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Membrane Blood Oxygenators: Oxygen Mass Transfer in a Gas/Membrane/Liquid System

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Abstract— **Despite the widespread use and the decades of continuous developments of the Membrane Blood Oxygenators, several aspects related to the membrane/blood interactions, circulating blood flow conditions and equipment design still need to be improved. Fundamental studies of the blood flow and blood/membrane interface are required to fully understand the effect of the membranes surface and of the conditions of circulation on the gas transfer. The oxygen mass transfer of integral asymmetric hemocompatible polyurethane-based membranes was investigated in a MBO surrogate system that allow the direct assessment to the oxygen fluxes. This system consists of a slit for water circulation as a surrogate blood flow channel and a constant pressure oxygen chamber separated by the membranes in study. A model of the oxygen mass transport in this system was previously verified. The oxygen fluxes were predicted for different conditions of operation. The effect of the circulation conditions and oxygen feed pressure on the required membrane area to assure oxygen physiological needs was investigated. The contribution of the liquid boundary layer resistance is evidenced by the increase of the oxygen fluxes with the increase of the liquid flow rates. The present benchmark device can accommodate membrane/boundary layer disruptors to promote flow fields, enhancing the oxygen mass transfer. Membrane/boundary layer disruptors composites are prepared by deposition of electrospunned fibers over the membranes surface. Their effect in the oxygen mass transfer and blood integrity is under investigation.**

I. INTRODUCTION

Membrane blood oxygenators (MBOs), are one of the main components of the perfusion system, and like natural lungs they are responsible for the gas exchanges. Patients need to be connected to these systems during cardiac surgeries where cardiopulmonary by-pass (CPB) is performed, allowing surgeons to operate in motionless and bloodless environment [1]. Blood oxygenators are also used in Extracorporeal Life Support (ECLS), the set of therapies that artificially supports pulmonary and/or cardiac system for long periods of time (days to weeks), allowing the organs to heal from lung and/or cardiac failure [2]. Different types of MBOs, with different materials, emerge along the decades of development. The paralel plates of the Land-Edwards oxygenator [3] and in the disposable coiled membrane oxygenator developed by Kolobow [4] included silicone membranes and allowed the introducing of the long term application due to the low blood damage that was inflicted. In the 70s the hollow fiber oxygenators began to be used in extracorporeal oxygenation [5]. To overcome the hydraulic resistance and boundary layer formation, crossflow hollow fiber oxygenators were developed where blood flowed outside of hollow fibers while oxygen was fed from the inside of the fiber lumens [6]. Coagulation issues associated to the silicon hollow fibers led to the introduction of polypropylene microporous membranes [7], [8]. These membranes had open pores with the diameter on the order of magnitude of 1 mm that greatly increased the mass transfer. Although, a new problem emerged: the plasma wetting, where plasma gradually infiltrates in the membrane porous, affecting the gas transport and possibly leading to device failure within days, requiring the replacement of the oxygenator [9]. Regarding the plasma wetting problems, composite hollow fibers incorporating a thin nonporous silicone layer as skin at the microporous fiber surface were developed. This hydrophobic material prevents and blocks the infiltration of plasma increasing the oxygenator longevity, although the rate of gas exchange was affected [10]. The de Pinho research group [11] developed noncommercial integral asymmetric polyurethane (PUR)-based membranes and companies such as MembranaGmbH developed asymmetric hydrophobic hollow fiber membranes of poly-methyl pentene (PMP), addressing the need of preventing the plasma infiltration [12]. Despite the widespread use and the decades of continuous development, several aspects related to the membrane/blood interactions, circulating blood flow conditions and equipment design still need to be improved [13], [14]. The development of the membranes for MBOs is deeply connected with the past evolution of the device itself, promoting great technological steps and clinical advantages. Membranes of different types and of different materials were incorporated in MBOs. From silicon rubber to polymethylpentene, the research has been focused on the development of more hemocompatible materials and on the enhancement of the flow management/mass transfer associated to the metabolic functions of the lung [15], [16]. The noncommercial integral asymmetric polyurethane (PUR)-based membranes synthesized and characterized by de Pinho et al. [11], [17] are casted in the flat-sheet configuration to be incorporated in flat-sheet MBOs. Their synthesis has been comprehensively investigated by the authors with the twofold objective of gas permeation and hemocompatibility enhancement [18]. Faria et al. [19] studied the oxygen permeation rates of integrally skinned asymmetric poly(ester urethane urea) PEUU100, PEUU95, PEUU90 and PEUU85 membranes prepared with PUR/PCL-diol weight ratios of 100/0, 95/5, 90/10, and 85/15, respectively. Using water in a surrogate system of a blood oxygenator, the oxygen mass transfer was modeled and the oxygen permeation rates were obtained varying the water flow rate and the O_2 feed

