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In vitro VV-ECMO mock circuit to quantify oxygen transfer across ARDS and ECMO weaning stages

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Abstract: A continuous dual-loop mock circuit for venovenous extracorporeal membrane oxygenation (VV-ECMO) was developed to quantify oxygenation contributions across simulated pathophysiological (acute respiratory distress syndrome, ARDS) and therapy stages (ECMO weaning). ARDS stages (mild to severe) were calibrated for simulated patients using Berlin-definition targets and model-derived setpoints. The calculation of relative partitioning, oxygen transfer rate, and gas exchange ratio was enabled by four-site blood gas measurement. The results indicate the presence of distinct plateaus and a consistent shift of oxygenation from ECMO to lung compartment during ECMO weaning. The setup provides a foundation for future gas exchange models and weaning strategies.

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I. Introduction

Acute respiratory distress syndrome (ARDS) is classified as mild, moderate, or severe based on the ratio of arterial oxygen partial pressure to inspired oxygen fraction ($P_{O2,a}/F_{i,O2}$) [1]. In cases of severe ARDS, venovenous extracorporeal membrane oxygenation (VV-ECMO) is employed to ensure systemic oxygen delivery and facilitate lung protective ventilation. During ECMO therapy and weaning maneuvers, the relative contributions of oxygen transfer between the native lung and the membrane oxygenator become key determinants of arterial oxygenation. In vivo, this partitioning can usually only be inferred indirectly (e.g., from flow or gas exchange calculations).

Several mathematical models describe cardiopulmonary gas-exchange with and without VV-ECMO, typically as compartment models. These range from integrated respiratory models without extracorporeal support [2] to VV-ECMO gas exchange models that incorporate shunt and, in some cases, recirculation [3],[4]. However, these frameworks remain purely computational and depend on parameter assumptions that are challenging to validate under controlled conditions. Complementary in vitro setups and lung models have been developed to examine individual subsystems (e.g., oxygenators, carbon dioxide removal, lung surrogates) [5], [6], [7].

Despite these developments, a continuous VV-ECMO mock circuit that explicitly separates lung, tissue, and extracorporeal compartments and permits controlled, repeatable modulation of ARDS severity with stepwise weaning has not been established. To address this gap, a blood-based dual-loop VV-ECMO mock circuit with dedicated lung and tissue exchange and ECMO modules was developed and characterized to quantify compartment-wise oxygen transfer across ARDS stages under standardized weaning maneuvers (Figure 1).

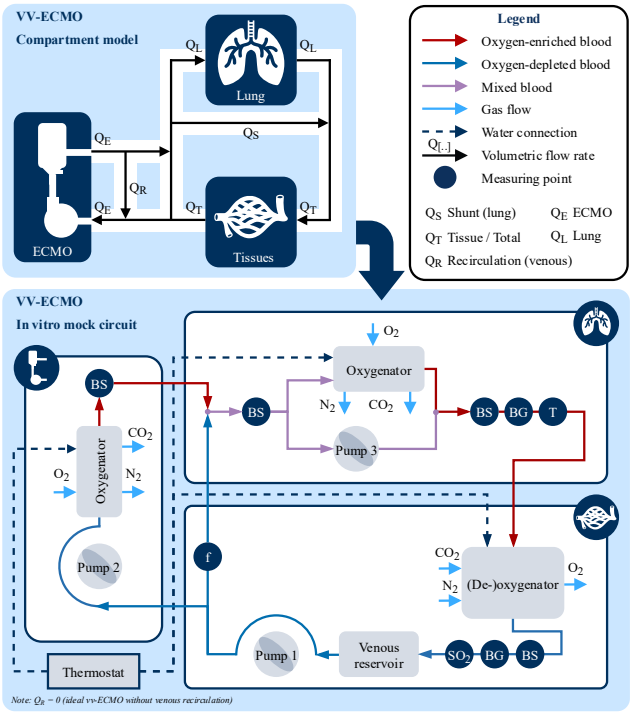

Figure 1: Compartment model (base) and resulting in vitro mock circuit with measuring points for temperature (T), flow (f), blood gases (BG), blood samples (BS) and oxygen saturation (S_{O2}).

