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Artificial lung: A biomedical engineering approach

Pulmón artificial: Un enfoque de ingeniería biomédica

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Abstract

This study explores recent advances in artificial lung technology from a biomedical engineering perspective, addressing the urgent need for alternatives to lung transplantation due to organ shortages and the rising prevalence of chronic respiratory diseases, such as COPD and pulmonary fibrosis. The analysis spans from extracorporeal membrane oxygenation (ECMO), used as temporary support, to implantable artificial lungs designed to autonomously replicate respiratory function. Key innovations are highlighted, including advanced biomaterials, microengineering, and 3D bioprinting aimed at enhancing biocompatibility and reducing coagulation and immune rejection risks. Notably, the decellularization of donated lungs and their repopulation with autologous cells emerges as a promising approach, offering sustainable solutions with reduced immunosuppression needs. Furthermore, biohybrid models and biomimetic microchanneled devices have demonstrated improved gas exchange efficiency and minimal inflammatory response. The development of implantable artificial lungs is thus positioned as a viable and innovative solution for chronic lung failure, requiring a multidisciplinary approach integrating biomedical engineering, biotechnology, and regenerative medicine.

Keywords: Artificial organs, artificial lungs, extracorporeal oxygenation, implantable technology.

Resumen

Este estudio explora los avances recientes en la tecnología del pulmon artificial desde una perspectiva de la ingeniería biomédica, abordando la necesidad urgente de alternativas al trasplante pulmonar debido a la escasez de órganos y al aumento en la prevalencia de enfermedades respiratorias crónicas, como la EPOC y la fibrosis pulmonar. El análisis abarca desde la oxigenación por membrana extracorpórea (ECMO), utilizada como soporte temporal, hasta pulmones artificiales implantables diseñados para replicar de manera autónoma la función respiratoria. Se destacan innovaciones clave, incluyendo biomateriales avanzados, microingeniería e impresión 3D biológica, orientadas a mejorar la biocompatibilidad y reducir los riesgos de coagulación y rechazo inmunológico. En particular, la descelularización de pulmones donados y su repoblación con células autólogas surge como un enfoque prometedor, que ofrece soluciones sostenibles con menor necesidad de inmunosupresión. Además, los modelos biohíbridos y los dispositivos biomiméticos con microcanales han demostrado una mayor eficiencia en el intercambio gaseoso y una respuesta inflamatoria mínima. El desarrollo de pulmones artificiales implantables se perfila, así como una solución viable e innovadora para la insuficiencia pulmonar crónica, que requiere un enfoque multidisciplinario que integre la ingeniería biomédica, la biotecnología y la medicina regenerativa.

Palabra clave: Órganos artificiales, pulmón artificial, oxigenación extracorpórea, tecnología implantable.

1 Introducción

In the dynamic field of biomedical engineering, technological innovation plays a crucial role in developing advanced solutions to address chronic diseases and improve the quality of life of patients. Among the most disruptive developments is the design of implantable artificial organs—devices intended to replicate biological organ functions to compensate for their deterioration or failure (Rondón *et al.*, 2024). In this context, implantable artificial lung engineering has emerged as a promising alternative for patients with end-stage respiratory diseases, offering a therapeutic option beyond organ transplantation (Petrella & Spaggiari, 2018; Petrosyan *et al.*, 2022).

The development of these devices is driven by the

increasing incidence of chronic respiratory diseases such as Chronic Obstructive Pulmonary Disease (COPD), idiopathic pulmonary fibrosis, and pulmonary hypertension, which significantly impair respiratory capacity and are among the leading causes of mortality worldwide (Humbert *et al*., 2022; Singh *et al*., 2022; Meyer, 2017; Podolanczuk *et al.*, 2023; Olsson *et al*., 2023; Elia *et al*., 2019). Despite advancements in mechanical ventilation techniques and extracorporeal membrane oxygenation (ECMO), these solutions are often temporary and require prolonged hospitalization (Sinha *et al*., 2023: Keller, 2020). Furthermore, the shortage of available donor organs poses a critical challenge in modern medicine, as fewer than 30% of donated lungs meet the viability criteria for transplantation, leaving thousands of patients without effective therapeutic options (Mody, 2023).

