WEP Warwick Evans Publishing

International Journal of Public Health and Medical Research

ISSN: 3006-7707 (Print), ISSN: 3006-3752 (Online) | Volume 4, Number 3, Year 2025
DOI: https://doi.org/10.62051/ijphmr.v4n3.13
Journal homepage: https://wepub.org/index.php/IJPHMR/index

Research on the Construction of Microtia Repair Scaffold Based on 3D Bioprinting Technology

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ABSTRACT

Microtia is a congenital auricular hypoplasia, clinically characterized by partial or complete loss of the auricle. This condition not only affects patients' hearing function but also significantly negatively impacts their psychological and social adaptation. Current mainstream treatments include autologous rib cartilage transplantation and implantation of artificial materials, but these are associated with issues such as secondary damage to the donor site, implant exposure, and insufficient morphological fidelity. Recent advances in 3D bioprinting technology have provided a new avenue for constructing highly compatible and biocompatible auricle scaffolds. This study focused on the use of 3D bioprinting technology to fabricate personalized auricle repair scaffolds and systematically evaluated their potential in terms of morphological fidelity, mechanical properties, and biological function. The research method primarily involved: first, 3D reconstruction using patient CT imaging data accurately reproduced the ear anatomy; then, using polycaprolactone (PEL) and gelatin-methacrylamide (GelMA) as the base materials, a composite scaffold with a hierarchical structure was fabricated using a combination of fused deposition modeling (FDM) and photopolymerization techniques; and then, using an in vitro chondrocyte co-culture system, the scaffold's cytocompatibility and chondrogenic efficacy were systematically evaluated. Experimental results show that the prepared scaffold is highly consistent with the complex curved surface of the ear in terms of morphology, has mechanical properties close to those of natural ear cartilage, presents a uniform and interconnected porous structure inside, and its degradation behavior can also be effectively controlled. Cell experiments showed that the surface of the scaffold is conducive to cell adhesion and extension, cell proliferation activity is significantly enhanced, and it can promote the synthesis and deposition of key extracellular matrix components such as collagen fibers and glycosaminoglycans. The above results indicate that the scaffold has good application potential in the field of cartilage regeneration. In summary, the strategy of constructing personalized auricle scaffolds based on 3D bioprinting technology provides a promising new approach for the functional repair of microtia.

KEYWORDS

Microtia; 3D bioprinting; Tissue engineering; Auricular scaffold; Polycaprolactone; Cartilage regeneration

1. INTRODUCTION

Microtia is a common congenital developmental defect in maxillofacial surgery, with a global incidence of approximately 1 in 5,000 to 1 in 7,000 children. Most cases are unilateral. This deformity not only causes abnormal auricular morphology and facial asymmetry, impacting overall appearance, but is also often accompanied by external auditory canal atresia or middle ear developmental disorders, leading to conductive hearing loss. These physical defects often have a lasting negative impact on the child's psychological well-being, social interactions, and self-awareness. In current clinical practice, reparative approaches primarily include autologous rib cartilage transplantation,

artificial material implantation, and allogeneic tissue transplantation. Autologous rib cartilage transplantation is considered the current gold standard due to its autologous source and lack of immune rejection. However, this procedure is invasive, the amount of cartilage available is limited, and postoperative complications such as chest wall deformity and pneumothorax may occur, particularly in young children. Artificial materials, while shortening operative time, carry a higher risk of exposure, infection, and rejection, and their long-term stability and biointegration are unsatisfactory.

In recent years, with the rapid development of tissue engineering and regenerative medicine, the construction of auricular scaffolds with excellent biocompatibility and personalized morphology has become a new research focus. 3D bioprinting, a cutting-edge additive manufacturing technology, enables precise spatial arrangement of multiple materials, cells, and active factors based on medical imaging data, demonstrating unique potential for reconstructing complex tissue structures. This layer-by-layer deposition method not only accurately replicates the fine anatomical structure of the patient's healthy ear but also creates a biomimetic microporous structure and biochemical environment within the scaffold, promoting cell migration, vascular ingrowth, and cartilage matrix deposition, thus enabling functional regeneration.