II. Material and methods

The developed in vitro mock circuit was evaluated in a validation case study and consists of lung, tissue, and ECMO compartments. It incorporates a lung shunt but no venous recirculation ($Q_R = 0$). The lung compartment includes pump 3 (Ismatec MCP Process) to control shunt flow (Q_S) and a lung-analog oxygenator (Terumo CAPIOX FX05) to represent the native lung. The tissue compartment consists of pump 1 (Ismatec MCP Process) and an oxygenator with an integrated venous reservoir (Terumo

CAPIOX FX25 Advance), mimicking systemic tissue metabolic load. The ECMO compartment includes pump 2 (Ismatec MCP Process) and an additional oxygenator (Terumo CAPIOX FX05). A thermostat (Labortechnik Meding T200), connected to all heat exchangers, ensures a normothermic perfusate temperature (37 °C). All components are connected via silicone tubing. Two flow regulators and a three-channel gas mixer (Q-CAL GMS 3_CH) are utilized to ensure precise gas supply. Venous and arterial blood samples are collected offline, with subsequent analysis performed using a blood gas analyzer (Radiometer ABL80 basic). Measurement equipment for continuous blood flow (Sonotec SonoFlow Co.55), blood gas and oxygen saturation (S_{O2}) monitoring (Terumo CDI 500) are integrated to facilitate trend observation and calibration.

The circuit was primed with 2 liters of heparinized Ringer's solution. The perfusate, 2 liters of anticoagulated porcine blood (heparin; 10.000 IU/liter; slaughter process), was added to the system and conditioned according to venous physiological reference values (healthy human). ARDS stages were implemented according to the Berlin definition [1] into severe, moderate, mild (A1-A3). Two patients types were simulated: one with ventilation ($F_{i,O2} = 0.6$) and one without ventilation ($F_{i,O2} = 0.21$). Target arterial p_{O2} and S_{O2} were computed. Compatible venous values and shunt fractions were taken from Zanella et al. [3] and used to calibrate the lung shunt at a total blood flow of 1.5 l/min. ECMO blood flow was adjusted between 1.3 and 0.1 l/min in discrete steps (W1-W6) to represent therapy and standardized weaning. At each setting, the circuit was allowed to reach quasi-steady state and blood samples were drawn at all four measurement sites. Difference-based relative partitions (e.g., based on Δp_{O2} and ΔS_{O2}), oxygen transfer rates ($\dot{V}_{O2}$), and gas exchange ratios ($r_{O2,ECMO}$) [8] were calculated.

III. Results and discussion

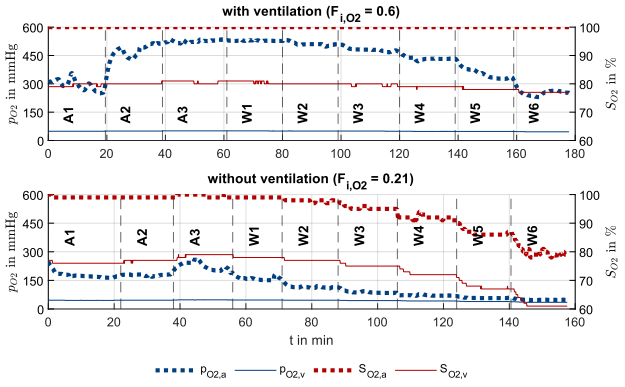

Figure 2: Continuous trend monitoring of venous (v) and arterial (a) oxygen partial pressure (p_{O2}) and saturation (S_{O2}) across ARDS severity (A1-3) and weaning steps (W1-6).

Continuous trend monitoring revealed distinct quasi-steady plateaus corresponding to the preset ARDS severities and subsequent systematic stepwise ECMO weaning (Figure 2). Difference-based relative partitioning indicated a progressive redistribution of oxygenation towards the lung compartment. This trend was observable for cases with and without ventilation. Content-based oxygen transfer analysis ($\dot{V}_{O2}$) confirmed the declining ECMO fraction, but estimates for the lung compartment were more sensitive to sources of error and occasionally yielded to negative values. Overall, $r_{O2,ECMO}$ demonstrated a significant decrease across weaning, indicating a shift of oxygenation contribution towards the lung compartment (Figure 3).

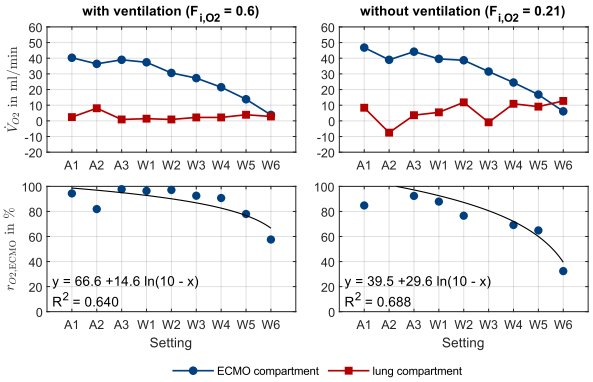

Figure 3: Significant decrease of ECMO oxygenation contribution with shift toward the lung compartment.

IV. Conclusions

The in vitro mock circuit and experimental procedures developed enable a systematic assessment of relative oxygen transfer in VV-ECMO. In addition, they provide a foundation for benchmarking gas exchange models and evaluating weaning strategies under controlled conditions. Future work will focus on enhancing automation, refining the system to address limitations (e.g., venous recirculation), and expanding the sample size.

Author's Statement

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