, into the design process, personalized drug delivery systems can be created, optimizing treatment outcomes and fostering patient adherence [30]. Therapeutic delivery stands as a crucial aspect of healthcare, and the advancements in 3D printing technology have revolutionized the landscape of drug delivery as shown in Table IV. The precision, customization, tailored release profiles, capacity to develop combination therapies, and patient-specific solutions offered by 3D printing have truly transformed therapeutic delivery. In contrast to conventional drug delivery approaches, 3D printing offers superior targeting precision, heightened treatment effectiveness, and increased patient contentment. As the field advances, ongoing research and innovation in 3D printing for therapeutic delivery are poised to open doors to even more personalized and efficacious healthcare interventions [31].

Significance of 3D Printing for Therapeutic Delivery

In recent years, 3D printing has emerged as a revolutionary technology in the field of therapeutic delivery, propelling the healthcare landscape towards personalized medicine. Its remarkable capacity to create intricate, patient-specific structures with precise control has opened unprecedented possibilities in healthcare interventions. Leveraging the capabilities of 3D printing, healthcare experts can presently conceive and produce personalized drug delivery mechanisms, implants, tissue support structures, and medical equipment, all meticulously crafted to cater to the specific requirements of individual patients [32]. A defining advantage of 3D printing in therapeutic delivery lies in its capability to fabricate complex geometries that prove challenging or even unattainable with traditional manufacturing methods. As an illustration, 3D-printed implants can be meticulously engineered to mirror the precise dimensions and contours of a patient's anatomical features, guaranteeing an ideal fit and functionality. Such a high degree of personalization markedly elevates patient comfort, diminishes the likelihood of complications, and augments the overall efficacy of the treatment [1]. Moreover, 3D printing offers a significant edge in achieving complex drug release profiles. While traditional drug delivery methods often entail simple drug release kinetics characterized by rapid initial release followed by a decline in drug concentration, certain therapeutic applications necessitate more sophisticated release patterns, such as pulsatile, sustained, or delayed release. Through 3D printing, researchers can engineer drug delivery systems with finely controlled release profiles, allowing for customized drug release kinetics tailored to the specific requirements of the therapeutic agent and the condition being treated [33]. Moreover, the utilization of various materials within 3D printing facilitates the direct integration of therapeutic substances, including drugs or growth factors, into the

Table IV SWOT Analysis of the Strengths, Weaknesses, Opportunities, and Threats in 3D Printing Technology

Strengths	Weaknesses
Customization: 3D printing allows for personalized fabrication of therapeutic delivery systems, enabling customized drug dosages, shapes, and release profiles to suit individual patient needs	Limited Materials: Although 3D printing offers material versatility, the available materials may still be limited compared to traditional manufacturing methods. The selection of appropriate materials for drug delivery, particularly for biodegradable systems, may pose challenges
Complex Geometry: 3D printing enables the creation of intricate and complex structures, allowing for the design of drug delivery systems with precise internal architectures and multi-functional features	Quality Control: Ensuring consistent quality and reproducibility of 3D-printed therapeutic delivery systems can be challenging, as variations in printer settings, material properties, and post-processing techniques can impact the final product
Rapid Prototyping: The quick turnaround time in 3D printing enables faster development and testing of novel therapeutic delivery systems, accelerating the research and development process	Regulatory Challenges: The regulatory landscape for 3D-printed therapeutic delivery systems is still evolving, and obtaining necessary approvals can be complex and time-consuming, potentially slowing down the translation of these technologies into clinical applications
Material Versatility: 3D printing can utilize a wide range of materials, including biocompatible polymers, metals, ceramics, and bioinks, offering flexibility in choosing the most suitable materials for drug delivery applications	
On-Demand Manufacturing: With 3D printing, therapeutic delivery systems can be produced on-demand, reducing the need for large-scale manufacturing and storage, and enabling decentralized production	
Opportunities	Threats
Personalized Medicine: 3D printing enables the customization of therapeutic delivery systems, opening doors to personalized medicine by tailoring treatments to individual patient characteristics, such as anatomy, disease state, and genetic profile	Cost: Currently, 3D printing technologies and materials can be relatively expensive, which may limit their widespread adoption for therapeutic delivery systems. Cost-effectiveness studies and advancements in materials and manufacturing processes are needed to address this concern
Novel Drug Delivery Strategies: 3D printing allows for the development of innovative drug delivery systems, including complex geometries, controlled release mechanisms, and combination therapies, which may enhance therapeutic efficacy and patient compliance	Intellectual Property and Counterfeiting: The ease of replicating 3D-printed objects raises concerns about intellectual property rights and the potential for counterfeit therapeutic delivery systems entering the market, compromising patient safety
Point-of-Care Manufacturing: 3D printing can facilitate the production of therapeutic delivery systems at the point of care, reducing transportation costs and time, enabling rapid response to specific patient needs, and potentially revolutionizing healthcare delivery	Long-Term Biocompatibility: The long-term biocompatibility and degradation behavior of 3D-printed therapeutic delivery systems need to be thoroughly evaluated to ensure safety and efficacy, as well as to address potential concerns about adverse reactions or tissue interactions

fabricated constructs. This groundbreaking capacity ushers in thrilling prospects for precise and regulated drug delivery, allowing for the release of medications at designated locations and in tailored dosages. Consequently, this approach minimizes systemic side effects, contributing to more effective therapeutic outcomes. The versatility of 3D printing also extends to the realm of combination therapies and multidrug delivery, where the synergistic effects of multiple therapeutic agents can significantly enhance treatment outcomes. By incorporating different drugs within a single dosage form, researchers can harness the benefits of synergistic drug interactions, improve treatment efficacy, and simplify the drug administration process for patients [34]. Beyond its influence on individualized drug delivery, 3D printing assumes a central role in tissue engineering and regenerative medicine. The production of intricate scaffolds and biocompatible frameworks via 3D printing empowers the generation of intricate tissues and organs, thereby offering invaluable utility in transplantation, disease modeling, and drug experimentation. This domain exhibits considerable potential for tackling the organ shortage predicament and propelling the boundaries of regenerative medicine forward [35–37].

3D printing has the potential to revolutionize the field of advanced drug formulations, particularly for poorly soluble or highly potent drugs. By leveraging the versatility of 3D printing techniques, researchers can develop novel drug formulations that enhance drug solubility, improve bioavailability, or enable targeted drug delivery. For instance, the incorporation of nanoscale drug carriers or encapsulating drugs within biocompatible polymers through 3D printing can enhance drug stability, control drug release kinetics, and facilitate targeted drug delivery to specific tissues or cells. Such advancements in drug formulation have the potential to address longstanding challenges in drug delivery and unlock new avenues for therapeutic interventions [35]. The significance of 3D printing in therapeutic delivery cannot be overstated. This transformative technology offers unparalleled precision, personalization, and customization in drug delivery, thereby facilitating patient-centric treatment approaches. With the ability to fabricate customized dosage forms, achieve complex drug release profiles, facilitate combination therapies, and develop advanced drug formulations, 3D printing holds tremendous promise in revolutionizing healthcare. As researchers continue to explore and optimize 3D printing techniques, further advancements in therapeutic delivery are expected, leading to improved treatment outcomes, enhanced patient satisfaction, and ultimately, a more personalized and effective healthcare landscape [29, 35]. 3D printing technology has emerged as a powerful tool in the realm of therapeutic delivery, reshaping the landscape of healthcare interventions. Its capacity to customize drug delivery systems, create patient-specific implants, and facilitate tissue engineering has unlocked new possibilities in personalized medicine and patient care. As we delve further into this article, we will explore the various applications, advancements, challenges, and future directions of 3D printing in therapeutic delivery, providing a comprehensive understanding of this transformative technology in healthcare [38].

Overview of 3D Printing in Therapeutic Delivery

One of the key advantages that sets 3D printing apart in therapeutic delivery is its unparalleled ability to create intricate and customized drug delivery systems. By leveraging a diverse range of biocompatible materials, 3D printers can fabricate structures with precise control over their architectures, geometries, and internal features. This remarkable capability empowers the generation of patient-specific drug delivery devices tailored to accommodate individual physiological variations, ultimately leading to heightened therapeutic efficacy and minimized side effects [36]. Moreover, 3D printing unlocks the potential for controlled and sustained drug release. Through adeptly incorporating drugs into biodegradable polymeric matrices or encapsulating them within 3D-printed micro/nanoparticles, researchers have achieved remarkable control over drug release kinetics. Such a capacity proves particularly invaluable for treating chronic diseases and conditions requiring long-term therapy, where maintaining consistent therapeutic levels and minimizing fluctuations are pivotal [39, 40]. Another noteworthy advantage of 3D printing in therapeutic delivery lies in its capacity to seamlessly integrate multiple therapeutic agents into a single dosage form. By expertly orchestrating the spatial distribution of drugs within a 3D-printed structure, multi-drug delivery systems can be tailored to target complex diseases or address multiple pathological factors simultaneously. This innovative approach holds the promise of synergistic effects, personalized combination therapies, and significantly enhanced treatment outcomes [41]. Notwithstanding these promising advancements, the realm of 3D printing for therapeutic delivery is not without challenges and limitations. One such hurdle lies in the meticulous selection of materials boasting requisite biocompatibility, mechanical properties, and controlled degradation characteristics. Research efforts remain ongoing to develop novel biomaterials that seamlessly align with 3D printing processes while offering optimal drug release profiles. Additionally, the regulatory landscape encompassing 3D-printed therapeutic delivery systems is still evolving, necessitating standardized manufacturing processes and the implementation of rigorous quality control measures to ensure utmost safety and efficacy [42]. In conclusion, 3D printing stands as a commanding force in the field of therapeutic delivery, presenting unparalleled opportunities for personalized medicine and precise drug administration as highlighted in Table V. The capacity to fabricate customized drug delivery systems, exercise precise control over drug release kinetics, and integrate multiple therapeutic agents offers immense potential for elevating treatment outcomes to new heights. However, it is imperative to address challenges related to material selection and regulatory considerations to fully harness the capabilities of 3D printing in therapeutic delivery. In the subsequent sections of this review, we shall delve deeper into specific applications, recent advancements, and the promising future prospects of 3D printing in therapeutic delivery [43].

