2. Redline S: The epidemiology of COPD, in Cherniak NS (ed), *Chronic Obstructive Pulmonary Disease*, Philadelphia, W.B. Saunders, 1991, pp. 225–234.
3. Fitzsimmons SC: The changing epidemiology of cystic fibrosis. *J Pediatr* 122: 171–179, 1993.
4. Meyer KC, Raghu G: Perspectives and future advances on the diagnosis and treatment of idiopathic pulmonary fibrosis, in Phan SH, Thrall RS (eds), *Pulmonary Fibrosis*, New York, Marcel Dekker, 1995, pp. 837–874.
5. Keck BM, White R, Breen TJ, Daily OP, Hosenpud JD: Thoracic organ transplants in the United States: a report from the UNOS/ISHLT Scientific Registry for Organ Transplants. Clin Transpl 37–46, 1994.
6. Davis RD Jr, Pasque MK: Pulmonary transplantation. Ann Surg 221: 14–28, 1995.
7. Spray TL: Transplantation of the heart and lungs of children. *Annu Rev Med* 45: 139–148, 1994.
8. Hayden A, Robert R, Kriett R, Smith CM, Nicholson K, Jamieson SW: Primary diagnosis predicts prognosis of lung transplant candidates. *Transplantation* 55: 1048–1050, 1993.
9. Fazzalari FL, Bartlett RH, Bonnell MR, Montoya JP: An intrapleural lung prosthesis: rationale, design, and testing. *Artif Organs* 18: 801–805, 1994.
10. Vaslef SN, Cook KE, Leonard RJ, Mockros LF, Anderson RW: Design and evaluation of a new, low-pressure loss, implantable artificial lung. *ASAIO J* 40: 522–526, 1994.
11. Mitruka BM, Rawnsley HM: *Clinical, Biochemical, and Hematological Reference Values in Normal Experimental Animals and Normal Humans*. New York, Masson Publishing, 1981.
12. Downing SW, Edmunds LH: Release of vasoactive substances during cardiopulmonary bypass. *Ann Thorac Surg* 54: 1236–1243, 1992.

Acute *In Vivo* Studies of the Pittsburgh Intravenous Membrane Oxygenator

MAHENDER MACHA, WILLIAM J. FEDERSPIEL, LAURA W. LUND, PATRICIA J. SAWZIK, PHILIP LITWAK, FRANK R. WALTERS, GARY D. REEDER, HARVEY S. BOROVETZ, AND BRACK G. HATTLER

The efficacy of an innovative intravenous membrane oxygenator (IMO) was tested acutely (6–8 hrs) in seven calves. The IMO prototypes consisted of a central polyurethane balloon within a bundle of hollow fibers with a membrane surface area of 0.14 m^2. The IMO devices were inserted through the external jugular vein into the inferior vena cava of anesthetized calves (68.9 ± 2.3 kg). Rhythmic balloon pulsation (60–120 bpm) was controlled with an intra-aortic balloon pump console. Oxygen sweep gas was delivered through the device at 3.0 L/min. Gas concentrations were monitored continuously by mass spectroscopy. The principal results were as follows: 1) oxygen and carbon dioxide exchange ranged from 125 to 150 ml/min/m^2 and 150 to 200 ml/min/m^2, respectively; 2) there was at least a 30–50% augmentation of gas exchange with balloon pulsation; 3) maximum exchange occurred with 60–90 bpm balloon pulsations; and 4) hemodynamic parameters remained unchanged. There were no device related complications, and the feasibility of insertion of the device by a cervical cut-down was established. These acute *in vivo* experiments show that the Pittsburgh IMO device can exchange oxygen and carbon dioxide gases *in vivo* at levels consistent with this current prototype design, and that intravenous balloon pulsation significantly enhances gas exchange without causing any end-organ damage. *ASAIO Journal* 1996;42:M609–M615.

From the Artificial Lung Program, Department of Surgery, Department of Chemical Engineering and the Bioengineering Program, University of Pittsburgh, Pittsburgh, Pennsylvania.

Reprint requests: William J. Federspiel, PhD, Artificial Lung Program, University of Pittsburgh, Room 428, Biotechnology Center, 300 Technology Drive, Pittsburgh, PA 15219.

The acute respiratory distress syndrome (ARDS) is associated with a high mortality rate (> 50%), despite the availability of advanced modes of ventilatory support and extracorporeal membrane oxygenation (ECMO).[1–4] Although most forms of acute lung injury are reversible, a significant proportion of adult patients require prolonged mechanical respiratory assistance that frequently leads to further pulmonary injury because of both volotrauma and barotrauma. Acute respiratory distress syndrome is associated with progressive interstitial edema, decreased pulmonary compliance, and decreased diffusion capacity.[5] The use of ECMO offers the possibility of "resting" the lungs to permit recovery of pulmonary function, but has failed to improve the survival for these patients because of significant complication rates. Intracorporeal oxygenation was first reported as an alternative to ECMO by Mortensen, with his intravenous oxygenator (IVOX) composed of hollow fiber membranes positioned in the venous system.[6,7] Clinical trials of the IVOX device showed average intravenous gas exchange rates of up to 28% of metabolic requirements.[8,9] The international multi-center clinical trial, which included 160 patients with acute respiratory failure, showed use of the device as a supplement to mechanical ventilation.[9] Use of the device was shown to improve blood gas partial pressures and to allow some patients a decrease in their level of respiratory support, but there was no significant improvement in survival.[9] Clinical investigators have concluded that higher gas exchange rates are needed for intravenous oxygenation to be an effective therapy for ARDS.

