Proceedings of ICMMGH 2026 Symposium: Biomedical Imaging and AI Applications in Neurorehabilitation
DOI: 10.54254/2753-8818/2026.AU28992

From Cells to Tissues: A Review of the Bioprinting Techniques for Organ Regeneration

Jiarui Hu

The Affiliated International School of Shenzhen, Shenzhen, China
hjr_07@qq.com

Abstract. Currently, the field of organ transplantation faces serious challenges such as organ supply shortages and immune rejection. As an emerging 3D printing technology, bioprinting holds promise as a potential solution to these issues. This paper aims to comprehensively analyze the core foundational elements, classification of key technologies, and application progress of bioprinting in organ regeneration. Through literature review and case studies, it explores the current status of bioprinting applications in constructing complex tissue and organ structures, identifying challenges such as bioink performance optimization, seed cell selection, and bioprinting precision. Empirical evidence demonstrates bioprinting's transformative potential for organ regeneration, but critical challenges persist—particularly in bioink biocompatibility, cell viability preservation, and structural durability of printed constructs—all requiring targeted research interventions. Future research should focus on developing novel bioinks, optimizing seed cell sources, and enhancing the precision and efficiency of bioprinting to advance organ regeneration technology.

Keywords: Bioprinting, Organ Regeneration, Bioink, Seed Cells, 3D Printing

1. Introduction

Organ transplantation is an effective treatment for end-stage organ failure, but the field currently faces numerous challenges. First, there is a severe shortage of organ supply. Globally, hundreds of thousands of patients await organ transplants each year, yet the number of donor organs falls far short of meeting demand. Second, post-transplant immune rejection is a major factor affecting success rates. Even when patients receive donor organs, rejection can lead to transplant failure, requiring lifelong immunosuppressant medications. As an emerging 3D printing technology, bioprinting has made remarkable progress in tissue engineering and regenerative medicine in recent years. By precisely depositing cells and biomaterials, bioprinting constructs complex tissue and organ structures, offering new hope for organ regeneration medicine. The core of bioprinting lies in bio-ink and seed cells. Bio-ink serves as the critical material, with its properties directly influencing the stability, biocompatibility, and functional realization of printed structures. Based on existing literature reviews and case analyses, this paper comprehensively summarizes the core foundational elements of bioprinting technology, its core technical classifications, and its application progress in organ regeneration. Through this literature review, the paper analyzes the classification and applications of bio-inks, the types and roles of seed cells, as well as the principles and applications

DOI: 10.54254/2753-8818/2026.AU28992

of major bioprinting techniques (such as inkjet bioprinting and laser bioprinting). This paper aims to explore the current application status of bioprinting technology in organ regeneration, identify technical challenges, and propose future research directions. Through these investigations, it seeks to provide researchers and practitioners with a comprehensive reference to enhance their understanding and application of bioprinting technology, thereby advancing the development of organ regeneration medicine.

2. The core fundamental elements of bioprinting technology

2.1. Bio-ink

Bio-ink is essential for tissue engineering and regenerative medicine, directly influencing the stability, biocompatibility, and functionality of printed structures. Bio-inks can be classified by application, composition, gelation mechanism, or the presence of scaffolds.

Natural bio-ink: Depending on the source of the materials, they are divided into synthetic biological ink and natural biological ink. Natural bio-inks have excellent biocompatibility and are conducive to the adhesion of cells for growth. For example, Type I collagen can be applied in various bioprinting technologies [1]. Type I collagen possesses two core advantages: high porosity and excellent biocompatibility. Its high porosity facilitates cell adhesion and proliferation—it can be electrospun into micro/nano-scale three-layer fibrous scaffolds for bionic vascular tissue engineering, and form 3D scaffolds composed of vertical highly porous collagen chains to support cell migration and infiltration. Biocompatibility stems from its ECM-mimicking composition, which replicates the native cellular microenvironment—thereby enhancing cell adhesion, proliferation, and directional migration through biochemical signaling pathways [1].

Composite bio-ink: Composite bio-inks combine natural and synthetic materials to leverage the benefits of both. These materials are synthesized through chemical or physical methods. For example, a rapidly formed supramolecular polypeptide–DNA hydrogel has been developed and used for in situ multilayer three-dimensional bioprinting. By alternating the deposition of two complementary bio-inks, designed structures can be printed. These structures exhibit high mechanical strength and geometric uniformity, maintaining their shape up to the millimeter scale without collapse.

