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Recent Advances and Challenges in 3D Bioprinting for Tissue Engineering

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A B S T R A C T

3D bioprinting is an emerging technology that enables the precise deposition of cells, biomaterials, and bioactive molecules to fabricate functional tissues and organs. Over the last decade, significant advances have been made in bioprinting techniques, bio-ink formulations, and applications in tissue engineering and regenerative medicine. This review summarizes the fundamental principles of 3D bioprinting, compares commonly used printing methods and bio-inks, and highlights their applications in developing engineered tissues and organ models. Key challenges —including vascularization, cell viability, mechanical stability, and clinical translation —are critically discussed. Finally, the review outlines future prospects such as 4D bioprinting, smart biomaterials, and personalized medicine, emphasizing the potential of bioprinting to revolutionize healthcare.

Introduction

Over the past few decades, printing technology has evolved from two-dimensional (2D) printing to 3D shaped printing. Just as Watson and Crick modeled the structure of DNA using a ball-and-stick model, 3D printing is now applied to visualize complex molecules, protein interactions, and to create customized laboratory tools. The concept of 3D printing was first described in 1986 by Charles W. Hull, who developed a technique called 'stereolithography', thin layers of ultraviolet light-curable materials in sequence to form a solid 3D object. (1)

Human organs are highly complex structures formed by the combined, functional organization of various tissue types. The cells in these organs are highly specialized and worked together to perform specific functions. Researchers are developing methods to fabricate 3D functional living human constructs with biological and mechanical characteristics necessary for restoration of tissue and organ function in clinical applications (2)

In bioprinting, cells and biomaterials are precisely deposited at the micrometer scale to create tissue-like structures. Unlike conventional 3D printing techniques that have been used to print temporary cell-free scaffolds for use in surgery, bioprinting requires a different technical approach that is compatible with depositing living cells. Several strategies are used in 3D bioprinting, including biomimicry, autonomous self-assembly and mini--tissue building blocks.

The advantages of bioprinting include accurate control of cell distribution, high resolution cell deposition, scalability, and cost-effectiveness. As a result, both the development and applications of bioprinting have expanded significantly over the past five years (3)

In this review, we discuss the basics of bioprinting, printing technologies, bio-ink design and characterization, major tissue applications, bottlenecks such as vascularization, cell viability, scalability, and regulatory issues and future directions including 4D bioprinting and AI integration.

Three – Dimensional (3D) Bioprinting

Three-dimensional (3D) bioprinting is an emerging technology with transformative potential in medical science.

Unlike conventional 3D printing, Bioprinting is defined as a computer-aided transfer process for simultaneous writing of living cells and bio-materials with a prescribed layer-by-layer stacking organization to create bio-engineered constructs for tissue engineering, regenerative medicine, or other biological studies. The major difference between 3D printing of tissue engineering and bioprinting are that bioprinting involves the printing of living cells and other biologics. It enables the placement of cells, proteins, DNA, drugs, and growth factors to guide tissue and organ formation, offering solutions to organ shortages (9). The 3-D bioprinting process involves three main steps: (Fig.1)

1. **Pre-processing**
2. P**rocessing**
3. **Post-processing**

Pre-Processing (Design and Preparation)

This step involves creating a digital blueprint of the tissue or organ to be printed. Medical imaging technologies such as MRI, CT scans, or ultrasound are often used to capture the patient's anatomy. The acquired images are then processed with computer-aided design (CAD) software to develop a precise 3D model. This design guides the bioprinter on the exact placement of cells, biomaterials, and growth factors layer by layer. Preprocessing also includes selecting suitable bioink (a mixture of living cells and biomaterials) based on the type of tissue being fabricated. (9)

Processing (Actual Bioprinting)

In this stage, the bioprinter fabricates the construct by depositing bioink in a layer-by-layer fashion, following the digital blueprint. The printer uses techniques like inkjet printing, extrusion printing, or laser-assisted printing to dispense cells and biomaterials.

The living cells are arranged in a way that mimics natural tissue architecture, with high spatial precision. The accuracy of this stage is critical, as it ensures proper cell distribution, nutrient pathways, and structural stability of the construct. (9)

Post-Processing (Maturation in Bioreactor)

After printing, the construct is not immediately functional; it requires further development. The printed structure is placed in a bioreactor, a controlled environment that supplies nutrients, oxygen, and growth factors. Here, cells undergo proliferation (multiplication), tissue remodeling, and maturation, allowing the structure to gain functionality. Post-processing ensures mechanical strength, vascularization (blood vessel formation), and biological activity of the construct. This step is essential whether the tissue is intended for transplantation, drug testing, or in vitro research. (9)

Printing Techniques

There are four main bioprinting technologies:

- Inkjet Bioprinting
- Extrusion – Based Bioprinting
- Laser – Assisted Bioprinting
- Stereolithography Bioprinting

While each bioprinting technology has both strengths and limitations, each may be utilized according to the

intended application to further develop the field of personalized medicine (16)

Inkjet Bioprinting

Inkjet 3D bioprinting was first introduced in 2003 by Wilson and Boland. First attempts to print live cells was performed using a specially adapted commercially available inkjet printers. An initial problem encountered when developing inkjet bioprinting was that the cells died during printing due to instantaneous drying out once on the substrate. The problem was overcome by encapsulating the cells in a highly hydrated polymer, this led to the development of cell-loaded hydrogels. In this technique, cells and biomaterials are dispensed as droplets generated through either thermal or piezoelectric mechanisms. (10)

In thermal inkjet printing, a heating element rapidly forms a vapor bubble within the printhead. The resulting pressure increases forces a droplet of bioink out of the nozzle. Although the thermal element can reach temperatures between 100 °C and 300 °C. Initially there have been concerns that such high temperatures would damage the cells however research has shown that the high temperatures are localized and are only present for a short time span. (10)

Piezoelectric-based apparatus uses acoustic waves to eject the bioink. This mechanism limits the use of highly concentrated and viscous bioinks as their viscosity dampens the applied acoustic/pressure waves, hindering the ejection of a droplet. Low viscosity is achieved by using low concentration solutions, a limiting factor for producing 3D structures. (10)

Inkjet bioprinting is of great interest as it exhibits high resolution and cell viability. With this process, accurate position of multiple cell types is possible. However, the limitations of vertical printing and restricted viscosities may mean that inkjet bioprinting needs to be combined with other printing techniques for future developments. (10)