Definition and Principles of 3D Printing

3D printinghas surfaced as a game-changing technology across various sectors. It boasts the capacity to construct three-dimensional objects incrementally, guided by CAD. Within the domain of therapeutic delivery, 3D printing has attracted considerable interest owing to its extraordinary adaptability and precision. This state-of-the-art technology enables meticulous deposition and solidification of materials, resulting in the formation of intricate structures with exceptional precision and complex geometries [44].

Advantages of 3D Printing in Therapeutic Delivery

Within the realm of therapeutic delivery, 3D printing presents a striking advantage by enabling the construction of personalized drug delivery systems and medical equipment customized to meet the unique requirements of individual patients. This capability is made possible through the utilization of diverse bioactive materials, including polymers, hydrogels, and even living cells, allowing for the direct integration of therapeutic substances into the printed constructs. Consequently, this empowers precise and regulated

Table V Comparative Analysis of Therapeutic Delivery Approaches, with Emphasis on 3D Printing-Based Delivery

Approach	Precision	Customization	Targeted Delivery	Patient Compliance	Impact on Treatment Outcomes	Advantages	Limitations	Refernecs
Traditional Drug Delivery	Moderate	Limited	General	Varies	Depends on drug formulation	Widely available and established	Lack of individual tailoring, potential side effects, limited efficacy	[162]
Nanoparticle Drug Delivery	High	Limited	Enhanced	Varies	Improved drug stability	Improved targeting and reduced side effects	Complexity of nanoparticle synthesis, potential toxicity	[163]
Liposomal Drug Delivery	High	Limited	Enhanced	Varies	Improved drug stability	Efficient intracellular delivery	Complexity of liposome production, limited scalability	[164, 165]
Implantable Devices	High	Limited	Targeted	High	Prolonged drug release	Continuous and localized drug delivery	Invasive implantation procedure, potential for complications	[166]
Inhalation Drug Delivery	Moderate	Limited	Localized	Varies	Rapid onset of action	Efficient and non-invasive	Limited to respiratory conditions, coordination challenges	[167]
Injectable Drug Delivery	High	Limited	Localized	High	Rapid onset of action	Quick and precise administration	Requires trained healthcare professionals, potential for needle-related issues	[168]
Oral Drug Delivery	Low	Limited	General	Varies	Convenient and non-invasive	Ease of administration, patient-friendly	Variability in drug absorption, potential for first-pass metabolism	[169]
3D Printing-Based Delivery	High	High	Targeted	High	Personalized and patient-specific	Customized drug dosage and release profiles	Limited range of printable materials, challenges in quality control and regulation	[35]

drug release, enhancing targeted therapeutic outcomes. This unprecedented capability opens up new frontiers in personalized medicine, where treatment strategies can be precisely tailored to specific patient requirements [45].

Types of 3D Printing Technologies Applicable to Therapeutic Delivery

Several 3D printing technologies find application in therapeutic delivery, each endowed with distinct advantages and limitations. The selection of a specific technology hinges upon the desired application, the materials involved, and the required resolution. In this context, we highlight some prominent types of 3D printing technologies commonly employed in therapeutic delivery:

Fused Deposition Modeling (FDM): FDM, a widely utilized 3D printing technique, employs thermoplastic filaments. The material is heated and then extruded through a nozzle, layer by layer, to craft the desired object. FDM bestows versatility in material selection and is particularly well-suited for fabricating drug-loaded matrices and scaffolds in tissue engineering application [46, 47].

Stereolithography (SLA): SLA employs a liquid resin that undergoes solidification upon exposure to a particular wavelength of light. The process involves incremental movements of a build platform, with a laser or projector selectively curing the resin in a layer-by-layer fashion, ultimately shaping the desired structure. SLA boasts high-resolution printing capabilities, making it suitable for intricate drug delivery systems and microfluidic devices [48, 49].

Selective Laser Sintering (SLS): SLS entails the use of a laser to selectively fuse powdered materials, such as polymers or ceramics, layer by layer. This technique allows for the fabrication of porous structures with precise control over pore size and interconnectivity. SLS proves particularly useful for creating drug-loaded implants and scaffolds for tissue regeneration [50].

Inkjet-based 3D Printing: This technology utilizes inkjet printheads to deposit droplets of bioinks containing cells or therapeutic agents onto a substrate as shown in Fig. 3. By meticulously controlling the deposition process, complex structures can be created, enabling the fabrication of tissue constructs and drug-loaded microcapsules [51].

To sum up, 3D printing has risen as a potent instrument within the sphere of therapeutic delivery, affording the capability to craft personalized drug delivery systems and medical equipment precisely attuned to the unique requirements of individual patients. Various 3D printing technologies, including FDM, SLA, SLS, and inkjet-based printing, provide unique advantages in terms of material versatility, resolution, and fabrication capabilities. As we explore the subsequent sections, we will delve deeper into the specific applications, recent advancements, and future prospects of these 3D printing technologies in the context of therapeutic delivery [8, 52].

Advantages and Limitations of 3D Printing in Therapeutic Delivery

The integration of 3D printing in therapeutic delivery offers numerous advantages that have the potential to revolutionize healthcare. These advantages include personalization, the ability to fabricate complex geometries, precise control over drug release, and rapid prototyping and manufacturing. However, several limitations such as material selection, resolution and scalability, and regulatory considerations need to be addressed to fully realize the potential of 3D printing in therapeutic applications [53, 54].

Personalization: 3D printing enables the customization of drug delivery systems and medical devices, catering to individual patient requirements. This personalized approach leads to more effective and targeted treatments, improving patient outcomes [55].

Complex Geometries: Through the application of 3D printing, it becomes feasible to create structures with

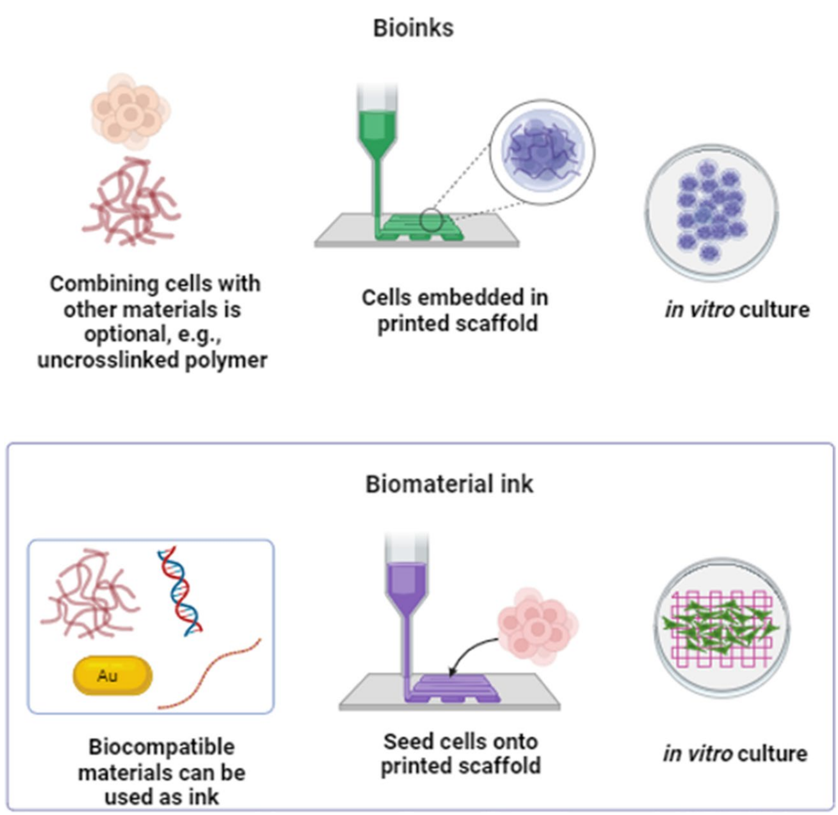

Fig. 3 Divergent Strategies in Tissue Engineering; In this visual representation, we underscore two divergent strategies within the realm of tissue engineering. To the left, the bioink methodology entails the integration of cells, polymers, and assorted materials into a formable bioink blend. This bioink is then administered into a scaffold, followed by subsequent *in vitro* incubation to stimulate tissue growth. On the right, the biomaterial ink approach centers on the utilization of biomaterials such as biopolymers, DNA, and nanomaterials for the direct fabrication of the scaffold. Subsequently, cells of interest are introduced onto the scaffold, with subsequent *in vitro* nurturing. These methodologies provide distinct avenues for tissue engineering, each endowed with unique merits and considerations. Image was generated by Biorender.com

complex geometries that prove difficult to achieve through traditional manufacturing techniques. This capacity opens the door to designing drug delivery systems capable of adapting to precise anatomical locations, thereby enhancing the effectiveness of therapeutic interventions [52, 56].

Controlled Drug Release: Incorporating therapeutic agents directly into printed structures enables precise control over drug release kinetics. This control allows for sustained or triggered release profiles, improving the efficacy and safety of therapeutic interventions [57].

Rapid Prototyping and Manufacturing: 3D printing expedites the processes of rapid prototyping and manufacturing, thereby reducing the time necessary for design refinements and expediting the transition from conceptualization to practical clinical application. This advantage is particularly valuable in emergency situations or for patients with urgent medical needs [58, 59].