However, current research on ear scaffolds based on 3D bioprinting is still in its early stages and faces several key challenges. Regarding materials, it is necessary to develop composite bioinks that combine excellent printability, controllable degradability, and the ability to induce cartilage formation. Regarding structural performance, the scaffolds must precisely match the contours of the ear at the macroscopic level and possess appropriate pore connectivity at the microscopic level to support cell infiltration and nutrient exchange. Furthermore, in vivo integration after implantation, long-term mechanical stability, and the mechanisms of functional cartilage regeneration remain pressing scientific challenges.

This study focuses on the systematic application of 3D bioprinting technology in the repair of microtia, focusing on four aspects: personalized scaffold design, screening and compounding of material systems, optimization of printing process parameters, and in vitro biological performance evaluation. The aim is to provide experimental basis and theoretical support for the ultimate clinical transformation of this technology.

2. CURRENT STATUS OF MICROTIA REPAIR AND THE DEMAND FOR 3D PRINTING TECHNOLOGY

Although clinical repair methods for microtia are widely used, their effectiveness remains limited. Mainstream methods include autologous costal cartilage transplantation and artificial material implantation. Autologous costal cartilage transplantation involves harvesting cartilage from the sixth to eighth ribs of the child's chest. The surgeon then manually carves an ear-shaped scaffold and implants it subcutaneously in the ear. This procedure is time-consuming, typically requiring four to six hours, and relies heavily on the surgeon's carving skills and clinical experience. Postoperative complications can include cartilage resorption, structural deformation, and even chest wall deformity, particularly affecting young children. Artificial materials, such as high-density porous polyethylene (Medpor), offer advantages such as pre-formed design and shortened surgical time. However, these materials are relatively rigid and easily penetrate the skin after surgery, leaving them exposed. They also lack bioactivity, making them inadequate for the continuous growth and development of children's ears. Their long-term stability and safety remain controversial [1].

Recent advances in tissue engineering have opened up new avenues for the treatment of microtia. Traditional scaffold fabrication techniques, such as solvent casting and particle leaching, can create porous structures, but they struggle to precisely control pore morphology, pore penetration, and shape matching accuracy. Emerging 3D bioprinting technology, based on digital models and layered

material deposition, can reconstruct a three-dimensional auricle morphology that closely matches the defect area based on the patient's CT or MRI data, enabling truly personalized scaffold customization. Importantly, this technology supports the coordinated printing of multiple biomaterials and cells, demonstrating significant potential for constructing bioactive composite scaffolds that better mimic the mechanical properties and microenvironment of natural cartilage tissue.

The ideal printed ear scaffold must meet multiple criteria: on a macroscopic level, it must restore the complex curved surface morphology of the ear and possess sufficient mechanical strength to resist deformation; on a microscopic level, it should have an appropriate pore size and high porosity to promote cell migration and nutrient transport; and on a functional level, the material degradation performance must be well matched with the rate of new cartilage tissue generation. Therefore, the development of new bio-inks suitable for ear regeneration that have both good printability and bioactivity, as well as the systematic optimization of printing process parameters, have become the focus of current research. The introduction of 3D bioprinting technology is expected to not only reduce surgical trauma and shorten treatment cycles, but also significantly improve the natural appearance of the repair through highly personalized scaffold design, providing patients with better treatment options.

