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Advancements in 3D-Printed Biomaterials for Personalized Medicine

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ABSTRACT

Recent advancements in 3D-printed biomaterials are revolutionizing personalized medicine by offering unprecedented levels of customization and precision in medical treatments. These technologies enable the creation of patient-specific implants, prosthetics, and drug delivery systems that are precisely tailored to individual anatomical and genetic profiles. Over the past few decades, a range of 3D printing technologies have been developed, utilizing various power sources to layer materials and replicate complex geometries. While not all technologies are feasible for personalized medicine, significant methods include inkjet printing, stereolithography, selective laser melting, electron beam melting, multi-jet modeling, fused deposition modeling, and classic extrusion techniques. Current research efforts are focused on printing with advanced biomaterials, such as biofunctional inks and decellularized extracellular matrices, which offer enhanced biological compatibility and promote tissue integration and regeneration. Despite promising advancements, challenges remain, including high costs, regulatory hurdles, and material limitations. Future research and interdisciplinary collaboration are crucial to overcoming these barriers, paving the way for more personalized and effective healthcare solutions. As a key driver of innovation, 3D printing holds transformative potential for the future of personalized medicine.

Keywords: 3d-printed biomaterials, Personalized implants, Biofunctional inks, Decellularized extracellular matrices, Drug delivery systems

Introduction

Over the past few decades, the field of personalized medicine, sometimes interchangeably called ‘patient-specific’ medicine, has gained significant momentum by tailoring treatments to individuals’ unique genetic and phenotypic profiles. Here, ‘personalization’ is not exclusively limited to the genetic profile; instead, it expands to include anatomical profile, microbiome, psychological factors, and even environmental characteristics.[1] This understanding facilitates the development of customized therapeutics for patients, thereby improving treatment efficacy, reducing side effects, and potentially lowering healthcare costs.[2] At the forefront of this innovative approach is the advent of advanced additive manufacturing technology, more commonly known as ‘3D printing,’ which, when employing biomaterials, opens a new meadow of unprecedented customization of materials going inside the body, as observed by Vanessa et al. The level of customization enabled by 3D printing can range from creating simple pediatric-friendly tablets to more complex custom bio-printed heart valves and vasculatures.[3] Additive manufacturing offers a transformative advantage in medical device manufacturing by enabling the processing of a wide range of materials, thus overcoming the limitations of traditional top-down approaches such as milling, machining, extrusion-based molding techniques, etc. Additive manufacturing is an amalgamation of advanced computer-assisted drawing (CAD) modeling, precision material deposition, and innovative layer-by-layer construction techniques, enabling the creation of complex, customized structures and components. Advancements in software have enabled the creation of micrometer-precision models of various tissues and anatomical supports, which is one of the factors that catapulted 3D printing technology.[4] These conventional methods often restrict customization, whereas additive manufacturing provides unprecedented flexibility and precision in tailoring medical devices to specific patient needs.[5] Traditional biomaterials such as natural and synthetic polymers, metal powders, and ceramics have been extensively explored and utilized in 3D bioprinting. However, current research is increasingly focused on biofunctional biomaterials, including decellularized extracellular matrix (dECM), cell aggregates and spheroids, composite bioinks, and acellular matrices. They provide natural scaffolds, enhance cell interactions, supporting cell growth, differentiation, and tissue formation. These techniques mimic natural tissues, improving regenerative outcomes in various applications. 3D printing enables the integration of multiple materials with various functionas and material properties into a bioligcally active form factor. These advanced materials are designed to integrate directly with functional tissues, offering enhanced biological compatibility and functionality for regenerative medicine applications.[6,7]

The scope of 3D-printed biomaterials extends beyond basic customization, delving into the realm of biomimetics. While biomimetics traditionally aims to replicate structures and processes found in nature, the focus in biomaterials is on replicating the functional characteristics of natural tissues. As observed by Raheem et al., this approach enhances the potential of 3D-printed biomaterials to work seamlessly with human biology, facilitating improved integration and functionality in medical applications.[8] This capability is also particularly crucial in personalized medicine, where treatments must be tailored to individual patient needs. For instance, Fabian et al. conducted multiple 3D scans of a patient’s cranium to recreate a custom cranial implant using selective laser melting (SLM) technology. This implant was 3D-printed using polyetheretherketone (PEEK), a high-performance polymer. The use of this patient-specific approach facilitated faster patient recovery by eliminating the need for intense X-ray exposure that might have been required with conventional repair methods[9] In another notable study by Hee-Gyeong Yi et al., a 3D-printed drug delivery patch was developed for pancreatic cancer treatment. This innovative patch utilizes 5-fluorouracil, polycaprolactone (PCL), and poly(lactic-co-glycolic) acid (PLGA) to enable controlled drug release directly at the tumor site. This approach addresses significant limitations associated with conventional oral or intravenous administration, such as poor solubility and systemic toxicity, enhancing treatment efficacy and patient outcomes.[10]

Personalized medicine represents a paradigm shift in modern healthcare, moving from a one- size-fits-all approach to a more precise and effective therapeutic strategy. The integration of 3D printing technology in this field not only enhances personalization but also accelerates the development and testing of new medical solutions. This review highlights the impact of 3D printing on personalized medicine by introducing state-of-the-art 3D printing technologies relevant to biomedical science, examining current and emerging applications in personalized medicine, and discussing the challenges and prospects of this technological integration.

Technological Advancements in 3D printing

Overview of 3d printing technologies

Additive manufacturing, commonly known as 3D printing, involves the layer-by-layer deposition of materials to create complex three-dimensional structures.[12] This process is inherently suitable for producing intricate geometries and customized designs, making it particularly valuable in biomedical applications. Figure 1 highlights all existing additive manufacturing principles and several techniques based on these principles. Although 3D printing was not initially developed exclusively for medical device construction, its ability to manufacture complex geometries has significantly increased its visibility and application in the medical sector.[13] Table 1 below provides an overview of the major techniques and their basic working principles, highlighting their relevance and utility in personalized medicine.

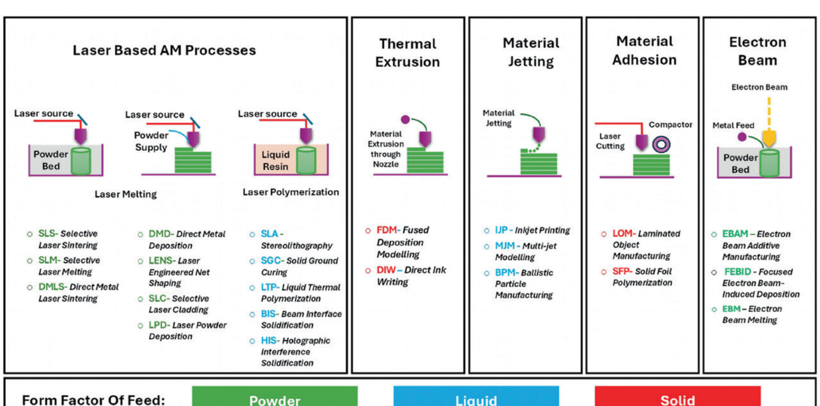

Fig 1 | Various types of additive manufacturing process. Inspired by Manu et al.,2022 under CC BY 4.0 [11]

Types of biomaterials and their application in personalized medicine

Each 3D printing technique has been developed with unique advantages that apply to a wide range of engineering and manufacturing applications. Initially, none of these techniques were created exclusively for medical device construction; however, they have since been adapted to meet the specific needs of medical devices and biological substances, as exemplified by the CELLINK3D Bioprinter.[31] Understanding the distinct processes and materials used in these technologies is crucial for optimizing their application in the construction and optimization of various medical devices.

