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Gas transfer model to design a ventilator for neonatal total liquid ventilation

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ABSTRACT

The study was aimed to optimize the gas transfer in an innovative ventilator for neonatal Total Liquid Ventilation (TLV) that integrates the pumping and oxygenation functions in a non-volumetric pulsatile device made of parallel flat silicone membranes. A computational approach was adopted to evaluate oxygen (O_2) and carbon dioxide (CO_2) exchanges between the liquid perfluorocarbon (PFC) and the oxygenating gas, as a function of the geometrical parameter of the device. A 2D semi-empirical model was implemented to this purpose using Comsol Multiphysics to study both the fluid dynamics and the gas exchange in the ventilator.

Experimental gas exchanges measured with a preliminary prototype were compared to the simulation outcomes to prove the model reliability. Different device configurations were modeled to identify the optimal design able to guarantee the desired gas transfer.

Good agreement between experimental and simulation outcomes was obtained, validating the model. The optimal configuration, able to achieve the desired gas exchange ($\Delta pCO_2 = 16.5$ mmHg and $\Delta pO_2 = 69$ mmHg), is a device comprising 40 modules, 300 mm in length (total exchange area = 2.28 m^2). With this configuration gas transfer performance is satisfactory for all the simulated settings, proving good adaptability of the device.

1. Introduction

The evaluation of gas transfer phenomena by numerical modeling is fundamental to design and optimize the performance of respiratory support devices [1,2]. This is particularly important when designing a ventilator prototype for neonatal Total Liquid Ventilation (TLV), since with this technique the fluid dynamics and gas transfer in the lungs and in the ventilator are completely different from conventional gas ventilation (GV), due to the use of liquid perfluorocarbons (PFC) to drive respiratory gases into the lungs [3,4].

TLV is studied as an alternative technique to GV for the treatment of pulmonary pathologies characterized by the lack or absence of endogenous surfactant (e.g. Neonatal Respiratory Distress Syndrome) that affect very low birth weight neonates (i.e. neonates with body weight at birth lower than 1 kg or gestational age lower than 28 weeks) [5,6]. Experimental animal studies proved that TLV is able to support pulmonary gas exchange while preserving lung structures and functions [7]. Moreover, liquid PFC is an optimal ventilation medium due to high oxygen (O_2) and carbon dioxide (CO_2) solubility and suitable chemical properties (i.e. low surface tension, high density, biocompatibility) [5,6]. However, different aspects of TLV have to be improved for a safe transition from the laboratory experience to the clinical application. A key role is played by the development of an advanced device able to safely support gas exchanges, while avoiding lung injury.

Several international research groups proposed various prototypes [8–12], all aimed to perform ventilation and PFC reconditioning (oxygenation, CO_2 removal, and temperature control). The most common strategy is the volume-controlled ventilation. However, to be safe, the volume control devices should be pressure limited, because high inspiratory pressure may induce barotrauma and excessive negative expiratory pressure, due to active PFC drainage, may cause airways collapse [13–15]. Despite these precautions, a number of drawbacks related to tidal volume regulation, gas exchange efficiency and control of the airway pressure are still affecting the outcomes of the trials with volumetric devices. To overcome these limitations, during the Round Table discussion at the "6th International Symposium on Perfluorocarbon Application and Liquid Ventilation" [16], the international scientific community working in TLV field has joined the efforts to define the main specifications TLV treatment has to comply with in terms of devices and controls to be implemented

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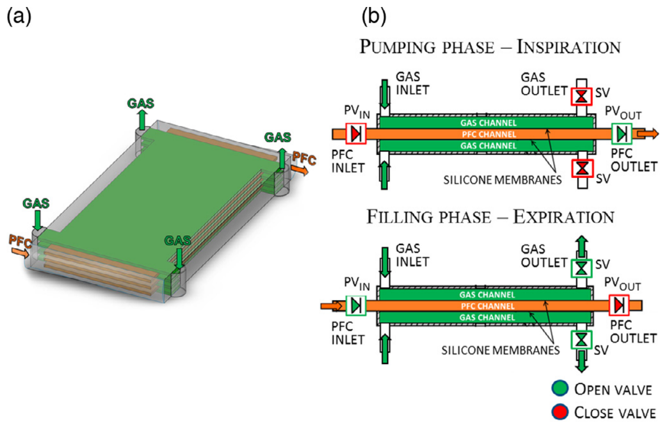

Fig. 1. Schematic configuration of the ventilator prototype: (a) 3D rendering of the Pro-Li-Ve, the arrows highlight the PFC (orange) and gas (green) inlets and outlets; (b) representation of a single Pro-Li-Ve functional module during the pumping (up) and filling (bottom) phases (PV_{IN}: PFC inlet passive valve, PV_{OUT}: PFC outlet passive valve, SV: gas outlet solenoid valve).

to guarantee the safety of the treatment. In this context, Robert et al. (2010) [17] proposed a new controller of their volumetric TLV ventilator [11] able to perform the expiration in pressure controlled strategy [17].

In compliance with the guidelines defined during the Round Table [16], our research group is investigating an alternative approach to develop an innovative Liquid Ventilator Prototype (Pro-Li-Ve) for the treatment of very preterm neonates, able to perform TLV in a lung-protective strategy. This device integrates the pumping and oxygenation functions in a non-volumetric pulsatile device, able to adjust the pumped PFC flow rate depending on the afterload (i.e. lung impedance) [18–20].