In this context, implantable artificial lungs stand at the intersection of biomedical engineering, nanotechnology, and bioengineering. These devices are being developed to integrate with the circulatory system and replicate respiratory function autonomously and continuously. The use of advanced biomaterials, 3D bioprinting, and computational fluid dynamics modeling has enabled the creation of high-efficiency gas exchange membranes and biomimetic devices that emulate the microstructure of pulmonary alveoli (Ates & Bartolo, 2023; Umur *et al*., 2023; Jin *et al*., 2025; Mathur *et al.*, 2025; Mirshafiei *et al*., 2024).

However, several technical challenges remain, particularly regarding biocompatibility, clot formation risk, and the ability of these devices to adapt to the patient's metabolic demands under dynamic physiological conditions (Anyanwu *et al*., 2024a; Menciassi & Iacovacci, 2020).

This study analyzes the key challenges and opportunities in developing implantable artificial lungs, with a focus on biomaterial selection, biocompatibility, bioregulatory aspects, and clinical feasibility. It also explores emerging strategies, including decellularized scaffolds and biohybrid models, which hold promise for achieving functional lung regeneration.

By integrating recent advancements in research and clinical studies, this work highlights the transformative potential of implantable artificial lungs in regenerative medicine and artificial organ engineering. It aims to inspire biomedical engineers, researchers, and healthcare professionals to develop innovative technologies that will shape the future of respiratory care.

The convergence of biotechnology, bioengineering, and artificial intelligence is expected to accelerate the development of personalized therapies and implantable artificial organs, bringing these innovations closer to becoming a tangible and accessible reality for patients suffering from severe respiratory failure (Wheeler 2025; Anyanwu *et al*., 2024b).

2 Methodology

A systematic review of the scientific literature was conducted to collect relevant information regarding tissue engineering principles, applied methodologies, recent advancements, and current challenges in the field.

a. Data Search and Collection: A comprehensive literature search was performed across several scientific databases, including PubMed, Frontiers, Wiley Online Library, the Royal Society of Chemistry, MDPI, ScienceDirect, SCOPUS, RedALyC, and Google Scholar. The search utilized key terms such as "artificial lung," "extracorporeal oxygenation," and "implantable technology" to ensure relevant coverage.
b. Information Selection and Refinement: The selected literature spanned the period from 2009 to 2025 to ensure an up-to-date and representative overview of the current state of the field. Reference management was performed using Mendeley (Elsevier, 2021), enabling the organization of sources by relevance and the exclusion of entries that did not meet predefined inclusion criteria.
c. Organization of Subtopics: Following the refinement of the collected data, a structured research framework was developed by organizing the content into thematic categories to facilitate a comprehensive analysis of the most relevant aspects of the study.
d. Data Analysis and Interpretation: A critical assessment of the selected studies was carried out, identifying emerging trends, knowledge gaps, and potential research opportunities. The insights obtained supported the formulation of evidence-based conclusions, which are presented in the results and discussion section (Rondón *et al*., 2023).

3 Results and Discussion

3.1 Implantable Artificial Lungs

The lungs are essential organs of the respiratory system, responsible for gas exchange, which enables the oxygenation of blood and the removal of carbon dioxide, a byproduct of cellular metabolism (Velleca *et al.*, 2023). Although breathing may seem like an automatic and simple process, it is, in fact, a highly complex and coordinated mechanism involving the joint action of the nervous, muscular, and cardiovascular systems (Powers & Dhamoon, 2023).

During inhalation, air enters through the nasal cavity and oral cavity, travels down the trachea, and reaches the

bronchi, which progressively branch into bronchioles that terminate in millions of alveoli. These microscopic structures provide an extensive surface area—approximately 70 m^2—where oxygen diffuses across the alveolar-capillary membrane into the bloodstream, while carbon dioxide diffuses in the opposite direction to be exhaled. The efficiency of this gas exchange is critical for maintaining acid-base balance and cellular metabolism (Tonelli & Harman, 2012; Soliyeva 2025; Aung *et al*., 2019).

The lungs possess sophisticated defense mechanisms that protect against pathogens and environmental pollutants. The respiratory mucosa is lined with microscopic cilia that propel mucus, along with trapped particles, toward the pharynx for clearance. However, various factors—such as genetic predisposition, prolonged exposure to pollutants, smoking, and respiratory infections—can compromise lung function (Karaca *et al*., 2025).