These technologies encompass a wide range of materials, including polymers, metals, ceramics, and composites, each selected for their specific properties and compatibility with biological systems. By leveraging these advanced manufacturing techniques, medical professionals can produce highly customized implants, prosthetics, anatomical models, and drug delivery systems that align precisely with individual patient anatomy and needs.[32] This capability enhances the efficacy of treatments and improves patient outcomes by reducing complications and accelerating recovery times.

Table 2 provides a comprehensive overview of various 3D printing technologies, detailing the processes, types of biomaterials employed, and their specific applications in personalized medicine.

Applications of 3D-Printed Biomaterials in Personalized Medicine

Personalizing a treatment can happen in *various* aspects of medical technology. It could either be a personalization during intervention or as a custom formulation of a drug based on genotypic factors. The bottom-up construction of materials offers unprecedented opportunities for customization, precision, and innovation, which is visible in almost all fields of medical engineering, as illustrated in figure 2.[43]

For instance, traditional manufacturing processes used for medical implant or prosthesis construction revolved around techniques like casting, machining, or molding. They often result in standardized products that do not account for individual anatomical differences. Customization using these methods is limited, time-consuming, and expensive. Prosthetics are typically made from a narrow range of materials, necessitating manual adjustments for fit. However, 3D printing allows for the creation of patient-specific implants and prosthetics with precise anatomical accuracy. This is achieved by using scans of a patient's body to generate 3D models for printing, ensuring a perfect fit.[44] Another emerging applcaiiton of 3D printing is seen in wound care. It offers personalized solutions such as custom dressings, skin grafts, and scaffolds that promote healing. Additionally, 3D printing enables the construction of tissues that closely mimic skin properties and are engineered

Table 1 | All 3D printing techniques and their working description

Technology	Description	Ref
Selective Laser Sintering (SLS)	Uses a laser to sinter powdered materials layer by layer, forming solid structures from polymers, metals, and ceramics.	14
Selective Laser Melting (SLM)	Utilizes a high-powered laser to fully melt metal powders, creating dense, intricate metal components.	15
Direct Metal Laser Sintering (DMLS)	Similar to SLS, but specifically for metals, it selectively sinters metal powders for high-detail parts.	16
Direct Metal Deposition (DMD)	Employs a laser to deposit metal powder or wire onto a substrate, customizing implants and tools layer by layer.	17
Laser Engineered Net Shaping (LENS)	Uses a laser to melt metal powder in precise patterns, minimizing waste while creating net-shaped components.	18
Selective Laser Cladding (SLC)	Metal powder is deposited onto surfaces using a laser, forming coatings to enhance implant surfaces.	19
Laser Powder Deposition (LPD)	Melts metal or ceramic powder using a laser, adding layers to personalize implant surfaces.	20
Stereolithography (SLA)	Cures liquid photopolymer resins with a UV laser, producing high-resolution anatomical models and guides.	21
Solid Ground Curing (SGC)	Uses UV lamps to cure entire layers of photopolymer simultaneously for large, detailed models.	22
Liquid Thermal Polymerization (LTP)	Involves heating liquid polymers to form solid structures for prosthetics and orthopedic devices.	23
Beam Interface Solidification (BIS)	Solidifies materials at their interface using focused beams, enabling precise micro-scale structures.	11
Holographic Interference Solidification (HIS)	Utilizes holographic techniques and light patterns to solidify materials, creating micro-structured surfaces.	11
Fused Deposition Modeling (FDM)	Extrudes thermoplastic filaments through a heated nozzle to create personalized anatomical models and devices.	24
Inkjet Printing (IJP)	Bioinks are deposited in droplets, layer by layer, for bioprinting tissues and drug delivery systems.	25
Multi-Jet Modeling (MJM)	Similar to IJP but with multiple jets depositing and curing photopolymers for high-resolution models.	15
Ballistic Particle Manufacturing (BPM)	Propels particles onto a substrate to build layers, fabricating custom medical devices.	26
Laminated Object Manufacturing (LOM)	Cuts and laminate sheets of material layer by layer for anatomical models.	27
Solid Foil Polymerization (SFP)	Uses layers of polymer foil, cut and bonded, to form solid structures for durable medical devices.	28
EBAM – Electron Beam Additive Manufacturing	Manufactures customized, high-strength implants tailored to individual patient anatomy, making it patient-specific.	29
FEBID - Focused Electron Beam-Induced Deposition	Enables precise nanoscale customization of biomaterials, improving biocompatibility and functionality in biosensor applications.	30
Electron Beam Melting (EBM)	Uses an electron beam to melt metal powder in a vacuum, forming high-density metal parts for implants.	15

to be multifunctional, delivering drugs locally with controlled release, thereby supporting tissue regeneration.[45]

Another unforeseen benefit of the additive manufacturing approach is that its rapid prototyping capabilities significantly decrease the time from design to production, enabling quicker delivery of customized solutions.[46]

When it comes to surgical guides and models, traditional manufacturing is limited by its standardization, which diminishes utility in complex or unique procedures. The production of custom models through conventional means is both expensive and time-consuming and often fails to capture the intricate details required for specific surgeries.[47] Conversely, 3D printing allows the construction of perfect surgical guides and anatomical models that precisely match a patient's anatomy. This enables surgeons to rehearse procedures on patient- specific models, thereby improving surgical accuracy and reducing operative time.

Bioprinting and tissue engineering also benefit greatly from 3D printing technology. Traditional methods struggle with replicating the complex architecture of tissues and organs, as scaffold-based approaches often lack precision and functionality. Manual scaffold creation is labor-intensive and imprecise, but 3D bioprinting facilitates the precise deposition of cells and biomaterials to create complex tissue structures that closely mimic natural tissues. This technology allows for the development of functional tissue constructs with vascularization, which is crucial for tissue survival and integration. 3D bioprinting holds immense potential for organ replacement and regenerative medicine, offering solutions to the pressing issue of organ shortages.[48]

The advantages of 3D printing can be seen across all aspects of personalized medicine. This technology is transforming the medical industry by addressing many challenges associated with current manufacturing approaches. As 3D printing continues to evolve, it promises further advancements and innovations in healthcare, ultimately improving patient outcomes and expanding the possibilities of medical treatment and education. The upcoming section will dive deeper into the integration of 3D printing in three main fields of personalized medicine that are expected to revolutionize medical technology in the near future.