Laser-assisted Bioprinting

Laser-assisted printing was initially developed to deposit metals onto receiver sheets. Odde and Renn later developed the technique to print viable embryonic chick spinal cord cells. (10) Laser-assisted bioprinting (LAB) consists of three parts: a donor-slide (or ribbon), a laser pulse and a receiver-slide. A ribbon is made of a layer of transparent glass, a thin layer of metal, and a layer of bioink. The bioink is transferred from the ribbon onto the receiver slide when the metal layer under the hydrogel is vaporized by a laser pulse. This scaffold-free technique has very high cell viabilities (>95) and a resolution between 10–50 μm. (10)

LAB has the ability to position multiple cell types with a high degree of accuracy, with several studies demonstrating singular the capability of positioning a singular cell per droplet. However, it is an expensive process to perform and suffers from low stability and scalability. It has shown great potential when combined with other biofabrication techniques (10) (13)

Extrusion – Based Bioprinting

Extrusion-based printing is a pressure-driven technology. The bioink is extruded through a nozzle, driven either by pneumatic or mechanical pressure, and deposited in a predesigned structure. The main advantage of extrusion bioprinting is the ability to print with very high cell densities. Despite its versatility and benefits, it has some disadvantages when compared to other technologies. The resolution is very limited, as a minimum feature size is generally over 100 μm, which is a poorer resolution than that of other bioprinting techniques.

This could limit its application for certain soft tissue applications that require small pore sizes for an improved tissue response, however could still be applicable to hard tissues with size larger than 10 mm. The pressure used for the extrusion of the material has the potential to alter the cell morphology and function, although several studies have reported. (10)

Extrusion-based bioprinting follows the directives of a computer model, applying mechanical or pneumatic pressure to distribute bio-ink through the nozzle. The freeform reversible embedding of suspended hydrogels approach dispenses low-viscosity bio-ink while simultaneously performing 3D bioprinting and cross-linking within a supportive hydrogel matrix. A leading innovation in the field integrates microfluidic chips with the dispensing head, enabling the distribution of multiple bio-inks through a single nozzle. This advanced method facilitates the rapid creation of complex and heterogeneous 3D tissue architectures (10)

Stereolithography Bioprinting

Stereolithography (SLA) is a well-known 3D bioprinting

method that depends on photopolymerization, wherein ultraviolet (UV) light cures a liquid resin into a solid polymer. In SLA, a photo initiator is integrated into the resin, which, upon exposure to UV light, executes a chemical reaction that generates free radicals. These free radicals cause the surrounding monomers to start polymerizing/crosslinking, which accelerates the resin's hardening. Both stereolithography and digital light processing bioprinting are based on the polymerization of photo-cross-linkable materials (light-sensitive polymers) using a precisely controlled light source. (10)

SLA is especially appropriate for applications in biomedical engineering and prototyping because of its precision, which enables the fabrication of complex and high-resolution features. The ability to control the exposure time and intensity of the UV light further enhances the accuracy and mechanical properties of the printed objects, thus broadening the scope of materials that can be utilized in SLA processes. (10)

Bioink and Biomaterials

Bioinks are an important component of 3D bioprinting. They contain living cells and biomaterials that simulate the extracellular matrix microenvironment. They are cross-linked or stabilised during or immediately after the bioprinting process to form a final shape that simulates the expected tissue structure. The properties that an ideal bioink should have include printability, adjustable gelation and fluidity to ensure high resolution and rapid prototyping of printing, modifiable chemical structure to achieve printing of specific tissue structures, high biocompatibility to accommodate living cells and support cell attachment, proliferation and differentiation, and sufficient mechanical strength and stability to maintain structural morphology. (4) (10)

Bio-inks used in 3D bioprinting are biomaterial solutions in hydrogel form, often containing or encapsulating target cell types and growth factors, extruded for construct fabrication. It comprises cells with biomaterials like hydrogel, spheroids and cell aggregates. The 3D hydrophilic polymeric materials known as hydrogels are created via physical or chemical cross-links, reversible or irreversible hydrogels, respectively. They show a unique capacity to absorb a lot of water without dissolving. Ideal bio-inks are non-toxic, non-immunogenic, and offer mechanical stability and integrity. Demonstrating appropriate biodegradability rates and promoting cell adhesion may also be beneficial depending on the specific project needs. Other factors for consideration include cytological elements, gelatin properties and crosslinking ability, cost, print time, industry scalability, and permeability. Specifically, crosslinked hydrogels are highly porous, supporting tissue reconstruction and regeneration by allowing cell–cell adhesion, proliferation, differentiation, and migration to populate scaffolds and nutrient delivery for cells' metabolic needs. (5) (6) (12)

Hydrogels can be used to prepare bioinks from synthetic and natural sources

1. Natural Polymer-Based Bioinks
2. Synthetic Polymer – Based Bioinks

Natural Polymer – Based Bioinks

Natural polymers (collagen, agarose, gelatin, alginic acid, chitosan (CS), etc.) have claimed central roles as bioinks for 3D bioprinting of tissues and organs due to their ability to provide adapted scaffolding systems for the structural and functional organization of cells. All possessing unique properties such as nontoxicity, biocompatibility, and biodegradability, making them well adapted for several tissue engineering applications (8) (15)

Collagen

Collagen type I is a key component of the ECM and is widely used as a biocompatible hydrogel for bioprinting. Viscoll, a collagen type I–based bioink, has demonstrated improved mechanical properties, printability, and good cell viability without requiring chemical crosslinking. Other natural ECM components like tropoelastin and decellularized ECM (dECM) have also been explored for tissue-specific bioprinting due to their preserved biochemical cues, though dECM often needs reinforcement because of its softness. Collagen type I bioinks have been used successfully to print corneal stromal constructs that mimic native tissue. Using the FRESH technique, researchers have also bioprinted complex heart structures with microvascularization and accurate anatomical features. Additionally, studies show that incorporating cells alters the rheological behavior of collagen bioinks, and that bioprinting does not negatively affect long-term cell viability. (8) (10)

Gelatin

Gelatin, a biodegradable protein derived from denatured collagen, is widely used in medical, pharmaceutical, and tissue engineering applications due to its safety and biocompatibility. Methacrylated gelatin has been successfully applied in fabricating cartilage and liver constructs. Studies show that encapsulated cells can significantly alter the viscosity and printability of gelatin-based bioinks. Visible-light crosslinkable gelatin-furfural bioinks have enabled the printing of various cell types with high viability and evidence of heterocellular interactions. Alginate–gelatin (Alg–Gel) bioinks have also been used to support MSC migration, proliferation, and differentiation, with pore structures and mechanical properties mimicking native dermal tissue. Additionally, Alg–Gel hydrogels combined with PCL and bioactive glass in 3D-printed scaffolds have shown high initial cell viability (>80%), though viability decreases after prolonged culture. (10)