Chronic Obstructive Pulmonary Disease (COPD) is a major cause of morbidity and mortality worldwide. This progressive disorder is marked by chronic inflammation and airway obstruction, resulting in impaired ventilation and eventual respiratory failure. Similarly, conditions such as idiopathic pulmonary fibrosis and pulmonary hypertension significantly reduce lung function, diminishing the body's ability to maintain adequate oxygenation (Wang, 2025, Agarwal *et al*., 2023).

In advanced stages of respiratory failure, patients often require oxygen therapy, mechanical ventilation, or, ultimately, lung transplantation. However, the limited availability of donor organs remains a significant barrier. Presently, fewer than 30% of donated lungs meet the eligibility criteria for transplantation, leaving many patients without viable treatment options (Cornea *et al*., 2024).

Organ allocation systems, such as the Lung Allocation Score (LAS), prioritize recipients based on disease severity and urgency. Nevertheless, the demand for donor lungs far exceeds the supply, underscoring the urgent need for alternative solutions. Implantable artificial lungs could partially or fully replace respiratory function in patients with terminal lung failure (Benvenuto & Arcasoy, 2021).

Biomedical engineering has been instrumental in the development of technologies designed to replace lung function. While extracorporeal membrane oxygenation (ECMO) remains the most widely used temporary support for acute respiratory failure, it presents limitations such as thrombosis risk and the necessity of anticoagulation therapy—factors that confine its application to hospital settings and short durations (Vyas & Bishop, 2023). However, ECMO has several limitations, including the risk of thrombosis and the need for anticoagulation therapy, restricting its use to hospital settings and relatively short treatment periods.

Recent advances in biomaterials and microengineering have facilitated the creation of sophisticated devices, including hollow fiber membrane gas exchangers that emulate alveolar function. Moreover, the application of 3D bioprinting has opened new pathways for the fabrication of biohybrid lungs, using decellularized scaffolds that can be repopulated with autologous cells to minimize immune rejection (Mathur *et al.*, 2025; Mirshafiei *et al*., 2024).

Cutting-edge research has led to the development of portable artificial lung prototypes capable of integrating with the circulatory system, offering improved mobility compared to conventional ECMO systems. These devices utilize bio0mimetic microchannels and polymer-based membranes to optimize gas exchange while minimizing clot formation and inflammatory responses.

As research in tissue engineering and nanotechnology advances, implantable artificial lungs are emerging as a realistic solution to address the growing crisis of respiratory failure (Rondón *et al*., 2025). The synergy between biomedical engineering, computational fluid dynamics, and cellular biotechnology continues to drive innovation in this field, promising improved quality of life for millions of patients worldwide.

3.2 Anatomy and Functionality

The lungs are the primary organs of the respiratory system and play a fundamental role in maintaining homeostasis through gas exchange. Located within the thoracic cavity and protected by the rib cage, they are covered by a double-layered pleural membrane that reduces friction during respiratory movements. Structurally, the lungs exhibit a three-dimensional architecture characterized by three surfaces and three borders. Their spongy texture and pinkish-gray coloration are due to extensive vascularization.

Biologically, the lungs possess a complex cellular organization that supports efficient respiratory function. They consist of a branching network of bronchi, bronchioles, and alveoli, where gas exchange occurs. In the alveoli, oxygen diffuses across a thin alveolar-capillary membrane and binds to hemoglobin in erythrocytes for systemic distribution. Carbon dioxide, produced during cellular metabolism, is transported from venous blood to the alveoli to be expelled during exhalation (Soliyeva, 2025; Tonelli & Harman, 2012).

In addition to their respiratory role, the lungs contribute to acid-base homeostasis by modulating carbon dioxide levels in the blood, which directly influence systemic pH. They also participate in blood pressure regulation through the renin-angiotensin system by converting angiotensin I into angiotensin II, a potent vasoconstrictor.

From an immunological standpoint, the lungs house numerous alveolar macrophages and dendritic cells, which play crucial roles in immune surveillance and the elimination of inhaled pathogens. This innate defense system is further supported by ciliated epithelial cells in the bronchial mucosa, which transport mucus and entrapped particles toward the pharynx for clearance (Adivitiya *et al*., 2021).