At the University of Pittsburgh, we are developing a novel intravenous membrane oxygenator (the IMO device) with an ultimate design goal for gas exchange of 50% of metabolic

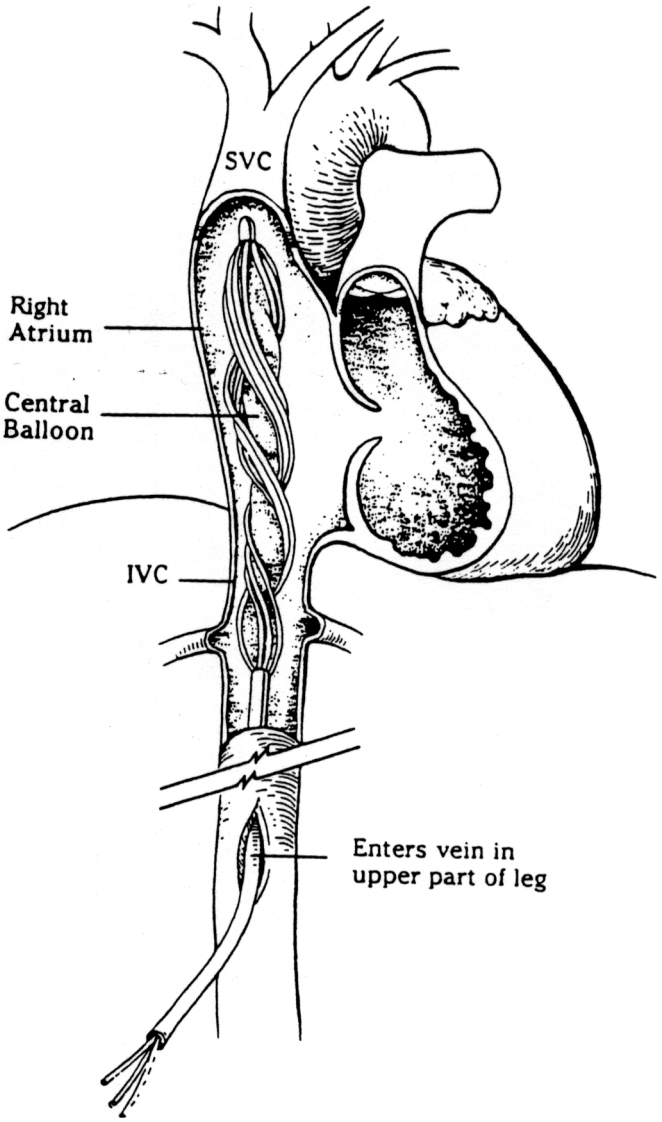

Figure 1. Schematic diagram of anatomic placement of the intravenous membrane oxygenator; SVC, superior vena cava; IVC, inferior vena cava.

requirements. The IMO device uses pulsation of a central polyurethane balloon within the hollow fiber membrane bundle[10-12] to induce active convective flow currents around the hollow fibers, thus augmenting gas exchange by reducing transport resistance associated with diffusional boundary layers at fiber membranes. The IMO device is in a phase of engineering development focused on increasing the efficiency of gas exchange so that the requisite 50% exchange levels can be accomplished in devices with < 0.5 m^2 fiber surface area. This article reports the results of recent acute *in vivo* studies of a scaled down IMO prototype aimed at preliminary assessment of IMO device exchange performance and biocompatibility *in situ*.

Materials and Methods

Device Description

The IMO device is composed of an elongated central polyurethane balloon that is surrounded by microporous hollow fiber membranes (**Figure 1**). The seven devices (D07 series) used in the *in vivo* studies incorporated plasma resistant fibers (PRF, Medtronic, Eden Prairie, MN), potted with Vorite epoxy (Caschem, Inc., Bayonne, NJ) into gas supply and removal manifolds made of Delrin (DuPont, Wilmington, DE). Three of the IMO devices had heparin coated (Carmeda, Medtronic) fiber bundles. All fiber bundles were of scaled down lengths (approximately 20 cm), but contained the maximum number of fibers consistent with peripheral venous insertion (approximately 720 fibers for the PRF 240 μm fibers). The devices averaged 0.14 m^2 in membrane surface area. A pneumatic delivery shaft extends from the cervical entry site of the device to the proximal manifold within the inferior vena cava to provide the requisite gas inflow and outflow paths for O_2, and the helium gas pathway for balloon inflation-deflation.

The IMO devices were tested *in vitro* before the acute animal studies to ensure proper function and gas exchange performance. The *in vitro* flow loop and methods are described elsewhere.[10,11] Oxygen exchange rates *in vitro* averaged between 60 and 80 ml/min/m^2 in water, with estimated exchange rates in blood being approximately 2.5-fold greater (150–200 ml/min/m^2). Maximal gas exchange rates typically occurred between 60 and 90 bpm balloon pulsation rate in these prototypes.

