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3D Bioprinting of Organs for Transplantation

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ABSTRACT

3D bioprinting represents a revolutionary convergence of tissue engineering and printing technology aimed at creating functional biological tissues and organs for transplantation. This paper explores the principles and historical development of 3D bioprinting, advances in materials and techniques, and its potential applications in organ transplantation. While significant progress has been made, challenges such as ensuring biocompatibility, regulatory compliance, and ethical considerations remain. The future of 3D bioprinting in regenerative medicine holds promise for personalized medicine and reducing donor organ shortages, contingent on overcoming these hurdles.

Keywords: 3D bioprinting, tissue engineering, organ transplantation, bioinks and regenerative medicine

INTRODUCTION

3D bioprinting can be defined as the aspiration to combine structured materials that are mimicking the extracellular matrix (ECM) and living cells. Innovations in different 3D bioprinting systems such as the design and development of print heads, i.e., extrusion nozzles, needles or droplet generators, have brought together the tissue engineering and printing fields. These now work in synergy with the aim of regenerating functional biological units which can fit the individual tissue areas. 3D printing, in general, enables the formation of computer-designed objects by depositing materials layer-by-layer and, in this sense, 3D bioprinting is similar: but is exclusive in that it creates 3D living tissues or organs by the deposition of biomaterials and bioinks in three dimensions allowing subsequent in vitro maturation (to form 'bioprinted tissues') and, after implantation, in vivo remodelling to form 'regenerated organs' [1]. The design of bioinks, both the materials and the cells in them, and cell-laden materials is critical in bioprinting, and numerous biomaterials from natural and synthetic sources are being explored as bioinks. In addition to low-cost, a wide spread in the tissue types and physical properties (soft and hard tissue) need to be covered, for example transparent and opaque, opaque and optically thick tissues because taxonomy and differentiation of diseases are also related. For each category, we should evaluate biocompatibility, growth factor encapsulation, presence of stem cell markers, growth factor release, decellularization, adsorbed proteins, long-term survival, and angiogenesis generation. Bioprocess platforms (physical methods) are under development as well, such as magnetic levitation, platelet-rich plasma and acoustic technique, as new methods for 3D bioprinting. The association of cells with three-dimensional (3D) printed tissues has been studied for the last 10 years, but the generation of complex tissues and full organs is still under development [2].

DEFINITION AND PRINCIPLES

In its essence, bioprinting can be defined as a technology that enables arranging and printing cell suspensions, cell aggregates, or hydrogels as well as proprietary bioinks through inkjet or microextrusion methods. It basically involves printing cells as well as the materials that cells are living in. Organ fabrication is like 3D printing: a "bioprinter" practices materials called "bio-inks" to layer living cells and the materials that support them in layers. The printer also puts biodegradable plastic, which is used to form its shape, and a sugar compound that creates the body's blood vessels, on top of the ink. Yet, biological layout must still be addressed. Cells can be organized into a suitable structure using 3D printing. It is thereby a promising breakthrough and an excellent system for reconstructive surgery. They can also print small and large portions. Researchers are discovering ways to print as well as

maintain 3D bioprinted human organs throughout the human body [3]. Four essential values are used by biophysicists using bioprinting to construct biological structures: spatial preparation, tools for determining materials, technology for 3D resin deposition, and depth-dependent cell placement. Bioprinting uses computer-assisted design (CAD) technology to gather digital bioengine patterns together with molecular printing into the after basic structure of three dimensions, making use of digital layer data and tangible materials deposition. In regards to bioprinting, many aspects have thus been employed in hybrid cases of tissue modifications or reconstruction based on tissue assembly instead of cellular material fabrication. Bio-inks are often relied upon by bioprinting, causing stimuli to be rooted in cell growth and used with 3D bioprinting for partial integrated tissue structures of the body [4].