Fibrin

Fibrin, formed from fibrinogen during the coagulation cascade, is a biodegradable and biocompatible protein that supports cell attachment, infiltration, angiogenesis, and wound healing. Because of these properties, fibrin and fibrinogen are widely used in tissue engineering and have been applied as bioinks in 3D bioprinting. Studies have shown that fibrin can be printed alone or in combination with thrombin to create functional constructs. Fibrin-based bioinks have been used to bioprint osteon-like structures containing HUVECs and hMSCs to enhance neovascularization, with optimized fibrin concentrations improving print resolution and cell viability. Hybrid constructs printed with polypropiolactone improved mechanical strength and supported angiogenic marker expression and blood vessel formation in vivo. Fibrin–gelatin composite bioinks have also enabled the fabrication of stable, porous cardiac constructs with high cardiomyocyte viability, proliferation, and marker expression, supporting coculture with fibroblasts. Both extrusion- and inkjet-based methods have been used for printing fibrin-derived materials. (10)

Silk

Silk, produced by insects and arachnids, is a highly biocompatible and hypoallergenic natural protein fiber traditionally used in wound dressings and sutures. Its main component, silk fibroin (SF), has excellent mechanical strength, biodegradability, and biocompatibility, making it a valuable biomaterial for tissue engineering and bioink formulation. Studies have shown that SF-based bioinks can support fibroblast growth and construct formation. Incorporating bacterial cellulose nanofibers into SF/gelatin hydrogels significantly improves mechanical strength and structural resolution, enabling scaffolds with micro- and macropores suitable for nutrient diffusion and cell infiltration. Silk fibroin–gelatin inks have also been used to 3D-print meniscus scaffolds that support fibrochondrocyte proliferation, phenotype retention, and matrix production, demonstrating strong compatibility both in vitro and in vivo (10)

Alginate

Alginate, a natural polysaccharide derived from brown algae and certain bacteria, is widely used in tissue engineering and drug delivery due to its tunable swelling, mechanical properties, degradation behavior, and biocompatibility. Alginate has been used alone and in combination with other biomaterials as a versatile bioink in various bioprinting platforms, including coaxial extrusion, droplet-based, and laser-assisted techniques, enabling the fabrication of vascular and heterogeneous tissue constructs. Recent studies showed that alginate–nanocellulose composites support high cell viability, adipocyte maturation, and strong in vivo angiogenesis. Research on alginate methacrylate systems revealed that longer grafting reactions produce stiffer, more homogeneous hydrogels with controlled swelling and degradation. Additionally, alginate–carrageenan composite scaffolds demonstrated good rheological properties, printability, and biocompatibility, confirming their suitability for 3D bioprinting applications. (10)

Synthetic Polymer- Based Bioinks

Synthetic polymers are also widely used in 3D bioprinting, including polyethylene glycol (PEG), PCL, polyvinylpyrrolidone (PVP), poly(l-lactic) acid (PLA), and poly(lactic-*co*-glycolic) acid (PLGA). They can be tuned to comply with tissue-specific degradation and mechanical property requirement of the target tissues and organs. Still, they represent only ≈10% of the systems used in bioprinting due to several limitations that hinder their translational applications (use of toxic solvents,

melting points higher than body temperature, difficulty to encapsulate cells). Moreover, the synthetic polymers usually lack sites for cellular recognition and other biological cues found in natural ECM for promoting cellular proliferation and differentiation. Though functionalization of synthetic bioinks can improve their biological properties, presence of adaptable side groups becomes a prerequisite for proper customization of a construct's mechanical and biological properties. (5) (8)

Polyethylene Glycol

Polyethylene glycol (PEG) is a highly biocompatible, low-cost synthetic polymer widely used in wound dressings, drug delivery, and as a bioink component. Although inherently non-adhesive, PEG hydrogels can support cell attachment when modified with peptides such as RGD. New PEG microgels created via thiol–ene click chemistry enable easy extrusion, strong post-printing stability, and high cell viability due to their modular, flexible structure. PEG-crosslinked bioinks have been optimized to balance flow properties with cell survival, highlighting the relationship between mechanical properties and functional tissue outcomes. Multiarm PEG systems and PEG-based degradable polymers incorporating nanosilicates have further advanced printability, mechanical tunability, and controlled release of therapeutic proteins. These PEG-derived bioinks support long-term cell viability and enable sustained delivery of proangiogenic factors, promoting endothelial cell migration. (10)

Polycaprolactone

Polycaprolactone (PCL) is a biodegradable but slowly degrading semicrystalline polymer often used as a structural material in bioprinting due to its high mechanical strength and printability. Studies have integrated PCL with bioactive materials to enhance tissue regeneration. For osteochondral tissue engineering, PCL scaffolds combined with nanohydroxyapatite and growth factors improved mechanical properties and supported adhesion, proliferation, and chondrogenic differentiation of hMSCs. Low-temperature extrusion and groove-assisted printing methods also enabled the incorporation of low-viscosity GelMA bioinks and PLGA-encapsulated cells without compromising scaffold strength or porosity, maintaining good cell viability. Another approach used PCL as an external support with TCP/alginate as internal filler to print bone defect constructs. This supporter model significantly enhanced mechanical strength, and although increasing TCP reduced cell viability, an optimal TCP/alginate ratio (1:4) yielded >80% survival after 7 days (15)

Polyvinylpyrrolidone

Polyvinylpyrrolidone (PVP) is a nontoxic, water-soluble polymer widely used in biomedical applications, including 3D bioprinting. Studies have shown that combining PVP with PCL improves the biological and mechanical performance of 3D-printed constructs. Adding fillers such as chondroitin sulfate (CS), alginic acid, and hyaluronic acid (HA) enhanced melting temperature and compressive strength, with PCL/3% PVP/1% CS showing the highest strength and PCL/3% PVP/1% HA showing the best cell viability. Using PVP in bioinks (0–3% w/v) improved printability by reducing cell adhesion and sedimentation, with 2.5% PVP giving the most stable cell distribution. PCL/PVP composite scaffolds made using electrohydrodynamic jet printing supported high cell proliferation and good biocompatibility. (15)

Pluronic

Pluronic, which is the trade name of poloxamer, is a synthetic block polymer composed of a hydrophobic polypropylene oxide (PPO) block and two hydrophilic polyethylene oxide (PEO) blocks. The Pluronic gel is a temperature-sensitive polymer with reversible gel properties; the gelation temperature of it depends on its type and concentration. Unlike gelatin and SA hydrogel, Pluronic is liquid at low temperatures (usually 4°C), forms a physical gel at high temperature (37°C), and can be dissolved in deionized water. Therefore, after printing scaffolds, lowering the temperature can remove Pluronic smoothly. Pluronic materials show better results in cartilage tissue engineering. The high concentration of Pluronic can meet the rheological and gelling conditions required for extrusion printing (8)

Nanocomposite hydrogel bioink

Despite the continuous investigations on natural and synthetic hydrogels in recent decades, it is still challenging to prepare tissue engineering scaffolds using single or mixed hydrogel materials, and some of the problems include weak mechanical properties, low cell activity, and poor processability. These difficulties have prompted researchers to find some suitable nanomaterials combined with hydrogels to improve the properties of

hydrogels. Nanocomposite hydrogels have a wide range of applications in the fields of tissue engineering and regenerative medicine. Summarized the methods and applications of nanomaterials in compounding hydrogel biopolymers. They found that the main natural biopolymers are SA and collagen derivatives.