Limitations of 3D Printing in Therapeutic Delivery

Material Selection: The availability of suitable materials for 3D printing, especially biocompatible and bioresorbable materials, remains a challenge. Further research and development are necessary to expand the range of materials compatible with 3D printing techniques [58].

Resolution and Scalability: Achieving high resolution and scalability simultaneously can be challenging. Printing small-scale intricate structures with high precision may require more time and resources, limiting the scalability of the process [60, 61].

Regulatory Considerations: The regulatory approval process for 3D-printed medical devices and drug delivery systems poses unique challenges. Ensuring the safety, efficacy, and quality control of these products requires compliance with rigorous regulatory standards [62, 63].

Applications of 3D Printing in Therapeutic Delivery

Fabrication of Patient-Specific Oral Dosage Forms: One significant advantage of 3D printing in therapeutic delivery is the ability to create patient-specific oral dosage forms. Traditional manufacturing methods often limit the production of oral medications to standardized formulations and sizes. However, with 3D printing, pharmaceutical companies can design and fabricate personalized dosage forms tailored to an individual's specific needs [64].

Utilizing 3D printing technologies such as FDM or SLS, drug-loaded matrices or tablets with precise geometries and drug release profiles can be produced. This customization allows for personalized dosing, optimizing therapeutic outcomes, and improving patient adherence to medication regimens. Furthermore, 3D printing enables the incorporation of multiple drugs or different dosages within a single tablet, facilitating combination therapy and simplifying treatment for patients with complex medication regimens [36, 65].

Personalized Drug Delivery Implants and Devices: In addition to oral dosage forms, 3D printing enables the fabrication of personalized drug delivery implants and devices. By combining biocompatible materials with therapeutic agents, 3D-printed implants can provide targeted and sustained drug release directly at the site of action. This localized drug delivery approach minimizes systemic side effects and maximizes therapeutic efficacy [66, 67]. For example, 3D-printed drug-eluting stents have been developed to treat cardiovascular diseases. These stents can be customized to match the patient's vascular anatomy and incorporate drugs that promote tissue healing and prevent restenosis. Similarly, personalized drug delivery devices, such as transdermal patches or inhalation devices, can be designed using 3D printing techniques to precisely control the release of drugs through the skin or respiratory system [68, 69]. In conclusion, the integration of 3D printing in therapeutic delivery offers significant advantages, including personalization, complex geometries, controlled drug release, and rapid prototyping and manufacturing. However, addressing limitations such as material selection, resolution and scalability, and regulatory considerations is crucial for fully harnessing the potential of 3D printing in therapeutic applications. As we delve further into this article, we will explore specific applications, recent advancements, and future prospects of 3D printing in therapeutic delivery, providing a comprehensive understanding of this transformative technology in healthcare [70, 71].

Tissue Engineering and Regenerative Medicine

Biofabrication of Complex Tissue Structures

Within the domain of tissue engineering and regenerative medicine, 3D printing assumes a central role by facilitating the biofabrication of intricate tissue structures. The fusion of biomaterials with living cells empowers researchers to generate 3D-printed constructs that replicate the structure and function of native tissues. This innovative methodology holds immense potential for applications in tissue repair and organ transplantation [36, 72]. Techniques like bioprinting, which involve the layer-by-layer deposition of bioinks containing cells and supporting materials, have successfully produced functional tissues such as skin, cartilage, and blood vessels. These biofabricated tissues can be utilized for drug testing, disease modeling, and, eventually, patient-specific tissue replacements [73, 74].

Scaffold-Based Approaches for Tissue Regeneration

Another notable application of 3D printing in tissue engineering pertains to the production of scaffolds. Scaffolds serve as transient supportive structures that oversee tissue regeneration by furnishing a platform for cell adherence, proliferation, and vascularization. 3D-printed scaffolds bring forth precise management of their physical and architectural attributes, allowing for customization of parameters such as pore size, porosity, and mechanical resilience [73, 75]. By incorporating bioactive factors and growth factors into the scaffold materials, researchers can promote cellular proliferation, differentiation, and tissue regeneration. These biofunctionalized scaffolds have demonstrated promise in various tissue engineering applications, including bone regeneration, wound healing, and organ-on-a-chip platforms for drug screening [76, 77].

Medical Devices and Implants: 3D-Printed Prosthetics and Orthotics

The field of prosthetics and orthotics has been revolutionized by 3D printing, allowing for the fabrication of customized devices with improved fit, functionality, and aesthetics. Traditional methods often involve labor-intensive and time-consuming processes to create individualized devices. However, 3D printing streamlines the production process, enabling rapid prototyping and customization [78, 79]. By leveraging 3D scanning technologies, patient-specific measurements can be obtained and used to design prosthetic limbs or orthotic braces that precisely match the patient's anatomy. Incorporating lightweight and durable materials, such as carbon fiber-reinforced polymers, 3D-printed prosthetics and orthotics offer enhanced comfort, mobility, and quality of life for individuals with limb loss or musculoskeletal conditions [80, 81].

Customized Implants and Surgical Instruments

Another significant application of 3D printing in therapeutic delivery is the creation of customized implants and surgical instruments. Traditional implants and instruments are often limited to standardized sizes and designs, which may not always meet the unique anatomical requirements of individual patients. 3D printing overcomes these limitations by allowing the fabrication of patient-specific implants and instruments based on medical imaging data [82]. In orthopedic surgery, for instance, 3D-printed implants can be tailored to fit precisely within a patient's bone defect, enhancing stability and promoting better osseointegration. Likewise, surgical guides and instruments can be custom-designed and 3D printed to assist surgeons in performing complex procedures with greater accuracy and efficiency [24, 83]. To sum up, 3D printing has brought about a revolution in therapeutic delivery, as depicted in Table VI. It has achieved this by facilitating the creation of tailored drug delivery systems, tissue-engineered constructs, and individualized medical equipment. In doing so, 3D printing has paved the way for personalized medicine and regenerative therapies. While there remains a need for additional research and development to address challenges related to material selection, resolution, scalability, and regulatory considerations, the potential of 3D printing in therapeutic applications is substantial. As technology continues to progress,

Table VI Significance of 3D Printing in Therapeutic Delivery

Aspect of 3D Printing in Therapeutic Delivery	Significance and Benefits
Personalized Drug Dosage Forms	3D printing enables the creation of patient-specific oral dosage forms, allowing precise drug dosing and tailored therapies for individual needs. This personalized approach can lead to improved treatment efficacy, reduced side effects, and enhanced patient compliance
Complex Tissue Scaffolds	By utilizing 3D printing to fabricate intricate tissue scaffolds, the regenerative medicine field benefits from the potential to engineer functional organs and tissues for transplantation. This revolutionary approach addresses the critical need for organ donors and offers hope for patients awaiting life-saving transplants
Patient-Specific Implants	The ability to create customized medical implants based on individual anatomical data enhances patient fit, reduces the risk of implant rejection, and improves surgical outcomes. 3D-printed implants offer enhanced functionality, compatibility, and comfort compared to traditional standardized implants, leading to better patient satisfaction and postoperative recovery
Controlled-Release Drug Delivery Systems	3D printing allows for the development of drug delivery systems with precise control over drug release profiles. This targeted and controlled drug delivery can improve treatment outcomes by ensuring therapeutic concentrations, minimizing side effects, and extending drug release durations, particularly useful for chronic conditions or complex treatment regimens
On-Demand Manufacturing	3D printing's decentralized production approach reduces the need for large-scale manufacturing and storage of therapeutic delivery systems. By producing devices, implants, and dosage forms on-demand, healthcare providers can optimize inventory, respond rapidly to patient needs, and potentially reduce overall healthcare costs

we can anticipate further breakthroughs and enhancements within the realm of therapeutic delivery, ultimately enhancing patient outcomes and reshaping the healthcare landscape [7, 59].

Advancements and Innovations in 3D Printing for Therapeutic Delivery

Material Selection and Biocompatibility

One significant advancement in 3D printing for therapeutic delivery is the development of specialized materials called bioinks for bioprinting applications. Bioinks are biocompatible materials that contain living cells and provide support for cell growth and tissue formation. They serve as the building blocks for creating complex biological structures with precise spatial control [84]. Bioinks are meticulously designed to replicate the characteristics of the native extracellular matrix (ECM) and foster a conducive environment for cell viability and growth. Typically, these materials comprise a blend of biomaterials, including natural polymers like collagen and gelatin, or synthetic polymers such as polycaprolactone and polyethylene glycol. They may also incorporate cell-adhesive molecules. Researchers have explored diverse approaches to enhance bioink formulations, including the integration of growth factors, signaling molecules, and other bioactive agents aimed at stimulating cell differentiation and facilitating tissue regeneration [85]. The incorporation of bioinks into bioprinting applications has surfaced as a highly promising path within tissue engineering and regenerative medicine. In this section, we present a thorough examination and discerning assessment of the current body of literature concerning bioinks. Our aim is to spotlight noteworthy discoveries, progressions, and constraints. Moreover, we acknowledge contrasting viewpoints and alternative stances to offer a well-rounded analysis of this swiftly evolving domain [86]. One significant finding in the literature is the successful incorporation of various therapeutic agents into 3D-printed structures for controlled drug release. Studies have demonstrated the integration of small molecules, proteins, growth factors, and nucleic acids within 3D-printed matrices or scaffolds. This approach offers spatial and temporal control over drug release, enabling targeted therapy and enhanced treatment outcomes [87]. For instance, there are reports of a 3D-printed scaffold that incorporates bone morphogenetic protein-2 (BMP-2) for the purpose of bone tissue engineering, leading to enhanced bone regeneration [88, 89].

