

AN EXPERIMENTAL AND THEORETICAL STUDY ON THE EFFECTS OF BLOOD FLOW PULSATILITY ON OXYGEN TRANSFER IN ARTIFICIAL LUNGS

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INTRODUCTION

Most present-day artificial lungs used with heart-lung machines during cardiopulmonary bypass, often referred to as oxygenators, are designed for and operated with a steady blood flow. Artificial lungs attached to the pulmonary circulation would receive pulsatile blood flow delivered by the right ventricle, RV, and pulsatility in these devices could affect the rate of gas transfer relative to what it would be with a steady flow at the same mean flow rate. The capability of oxygenators to transfer gas depends on the blood flow rate through the device. At steady, low flow rates the hemoglobin becomes fully saturated early within these devices and their capability is underutilized. Superposing a pulse on such flows may make the device less efficient but still capable of fully saturating the hemoglobin and have little effect on the overall rate of oxygen transfer. At steady high flow rates, on the other hand, the oxygenator may not be capable of oxygenating the hemoglobin. Superposing a pulse on the steady flow may result in reduced outlet saturation.

A common form for representing heat/mass transfer to fluids flowing steadily through packed beds of particles or across tightly packed rods or fibers is, for mass transfer in the latter [1]:

$$Sh = \phi Sc^{1/3} Re^\beta, \quad (1)$$

in which Sh = Sherwood number, Sc = Schmidt number, Re = Reynolds number. The constants ϕ and β depend on the arrangement and uniformity of the rod or fiber spacing. By rearranging equation (1), the local mass transfer coefficient, k , can be expressed as:

$$k = \phi \frac{(1 - V_f) D}{V_f d} \left(\frac{v}{D} \right)^{1/3} \left(\frac{Q}{V_f A_f} \right)^\beta \left(\frac{V_f d}{(1 - V_f) v} \right)^\beta (1 + \lambda)^{1/3}. \quad (2)$$

In which V_f = bundle void fraction, d = outside diameter of the rods or fibers, D = molecular diffusivity of the mass transferring specie, v = kinematic viscosity of the fluid, Q = fluid flow rate, A_f = gross frontal area of packed bundle, and $\lambda = 1.34(C_{Hb}/\alpha)(dS/dP)$, C_{Hb} = hemoglobin concentration, α = solubility of oxygen in blood, S = fractional saturation of hemoglobin with oxygen, P = partial pressure of oxygen in the blood, and dS/dP = slope of the oxyhemoglobin dissociation curve [2]. Equation (1) is a correlation that has been

established for steady flow at low Reynolds Numbers, less than about 10. If the Womersley number is less than 1, it may be used for unsteady flow in which the Re is time varying, i.e., quasi-steady flow.

This paper demonstrates the pulsatility effects on the rate of oxygen transfer with some in vitro tests on commercial oxygenators, and applies the theory to the experimental conditions.

MATERIALS AND METHODS

In vitro tests

In vitro tests were performed on six commercial oxygenators, three SARNs pediatric oxygenators (rated flow rate up to 2.5 l/min) and three DIDEKO D701 MasterFlow 34 infant oxygenators (rated flow rate up to 1.5 l/min). The fiber bundle for both oxygenators is made of microporous fibers. The experimental setup is mainly composed of two polyethylene reservoirs, a pulsatile pump (Harvard Pulsatile Blood Pump, Harvard Apparatus, Holliston, MA), a compliance chamber, and a commercial oxygenator. Approximately 20 l of fresh bovine blood was anticoagulated with heparin (10,000 U/l) and EDTA (1g/l), passed through a milk hair filter (Kendall, Boston, MA) into a polyethylene reservoir and recirculated until standard conditions were reached. Partial pressures of O_2 and CO_2 were adjusted by varying the O_2 , N_2 and CO_2 percentages in the sweep gas mixture. Sodium bicarbonate was used to adjust base excess and pH. Once standard inlet blood conditions were achieved, the test phase began using a single-pass technique. In all experiments, the pulsatile pump with the compliance chamber was first used and then the pulsatile pump alone. The compliance was such that the flow pulsatility was essentially completely damped. Three values of mean flow rate were used for each of the two flow shapes tested. The average flow rate varied from 0.6 to 2.2 l/min. The different values were obtained by varying stroke volume, without changing the frequency, nor the systole/diastole ratio. The Reynolds numbers for the average flow rates varied from 2 to 8. The Womersley number, calculated as the root of $[V_f d / (2(1 - V_f))]^2 \cdot (\omega/v)$, in which $\omega = 2\pi f$ and f = fundamental frequency of the flow rate waveform in Hz, was equal to 0.3 for the SARNs devices and 0.2 for the DIDEKO devices.

The gas mixing was composed of 50% oxygen and 50% nitrogen. For each combination of average flow rate and flow rate shape, two inlet and two outlet samples were collected and put in ice until they were analyzed. The inlet and outlet samples were taken simultaneously. Flow rates and pressures were recorded when the blood samples were taken. The oxygen transfer rate was calculated as:

$$\dot{V}_{O_2} = \bar{Q} \alpha \Delta P + 1.34 \bar{C}_{Hb} \bar{Q} \Delta S \quad (3)$$

in which ΔP is the difference between P_{out} and P_{in} (each averaged over the two samples); \bar{Q} is the average blood flow rate; ΔS is the difference between the outlet and inlet hemoglobin saturation, calculated using the Hill equation, with parameters valid for bovine blood and P and pH values averaged over the two samples.