The structural and functional complexity of the lungs poses a significant challenge for biomedical engineering in designing devices capable of replicating these processes un-

der physiological conditions. Developing implantable artificial lungs requires a deep understanding of respiratory biomechanics, material biocompatibility, and seamless integration with the circulatory system without provoking adverse immune responses.

Advances in biomaterials have facilitated the development of high-efficiency gas exchange membranes inspired by the ultrastructure of alveoli. These have improved extracorporeal oxygenation in devices such as ECMO. Concurrently, tissue engineering has made progress in fabricating decellularized lung scaffolds—donor lungs stripped of immunogenic cells while preserving extracellular architecture—enabling repopulation with autologous cells (Nwanna-Nzewunwa & Keshavamurthy, 2025).

Biomedical engineering has also contributed to the development of microfluidic devices and 3D bioprinting technologies that allow the creation of scaled lung models. These platforms are being used to test pulmonary toxicology and regenerative therapies, further advancing the field (Fleck *et al.,* 2024).

With the rising prevalence of chronic pulmonary diseases such as COPD and idiopathic pulmonary fibrosis, integrating pulmonary biology with biomedical engineering becomes increasingly essential. The convergence of materials science, computational fluid dynamics, and regenerative medicine offers new perspectives for creating artificial lungs that can not only extend patient survival but also restore respiratory functionality in a sustainable and efficient manner (Beghé *et al*., 2021; Ghosh *et al*., 2022).

3.3 Historical Background

The origins of artificial lung development can be traced back to the 19th century, when it was discovered that blood could be oxygenated outside the human body. This breakthrough laid the foundation for technologies capable of replacing pulmonary function and ultimately led to the creation of the heart-lung machine in the 1950s, which enabled prolonged cardiac and pulmonary surgeries by facilitating extracorporeal circulation.

A major milestone occurred in 1972, when Hill and colleagues successfully employed a heart-lung machine to provide respiratory support to a patient with pulmonary failure. This achievement marked a turning point in modern medicine, paving the way for further advancements aimed at extending the use of such devices beyond short-term surgical procedures (Makdisi & Wang, 2015).

Over the following decades, significant advancements were made in extracorporeal membrane oxygenation (ECMO) technology, which emerged as a critical tool for patients with acute respiratory failure. ECMO has proven especially valuable in intensive care settings, including for patients suffering from acute respiratory distress syndrome (ARDS) and severe cases of avian flu, SARS, and COVID-19. Despite its benefits, ECMO is limited by factors such as the need for prolonged anticoagulation, thrombosis risk, and the dependence on bulky equipment, which restricts patient mobility (Nwanna-Nzewunwa & Keshavamurthy, 2025; Sinha *et al*., 2023).

In response to the limitations of ECMO, research has shifted toward developing more advanced artificial lungs using approaches such as hollow fiber membranes, biomimetic microfluidic systems, and biohybrid devices. A recurring challenge across these technologies is the biocompatibility of materials. Prolonged contact between blood and synthetic surfaces can activate immune responses, promote clot formation, and impair gas transfer efficiency, limiting the long-term viability of such devices (Fleck *et al.,* 2024; Thompson *et al*., 2020).

To overcome these obstacles, scientists have investigated strategies such as coating gas exchange membranes with endothelial cells, which mimic the inner lining of blood vessels and reduce coagulation cascade activation. Nanotechnology has also enabled the development of materials with antimicrobial and anticoagulant properties, significantly enhancing the safety and biocompatibility of implantable devices (Jin *et al*., 2025; Pflaum *et al*., 2021).

In the search for more sustainable and biocompatible solutions, researchers have explored the development of decellularized pulmonary scaffolds, a technique in which cells from donated lung tissue are removed, leaving behind an immunogen-free extracellular matrix. This matrix can be repopulated with the patient's own cells, providing a three-dimensional architecture conducive to tissue regeneration and minimizing the risk of immune rejection (Gomes *et al*., 2025).