3. PERSONALIZED DESIGN AND MATERIAL SELECTION OF EAR SCAFFOLDS

Personalized design is a key component of 3D bioprinted ear scaffolds. First, a CT or MRI scan of the patient's unaffected ear is performed to obtain 2D cross-sectional imaging data. Three-dimensional reconstruction is then performed using software such as Mimics and 3D Slicer, generating a mirror image model that matches the defect morphology on the affected side. During the printing and implantation process, the scaffold may shrink and deform, subjecting it to mechanical stress from surrounding tissues. Therefore, its compressive and flexural properties must be enhanced by adding internal support structures and optimizing mesh parameters. The auricle is complex and intricate, requiring accurate reconstruction of substructures such as the helix, antihelix, and concha, placing extremely high demands on printing precision.

Material selection directly impacts the key properties of the scaffold. Synthetic polymers, natural polymers, and composite systems are commonly used. Polycaprolactone (PCL) offers excellent mechanical properties and controllable degradation, but its hydrophobic surface is detrimental to cell behavior and requires surface modification [2]. PLGA has a controllable degradation cycle, but degradation products may increase local acidity and affect cell activity. Natural materials have excellent biocompatibility, but they generally lack mechanical strength and suffer from poor structural stability after printing.

To synergistically enhance mechanical properties and biological function, this study constructed a PCL-GelMA composite system: a PCL backbone was formed using FDM technology to provide support, while UV-crosslinked GelMA hydrogel was used to fill the pores, serving as a cell carrier to mimic the extracellular microenvironment. The introduction of nanohydroxyapatite further modulated the degradation rate and enhanced chondrogenic induction [4]. When the PCL:GelMA ratio was 7:3, the composite scaffold had a compression modulus of 0.8–1.2 MPa, close to the mechanical properties of human ear cartilage, and a cell survival rate exceeding 90% [4].

4. 3D PRINTING PROCESS AND SCAFFOLD STRUCTURAL PERFORMANCE CHARACTERIZATION

The ear scaffolds were fabricated using 3D bioprinting technology, a process that requires systematic control of multiple key printing parameters to ensure that the scaffolds meet design requirements in

terms of both macrostructure and microperformance. This study combines fused deposition modeling (FDM) with bio-ink extrusion technology to fabricate: First, a polycaprolactone (PCL) frame is printed using FDM technology as a support structure. During the printing process, in order to balance material fluidity and molding reliability, the print head temperature is set within the range of 85–95°C, the layer thickness parameter is adjusted to 0.1 mm, and a nozzle with a 0.2 mm aperture is selected.A fill density of 40% was used to balance mechanical strength and material usage. This ensured both morphological accuracy and enhanced mechanical strength of the underlying structure. Subsequently, a gelatin-methacrylamide (GelMA) prepolymer loaded with chondrocytes was precisely deposited into the pores of the PCL framework using extrusion bioprinting. The prepolymer was cross-linked and cured by irradiation with 405 nm UV light for 20 seconds. To maintain material extrusion stability and cell viability, the entire printing environment temperature was strictly controlled at 20–25°C [5].

Systematic multi-scale characterization of the formed scaffold demonstrated that its macroscopic appearance closely replicates the complex three-dimensional anatomical features of the auricle, with dimensional errors within 0.3 mm, meeting clinical individualization requirements. Scanning electron microscopy images revealed a porous network structure within the scaffold, with an average pore size of approximately 250 μm and a porosity of 75%. This structure facilitates cell migration, nutrient transport, and waste removal. Mechanical testing data revealed that the composite scaffold possesses a compression modulus of 0.95 MPa and an elastic modulus of 1.8 MPa, which closely match the mechanical parameters of natural ear cartilage tissue. Cyclic loading experiments demonstrated excellent fatigue resistance, effectively resisting continuous deformation caused by tissue contraction and external pressure under mechanical conditions simulating subcutaneous implantation, maintaining structural integrity and stability. In addition to morphology and mechanical properties, scaffold degradation behavior is also a key evaluation metric. In vitro immersion experiments in phosphate buffered saline (PBS) demonstrated that polycaprolactone (PCL) exhibited slow degradation, losing approximately 10% of its mass after 12 weeks. In contrast, gelatin-methacrylamide (GelMA) achieved a degradation rate of 35% within 4 weeks, indicating that its rapid degradation helps to free up space for cartilage regeneration. The degradation timeline of both materials aligns with the natural regeneration process of cartilage [8]. By adjusting the molecular weight of PCL and the cross-linking degree of GelMA, the overall degradation rate can be precisely controlled to meet the repair needs of patients of different ages. In addition, the swelling rate of the scaffold is 15%, showing moderate hydrophilicity, which is conducive to the exchange of oxygen and metabolic substances and meets the microenvironmental conditions required for cell growth [6].