Tissue Engineering and Regenerative Medicine

Tissue engineering and regenerative medicine focus on repairing or replacing damaged tissues or organs, which would otherwise require allografts, autografts, xenografts, or, in severe cases, organ transplantation.[49] A fundamental strategy in this field involves the creation of scaffolds that offer a structural framework conducive to cell attachment, proliferation, and differentiation. These scaffolds are meticulously engineered to replicate the natural microenvironment, comprising a complex array of connective tissues that conventional manufacturing techniques cannot reproduce. The bottom-up approach in scaffold fabrication technology facilitates the development of intricate, customizable structures that closely mimic the native extracellular matrix (ECM) of tissues. With a CAD-based designing tool, researchers can make scaffolds with precise control over pore size, geometry, and mechanical properties and print them according to specific tissue types and patient needs.[50]

For example, a study presented by Lin Gong et al. explores a novel approach to osteochondral tissue engineering through the development of an interleukin-4-loaded bi-layer scaffold fabricated using advanced 3D printing techniques. The scaffold combines a radially oriented GelMA hydrogel upper layer hosting IL-4 with a PCL-HA lower layer, utilizing DLP and FDM methods for precise architectural control, as shown in figure 3. The IL-4 supports the protection and maintenance of chondrocyte phenotype alongside anti-inflammatory properties. The scaffold enhances osteochondral

Table 2 | A process description of various types of biomaterials, suitable 3D printing techniques, and their applications in personalized medicine

Types of Biomaterials	Suitable 3D Printing Technique	Potential Application in Personalized Medicine	Ref
Metals	SLS, SLM, DMLS, EBM	Custom implants and prosthetics, such as orthopedic and dental implants, with precise anatomical matching.	33
Polymers	FDM, SLA, IJP, MJM	Personalized prosthetics, anatomical models, surgical guides, and drug delivery systems tailored to individual patient needs.	34
Ceramics	SLS, LDP	Bone grafts and dental applications with high biocompatibility and mechanical strength for patient-specific requirements.	35
Composites	FDM, SLA	Hybrid materials for load-bearing implants and scaffolds that combine the properties of multiple biomaterials for enhanced function.	36
Bio-inks	IJP, MJM,	Bioprinting of tissues and organs using living cells, proteins, and growth factors for regenerative medicine and tissue engineering.	37
Decellularized Extracellular Matrix (dECM)	IJP	For the construction of natural scaffolds for cell growth and tissue development which are beneficial in tissue engineering and regenerative medicine.	38,39
Cell Aggregates and Spheroids	IJP, MJM	Formation of complex tissue structures for organ printing and regenerative medicine applications.	37
Composite Bioinks	IJP	Fabrication of complex tissues with varied mechanical and biological properties for personalized treatments.	37
Acellular Matrices	SLA	Scaffolds for cell seeding and tissue regeneration, supporting the growth of patient-specific tissues.	38
Thermoplastics	FDM, LOM	Manufacturing custom-fit medical devices, orthopedic supports, and patient-specific anatomical models.	40
Thermoset Polymers	SLA, SGC	Durable prosthetics and implants with tailored mechanical properties for individual patients.	41
Hydrogels	IJP, MJM	Used for creating a cellular microenvironment that supports natural cell growth, with potential applications in tissue engineering and regenerative medicine.	41
Resins	SLA, BIS	High-resolution anatomical models and surgical guides for precise surgical planning.	40
Biodegradable Polymers	FDM, SLA	Temporary implants and scaffolds that degrade in the body, reducing the need for surgical removal.	42

regeneration by promoting cell adhesion and proliferation, reducing inflammation, and supporting osteogenic differentiation. In a rabbit model, the scaffold significantly improved cartilage and bone repair compared to non-treated groups. This innovative scaffold design offers a promising therapeutic strategy for effectively treating osteochondral defects.[51]

In another study, Szojka et al. developed 3D-printed polycaprolactone (PCL) scaffolds that mimicked the extracellular matrix of the meniscus using biomimetic fiber architecture. The scaffolds demonstrated excellent mechanical properties, effectively replicating the native meniscus's structure, making them promising candidates for meniscus tissue engineering and future regenerative medicine applications.[52] Similarly, Jia et al. developed a 3D bioprinting approach for fabricating perfusable vascular structures with highly ordered arrangements. Using a blend bioink composed of gelatin methacryloyl, sodium alginate, and 4-arm poly(ethylene glycol)-tetra-acrylate, the researchers produced 3D perfusable hollow tubes. The bioink was designed to be cell-responsive, effectively supporting the spreading and proliferation of encapsulated endothelial and stem cells. The bioprinted constructs led to the formation of biologically relevant, highly organized, and perfusable vessels, demonstrating the potential for creating complex vascular networks essential for tissue regeneration applications. This work highlights the innovative use of 3D printing technology in developing scaffolds and constructs that advance tissue regeneration, showcasing its potential to revolutionize tissue engineering and regenerative medicine.[53]

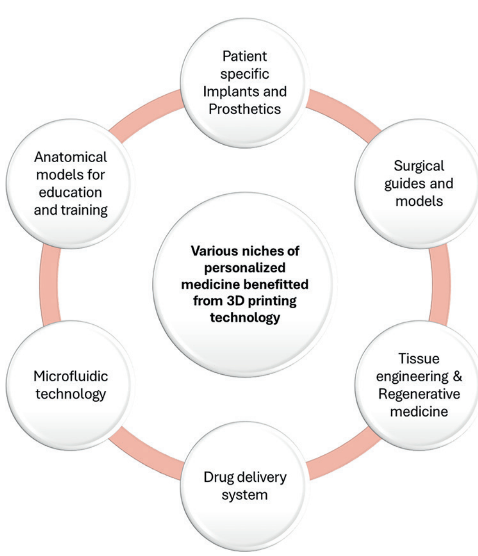

Fig 2 | Various niches of personalized medicine benefitted from the 3D printing technology

Implantable Devices and Prosthetics

Implantable devices and prosthetics are integral to modern medicine, providing essential solutions for restoring function and enhancing the quality of life for patients with damaged or missing body parts. Traditional implants and prosthetics often face challenges related to fit, biocompatibility, and long-term stability within the human body. In many cases, implanted devices require revision surgery, necessitating their removal after serving their intended function.[54,55] However, certain devices, such as hip implants, knee implants, and heart valves, are designed to remain in the body for extended

