Bioartificial Lungs: A Promising Alternative to Traditional Organ Transplantation

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ABSTRACT

End-stage lung disease remains a major clinical challenge due to donor shortage and chronic rejection after transplantation. Bioartificial lung engineering using patient-derived cells offers a promising alternative by enabling the creation of functional three-dimensional tissues capable of gas exchange. Preclinical studies have demonstrated successful implantation in animal models; however, key challenges remain, including scaffold optimization, vascularization, and functional maturation to ensure long-term in vivo performance. The development of personalized lung grafts represents a critical step toward clinically translatable therapies, as well as advanced platforms for airway reconstruction and disease modeling.

INTRODUCTION

Chronic obstructive pulmonary disease affects approximately 25 million people worldwide, with an estimated 12,000 deaths annually in the United States. Lung transplantation remains the only definitive treatment for end-stage lung disease; however, donor scarcity and the low suitability of available lungs, only 10–20%, severely limit its clinical impact. Thousands of patients remain on the transplant waiting list each year, a number that has remained relatively unchanged for over a decade. In addition, long-term transplant outcomes are negatively affected by chronic rejection and the adverse effects associated with lifelong immunosuppressive therapy.

Tissue-engineered lungs represent a promising alternative aimed at generating functional, transplantable organs capable of restoring gas exchange. Current approaches focus on recreating the extracellular matrix using polymers and natural biomaterials such as collagen, Matrigel, and Gelfoam, which are essential for maintaining lung architecture and guiding pulmonary cell differentiation. These strategies aim to overcome donor limitations and advance personalized and regenerative therapies for patients with end-stage respiratory failure.

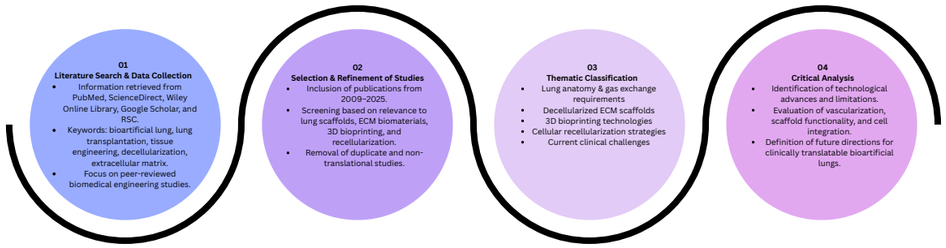
OBJECTIVES

To evaluate the clinical limitations of lung transplantation, including donor shortage, low organ suitability, and long-term complications associated with immunosuppressive therapy.

To analyze current tissue engineering strategies for bioartificial lung development, focusing on decellularized extracellular matrix scaffolds and biomaterial-based approaches for lung regeneration.

To assess the potential of bioartificial lungs as a regenerative and personalized therapeutic alternative capable of restoring functional gas exchange and addressing end-stage respiratory failure.

METHODOLOGY



DATA

Approach	Purpose	Key Findings	Limitations
Decellularization	Remove cells, preserve ECM scaffold	Maintains native lung architecture & mechanics	Possible ECM damage, incomplete removal
Recellularization	Seed epithelial/endothelial cells	Partial gas exchange in animal models	Poor cell distribution, low maturation
3D Printing	Fabricate custom lung structures	High design control & biomimicry	Insufficient alveolar resolution
Biomaterials	Support cell growth & differentiation	Promotes adhesion & tissue formation	Limited long-term stability
Overall Outcome	Functional lung substitutes	Promising preclinical results	Vascularization & durability remain critical challenges

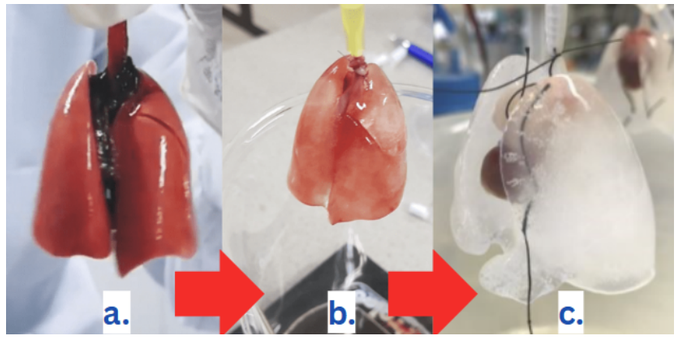


Figure 1. Stages of the lung decellularization process: a) Native lung; b) Lung during decellularization; c) Fully decellularized lung.

ANALYSIS AND RESULTS

Decellularized lung scaffolds successfully preserve the native extracellular matrix architecture, providing a suitable platform for cell adhesion and tissue organization. Recellularization with epithelial and endothelial cells has demonstrated partial restoration of gas exchange in preclinical animal models, confirming the biological feasibility of engineered lungs. However, long-term function remains limited by insufficient vascularization, incomplete tissue maturation, and reduced mechanical stability. Advances in 3D bioprinting and bioink development have enabled the fabrication of biomimetic lung constructs with tunable properties, although current technologies still lack the resolution required to reproduce the alveolar–capillary interface. Overall, bioartificial lungs show strong structural and regenerative potential but remain in the experimental stage and require further optimization before clinical translation.

CONCLUSION

Bioartificial lung engineering represents a promising strategy to address the limitations of donor organ availability and the long-term complications associated with lung transplantation. Decellularized extracellular matrix scaffolds, recellularization with patient-derived cells, and advances in 3D bioprinting have demonstrated structural feasibility and partial functional performance in preclinical models. However, critical challenges, including adequate vascularization, immune stability, and full tissue maturation, must be addressed before clinical implementation. Despite these limitations, bioartificial lungs offer a powerful platform for regenerative therapies, disease modeling, and drug testing, underscoring their potential impact on the future of personalized medicine and treatment for end-stage respiratory failure.

FUTURE WORK

Future studies should prioritize improving vascularization and optimizing recellularization using patient-specific iPSCs to enhance tissue maturation and reduce immune rejection. Advances in high-resolution 3D bioprinting and perfusion bioreactors are needed to recreate the alveolar–capillary interface and support long-term functionality. Large-animal models will be essential to evaluate scalability, physiological performance, and clinical safety prior to human translation.

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