Animal Experiments

Seven female calves (68.9 ± 2.3 kg) were pre medicated with 0.5 mg/kg atropine, induced with 11 mg/kg brevital (Eli Lilly and Co., Indianapolis, IN), and intubated endotracheally. Isoflurane (1–2.5%) was mixed with low flow oxygen and room air (1:1), and the animal was placed on a volume controlled ventilator (Penlon AM1000, Abingdon, UK). The left cervical region was incised to expose the jugular and carotid vessels. An 18 gauge arterial catheter in the right carotid artery was connected to a fluid filled pressure transducer (Baxter Healthcare Corp., Edwards Division, Irvine, CA). A 7 Fr Swan-Ganz thermodilution catheter connected to a cardiac output monitor (Model SAT-2, Baxter Healthcare Corp.) was placed in the right external jugular and advanced approximately 50 cm into the pulmonary artery. A 4 Fr pediatric pulmonary artery catheter (Arrow International, Reading, PA) was placed in the left femoral vein and advanced into the inferior vena cava (30 cm). A pressure and electrocardiograph monitor (Hewlett-Packard, Andover, MA) were used to monitor arterial, pulmonary, central venous, and inferior vena caval pressures. Blood gas tensions were measured with a blood gas machine (Model 505, ABL Radiometer, Copenhagen, Denmark) and co-oximeter (Model 482, Instrumentation Laboratory, Lexington, MA). Anticoagulation was monitored by measurement of activated clotting times (ACT) using an ACT measuring device (Hemachron Jr., International Teledyne Corp., Edison, NJ). Continuous mass spectroscopy was used for measurement of oxygen and carbon dioxide gas exchange rates (Marquette Electronics, Milwaukee, WI). A Gould recorder (Gould, Inc., Cleveland, OH) was used for data collection. Body temperature was maintained at 37°C by the use of a heating pad.

Baseline hemodynamic data and arterial and venous gas tensions were obtained. The animal was then heparinized

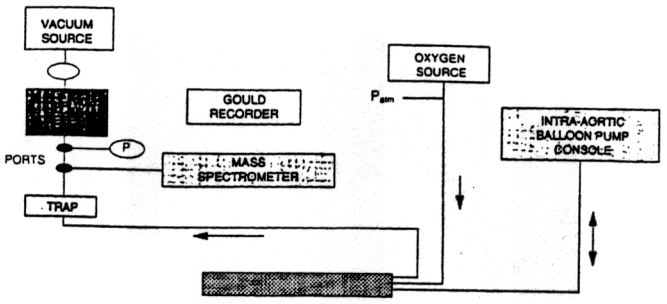

Figure 2. Schematic of intravenous membrane oxygenator, associated equipment, and pneumatic circuitry for determination of gas exchange rates.

with 400 units/kg and a Satinsky clamp was placed on the external jugular. The IMO device was soaked in 25% human albumin immediately prior to insertion through the external jugular vein. By furling the IMO device fully, it was advanced caudally, with the tip of the device extending to the inferior vena cava.

Oxygenator sweep gas (100% O_2) was delivered through the IMO at 3 L/min under vacuum pressure. Since the IMO devices were scaled down prototypes, mechanical ventilation was continued at normal rates (0.3 L/kg min ventilation and 50% FIO_2) to provide adequate respiratory support of the animal. In several experiments a ventilator challenge was performed by decreasing minute ventilation 50%. Balloon pulsation was performed at either 60, 90, and/or 120 bpm for variable time periods, with static inflation of the balloon serving as control in several experiments. Hemodynamic values and blood gas tensions were obtained at each 15–30 min interval, and after each change in balloon pump setting. Plasma free hemoglobin was measured at 1, 2, 4, and 6 hrs. Heparin was administered continuously as an IV drip (initially 0.5–1.0 mg/kg/hr; in the first two experiments only bolus doses were given). ACT was determined hourly and maintained at 400–450 sec with repeat heparin boluses and adjustment in the IV drip as needed. Crystalloid solution was administered at 100 ml/hr, and the animal was maintained under general anesthesia. In the latter two experiments, anesthesia was reduced to observe changes in IMO function during the awake state. At the completion of the study, the animal was fully anesthetized and sacrificed with an injection of potassium chloride. Thoracic and abdominal organs, as well as the vascular structures, were examined at necropsy and the explanted device was carefully examined. All animal procedures were conducted under the supervision of a staff veterinarian, and were in accordance with NIH and University guidelines for the care and use of experimental animals.

Pneumatic Circuitry and Gas Exchange Rates

The gas exchange rate of the IMO device cannot be determined reliably from vena caval blood gas measurements upstream and downstream of the device due to the multiple sources of venous blood flow into the vena cava (i.e., iliac, portal, hepatic, brachiocephalic, azygos). Determination of all the requisite blood flow rates and gas tensions is not feasible. Accordingly, gas exchange rates are determined from gas-side measurements. The implanted IMO, associated equipment, and pneumatic circuitry are schematically demonstrated in **Figure 2.** The sweep gas flow through the IMO device is driven by a vacuum attached to the gas pathway from the distal manifold. The sweep gas exiting the IMO flows through a moisture trap, gas flow meter, and flow regulating valve before reaching the vacuum source. Sample ports after the moisture trap are used for pressure measurement and measurement of effluent gas concentrations by a mass spectrometer. The sweep gas flowing into the IMO device comes from a 100% oxygen source downregulated to near atmospheric pressure. A third pathway in the IMO device is used to pulsate the central balloon with helium gas and is connected to an intra-aortic balloon pump console (Datascope Corp., Oakland, NJ).

