SmartReactors

ECMO AND CPB: SCIENTIFIC ADVANCES AND FUTURE DIRECTIONS

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1.0 Introduction

Extracorporeal Membrane Oxygenation (ECMO) and Cardiopulmonary Bypass (CPB) are fundamental approaches in the management of patients with severe cardiac and respiratory failure. Their clinical significance lies in their ability to serve as bridges to recovery, transplantation and for mechanical support in cases refractory to conventional therapies. While CPB is primarily employed as a short-term circulatory solution during cardiac surgery to replace heart and lung function, ECMO is designed to provide prolonged extracorporeal support enabling sustained oxygenation for critically ill patients. Initially developed as a supplement to CPB systems, ECMO has evolved into a vital component of intensive care treatment, capable of temporarily replacing heart and lung functions. Despite the life-saving capabilities of ECMO and CPB, both systems are associated with complications, such as thrombosis and impaired gas exchange, limiting their overall effectiveness. Smart Reactors Camouflage™ Coating technology is a novel solution that addresses these complications. This advanced surface coating reduces the risk of blood clots, inflammation and facilitates efficient gas exchange. Advancements in ECMO and CPB systems have led to significant refinements, with innovations such as Camouflage™ coating transforming the management of patients with life-threatening cardiopulmonary compromise. This paper explores the clinical importance of ECMO and CPB, with a focus on recent technological advancements that are shaping the future of these life-saving interventions. It also explores how Smart Reactors Camouflage™ offers an innovative solution to overcome the current limitations of both ECMO and CPB systems, enhancing safety, efficiency, and long-term patient outcomes.

Fig 1: Extracorporeal Blood circuit

1.1 Scope and Significance of ECMO and CPB

ECMO has dramatically evolved over the last 40+ years, transforming from a cardiopulmonary bypass adjunct into a therapy for patients with severe cardiac and respiratory failure. It provides temporary support by oxygenating blood outside the body and returning it to systemic circulation. ECMO plays a central role in managing acute respiratory distress syndrome (ARDS), cardiogenic shock, post-cardiotomy failure, severe acute asthma and serves as a bridge to heart or lung transplantation [1]. Its scope extends beyond traditional intensive care units (ICU) to emergency departments, operating rooms and even prehospital environments facilitated by advances in portable and biocompatible ECMO systems. CPB is a technique that temporarily assumes the function of the heart and lungs by diverting venous blood away from the heart, oxygenating it and removing carbon dioxide via an external oxygenator. It subsequently returns the oxygenated blood to systemic circulation using a mechanical pump (heart-lung machine). The process is tightly regulated to maintain adequate tissue perfusion and metabolic stability. The clinical significance of ECMO and CPB lies in their ability to stabilize hemodynamics and gas exchange, effectively allowing time for myocardial, pulmonary recovery or transition to definitive therapies such as ventricular assist devices and transplantation [1]. Despite their transformative potential, ECMO and CPB remain resource-intensive and require multidisciplinary management to prevent complications. Survival outcomes vary for both systems (CPB ~ 95%, ECMO ~ 55%) depending on clinical indication, patient population and specific modality of support used.

1.2 Veno-Venous and Veno-Arterial ECMO

Veno-venous (VV)-ECMO is primarily used for patients experiencing life-threatening conditions such as ARDS where lung function is compromised. In VV-ECMO, blood is withdrawn from a central vein, typically the femoral or internal jugular vein and passed through an oxygenator where gas exchange occurs. The oxygenated

blood is returned to venous circulation from the right atrium to circulate through the pulmonary vasculature, and into systemic circulation (Fig. 2) [2]. The two principal techniques employed are double-lumen cannulation or multiple cannulations. When using a double-lumen cannula, the tip is advanced from the insertion point at the right jugular vein into the right atrium and further into the inferior vena cava. When using multiple cannulas, the drainage cannula is usually placed in either the superior, inferior vena cava or femoral vein.

Veno-arterial (VA)-ECMO is often used for patients with combined cardiac and respiratory failure or profound cardiogenic shock. Venous blood is drained from a large central vein, oxygenated outside the body and then returned into the arterial system, effectively substituting for both cardiac output and gas exchange (Fig. 3). In VA-ECMO, cannulation can be performed either centrally or peripherally. In central cannulation, a drainage cannula is inserted in the right atrium or superior vena cava, and a return cannula is inserted in the aorta allowing blood to be drained directly into the arterial system. In contrast, peripheral cannulation can be performed in multiple configurations, some of which are the femoral-femoral, where drainage cannula is placed in the femoral vein and the return cannula is placed in the femoral artery.