Although decellularization has shown success in experimental models, its clinical implementation faces several obstacles. One major challenge is the limited availability of suitable donor lungs for this process. Furthermore, cell repopulation remains complex, as it requires the efficient integration of multiple cell types, including pneumocytes, fibroblasts, and endothelial cells, to fully restore pulmonary function (Golebiowska *et al.,* 2024).

Advances in bioengineering and nanotechnology have enabled the emergence of innovative strategies for implantable artificial lung development, including:

- Biohybrid models, which integrate synthetic frameworks with biological tissues to improve functionality and biocompatibility.
- Low-energy oxygenation systems, designed to reduce reliance on mechanical pumps and enhance patient mobility.
- 3D-printed pulmonary scaffolds, fabricated from advanced biomaterials that replicate alveolar microstructures and support cellular integration.
- Autonomous artificial lungs, aiming to eliminate dependence on external devices while maintaining efficient gas exchange.

As science and technology continue to evolve, the integration of tissue engineering, nanotechnology, and biohybrid systems is paving the way for the next generation of

implantable artificial lungs. These innovations represent a promising alternative for treating end-stage pulmonary diseases, with the potential to improve patient outcomes and reduce dependence on organ transplants. Although challenges persist, ongoing research is steadily bringing these devices closer to clinical reality (Mirshafiei *et al*., 2024; Mathur *et al*., 2025; Hannover Medical School, 2021; (Nwanna-Nzewunwa & Keshavamurthy, 2025; Vyas & Bishop, 2023).

3.4 Lung: Current Demand and respiratory pathologies

The persistent shortage of donated lungs and the limited availability of viable organs for transplantation have stimulated research into advanced therapeutic alternatives, such as the development of implantable artificial lungs. Currently, less than one-third of donated lungs meet viability criteria for transplantation, underscoring the urgent need for innovative technologies that can effectively replicate pulmonary function in patients with end-stage respiratory failure (Alvarez *et al.*, 2010; Khayatan *et al*., 2025; Noiseux *et al*., 2009; Barnard, 2020).

Although lung transplantation remains the most effective treatment for severe pulmonary conditions, it is typically reserved for patients who have exhausted all conventional therapies (Arens *et al*., 2020). The main diseases that may necessitate lung transplantation include:

- Chronic Obstructive Pulmonary Disease (COPD): A progressive disorder encompassing emphysema and chronic bronchitis, characterized by airflow obstruction and declining lung function.
- Cystic Fibrosis: A genetic disorder marked by thick mucus accumulation in the airways, leading to recurrent infections and progressive respiratory impairment.
- Idiopathic Pulmonary Fibrosis (IPF): A chronic disease characterized by irreversible scarring of lung tissue, which severely limits gas exchange.
- Pulmonary Hypertension: Elevated pressure in the pulmonary arteries that can result in right heart failure.
- Alpha-1 Antitrypsin Deficiency: A genetic condition that reduces lung protection against inflammation, predisposing patients to emphysema (Stoller, 2025).
- Bronchiectasis: Permanent dilation of the bronchi, leading to mucus retention, recurrent infections, and functional deterioration.
- Occupational Lung Diseases: Conditions resulting from long-term exposure to toxic agents such as asbestos, silica, or coal dust, often culminating in pulmonary fibrosis.

Although lung transplantation remains the most effective intervention, its application is limited to patients who have exhausted all conventional therapeutic options (Arens *et al*., 2020). The main pulmonary diseases that may necessitate a transplant include:

- Chronic Obstructive Pulmonary Disease (COPD): A progressive condition that includes emphysema and chronic bronchitis, leading to airflow obstruction and significant lung function deterioration.
- Cystic Fibrosis: A genetic disorder that causes the accumulation of thick mucus in the airways, leading to recurrent infections and progressive lung damage.
- Idiopathic Pulmonary Fibrosis (IPF): A disease characterized by irreversible scarring of lung tissue, reducing gas exchange capacity.
- Pulmonary Hypertension: Increased blood pressure in the pulmonary arteries, which can lead to right-sided heart failure and the need for a transplant.
- Alpha-1 Antitrypsin Deficiency: A genetic condition that compromises pulmonary protection against chronic inflammatory processes, facilitating the development of emphysema (Stoller 2025).
- Bronchiectasis: Abnormal and permanent dilation of the airways, resulting in recurrent infections and progressive lung function deterioration.
- Occupational Lung Diseases: Prolonged exposure to toxic substances such as asbestos, coal dust, or silica, which can lead to severe pulmonary fibrosis.