New bio-ink: The photo-crosslinked silk fibroin (SF) bioink for 3D bioprinting has key improvements: it optimizes rheological performance via compounding gelatin/sodium alginate or in-situ photocrosslinking to address poor printability of pure SF; GMA modification avoids acidic by-products, while thiol-ene chemistry resists oxygen inhibition. Crosslinking systems like $Ru(bpy)_3^{2+}$/persulfate accelerate gelation; shift to visible light sources (>405 nm) and biocompatible initiators (LAP, $Ru(bpy)_3^{2+}$/SPS) for better cytocompatibility; and form composites with synthetic (e.g., 4-arm PEG acrylate) or natural polymers (e.g., nanocellulose) to enhance mechanical properties. It retains SF's high biocompatibility and controllable biodegradability, while featuring mild, efficient, spatiotemporally controllable photocrosslinking, adjustable rheology/mechanical performance, high printing precision (macro-to micro-nano scale), and wide applicability in tissue engineering [2].

2.2. Seed cell

Seed cells refer to those in regenerative medicine that possess the potential for proliferation and differentiation, and can participate in tissue formation or functional repair. They are responsible for

DOI: 10.54254/2753-8818/2026.AU28992

ultimately forming functional tissues, such as muscle contraction, nerve conduction, substance secretion, etc. Seed cells are mainly classified as autologous cells, allogeneic cells, and stem cells. Cellular therapies, also known as cell therapy, cell transplantation, or cytotherapy, involve the injection, grafting, or implantation of autologous or allogeneic living cells into patients to achieve therapeutic effects, and are often combined with biomaterial scaffolds to support and guide cells during and after transplantation. Advancements in 3D printing enable precise spatial arrangement of multiple cells and biomaterials, thereby enhancing cell delivery efficiency and scaffold integration. 3D-printed scaffolds enable two distinct cell delivery paradigms: (1) Post-printing seeding—benefiting from process flexibility but limited by initial cell adhesion, a challenge mitigated by hydrogel encapsulation; and (2) Bioink embedding—delivering superior cell spatial precision and loading efficiency, albeit demanding stringent environmental control to accommodate cellular sensitivity to mechanical and chemical stresses during printing [3].

3. Classification and principles of core technologies in bioprinting

3.1. Inkjet bioprinting

Inkjet 3D bioprinting, a crucial part of 3D bioprinting, creates native-like tissues/organs by depositing cell-laden droplets. These tissues/organs are designed to be transplantable into the human body to replace damaged ones [4]. 3D inkjet printing technology mainly includes three types: continuous inkjet (CIJ) printing, drop-on-demand (DOD) inkjet printing, and electrohydrodynamic (EHD) inkjet printing.

DOD inkjet printing, unlike CIJ printing, emits droplets only when the ejection signal is provided, enabling better controllability of the formed droplets [4]. This advantage is particularly critical in the processing of sensitive cell types such as mesenchymal stem cells (MSCs). Moreover, the 3D microspheres constructed in combination with alginate (which has good biocompatibility and can be completely degraded within 8 weeks) can not only provide stable structural support but also ensure appropriate permeability, thus meeting the requirements for cell growth and differentiation. The 3D bio-printed microspheres constructed by BES(Bio-electrospraying, a type of DOD inkjet printing)can effectively overcome the limitations such as the slow differentiation of HUMSCs and the difficulty in focusing on specific areas.

EHD inkjet 3D bioprinting uses an electric force to emit bioink droplets instead of the pressure pulse used in DOD 3D bioprinting. Its main advantages are high resolution and wide viscosity adaptability, making it suitable for manufacturing microscopic fine structures. However, it still needs to overcome challenges related to "single droplet controllability" and "long-term cell maintenance." Currently, it is often combined with other technologies to compensate for its shortcomings [4].

3.2. Laser-based printing

Stereolithography operates as a vat photopolymerization system where photocurable bioinks undergo layer-by-layer solidification through UV/visible light irradiation, enabling precise 3D construct fabrication. Among the advantages of SLA is its capacity to rapidly cure at physiological temperatures, which facilitates the production of constructs suitable for regenerative medicine applications [3]. SLA is primarily utilized in drug delivery systems, dental applications, and tissue engineering scaffolds. However, its primary disadvantages include exclusive compatibility with photocurable bioinks, the risk of cytotoxicity, the difficulty in achieving precise spatial co-localization of multiple cell types, and high costs [3].