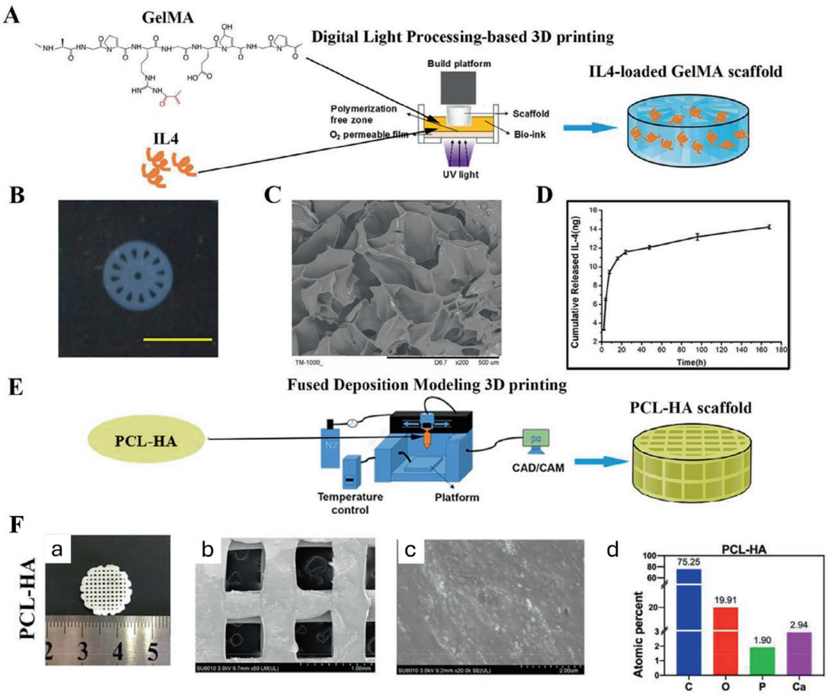

Fig 3 | Fabrication and Characterization GelMA +PCL hybrid scaffold: (A) A schematic representation of the IL-4-loaded GelMA scaffold created using the DLP 3D printing system. (B) A photographic image of the GelMA scaffold, with a scale bar indicating 5 mm. (C) A SEM image of the GelMA scaffold, with a scale bar of 500 μm. (D) IL-4 release from the GelMA hydrogel (n=3). (E) A schematic of the PCL-HA scaffold produced by the FDM 3D printing system. (F) A photographic image of PCL HA alongside SEM and the EDS spectra. Adopted from Lin Gong et al.,2020 under CC BY 4.0 [51]

periods.[56] A significant issue contributing to the failure of these implants is biomimetic mismatch, where the mechanical and biological properties of the implant do not adequately replicate those of the surrounding tissues, leading to issues like stress shielding.[57,58] The advent of 3D printing technology offers a transformative solution by enabling the design and fabrication of personalized implants that precisely match the patient's anatomy and physiological requirements. This technology allows for the creation of implants that are tailored to the unique contours and biomechanical properties of individual patients, reducing the risk of immune rejection and improving integration with host tissues.[59] By minimizing the immunological response, 3D-printed implants have the potential to enhance the longevity and effectiveness of implantable devices and prosthetics, marking a significant advancement in personalized medicine.

One of the finest examples is from work carried out by Pearlin et al., which evaluates the biological performance of a gyroid-based Ti6Al-4V implant material compared to a dense alloy counterpart using a rabbit tibia model, as shown in figure 4. The gyroid structure's porous architecture enhances bone ingrowth, leading to a bone volume/total volume (BV/TV) ratio 11 times higher than that of dense metal. The presence of pores that functionally mimic the human bone architecture has helped the tissue quickly realign to the newly added metal. The pores also facilitate angiogenesis, as confirmed by bone growth within the porous structure, which is absent in dense metal. The study confirms superior osteointegration and new blood vessel formation in the gyroid structure, highlighting its potential for improved bone healing and remodeling. This design leverages 3D printing and biomimetic approaches to mimic natural bone, offering promising applications in orthopedic implantology.[60]

J. Fu et al. conducted a study using a swine model to evaluate the effectiveness of 3D-printed porous prostheses for reconstructing acetabular bone defects. The findings demonstrated that the prostheses exhibited excellent porosity, pore size, stiffness, and elastic modulus, providing superior anatomical matching and enhancing stability. Despite being conducted on minipigs, the study underscores the potential of 3D-printed porous augments in treating severe acetabular bone defects, suggesting significant promise for future clinical applications in orthopedic surgery.[61] In another approach, W. Peng et al. designed an anatomically conforming pelvic prosthesis using 3D printing for pelvic reconstruction in patients with complex pelvic tumors. Given the challenges of vascular invasion, which often necessitate tumor resection and hemipelvic replacement, the study demonstrated that 3D-printed prostheses offer anatomically tailored solutions for such reconstructions. This research highlights the potential of 3D printing to create personalized implants that address the complexities of pelvic tumors, underscoring its value in providing customized solutions for challenging surgical scenarios.[62]

Drug Delivery Systems

Drug delivery is one of the most advanced and emerging applications benefiting from 3D printing technology. At first glance, these two technologies may seem unrelated. However, the integration of a bottom-up manufacturing approach has enabled a more patient-centric model of therapeutics than ever before.[63] One significant advantage is the development of personalized combination drugs tailored to a patient's physiological and genetic factors. This personalization aids in the management of polypharmacy, which is crucial for patients with multiple chronic conditions.[64] Furthermore, 3D printing allows for the creation of drug carriers with specific shapes and surfaces that can target particular tissues or cells, thereby improving the efficacy of treatments and reducing side effects.[65] Another technological advancement offered by 3D printing in drug delivery is its ability to enable layer-by-layer fabrication of certain drugs. This process allows for the incorporation of heat-sensitive or unstable compounds that would otherwise degrade during traditional manufacturing processes.[66] Additionally, some studies have successfully created orally disintegrating tablets using 3D printing, highlighting the technological leap made possible by additive manufacturing.[67] These advancements demonstrate the potential of 3D printing to revolutionize drug delivery by offering precise control over dosage forms, release profiles, and drug stability.

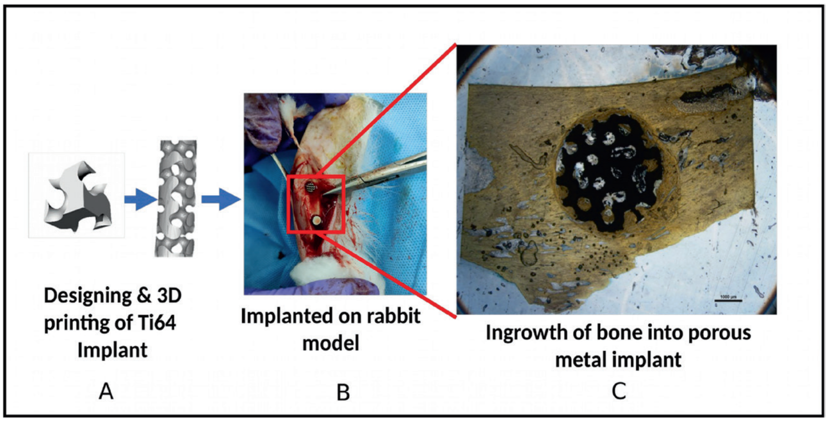

Fig 4 | Experimental approach for 3D printing metal mimicking natural human *bone*. (A) TPMS-based gyroid implants are designed to be porous and 3D printed using SLM technology. (B) The porous implant is surgically put on the rabbit tibia. (C) Histological analysis of the bone after six weeks of implantation. Adopted from Pearlin et al., 2024 under CC BY 4.0[60]

In a study commissioned by Peeyush et al., the authors explore the use of desktop vat photopolymerization (stereolithography) to create 3D-printed nanocomposite pills for drug delivery, focusing on berberine, a nutraceutical with limited gut absorption, as shown in figure 5. Researchers designed hydrogel nanoparticles loaded with berberine and embedded them into biocompatible resin matrices using stereolithography. The resultant pills demonstrated high print fidelity, with hydrogel nanoparticles evenly distributed within the matrix. Characterization showed efficient nanoparticle formation with a mean size of 95.05 nm. The pills exhibited significant swelling and drug release in acidic environments, releasing 50.39% of berberine within 4 hours and a maximum of 77.96% over 48 hours. This approach aims to enhance berberine's bioavailability and gastrointestinal absorption by facilitating controlled release through a 3D-printed delivery system. The study highlights the potential of 3D printing in developing advanced drug delivery systems and opens avenues for customized pharmaceutical applications.[68]

A study by Ahmed et al. created a patient-specific drug delivery approach using 3D-printed tablets containing glimepiride (GLMP) and rosuvastatin (RSV) for diabetic dyslipidemia management. By developing a self-nano emulsifying drug delivery system (SNEDDS) with curcumin oil, these drugs were incorporated into semi-solid pastes and subsequently 3D- printed. Characterization tests demonstrated good mechanical properties, consistent drug content, and enhanced dissolution rates compared to non-SNEDDS tablets. The 3D-printed tablets showed superior pharmacokinetics and relative bioavailability, suggesting their potential as a personalized therapy option for metabolic disorders, although clinical trials are needed to confirm safety and efficacy.[69] The beneficial leap of personalized medicine with the help of 3D printing extends far beyond a few applications, as more and more medical fields are employing this bottom-up manufacturing approach for its obvious benefits.