Mass balances for CO_2 and O_2 in the IMO sweep gas pathway (assuming 100% oxygen at the inlet) indicate that their respective exchange rates are given by $\dot{V}_{CO2} = Q_{out}F_{CO2}$ and $\dot{V}_{O2} = Q_{in} - Q_{out}F_{O2}$, where Q represents sweep gas flow rate leaving (Q_{out}) or entering (Q_{in}) the IMO device, and F represents the fractional gas concentration of CO_2 and O_2 measured in the exiting pathway. The sweep gas flow rate is typically much greater than O_2 and CO_2 exchange rates, and hence the difference in Q_{in} and Q_{out} is small. Thus, for simplicity, the O_2 exchange rate is often estimated as $\dot{V}^*_{O2} = Q_{out}(1 - F_{O2})$, where the asterisk indicates an estimated value. Combining these O_2 exchange rate expressions, and using the overall mass balance, $Q_{in} - Q_{out} = \dot{V}_{O2} - \dot{V}_{CO2}$, leads to

$$\dot{V}_{O2} = \dot{V}^*_{O2} + (\dot{V}_{O2} - \dot{V}_{CO2}) \quad (1)$$

Accordingly, unless the O_2 and CO_2 exchange rates are balanced exactly, the actual O_2 exchange rate, $\dot{V}_{O2}$, will differ from the estimated value, $\dot{V}^*_{O2}$, and the relative difference can be appreciable (the size of CO_2 and O_2 exchange imbalance). The additional measurement of Q_{in} offers no realizable improvement, because both flow meters (Q_{in} and Q_{out}) would need to be accurate and matched down to a flow rate of the order of $\dot{V}_{O2} - \dot{V}_{CO2}$, a small flow rate relative to the range of sweep gas

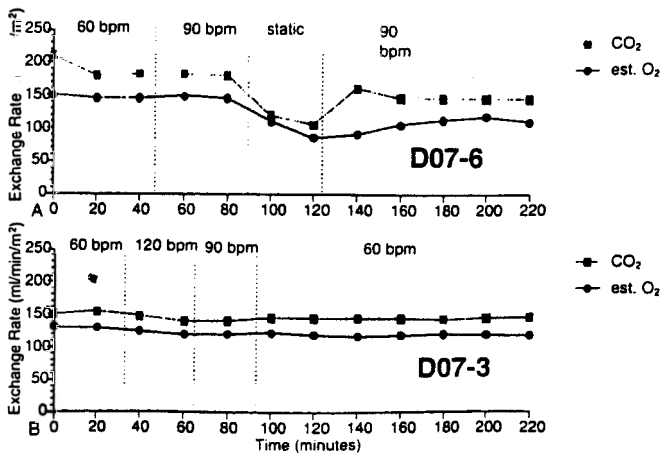

Figure 3. Carbon dioxide and oxygen exchange rates during the course of two animal experiments DO7-6 **(A)**, and DO7-3 **(B)**; bpm, beats per minute. Static balloon inflation leads to decreased exchange rates **(a)**.

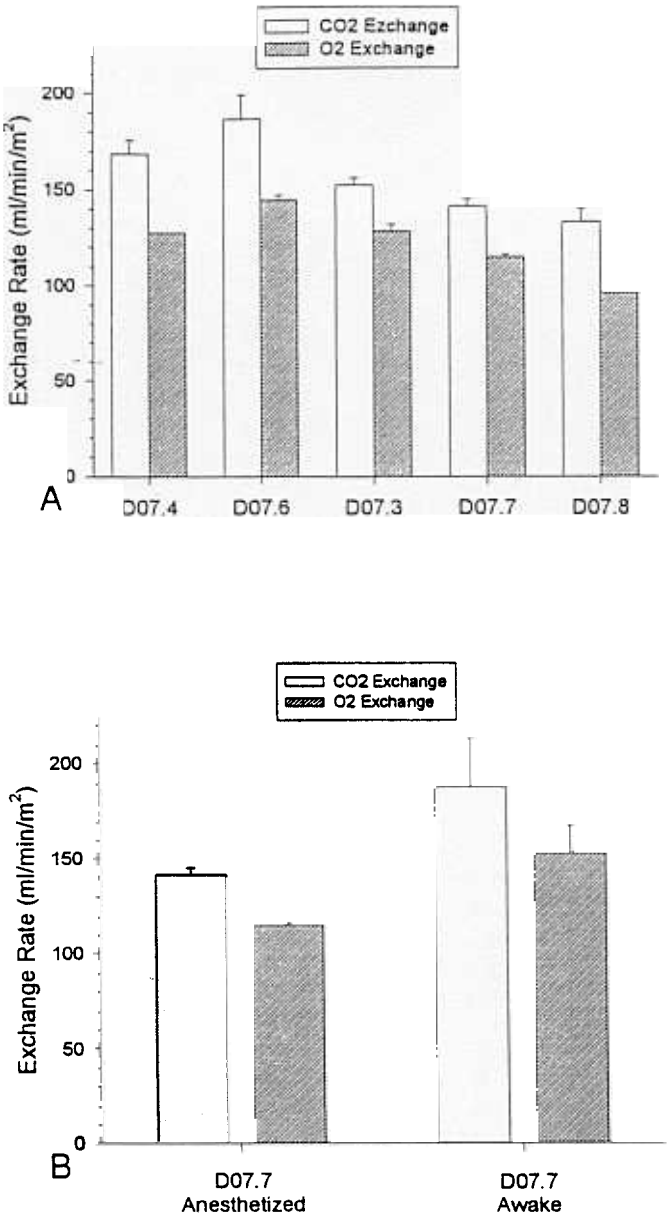

Figure 4. Sustained carbon dioxide and oxygen exchange rates in five acute experiments **(A)**, and representative change in exchange rates upon awakening the animal **(B)**.