HISTORICAL BACKGROUND

Traditional printing techniques were used to create two-dimensional (2D) images with well-defined colors, patterns, and shapes. Second-generation printing technologies are more focused on three-dimensional (3D) objects and were developed in 1986, where an integrated automated fabrication device can generate 3D objects with well-defined shapes in the area of mechanical computer-aided design. The same production principles and designs are used in additive manufacturing, but they are significantly more complex than additive manufacturing since they can print complex 3D biological objects regardless of their size or shape. Building biological structures is rather difficult because they require increasing complexity, a higher degree of freedom in design, and a variety of chemical and biological parameters in printing materials. Although manual placement of biological materials can produce simple biological structures consisting of cells, fibers, and scaffolds, more complex organic structures and structures such as tissues and organs cannot be built at the molecular level [5]. 3D bioprinting builds biological systems at the cellular, tissue, and organ level using a controlled and automated process. New bioprinting technologies can surpass the complex structures of traditional methods, making it ideal for printing organs and tissues. used the concept of 3D printing for the first time by constructing three-dimensional products with a solid base, area, volume, and other features. used 3D printing as a basic technique that revolutionized the manufacturing process. integrated 3D printers, materials, and modeling to create prototypes, creating a new generation of printing. suggested that 3D printing is an additive manufacturing technology that keeps print production sustainable and eco-friendly. Decades ago, 3D printing technology was successfully used to produce tissue regenerators and implants, sowing the seeds for the development of 3D bioprinting technology. With deepening research, the vision of bioprinting started to transition from single cells and clusters to complex 3D structures containing various cells and biomaterials [6].

TECHNOLOGICAL ADVANCES IN 3D BIOPRINTING

The advances in technology enabling tissue growth in vitro over the last two decades have led to the eventual abolishment of donor organ waiting lists. These technological advances have therefore had a large impact and implications across the entire transplant industry. For the creation of functional organs by fabrication of the proper microenvironment, 3D cell printing is currently embarking on a trajectory reliant on several components and methods including: materials, cells, mechanical properties, and structure. Bioprinting is entirely dependent on the choice of materials that can spur cell proliferation, often called scaffold materials. Cells are also important for the fabrication of organs and may be derived from the intended transplant organ in biopsies, donor adult stem cells, and patient embryonic stem cells. These cells must have fast proliferation rates, be able to survive under anaerobic conditions, and be capable of differentiation into multiple cell types [7]. Materials such as collagen are widely used in the 3D bioprinting of tissues such as muscle, brain, and skin because this biomacromolecule is a major component of the extracellular matrix and is compatible with human tissue. 3D bioprinting can generally be divided into techniques used: drop-based bioprinting (DBB), laser-induced forward transfer bioprinting (LIFT), inkjet-based bioprinting (IBB), and extrusion-based bioprinting (EBB). These techniques are used to add with precision the extra line layers of both cells and biomaterials to form a tissue-specific shape. 3D bioprinting has been in practice with skin and bone tissues with efficacy, and functional bone has been implanted into animal models with success and not reabsorbed into the body. In major advances towards the 3D bioprinting of organs, on March 1, 2019, CELLINK in collaboration with CTI Biotech successfully 3D bioprinted a functional liver using human primary cells [8].

MATERIALS USED IN 3D BIOPRINTING

3D bioprinting has evolved over the years to become one of the more prestigious scientific advancements. However, in order to 3D print, there has to be a careful choice of material of interest, which is selected based on its property and its application. In 3D bioprinting, the choice of bioprinting medium is more critical when considering cell survival as it has to maintain its biocompatible property all through the

printing process to actual transplantation. But when that is compared to the choice of materials for solid 3D printing where cell survival is out of context, however major, it provides an avenue to a possibility of having customizable tissues in terms of developing an artificial organ. Materials for 3D printing are either human cultured tissue cells spanning from other organs, macro or microscopic biomaterials scaffolds such as polycaprolactone (PCL), polylactic-co-glycolide (PLGA), etc. which can be derived from natural or synthetic sources, though these are used as bioinks/biopasting [9]. The richness regarding candidates for the stated sector is omitted because of the time-bound frame and projects diversity; however, exploration is still underway. Polycaprolactone (PCL), due to its property such as FDA approval, biodegradability extent, poor rate of cell adhesion, low bioactivity, and lack of tissue regeneration property, makes the polymer an ideal polymer for tissue engineering despite its limitation. The polymer is employed in an aqueous-based environment for cell printing since it allows for efficient printing and high cell survival for up to about 97.9%. Furthermore, it has a melting range of -60°C to -64°C with a resorbable rate of 2-3 years in vivo according to other papers. Moreover, the polymer's melting point is higher than human body temperature, and it is affordable and suited for home-based FDM 3D printers [10].