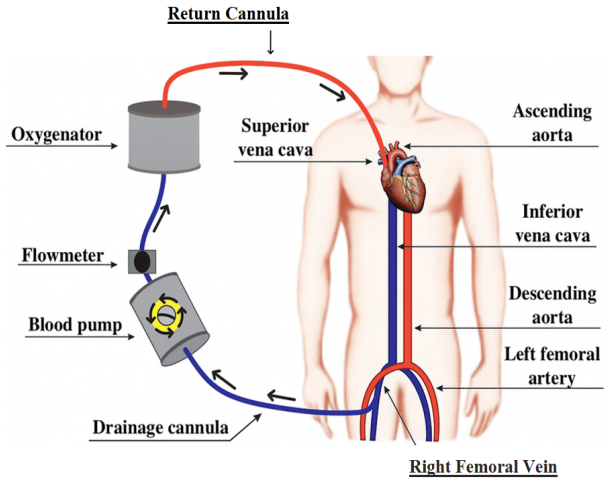


Fig 2: Image showing VV-ECMO circuit setup

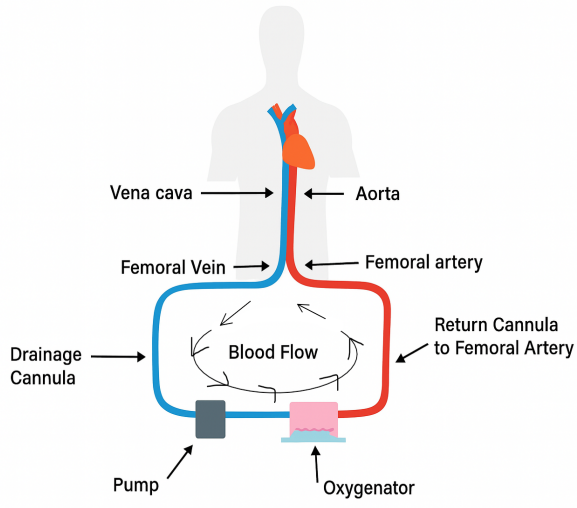


Fig 3: Image showing VA-ECMO circuit setup.

1.3 Overview of CPB Systems

CPB systems are essential for facilitating cardiac surgery by temporarily replacing the functions of the heart and the lungs. These systems typically include a venous reservoir, oxygenator, pump and tubing that directs blood flow outside of the body, where it is oxygenated and returned to the arterial circulation (Fig. 4). Conventional CPB typically employ an open, uncoated venous reservoir and roller pump mechanism. This configuration exposes the patient's blood to substantial blood blood-air interface, which can activate inflammatory pathways and contribute to a systemic inflammatory response. In contrast, miniaturized extracorporeal circulation (MECC) systems represent a more biocompatible approach, employing a closed circuit with active venous drainage and a centrifugal pump. This design minimizes blood contact with air and artificial surfaces, reduces mechanical trauma, and eliminates cardiotomy suction, thereby limiting inflammatory mediator activation and microembolization. MECC has been associated with improved hemodynamic stability, enhanced tissue oxygenation, and a reduction in postoperative complications, making it a promising alternative to traditional CPB systems.

2.0 Advancements in CPB & ECMO

In 1953, Dr. John Gibbon achieved the first successful clinical application of a heart-lung machine, utilizing a roller pump-driven CPB circuit to facilitate the surgical repair of an atrial septal defect under total extracorporeal circulation. ECMO was developed later in the 1970s as an experimental therapy of CPB for long-term support in neonatal respiratory failure. CPB and ECMO have since undergone remarkable evolution in modern critical care. This transformation has been propelled by continuous advancements in both technologies and clinical protocols. In CPB, the integration of AI-driven clinical decision support tools enables safer and individualized protocols. Innovations in biocompatible coatings with advanced hemocompatible surfaces have significantly decreased clot formation and inflammatory activation, improving outcomes and equipment durability. Additionally, CPB systems now emphasize miniaturized, closed-circuit designs with reduced blood-air exposure and priming volumes minimizing hemodilution. Recent advances in ECMO include, the emergence of levitated centrifugal pumps combined with biocompatible polymethylpentene (PMP) membrane oxygenators markedly improving flow dynamics and gas transfer efficiency while mitigating hemolysis and inflammatory activation.