flow rates involved. In our study, we reduce the sweep gas flow rate (from 3 L/min to < 1 L/min) during the O_2 exchange measurement only. Since CO_2 exchange is flow dependent whereas that for O_2 is essentially flow independent, reducing the sweep gas flow rate reduces $\dot{V}_{CO2}$ (which at normal sweep gas flow rates usually exceeds $\dot{V}_{O2}$) and helps ensure that the estimated O_2 exchange rate does not represent an overestimate. Furthermore, reducing the sweep gas flow rate increases the O_2 concentration difference in the gas stream (in–out) and, hence, reduces any analysis error associated with computing the difference $(1 - F_{O2})$.

Results

The IMO devices were evaluated acutely in seven calves, with study periods ranging from 3 to 8 hrs, and averaging 6 hrs in duration. The O_2 and CO_2 gas exchange during two representative experiments is shown in **Figures 3a and b.** In both cases, the O_2 exchange rate with balloon pulsation ranged from 125 to 150 ml/min/m², whereas that for CO_2 ranged from 150 to 200 ml/min/m². One experiment (D07-6 device, **Figure 3a)** included a control period with no balloon pulsation. The balloon was pulsed initially at 60 bpm, and CO_2 and O_2 exchange rates stabilized at 180 ml/min/m² and 150 ml/min/m², respectively. There was no significant augmentation in exchange rate with increased balloon pulsation to 90 bpm, but a rapid and significant decline in exchange rates occurred for both CO_2 and O_2 immediately after cessation of balloon pulsation. During the 30 min static control period, exchange rates for CO_2 and O_2 fell by more than 50% to 100 ml/min/m² and 80 ml/min/m², respectively. Resumption of balloon pulsation at 90 bpm increased exchange rates, but only to levels just over 70% of the pre control values, to 140 ml/min/m² for CO_2 and 110 ml/min/m² for O_2.

Reduced levels of gas exchange after a no-pulsation control period (relative to control gas exchange) occurred in each acute experiment involving a period of balloon inactivity. We attributed this to initiation of some thrombus formation within the fiber bundle during the stasis period, which could aggregate fibers sufficiently to reduce effective gas exchange surface area. Accordingly, the no-pulsation control period was eliminated from the experimental protocol, resulting in stable O_2 and CO_2 exchange rates during the entire acute period, as indicated in **Figure 3b** (for the D07-3 device). Here, the CO_2 exchange rate was approximately 150 ml/min/m², and the O_2 rate was 130 ml/min/m². The

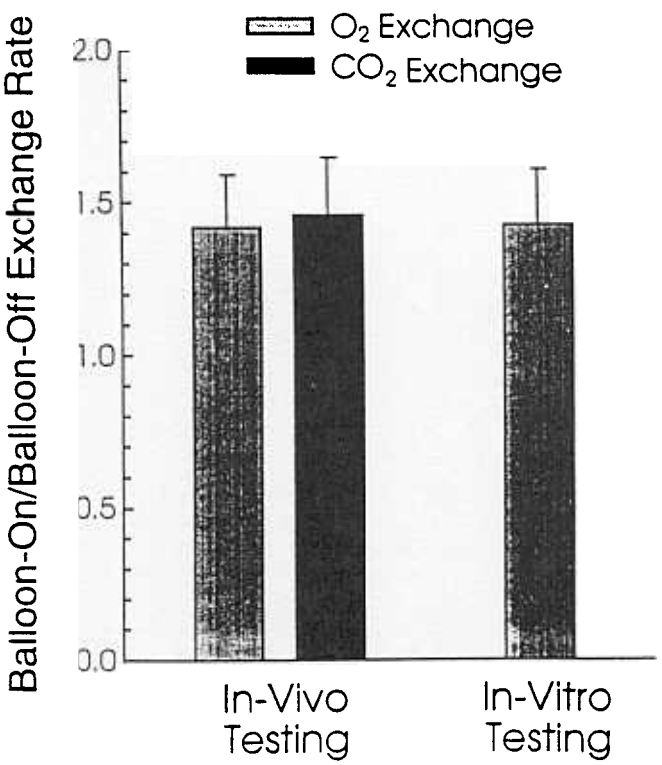

Figure 5. The ratio of exchange rates with balloon pulsation to no pulsation for carbon dioxide and oxygen under *in vivo* and *in vitro* conditions.