While bioinks have shown tremendous progress, it is crucial to acknowledge limitations and alternative perspectives in the existing literature as shown in Table VII. One key challenge lies in achieving spatial control over multiple cell types, their organization, and the formation of complex tissue architectures. Furthermore, the lack of standardized protocols and characterization techniques for assessing the quality and functionality of printed constructs hinders the reproducibility and comparability of results across different studies. Efforts should be made to establish standardized protocols and characterization methods to facilitate the advancement and translation of bioprinting technologies. Another viewpoint to consider is the ethical and regulatory aspects associated with bioprinting and the use of bioinks. The translation of bioprinting technologies to clinical

Table VII Diverse Applications of 3D Printing in Tissue Engineering and Regenerative Medicine

Application	Description	Advantages/ Benefits
Customized Tissue Grafts	3D printing enables the fabrication of patient-specific tissue grafts, such as skin, cartilage, and bone, offering a precise fit and potential for improved integration	- Reduced rejection rates in grafts - Faster healing and better patient outcomes
Bioprinting of Organs	Researchers are exploring 3D bioprinting techniques to create functional organs, including liver, kidney, and heart, to address the organ transplant shortage	- Potential to eliminate the need for organ transplantation waiting lists - Personalized organ manufacturing
Scaffold-Based Approaches	3D-printed scaffolds serve as a framework for cell growth and tissue regeneration, facilitating the repair of damaged or diseased tissues	- Enhanced tissue regeneration with improved structural support - Tailored to patient-specific requirements
Vascularization	3D printing aids in the creation of vascular networks within engineered tissues, promoting nutrient supply and waste removal for enhanced viability	- Improved tissue survival through better oxygen and nutrient delivery - Accelerated tissue integration
Drug Delivery Platforms	3D-printed constructs can be designed to serve as drug delivery platforms, allowing localized and controlled release of therapeutic agents for regenerative purposes	- Targeted and sustained drug release at the site of interest - Reduced systemic side effects
Disease Modeling	Patient-specific 3D-printed tissue models mimic pathological conditions, enabling the study of diseases, drug testing, and personalized treatment evaluation	- Precise disease representation for accurate research and testing - Tailored treatment strategies

applications raises concerns regarding safety, long-term stability, and the ethical implications of printing functional human organs or tissues. Addressing these concerns requires interdisciplinary collaboration involving scientists, ethicists, and regulatory bodies to establish guidelines and frameworks that ensure responsible and ethical use of bioprinting technologies [90, 91]. In summary, bioinks represent a remarkable advancement in 3D printing for therapeutic delivery, offering the potential for creating complex biological structures with controlled drug release capabilities. Although significant progress have been taken, there remains a need for deeper exploration into challenges associated with spatial precision, standardization, and ethical dimensions. As researchers persist in their efforts to investigate and enhance these technologies, the prospects for bioprinting in revolutionizing tissue engineering and regenerative medicine remain highly promising. Ultimately, such advancements stand to benefit patients on a global scale [15, 92].

Integration of Therapeutic Agents into 3D-Printed Structures: Another pivotal advancement in the field of 3D printing for therapeutic delivery lies in the seamless integration of therapeutic agents into 3D-printed structures. By incorporating drugs, growth factors, or other therapeutic molecules directly into the printing process, researchers can engineer functional structures with localized and controlled drug release capabilities [93, 94]. Through meticulous material selection and innovative design, 3D-printed structures can effectively act as sophisticated drug delivery systems, enabling sustained release of therapeutics at specific sites of action. For instance, researchers have successfully embedded antibiotics into 3D-printed bone scaffolds, effectively preventing post-surgical infections. The precise control over release kinetics allows 3D-printed structures to offer targeted therapy, minimize systemic side effects, and significantly enhance overall treatment outcomes [33]. The integration of therapeutic agents into 3D-printed structures has garnered substantial attention as a promising approach for advanced drug delivery systems. In this section, we present a thorough analysis and critical evaluation of the existing literature on this groundbreaking topic, meticulously highlighting key findings, advancements, and limitations. Our analysis also takes into account opposing viewpoints and alternative perspectives, providing a balanced outlook that acknowledges differing opinions and limitations in the field [34]. A remarkable finding in the literature is the successful incorporation of various therapeutic agents into 3D-printed structures, empowering precise control over drug release. Among the therapeutic agents that have been incorporated are small molecules, proteins, growth factors, and nucleic acids, each serving a specific therapeutic purpose within the 3D-printed matrices or scaffolds. This approach offers not only spatial but also temporal control over drug release, presenting an exciting opportunity for targeted therapy and substantially improved treatment outcomes [95]. For instance, Kawai et al. (2021) conducted pioneering work by developing a 3D-printed scaffold loaded with bone morphogenetic protein-2 (BMP-2), leading to remarkable advancements in bone tissue engineering and enhanced bone regeneration [96].

Furthermore, the utilization of 3D printing techniques enables precise distribution of therapeutic agents within the printed structures. This spatial control enables the creation of highly sophisticated drug delivery systems, such as multicompartment devices or gradient release profiles. Through meticulous design and architectural planning, researchers can achieve differential drug release rates, effectively mimicking physiological conditions and optimizing therapeutic efficacy. Nonetheless, it is vital to be cognizant of potential challenges associated with achieving uniform distribution and homogeneity of the incorporated agents throughout the printed structures [29]. While the integration of therapeutic agents into 3D-printed structures shows immense promise, it is equally important to acknowledge limitations and alternative perspectives within the existing literature. A key challenge lies in the selection and compatibility of materials used for 3D printing with therapeutic agents. Different drugs or biologics may possess varying chemical properties and stability requirements, necessitating meticulous consideration during the formulation of bioinks or printable materials [97]. Moreover, the potential interactions between drug molecules and the printing process itself, such as exposure to high temperatures or shear forces, may impact the stability or activity of the therapeutic agents. Thus, further research is imperative to optimize the formulation and printing parameters to ensure the integrity and efficacy of the incorporated agents [98]. Moreover, the regulatory considerations and approval processes for 3D-printed drug delivery systems present formidable challenges. The complexity associated with integrating therapeutic agents within 3D-printed structures may necessitate additional scrutiny in terms of safety, quality control, and long-term stability. Regulatory agencies may demand compelling evidence regarding the compatibility, stability, and controlled release profile of the integrated agents before approving their clinical use. To overcome these challenges, it is of utmost importance to address regulatory considerations and engage in close collaboration with regulatory bodies to facilitate the seamless translation of 3D-printed drug delivery systems into clinical practice [99]. In conclusion, the integration of therapeutic agents into 3D-printed structures signifies an exciting and promising avenue for advanced drug delivery systems. The ability to achieve controlled drug release and spatial control within the printed structures holds great potential for personalized medicine and targeted therapies. However, it is crucial to confront challenges related to material compatibility, formulation optimization, and regulatory considerations. Future research endeavors should prioritize overcoming these limitations and establish comprehensive guidelines to support the safe and effective translation of 3D-printed drug delivery systems [9].

Multi-material and Multi-functional Printing

Advancements in 3D printing technology have ushered in a new era of multi-material printing, revolutionizing various applications by integrating distinct materials within a single 3D-printed device or construct. This innovation has resulted in enhanced functionality and performance, as different materials like polymers, metals, ceramics, and composites offer tailored mechanical, electrical, thermal, or biological properties that can be precisely engineered to meet specific requirements [100]. For example, in the field of prosthetics, the utilization of multi-material printing has facilitated the fabrication of personalized sockets featuring both sturdy structural elements and adaptable interfaces. This innovation has resulted in heightened comfort and functionality for users. Likewise, within drug delivery systems, the amalgamation of biocompatible polymers with hydrogels or porous materials enhances the precision of drug release kinetics, consequently bolstering therapeutic effectiveness [7]. In this section, we undertake a comprehensive analysis and critical evaluation of the existing literature on multi-material and multi-functional printing, with a focus on findings, advancements, and limitations of this cutting-edge technology. By acknowledging opposing viewpoints and alternative perspectives, we strive to provide a balanced analysis that encompasses differing opinions and limitations within the field. One key finding in the literature is the successful combination of different materials in 3D printing to create objects with enhanced functionality and performance. Researchers have delved into diverse methodologies for the integration of materials possessing distinct properties, thereby enabling the creation of intricate structures customized to specific characteristics. For instance, it has been demonstrated the integration of conductive materials into 3D-printed structures, enabling the creation of functional electronic devices [101]. Moreover, the use of multi-material printing has facilitated the development of objects with gradient properties. This design approach offers unique opportunities, particularly in tissue engineering, where the seamless integration of different materials can mimic the complex gradients found in natural tissues. However, precise control and optimization of material transitions within printed objects pose challenges that warrant consideration [102].

While multi-material and multi-functional printing show great promise, it is essential to acknowledge limitations and alternative perspectives in the existing literature. One significant challenge lies in achieving strong interfacial adhesion between different materials. Ensuring compatibility and bonding between dissimilar materials is crucial to avoid delamination or weak interfaces within the printed objects. Additionally, the compatibility of materials with the 3D printing process itself, such as their melt or cure temperatures, viscosity, or curing kinetics, can pose challenges for successful multi-material printing. Further research is needed to develop innovative approaches or surface treatments that promote better material compatibility and interfacial adhesion [103].

