AN ARTIFICIAL LUNG BASED ON GAS EXCHANGE AND BLOOD FLOW OPTIMIZATIONS

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ABSTRACT
This work presents a fluidic system and its use as an extracorporeal, diffusive gas exchange device for the modification of the oxygen and carbon dioxide partial pressure in blood. We report layout specifications and flow parameter, which meet the conflicting requirements of an effective gas exchange. Evaluation models with 400 parallel micro channels and a gas compartment bordering the micro channels on two sides were fabricated. Their gas exchange was characterized. The occurrence of a cell free blood plasma layer at the channel walls was analyzed using a laser scanning microscope. With the introduced method no plasma layer was detected.

KEYWORDS: extracorporeal gas exchange, silicone rubber, highly parallelized micro channels, cell free blood plasma layer.

INTRODUCTION

The main task of artificial lungs or, more in detail, extracorporeal, diffusive gas exchange devices is to oxygenate a patient's blood and to remove carbon dioxide from it in an extracorporeal blood circulation. It is applied if the diseased natural lung of a patient needs to be supported while not further harming it by mechanical ventilation. For an effective gas exchange such a gas exchange device has to meet conflicting requirements as for the layout and the flow parameters. On the one hand it is necessary to realize a long contact time between blood and ventilation gas on the other hand a short diffusion length is essential to provide a sufficient gas exchange. Furthermore an adequate volume flow is essential to ensure that the amount of aerated blood is large enough to supply the patient's body. Although, a high volume flow requires large cross sections and a high flow velocity, the former increases the diffusion lengths, while a high flow velocity reduces the contact time. Both lower the gas exchange capacity to a large extent. Besides, while the blood is flowing through micro channels the cells within it will move to the center of the channel due to the occurring velocity gradient in the laminar flow. By this so called axial migration a cell free blood plasma layer at the channel wall might be formed. Such a cell free layer increases the diffusion length for the gases to the red blood cells (RBCs) which mainly carry the gases, bound to their hemoglobin, through the body. These conflicting requirements and their drawbacks for the system are summarized in Table 1.

Table 1. Main conflicting requirements of an effective supply with oxygen and removal of carbon dioxide in an extracorporeal blood circuit with optimized parameter set for the here presented device

Requirements	Possible realization	Drawback for the system	Optimized parameter set
Adequate volume flow	large channel cross section	increases diffusion length	0.1 mm x 1 mm
	high flow velocity	reduces contact time between gas and blood; reduces hemocompatibility [1] may increase the cell free blood plasma layer	20 mm/s
Long contact time between blood and ventilation gas	low flow velocity	reduces volume flow	20 mm/s
	long channel length	reduces hemocompatibility	150 mm
Short diffusion length	thin membranes	fabrication becomes complex; reduces mechanical stability	100 µm
	low channel height	reduces channel cross section	100 µm

THEORY

Within the here presented system the blood to be modified is guided in micro channels covered by thin membranes made of polydimethylsiloxane (PDMS) on both sides. On the other side of the membrane borders the compartment for the ventilation gas flow (e.g. oxygen). The schematic set up is shown in Figure 1. The diffusive gas exchange occurs between the blood and the ventilation gas across the PDMS membrane, driven by the partial pressure gradient. Therefore, PDMS is chosen as material due to its high permeability.

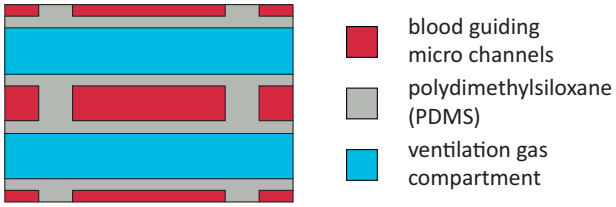

Figure 1: Cross section of the schematic set up of the extracorporeal, diffusive gas exchange device. The blood gas partial pressures are modified by diffusion between blood and ventilation gas via a membrane made in PDMS. The alternating stacking of layers for blood and for ventilation gas allows a high degree of parallelization and therefore an increased volume flow through the device.

To realize short diffusion lengths and an adequate volume flow while reducing the necessary flow velocity, the blood is guided in micro channels with a height of 100 µm. This height is a compromise between the diffusion length and the pressure drop determined by simulation of the gas exchange [2] and calculation of the pressure drop within the flow. In order to still ensure an adequate volume flow, the micro channels are highly parallelized. The realization of devices with several hundreds of micro channels makes a stacked set-up with alternating layers for the blood and the ventilation gas essential. The channel length is 150 mm to balance the reduction of the contact time by the necessary flow velocity of approx. 20 mm/s. Figure 2 shows an evaluation model (EM) with 400 parallel micro channels which was fabricated according to these layout specifications. The fabrication chain for the realization of such a system was presented at µTAS 2012. [3]