2.1 Advancements in Pump Engineering

The evolution of pump technologies has significantly enhanced the safety and efficacy of extracorporeal support. Historically, peristaltic pumps have been the standard choice for CPB support, utilizing a rotating mechanism that compresses flexible tubing against a curved track to propel blood flow (Fig. 4). However, these systems often present limitations, primarily related to mechanical stress exerted on the circuit tubing. The generation of high positive pressures downstream of the pump, in combination with repetitive compression, increases the risk of tubing rupture. To mitigate this risk, extended lengths of tubing are often required to allow for repositioning within the roller-head further increasing the circuit size, priming volume and patient exposure to non-biological surfaces. Modern centrifugal pumps are the current standard in ECMO, particularly those utilizing seamless, low-friction technology offer significantly improved performance and efficiency [3]. These systems enable the use of small circuits with lower priming volumes reducing damage to blood cells and the incidence of haemolysis. Hemolysis occurs when excessive shear forces within the circuit, particularly at the pump-impeller interface leading to the release of free haemoglobin into the plasma. This can result in complications such as acute kidney injury, increased inflammation, and impaired oxygen delivery. Modern centrifugal pump designs and biocompatible coatings aim to reduce these risks, thereby improving hemocompatibility and patient outcomes.

Magnetically levitated pumps are one of the most promising developments using magnetic fields to levitate and rotate the impeller, eliminating mechanical friction and contact between moving parts of the pump and the blood. Maglev pumps, operating without mechanical contact, minimize blood trauma such as haemolysis and platelet activation, allowing for prolonged use without replacement.

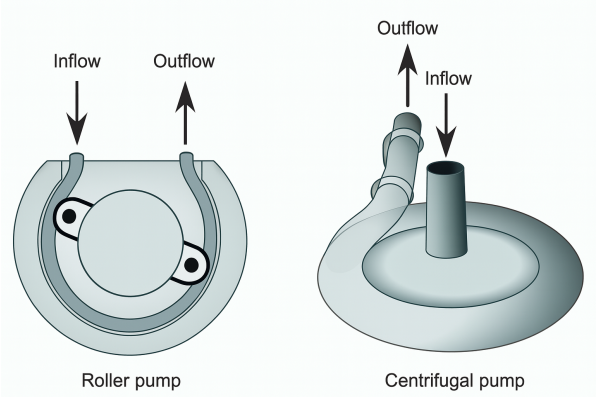


Fig 4: Roller-Head Pump used in CPB and Centrifugal pump used in ECMO

2.2 Innovations in Membrane Oxygenators

Current oxygenator technology has evolved with the adoption of polymethylpentene (PMP) hollow-fibre membranes, largely replacing older materials such as polypropylene. PMP membrane oxygenators are the standard in ECMO support, however, their use in CPB is selective, typically only reserved for prolonged procedures or in cases where ECMO is anticipated. PMP is a polymer featuring an asymmetric pore structure and outer skin layer designed to deliver gas exchange efficiency through reduced resistance and enhanced biocompatibility (Fig. 5). This enables prolonged extracorporeal support while minimizing plasma leakage and inflammatory activation. Integration of sensor technology into oxygenators and pump systems now permits real-time monitoring of blood gases, pressures and flow dynamic's allowing close-loop automated regulation of extracorporeal parameters to optimize

oxygen delivery and carbon dioxide removal. These advances collectively allow for safer, more effective support tailored to the patients evolving clinical condition.