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pressure. Results showed that the oxygen permeation was totally controlled by the membrane resistance for PEUU100 and PEUU85 membranes. The higher oxygen fluxes were obtained by the PEUU 95 and PEUU 90 membranes reflecting the lower membrane resistance to permeation.

In the present work, the flow conditions in a surrogate system of an MBO with the PEUU95 and PEUU90 membranes that minimize the membrane area needed to assure the oxygen physiological needs of an adult are predicted using the model validated by Faria et al. [19].

II. EXPERIMENTAL

A. Poly(ester urethane urea) membrane synthesis

Integrally skinned asymmetric poly(ester urethane urea) (PEUU) membranes were prepared by a modified version of the phase inversion technique as described in [19]. In this process, two prepolymers, a polypropylene oxide-based polymer (PUR) (MW: 3500) and a polycaprolactone-diol (PCL-diol) (MW: 530) reacted in a homogeneous phase solvent system of dimethyl formamide (DMF) and diethyl ether (DEE), at a weight ratio DMF/DEE of 3, and was catalyzed by stannous octoate. Casting solutions with PUR/PCL-diol weight percentage (wt.%) ratios of 100/0, 95/5, 90/10, and 85/15 were prepared in a solvent mixture of DMF/DEE, where the weight ratio of total polymer to total solvent was kept constant and equal to 2/3. The solutions were cast onto a glass plate with a 250 μm casting knife and after 30 s of solvent evaporation time were quenched into a gelation bath of deionized water to yield the PEUU100, PEUU 95, PEUU 90, and PEUU 85 membranes. After 12 h in the gelation bath, the resulting membranes were detached from the glass plate.

B. Mini-oxygenator as a surrogate of a flat-sheet blood oxygenator

The oxygen permeation experiments carried out by Faria et al. [19] were performed in a device surrogate of a flat-sheet blood oxygenator, composed of three main units: unit 1, the bottom unit containing the gas compartment; unit 2, the middle unit that defines the surface area contacting the water flow; and unit 3, the top unit that defines the height (2Y = 0.06 cm) of the water flow chamber and seals the entire device. Unit 1 has a top acrylic glass plate containing a perforated zone for the oxygen permeation through the membrane with 8.7 cm^2 of open area. The PEUU membrane is placed with the active dense layer surface faced upward, between units 1 and 2, which are then compressed together by screws and sealed by an O-ring gasket. Unit 3 is then attached to the top of unit 2 by another series of screws, and another O-ring gasket provides the necessary sealing between the units. The compartment, where the liquid stream to be oxygenated circulates in the z-direction, is separated from the oxygen compartment that is kept at constant pressure, pO_2, by a flat-sheet integral asymmetric PEUU membrane. The compartment where the liquid circulates is a slit with dimensions 2X $\times$ 2Y $\times$ Z and is characterized by the Y dimension being very small compared to the other two dimensions. Fig. 1 shows a scheme of the setup used for the water oxygenation experiments. The mini-oxygenator flow channel is fed with deionized water by a peristaltic pump and connected to a well-mixed reservoir of constant volume, V, downstream from its exit that is immersed in a thermostatized bath to keep the temperature constant at 25°C. Polyvinyl chloride tubing ensures a mock circulatory flow loop, and the slit geometry of the liquid flow channel assures that the water circulates in a fully developed laminar flow inside the mini-oxygenator. The oxygenated water exiting the flow channel circulates through a well-mixed vessel with a constant volume, 0.678 L, where the oxygen concentration in the liquid is measured as a function of time by a fiber optic oxygen sensor (FOXY-R, Ocean Optics, Largo, Florida, USA). The water flow rates imposed were 2.0, 2.5, and 3.0 L/min, and pure oxygen was administered to the gas compartment of the mini-oxygenator at feed pressures of 30 and 60 kPa. Moreover, a helium sparger to perform the water deoxygenation prior to the oxygenation experiments is also immersed in the reservoir. A pressure regulator and a vacuum pump precede the oxygen compartment.

