

In Vitro Testing of the 0.6 M² SciMed Membrane Oxygenator for Use in Neonatal Extracorporeal Membrane Oxygenation

Krisa P. Van Meurs, MD⁺, Gerald T. Mikesell, BS CCP^{*}, Joseph P. Hearty, III, CCP^{*},
Winslow R. Seale, MS⁺, Oswaldo Rivera, BS[#], Billie L. Short, MD⁺

⁺Departments of Neonatology, ^{*}Cardiovascular Perfusion and [#]Biomedical Engineering,
Children's National Medical Center and
George Washington University School of Medicine, Washington, D.C.

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Abstract

Prior to the introduction of the 0.6 M² SciMed membrane oxygenator, the 0.8 M² membrane was the only oxygenator FDA-approved for long-term bypass. The performance of the 0.6 M² SciMed membrane oxygenator was examined using a modified test protocol suggested by the Association for Advancement of Medical Instrumentation for testing gas exchange devices. Four 0.6 M² SciMed membrane oxygenators were tested *in vitro* using filtered ovine blood and a customized test circuit designed to provide a continuous source of deoxygenated, CO₂-laden blood. Venous blood delivered to the test membrane had an oxygen saturation of 65 ± 2%. Testing confirmed good oxygenation throughout the manufacturer's specified blood flow range. Transfer rates of CO₂ measured for the 0.6 M² SciMed membrane oxygenator were comparable to those of the 0.8 M² membrane up to a blood flow rate of 400 ml/minute. Further increases in blood flow did not augment CO₂ transfer rates. Use of the 0.6 M² SciMed membrane oxygenator for neonatal extracorporeal membrane oxygenation (ECMO) should be limited to the lower blood flow range and to infants not likely to experience significant hypercarbia, if such infants can be accurately identified.

Introduction

Neonatal extracorporeal membrane oxygenation (ECMO) has been used in over 4800 infants to date.¹ Neonatal ECMO is used to supply cardiorespiratory support for infants failing conventional ventilatory therapy and differs from routine cardiopulmonary bypass in the use of low-flow (20-120 cc/kg), low-heparin (activated clotting times of 180 - 250 seconds) and longterm (average run of 130 hours) techniques.² It is therefore important to have a membrane lung with good O₂ and CO₂ transfer capabilities over time, and good blood flow characteristics to decrease the formation of fibrin and clots.

This paper is a report on the gas exchange properties of the 0.6 M² SciMed membrane oxygenator^a to determine its

suitability for general use in neonatal extracorporeal membrane oxygenation (ECMO). The SciMed membrane oxygenator is the only FDA-approved device for long-term bypass. Previously, the 0.8 M² SciMed membrane oxygenator was the only SciMed membrane available for neonatal ECMO, but recently the 0.6 M² membrane was introduced for possible use. Because of the smaller surface area of the 0.6 M² membrane, the focus of this evaluation was CO₂ transfer.

Materials and Methods

The test procedure was modified from the draft standard suggested by the Association for Advancement of Medical Instrumentation for testing gas exchange devices.^{3,5} Four 0.6 M² and four 0.8 M² SciMed membrane oxygenators were tested *in vitro* using filtered ovine blood. All pressure readings were corrected for atmospheric conditions before use in calculations. All numerical data are reported as the mean and standard deviation of all measurements. Oxygen

Address correspondence to: Krisa P. Van Meurs, M.D.
Stanford University School of Medicine Department of
Pediatrics, 750 Welch Road, Suite 315 Palo Alto, CA
94304 (415) 723-5711

TABLE 1: SPECIFICATIONS OF THE SCIMED 0600

Manufacturer's Specifications:	
Surface area (m ²)	.6
Static priming volume (mL)	9.0
Maximum gas flow rate (L/min)	1.8
Recommended blood flow rate (L/min)	Up to 1.0
Recommended sizing by Pt weight (Kg)	Up to 10
Blood port dimensions (inches)	1/4
Measured:	
Length (cm)	17.0
Mid-section diameter (cm)	6.7
Overall envelope dimensions	
Width (m)	.13
Length (m)	2.97
Effective surface area (m ²)	
Width (m)	.12
Length (m)	2.49

The envelope and spool are the same as used in the 0400 except that the envelope is lengthened to provide 0.6 m² surface area.

and carbon dioxide transfer rates were determined only over the range of the manufacturer's rated specifications for blood and gas flow (Table 1).