Challenges and Limitations

3D printing has undoubtedly emerged as a transformative technology in personalized medicine, expanding its capabilities to provide precise and customizable solutions for a range of medical applications. Despite this promise, the complete adoption of 3D printing in medical science faces technical and biological challenges that prevent it from being the holy grail.

A significant barrier to the integration of 3D printing in personalized medicine is the high capital cost associated with the technology.[70] Although the cost of consumer-grade 3D printers is decreasing, advanced application-oriented technologies still require substantial investment. For instance, an industrial-grade electron beam melting (EBM) metal 3D printer from GE Additive costs approximately $500,000, with an additional 10-15% in annual maintenance costs and $250 to $1,000 per kilogram of powder feed used.[71] This financial burden limits access, particularly in low-resource settings where healthcare budgets are already constrained.

A wide range of biomaterials are suitable for 3D printing; however, there is currently no perfect material that can sustainably serve as an implant. An ideal biomaterial would possess exceptional biocompatibility, mechanical properties similar to those of human tissue, and superior processability to facilitate the construction of implants. Additionally, some of these materials need to be easily degradable and economical for widespread use. This combination of attributes is not yet available in any single biomaterial, highlighting the need for further research and development. There is a significant opportunity to develop new biomaterials compatible with existing 3D printing technologies, which would enable the creation of more effective and reliable medical implants. Advances in this area could lead to improved patient outcomes and expand the applicability of 3D printing in personalized medicine.[72,73]

Seamlessly integrating 3D printing technology into existing medical workflows presents a significant challenge. The medical industry has long relied on mature processing techniques, such as machining and molding, which are major driving factors behind current cost structures. Due to the initial high capital investment required for additive manufacturing technology, it has yet to become an economical and viable choice for many hospitals.[74] Additionally, the process of integrating 3D printing into medical workflows often requires the use of multiple software platforms. These platforms are typically designed to meet the needs of biomedical engineers, making them difficult for medical professionals to master. Developing an integrated platform that allows for seamless communication between healthcare providers, engineers, and manufacturers is crucial for

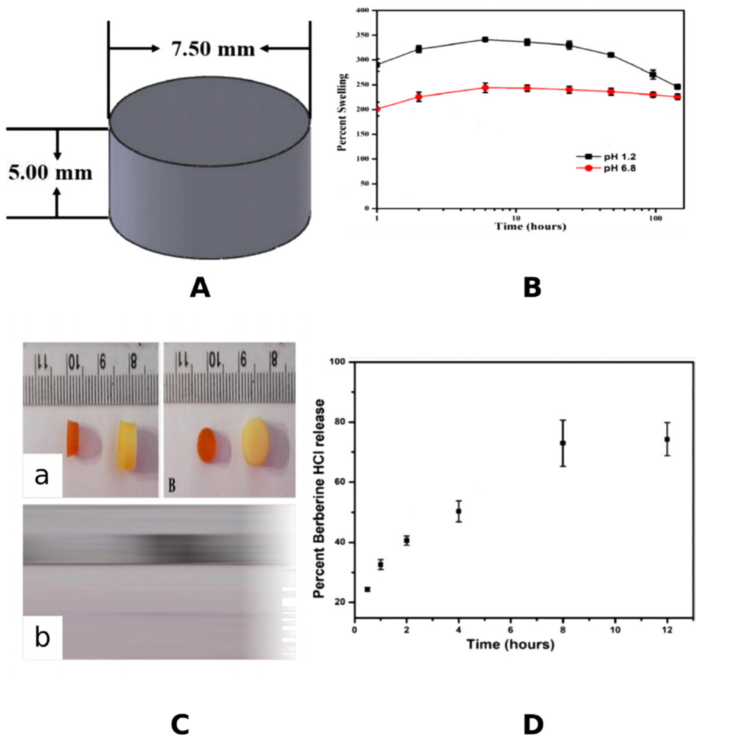

Fig 5 | Overview of 3D-Printed Nanocomposite Drug Delivery System
(A) CAD model showcasing the dimensions of the drug delivery system, (B) Swelling behavior analysis in both gastric and intestinal environments, highlighting higher swelling under acidic conditions, (C) Volumetric changes of the nanocomposite pills illustrating swelling-induced dimensional alterations, (D) Berberine-HCl release profile from the nanocomposite pills, demonstrating drug release over time in different pH environments. Adopted from Peeyush et al.; 2022 under CC BY 4.0[68]

facilitating the widespread adoption of 3D printing in personalized medicine.[73]

While 3D printing offers transformative potential in personalized medicine and implant design, several challenges hinder its widespread adoption. Longer lead times compared to standard implants, a lack of intraoperative flexibility, the need for post-processing after 3D printing, and various regulatory concerns are major obstacles that need to be addressed.[73,75,76] To maximize the efficacy and integration of 3D printing into clinical practice, these technical and biological challenges must be overcome. Ongoing advancements in technology, combined with regulatory developments, will be essential in addressing these limitations and realizing the full potential of 3D-printed medical solutions.

Future Directions and Conclusion

The future of 3D printing in personalized medicine is promising, with significant advancements in pharmaceuticals and bioprinting. This technology enables personalized drug dosage forms tailored to individual needs, improving treatment for pediatric and geriatric populations.[77] 3D printing can also create combination pills with various release profiles, enhancing patient compliance. In bioprinting, the focus is on fabricating tissues and organs, such as skin, bone, and even complex structures like the heart.[78] Another area where 3D prnting could be a breakthrough is in the clinical practice by providing accurate models for surgical planning and medical education. Integration with Aritifical Intelliegnce (AI), Virtual Reality (VR), and Augmented Reality (AR) could further enhance these applications. These tenologies would enable precise, patient-specific designs thereby brinding gap of geometric deviation between CAD model and 3d pmrinted structure. AI can analyze patient data , help in design optimzaiton to create tailored medical devices or implants. VR allows surgeons to visualize and plan complex procedures with 3D models before printing, enhancing accuracy while AR can guide practitioners during surgery by overlaying 3D-printed models onto the patient, ensuring perfect alignment and fit, ultimately improving outcomes in personalized medical treatments.[79,80] However, challenges remain, including regulatory concerns, material limitations, and high costs. Addressing these issues through continued research and technological advancements will be crucial for fully realizing the potential of 3D printing in personalized medicine, ultimately transforming healthcare by offering safer, more effective, and tailored treatments for patients.