Moreover, the scalability and efficiency of multi-material printing techniques are areas of concern. Additional steps, such as material switching or nozzle changes, may increase printing time and complexity. Scaling up the process to larger volumes or industrial applications may pose challenges in terms of process reliability, speed, and cost-effectiveness. Future research should focus on developing efficient and high-throughput multi-material printing techniques to overcome these limitations [104, 105]. In conclusion, the integration of multiple materials in 3D printing has opened exciting avenues for enhanced functionality and performance of printed objects. The ability to tailor material properties allows for the creation of complex structures with unique characteristics as summarize in Table VIII. However, challenges related to material compatibility, bonding, scalability, and efficiency need to be addressed. By addressing these limitations, we can unlock the full potential of multi-material printing for diverse applications, ultimately advancing the field of 3D printing for therapeutic delivery [106]. Integration of Nanoparticles for Targeted Drug Delivery: The convergence of nanotechnology and 3D printing has given rise to a new era of targeted drug delivery systems. By incorporating nanoparticles within 3D-printed structures, researchers can augment the therapeutic efficacy and specificity of drug delivery. Nanoparticles serve as carriers that encapsulate drugs, shielding them from degradation and facilitating their precise delivery to specific cells or tissues [107]. An exemplary illustration of this synergy is the integration of magnetic nanoparticles into 3D-printed scaffolds or implants, enabling precise drug targeting through the application of external magnetic fields. Similarly, nanoparticles functionalized with specific ligands can selectively bind to particular cell receptors, offering targeted therapies for diseases such as cancer. The amalgamation of nanotechnology and 3D printing expands the therapeutic options available and lays the groundwork for the advancement of personalized medicine [108].

Surface Modification of 3D-Printed Structures for Enhanced Interactions

Surface modification assumes a pivotal role in enhancing the interactions between 3D-printed structures and biological entities. By introducing nanoscale attributes, coatings,

Table VIII Bioinks for Bioprinting Applications: A Comprehensive Overview of Composition, Rheological Properties, Biocompatibility, Bioprinting Techniques, and Potential Applications

Bioink Type	Composition	Rheological Properties	Biocompatibility	Bioprinting Techniques	Potential Applications
Alginate-based Bioinks	Alginate, Collagen, Fibrin, Gelatin, etc	Shear-thinning	High	Extrusion-based, Inkjet, Laser-assisted	Tissue constructs, organoids, wound healing
Hyaluronic Acid-based Bioinks	Hyaluronic Acid, Chitosan, Silk, etc	Thixotropic	Good	Extrusion-based, Inkjet, Laser-assisted	Drug delivery, tissue repair, regenerative medicine
PEG-based Hydrogels	Polyethylene Glycol (PEG) derivatives	Thixotropic	Excellent	Extrusion-based, Inkjet	Controlled drug release, artificial organs
PLA-PLGA Blends	Polylactic Acid (PLA)—Polyglycolic Acid (PLGA)			Inkjet	Implants, disease modeling, drug testing
Gelatin-Methacrylate Bioinks	Gelatin, Methacrylate, Photoinitiator, etc	Tunable viscosity	Good	Extrusion-based	Organ-on-a-chip, microfluidics, tissue constructs
Cell-laden Nanocomposite Bioinks	Synthetic polymers, Nanoparticles, Cells			Laser-assisted	Multi-material bioprinting, tissue constructs

or biomolecules onto the surface of 3D-printed constructs, researchers can stimulate cell adhesion, regulate immune reactions, and enhance the biocompatibility of the printed materials [109]. Various surface modification techniques, such as plasma treatment, electrospinning, or layer-by-layer assembly, can be employed to tailor the surface properties of 3D-printed structures. These modifications effectively promote cell attachment and proliferation, facilitate tissue integration, and minimize adverse reactions. The precise control over surface characteristics empowers researchers to optimize the performance and biocompatibility of 3D-printed devices and implants [110]. To summarize, the progress and innovations in 3D printing for therapeutic delivery have significantly expanded the frontiers of personalized medicine, tissue engineering, and precise drug delivery. Key developments such as bioinks, the incorporation of therapeutic substances, and the capacity to fabricate complex multi-material and multi-functional structures have brought about a revolution in the field. Additionally, the synergy between nanotechnology and 3D printing has facilitated accurate drug delivery and enhanced interactions with biological systems. As ongoing research and development in this domain advance, we can anticipate further breakthroughs that will reshape the landscape of therapeutic delivery, ultimately leading to improved patient outcomes and the continued advancement of healthcare [111, 112].

Challenges and Future Directions

The domain of 3D printing has experienced notable progress in a multitude of sectors, encompassing healthcare, aerospace, and manufacturing. Nonetheless, it is marked by a host of challenges and constraints that are instrumental in shaping the future trajectory of this technology. In this section, we offer a thorough examination and astute assessment of these challenges and potential future pathways in 3D printing. Our approach includes the acknowledgment of contrasting viewpoints and alternative perspectives to provide a comprehensive and balanced analysis of diverse opinions and limitations within the field [113]. One of the key challenges in 3D printing is the limited range of printable materials. Although 3D printing encompasses polymers, metals, ceramics, and composites, the selection is still relatively restricted compared to traditional manufacturing methods. Expanding the range of printable materials is crucial to meet diverse requirements and address limitations in material properties, such as strength, flexibility, or thermal stability. The development of multi-functional materials, such as self-healing polymers or shape-memory alloys, can introduce new capabilities and enhance the performance of 3D-printed objects [114]. Another challenge lies in the scalability and production efficiency of 3D printing. Current printing processes may suffer from limited production speed and capacity, making it challenging to meet the demands of large-scale manufacturing. Improving printing speed, enhancing throughput, and optimizing printing parameters are crucial aspects for the widespread adoption of 3D printing in industrial applications. Additionally, developing hybrid approaches that combine 3D printing with other manufacturing techniques, such as injection molding or machining, can potentially overcome the limitations in production efficiency [115]. Furthermore, the lack of standardization in 3D printing processes, materials, and design files poses challenges for interoperability and quality control. The absence of standardized file formats, printing protocols, and post-processing techniques can hinder the exchangeability and reproducibility of 3D-printed objects.

Standardization efforts are required to establish guidelines and best practices that ensure compatibility, consistency, and quality across different printers, materials, and applications. Collaborative initiatives involving industry, academia, and regulatory bodies are necessary to develop comprehensive standards for the field [61, 116]. Despite these challenges, several future directions can shape the evolution of 3D printing. One direction involves advancements in multi-material printing and the integration of different functionalities. Exploring novel materials, such as conductive inks or biocompatible polymers, and developing techniques for precise material placement and transition can open up new possibilities for diverse applications. Additionally, the integration of 3D printing with other emerging technologies, such as nanotechnology or artificial intelligence, holds promise for further innovation and advancement in the field [61, 117]. Moreover, the development of sustainable and environmentally friendly approaches in 3D printing is gaining importance. The reduction of waste, the use of recycled materials, and the exploration of bio-based or biodegradable materials are essential considerations for the future of 3D printing. Implementing circular economy principles and optimizing energy consumption and material usage can contribute to a more sustainable and responsible practice of 3D printing [118]. In conclusion, while 3D printing has made significant strides, challenges and limitations persist in the field. The expansion of printable materials, improvements in scalability and production efficiency, and standardization efforts are crucial for the future development and adoption of 3D printing. Additionally, exploring advancements in multi-material printing, integration with other technologies, and sustainable practices can further enhance the capabilities and impact of 3D printing. Future research and collaborative efforts are necessary to address these challenges and shape the future direction of 3D printing [119]. Some of the major challenges in 3D printing are discussed below.

Evaluation of the Economic and Cost-Effectiveness of 3D-Printed Therapeutic Delivery Systems Compared to Traditional Approaches

The economic and cost-effectiveness evaluation of 3D-printed therapeutic delivery systems compared to traditional approaches is a pivotal aspect in determining the viability and widespread adoption of this technology in healthcare settings. While the apparent advantages of 3D printing in therapeutic delivery highlight its importance, it remains crucial to conduct a comprehensive evaluation of the economic ramifications, cost-effectiveness, and enduring value associated with the adoption of 3D-printed solutions as opposed to conventional methodologies [120]. At the forefront of evaluating the economic impact of 3D printing is the consideration of the initial investment required for setting up the infrastructure, encompassing the cost of 3D printers, materials, and supporting equipment. Although the upfront costs associated with acquiring 3D printing technology can be substantial, it is crucial to take into account the potential long-term benefits and cost savings that can be achieved through the utilization of 3D-printed therapeutic delivery systems [121]. One area where 3D printing can offer economic benefits is in the manufacturing of medical devices and implants customized for individual patients. Traditional manufacturing techniques frequently involve intricate and labor-intensive procedures, which result in higher costs and extended production schedules. In contrast, 3D printing enables the direct fabrication of customized devices based on patient-specific anatomical data, mitigating the need for manual customization and streamlining the production workflow. This can lead to cost savings in terms of reduced labor, material waste, and inventory management [122]. Furthermore, 3D printing facilitates the consolidation of multiple components into a single printed structure, thereby obviating the need for assembly and reducing associated costs. This aspect can be particularly advantageous in the production of complex medical devices or drug delivery systems necessitating intricate designs and precise integration of various functionalities. The capability to create multi-material and multi-functional objects in a single printing process enhances efficiency and potentially reduces overall production costs [123]. Integral to evaluating the economic viability of 3D-printed therapeutic delivery systems is cost-effectiveness analysis. Such studies compare the costs and outcomes of 3D-printed interventions with those of conventional approaches, taking into account factors like treatment efficacy, patient outcomes, quality of life, and long-term cost implications [30]. In certain cases, the use of 3D-printed therapeutic delivery systems has demonstrated cost-effectiveness when juxtaposed with traditional methods. For example, in orthopedics, the production of customized orthotic devices or implants using 3D printing has shown potential cost savings by diminishing the need for repeated fittings, adjustments, and revisions. Additionally, the enhanced patient comfort, functionality, and long-term outcomes associated with personalized 3D-printed solutions can contribute to overall cost-effectiveness by minimizing the need for subsequent interventions or rehabilitative care [124]. In the context of drug delivery systems, 3D printing's precise control over drug release profiles and optimized dosing can potentially improve treatment efficacy while reducing medication waste and associated costs. By tailoring drug delivery systems to individual patient needs, 3D printing offers the potential for personalized medicine and targeted therapies, maximizing therapeutic outcomes while minimizing adverse effects [125, 126]. However, it is crucial to acknowledge that the cost-effectiveness of 3D printing in therapeutic delivery is influenced by various factors, including the specific medical condition, the complexity of the intervention, the availability of alternative treatment options, and the healthcare system in which it is implemented. Economic evaluations should consider the entire patient care pathway, encompassing preoperative planning, surgical procedures, postoperative care, and long-term follow-up, to comprehensively assess the value proposition of 3D-printed therapeutic delivery systems [127]. Moreover, the long-term cost implications and sustainability of 3D printing in healthcare must be evaluated. While 3D printing can offer cost savings in certain aspects of care delivery, factors such as material costs, maintenance and upgrade expenses, regulatory compliance, and ongoing research and development efforts should be considered in assessing the overall economic impact [128]. In conclusion, the evaluation of the economic and cost-effectiveness of 3D-printed therapeutic delivery systems compared to traditional approaches is critical in determining the value proposition and feasibility of implementing this technology in healthcare settings. While initial investments in 3D printing infrastructure can be substantial, potential long-term cost savings, increased efficiency, and improved patient outcomes may justify the adoption of 3D-printed solutions. Cost-effectiveness analysis, taking into account treatment efficacy, patient outcomes, and long-term cost implications, can provide insights into the economic viability of 3D printing in therapeutic delivery. Sustained research efforts, exhaustive economic assessments, as demonstrated in Table IX, and collaborative endeavors involving various stakeholders are indispensable to gain a comprehensive understanding of the economic consequences and to unlock the potential advantages of integrating 3D printing into healthcare [129].