This part reviews the commonly used nanomaterial composite hydrogels, such as inorganic nanomaterials, carbon-based nanomaterials, and nanofiber-based materials. A few researchers also use gold nanomaterials mixed with hydrogels as printed bioinks. (8)

3D Bioprinting and Tissue Engineering

Bioprinting technology has gained significant attention for its potential to fabricate biomaterials for tissue and organ engineering. As one of the body's most complex multilayered organs, the skin has been a major focus of bioprinting research, particularly for the reconstruction or regeneration of burn injuries. In this context, Kim *et al.,* developed a novel 3D human skin model by integrating extrusion and inkjet bioprinting modules. This hybrid approach proved to be time-efficient by combining the strengths of two distinct bioprinting techniques. (1)

Despite advancements in engineered skin, Albanna *et al.,* introduced an innovative design and proof-of-concept for a mobile skin bioprinting system capable of rapid, on-site treatment of large wounds.

Their method used epidermal keratinocytes and dermal fibroblasts embedded in a collagen hydrogel to enable precise deposition and rapid cross-linking. When compared with clinically used cell-spraying methods, the results showed no significant difference in wound closure or re-epithelialization. (17)

Parallel to progress in skin bioprinting, bone bioprinting has emerged as a promising technique for repairing damaged bone tissue. Its workflow typically includes material and cell selection, scaffold fabrication, cell culture, viability assessment, and in vivo evaluation. Beyond the notable work of Lee *et al.,* on in vitro differentiation and in vivo bone regeneration, Byambaa *et al.,* employed an extrusion-based direct-write bioprinting strategy to fabricate microstructured bone-like constructs with perfusable vascular lumens using gelatin methacryloyl (GelMA) hydrogels. Their approach provides a valuable framework for producing cell-laden constructs aimed at treating large bone defects. (14)

Overall, bioprinting has been applied to a wide range of tissues, with numerous studies demonstrating successful fabrication of structures resembling native organs such as the pancreas, neural tissue, cartilage, cardiac tissue, lungs, and muscle. Most of these have been produced using advanced 3D bioprinting techniques, highlighting the technology's broad potential in tissue engineering and regenerative medicine. (18)

Application of bioprinting in tissue engineering and regeneration, there are several tissue constructions imitating native organs such as pancreas, neural, cartilage, cardiac, lung, or muscle.

Almost all of them have been progressively bioprinted using 3D bioprinting techniques. A summary of the most recent and applicable works relating to the tissue generation/replacement using bioprinting are: (19)

Applications of 3D Bioprinting

3D bioprinting has become a transformative technology because it enables the precise placement of cells, biomaterials, and growth factors to fabricate tissues that mimic natural human structures. Its applications span multiple fields: (7)

Tissue Engineering

Skin Tissue (Skin Grafts)

Used for burn patients, diabetic ulcers, and wound healing. Bioprinted skin layers can include epidermis and dermis, and even hair follicles in advanced models. Some companies have already tested in situ bioprinting on wounds. (6) (7)

Bone and Cartilage Tissue

Widely bioprinted for orthopedic repair. Uses materials like PCL, collagen, GelMA, hydroxyapatite. Cartilage constructs have been printed with natural shape and mechanical properties. (7)

Vascularized Tissues

Bioprinting can create micro-channels and blood vessel networks. Essential for thick, functional tissues (heart, liver, kidney). Techniques: coaxial printing, sacrificial inks (Pluronic F127), angiogenic factors. (7)

Figure.1 (The steps involved in bioprinting Process)

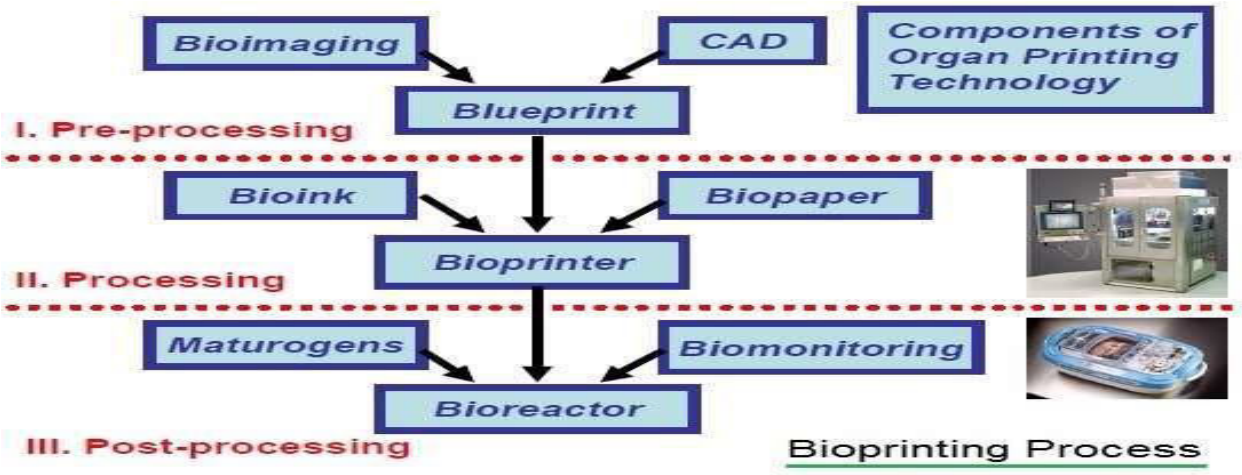

Fig.2 (Inkjet Bioprinting)