The test circuit utilized a 4" Picker roller pump with digital readout^b which was calibrated by repeated timed volume collections. A Sarns 7000 roller pump^c and a 3.3 M² Terumo hollow fiber oxygenator^d comprised the control circuit. Terumo 700 ml reservoir bags were used for the blood reservoirs. A Perkin Elmer MGA 1100 Mass Spectrometer^e was used for direct measurement of gas composition in and out of both the test and control membranes. Oxygen saturations in the blood were monitored with a Bentley Oxysat meter^f. Temperatures and pressures were measured with a Hewlett-Packard 78200 physiologic monitoring system^g. Gas delivery to the oxygenators was controlled with a Sarns triple-flow meter^h and O₂ and N₂ content were regulated by a Sechrist Air/O₂ blenderⁱ. A Cincinnati Sub-Zero Hemotherm heater/cooler system^j maintained blood temperatures at 37°C. Blood gases were analyzed using a CIBA/Corning 168 pH/blood gas analyzer^k and hematocrits were calculated using a Damon/IEC hematocrit centrifuge and reader^l.

Test apparatus

The test apparatus consisted of two separate, but integrated circuits (Figure 1). Two 700 ml Terumo reservoir

- a SciMed, Inc., Minneapolis, MN
- b Picker International, Ossining, NY
- c Sarns 3M Health Care, Ann Arbor, MI
- d Terumo Corp., Piscataway, NJ
- e Marquette Gas Analysis Corp., St. Louis, MO
- f Bentley Laboratories Division, Baxter Healthcare Corp., Irvine, CA
- g Hewlett-Packard, Waltham, MA
- h Sarns 3M Health Care, Ann Arbor, MI
- i Sechrist Industries, Medical Products Division, Anaheim, CA
- j Cincinnati Sub-Zero Products, Cincinnati, OH
- k Ciba Corning Diagnostics Corp., Medfield, MA
- l IEC-MB, Needham Heights, MA

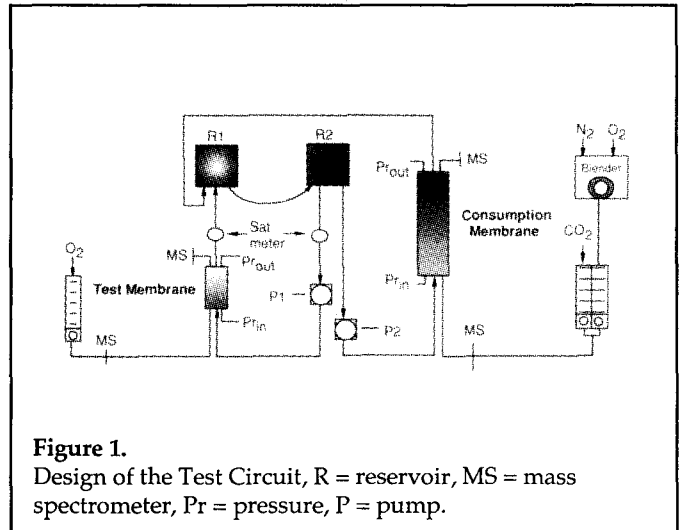


Figure 1. Design of the Test Circuit, R = reservoir, MS = mass spectrometer, Pr = pressure, P = pump.

bags were connected from the outlet of reservoir 1 to the return or venous port of reservoir 2. Reservoir 1 functioned as the blood return and mixing chamber. Blood from both the test circuit and the oxygen consumption circuit returned to reservoir 1 was mixed and shunted to reservoir 2. Blood exiting reservoir 2 flowed through a Bentley Oxysat sensor cell thus measuring the test membrane input oxygen saturation continuously. A 1/4" x 1/4" leurock connector was placed in-line proximal and distal to the test membrane to allow sampling. Gas flow to the membrane had a FiO₂ of 1.00. Gas flow in and out of the membrane was analyzed by mass spectrometry. Pre- and post-membrane blood flow pressures were measured continuously.