3D printing is undeniably a key promoter of personalized medicine, driving innovation and transformation across the field. Every day, new advancements are added to the existing pool of 3D printing knowledge. On one hand, this technology is revolutionizing personalized medicine by enabling the creation of patient-specific implants, prosthetics, and drug delivery systems. On the other hand, there are progress-hindering challenges that can only be overcome through smart engineering in biomaterials, refining process flows, and devising new integration strategies within existing healthcare systems. Decades of research are still essential to overcoming these challenges, ultimately improving patient outcomes and transforming healthcare through more precise, individualized therapies. Continued advancements in 3D printing technology, along with interdisciplinary collaboration, will pave the way for a new era of personalized medicine that tailors treatments to the unique needs of each patient.

References

1 Agamah FE, Thomford NE, Hassan R, Allali I, Elsheikh SSM, Dandara C, et al. Drug response in association with pharmacogenomics and pharmacomicrobiomics: towards a better personalized medicine. Brief Bioinform n.d.;22:1-14. doi: 10.1093/bib/bbaa292.
2 Harvey A, Brand A, Holgate ST, Kristiansen L V., Lehrach H, Palotie A, et al. The future of technologies for personalised medicine. N Biotechnol 2012;29:625-33. doi: 10.1016/J.NBT.2012.03.009
3 Vaz VM, Kumar L. 3D Printing as a Promising Tool in Personalized Medicine. AAPS PharmSciTech 2021;22:1-20. doi: 10.1208/S12249-020-01905-8/TABLES/3
4 Comminal R, Serdeczny MP, Pedersen DB, Spangenberg J. Numerical Modeling of the Material Deposition and Contouring Precision in Fused Deposition Modeling 2018:1855-64.
5 Wacogne B, Py S, Guitton A, Charrière K, Pazart L. Medical devices development: the bottom-up or the top-down approach? Int J Biosens Bioelectron 2017;Volume 3. doi: 10.15406/IJBSBE.2017.03.00079