DOI: 10.54254/2753-8818/2026.AU28992

Selective Laser Sintering employs powdered materials (polymers/ceramics/metals) that undergo localized fusion via high-energy laser scanning, followed by sequential layer deposition to build 3D architectures with complex geometries. This method can produce components with high mechanical strength and complex pores, which are suitable for the preparation of "hard tissue scaffolds" and "load-bearing medical devices" in regenerative medicine. It has the advantages of high compatibility with rare materials and excellent mechanical properties, but it also has the disadvantages of low cell compatibility, slow printing speed and poor surface quality. Therefore, in regenerative medicine, it is mainly applied to hard tissue engineering, such as bones and teeth, as well as non-cellular medical devices [3].

3.3. Extrusion bioprinting

The basic principle of 3D extrusion bioprinting is to extrude bioinks—composed of natural (e.g., alginate, collagen), synthetic (e.g., polycaprolactone [PCL]), or composite polymers (e.g., polymer + hydroxyapatite [HAp]) along with living cells (or cell-free)—layer by layer according to a pre-designed structure using mechanical forces from pneumatic, piston, or screw-driven systems. Subsequently, the bioink is solidified via crosslinking mechanisms such as ionic crosslinking (e.g., alginate binding with Ca^{2+}), thermal crosslinking (e.g., temperature-sensitive gelation of gelatin), photo-crosslinking (e.g., UV-induced curing of gelatin methacryloyl [GelMA]), or enzymatic crosslinking (e.g., thrombin-catalyzed fibrin formation). This process forms 3D scaffolds or constructs with specific structural, mechanical, and biological properties to mimic natural tissues/organs, which are applied in tissue engineering (for repairing damaged tissues) and combating infectious diseases (for constructing in vitro tissue/virus models).

Its advantages are diverse mechanical driving methods adaptable to various bioinks, the ability to print multiple materials for balanced biocompatibility and mechanical strength, a wide application range covering skin, bone, cartilage, and heart repairs, the potential for enhanced structural biomimicry through multi-material and coaxial printing, and relatively simple operation. However, it has limitations such as low printing resolution (around 100 μm, making fine structures like capillaries difficult to achieve), a core bioink contradiction (high viscosity improves structural fidelity but damages cells, while low viscosity ensures cell viability but leads to structural collapse), cell damage from extrusion stresses, difficulty in vascularizing large-volume constructs (prone to hypoxia and necrosis), ethical and safety concerns with some materials (e.g., Matrigel batch variation, FBS controversies), insufficient mechanical strength of natural materials, and low biological activity of synthetic materials, necessitating composite materials for optimization [5].

4. The progress of bioprinting technology in the field of organ regeneration

4.1. Regeneration of hollow organs

To achieve functional re-epithelialization—critical for establishing infection-resistant mucosal barriers—researchers have developed fibrin-coated polycaprolactone scaffolds via 3D bioprinting, where mesenchymal stem cells are precisely encapsulated within the fibrin matrix to promote mucosal regeneration. In rabbit tracheal defect models, this approach achieved ciliary regeneration at 8 weeks post-operation, with ciliary beating frequency matching that of native tissue. Additionally, by integrating CT imaging and CAD modeling, patient-specific tracheal grafts have been printed, effectively promoting surface re-epithelialization and validating the functionality of the neoepithelium.

DOI: 10.54254/2753-8818/2026.AU28992

Regarding cartilage regeneration, to construct C-shaped cartilaginous rings that maintain tracheal patency, researchers have combined 3D-printed polycaprolactone/collagen scaffolds with decellularized aortic matrices. After seeding with chondrocytes and mesenchymal stem cells, these constructs formed tracheal structures with satisfactory mechanical properties in rabbit models. Alternative approaches include printing hollow corrugated poly(L-lactide-co-caprolactone) scaffolds, where gelatin sponges loaded into grooves enable sustained release of transforming growth factor-β1 to enhance cartilage regeneration. In vascular reconstruction, to establish a microvascular network essential for cell survival, pre-vascularized bilayer tubular scaffolds—composed of polylactic acid, polycaprolactone, and collagen fibers—have been developed. These scaffolds reduced immune responses and promoted the formation of new capillary networks in murine models [6].