The test circuit continued to a Bentley Oxysat sensor cell for post-membrane oxyhemoglobin saturation measurement and then returned to reservoir 1. A second circuit attached to reservoir 2 was connected to the Terumo 3.3 M² hollow fiber oxygenator. The Terumo oxygenator functioned as an oxygen consumption and carbon dioxide generating device by supplying a nitrogen-oxygen-carbon dioxide gas mixture to the membrane. Measurement by mass spectrometry of the inlet and outlet gases to and from the Terumo oxygenator allowed repetition of test conditions. Blood flowed through the oxygenator and returned to reservoir 1 to mix with the blood returned from the test circuit. A constant blood temperature was maintained by a Cincinnati Sub-Zero hemotherm connected to the Terumo oxygenator.

Blood Inlet Conditions:

Oxyhemoglobin saturation	65 ± 2%
Hemoglobin	9 ± 1 g/dl
PaCO ₂	45 ± 5 Torr and 60 ± 5 Torr
Temperature	37 ± 1 °C

Using the mass spectrometer, membrane inlet and outlet O₂ and CO₂ were measured. This allowed for direct

calculation of oxygen and carbon dioxide transfer at various blood flow levels. The blood inlet and outlet pressures were measured at the various flow levels. Blood oxyhemoglobin, PaO_2 and PaCO_2 were measured on the inlet and outlet sides of the test membranes. Temperature was monitored and maintained at 37°C . Using the Timemeter gas/flow/pressure/volume system, the gas outlet flow was measured as a percentage of the total gas flow at the gas inlet ports.

Calculation of O_2 and CO_2 transfer was performed as follows:

$$\text{O}_2 \text{ transfer rate} = \text{ml O}_2 \text{ (STPD)}/\text{min}$$

$$\text{O}_2 \text{ transfer} = Q \times (1/100) \times (\text{VO}_2 \text{ outlet} - \text{VO}_2 \text{ inlet})$$

where Q = blood flow rate (ml/min)

where $\text{VO}_2 \text{ outlet}$ = blood O_2 content (ml O_2 /100 ml blood)

where $\text{VO}_2 \text{ inlet}$ = blood O_2 content (ml O_2 /100 ml blood)

CO_2 transfer rate: (by analysis of gas stream)

$$\text{CO}_2 \text{ transfer} = \text{gas flow} \times \text{delta } \% \text{ CO}_2$$

where gas flow = gas flow rate (ml [STPD]/min) exiting the gas phase of oxygenator

delta % CO_2 = the change in CO_2 concentration between the inlet and outlet gas ports

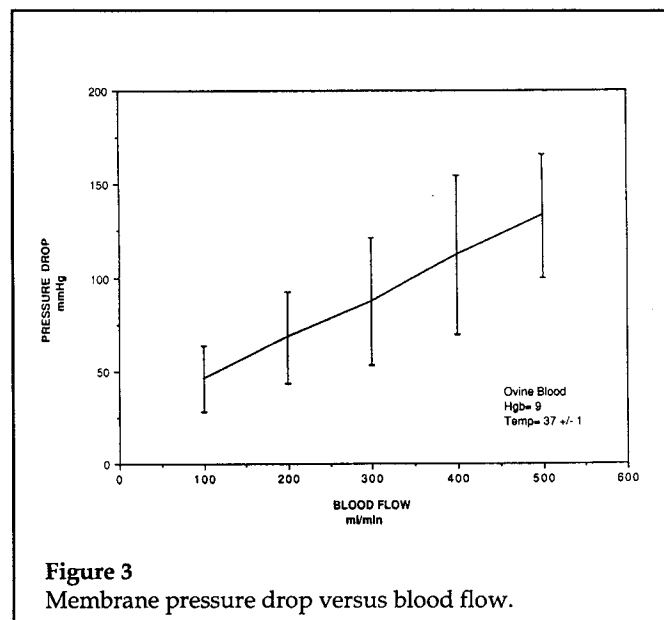
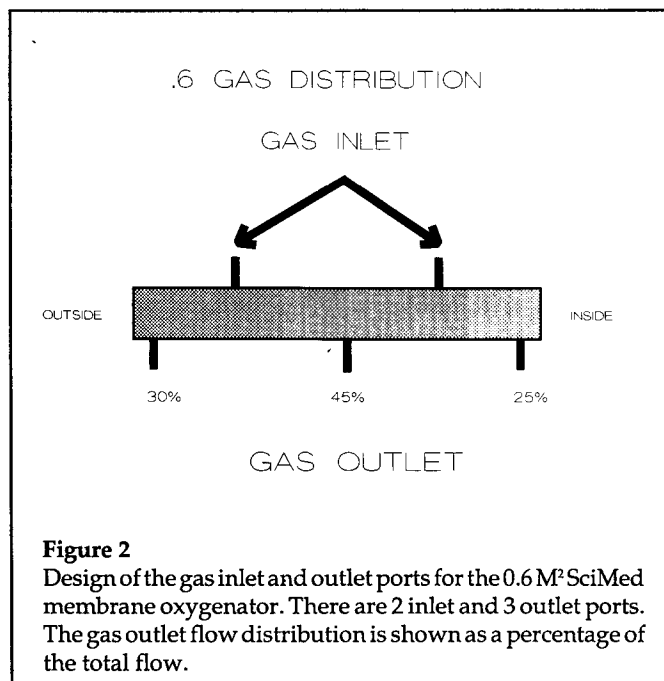
Results