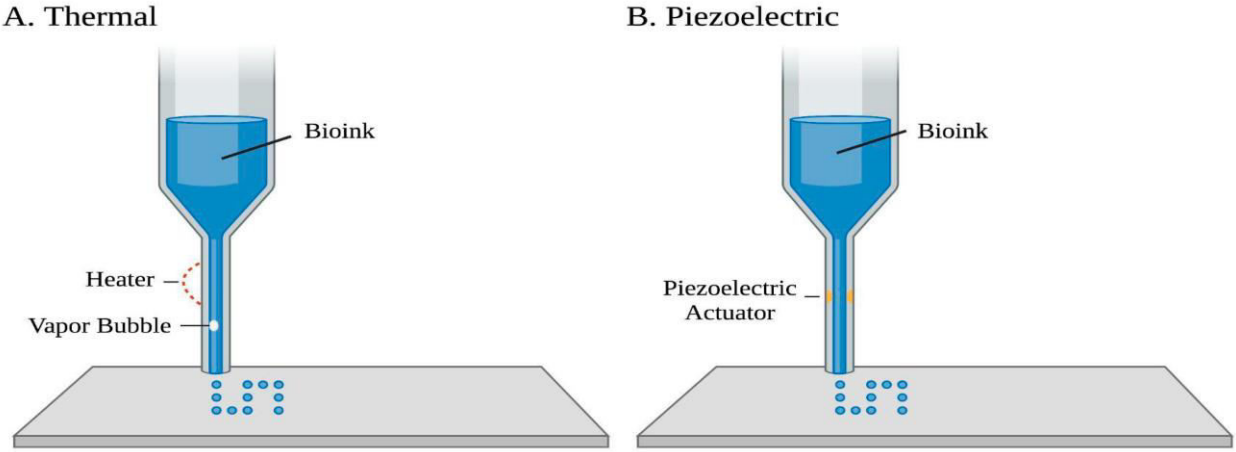

Fig.3 (Laser – Assisted Bioprinting)

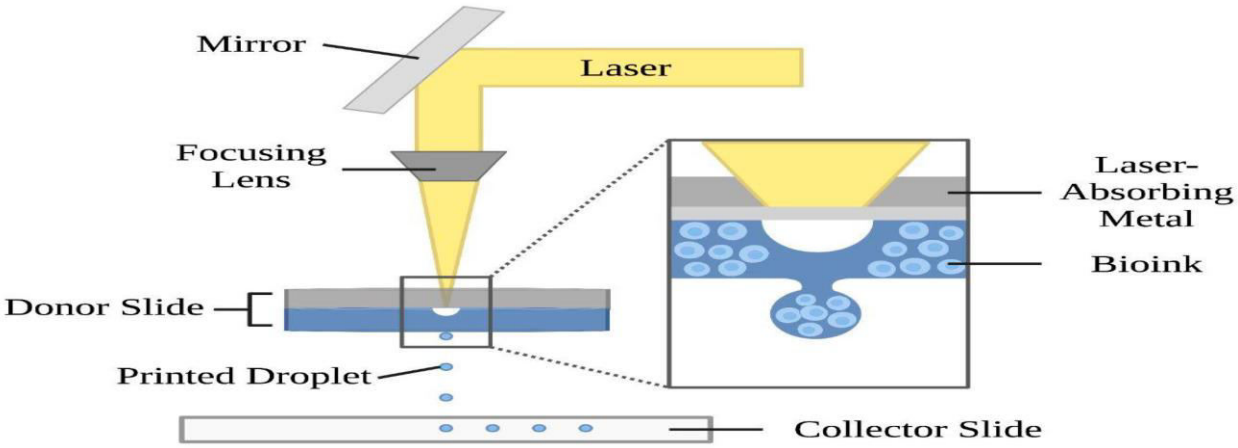

Fig.4 (Extrusion-based printing)

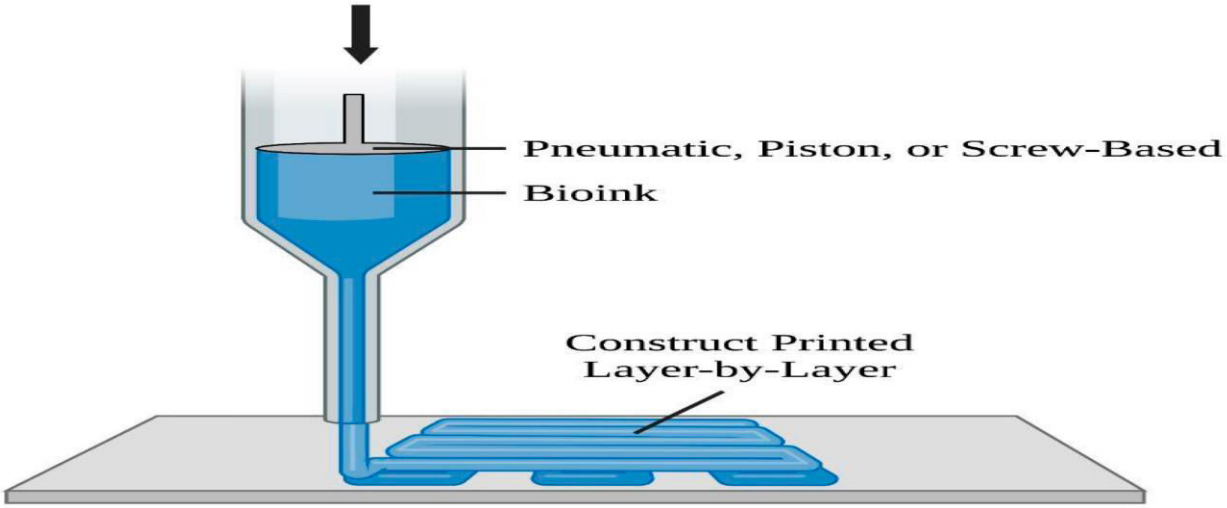

Fig.5 (Stereolithography)

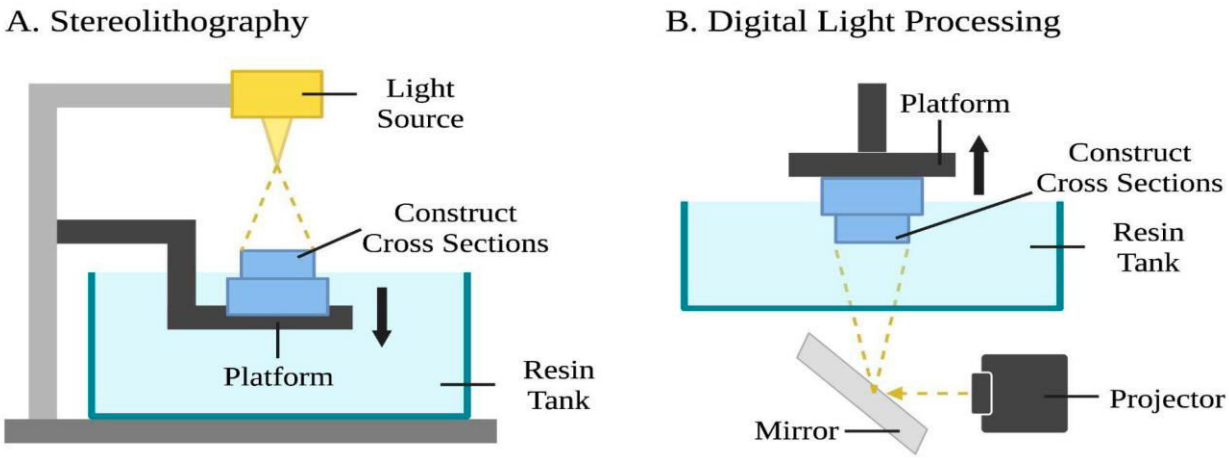

Table.1 The advantages and disadvantages for different 3D bioprinting technologies