6 Cai Y, Chang SY, Gan SW, Ma S, Lu WF, Yen CC. Nanocomposite bioinks for 3D bioprinting. Acta Biomater 2022;151:45-69. doi: 10.1016/J.ACTBIO.2022.08.014
7 Wan H, Xiang J, Mao G, Pan S, Li B, Lu Y. Recent Advances in the Application of 3D- Printing Bioinks Based on Decellularized Extracellular Matrix in Tissue Engineering. ACS Omega 2024;9:24219-35. doi: 10.1021/ACSOMEGA.4C02847/ASSET/IMAGES/LARGE/AO4C02847_000 6.JPEG
8 Raheem AA, Hameed P, Whenish R, Elsen RS, Aswin G, Jaiswal AK, et al. A Review on Development of Bio-Inspired Implants Using 3D Printing. Biomimetics 2021, Vol 6, Page 65 2021;6:65. doi: 10.3390/BIOMIMETICS6040065
9 Kropla F, Winkler D, Lindner D, Knorr P, Scholz S, Grunert R. Development of 3D printed patient-specific skull implants based on 3d surface scans. 3D Printing in Medicine 2023 9:1 2023;9:1-10. doi: 10.1186/S41205-023-00183-X
10 Yi HG, Choi YJ, Kang KS, Hong JM, Pati RG, Park MN, et al. A 3D-printed local drug delivery patch for pancreatic cancer growth suppression. J Control Release 2016;238:231-41. doi: 10.1016/J.JCONREL.2016.06.015
11 Srivastava M, Rathee S, Patel V, Kumar A, Koppad PG. A review of various materials for additive manufacturing: Recent trends and processing issues. Journal of Materials Research and Technology 2022;21:2612-41. doi: 10.1016/J.JMRT.2022.10.015
12 Abdulhameed O, Al-Ahmari A, Ameen W, Mian SH. Additive manufacturing: Challenges, trends, and applications. Advances in Mechanical Engineering 2019;11:1-27. doi: 10.1177/1687814018822880
13 Vignesh M, Ranjith Kumar G, Sathishkumar M, Manikandan M, Rajyalakshmi G, Ramanujam R, et al. Development of Biomedical Implants through Additive Manufacturing: A Review. Journal of Materials Engineering and Performance 2021 30:7 2021;30:4735-44. doi: 10.1007/S11665-021-05578-7.
14 Mazzoli A. Selective laser sintering in biomedical engineering. Med Biol Eng Comput 2013;51:245-56. doi: 10.1007/s11517-012-1001-x
15 Gokuldoss PK, Kolla S, Eckert J. Additive manufacturing processes: Selective laser melting, electron beam melting and binder jetting-selection guidelines. Materials 2017;10:1-11. doi: 10.3390/ma10060672
16 Cerea M, Dolcini GA. Custom-Made Direct Metal Laser Sintering Titanium Subperiosteal Implants: A Retrospective Clinical Study on 70 Patients. Biomed Res Int 2018;2018. doi: 10.1155/2018/5420391
17 Choi J, Song L, Mazumder J. Additive Manufacturing by Direct Metal Deposition 2011.
18 Revathi A, Das M, Balla VK, Devika D, Sen D, … Surface engineering of LENS-Ti-6Al-4V to obtain nano-and micro-surface topography for orthopedic application. … , Biology and Medicine 2019.
19 Chivel Y. New approach in selective laser cladding. Procedia CIRP 2018;74:172-5. doi: 10.1016/J.PROCIR.2018.08.075
20 Laser metal deposition (LMD) | Höganäs n.d. https://www.hoganas.com/en/powder- technologies/additive-manufacturing-metal-powders/laser-metal-deposition-lmd/ (accessed August 2, 2024).
21 Moniruzzaman M, O'neal C, Bhuiyan A, Egan PF. Design and mechanical testing of 3d printed hierarchical lattices using biocompatible stereolithography. Designs (Basel) 2020;4:1-14. doi: 10.3390/designs4030022
22 Zhang X, Zhou B, Zeng Y, Gu P. Model layout optimization for solid ground curing rapid prototyping processes. Robot Comput Integr Manuf 2002;18:41-51. doi: 10.1016/S0736-5845(01)00022-9
23 Liao WC, Hsu SLC. A novel liquid thermal polymerization resist for nanoimprint lithography with lowshrinkage and high flowability. Nanotechnology 2007;18:065303. doi: 10.1088/0957-4484/18/6/065303
24 García-Dominguez A, Claver J, Sebastián MA. Integration of Additive Manufacturing, Parametric Design, and Optimization of Parts Obtained by Fused Deposition Modeling (FDM). A Methodological Approach. Polymers (Basel) 2020;12:1-27. doi: 10.3390/POLYM12091993
25 Christensen K, Xu C, Chai W, Zhang Z, Fu J, Huang Y. Freeform inkjet printing of cellular structures with bifurcations. Biotechnol Bioeng 2015;112:1047-55. doi: 10.1002/bit.25501
26 Tamir TS, Xiong G, Shen Z, Leng J, Fang Q, Yang Y, et al. 3D printing in materials manufacturing industry: A realm of Industry 4.0. Heliyon 2023;9:e19689. doi: 10.1016/J.HELIYON.2023.E19689
27 Feygin M, Hsieh B. Laminated Object Manufacturing (LOM): A Simpler Process 1991. doi: 10.15781/T2PV6BQ54
28 Wendel B, Rietzel D, Kühnlein F, Feulner R, Hülder G, Schmachtenberg E. Additive Processing of Polymers. Macromol Mater Eng 2008;293:799-809. doi: 10.1002/MAME.200800121
29 Moiduddin K, Mian SH, Elseufy SM, Abdo BMA, Aboudaif MK, Alkhalefah H. Craniofacial Reconstruction with Personalized Lightweight Scaffold Fabricated Using Electron-Beam Additive Manufacturing. Metals 2022, Vol 12, Page 552 2022;12:552. doi: 10.3390/MET12040552
30 An T, Wen J, Dong Z, Zhang Y, Zhang J, Qin F, et al. Plasmonic Biosensors with Nanostructure for Healthcare Monitoring and Diseases Diagnosis. Sensors 2023, Vol 23, Page 445 2022;23:445. doi: 10.3390/S23010445
31 Ke D, Niu C, Yang X. Evolution of 3D bioprinting-from the perspectives of bioprinting companies. Bioprinting 2022;25:e00193. doi: 10.1016/J.BPRINT.2022.E00193
32 Alzoubi L, Aljabali AAA, Tambuwala MM. Empowering Precision Medicine: The Impact of 3D Printing on Personalized Therapeutic. AAPS PharmSciTech 2023 24:8 2023;24:1-33. doi: 10.1208/S12249-023-02682-W
33 Bai L, Gong C, Chen X, Sun Y, Zhang J, Cai L, et al. Additive Manufacturing of Customized Metallic Orthopedic Implants: Materials, Structures, and Surface Modifications. Metals 2019, Vol 9, Page 1004 2019;9:1004. doi: 10.3390/MET9091004
34 Youssef A, Hollister SJ, Dalton PD. Additive manufacturing of polymer melts for implantable medical devices and scaffolds. Biofabrication 2017;9:012002. doi: 10.1088/1758- 5090/AA5766
35 Dadkhah M, Tulliani JM, Saboori A, Iuliano L. Additive manufacturing of ceramics: Advances, challenges, and outlook. J Eur Ceram Soc 2023;43:6635-64. doi: 10.1016/J.JEURCERAMSOC.2023.07.033
36 Prem Ananth K, Jayram ND. A comprehensive review of 3D printing techniques for biomaterial-based scaffold fabrication in bone tissue engineering. Annals of 3D Printed Medicine 2024;13:100141. doi: 10.1016/J.STLM.2023.100141
37 Dey M, Ozbolat IT. 3D bioprinting of cells, tissues and organs. Scientific Reports 2020 10:1 2020;10:1-3. doi: 10.1038/s41598-020-70086-y
38 Elomaa L, Keshi E, Sauer IM, Weinhart M. Development of GelMA/PCL and dECM/PCL resins for 3D printing of acellular in vitro tissue scaffolds by stereolithography. Materials Science and Engineering: C 2020;112:110958. doi: 10.1016/J.MSEC.2020.110958
39 Dzobo K, Motaung KSCM, Adesida A. Recent Trends in Decellularized Extracellular Matrix Bioinks for 3D Printing: An Updated Review. International Journal of Molecular Sciences 2019, Vol 20, Page 4628 2019;20:4628. doi: 10.3390/IJMS20184628. Cornejo J, Cornejo-Aguilar JA, Vargas M, Helguero CG, Milanezi De Andrade R, Torres- Montoya S, et al. Anatomical Engineering and 3D Printing for Surgery and Medical Devices: International Review and Future Exponential Innovations. Biomed Res Int 2022;2022:6797745. doi: 10.1155/2022/6797745
41 Touri M, Kabirian F, Saadati M, Ramakrishna S, Mozafari M. Additive Manufacturing of Biomaterials – The Evolution of Rapid Prototyping. Adv Eng Mater 2019;21:1800511. doi: 10.1002/ADEM.201800511
42 Nair LS, Laurencin CT. Biodegradable polymers as biomaterials. Progress in Polymer Science (Oxford) 2007;32:762-98. doi: 10.1016/j.progpolymsci.2007.05.017
43 Katakam P, Dey B, Assaleh FH, Hwisa NT, Adiki SK, Chandu BR, et al. Top-Down and Bottom-Up Approaches in 3D Printing Technologies for Drug Delivery Challenges. Critical Reviews™ in Therapeutic Drug Carrier Systems 2015;32:61-87. doi: 10.1615/CRITREVTHERDRUGCARRIERSYST.2014011157
44 Giannatsis J, Dedoussis V. Additive fabrication technologies applied to medicine and health care: A review. International Journal of Advanced Manufacturing Technology 2009;40:116-27. doi: 10.1007/S00170-007-1308-1/METRICS
45 de Oliveira RS, Fantaus SS, Guillot AJ, Melero A, Beck RCR. 3D-Printed Products for Topical Skin Applications: From Personalized Dressings to Drug Delivery. Pharmaceutics 2021, Vol 13, Page 1946 2021;13:1946. doi: 10.3390/PHARMACEUTICS13111946
46 Attaran M. The rise of 3-D printing: The advantages of additive manufacturing over traditional manufacturing. Bus Horiz 2017;60:677-88. doi: 10.1016/J.BUSHOR.2017.05.011
47 Shea GK-H, Wu KL-K, Li IW-S, Leung M-F, Ko AL-P, Tse L, et al. A review of the manufacturing process and infection rate of 3D-printed models and guides sterilized by hydrogen peroxide