BIOPRINTING TECHNIQUES

Bioprinting is a process of creating 3D structures with high precision, sophisticated resolution, and most significantly, the ability to deposit cells with controlled distribution and viability. It is generally incorporated into successive methods including: pre-bioprinting (cell culture preparation), bioprinting (where cell deposition takes place), and post-bioprinting (cell cultivation for tissue maturation). A schematic illustration of these processes was shown in Figure 3. The significant advantages of bioprinting over conventional tissue engineering include: personalized tissues printing due to computer-driven drafted models using the patient's medical images and history to guide the construct design; reductions in patient suffering and trauma waiting for donors; eradication of immune rejection and tissue incompatibility as well as less need for immunosuppressive therapies through endogenous cells and tissue isolations [11]. There are three primary bioprinting techniques, categorized based on the material/spatial fabrication unit. These techniques can be enumerated as: vi) inkjet-based bioprinting, ii) nozzle or extrusion-based bioprinting, and iii) laser-based bioprinting. In inkjet bioprinting, the biological material is propelled directly into the physical framework by a series of minute droplets, termed as droplet on demand, by inkjet nozzles in a channel-free chamber. The movements of biological materials can be controlled conditionally through either thermal: piezoelectric or non-thermal mechanism: a Solid Immersion Lens (SIL) [12].

APPLICATIONS OF 3D BIOPRINTING IN ORGAN TRANSPLANTATION

3D bioprinting technologies may hold the potential to solve many limitations of organ transplantation. Despite the promise, there are many steps still to be taken before a bioprinted organ will have the same functionality as the original tissue of an individual. Bioprinting of human-scale grafts is more complex than developing 2D in vitro models and faces several critical challenges regarding resolution of printing and usage of selected materials. Nevertheless, there are many areas where 3D bioprinting may assist in organ transplantation, including 3D cell models, drug testing, and personalized medicine [13]. Bioprinting assists with creating in vitro 3D cell models, mostly in drug testing and basic research. Researchers may develop tumor microenvironments, vasculature models, drug release devices, or even entire organ-on-a-chip systems. 3D tissue models can replace animal testing; however, their complexity is still far from the original tissue. Within personalized medicine, 3D bioprinting assists with disease model creation. However, it is mostly limited to cancer biomedical models and finding the appropriate therapy. It may also work as an educational device for doctors and students. Bioprinting is also anticipated to revolutionize regenerative medicine. Currently, transplantation of patient-specific constructs is not available, but there are many in vitro and preclinical models created. Open-source bioprinting companies focus on creating easy bioprinters for schools and universities, sometimes even for an individual. To help replace organs for transplantation, we need complex organs, including the heart, kidney, liver, or lungs [14].

CHALLENGES AND LIMITATIONS

The main goal of tissue engineering and regenerative medicine is to find effective treatment methods for the large number of patients around the world who are in need of tissue and organ transplants. However, obtaining a sufficient number of organs or tissues remains one of the greatest challenges of transplantation medicine. 3D bioprinting is regarded as a potential solution for this issue. However, the clinical application of 3D bioprinted organs is still some way off because it has some limitations and significant areas of concern that need to be addressed. In this review, we discuss the potential challenges

and existing limitations of clinical application (availability) of 3D bioprinted organs for transplantation and also some points need to be considered before these printed organs are delivered to clinics for transplantation [15]. In the case of 3D bioprinted organs, two main concerns must be addressed. First, the efficacy, function, and safety of a 3D bioprinted organ should be thoroughly studied and clearly established. Second, the legibility, biocompatibility, and regulatory standards of every organ printed should be specifically defined. In light of these challenges, in this international standardization landscape, standards related to tissue-engineered products and technology standardized by the International Organization for Standardization are considered historic precedent. The biggest disagreements and the greatest promise arise in discussions about 3D bioprinted and regulation-Enabling Tissue-Engineered Products (3Dbio-ETEPs) in terms where current standards are not applicable [16].