Validation of the quasi-steady theory

The quasi-steady theory was validated by comparing the *in vitro* test results with the predictions calculated by applying the theory to the commercial oxygenators. By equating the local oxygen transfer rate at the fiber surfaces to the oxygen uptake by the blood, the local instantaneous mass transfer coefficient, k , can be shown to be:

$$k = Qd(1+I)(dP/dx)/[4A_f(1-V_f)(P_g-P)] \quad (4)$$

in which P_g = partial pressure of the oxygen on the gas side, and Q = time varying blood flow rate. Equating equations (2) and (4) gives

$$\frac{dP}{dx} = \frac{4}{V_f} \left(\frac{1-V_f}{d} \right)^{2\beta} \left(\frac{A_f V}{Q} \right)^{1-\beta} \left(\frac{D}{v} \right)^{2/3} \frac{(P_g - P)}{[1 + \lambda(P)]^{2/3}} \quad (5)$$

for the gradient of the oxygen partial pressure along the blood path x . Equation (5) is numerically integrated, from $x = 0$ to $x = L$ to obtain the change in oxygen partial pressure from P_{in} at the entrance to P_{out} at the exit. The parameters needed for the integration of equation (5) were set to the recorded experimental values or calculated from recorded values.

RESULTS

Figure 1 compares the measured *in vitro* specific oxygen transfer for pulsatile flow, V_{O_2-p} with those for steady flow, V_{O_2-s} , grouped for the three levels of average flow rate used in the experiments. The average decrease is 10%, with a maximum decrease of 25%. A paired t-test was applied to the data and confirmed the hypothesis that the mean value of V_{O_2-s} is significantly greater than the mean of V_{O_2-p} ($p < 0.001$). To test the agreement between theory and experiments we used the statistical method proposed by Bland and Altman [3] (Fig. 2).

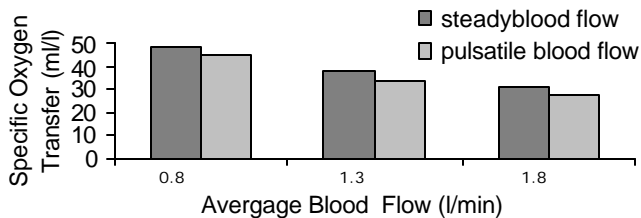


Figure 1. Results of the gas transfer experiments.

The 95% of the differences between the measured V_{O_2-p} values and those predicted lie between the limits $d-1.95s$ and $d+1.95s$, being d the average and s the standard deviation of the differences. These limits are -4.5 ml/l and 3.6 ml/l (Fig. 6). The average difference is -0.5 ml/l, corresponding to a percent value of -1.5%; this value is not significantly different from zero ($p > 0.3$), i.e. it does not represent a consistent bias. The percent difference between measured and

predicted V_{O_2-p} ranges between -11% and 9%. A paired t-test was applied to the data and confirmed the hypothesis that the mean value of the measured V_{O_2-p} is not significantly different from the mean of those theoretically predicted ($p > 0.3$).

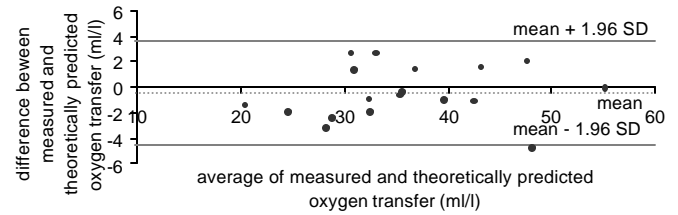


Figure 2 Comparison between measured and theoretically predicted oxygen transfer (Bland-Altman test).

CONCLUSIONS

The purpose of this study is to evaluate the effect of pulsatile flow on oxygen transfer in artificial lungs, a crucial item for thoracic artificial lungs that receive blood from the right heart [4]. Commercial oxygenators, usually operated with essentially steady flow, are often designed to "over saturate the blood" (i.e., produce an outlet partial pressure of oxygen much greater than 100 mmHg) when used with 100% oxygen at the 'rated blood flow rate'. Little or no differences between steady and pulsatile flow would be expected at these conditions. We used 50% oxygen to avoid over saturation and indeed we could observe a 10% average reduction in oxygen transfer with pulsatile blood flow in respect to steady blood flow. Equations borrowed from heat transfer theory [3] have been shown to adequately predict oxygen transfer under steady flow conditions [1]. The same theory has been applied in the present study to pulsatile flow conditions using the instantaneous values of flow rate in equation (1), i.e., assuming quasi-steady conditions. The Reynolds numbers for these flows were between 1 and 8 and the Womersley numbers were 0.3 and 0.2, indicating quasi-steady conditions are reasonable.

These results have implications in the design of implantable artificial lungs, in which the number of fibers – and therefore the maximum average flow rate – is limited by the need for a low resistance, compact device. The rated blood flow rate may be that necessary to meet basal metabolic demands. An increase in metabolic demands, resulting in an augmented cardiac output, would result in a less than proportional increase in oxygen transfer rate. We conclude that a compliance should be included in the design of all implantable thoracic artificial lungs (TAL).

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