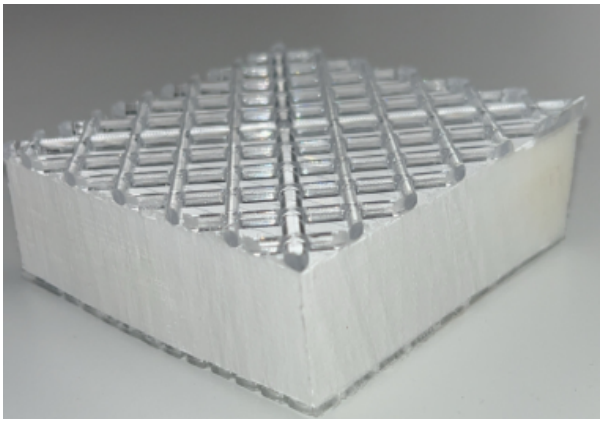


Fig 5: Cross sectional image of PMP hollow-fibre membrane in an oxygenator

2.3 Mobile Systems for Critical Care

The miniaturization of CPB systems has significantly expanded their clinical utility, transforming extracorporeal therapy from a modality once confined to ICU into one suitable for transport and field deployment. These compact systems enable rapid initiation of life-saving circulatory and respiratory support in diverse settings, improving accessibility and outcomes in time-critical settings. Portable ECMO consoles such as Cardiohelp by Getinge and ECMOLIFE by (Eurosets), integrate pumps, oxygenators and monitoring systems into compact battery-operated units [4]. These devices maintain full cardiopulmonary support capabilities enabling critical life-saving interventions during transport. Advances in cannula design using flexible, atraumatic materials further enhance patient mobility and reduce vascular complications. Emerging wearable ECMO technologies incorporate compact power sources, integrated controls and capabilities to facilitate long-term extracorporeal support outside the intensive care environment.

2.4 Advances in Biocompatible Surfaces

Biocompatibility remains central to reducing ECMO and CPB associated complications such as coagulation cascade activation, platelet adhesion and systemic inflammation. Recent innovations such as Smart Reactors Camouflage™ technology has emerged to minimize thrombogenicity and mitigate risk of inflammatory responses to the extracorporeal circuit. This surface coating collectively improves the durability, hemocompatibility and safety of ECMO and CPB systems, particularly for prolonged support necessitated by chronic respiratory or cardiac failure. Unlike traditional heparin coatings**,** which may pose risks such as heparin-induced thrombocytopenia (HIT), advanced biocompatible coatings like Camouflage™ offer a non-heparin-based alternative that reduces thrombosis. Biocompatible coatings like Camouflage™ utilized for cannulas, tubing, oxygenator membranes not only extend circuit longevity but also reduce the risk of clot formation and associated device failures. Together, these advancements represent a paradigm shift in ECMO and CPB design, moving from inert materials to bifunctional interfaces that interact with blood improving patient outcomes and enabling longer, safer extracorporeal support.

3.0 Clinical Complications in ECMO and CPG Therapies

While ECMO and CPG therapies provide life-saving support in cases of cardiac and respiratory failure, they are inherently complex interventions associated with a broad range of clinical complications. The most common encountered challenges are related to anticoagulation management, cerebrovascular infection and inflammation.

3.1 Thromboembolic Risk Management

One of the most fundamental challenges in ECMO and CPB management is targeting optimal anticoagulation strategies for the prevention of circuit thrombosis while attenuating the risk of bleeding. Thrombosis is a prevalent occurrence and a major concern for patients on ECMO and CPB therapy. Exposure of the patients' blood to foreign substances, non-physiological shear-stress, and alteration of critical illness increases the risk of a thrombotic event to occur. Clot formation can obstruct critical circuit components such as the oxygenator, pump head or cannulas leading to impaired flow, compromised gas exchange and ultimately oxygenator failure. This can be indicated by a rise in transmembrane pressure often requiring urgent circuit exchange. Furthermore, thrombosis can elevate intraluminal shear forces, which in turn can induce hemolysis, activate leukocytes and initiate an inflammatory response. Utilizing target anticoagulants like bivalirudin guided by real time parameters e.g. ACT, helps maintain therapeutic ranges

without over treatment. In CPB, high dose unfractionated heparin is used to achieve an ACT>400 seconds. ECMO requires lower-dose prolonged anticoagulation typically heparin infused monitored by ACT or anti-Xa levels. Advances in surface coatings such as Smart Reactors Camouflage™ Coating may reduce thrombogenicity, minimizing the need for high-dose systemic anticoagulation.

3.2 Cerebrovascular Embolization

The potential for cerebral embolization constitutes a major neurological risk in the context of ECMO and CPB therapy. Patients receiving extracorporeal support are at risk of ischemic stroke as a result of thromboembolism. In patients on VA- ECMO with blood return to the femoral artery, it is possible for the vessels to receive poorly oxygenated blood from the dysfunctional lungs while the remainder of the body is perfused by well-oxygenated blood from the ECMO circuit. This is known as Harlequin syndrome and can lead to chronic cerebral hypoxia. Optimizing blood flow and maintenance of mean arterial pressure helps to ensure sufficient perfusion to vital organs including the brain.