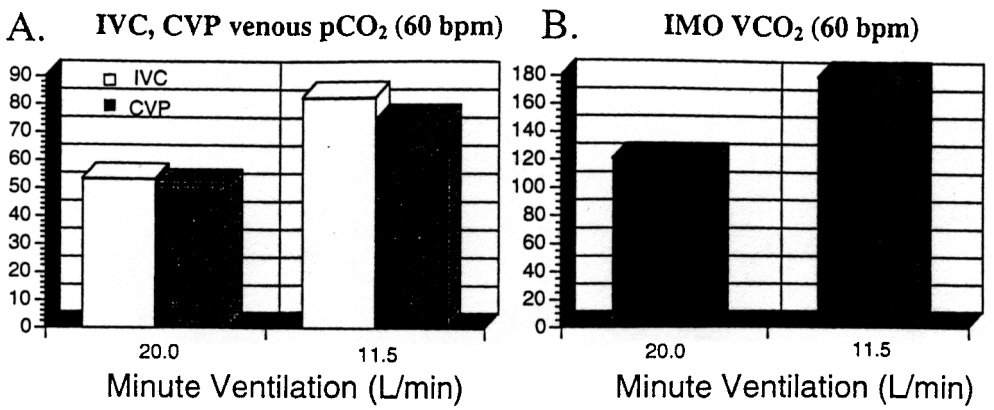

Figure 6. Ventilator challenge increases inferior vena cava and central venous pressure pCO_2 gradient **(A)**, and CO_2 exchange rate (VCO_2) **(B)**; IVC, inferior vena cava; CVP, central venous pressure; Ve, minute ventilation (L/min).

change in exchange rates was less than 10% during the acute time course. Augmenting pulsation beyond 60 bpm did not significantly improve exchange rates of either CO_2 or O_2.

Figure 4 summarizes representative sustained exchange rates found in the acute experiments. Only results from the last five animal tests are included, because the first two acute experiments involved establishing the anticoagulation regimen and balloon pulsation protocols, and the gas exchange rates were not representative of *in vitro* performance. Maximal sustained CO_2 exchange rate was 185 ml/min/m^2, and maximal sustained O_2 exchange rate was 140 ml/min/m^2. It is notable that there was an approximately 10–15% decline in both CO_2 and O_2 exchange rates with the IMO devices that were heparin bonded (DO7-3, DO7-7, DO7-8). Exchange rates increased 30–35% upon awakening the animal **(Figure 4b).** Balloon pulsation had a very significant effect on exchange rates **(Figure 5).** The effective exchange rates increased by 50% with balloon pulsation. These results are consistent with those from *in vitro* testing.

The IMO devices responded appropriately to ventilatory challenge (50% reduction in Ve). **Figure 6** depicts the typical change in exchange rates observed with ventilator challenge during 60 bpm balloon pulsation. The inferior vena cava (IVC) and central venous pressure (CVP) pCO_2 increased from 53 to 82 mmHg, and 51 to 75 mmHg, respectively. At the same time, the CO_2 exchange rate increased markedly from 120 to 180 ml/min/m^2 (50%).

The IMO devices tested were scaled down prototypes with surface areas of approximately 0.14 m^2, or three-fold to four-fold less than we estimate is ultimately compatible with vena caval placement. Accordingly, the IMO devices were not expected to impact significantly on the blood gas levels of the animal (but would respond appropriately to them, as in the ventilatory challenge described above.) Arterial O_2 and CO_2 tensions were altered moderately during the course of the studies; a representative example is shown in **Figure 7.** Mean arterial pO_2 and pCO_2 during the DO7-3 experiment were 280 ± 14 mmHg (base 212 mmHg) and 40 ± 0.3 mmHg (base 38 mmHg), respectively. During balloon pulsation, venous pCO_2 typically was diminished, particularly at the central venous location. For example, IVC and CVP pCO_2 were 42 ± 2 mmHg (base 42 mmHg) and 39 ± 1 mmHg (base 43 mmHg), respectively. The IVC and CVP pO_2 were 57 ± 4 mmHg (base 44 mmHg) and 80 ± 3 mmHg (base 59 mmHg), respectively. The rise in arterial pO_2 after 30 min coincided with the increase in cardiac output after decreasing pulsation from 120 to 90 bpm. The CVP pO_2 also rose significantly at this point.

The hemodynamic response to the IMO device within the vena cava was minimal despite prolonged periods of balloon pulsation. **Figure 8** shows the changes in mean arterial pressure, pulmonary artery pressure, CVP, and IVC pressure during the course of a representative 5 hr study (DO7-3). Heart rate was 103 ± 2 bpm (base 105 bpm), mean arterial pressure 97 ± 2 mmHg (base 96 mmHg), pulmonary artery pressure 31 ± 1 mmHg (base 22 mmHg), CVP 9 ± 1 mmHg (base 10 mmHg), and IVC 21 ± 1 mmHg (12 mmHg). The cardiac output was 7.1 ± 0.2 L/min (base 7.2 L/min). There was a slight decrease in cardiac output to 5.8 L/min after increasing balloon pulsation to 120 bpm. This was observed in several experiments. The pressure drop across the IMO was 12.1 ± 0.6 mmHg (base 2.0 mmHg).