The device geometry and fluid dynamics have to be optimized to obtain the desired gas exchange performance, in particular to improve CO_2 removal, which is the main limiting issue in this kind of devices, due to the low partial pressure difference between the 2 compartments [21]. A computational approach is a useful tool for the design process, allowing the optimization of the device prior to construct the prototypes.

The aim of this study was to implement a two-dimensional (2D) semi-empirical computational model to study O_2 and CO_2 exchange between the PFC and the oxygenating gas mixture, as a function of the parameters of the device. The effect on gas exchange exerted by different geometries and ventilation parameters was analyzed to define the best device configuration, able to guarantee the desired gas transfer.

2. Materials and methods

The design of the new prototype consists in a modular device comprising several functional modules, each made of two flat parallel semi-permeable silicone membranes (Fig. 1). The liquid PFC flows in each module between the two membranes (PFC-channel) that are externally lapped by gas. Unidirectional PFC flow is obtained with 2 one-way passive valves placed upstream (PV_{IN}) and downstream (PV_{OUT}) the device. The gas-side inlet is connected to a line of compressed oxygenating gas, while the outlet is connected to the atmosphere through an active Solenoid Valve (SV). During the inspiration phase of the respiratory cycle the PFC is actively pumped (pumping phase): SV is close and gas fills and pressurizes the gas side causing tidal volume (TV) ejection. The gas pumping pressure is set by the user via a pressure regulator to adjust the desired TV. During the expiration phase, SV opens to scavenge gas into the atmosphere; therefore, PFC flows into the device due to hydrostatic preload (filling phase). Gas flow is maintained during the filling phase to improve

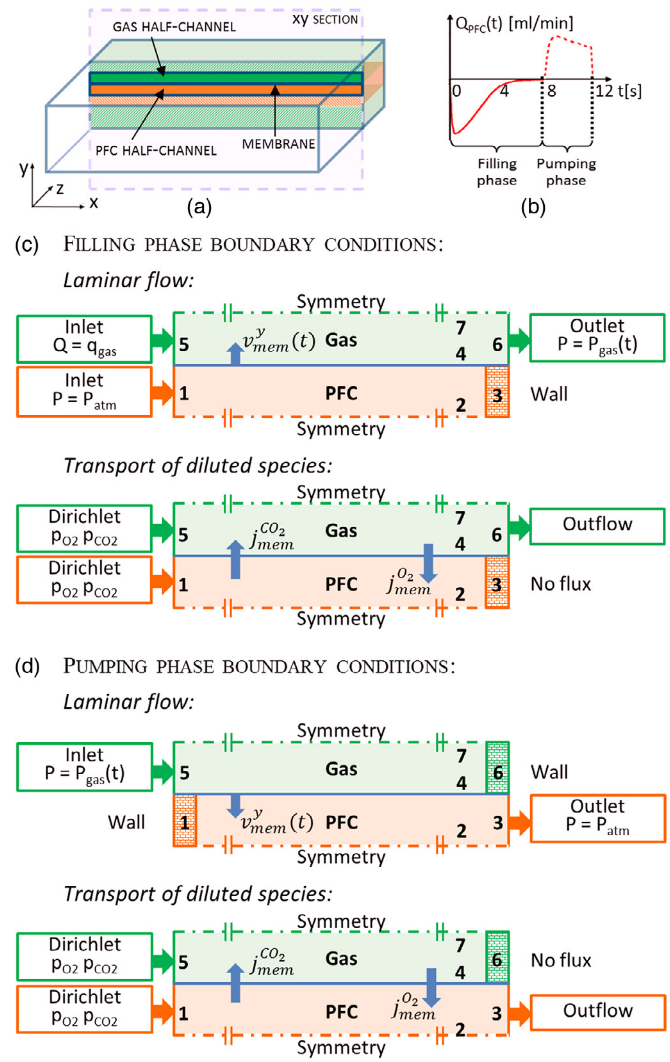

Fig. 2. 2D computational model domain and boundary conditions: (a) geometry of the 2D longitudinal central section: the gas and PFC half-channels used as computational domain are highlighted in the figure; (b) PFC flow rate during the respiratory cycle (solid line = filling phase, dashed line = pumping phase); (c–d) boundary conditions applied at the boundaries during the filling (c) and the pumping (d) phases, for the *laminar flow* and *transport of diluted species modules*.

CO_2 removal from PFC. The PFC flow rate and airway pressure are real-time monitored during the respiratory cycle by an ad hoc implemented control software [22] in order to measure the TV and avoid barotrauma.

The gas exchange occurring in this device strongly depends on the constructive parameters (e.g. shape and dimensions of the silicone membranes, number of modules, etc.). The optimization of the PFC fluid dynamics and gas transfer into each functional module was performed adopting the computational approach described in the following.

2.1. Computational model

In order to reduce the computational cost and simplify the model, the three-dimensional geometry of the oxygenating device was simplified and simulated with a two-dimensional computational model representing one longitudinal section of one functional module (Fig. 2a). To avoid any possible shortcomings introduced by this approximation that neglects flow variations with the depth of the device, a semi-empirical model was implemented, in which an experimental coefficient ξ was introduced. This multiplicative coefficient