INTRODUCTION

Acute and chronic diseases of the lung are currently a major healthcare problem. Each year nearly 350,000 Americans die of some form of lung disease [1]. Most lung disease is chronic, and an estimated 30 million Americans are now living with chronic lung disease. Artificial lungs provide respiratory support independent of the lungs and allow a reversibly injured lung to rest and heal [1]. However, current artificial lung design is far from matching the gas exchange power of the natural human lungs. Current artificial lung devices utilize hollow fibers permeable to gas diffusion. Blood is pumped over the fibers while pure oxygen gas is pumped through the lumen of the fibers and the carbon dioxide and oxygen can passively diffuse down their concentration gradients. The natural lung has an effective surface area of 100-150 m² supporting gas exchange ranging from resting levels for both O2 and CO2 to 10–20 times that under exercise conditions [1], and it does so using room air as its oxygen supply gas. Current hollow fiber blood oxygenators have membrane surface areas of about 1-4 m², and even using pure oxygen gas struggle to support resting metabolic needs.

The most significant resistance to gas exchange in hollow fiber blood oxygenators is the diffusional boundary layer. The diffusional boundary layer is a thin layer of fluid at the fiber surface in which the fluid velocity ranges from zero at the wall up to the bulk fluid velocity at the boundary limit [4]. This region of low flow severely limits how quickly the oxygen and carbon dioxide can diffuse down their respective concentration gradients. The hollow fibers are about 300 µm in diameter, while the boundary layer is about 50 µm in thickness. By introducing active micro-mixing at the fiber surface, we hope to disrupt this layer, thereby greatly improving the gas exchange efficiency of the oxygenator.

Several prior studies have demonstrated micro-mixing generated by small particles. In a related study, Geng et al. demonstrated an increase in gas exchange using oscillating microbubbles. They utilized a silicon membrane that is permeable to gas exchange, and pumped CO2 saturated water over the surface, measuring the CO2 removal with and without the bubbles. The bubbles were trapped on the membrane surface, and oscillated via a piezoelectric actuator. They were able to demonstrate a 25% increase in CO2 removal with the oscillating bubbles compared to the control without bubbles [2]. These bubbles can also be excited by an external ultrasound field, eliminating the need to actuate the fibers [5]. Another group was able to demonstrate micro-mixing generated by rotating magnetic nanoparticles. The magnetic nanoparticles were attached to a small tether which was attached to a membrane surface. A saline solution was pumped over the membrane surface, which was then subjected to a rotating magnetic field. The magnetic field caused the nanoparticles to rotate and generate small turbulences on the membrane surface [3].
Gas exchange efficiency is defined as the CO2 parts per million removed multiplied by the sweep gas flow rate (oxygen in this case) divided by the total exposed fiber surface area. The gas exchange system is set up as follows. A reservoir of water is first mixed with CO2 until the partial pressure of CO2 is 45±5 mmHg, which is consistent with normal human blood ranges. The water is then pumped with a peristaltic pump through the device and out into a waste container. Pure oxygen gas is pumped through the lumen of the fibers in a direction opposite fluid flow. The outlet gas is pumped out with a vacuum pump into a CO2 analyzer which measures the parts per million of CO2 in the outlet gas. The device can be set up such that the fibers are directly exposed to an ultrasound signal or rotating magnetic field.

RESULTS

Overall, we were not able to demonstrate any increase in gas exchange efficiency with the two different oscillating microparticles. Our control data showed a baseline gas exchange efficiency of ~80 mL CO2/(min*m²) with an intradevice standard deviation about 2%. The data for the microbubble gas exchange is shown below in figure 2.

As shown, there is no change between efficiency of the devices with or without an ultrasound signal. Additionally, the efficiency of all groups is within the variability of the control devices, i.e., no microbubbles. The results for the magnetic nanoparticle gas exchange are shown below.

As shown, the magnetic nanoparticles actually decreased gas exchange efficiency at a consistent level of about 20%, and varying magnetic field strengths and frequencies had no effect on gas exchange efficiency.

DISCUSSION

The results of this study were not able to demonstrate any positive effect of oscillating microparticles on gas exchange efficiency. The negative effect of the magnetic nanoparticles could possibly be attributed to the particles blocking some of the pores of the fiber, but ultimately is unknown. The most likely reason for no noticeable effect on gas exchange is the fact that the boundary layer is about 50 µm while the microbubbles used were on average 2 µm in diameter and the magnetic nanoparticles were about 25 nm in diameter, over an order of magnitude smaller than the layer they hope to disrupt. Additionally, the bubbles only last on the order of minutes, while a functional device must operate over the course of days to months. The devices would also have to undergo experiments in blood to determine any negative effects such as hemolysis, and finally extended animal trials. In conclusion, the oscillating microparticles tested do not hold much promise for improving the gas exchange efficiency of hollow fiber oxygenators. Active mixing remains a potentially promising field, perhaps larger, more stable particles could be tested in the future.

ACKNOWLEDGMENTS

NIH RO1 Grant, Dr. Ranil Wickramasinghe at the University of Arkansas MAST Center and Dr. Xucai Chen at the Center for Ultrasound Molecular Imaging and Therapeutics

REFERENCES