Bioprinting technologies	Advantages	Disadvantages
Stereolithographic	High ink viscosity; high resolution; cost effective	Low cell density; average formation time
Laser-Assisted Bioprinting	High ink viscosity; high resolution	Average formation time; low printed speed; low cell viability
Extrusion Bioprinting	Cost effective; low cell viability	Slow speed; low formation time; low resolution
Inkjet Bioprinting	Cost effective; high printed speed	Low cell density; low resolution

Table: Summary of recent works in tissue generation/replacement.

Application	Research description	Results
Muscle tissue engineering	Prototyping PCL-based tissue constructs in organ printing	An alternative approach in polymers application in bioprinting Construction of muscle without disturbing the vascular network
	Development of musculotendon unit (MTU) using PU and PCL as structural units	Indicating acceptable elastic property and an acceptable candidate in muscle printing
Neural tissue engineering	Development of a neural mini-tissue construct by micro-extrusion bioprinting	Viable cell in construct and differentiate in situ to functional neurons Forming synaptic contacts and networks
	Development of a handheld reactive printing technique for 3D bioprinting of multi-layer brain-like structure	Fabrication of discrete cell-containing layers Developing 3D in vitro model to consider neural circuit formation
	Using inkjet bioprinting to show an artificial neural tissue 3D model by using multiple hydrogel types	Capable of evaluating of cellular behavior and application in neural tissue regeneration
Lung tissue engineering	In vitro human air-blood tissue barrier analog fabrication using valve-based inkjet bioprinting	The first step of bioprinted lung tissue
Cartilage tissue engineering	Preparation of pure-phase L2C4S4 scaffold using extrusion-based bioprinting	Display controlled biodegradability and good apatite-mineralization ability A feasible strategy for osteochondral reconstruction
	Modification of inkjet bioprinting to enhance the biocompatibility of polymer and decreasing the viscosity	Enhancement in ease of bioprinting the cartilage tissue
	Development of new device 'Biopen' that allow using 3D bioprinting and manual control during surgical with/without live cell	Capable of multi-ink bioprinting for in vivo application Repairing full-thickness chondral defects in a large animal Ovine model
	Development of hybrid system using electrospinning and inkjet printing to produce scaffolds for cartilage tissue regeneration	Capable of refining the fabrication of functional complex cartilage tissue using oriented fibers
	Designing a cartilage extracellular matrix (CECM)-functionalized alginate bioink for bioprinting using an extrusion-based bioprinter	Ability of supporting post-printing viability and robust chondrogenesis in vitro Proposition of a novel class of functionalized bioinks
Pancreas tissue engineering	Developing pancreatic tissue-derived bioink using decellularization process by micro-extrusion based printing	Enhancement in the viability of cells Increase in pancreatic functions
	Investigation a scale-up fabrication of scaffold-free tissue standards using extrusion-based bioprinting	Capable of pancreatic tissue regeneration after hybrid fabrication Rapid fusion capability and high viability
	Using extrusion-based printing for testing controlled release of anticancer drug against pancreatic cancer	Ability of applying 3D printing for local delivery of drugs

Cardiac Tissues

Used to create heart patches for repairing damage after heart attacks. Enables printing of anisotropic muscle fibers similar to real myocardium. (7)

Liver and Kidney Tissues

Used mainly for drug testing and disease models. Some groups have printed liver lobule–like structures with metabolic activity. (7) (10)

Regenerative Medicine

Organ-on-a-Chip Models

Micro-tissues printed on chips to simulate organ function. Used for testing drug absorption, metabolism, toxicity. (8)

Personalized Implants

Patient-specific ear, nose, airway, and bone structures.

Use patient MRI/CT scans → convert to 3D model → bioprint implant. (24)

In Situ Bioprinting (Printing Directly on the Body)

Bioprinters applied directly at wound/injury site. Examples: in-situ cartilage printing, skin printing over a burn. (25)

Cancer Research

Tumor Microenvironment Models

3D bioprinting recreates cancer–stromal interactions. Better than 2D cultures for understanding tumor growth and drug resistance. (24)

Personalized Cancer Treatment

Patient's tumor cells → bioprinted tumor → screen drugs for best response. (24) (25)

Pharmaceutical & Drug Testing Applications

Drug Screening

More accurate prediction of human responses than animal models. Bioprinted liver, kidney, or heart tissues used to test drug toxicity. (24)

High-Throughput Screening

Automated bioprinting allows rapid production of hundreds of tissue samples.

Cosmetic Testing (Animal-Free Testing)

Bioprinted human skin is now used by cosmetic companies as an alternative to animal testing. Regulatory agencies accept human-derived skin models for safety testing. (24)

Education & Research Models

Bioprinted ear, bone, heart, and liver models help medical students learn anatomy and surgical procedures. (24)

Future Application: Whole Organ Bioprinting

Still in early stages, but progress is ongoing toward: Bioprinted hearts, Kidneys, Pancreas, Lungs (24)

Challenges and Prospects

Modeling the lung presents unique challenges related to its structure, mechanical properties, dynamic environment, and other important physiological attributes. Many efforts have been dedicated to developing *in vitro* models that allow studying disease evolution and the biodistribution of drugs delivered through the pulmonary route, and significant progress has been made in the development of organ-on-chip models, microtissues, and organoids. 3D bioprinting offers potential advantages for the development of pulmonary models, but the field is still in the early stages of exploration and optimization to achieve the long-term goal of printing a functional lung. Current efforts in 3D bioprinting are limited because the technology does not yet provide the control or the resolution required to model lung tissue in detail. Nevertheless, the results produced so far show that this technology has an enormous potential that still needs to be unlocked. (22)