Given the considerable risks and limited accessibility associated with lung transplantation, biomedical engineering has focused on enhancing the viability of donor lungs and advancing the development of implantable devices that can replicate essential lung functions (Velleca *et al*., 2023; Podolanczuk *et al*., 2023; Meyer, 2017; Nwanna-Nzewunwa & Keshavamurthy, 2025; Cornea *et al*., 2024; Karaca *et al*., 2025).

3.5 Technological Advances in Implantable Artificial Lungs

3.5.1 Ex Vivo Lung Perfusion (EVLP): Expanding Lung Transplant Availability

In an effort to expand the pool of transplantable lungs, ex vivo lung perfusion (EVLP) systems have been developed to assess, preserve, and rehabilitate donated lungs outside the body prior to transplantation. One notable example is the XVIVO Perfusion System (XPS), an advanced platform that facilitates functional recovery of marginal lungs by maintaining them at normothermic conditions while circulating an oxygenated, nutrient-rich perfusate.

The XPS utilizes the STEEN Solution Perfusate to perfuse lungs with an oxygen-enriched fluid containing essential nutrients and proteins under normothermic conditions, thereby enhancing tissue viability. This system also incorporates advanced monitoring technologies—including X-ray imaging, computed tomography (CT), and weight sen-

sors—that enable precise assessment of organ quality before transplantation.

According to Nakata et al. (2025), EVLP represents a major breakthrough in the field of lung transplantation. It not only allows for infection control and inflammation reduction, but also significantly improves pulmonary function prior to surgery. By enabling the evaluation and rehabilitation of initially non-viable lungs, EVLP has emerged as a transformative strategy to increase transplant success rates and improve patient outcomes (Krishnan *et al*., 2025; Mallea *et al*., 2022).

3.5.2 Biohybrid Lung and Extracorporeal Membrane Oxygenation (ECMO)

The Hannover Medical School (MHH) is currently developing a biohybrid lung based on extracorporeal membrane oxygenation (ECMO) technology. ECMO systems have already been used clinically in patients with severe respiratory failure, including those with critical COVID-19 infections in intensive care units (ICUs), providing temporary support by oxygenating blood outside the body (Alabdullh *et al*., 2023).

Despite its clinical utility, prolonged ECMO use presents major limitations, including thrombosis and immune activation caused by continuous blood contact with artificial surfaces. These complications not only increase patient risk but also limit the duration of ECMO support and its viability for long-term respiratory assistance.

To mitigate these challenges, Dr. Bettina Wiegmann from the Lower Saxony Center for Biomedical Engineering (NIFE) is spearheading research on advanced cellular coatings for ECMO components. Her team is genetically modifying endothelial cells to line gas exchange membranes and blood pumps, thereby reducing immune activation and enhancing hemocompatibility. These innovations aim to extend the functional lifespan of ECMO systems and move toward safer, long-term respiratory support (Orizondo & Cook, 2024; Hannover Medical School, 2021; Pflaum *et al*., 2021).

3.5.3 Implantable Artificial Lungs: Innovation for the Future

Implantable artificial lungs have emerged as one of the most promising solutions for managing chronic respiratory failure. These devices are engineered to integrate with the circulatory system and replicate pulmonary function in an autonomous and continuous manner, offering long-term respiratory support without the need for external systems.

The most advanced prototypes employ synthetic membranes connected to the vascular system via tubing and silicone cannulas. These structures enable gas exchange through oxygen diffusion and carbon dioxide elimination, closely mimicking natural lung function.

Recent technological developments include:

- Gas exchangers with hollow fiber membranes, which serve as temporary respiratory support for patients awaiting lung transplantation.
- Microchannel-based devices, inspired by alveolar microstructures, that enhance gas diffusion efficiency.
- Advanced extracorporeal systems, which have proven critical in sustaining life during severe respiratory failure and act as bridges to transplantation.

One innovative prototype replicates the anatomical structure and size of a human lung using ultra-thin silicone rubber vessels—thinner than a human hair. With a volume comparable to that of a natural lung, the device is designed to operate using the patient's own cardiac pressure, potentially eliminating the need for external mechanical pumps.