Integration of 3D-Printed Therapeutic Interventions: Understanding Patient Perspectives and Acceptance

The successful implementation and widespread adoption of personalized 3D-printed therapeutic interventions in healthcare depends significantly on understanding patient perspectives and acceptance of this innovative technology. Patient-centered care places significant emphasis on engaging patients in decision-making processes, taking into account their values, preferences, and experiences. Consequently, it is essential to delve into how patients perceive and embrace these personalized treatments, examining their expectations, apprehensions, and the overall influence on their healthcare journey. This section presents a comprehensive review of existing literature on patient perspectives and acceptance of personalized 3D-printed therapeutic interventions, highlighting key findings and offering insights into the implications for clinical practice [130, 131].

Patient Perceptions and Expectations

Patient perceptions and expectations of personalized 3D-printed therapeutic interventions play a pivotal role in influencing their acceptance and satisfaction with these treatments. Studies have identified several key factors that shape patient attitudes towards 3D printing in healthcare [132]. An essential factor is the perception of personalization and its impact on treatment outcomes. Patients often view personalized 3D-printed therapeutic interventions as innovative and tailored to their specific needs. The ability to customize medical devices, implants, or drug delivery systems based on individual anatomical data instills a sense of confidence and reassurance in patients. This personalized approach is associated with improved treatment efficacy, better functional outcomes, and enhanced quality of life, which positively influences patient acceptance [12, 133–135]. Additionally, patients appreciate the potential for reduced treatment complexity and improved surgical outcomes through the use of 3D-printed interventions. The ability of 3D printing to streamline surgical procedures, reduce surgical time, and minimize invasiveness is valued by patients as it may result in shorter hospital stays, faster recovery, and reduced postoperative complications. Patient perceptions of the potential benefits, such as improved treatment outcomes, reduced pain, and enhanced functionality, contribute to their acceptance and willingness to undergo personalized interventions [136, 137].

Challenges and Concerns

Despite the potential advantages, patients may also harbor concerns and reservations regarding personalized 3D-printed therapeutic interventions. One common concern is the safety and long-term durability of 3D-printed medical devices and implants. Patients may worry about the reliability and performance of 3D-printed interventions, particularly when compared to established, conventional treatments. Addressing these concerns requires clear communication regarding the safety standards, regulatory compliance, and rigorous testing protocols associated with 3D-printed therapeutic interventions [63, 138]. Another challenge is the accessibility and affordability of personalized 3D-printed treatments. While 3D printing holds the promise of customization, the availability and cost-effectiveness of these interventions can vary. Patients may express concerns about the accessibility of 3D printing technology, especially in regions with limited resources or underdeveloped healthcare infrastructure. Furthermore, the financial implications of personalized 3D-printed treatments, including potential costs not covered by insurance, can be significant barriers for some patients. Addressing these challenges involves considering the cost-effectiveness of 3D printing, expanding access to

Table IX Nanomaterials for Targeted Drug Delivery in Biomedical Applications

Nanoparticle Type	Advantages	Challenges	Current Applications	Limitations	Recent Advances	References
Liposomes	- Encapsulation of hydrophobic drugs	- Short circulation half-life	Cancer therapeutics, gene delivery, vaccines	High susceptibility to enzymatic degradation	PEGylation for prolonged circulation	[164]
	- Targeted drug delivery	- Premature drug release		Rapid clearance by the mononuclear phagocyte system	Surface modifications for enhanced stability	[165]
	- Biocompatibility	- Limited drug loading capacity		Limited scalability for large-scale production	Remote-triggered drug release	[170]
	- Controlled drug release	- Instability during storage			pH-sensitive liposomes for intracellular release	[171]
Polymeric	- Tunable drug release profiles	- Potential toxicity of polymer residues	Controlled release systems, nanogels	Incomplete drug release	Co-delivery of multiple drugs for combination therapy	[172]
Nanoparticles	- High drug loading capacity	- Lack of uniformity in particle size	Drug targeting and imaging agents	Burst release effect	Surface modification for improved stability	[173]
	- Targeted drug delivery	- Burst release effect	Nanomedicine, wound healing	Potential toxicity	Crosslinked nanoparticles for prolonged release	[174]
	- Stability in circulation	- Incomplete drug release		Drug leakage from polymer matrix	Biodegradable polymers for reduced toxicity	[175]
	- Biocompatibility					
Inorganic	- High stability in various conditions	- Potential accumulation in organs	Targeted cancer therapy, imaging agents	Long-term toxicity	Multifunctional nanoparticles for theranostics	[176]
Nanoparticles	- Controlled drug release	- Limited targeting capability	Inflammatory disease treatment	Limited targeting efficiency	Mesoporous structures for enhanced drug loading	[177]
	- Multifunctionality (e.g., imaging)	- Clearance by the reticuloendothelial system				[107]
	- Potential for combination therapy	- Potential toxicity				[107, 156]
	- Versatile surface modifications					
Dendrimers	- Precise control of structure	- Cytotoxicity and immunogenicity	Drug delivery, gene therapy	Complexity of synthesis	Targeted dendrimer therapeutics	[178]
	- High drug payload	- Complex synthesis process	Diagnostic imaging	Limited drug loading capacity	Dendrimer-based nanoparticles for improved targeting	[179]
	- Potential for multifunctionality	- Limited drug release kinetics				[179]
	- Biodegradable	- Low drug loading capacity				
	- Targeting ligands for enhanced specificity					[179]
Nanogels	- High water content for hydrophilic drug delivery	- Potential for burst release	Sustained drug release	Complex preparation process	Multifunctional nanogels for combination therapy	[180]
	- Controlled drug release	- Complex preparation process	Imaging agents, protein delivery	Limited drug loading capacity	pH- or temperature-sensitive nanogels	[181]

Table IX (continued)

Nanoparticle Type	Advantages	Challenges	Current Applications	Limitations	Recent Advances	References
	- Biocompatibility	- Limited drug loading capacity		Limited stability during storage	Stimuli-responsive nanogels	
	- Versatile drug entrapment	- Limited stability during storage		Limited scalability for large-scale production		[182]
	- Potential for stimuli-responsive drug release					
Solid Lipid	- Enhanced drug stability and protection	- Limited drug loading capacity	Drug delivery, cancer therapy	Limited drug loading capacity	Solid lipid nanoparticles for oral delivery	[183]
Nanoparticles	- Sustained drug release	- Complexity of preparation process	Diagnostic imaging	Limited scalability for large-scale production	Nanostructured lipid carriers for improved stability	[184]
	- Biocompatibility	- Potential for drug leakage		Drug leakage from lipid matrix	Lipid-based nanoparticles for targeted delivery	[107]
	- Targeted drug delivery					
	- Versatile surface modifications					[138]
Carbon-Based	- High drug loading capacity	- Limited solubility in aqueous solutions	Drug delivery, cancer therapy	Potential toxicity	Functionalized carbon nanoparticles for targeting	[185]
Nanoparticles	- Targeted drug delivery	- Potential toxicity and long-term biocompatibility	Diagnostic imaging	Limited solubility in aqueous solutions	Carbon-based nanoparticles for combination therapy	[163]
	- Photothermal and photodynamic therapy capabilities	- Difficulty in large-scale production				[186]
	- Stability and tunable drug release					
Metallic	- Plasmonic properties for enhanced drug release	- Potential toxicity and biocompatibility	Drug delivery, cancer therapy	Potential toxicity	Combination therapies using metallic nanoparticles	[187]
Nanoparticles	- Magnetic targeting for site-specific delivery	- Aggregation and instability	Imaging agents, theranostics	Aggregation and instability	Smart magnetic nanoparticles for drug release	[188]
	- Photothermal and photodynamic therapy capabilities	- Complex surface functionalization		Limited drug loading capacity	Multi-functional magnetic nanoparticles	[189]
	- Controlled drug release					
Silica-Based	- High surface area for drug loading	- Potential toxicity and biocompatibility	Drug delivery, gene therapy	Potential toxicity	Mesoporous silica nanoparticles for drug delivery	[190]
Nanoparticles	- Stabilization of drugs and enhancement of solubility	- Limited drug loading capacity	Diagnostic imaging	Limited drug loading capacity	Surface modification for targeted delivery	[163]
	- Mesoporous structure for controlled release	- Potential for aggregation and instability		Limited stability during storage	Silica-based nanoparticles for combination therapy	[191]
	- Biocompatibility					

the technology, and exploring reimbursement options to ensure equitable availability [63, 139].