plasma and utilized intra-operatively. 3D Printing in Medicine 2020 6:1 2020;6:1-11. doi: 10.1186/S41205-020-00061-W
48 Mudigonda J. 3D bioprinting of tissues and organs: A comprehensive review of the techniques, recent advances, and their applications in organ engineering and regenerative medicine. Advances in 3D Bioprinting 2023:1-54. doi: 10.1201/9781351003780- 1/3D-BIOPRINTING-TISSUES-ORGANS-JAHNAVI-MUDIGONDA
49 Messner F, Guo Y, Etra JW, Brandacher G. Emerging technologies in organ preservation, tissue engineering and regenerative medicine: a blessing or curse for transplantation? Transplant International 2019;32:673-85. doi: 10.1111/TRI.13432
50 Gaspar VM, Lavrador P, Borges J, Oliveira MB, Mano JF. Advanced Bottom-Up Engineering of Living Architectures. Advanced Materials 2020;32:1903975. doi: 10.1002/ADMA.201903975
51 Gong L, Li J, Zhang J, Pan Z, Liu Y, Zhou F, et al. An interleukin-4-loaded bi-layer 3D printed scaffold promotes osteochondral regeneration. Acta Biomater 2020;117:246-60. doi: 10.1016/J.ACTBIO.2020.09.039
52 Szojka A, Lalh K, Andrews SHJ, Jomha NM, Osswald M, Adesida AB. Biomimetic 3D printed scaffolds for meniscus tissue engineering. Bioprinting 2017;8:1-7. doi: 10.1016/J.BPRINT.2017.08.001
53 Jia W, Gungor-Ozkerim PS, Zhang YS, Yue K, Zhu K, Liu W, et al. Direct 3D bioprinting of perfusable vascular constructs using a blend bioink. Biomaterials 2016;106:58-68. doi: 10.1016/J.BIOMATERIALS.2016.07.038
54 Prakasam M, Locs J, Salma-Ancane K, Loca D, Largeteau A, Berzina-Cimdina L. Biodegradable Materials and Metallic Implants—A Review. J Funct Biomater 2017;8. doi: 10.3390/JFB8040044
55 Lozano CM, Samundeeswari S, Araujo-Espinoza G, Shanmugasundaram S. Impact of Increased Life Expectancy on Orthopaedic Trauma Implantology. Handbook of Orthopaedic Trauma Implantology 2023:951-64. doi: 10.1007/978-981-19-7540-0_53
56 Chen Q, Thouas GA. Metallic implant biomaterials. Materials Science & Engineering R 2015;87:1-57. doi: 10.1016/j.mser.2014.10.001
57 Arabnejad S, Johnston B, Tanzer M, Pasini D. Fully porous 3D printed titanium femoral stem to reduce stress-shielding following total hip arthroplasty. J Orthop Res 2017;35:1774-83. doi: 10.1002/JOR.23445
58 Ridzwan MIZ, Shuib S, Hassan AY, Shokri AA, Mohammad Ibrahim MN. Problem of stress shielding and improvement to the hip implant designs: A review. Journal of Medical Sciences 2007;7:460-7. doi: 10.3923/JMS.2007.460.467
59 Kelly SH, Shores LS, Votaw NL, Collier JH. Biomaterials Strategies for Generating Therapeutic Immune Responses. Adv Drug Deliv Rev 2017;114:3. doi: 10.1016/J.ADDR.2017.04.009
60 Khan PA, Raheem A, Kalirajan C, Prashanth KG, Manivasagam G. In Vivo Assessment of a Triple Periodic Minimal Surface Based Biomimmetic Gyroid as an Implant Material in a Rabbit Tibia Model. ACS Materials Au 2024. doi: 10.1021/ACSMATERIALSAU.4C00016/ASSET/IMAGES/LARGE/MG4C00016_0009.JPEG
61 Fu J, Xiang Y, Ni M, Qu X, Zhou Y, Hao L, et al. In Vivo Reconstruction of the Acetabular Bone Defect by the Individualized Three-Dimensional Printed Porous Augment in a Swine Model. Biomed Res Int 2020;2020. doi: 10.1155/2020/4542302
62 Peng W, Zheng R, Wang H, Huang X. Reconstruction of Bony Defects after Tumor Resection with 3D-Printed Anatomically Conforming Pelvic Prostheses through a Novel Treatment Strategy. Biomed Res Int 2020;2020:8513070. doi: 10.1155/2020/8513070
63 Chatterjee P, Chakraborty C. Emergence of 3D Printing Technology in the Intelligent Healthcare Systems: A Brief Drug Delivery Approach. Intelligent Healthcare: Infrastructure, Algorithms and Management 2022:395-420. doi: 10.1007/978-981-16-8150-9_18
64 BG PK, Mehrotra S, Marques SM, Kumar L, Verma R. 3D printing in personalized medicines: A focus on applications of the technology. Mater Today Commun 2023;35:105875. doi: 10.1016/J.MTCOMM.2023.105875
65 Afsana, Jain V, Haider N, Jain K. 3D Printing in Personalized Drug Delivery. Curr Pharm Des 2019;24:5062-71. doi: 10.2174/1381612825666190215122208
66 Abdella S, Youssef SH, Afinjuomo F, Song Y, Fouladian P, Upton R, et al. 3D Printing of Thermo-Sensitive Drugs. Pharmaceutics 2021, Vol 13, Page 1524 2021;13:1524. doi: 10.3390/PHARMACEUTICS13091524
67 Fina F, Madla CM, Goyanes A, Zhang J, Gaisford S, Basit AW. Fabricating 3D printed orally disintegrating printlets using selective laser sintering. Int J Pharm 2018;541:101-7. doi: 10.1016/J.IJPHARM.2018.02.015
68 Sharma PK, Choudhury D, Yadav V, Murty USN, Banerjee S. 3D printing of nanocomposite pills through desktop vat photopolymerization (stereolithography) for drug delivery reasons. 3D Printing in Medicine 2022 8:1 2022;8:1-10. doi: 10.1186/S41205-022-00130-2
69 Ahmed TA, Felimban RI, Tayeb HH, Rizg WY, Alnadwi FH, Alotaibi HA, et al. Development of Multi-Compartment 3D-Printed Tablets Loaded with Self-Nanoemulsified Formulations of Various Drugs: A New Strategy for Personalized Medicine. Pharmaceutics 2021, Vol 13, Page 1733 2021;13:1733. doi: 10.3390/PHARMACEUTICS13101733
70 Choonara YE, Du Toit LC, Kumar P, Kondiah PPD, Pillay V. 3D-printing and the effect on medical costs: a new era? Expert Rev Pharmacoecon Outcomes Res 2016;16:23-32. doi: 10.1586/14737167.2016.1138860
71 How Much Does a Metal 3D Printer Cost? | All3DP Pro n.d. https://all3dp.com/2/how-much- does-a-metal-3d-printer-cost/ (accessed August 4, 2024)
72 Yadav D, Garg RK, Ahlawat A, Chhabra D. 3D printable biomaterials for orthopedic implants: Solution for sustainable and circular economy. Resources Policy 2020;68:101767. doi: 10.1016/J.RESOURPOL.2020.101767
73 Oropallo W, Piegl LA. Ten challenges in 3D printing. Eng Comput 2016;32:135-48. doi: 10.1007/S00366-015-0407-0/METRICS
74 Pavlish-Carpenter S. The Effects of Emerging Technology on Healthcare and the Difficulties of Integration. Honors Undergraduate Theses 2018
75 Pugliese L, Marconi S, Negrello E, Mauri V, Peri A, Gallo V, et al. The clinical use of 3D printing in surgery. Updates Surg 2018;70:381-8. doi: 10.1007/S13304-018-0586- 5/METRICS
76 Attaran M. 3D Printing: Enabling a New Era of Opportunities and Challenges for Manufacturing. International Journal of Research in Engineering and Science (IJRES) ISSN 2016;4:30-8
77 Varghese R, Sood P, Salvi S, Karsiya J, Kumar D. 3D printing in the pharmaceutical sector: Advances and evidences. Sensors International 2022;3:100177. doi: 10.1016/J.SINTL.2022.100177
78 Lozano R, Stevens L, Thompson BC, Gilmore KJ, Gorkin R, Stewart EM, et al. 3D printing of layered brain-like structures using peptide modified gellan gum substrates. Biomaterials 2015;67:264-73. doi: 10.1016/j.biomaterials.2015.07.022
79 Popov V V., Kudryavtseva E V., Katiyar NK, Shishkin A, Stepanov SI, Goel S. Industry 4.0 and Digitalisation in Healthcare. Materials 2022, Vol 15, Page 2140 2022;15:2140. doi: 10.3390/MA15062140
80 Tene T, Vique López DF, Valverde Aguirre PE, Orna Puente LM, Vacacela Gomez C. Virtual reality and augmented reality in medical education: an umbrella review. Front Digit Health 2024;6. doi: 10.3389/FDGTH.2024.1365345