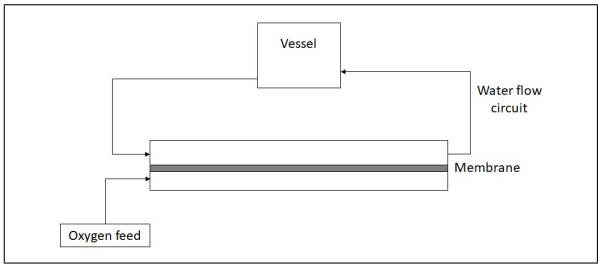

Fig. 1: Scheme of the mini-oxygenator circuit.

A time differential mass balance to the well-mixed vessel of volume V, yields

$$V\frac{dC_{O_2}}{dt} = J_{O_2}A \tag{1}$$

where $\mathrm{dC_{O_2}/dt}$ is the slope of the experimental curves, C_{O_2} (mol/cm^3) vs. time (min), measured by the FOXY-R oxygen sensor and J_{O_2} is the oxygen flux permeating through the open surface area of the membrane, A.

C. Modeling oxygen mass transfer in a gas chamber/membrane/water flow channel system

The modeling of the oxygen mass transfer in the system was performed assuming that: the O_2 mass transfer results from the convective contribution in the z direction and the diffusive contribution in the y direction; the flow is fully developed, unidimensional and characterized by a parabolic velocity profile; the very small distance of penetration of O_2 in the y direction can be approximated by the straight line; and the liquid phase can be aproximated to a semi-infinite medium. The O_2 permeation fluxes can be predicted by (2) [19]:

$$\left\langle J_{O_2}\big|_{y=0}\right\rangle = \frac{3D_{O_2l}\left(C_{O_21} - C_{O_20}\right)}{2\Gamma\left(\frac{4}{3}\right)}\left(\frac{a}{9D_{O_2l}Z}\right)^{1/3} \tag{2}$$

III. RESULTS AND DISCUSSION

Faria et al. [19] studied the O_2 permeation fluxes for the PEUU 100, PEUU 95, PEUU 90, and PEUU 85 membranes in a surrogate system of a MBO varying the oxygen feed pressures between 30 and 60 kPa and the water flow rates from 2.0 to 3.0 L/min. By measuring the oxygen average concentrations as function of time it was observed that the evolution with time of the oxygen average concentration follows a three-regime pattern: (1) a linear variation of the O_2 consentration vs. time for the initial short times range; (2) a nonlinear variation in the intermediate time range; and (3) a plateau for larger times. The slopes, $\mathrm{dC_{O_2}/dt}$, of the experimental straight lines, $\langle C_{O_2} \rangle$ vs. time, for the short times range, were used to determine by (1) the experimental oxygen permeation fluxes, $J_{O_2} = \frac{V}{A}\frac{dC_{O_2}}{dt}$, in this range. As a general trend for membranes PEUU 100, PEUU 95, and PEUU 90, J_{O_2} increases with the cross-flow velocity. The PEUU 100 and the PEUU 85 membranes displayed the lowest J_{O_2} , and were nearly independent on the cross-flow velocity.This was a clear evidence of the oxygen permeation being totally controlled by the membrane resistance as expected by the very thick active layer. The higher oxygen fluxes displayed by the PEUU 95 and PEUU 90 membranes reflect the lower membrane resistance to permeation. As a consequence, the contribution of the liquid boundary layer resistance is evidenced by the increase of the oxygen fluxes with the increase of the feed flow rates. Oxygen permeation fluxes for the PEUU95 and PEUU90 membranes predicted by the convection/diffusion model validated by Faria et. al [19] are shown in Table I. It was verified that the predicted fluxes increase with the increase of the cross-flow velocity and the O_2 feed pressure. The predicted oxygen permeation fluxes are very close to the experimental ones obtained by Faria et al. [19] .