Another major advancement is the biohybrid lung based on ECMO principles, which uses hollow polymer fibers to simulate alveolar function and enhance gas exchange. This approach is currently being advanced at Hannover Medical School—Europe's leading center for lung transplantation—underscoring its potential clinical significance (Vos *et al*., 2025; Fleck *et al*., 2024; Blauvelt *et al*., 2021).

3.6 Challenges and Opportunities

The clinical translation of implantable artificial lungs is hindered by several technological and biological challenges. However, these limitations also present opportunities for innovation. The following are the most critical barriers and corresponding research directions in this field:

- Biocompatibility and Risk of Coagulation: A major challenge lies in ensuring that synthetic materials used in artificial lungs are biocompatible. Blood contact with non-biological surfaces can activate the coagulation cascade, increasing the risk of thrombosis. Current research focuses on bioactive surface coatings and the use of genetically modified endothelial cells to reduce clot formation and improve hemocompatibility.
- Enhancing Gas Exchange Efficiency: Artificial devices must match or exceed the efficiency of natural lungs in gas exchange. Efforts are underway to design high-permeability hollow fiber membranes and microchannel-based systems that replicate the alveolar interface, optimizing oxygen diffusion while minimizing resistance to blood flow.
- Support Technology and Miniaturization: Current extracorporeal systems like ECMO are bulky and require constant medical supervision, limiting their use to hospital settings. A major research focus is the miniaturization of these systems through microfluidics and bioinspired design to create compact, autonomous devices suitable for long-term implantation.
- Biohybrid Models and Decellularized Scaffolds:

Combining synthetic and biological elements offers a promising route for functional lung replacements. Decellularized lung scaffolds preserve the three-dimensional architecture of native tissue and, when repopulated with autologous cells, can minimize immune rejection and support functional tissue regeneration.

Regulations and Clinical Trials: Transitioning from laboratory research to clinical use requires adherence to rigorous safety and efficacy standards established by regulatory agencies such as the Food and Drug Administration (FDA) and European Medicines Agency (EMA). Extensive validation through preclinical models and controlled clinical trials is essential to demonstrate the reliability, safety, and performance of implantable artificial lungs.

4 Conclusion

The development of implantable artificial lungs represents a significant milestone at the intersection of biomedical engineering and regenerative medicine, with the potential to revolutionize the treatment of chronic lung diseases and end-stage respiratory failure. The increasing shortage of viable donor organs has driven research into innovative technological solutions aimed at efficiently and safely replicating lung function.

From a biomedical engineering perspective, advancements in biomaterials, nanotechnology, and 3D bioprinting have led to the creation of highly sophisticated devices capable of integrating with the patient's circulatory system and optimizing gas exchange. Hollow fiber membrane gas exchangers, biomimetic microchannel devices, and biohybrid lungs are promising solutions designed to overcome the limitations of extracorporeal membrane oxygenation (ECMO), offering more sustainable alternatives with a lower risk of complications.

One of the most critical challenges in this field is the biocompatibility of the materials used, as prolonged interaction with blood can induce adverse immune responses and clot formation. Tissue engineering has addressed this issue through the decellularization of donor lungs, which retain the extracellular architecture and can be repopulated with autologous cells, thereby reducing the risk of rejection. Furthermore, the integration of biohybrid models, which combine synthetic structures with living cells, represents a key strategy to enhance the functionality and viability of implantable artificial lungs.

With advancing technology, miniaturization and autonomous device development have become top priorities to enhance patient mobility and reduce reliance on bulky equipment. Optimizing device design through computational fluid dynamics modeling and 3D printing of pulmonary scaffolds will significantly improve efficiency, bringing clinically viable artificial lungs closer to reality.

From a biomedical perspective, the future of implantable artificial lungs will depend not only on technological improvements but also on rigorous validation through preclinical studies and clinical trials to ensure their safety and efficacy. Collaboration between biomedical engineers, physicians, and biotechnology researchers will be crucial for the successful implementation of these innovations in clinical practice, offering new hope to patients with chronic respiratory failure and reducing exclusive reliance on lung transplants.

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