Ethical Considerations

Ethical considerations surrounding personalized 3D-printed therapeutic interventions also influence patient perspectives and acceptance. Patients value transparent communication regarding the use of their personal data, including medical imaging data used for 3D printing. Informed consent and privacy protection are essential to build patient trust and ensure ethical practice. Engaging patients in shared decision-making processes, involving them in discussions about the benefits, risks, and alternatives of personalized 3D-printed interventions, is essential to respect patient autonomy and promote ethical healthcare practices [140, 141]. Moreover, patients may have ethical concerns related to the potential overutilization of 3D-printed interventions. The allure of customization and innovation may lead to unwarranted utilization of 3D printing technology. Clinicians and researchers should carefully consider the appropriateness and necessity of personalized 3D-printed interventions, ensuring that they are used judiciously and when they offer clear advantages over conventional treatments [142, 143].

Improving Patient Education and Engagement

To enhance patient acceptance and engagement with personalized 3D-printed therapeutic interventions, effective patient education is essential. Clear and comprehensive communication about the benefits, limitations, and potential risks associated with 3D printing should be provided to patients. Educational materials, visual aids, and interactive platforms can be utilized to help patients understand the technology, its applications, and their role in decision-making processes [144, 145]. Additionally, healthcare professionals should actively engage patients in discussions about personalized 3D-printed interventions. Understanding patient preferences, values, and concerns can help align treatment decisions with patient goals and improve shared decision-making. Patient support groups, educational workshops, and access to expert opinions can also contribute to patient empowerment, facilitating their acceptance and engagement with personalized 3D-printed therapeutic interventions [146]. Exploring patient perspectives and acceptance of personalized 3D-printed therapeutic interventions is vital for their successful implementation and utilization in clinical practice. Patient perceptions of personalization, expectations of improved treatment outcomes, and the potential for reduced treatment complexity are factors that positively influence patient acceptance. However, concerns regarding safety, accessibility, affordability, and ethical considerations should be addressed to ensure patient trust and facilitate informed decision-making. Improving patient education, engagement, and shared decision-making processes can enhance patient acceptance and foster a patient-centered approach in the integration of personalized 3D-printed therapeutic interventions in healthcare [147].

Environmental Impact and Sustainability Assessment of 3D Printing in Healthcare

As the field of healthcare embraces 3D printing technology, it becomes imperative to assess the environmental impact and sustainability considerations associated with its implementation. While 3D printing offers numerous advantages in terms of customization, rapid prototyping, and on-demand manufacturing, it is crucial to evaluate its implications for resource consumption, waste generation, energy usage, and overall environmental sustainability. This section reviews the existing literature on the environmental impact of 3D printing in healthcare, highlighting key findings and providing insights into the sustainability considerations that need to be addressed [148, 149].

Resource Consumption and Waste Generation

The utilization of 3D printing in healthcare demands various raw materials, including polymers, metals, ceramics, and bioinks. The extraction, production, and transportation of these materials contribute to environmental impact, particularly concerning energy consumption and greenhouse gas emissions. Additionally, the disposal of unused or failed prints and post-processing waste add to the overall waste generation [150]. To mitigate resource consumption and waste generation, several strategies can be implemented. One approach is optimizing the design of 3D-printed objects to minimize material usage while maintaining structural integrity. Techniques such as topology optimization and lattice structures can reduce material waste and enhance the sustainability of 3D printing. Moreover, recycling and reusing materials can help minimize waste and decrease the environmental footprint of 3D printing processes [44].

Energy Consumption

Energy consumption is another important consideration when assessing the environmental impact of 3D printing on healthcare. 3D printers, particularly those used for large-scale production, consume significant amounts of energy during the printing process. The energy requirements for heating, melting, and curing materials can contribute to greenhouse gas emissions and resource depletion.

To mitigate energy consumption, it is prudent to explore energy-efficient printing methods and equipment. Progress in printer technology, including low-energy consumption printers, energy recovery systems, and fine-tuned printing parameters, can contribute to a reduction in environmental footprint. Furthermore, the adoption of renewable energy sources like solar or wind power to fulfill the energy demands of 3D printing facilities can bolster sustainability efforts [151, 152].

Life Cycle Assessment

The use of life cycle assessments (LCAs) stands as an effective approach to gauge the environmental repercussions of 3D printing in healthcare. LCAs involve a comprehensive analysis of the complete life cycle of a product or process, encompassing everything from raw material extraction to disposal, thereby enabling a thorough evaluation of the environmental impact. By conducting LCAs, researchers can identify hotspots of environmental impact and develop strategies to mitigate them [153]. LCAs of 3D printing within the healthcare sector have yielded significant insights. Notably, research has illuminated that the environmental consequences of 3D printing are subject to variation contingent on the particular application, choice of materials, and printing methodologies employed. Acquiring a nuanced comprehension of these distinctions is paramount for identifying opportunities to enhance sustainability in these processes. LCAs can guide the selection of materials, printing methods, and post-processing techniques that minimize environmental impact and promote sustainability [154].

Material Selection and Biodegradability

Choosing the right materials for 3D printing in healthcare is critical for environmental sustainability. Researchers are exploring biodegradable and bio-based materials as alternatives to traditional petroleum-based polymers. Biodegradable materials have the advantage of reducing long-term environmental impact by decomposing naturally over time [155]. Additionally, the development of bioinks and biomaterials derived from renewable resources, such as cellulose or algae-based materials, can contribute to the sustainability of 3D printing in healthcare. These materials can minimize the reliance on fossil fuels and reduce the carbon footprint associated with 3D printing processes [156].

Table X Economic and Cost-Effectiveness Assessment of 3D-Printed Therapeutic Delivery in Healthcare

Factors	Evaluation
Initial Investment Costs	Significant upfront costs for 3D printing technology, including 3D printers, materials, and supporting equipment
	Potential long-term cost savings through on-demand manufacturing and reduced need for inventory storage
Material Selection	Versatility in material options, including biocompatible polymers, metals, ceramics, and bioinks
	Challenges in selecting appropriate materials for biodegradable systems due to limited availability
Production Efficiency	Rapid prototyping capabilities allow for faster development and testing of novel therapeutic delivery systems
	Potential to streamline production workflow and reduce labor costs
Quality Control	Ensuring consistent quality and reproducibility is challenging due to variations in printer settings and materials
	Rigorous quality control measures required for regulatory compliance
Patient Outcomes	Personalized 3D-printed interventions may improve treatment efficacy and patient satisfaction
	Customized implants and devices can lead to better patient fit and functionality
Long-Term Value	Reduced treatment complexity and improved surgical outcomes reported in orthopedic and dental applications
	Studies on long-term cost implications needed for comprehensive evaluation
Regulatory Considerations	Evolving regulatory landscape for 3D-printed therapeutic delivery systems
	Time-consuming process to obtain necessary approvals for clinical applications
Ethical Implications	Ensuring patient privacy, equitable access, and informed consent is crucial
	Ethical considerations of personalized medicine and overutilization of 3D-printed interventions should be addressed
Cost-Effectiveness Analysis	Comparative studies show cost-effectiveness in orthopedic and dental applications
	Varied results in other medical specialties warrant further research
Sustainability Considerations	Resource consumption and waste generation associated with 3D printing
	Energy consumption and greenhouse gas emissions
	Life cycle assessments can help identify areas for sustainability improvements
	Biodegradable materials and eco-friendly printing techniques should be explored
	Establishing regulatory frameworks and standards for environmentally conscious practices

Table XI Environmental Impact and Sustainability Assessment of 3D Printing in Healthcare

Factors	Description	Data/Metrics	Comparative Analysis	References
Resource Consumption	- Use of raw materials (polymers, metals, ceramics, bioinks) and their impact on energy consumption and greenhouse gas emissions	- Quantity of raw materials used for a typical print	- Comparison of resource consumption in 3D printing vs. traditional manufacturing methods	[192]
	- Disposal of unused or failed prints and post-processing waste	- Amount of waste generated per print	- Environmental impact of waste disposal	[150, 158]
Energy Consumption	- Energy requirements during the printing process, including heating, melting, and curing of materials	- Energy consumption per print	- Comparison of energy usage in 3D printing vs. traditional methods	[151, 154]
	- Contribution to greenhouse gas emissions and resource depletion	- CO_2 equivalent emissions per print	- Comparison of emissions with other manufacturing processes	[193]
Life Cycle Assessment (LCA)	- Analysis of the entire life cycle of 3D-printed products, from raw material extraction to disposal	- LCA results for key environmental impact categories	- Evaluation of environmental impacts throughout the product life cycle	[153]
Material Selection	- Consideration of biodegradable and bio-based materials as alternatives to petroleum-based polymers	- Percentage of biodegradable materials used	- Environmental benefits of using biodegradable materials	[194]
	- Reducing the reliance on fossil fuels and minimizing the carbon footprint	- Carbon footprint per unit of material	- Comparison of carbon footprints with conventional materials	[195]
Regulatory Framework	- Establishing guidelines for environmentally conscious 3D printing practices	- Number of regulatory guidelines or standards	- Impact of regulatory guidelines on sustainability	[66, 99]
	- Encouraging the use of eco-friendly materials and promoting energy-efficient printing processes	- Number of eco-friendly material certifications	- Effect of eco-friendly materials on resource consumption	[196]
Material Recycling	- Implementation of recycling and reusing strategies to minimize waste generation	- Percentage of recycled materials used	- Comparison of waste reduction through recycling	[132]