TABLE I: Predicted O_2 permeation fluxes for the PEUU 95 and the PEUU 90 Membranes.

pO_2(kPa)	Q(L/min)	PEUU95	PEUU90
30	2.0	12	13
	2.5	12	14
	3.0	13	14
60	2.0	24	26
	2.5	24	27
	3.0	25	28

O_2 permeation fluxes have units of $10^{-10}\mathrm{molcm^{-2}s^{-1}}$

A MBO must deliver 250 $\mathrm{cm^3(STP)/min}$ of O_2 to blood [12]. Taking this into account and the permeation fluxes predicted by the validated model, the area of membrane PEUU 90 necessary to satisfy this requirment was estimated. Table II shows the predicted membrane area of PEUU 90 for the operation conditions of the work of Faria et al. [19] to assure the O_2 physiological requirements. Being the required membrane area dependent on the O_2 permeation fluxes it is observed that it decreases with the parameters that promote the increasing of the fluxes. The required membrane area decreases with the increase of the circulation flow and with O_2 feed pressure.

TABLE II: Predicted membrane area of PEUU 90 to assure the O_2 physiological requirements.

PO_2(kPa)	Q(L/min)	A(m^2)
30	2.0	14
	2.5	13
	3.0	13
60	2.0	7
	2.5	7
	3.0	6

The influence of the circulation flow on the membrane area of PEUU90 required to assure the O_2 physiological needs is plotted in Fig. 2. It is possible to note that for small values of flow, a small variation of the flow circulation has great impact on the reduction of the required membrane area. However, after increasing of circulation flow above 15 L/min there is not a significant reduction in the required membrane area. Furthermore, blood demage must be considered since higher circulation flows origin higher shear stresses.

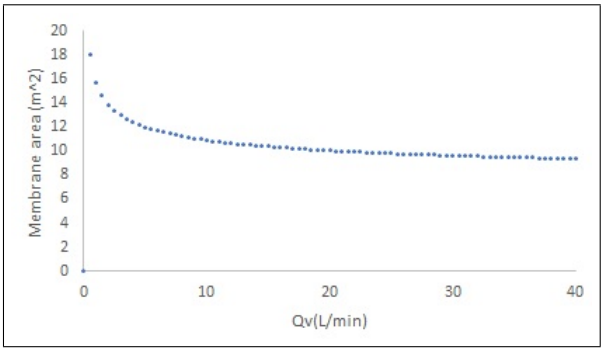

Fig. 2: Influence of the circulation flow on the membrane area required to assure the O_2 physiological needs.

The influence of the O_2 feed pressure on the membrane area of PEUU90 required to assure the O_2 physiological needs is plotted in Fig. 3. Similarly to the effect of the circulation flow in the reduction of the required membrane area, a small variation of the O_2 feed pressure for small values of flow has great impact on the reduction of the required membrane area until a pressure of 200 kPa is reached. After this there is no significant reduction in required membrane area.

IV. CONCLUSIONS

Previous works showed that, in a surrogate system of a MBO, the oxygen permeation of membranes PEUU 85 and PEUU 100 was totally controlled by the membrane resistance. The higher oxygen fluxes were obtained for the PEUU 95 and PEUU 90 membranes reflecting the lower membrane resistance to permeation. The effect of the circulation flow and of the O_2 feed pressure in the membrane area to assure the oxygen metabolic needs of an adult was investigated. Results show that after certain value of the

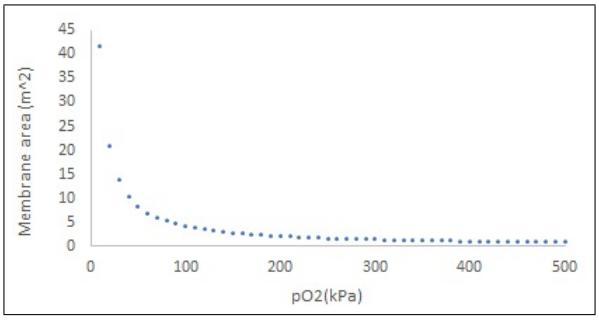

Fig. 3: Influence of the O_2 feed pressure on the membrane area required to assure the O_2 physiological needs.

parameter the effect on the required membrane area is no longer significant. The combined effect of the circulation flow and the O_2 feed pressure must be investigated taking into account the limitations regarding blood integrity. In this case, where the O_2 mass transfer is controlled by the liquid boundary layer, the optimization of the circulation conditions and the introduction of boundary layer disruptors and mixing promoters can improve the mass transport. The present benchmark device can accommodate membrane/boundary layer disruptors to promote flow fields, enhancing the oxygen mass transfer. Electrospunned fibers can be deposited over the membranes surface to act as obstacles on the liquid flow and its effect in the oxygen mass transfer and blood integrity is under investigation.

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