The design of the gas inlet and outlet ports for the 0.6 M^2 membrane is shown in Figure 2. There are 2 gas inlet ports and 3 gas outlet ports. The gas outlet flow distribution was as follows: 25% inside port (port located closest to the central spool), 45% middle port and 30% outside port.

The pressure drop across the 0.6 M^2 membrane increased from 50 ± 17 mmHg to 125 ± 58 mmHg as blood flow increased from 100 to 500 ml/min (Figure 3). There was considerable variation in pressure drop measured for the 4 membranes resulting in a large standard deviation. This would appear to be related to the variation of tension in the wrapping of the silicon membrane on the spool, but showed no effect on membrane function.

The transfer rate of O_2 was calculated to range from 14.5 ± 1.3 to 36 ± 2.1 ml/min for blood flows from 100 to 500 ml/min for the 0.6 M^2 membrane. The oxygen transfer rate of the 0.8 M^2 membrane was not significantly different.

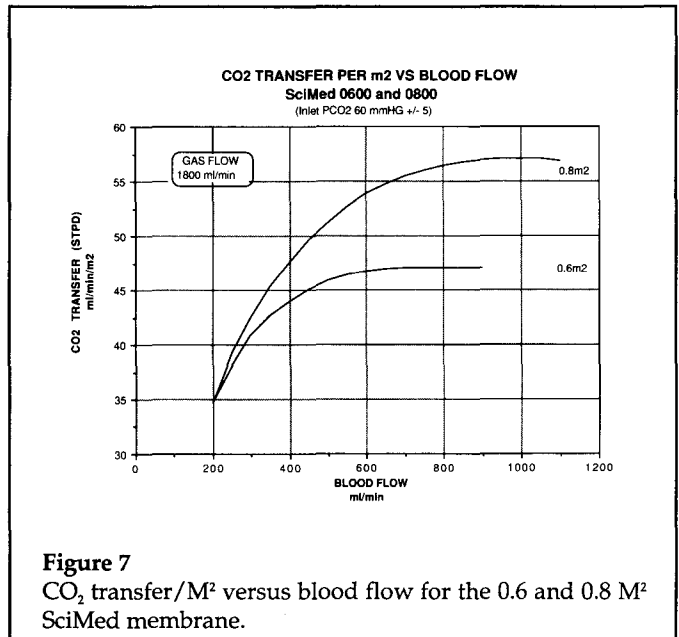
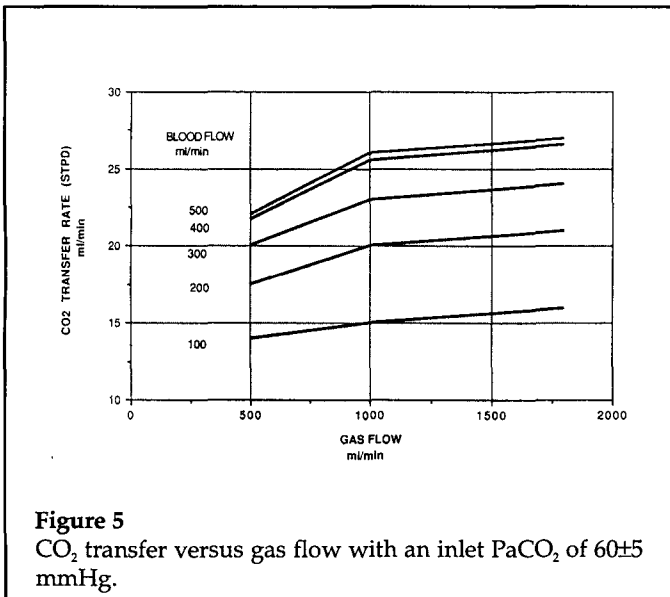
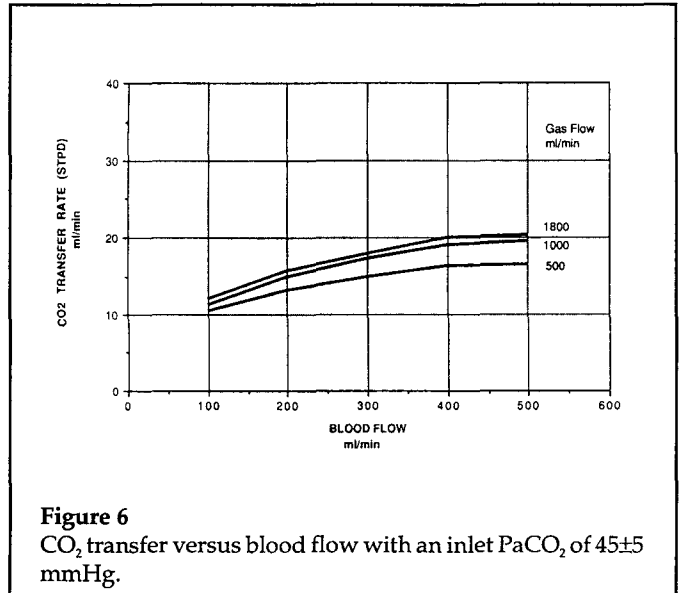
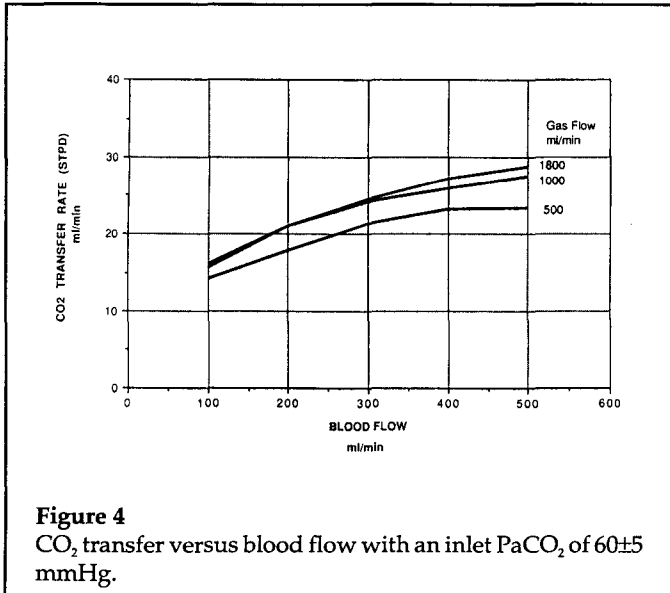
The 0.6 M^2 membrane, with an inlet PaCO_2 of 60 ± 5 Torr and a gas flow of 500 ml/min, showed a CO_2 transfer of 16.6



± 1.1 to 27.0 ± 2.8 ml/min with blood flow ranging from 100 to 500 ml/min. Maximum CO_2 transfer was found with a gas flow of 1800 ml/min and ranged from 19.2 ± 8.7 to 24.6 ± 3.8 ml/min with blood flows of 100 to 500 ml/min (Figure 4).