4.2. Regeneration of parenchymal organs

Current technologies cannot yet produce regenerative parenchymal organs for transplantation. However, research on 3D bioprinted organoids has made significant progress. In liver organoids, a team led by Pang Yuan from Tsinghua University and others used cell cluster printing to construct liver tissue models with enhanced cell interactions and activity. Another team created vascularized liver sinus models using 3D bioprinting. In the field of heart organoids, the world's first live heart organoid with a diameter exceeding 1 centimeter was successfully cultivated in Shanghai in August 2025, derived from human stem cells, with natural activity and low immunoreactivity [7]. 3D printing technology, as an important auxiliary technique for liver surgeries, can be based on the patient's CT/MRI data and cell characteristics to print personalized implants or grafts (such as those containing branch blood vessels and with liver functions), thereby addressing the issues of graft shortage and immune rejection [8].

It can not only construct functional myocardial tissues and autologous scaffolds that can simulate the natural extracellular matrix through bioinks such as alginate, gelatin, fibrin, and collagen, and induce stem cells to differentiate into mature cardiac tissues to repair damaged blood vessels, valves and myocardium, effectively addressing the challenges of scarce donors and immune rejection in the treatment of end-stage CVD (for example, after 3 weeks of implanting a silicone tube containing fibrin gel in rats, the tissue inside the tube was close to normal myocardium); but also based on data such as CT and cardiac magnetic resonance imaging (CMR), it can construct patient-specific models to assist in the preoperative precise planning (determining the best surgical plan), surgical simulation (predicting PVL) and risk control for complex diseases such as congenital heart disease, coronary heart disease, heart valve disease (such as TAVR for transcatheter aortic valve replacement) [9].

4.3. Clinical case

A study enrolling 13 patients with liver cancer explored the application of 3D printing in assisting ultrasound-guided microwave ablation of liver cancer, focusing on a critical clinical challenge: intraoperative ultrasound exhibits a low recognition rate for small liver cancers (<2 cm in diameter), which easily leads to puncture deviation and repeated punctures, increasing treatment risks. To address this issue, the core approach of the study was to construct 3D printed models using patients' CT scan data; these models were then used to assist intraoperative ultrasound in localizing liver cancers and further guide the liver microwave ablation procedure. The key findings revealed that the positioning accuracy of this combined method reached 76.92% (10 out of 13 patients were accurately localized), while the number of repeated punctures was significantly reduced, and the

DOI: 10.54254/2753-8818/2026.AU28992

safety of percutaneous microwave ablation of the liver was enhanced. The pioneering significance of this study is that it effectively solves the clinical problem of "intraoperative invisibility of small liver cancers" and provides a dual guarantee of "3D printed physical positioning + ultrasound guidance" for minimally invasive ablation therapy of liver cancer. Although the current study has a small sample size, it lays an important foundation for future large-sample clinical studies to further verify the technology's effectiveness and universality [10].

5. Current challenges and future outlook

5.1. Challenges

The ink materials used in bioprinting have issues related to cell compatibility and in vivo adaptability. The existing materials are insufficient to meet the complex clinical requirements and cannot support the application of high-precision medical scenarios such as organ repair. At the precision regulation level, the core "intelligent transformation" characteristic underpinning 4D bioprinting requires activation through external stimuli such as thermal, optical, or magnetic fields. Furthermore, to ensure biosafety and structural integrity, the responsive temperature of printing materials must strictly align with the human physiological temperature of 37°C—a threshold that current technological systems have yet to reliably achieve due to challenges in high-precision thermal control.

Regarding resolution, bioink formulations have made some progress in cellular compatibility and in vivo adaptability, but they still fall short of meeting complex clinical demands. Existing 4D-printed structures are largely limited to simple folding or assembly patterns, failing to replicate the intricate multi-layered and multi-dimensional anatomical structures needed for organ replication. The current technological framework also lacks precise spatiotemporal control over material deformation, which is necessary for synchronization with natural tissue growth and dynamic repair processes. In the context of immune rejection, although current bioink materials for bioprinting exhibit a certain degree of cellular compatibility, they suffer from insufficient bio-inertness and inadequate simulation of human tissue characteristics. Post-implantation, these materials are readily identified by the immune system as foreign bodies, triggering immune attacks.

5.2. Future

The interdisciplinary integration of organoid science and 3D bioprinting leads biomedical research. This interdisciplinary field harnesses two pivotal technological advancements: (1) precise regulation of iPSC differentiation pathways, and (2) microfluidic-enabled biomimetic scaffold fabrication—collectively unlocking unprecedented multidimensional potential for future biomedical applications. In healthcare, it facilitates developing personalized bio-inks from patient-specific cells, advancing personalized medicine via customized skin/bone scaffold transplants and targeted cancer therapies. It also drives breakthroughs in regenerative medicine by addressing vascularization issues in kidney and cardiac organoids, ultimately supporting functional regeneration of damaged organs. Furthermore, high-throughput drug screening platforms using 3D-printed tumor organoids enable accurate in vivo ADME process simulation, greatly reducing toxicity prediction biases in preclinical drug development.