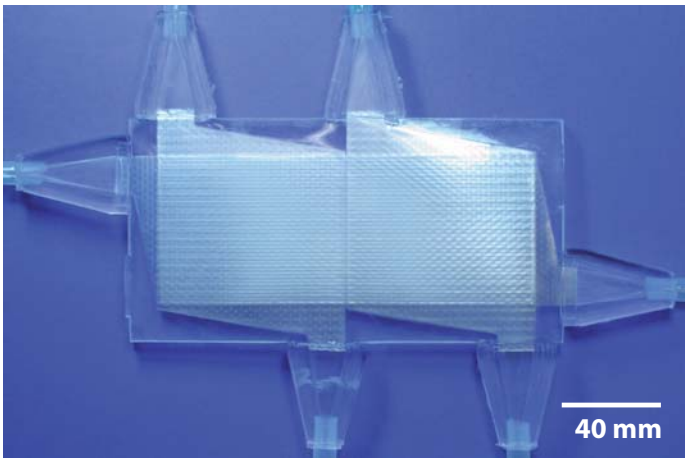

Figure 2: Fabricated evaluation model of the extracorporeal gas exchange device with 400 parallel micro channels. This system serves two ventilation gas inlets and outlets each and one blood inlet and outlet each.

Figure 3: Simplified evaluation model used for the analysis of the cell free blood plasma layer. In this image the simplified EM is filled with dyed water.

EXPERIMENTAL

The gas exchange of the artificial lung is characterized using three EMs with 120 micro channels each arranged in three layers. The EMs are fabricated as mentioned before [3]. The experiments are conducted with heparinized porcine whole blood. The conditioning of the blood is performed according to ISO 7199 [4]. The blood flows with 20 mm/s through the EM. Pure oxygen is used as ventilation gas. The gas partial pressures are measured in blood samples before and after the blood passed the EM with a clinical blood gas analyzer.

To investigate the cell free plasma layer simplified EMs (Figure 3) are used having the same channel cross sections as the original EMs but less as well as shorter channels and no gas compartment. The simplified EM is mounted beneath an upright confocal laser scanning microscope (Zeiss LSM 510 META) and human whole blood flows through it with a velocity of 20 mm/s. The reflected light intensity (wavelength 633 nm) is detected for several planes along the channel height (z-axis). Therefore the interfaces (the blood membrane interface and cell membranes of blood cells) and their z-position within the simplified EM are recognized by an increase in the intensity of the reflected light. By this method we are able to detect plasma layers of 1 µm thickness reliably.

RESULTS AND DISCUSSION

Leakage-free evaluation models with 120 micro channels were realized. Figure 4 shows the gas transfer of oxygen (59 to 60 ml/l_{blood}) and carbon dioxide (approx. 71 to 74 ml/l_{blood}) and its weak dependency on the ventilation gas flow (increase of 3% while gas flow increases by 500%). The average flow velocity was 20 mm/s, which leads to a volume flow through the EM of 15 ml/min.

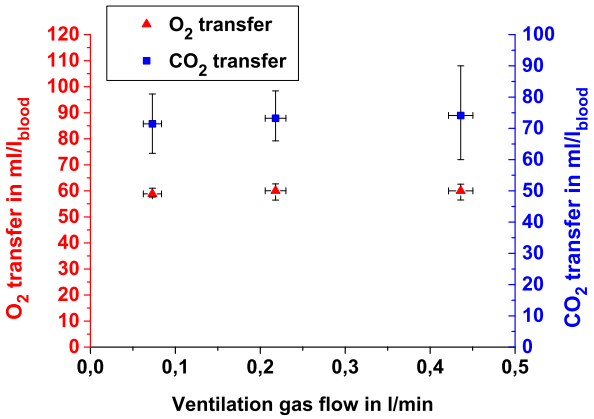

Figure 4: Average of gas transfer to porcine whole blood flowing with an average velocity of 20 mm/s in 3 different, 120 micro channel EMs. For each EM 3 measurements are performed. The y-error bars correspond to the range of the measurement results. Pure oxygen is used as ventilation gas. The x-error bars correspond to the gas flow measurement uncertainty.

For a flow velocity of 20 mm/s and a physiological hematocrit of whole blood of 44% no plasma layer is detected and therefore no significant increase in the diffusion length by a cell free blood plasma layer occurs. In the here presented channel geometry, a detectable cell free plasma layer was observed for a maximum hematocrit of 25% and a flow velocity of at least 167 mm/s.

CONCLUSION

It was shown that the here presented device is applicable as extracorporeal gas exchange device regarding the amount of gas transfer to and from blood. To realize the necessary volume flow through it, the device needs to be further up scaled. So far no limitation of the number of stacked layers is obvious, especially if the fabrication is automatized.

The investigation of the cell free blood plasma layer showed, that no significant increase of the diffusion length occurs due to the axial migration. To detect a cell free blood plasma layer, the blood needs to be diluted significantly and to flow with a more than eightfold higher velocity compared to the aimed application and flow conditions.

To finally judge the applicability of the here presented device as an extracorporeal, diffusive gas exchange device, or in short an artificial lung, further investigations need to be performed concerning the hemocompatibility. But also here first results were promising.

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