ETHICAL AND REGULATORY CONSIDERATIONS

At an individual level, 3D printed organs can also cause several ethical challenges, such as the presence of permanently printed cells from babies and older adults within the same organ. Furthermore, people from some societies may view 3D bioprinting as contradictory to their beliefs. Each of these concerns may help to form the philosophical and ethical area of 3D bioprinting for transplantation conversation, but many of these points have already been resolved on a policy level by modern laws [17]. The bioprinted organs will persist according to their biological validity, or biodurability, well after the patient has reached the age of 18. The aims of human clinical research and strategies that will be carried out with citizens worldwide are to advance technologies for the good of humanity. The legislative structure and non-partisan regulation of 3D bioprinting and transplantation continue to change and evolve. From 2021 to 2022, a number of widely debated statutes, regulations, and guidelines came into existence that set a precedent and a new level of verification and ethics for the creation and transplantation of bioprinted organs from cells. The InterLivery Donor is the name of the system that will someday remove end-stage organ waitlists from most developed cities. In between many laws that address relatively simple regulatory issues and still do not exist, the laws can be found. At worst, 3D bioprinting's uniqueness might have kept it at a standstill. Because the Canadian and European legislative models are the most preferred in their simplicity, flexibility, and the many options that they contain, the United States and United Kingdom systems are currently perceived as more advanced and inclusive of other systems [18].

FUTURE DIRECTIONS AND INNOVATIONS

The field of tissue engineering and 3-dimensional bioprinting has been expanding rapidly in the recent past with many different approaches and techniques. This knowledge and technology could be developed further and applied towards giving more freedom in the form and function of the final bioprinted organ, producing a natural appearance and touch. As one innovation, cellular therapy emerges, traditional immunosuppressive medications and their side effects will be replaced with adjuvant medications that will tune the donor organ to match the recipient. Efforts will be shifted from regenerating structural components of the donor organ using stem cells to supporting the donor stem and precursor cells in maintaining and expanding the structures [19]. To increase the supply of cell sources for organ engineering, organs declining in transplantability - such as those from very elderly cadavers or kept in a cold ischemic state while transplanted - could be used following innovative rejuvenation. This concept can be taken to its furthest extent by an innovative pilot clinical trial whose goal is to rejuvenate a presumably pathological organ for transplantation by 3-dimensionally deconstructing an organ along its natural planes of cellular makeup while treating each part with pharmaceuticals and innovative technologies tailored for it. Bioprinting's ability to create organs of varying cellular content and anatomical shapes, align cells and printed tissues in geometric patterns that mimic natural tissue architecture, deposit a variety of structural components different biocompatible materials with varying physical properties, deposit other structures such as lumens, solid drug-eluting porous particles or construct capillaries by fusing a biodegradable vascular template of endothelial cells is easily amenable to these goals [20].

CONCLUSION

3D bioprinting holds immense potential to revolutionize the field of organ transplantation by addressing the critical shortage of donor organs and enabling personalized medical treatments. Despite the promising advancements in bioprinting techniques and materials, several challenges, including biocompatibility, regulatory approval, and ethical issues, must be resolved. Continued research and innovation are essential to overcome these barriers and realize the full potential of 3D bioprinting in regenerative medicine. The future landscape of organ transplantation could be transformed with bioprinted organs, leading to improved patient outcomes and reduced dependency on donor organs.