Regulatory Framework and Standards

To ensure the environmental sustainability of 3D printing in healthcare, the establishment of regulatory frameworks and standards is essential. Regulatory bodies can play a crucial role in setting guidelines and requirements for environmentally conscious 3D printing practices. This includes encouraging the use of eco-friendly materials, promoting energy-efficient printing processes, and enforcing responsible waste management [61]. Moreover, industry collaborations, certification programs, and eco-labeling initiatives can facilitate the adoption of sustainable practices in 3D printing. By creating incentives and recognition for environmentally friendly approaches, these efforts can drive the implementation of sustainable 3D printing processes in healthcare [157]. Assessing the environmental impact and sustainability considerations associated with 3D printing in healthcare is crucial for responsible implementation and long-term viability. Strategies to minimize resource consumption, reduce waste generation, and optimize energy usage should be implemented. Conducting life cycle assessments can provide valuable insights into the environmental impact of 3D printing processes and guide sustainability improvements. Material selection, biodegradability, and the establishment of regulatory frameworks and standards also contribute to the sustainability of 3D printing in healthcare as shown in Tables X, XI and XII. By considering these environmental considerations and promoting sustainable practices, the healthcare industry can embrace 3D printing technology while minimizing its ecological footprint [158, 159].

The transformative potential of 3D printing in healthcare is evident in a wide range of applications, where it enables personalized and patient-specific therapeutic interventions. This section highlights several examples that showcase the revolutionary impact of 3D printing in improving medical treatments and patient outcomes. In severe burn injuries, traditional skin grafting involves harvesting skin from another part of the body, leading to additional pain and scarring. 3D bioprinting presents a solution by utilizing the patient's own cells and a bioink to craft personalized skin grafts that closely mimic the characteristics of natural skin. This method diminishes the requirement for invasive treatments and delivers a result that is both more natural and aesthetically appealing to the patient [1, 27]. Furthermore, Cancer patients undergoing radiation therapy often require shielding devices to protect healthy tissues. 3D printing enables the creation and manufacturing of personalized shielding devices tailored to the individual patient's unique anatomy. This approach guarantees accurate coverage and mitigates the potential for complications associated with

Table XII Diverse Applications of 3D Printing in Healthcare

Application	Description
Dental Restorations	3D printing enables the creation of precise and custom-fit dental crowns, bridges, aligners, and dentures based on digital scans [197]
Prosthetics and Orthotics	3D printing provides affordable and customizable prosthetic limbs, orthotic devices, and braces tailored to individual patient needs [198]
Surgical Tools and Guides	Patient-specific surgical guides assist surgeons in accurate implant placement and complex surgeries, improving precision and safety [199]
Customized Surgical Implants	Patient-specific 3D-printed implants, like cranial plates or spinal cages, offer improved fit, reduced surgery time, and better outcomes [200]
Anatomical Models	Realistic 3D-printed anatomical models aid in surgical planning, medical education, and patient communication for better outcomes [136]
Drug Delivery Systems	Intricate 3D-printed systems can release medication at controlled rates, target specific areas, or provide personalized dosage forms [33]
Tissue Engineering	3D printing enables the fabrication of scaffolds and structures for tissue regeneration, including bone, cartilage, skin, and organs [201]
Biofabrication of Organs	Layering cells and biomaterials using 3D printing technology shows promise in creating functional organs and tissues for transplantation [202]
Hearing Aid Shells	3D printing allows to produce customized and comfortable hearing aid shells that perfectly fit the individual's ear canal [203]
Ophthalmic Devices	3D printing can create personalized contact lenses, ocular prosthetics, and surgical guides for procedures like LASIK or cataract surgery [204]
Respiratory Devices	Customized 3D-printed airway splints, masks, or ventilation components can improve comfort and treatment outcomes for respiratory conditions [205]
Surgical Planning and Simulation	3D-printed models aid in surgical planning, simulation, and practice, reducing risks, optimizing surgical outcomes, and improving training [134]
Rehabilitation and Assistive Devices	3D printing offers personalized solutions for rehabilitation aids, mobility devices, ergonomic tools, and customized braces or splints [206]

radiation exposure [38]. 3D printing has transformed the field of prosthetics by enabling the customization of prosthetic limbs to match the patient's unique specifications. This results in improved comfort, mobility, and quality of life for individuals with limb loss [160]. Besides, 3D printing has revolutionized dentistry by enabling the fabrication of precise and custom-fit dental crowns, bridges, and aligners in a single visit. This approach saves time, improves patient comfort, and enhances aesthetics [161]. 3D printing facilitates the creation of complex drug delivery systems capable of controlled medication release or precise targeting within the body. This capability enhances treatment effectiveness and paves the way for personalized medicine [55, 107]. In additions, Surgeons can benefit from patient-specific surgical guides produced through 3D printing. These guides assist in accurately placing implants or performing complex surgeries, improving surgical precision and patient safety [143]. Moreover, Medical education and surgical planning have been revolutionized by 3D printing, as it allows for the creation of realistic anatomical models based on patient-specific imaging data. These models enable surgeons to visualize complex structures and plan surgeries with greater precision and confidence [63]. 3D printing provides affordable and customized assistive devices for individuals with disabilities. From prosthetic limbs to adaptive equipment like wheelchair accessories, 3D printing improves the quality of life for people with mobility limitations [31]. 3D printing empowers the fabrication of surgical implants customized to the patient's unique anatomy, such as hip or knee replacements. The outcome is a superior fit, reduced surgical duration, and improved post-operative results [83]. One of the most promising applications of 3D printing is in the field of regenerative medicine. Researchers are exploring the use of 3D printing to create functional organs and tissues by layering cells and biomaterials. This breakthrough technology has the potential to revolutionize transplantation medicine and address the critical shortage of organ donors [57]. These examples highlight the incredible versatility and potential of 3D printing in healthcare. By enabling personalized and patient-specific therapeutic interventions, 3D printing is transforming medical treatments, improving patient outcomes, and paving the way for a more patient-centered approach to healthcare. As research and development in 3D printing continue, we can expect even more innovative applications that will further revolutionize the field of healthcare.

Conclusion

This comprehensive overview delves into the definition, principles, and various types of 3D printing technologies applicable to therapeutic delivery. We have explored the advantages and limitations of 3D printing in this field, highlighting its potential to revolutionize healthcare through customized drug delivery systems, advances in tissue engineering and regenerative medicine, and the production of medical devices and implants. Applications of 3D printing in therapeutic delivery encompass patient-specific oral dosage forms, personalized drug delivery implants and devices, biofabrication of complex tissue structures, scaffold-based approaches for tissue regeneration, and the production of 3D-printed prosthetics, orthotics, customized implants, and surgical instruments. These applications have the potential to enhance treatment outcomes, improve patient comfort and compliance, and enable personalized medicine. The implications of 3D printing in therapeutic delivery are profound and far-reaching. Customized drug delivery systems can enable precise dosing and targeted therapy, minimizing side effects and maximizing treatment efficacy. Applications in tissue engineering and regenerative medicine hold the potential to generate functional organs and tissues for transplantation, addressing the pressing issue of organ donor shortages. Additionally, 3D-printed medical devices and implants offer enhanced functionality, better patient fit, and improved surgical outcomes. The integration of therapeutic agents into 3D-printed structures opens up possibilities for controlled drug release, prolonged drug delivery, and personalized treatment approaches. This has the capacity to bring about a revolution in medication administration and the care of chronic conditions, ultimately leading to better patient outcomes and an enhanced quality of life. Nevertheless, despite notable advancements in the field of 3D printing in therapeutic delivery, there remain several areas that necessitate continued research and development. Key areas include:

Material Selection and Biocompatibility: Continued research focused on the development of biocompatible materials and bioinks for 3D printing holds the potential to broaden the spectrum of therapeutic agents that can be incorporated into printed constructs. Enhancing our comprehension of material characteristics and their interplay with biological systems assumes pivotal importance in driving advancements in the field.

Multi-material and Multi-functional Printing: Exploring new techniques for combining different materials within a single 3D-printed structure can enhance functionality and enable the creation of complex, multi-component devices. Integration of sensors, electronics, and smart functionalities into 3D-printed systems is an exciting avenue for exploration.

Nanotechnology in 3D Printing: Investigating the integration of nanoparticles into 3D-printed structures for targeted drug delivery and surface modification is an emerging field. Further research is needed to optimize the incorporation of nanoparticles and understand their impact on therapeutic efficacy and biocompatibility.

Regulatory Considerations and Standardization: Establishing clear regulatory guidelines and standards for 3D-printed therapeutic delivery systems is essential. Collaborative efforts among researchers, industry, and regulatory bodies are needed to ensure safety, efficacy, and quality control.

Ethical and Legal Implications: The ethical and legal implications of 3D printing in therapeutic delivery must be carefully considered. Ongoing discussions and collaborations are necessary to address concerns related to patient privacy, equitable access, intellectual property, and liability. In conclusion, 3D printing has the potential to revolutionize therapeutic delivery through customized drug delivery systems, tissue engineering, regenerative medicine, and the production of medical devices and implants. While challenges exist, ongoing research and development efforts in material science, multi-material printing, nanotechnology, and regulatory considerations will drive the field forward. The future of therapeutic delivery is promising, and with continued innovation and collaboration, we can unlock the full potential of 3D printing to transform healthcare and improve patient outcomes.

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Declarations

Conflict of Interest Authors declare no conflict of interest.

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