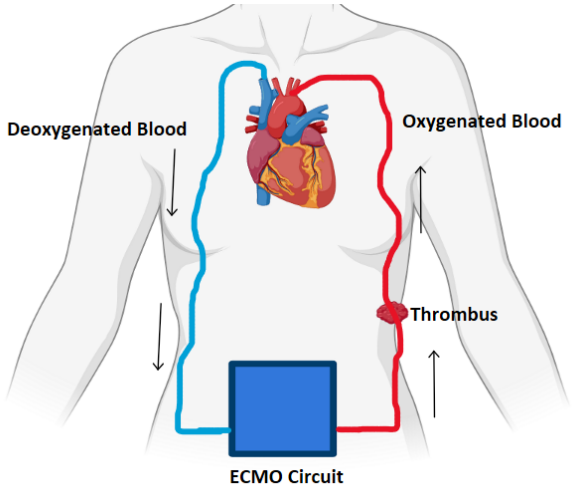


Fig 6: Blood clot has become part of the bloodstream,

3.3 Left Ventricular Unloading

In VA-ECMO, challenges related to left ventricular (LV) distension and inadequate unloading are frequently encountered, significantly impacting patient outcomes. While VA-ECMO provides robust circulatory support by diverting venous blood through an extracorporeal circuit for oxygenation and returning it to the arterial system, this aortic flow can substantially increase LV afterload, leading to elevated pressure within the left ventricle. This can impair LV function, contribute to pulmonary congestion, and exacerbate myocardial dysfunction. Inadequate LV unloading during CPG increases myocardial wall tension leading to a higher oxygen demand and leads to fluid transudation into the alveoli.

3.4 Associated Infections

The insertion of cannulas provides potential entry points for infections. Adhering to aseptic technique during cannulation and closely monitoring for signs of infection e.g. fever or elevated inflammatory markers, is essential for ensuring patient safety and preventing complications. Extracorporeal patients with prolonged support are susceptible to systemic infections due to foreign materials in the circuit. Close surveillance for signs of sepsis and proactive infection control measures is imperative in minimizing the risk of complications [4].

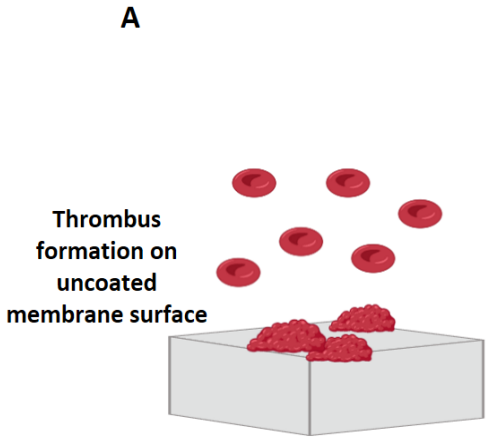
4.0 Trends and Global Market Expansion in ECMO and CPB

The ECMO and CPB market has experienced notable growth in recent years, attributed by the increasing demand for advanced extracorporeal support in critical care. As of 2025, the global ECMO system market is valued at USD 601.06 million and is projected to grow to USD 750.10 million by 2030. VA-ECMO retained 55% of the extracorporeal system market in 2024 reflecting its dual heart-lung support versatility. While North America remains the dominant market due to advanced healthcare infrastructure, Asia-Pacific is the fastest growing region driven by expanding hospital capacity. Current market trends involve the development of user-friendly systems, long-lasting oxygenators and AI-driven perfusion control algorithms, all aimed at enhancing patient outcomes while minimizing complications such as hemolysis, thromboembolism and inflammation. Leading manufacturers include Getinge, Medtronic, LivaNova, Terumo, and Abiomed. The Abiomed Breethe OXY-1 System was cleared in 2020 for cardiopulmonary bypass and short-term ECMO support, with expanded use under emergency authorization during the COVID-19 pandemic. LivaNova's Essenz Heart–Lung Machine received FDA 510(k) clearance in March 2023, followed by its Essenz In-Line Blood Monitor in August 2023, both approved for use during cardiopulmonary bypass procedures.

Current trends focus on user-friendly systems, durable oxygenators, AI-driven perfusion controls, and biocompatible coatings such as Smart Reactors Camouflage™, all aimed at enhancing safety, reducing complications such as thrombosis, and enabling longer support durations.