Direct bioprinting is a suitable option when the application does not require recreating the cellular microenvironment. In the case of implants, where the most important aspects are biocompatibility, biodegradability and the mechanical properties of the printed structure, along with how it behaves when introduced in the body, optimizing the bioink to me*et al.,*1 these requirements has proven to be a successful strategy. On the other hand, when trying to create models to study organ function or drug performance, it is ideal that cell behavior can be deliberately modulated to mimic the natural microenvironment by changing the properties of the printed constructs (like the mechanical

or biochemical characteristics. In these cases, the priority when designing the bioink should be aimed at recreating the natural cell microenvironment while still being able to print the target structure, and the optimization of the bioink to obtain the desired rheological properties should be treated as secondary aspect. To succeed in the printing process while satisfying these opposing requirements, applying more complex protocols than direct bioprinting can be the answer. (20) (22)

So far, the most elegant and advanced 3D bioprinted structures have been obtained by taking advantage of creative strategies while printing, like using sacrificial materials, printing more than one material at a time (coaxial nozzle and multi-bioink printing), or mixing strategies into one printing protocol. The last decade has shown us that trying to optimize an ink to create an environment suitable for cells and at the same time obtain appropriate rheological and mechanical properties is challenging and has usually fallen short in one of those aspects. The printing strategies described have been successful because they allow to optimize the bioink so the printed structure resembles the natural microenvironment of the cells, and the sacrificial material can be optimized to obtain the required properties that allow a good printing. There will always be room to improve equipment design and bioink properties, but it is important to also pay attention to the printing strategy used. (22)

In this review, several examples are presented where complex structures were successfully printed at high resolution by taking advantage of matrix support and the use of sacrificial inks. Exploring creative ways of combining current developed printing strategies can open a new set of possibilities and allow printing complex constructs that resemble anatomical structures. The use of sacrificial matrices has shown that it is possible to print bioinks with poor printability, and the use of sacrificial inks has made printing vasculatures feasible, one of the biggest challenges of direct bioprinting strategies. These strategies also make it possible to print ECM-based bioinks, which should be explored more in depth for the development of accurate models to study the pulmonary tissue and disease. An additional aspect that needs to be explored in more detail is how cells modify the mechanical properties of the printed structures. The metabolic activity of the cells that populate the construct has the potential to alter the mechanical properties of the material through degradation or the deposition of ECM components. These aspects can be leveraged when designing bioinks for model systems, but further studies are required to understand the interplay between cells and the 3D bioprinted matrices. Another important aspect to consider when designing a model, is the final purpose for which it is being created. Available technologies do not allow yet to print a fully functional lung organ, so deciding which aspects are more relevant to the application that is being developed will help to choose the right technology, printing materials and strategies suitable for the cells to be cultured. (22)

Future Prospect

The creation of complex human tissue arrays and organoids has not gone unnoticed by researchers around the world looking to better create 3D models of complex diseases such as cancer. The production of 3D vascularised tumor models “organ on a chip” has been created to better understand the complex interplay between cancer and multi-organ metastasis and paracrine signaling mechanisms in the regulation of breast cancer metastasis. This novel utilization of 3D printing has the potential to advance our understanding of complex disease and develop novel personalized treatments for diseases such as caner which currently account for one in seven deaths worldwide. The continued development and application of this base technology promises to 1 day make the creation of bespoke tissue engineered constructs and “made to order” solid complex organs a reality. The technological revolution in the last two decades has seen the development of intelligent bio-inks, refinement of printing techniques and production of novel biomaterials to facilitate the creation of custom scaffolds to support cellular growth. Since 2014 a number of 3D bioprinting companies, start-ups and R&D spinouts have entered the market contributing to the commercial development of this novel technology and creating a projected market value based on the early success and novel application of 3D bioprinted products. With a market value estimated at around $680 Million in 2016, industry reports project growth to reach $1.9 Billion by 2027. (26)

In conclusion, 3D printing and bioprinting has the potential to be the single biggest technological disruptor to the current model for design and delivery of healthcare and research in this century. The incorporation of human cells and biocompatible materials into 3D printing practice is set to deliver a paradigm shift in the application of 3D printing for

surgery, offering the potential to 3D print living tissue and organs. The promise to 3D print de novo body parts, obviate the need for organ transplantation and to replace the role of animals in the development and testing of novel drugs, means patients could potentially have access to a bespoke treatments at every point in their healthcare journey. (26)

The diverse applications of bioprinting technology have already been demonstrated on a global scale, leading to the production of novel constructs from vessels and composite tissue, to organoids and complex cellular and tissue models for drug, cosmetic and experimental testing. The 3D bioprinting market has seen off shoot companies set up to corner a specific sub-set of the production and manufacturing of complex 3D printed tissues; from desktop 3D bioprinters and bioinks, to scaffolds pre-loaded with and without growth factors generating a market value in the $US billions. The diversification of this technology and its associated components demonstrate the key issue with this extraordinary technology and potential difficulty in harnessing its true potential; the lack of "end to end" visibility by any one agency.

The translation of 3D printed constructs into clinical practice is challenging. The optimization of the translational pathway demands concerted efforts from scientists, engineers and clinicians, contextualized within an infrastructure in which an effective supply chain exists. It is no longer sufficient for scientists, clinicians and regulatory bodies to exist in operational silos: there is a need for a collaborative effort to translate this impactful technology into a real-world healthcare setting. In order to harness the true potential of 3D printing in surgery, surgeons will need to keep abreast of developments in the field, identify niches in which this technology can be applied and encourage its integration into mainstream surgical practice. With incremental advances in 3D printing and bioprinting expected over the next century, the impact on the future of surgery could be transformational. (26)

Author Contributions

S. Teresa: Investigation, formal analysis, writing—original draft. M. Flory Shobana: Validation, methodology, writing—reviewing. K. Akash:—Formal analysis, writing—review and editing. J. Julit Merlin: Investigation, writing—reviewing. S. Reshmi: Resources, investigation writing—reviewing. M. Yugesh: Validation, formal analysis, writing—reviewing.

Data Availability

The datasets generated during and/or analyzed during the current study are available from the corresponding author on reasonable request.

Declarations

Ethical Approval Not applicable.

Consent to Participate Not applicable.

Consent to Publish Not applicable.

Conflict of Interest The authors declare no competing interests.