The plasma free hemoglobin levels reached a maximum of 41.5 mg% at 4 hrs in one experiment. Average at baseline, 1, 2, 4, and 6 hr levels are shown in **Figure 9.** Necropsy showed no organ disease. There was no evidence of thromboembo-

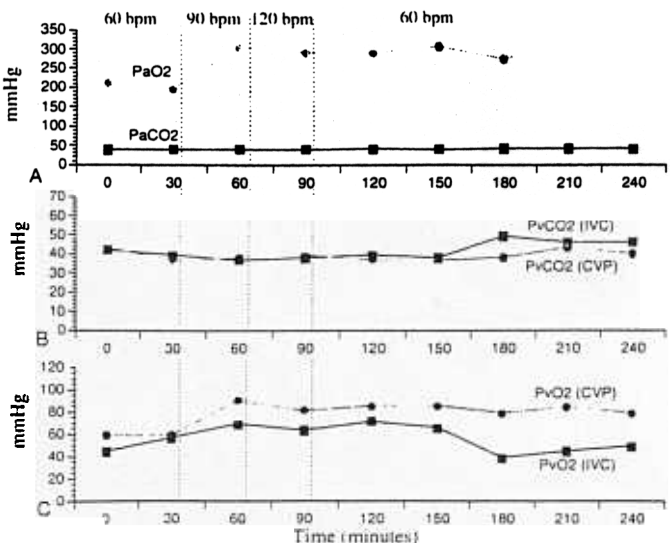

Figure 7. Arterial and venous gas tensions during the course of experiment DO7-3; IVC, inferior vena cava; CVP, central venous pressure; bpm, beats per minute.

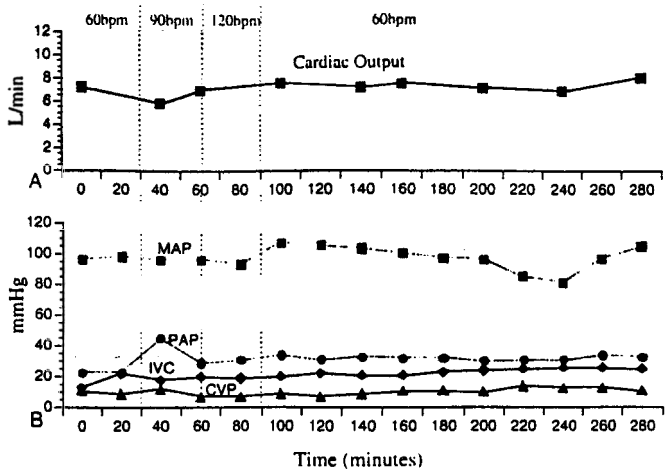

Figure 8. (A) Cardiac output changes during 5 hrs of intravenous membrane oxygenator (IMO) balloon pulsation at 60, 90, and 120 bpm (D07-3); **(B)** Measured pressures during IMO balloon pulsation; MAP, mean arterial pressure; PAP, pulmonary artery pressure; IVC, inferior vena caval pressure; CVP, central venous pressure; bpm, beats per minute.

lus in the lungs or other organs. There was evidence of partially kinked fibers in two experiments. No vena caval injuries were identified, and there was no significant thrombosis associated with the device.

Discussion

We report the results of our first series of acute large animal experiments with the current prototype D07. The exchange rates observed were consistent with the levels obtained in our flow loop circuit. Oxygen exchange ranged from 125 to 150 ml/min/m^2, and CO_2 exchange ranged from 150 to 200 ml/min/m^2. These exchange rates are comparable to the rates obtained by the IVOX device, and would be expected to be significantly higher with a scaled up version that potentially would be used in patients.

Other intravenous oxygenators, such as the IVOX, have relied on venous blood flow for gas exchange. The membrane surface boundary resistance in the fluid phase is considered a major impediment to significant exchange rates.[13] Clinical trials have showed O_2 exchange rates in the range of 28–85 ml/min, and CO_2 rates of 21–87 ml/min, which were considered to be approximately one third of physiologic requirements.[8,9] Efficiency of exchange increased with increasing size of the device. Early clinical trials with the IVOX in patients with severe respiratory failure have showed improved respiratory status in some patients, but no significant change in survival.[9] As a result, design alternatives to the IVOX device are under investigation. Makarewicz *et al.*[14] have described a "screw-type" intravenous oxygenator that rotates, increasing convection around fibers and increasing oxygen transfer rates *in vitro*.

Our approach has been to incorporate balloon pulsation within radially arranged membrane fibers to maximize flow velocity over the membrane surface and increase gas exchange efficiency. *In vitro* studies using fluorescent image tracking velocimetry have confirmed that the velocity profiles adjacent to the fiber are altered markedly with balloon pulsation.[10] Numerous prototypes have been tested *in vitro* in a mock loop circuit, showing improved exchange characteristics with balloon pulsation. Hollow fiber membrane characteristics also have been modified to achieve maximal exchange rates.[9–11]

The efficiency of gas exchange observed with balloon pulsation was approximately twice as great as without pulsation. The improvement in both O_2 and CO_2 exchange was similar. Balloon pulsation rates between 60 and 90 bpm were found to be optimal. Arterial gas tensions were elevated mildly during IMO function. The impact on arterial blood gases would be expected to be significantly increased with a scaled up prototype (0.5 m^2). Interpretation of venous blood gas tensions must take into consideration the effect of blood mixing, which is difficult to quantify. Nevertheless, venous O_2 and CO_2 gradients were altered markedly with balloon pulsation and even greater during ventilator challenge. The hemodynamic effects of balloon pulsation within the vena cava were minimal. There were no device failures. The occurrence of fiber bending was noted in several experiments; this occurred presumably during device insertion.