Interestingly, at this maximal blood flow, gas exchange was not significantly different at gas flows of 1000 and 1800 ml/min. Figure 5 shows the lack of significant increase in CO_2 exchange as gas flow is increased from 1000 to 1800 ml/min with blood flows of 100 to 500 ml/min.

The transfer rate of CO_2 as a function of blood flow with an inlet PaCO_2 of 45 ± 5 Torr is shown in Figure 6. The



absolute CO₂ transfer rates are decreased with an inlet PaCO₂ of 45 (12.5 ± 0.8 to 20.9 ± 2.1 ml/min with a gas flow of 500 ml/min and 14.4 ± 2.1 to 26.0 ± 2.9 with a gas flow of 1800) compared to 60, although the curves are essentially the same. Transfer is maximal at a blood flow of 400 ml/min.

In comparison, using the 0.8 M² membrane at a gas flow of 1800 ml/min, CO₂ transfer was 17.2 ± 1.7 to 36.0 ± 1.1 ml/min at flows of 100 to 500 ml/min. Increasing blood flow to the maximum rated flow (1200 ml/min) increased CO₂ transfer to 39.1 ml/min.

Transfer rates of CO₂ per meter squared as a function of blood flow for the 0.6 and 0.8 M² SciMed membranes are displayed in Figure 7. The gas flow was fixed at 1800 ml/min. The transfer rates of CO₂ for the two membranes are comparable at a blood flow less than 400 ml/min. As blood

flow increases, the CO₂ transfer per meter squared is superior in the 0.8 M² SciMed membrane.

Discussion

The CO₂ transfer rates for the 0.6 M² SciMed membrane are maximal at a blood flow of 400 ml/min and a gas flow of 1800 ml/min. Further increases above 400 ml/min do not augment CO₂ transfer. The manufacturer's maximum recommended gas flow is 1800 ml/min. Exchange of CO₂ was found to be only minimally increased with gas flows higher than 1000 ml/min. Comparison of the 0.6 and 0.8 M² membranes shows that CO₂ transfer per meter squared is comparable up to a flow of 400 ml/min, but beyond 400 ml/min CO₂ transfer for the 0.8 M² membrane is quite su-

terior.

The physical construction of the SciMed membrane allows for channeling of blood flow through the device and a subsequent loss of effective membrane surface area. Some evidence of this was shown with the significant variation of pressure drop across different membranes at various blood flows. Single pass dye flow studies have shown a loss of up to 40 percent of total surface area due to preferential flow patterns through the membrane which may increase the risk for fibrin and clot formation in this device (unpublished data from our laboratory). This becomes of particular concern in neonatal ECMO where anticoagulation is managed differently than in heart surgery.⁶ In an attempt to control intracranial bleeds and other problems related to systemic heparinization, these patients are maintained on low dose heparin. Clot formation in the membrane is a consequence. Because of the smaller surface area of the 0.6 M² membrane, loss of effective surface area related to clot formation may critically compromise CO₂ transfer. Although oxygen transfer is not the limiting factor, use of this membrane should be limited to the lower flow ranges and to infants not likely to experience significant hypercarbia if such infants can be identified.

References

1. Extracorporeal Life Support Organization Neonatal Registry; with permission.
2. Short BL, Miller MK, Anderson KD: Extracorporeal membrane oxygenation in the management of respiratory failure in the newborn. *Clin Perinatol* 14(3):737-748, 1987.
3. Standard for Blood/Gas Exchange Devices—draft, Association for Advancement of Medical Instrumentation, Arlington, Virginia.
4. Kolobow T and Bowman RL: Construction and evaluation of an alveolar membrane artificial heart-lung. *Trans Amer Soc Artif Int Organs* 9:238-41, 1963.
5. Galletti PM, Richardson PD, Snider MT, Friedman LI: A standardized method for defining the overall gas transfer performance of artificial lungs. *Trans Amer Soc Artif Int Organs* 18:359-368, 1972.
6. Children's National Medical Center ECMO Specialist Manual, 5th Edition, 1989.