5.0 The Role of Camouflage™

Surface modifications are pivotal in optimizing the safety and efficacy of extracorporeal support systems. Smart Reactors Camouflage™ coating technology represents a significant advancement in this field. This non-pharmaceutical, hemocompatible surface coating is engineered to enhance the performance of blood-contacting devices. By reducing thrombotic and inflammatory responses, supporting efficient gas exchange, Camouflage™ enhances biological integration for extracorporeal support. Camouflage™ coating technology functions to effectively conceal the surface of the device preventing direct interaction with the surrounding circulating blood. It achieves this by attracting non-inflammatory proteins from the patients' blood to the coated surface. This advanced interface regulates blood-material interactions, minimizing the biological responses that lead to clot formation and immune system activation.



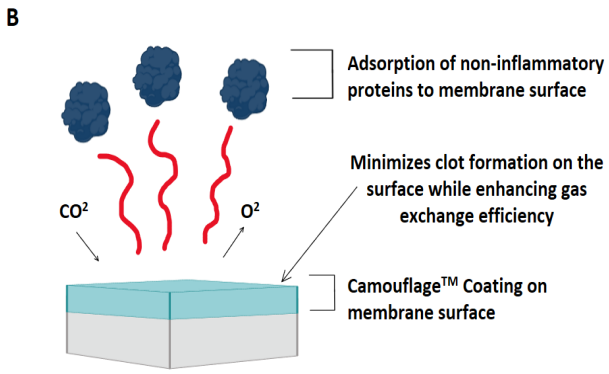


Fig 7: Smart Reactors Camouflage™ Coating Mechanism of Action on oxygenator membrane (A) Uncoated membrane surface with thrombus formation. (B) Camouflage Coated membrane surface reducing inflammation, thrombosis and supporting efficient gas exchange

5.1 Camouflage™ Clinical Benefits

Reduced Thrombosis Risk

By promoting a smooth, biologically inert and blood-compatible surface, Camouflage™ technology minimizes platelet adhesion, thereby significantly reducing the risk of thrombus formation within the extracorporeal circuit.

Enhanced Gas Exchange

By maintaining a clean membrane surface, Camouflage™ preserves the diffusion gradients essential for optimal gas exchange. As a result, the efficiency of oxygen transfer and carbon dioxide removal is sustained over time, ensuring consistent extracorporeal performance and reducing the need for frequent oxygenator replacement.

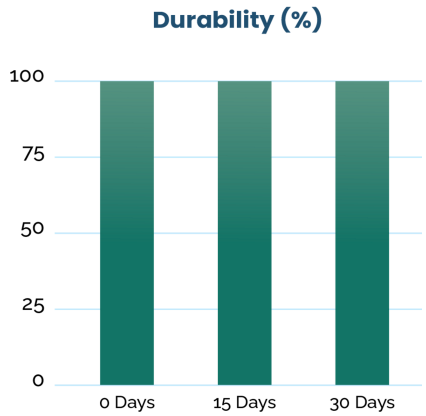


Fig 8: Graph indicating Camouflage™ coating on ECMO tubing exhibiting minimal degradation during 30-day saline solution flow test of 6 liters per minute at 37⁰C

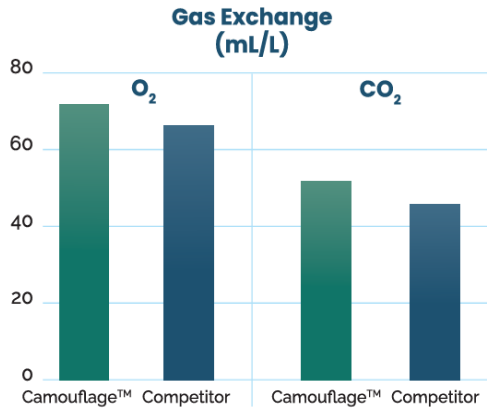


Fig 9: Camouflage™ coating exhibits excellent gas exchange properties with minimal impact on oxygen and carbon dioxide rates

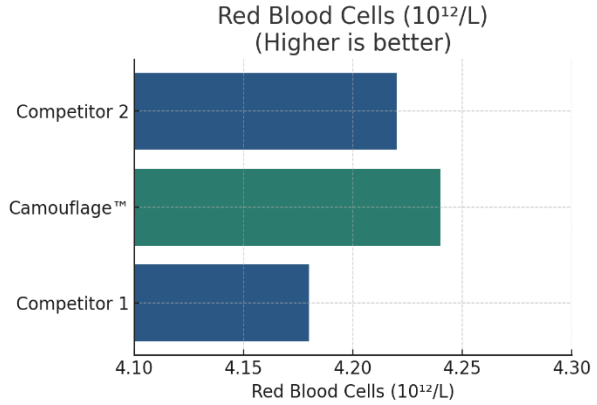


Fig 10: Camouflage™ exhibiting higher red blood cell count than competitor coatings