Chronic studies are planned to further characterize the exchange rates over longer periods. In addition, a smoke inhalation challenge may provide a more clinically relevant respiratory model to test the device in animals.[15]

Conclusions

The goal of our ongoing development of the Pittsburgh IMO is to design an intravenous oxygenator that temporarily will provide respiratory support and replace or supplement mechanical ventilation. A simpler, safer, and cost-effective alternative to ECMO is required to allow earlier intervention whereas pulmonary parenchymal damage still may be reversible. The potential benefits of an intravenous oxygenator that lies in the vena cava and allows gas exchange to occur for patients with acute respiratory failure are significant. In addition to allowing the lung injury associated with ARDS

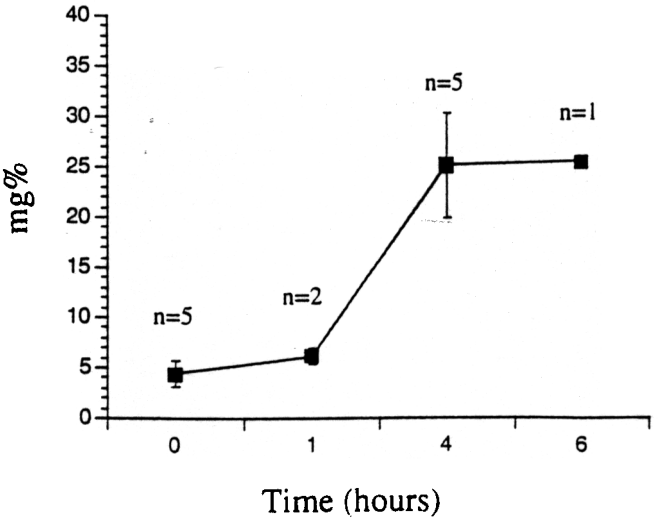

Figure 9. Plasma free hemoglobin levels (± SEM) for combined acute experiments.

to recover, it theoretically would allow patients to maintain mobility and may eventually provide a means for long-term "respiratory dialysis."

Our *in vivo* results confirm that the Pittsburgh IMO, which incorporates balloon pulsation with an intravenous oxygenator, can achieve O_2 and CO_2 exchange rates that are consistent with *in vitro* results, and that balloon pulsation is a simple and effective method of augmenting exchange efficiency without compromising hemodynamic stability.

Acknowledgments

This work was supported by the U.S. Army Medical Research, Development, Acquisition, and Logistics Command under Contract No. DAMD17-94-C-4052. The views, opinions, and/or findings contained in this report are those of the authors and should not be construed as an official Department. of the Army position, policy, or decision unless so designated by other documentation.

The authors thank Medtronics Inc. and the McGowan foundation for their support.

References

1. Ichiba S, Bartlett RH: Current status of extracorporeal membrane oxygenation for severe respiratory failure. *Artif Organs* 20: 120–123, 1996.
2. Snider MT, Campbell DB, Dofke WA, *et al:* Venovenous perfusion of adult and children with severe acute respiratory distress syndrome. *ASAIO Transactions* 34: 1014–1020, 1988.
3. Gattinoni L, Pesenti A, Rossi GP: Treatment of acute respiratory failure with low-frequency positive-pressure ventilation and extracorporeal removal of CO_2. *Lancet* 2: 292–294, 1980.
4. Pesenti A, Gattinoni L, Kolobow T, *et al:* Extracorporeal circulation in adult respiratory failure. *ASAIO Transactions* 34: 43–47, 1988.
5. Kolobow T, Moretti MP, Fumagalli R, *et al:* Severe impairment in lung function induced by high peak airway pressure during mechanical ventilation. *Annual Review of Respiratory Disease* 135: 312–315, 1987.
6. Mortensen JD: An intravenacaval blood gas exchange (IVCBGE) device. *ASAIO Trans* 33: 570–573, 1987.
7. Mortensen JD, Berry G: Conceptual and design features of a practical, clinically effective intravenous mechanical blood oxygen/carbon dioxide exchange device (IVOX). *Int J Artif Organs* 12: 384–389, 1989.
8. High KM, Snider MT, Richard R, *et al:* Clinical trials of an intravenous oxygenator in patients with adult respiratory distress syndrome. *Anesthesiology* 77: 856–863, 1992.
9. Conrad SA, Bagley A, Bagley B, *et al:* Major findings from the clinical trials of the intravascular oxygenator. *Artif Organs* 18: 846–863, 1994.
10. Hattler BG, Johnson PC, Sawzik PJ, *et al:* Respiratory Dialysis: a new concept in pulmonary support. *ASAIO J* 38: M322–M325, 1992.
11. Reeder GD, Hattler BG, Rawleigh J, *et al:* Current progress in the development of an intravenous membrane oxygenator. *ASAIO J* 39: M461–M465, 1993.
12. Hattler BG, Reeder GD, Sawzik PJ, *et al:* Development of an intravenous membrane oxygenator (IMO): enhanced intravenous gas exchange through convective mixing of blood around hollow fiber membranes. *Artif Organs* 18: 806–812, 1994.
13. Mockros LF, Weissman MH: The artificial lung, in Brown JHU, Jacobs JE, Stark L (eds), *Biomedical Engineering,* Philadelphia, Green and Stratton, 1971, pp. 325–347.
14. Makarewicz AJ, Mockros LF, Anderson RW, *et al:* A pumping intravascular artificial lung with active mixing. *ASAIO J* 39: M466–M469, 1993.
15. Zwischenberger JB, Cox CS, Minifee PK, *et al:* Pathophysiology of ovine smoke inhalation injury treated with extracorporeal membrane oxygenation. *Chest* 103: 1582–1586, 1993.