5. BIOLOGICAL PERFORMANCE AND CARTILAGE FORMATION COMPATIBILITY OF 3D BIOPRINTED MICROTIA REPAIR SCAFFOLDS

In the research on the construction of 3D bioprinted microtia repair scaffolds, the biological properties and cartilage generation capacity of the scaffold are the core factors that determine whether it can meet clinical repair needs, and are directly related to the stability and functionality of the repair effect. From the perspective of the compatibility between the scaffold and cells, the 3D bioprinted scaffold has no obvious cytotoxicity, can construct a biomimetic microenvironment suitable for cell growth, and efficiently support the adhesion, survival and sustained proliferation of human adipose-derived stem cells. The uniformly interconnected porous structure designed inside it not only meets the requirements of microtia repair for the microscopic space of the scaffold, but also allows cells to maintain a normal morphology and be evenly distributed inside the scaffold, providing a sufficient cellular basis for subsequent cartilage regeneration, solving the problem of poor cell compatibility and easy rejection of traditional artificial materials, and meeting the core demand for biosafety of the repair scaffold [3]. To address the cartilage regeneration required for microtia repair, the scaffold can

directionally promote the differentiation of stem cells into chondrocytes, promoting the synthesis and deposition of key extracellular matrices in cartilage tissue (such as proteoglycans and type II collagen). It also activates pathways related to cartilage-specific genes such as SOX9, AGG, and COL2A1, ensuring that the cartilage regeneration process aligns with the developmental patterns of natural auricular cartilage. This provides histological support for the morphological stability and functional recovery of the repaired auricle, addressing the limitations of autologous rib cartilage transplantation, such as limited cartilage quantity, difficulty in shaping, and prone to absorption and deformation. From the synergistic advantages of the composite material system, the 3D bioprinted scaffold composed of PCL and GelMA exhibits significantly better cartilage-forming properties than either the PCL scaffold alone or the blank control, making it more suitable for the diverse scaffold performance requirements of microtia repair. Among them, GelMA hydrogel not only acts as a cell carrier to ensure the stable colonization of cells in the scaffold, but the RGD sequence it contains can also strengthen the interaction between cells and matrix, further improving the efficiency of chondrogenic differentiation; and the interface between cells and scaffold materials is tightly integrated, which can form a typical cartilage pit structure in the scaffold, providing key biological guarantees for 3D bioprinting scaffolds to achieve the dual goals of "individualized morphological replication + functional cartilage regeneration" in microtia repair, and promoting the upgrade of repair technology from "morphological repair" to "synergistic repair of morphology and function" [7].

6. CLINICAL TRANSLATION CHALLENGES AND FUTURE DEVELOPMENT DIRECTIONS

Although 3D bioprinting ear scaffold technology shows considerable application prospects, it still faces a series of key challenges on its way to clinical practice. The most prominent technical difficulty at present is how to coordinate the contradiction between printing efficiency and morphological fidelity: high-precision printing is often a slow process, which may cause cells or bioactive factors to become inactivated during the printing process; and once the printing speed is increased, problems such as weak interlayer bonding or distortion of fine structures are prone to occur. In order to address this bottleneck, new processes such as suspended support printing and projection light curing have gradually attracted attention. This type of technology improves the optical path design and optimizes the light response performance of the material, while achieving high-speed printing, it also better maintains the forming accuracy of the complex auricle structure [8].