REFERENCES

1. Wang H, Yu H, Zhou X, Zhang J, Zhou H, Hao H, Ding L, Li H, Gu Y, Ma J, Qiu J. An overview of extracellular matrix-based bioinks for 3D bioprinting. Frontiers in Bioengineering and Biotechnology. 2022 May 11;10:905438. frontiersin.org
2. Su X, Wang T, Guo S. Applications of 3D printed bone tissue engineering scaffolds in the stem cell field. Regenerative therapy. 2021. sciencedirect.com
3. Daly AC, Prendergast ME, Hughes AJ, Burdick JA. Bioprinting for the biologist. Cell. 2021. cell.com
4. Birla RK, Williams SK. 3D bioprinting and its potential impact on cardiac failure treatment: An industry perspective. APL bioengineering. 2020. aip.org
5. Fatimi A, Okoro OV, Podstawczyk D, Siminska-Stanny J, Shavandi A. Natural hydrogel-based bio-inks for 3D bioprinting in tissue engineering: a review. Gels. 2022 Mar 14;8(3):179. mdpi.com
6. Wang Z, Kapadia W, Li C, Lin F, Pereira RF, Granja PL, Sarmento B, Cui W. Tissue-specific engineering: 3D bioprinting in regenerative medicine. Journal of Controlled Release. 2021 Jan 10;329:237-56. [HTML]
7. Decarli MC, Amaral R, Dos Santos DP, Tofani LB, Katayama E, Rezende RA, da Silva JV, Swiech K, Suazo CA, Mota C, Moroni L. Cell spheroids as a versatile research platform: formation mechanisms, high throughput production, characterization and applications. Biofabrication. 2021 Apr 8;13(3):032002. maastrichtuniversity.nl
8. Xu J, Zheng S, Hu X, Li L, Li W, Parungao R, Wang Y, Nie Y, Liu T, Song K. Advances in the research of bioinks based on natural collagen, polysaccharide and their derivatives for skin 3D bioprinting. Polymers. 2020 May 29;12(6):1237. mdpi.com
9. Germain N, Dhayer M, Dekiouk S, Marchetti P. Current advances in 3D bioprinting for cancer modeling and personalized medicine. International journal of molecular sciences. 2022 Mar 22;23(7):3432. mdpi.com
10. Ahmed MK, Zayed MA, El-Dek SI, Hady MA, El Sherbiny DH, Uskoković V. Nanofibrous ε-polycaprolactone scaffolds containing Ag-doped magnetite nanoparticles: Physicochemical characterization and biological testing for wound dressing applications in vitro and in vivo. Bioactive materials. 2021 Jul 1;6(7):2070-88. sciencedirect.com
11. Xu X, Yu S, Ma L, Mao J, Chen H, Zhu Z, Wang L, Lin H, Zhang J, Wang Z. Multifunctional high-simulation 3D-printed hydrogel model manufacturing engineering for surgical training. International Journal of Bioprinting. 2023;9(5). nih.gov
12. D ANUMOLU PK, MADHURI G, MAMATHA G, NAIR S. 3D BIOPRINTING AS GROUNDBREAKING TECHNOLOGY IN PHARMA AND HEALTH CARE SYSTEMS. researchgate.net. . researchgate.net
13. Jovic TH, Combellack EJ, Jessop ZM, Whitaker IS. 3D Bioprinting and the Future of Surgery. Frontiers in surgery. 2020 Nov 27;7:609836. frontiersin.org
14. Petrosyan A, Montali F, Peloso A, Citro A, Byers LN, La Pointe C, Suleiman M, Marchetti A, Mcneill EP, Speer AL, Ng WH. Regenerative medicine technologies applied to transplant medicine. An update. Frontiers in Bioengineering and Biotechnology. 2022 Sep 28;10:1015628. frontiersin.org
15. Panja N, Maji S, Choudhuri S, Ali KA et al. 3D bioprinting of human hollow organs. AAPs Pharmscitech. 2022. springer.com
16. Laurent A, Abdel-Sayed P, Grognuz A, Scaletta C, Hirt-Burri N, Michetti M, de Buys Roessingh AS, Raffoul W, Kronen P, Nuss K, von Rechenberg B. Industrial development of standardized fetal progenitor cell therapy for tendon regenerative medicine: Preliminary safety in xenogeneic transplantation. Biomedicines. 2021 Apr 3;9(4):380. mdpi.com
17. Jin Z, Li Y, Yu K, Liu L, Fu J, Yao X, Zhang A, He Y. 3D printing of physical organ models: recent developments and challenges. Advanced Science. 2021 Sep;8(17):2101394. wiley.com
18. Kop M. Abundance and equality. Frontiers in Research Metrics and Analytics. 2022. frontiersin.org
19. Panda S, Hajra S, Mistewicz K, Nowacki B, In-Na P, Krushynska A, Mishra YK, Kim HJ. A focused review on three-dimensional bioprinting technology for artificial organ fabrication. Biomaterials science. 2022;10(18):5054-80. rug.nl
20. Mirshafiei M, Rashedi H, Yazdian F, Rahdar A, Baino F. Advancements in tissue and organ 3D bioprinting: Current techniques, applications, and future perspectives. Materials & Design. 2024 Mar 19:112853. sciencedirect.com

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