References

1. Papaioannou, T. G., Manolesou, D., Dimakakos, E., Tsoucalas, G., Vavuranakis, M., & Tousoulis, D. (2019). *3D bioprinting methods and techniques: Applications on artificial blood vessel fabrication*. Acta Cardiologica Sinica, 35(3), 284–289. https://doi.org/10.6515/ACS.201905_35(3).20181115A
2. Rahman, M., Prodh an, S. A.-h., Islam, R., Mahmud, A., & Hossain, K. R. (2024). *Review of the 3D bioprinting methods and materials applicable in 4D bioprinting. Tribology and Materials, 3*(2), 81–95. https://doi.org/10.46793/tribomat.2024.009
3. Lam, E. H. Y., Yu, F., Zhu, S., & Wang, Z. (2023). 3D bioprinting for next-generation personalized medicine. *International Journal of Molecular Sciences, 24*(7), 6357. https://doi.org/10.3390/ijms24076357
4. Bramhe, P., Rarokar, N., Kumbhalkar, R., & Saoji, S. (2024). Natural and synthetic polymeric hydrogel: A bioink for 3D bioprinting of tissue models. *Journal of Drug Delivery Science and Technology, 101*, 106204. https://doi.org/10.1016/j.jddst.2024.106204
5. Groll, J., Burdick, J. A., Cho, D. W., Derby, B., Gelinsky, M., Heilshorn, S. C., … Yoo, J. J. (2018). Biofabrication: Reappraising the definition of an evolving field. *Biomaterials Science, 6*(5), 1154–1159. https://doi.org/10.1039/c7bm00765e
6. Laakso, T. (2021). *Different types of 3D bioprinting techniques: Bioprinting skin* (Bachelor's thesis, Tampere University). Trepo — Tampere University Repository. https://trepo.tuni.fi/bitstream/handle/10024/132732/LaaksoTuulia.pdf?sequence=2

7. Abu Owida, H. (2022). Developments and clinical applications of biomimetic tissue regeneration using 3D bioprinting technique. *Applied Bionics and Biomechanics, 2022*, Article 2260216. https://doi.org/10.1155/2022/2260216
8. Fang, W., Yang, M., Wang, L., Li, W., Liu, M., Jin, Y., Wang, Y., Zhang, K., & Fu, Q. (2023). *Hydrogels for 3D bioprinting in tissue engineering and regenerative medicine: Current progress and challenges. International Journal of Bioprinting, 9*(5), 759. https://doi.org/10.18063/ijb.759
9. Saini, G., Segaran, N., Mayer, J. L., Saini, A., Albadawi, H., & Oklu, R. (2021). *Applications of 3D bioprinting in tissue engineering and regenerative medicine. Journal of Clinical Medicine, 10*(21), 4966. https://doi.org/10.3390/jcm10214966
10. Jin, X., Li, Y., Tang, X., Tong, R., & Sun, W. (2019). *Current advances in 3D bioprinting technology and its applications for tissue engineering. Polymers, 12*(12), 2958. https://doi.org/10.3390/polym12122958
11. Gungor-Ozgüven, M., Dursun, T., & Ozturk, S. (2020). *An overview on materials and techniques in 3D bioprinting toward biomedical application. Current Research in Biotechnology, 2*, 68–76. https://doi.org/10.1016/j.crbiot.2020.05.001
12. Zhao, L., Zhang, Y., Zhao, X., Chao, Y., Huang, Y., & Zhang, Z. (2021). Recent advances in 3D bioprinting of vascularized tissue constructs. *International Journal of Bioprinting, 7*(3), 259. https://doi.org/10.1016/j.ijbiopr.2020.03.170
13. Li, J., Chen, M., Fan, X., & Zhou, H. (2024). 3D bioprinting of functional tissues and organs: Technological advances and translational challenges. *Bioengineering, 8*(1), 78. https://doi.org/10.3390/bioengineering8010078
14. Li, X., Liu, J., Gong, H., & Xu, Y. (2021). Direct-writing 3D bioprinting of enhanced tissue constructs with printability optimization. *Biotechnology and Bioengineering, 118*(12), 4899–4909. https://doi.org/10.1002/bit.25493
15. Gao, Q., Jin, Y., & Wang, Z. (2020). Recent developments in 3D bioprinting of functional tissue models. *Advanced Nanobiomed Research, 2*(3), 2000097. https://doi.org/10.1002/anbr.202000097
16. Xu, K., Yang, Y., & Wang, Q. (2018). A review on 3D printing of polymer biomaterials. *Materials, 11*(11), 2199. https://doi.org/10.3390/ma11112199
17. Liu, X., Zhang, Z., & Wang, P. (2024). Bioprinting strategies for tissue regeneration: Recent progress and future trends. *Bioengineering, 10*(7), 842. https://doi.org/10.3390/bioengineering10070842
18. Murphy, S. V., & Atala, A. (2017). 3D bioprinting of tissues and organs. *Biomaterials, 134*, 107–123. https://doi.org/10.1016/j.biomaterials.2017.03.057
19. Zhang, Y. S., Yue, K., Aleman, J., Moghaddam, K. M., Bakht, S. M., Yang, J., & Khademhosseini, A. (2020). A comparison of stem cell performance in fabricating scaffold-based and scaffold-free 3D tissue models using bioprinting. *Frontiers in Surgery, 7*, 609836. https://doi.org/10.3389/fsurg.2020.609836
20. Khan, I., Saeed, K., & Khan, I. (2018). Nanostructured materials and their applications in drug delivery. *Journal of Nanomaterials, 2018*, 6497242. https://doi.org/10.1155/2018/6497242
21. Mironov, V., *Trends in Biotechnology Editorial Board* (2022). 3D bioprinting goes mainstream. *Trends in Biotechnology, 40*(9), 897–899. https://doi.org/10.1016/j.tibtech.2022.02.008
22. Alvarez, M. M., & Khademhosseini, A. (2021). Bioprinting strategies for engineered tissues: Advancing application-specific design. *Frontiers in Bioengineering and Biotechnology, 9*, 773511. https://doi.org/10.3389/fbioe.2021.773511
23. Kidambi, S. P. (2015). *3D bioprinting*. In S. P. Kidambi (Ed.), Biofabrication: Micro- and Nano-fabrication, Printing, Patterning and Assemblies (pp. xx–xx). Springer. https://books.google.co.in/books?id=vcEOCAAAQBAJ
24. He, Y., & Gu, W. (2021). Bioprinting materials and strategies for tissue engineering. *Journal of Biomedical Materials Research Part B: Applied Biomaterials, 109*(8), 909–919. https://doi.org/10.1002/jbm.b.33826
25. Li, J., Chen, M., Fan, X., & Zhou, H. (2021). 3D bioprinting techniques and applications in regenerative medicine. *Signal Transduction and Targeted Therapy, 6*(1), 101. https://doi.org/10.1038/s41392-021-00566-8
26. Anjum, S., Tariq, M., & Qureshi, W. (2020). Review on 3D bioprinting – Principles, applications and recent advances. *Frontiers in Medical Technology, 2*, 607648. https://doi.org/10.3389/fmedt.2020.607648

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