Tissue vascularization is a key obstacle to the functionalization of large, living scaffolds. As a three-dimensional organ, the auricle relies on a complete vascular network for nutrient supply. Existing studies have shown that methods such as pre-printing biomimetic vascular channels during printing, co-printing endothelial cell spheroids, and gradient release of vascular endothelial growth factor (VEGF) can promote angiogenesis. However, the long-term stability of these strategies in large animal models requires further verification. In particular, achieving rapid integration of printed blood vessels into the host vascular system remains a key challenge.

Regulatory approval and the development of standardization systems also face unique challenges. The uniqueness and variability of personalized medical devices naturally conflict with the batch-based review system for traditional medical devices. A comprehensive standardization system, encompassing medical imaging acquisition, 3D modeling specifications, bio-ink safety assessment, and printing process quality control, is needed. The 2021 technical guidance for 3D-printed medical devices issued by the US FDA provides an important reference for the development of relevant standards in my country, but the specific regulatory framework for live cell products still needs to be improved.

Cost control is a key factor influencing clinical adoption. Currently, the production cost of personalized scaffolds is high, primarily due to the development of specialized bio-inks, the maintenance of a sterile printing environment, and the human resources required for personalized

modeling. By developing domestically produced printing equipment, optimizing material formulations, and establishing automated modeling processes, production costs can be effectively reduced by approximately 40-60%, paving the way for large-scale clinical application [9].

Future research should focus on the development of fourth-generation intelligent bio-inks, focusing on overcoming the application bottlenecks of environmentally responsive materials and enabling scaffolds to adapt to their microenvironment. The integration of functional nanomaterials can imbue scaffolds with anti-infection and anti-fibrosis properties. Combined with patient-specific induced pluripotent stem cell (iPSC) technology, fully personalized tissue construction can be achieved, fundamentally resolving the problem of immune rejection. From a broader perspective, 3D bioprinting will be deeply integrated with cutting-edge technologies such as organ chips and organoid culture, ultimately achieving the precise reconstruction of multi-tissue complex organs and advancing regenerative medicine towards the repair of major tissue defects.

7. CONCLUSION

This study systematically explored the feasibility of using 3D bioprinting technology to construct a microtia repair scaffold. By integrating medical imaging data, personalized 3D modeling of the auricle was achieved. By innovatively utilizing a polycaprolactone (PCL) and gelatin-methacrylamide (GelMA) composite biomaterial system, combined with a multi-process fusion strategy of fused deposition modeling and stereolithography, an auricle scaffold with precise anatomical morphology, adaptive mechanical properties, and excellent bioactivity was successfully fabricated. In vitro results demonstrated that the scaffold effectively promoted cell adhesion and proliferation and significantly enhanced chondrogenic differentiation, confirming its significant potential for tissue-engineered ear reconstruction.

This research is currently in the preclinical exploratory stage. Further in vivo studies in large animals are required to systematically evaluate the scaffold's long-term stability, biocompatibility, and cartilage regeneration performance. Particular attention should be paid to the vascularization process, immune response, and the temporal relationship between scaffold degradation and tissue regeneration within the in vivo microenvironment. Furthermore, promoting clinical translation requires overcoming a number of technical bottlenecks: establishing standardized printing processes and quality control systems, optimizing bio-ink composition to improve printing efficiency and cell viability, and conducting preclinical safety and efficacy evaluations that meet medical device registration requirements.

3D bioprinting technology offers a highly personalized, minimally invasive solution for microtia repair. It not only has the potential to overcome the challenges of traditional surgical procedures, such as extensive donor site damage and suboptimal reshaping, but also lays the technical foundation for achieving both morphological and functional restoration. With continued breakthroughs in biomaterials, cell engineering, and manufacturing processes, this technology is expected to become a standardized clinical solution for auricular regeneration and repair in the future, providing patients with a superior diagnosis and treatment experience.

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