This integration enhances the functionality of biodegradable polycaprolactone (PCL)-gelatin composite scaffolds, facilitating tissue engineering for intricate structures such as neural-integrated cartilage and vascularized intestinal tissues. Integrating bioactive components (e.g., cholinesterase,

DOI: 10.54254/2753-8818/2026.AU28992

tumor-specific antibodies) with carbon nanotubes through printing technologies facilitates the development of ultrasensitive biosensors, achieving picogram-level detection limits for applications like organophosphorus residue monitoring and early cancer screening. As these technologies advance, the field is poised to substantially ease global donor organ shortages through standardized artificial organ production, rebalancing the long-standing gap between clinical demand and transplant supply. Moreover, it will drive transformative shifts in healthcare: toward "precision repair"; in drug development: toward "in vitro human simulation"; and in biomanufacturing: toward "functional living constructs." This progression will provide critical technical support for global health security and sustainable development, fueling continuous innovation from basic biomedical research to clinical translation.

6. Conclusion

This review examines bioprinting as a strategy to tackle organ shortage and immune rejection in transplantation and its role in organ regeneration. It highlights that diverse bioinks (natural, synthetic, composite, and photo-crosslinked) and seed cell populations (autologous, allogeneic, and stem cells) form a strong technical basis for bioprinting. Key technologies like inkjet, laser-based (e.g., SLA, SLS), and extrusion systems have shown promise in reconstructing hollow organs and advancing parenchymal organoids, with initial clinical success in procedures like ultrasound-guided microwave ablation of small liver cancers. However, challenges remain, including suboptimal bioink performance, insufficient printing precision for microscale structures, and post-implantation immune rejection risks. Future progress will depend on interdisciplinary efforts to develop patient-specific bioinks, address vascularization issues in large constructs, and improve spatiotemporal control. These advancements will drive bioprinting's clinical translation, potentially alleviating global organ shortages and transforming regenerative medicine.

References

[1] Li, Y., Yue, W., Xu, T., Hu, H. L., & Li, S. (2024). Research progress on bioinks for 3D bioprinting (Jiyu 3D shengwu dayin de shengwu yimo yanjiu jinzhan). Biomedical Engineering and Clinical Medicine, 28(6), 869-877. https: //doi.org/10.13339/j.cnki.sglc.20241023.014 (in Chinese).

[2] Pan, X. P., et al. (2024). Research Progress of Photo-Crosslinked Silk Fibroin Bio-3D Printing Ink. Silk, 61(8), 50-59.

[3] Sousa, A. C., et al. (2025). Three-Dimensional Printing/Bioprinting and Cellular Therapies for Regenerative Medicine: Current Advances. Journal of functional biomaterials, 16(1), 28.

[4] Zhao, D. K., et al. (2022). Inkjet 3D bioprinting for tissue engineering and pharmaceutics. Journal of Zhejiang University-Science A (Applied Physics & Engineering), 23(12), 955-973.

[5] Chen, X. B., Fazel Anvari-Yazdi, A., Duan, X., Zimmerling, A., Gharraei, R., Sharma, N. K., Sweilem, S., & Ning, L. (2023). Biomaterials / bioinks and extrusion bioprinting. Bioactive materials, 28, 511–536.

[6] Pan, Z. Y., et al. (2022). Latest Research Progress and Applications of Bioprinting Technology in the Field of Tissue-Engineered Trachea. Chinese Journal of Tissue Engineering Research, 26(27), 4393-4400.

[7] Zhang, J., & Gu, Q. (2025). Bio-3D Printing of Complex Organoids. Chinese Journal of Cell Biology, 47(9), 2205-2220.

[8] Sun, Y., et al. (2024). Application Progress of 3D Printing Technology in Liver Surgery. Journal of Practical Clinical Medicine, 28(17), 131-136 (in Chinese).

[9] Wang, Z. L., & Jin, J. (2023). Research Progress of 3D Bioprinting Technology in Cardiac Tissue Engineering. Biomedical Engineering and Clinical Medicine, 27(3), 388-391.

[10] Zhang, Y., et al. (2023). Preliminary study of 3D printing technology for extracorporeal positioning guide assisted ultrasound-guided microwave ablation of the liver. Expert review of medical devices, 20(12), 1227–1233.