Minimized Immune Reactions

Camouflage™ is engineered to enhance biocompatibility ensuring blood-contacting devices integrate smoothly into the body without triggering excessive immune responses. This coating promotes a more stable and biological surface supporting both device function and patient safety over prolonged use.

Increased Device Longevity

Camouflage™ demonstrates its effectiveness in device longevity through its hemocompatibility by maintaining ECMO and CPB component functionality while reducing overall maintenance requirements. This contributes to enhanced system reliability and improved patient safety.

Ultra-Thin

Camouflage™ coating is just a few nanometres thick and is suitable for a broad range of applications within the medical device space. This ultra-thin coating does not impede gas exchange permeability on perfusion devices and is custom developed to avoid thrombus formation.

6.0 Camouflage™ Analysis

Hemocompatibility

The reduced PMN elastase levels are observed with Smart Reactors' Camouflage™ coating indicating a lower propensity for initiating an inflammatory response. This reduction, when compared to phosphoryl choline (PC) and albumin-based coatings, indicates Camouflage™ interacts favourably with blood components (Fig. 10). A reduced inflammatory response is a critical marker of hemocompatibility reflecting minimized risk of thrombotic complications often seen with extracorporeal circuits.

Anti-Inflammatory

Camouflage™ coating minimizes the interaction with white blood cells and reduces the inflammatory response. Camouflage™ coating minimizes interaction with white blood cells, significantly reducing the activation of an inflammatory response. Data demonstrates white blood cells exhibiting minimal adhesion to the surface (Fig. 11).

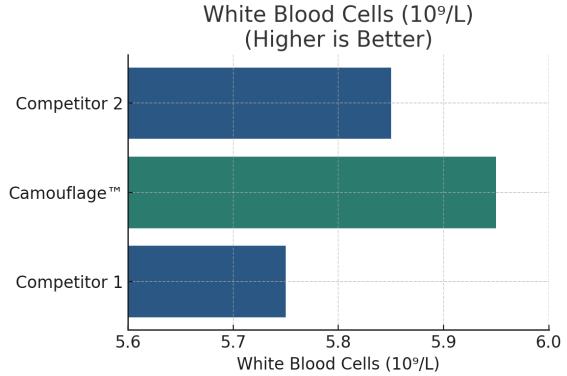


Fig 11: White Blood Cell Levels

7.0 Future Directions

Future directions in ECMO and CPB revolve around the ongoing miniaturization, integration, and enhanced biocompatibility of these extracorporeal systems to expand their applicability beyond conventional ICU settings. Future research will emphasize the development of integrated sensor arrays and intelligent control algorithms that dynamically adjust perfusion parameters in response to physiological feedback, thereby optimizing oxygen delivery while minimizing complications such as thrombosis. Additionally, advances in novel biocompatible coatings such as Smart

Reactors Camouflage™ will improve thrombogenicity, reduce inflammation and promote efficient gas exchange driving continued innovation in perfusion science and extracorporeal technologies.

8.0 Conclusion

ECMO and CPB are advanced therapies that play pivotal roles in managing critically ill patients with severe cardiac and respiratory failure. Recent scientific advancements such advanced centrifugal pumps, PMP oxygenators, portable and miniaturized extracorporeal support systems and biocompatible coatings such as Camouflage™ have markedly improved the safety, efficacy, in diverse clinical settings. Innovations continue in circuit design, anticoagulation strategies, and patient monitoring, which will aim to enhance patient survival. Despite these advancements, ECMO and CPB remain resource-intensive processes with substantial risks and limitations. Challenges persist in optimizing patient selection and minimizing complications such as thrombosis. Smart Reactors' Camouflage™ coating exemplifies the next frontier in enhancing ECMO and CPB biocompatibility by reducing inflammatory responses, thrombotic risk and preserving gas exchange efficiency. As surface engineering technologies continue to advance, this coating has the potential to redefine safety benchmarks and enhance the durability of extracorporeal life support, even in the most challenging clinical environments.

9.0 References

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