Blood Oxygenation Control by Vacuum Drawn Mixture of Room Air and Oxygen in a Membrane Oxygenator

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Purpose

Oxygen transfer function curves were created for the 1.5 m^2 Sci-Med Spiral membrane oxygenator* in a canine, left heart bypass preparation. The effects of altering the ventilating gas partial pressure of oxygen ($VGpO_2$) on blood oxygenation were quantitated at fixed values of oxygenator blood residence time (t), blood hemoglobin concentration (Hb) and venous blood % O_2 saturation of hemoglobin (SvO_2).

A clinical patient experience employing vacuum ventilation and altering the $VGpO_2$ to control PaO_2 in the Sci-Med Membrane system is reported.

Applying vacuum to the outlet of the gas path of a continuous membrane oxygenator has the following advantages: 1) the gas sweep rate may be increased to blow off more CO_2 when retention occurs without the sequelae of pressurizing the gas path,[1] 2) the pressure gradient for gaseous microemboli to pass through pin hole leaks in the membrane is toward the gas path (viscous blood will not pass through pin hole leaks)[3] and 3) the pressurization of the gas path above one atmosphere and increasing the partial pressure gradient for oxygenation does not occur aiding in avoiding high PaO_2's.[3]

Background

The volume of O_2 gas transported across an artificial membrane per unit time ($\dot{V}O_2$) is determined by many variables including the solubility of O_2 in blood(s), the diffusibility of O_2 across the membrane material and in the blood (D), the venous O_2 partial pressure (PvO_2) and the distance O_2 must diffuse to reach the red blood cell (l):[1]

$$\dot{V}O_2 = \frac{[VGpO_2 - PvO_2] \times s \times D \times t}{l} \quad \text{Eq. 1}$$

The volume of O_2 per unit time that the tissue extract from the blood may be quantitated as;

$$\dot{V}O_2 = \frac{[[PaO_2 - PvO_2] \times s] + \left[\frac{[SaO_2 - SvO_2]}{100} \times 1.34 \times Hb\right]}{100} \times C.O. \quad \text{Eq. 2}$$

where: SaO_2 is the arterial % O_2 saturationof Hb
C.O. is the cardiac output in ml/min
1.34 is the volume of O_2 that 1 gram of Hb can carry

An equilibrium is reached during total heart lung bypass when the $\dot{V}O_2$ extracted by the tissue is matched by the $\dot{V}O_2$ delivered by the oxygenating device, hence:

$$\frac{[(PaO_2 - PvO_2) \times s] + \left[\frac{(SaO_2 - SvO_2)}{100} \times 1.34 \times Hb\right]}{100} \times C.O. = \frac{[VGpO_2 - PvO_2] \times s \times D \times t}{l} \quad \text{Eq. 3}$$

If the temperature is not altered and extreme changes in hematocrit are avoided, the solubility and diffusibility coefficients will not change and may be deleted

* Sci-Med Life Systems Inc., 13000 County Rd. 6 Minneapolis MN 55441

along with the other constants to yield the following proportionality;

$$PaO_2 \propto \frac{\frac{[VGpO_2 - PvO_2] \times t}{l}}{C.O.} - [SaO_2 \times Hb] + [SvO_2 \times Hb] + PvO_2 \quad \text{Eq. 4}$$

Equation four may be used to predict the direction of change in PaO_2 as alterations are made in the independent variables on the right side of the equation. For example, decreasing the SvO_2 and the PvO_2 will decrease the PaO_2 holding other variables constant. Increasing the forcing function for O_2 diffusion across the membrane, $(VGpO_2 - PvO_2)$ or the residence time in the oxygenating device will increase the PaO_2 holding all other variables equal. Increasing the cardiac output or distance that O_2 has to diffuse to reach a red cell or the hemoglobin concentration will decrease the PaO_2 if other variables do not change.

Equation five states the relationship between C.O. and t in seconds/m^2 membrane surface area for one milliliter of blood.[2]

$$\frac{\text{blood residence time}}{m^2} = \frac{\frac{\text{oxygenator dynamic volume (ml)}}{\text{C.O. (ml/sec)}}}{\text{membrane surface area } (m^2)} \quad \text{Eq. 5}$$

$$\text{dynamic volume} = \text{static volume} + (\text{compliance} \times \text{average membrane blood path pressure}) \quad \text{Eq. 6}$$

Increasing C.O. decreases t. Employing an oxygenator with greater surface area and dynamic prime volume, increases t and the PaO_2, holding the C.O. and the venous blood oxygen content constant.

If the effect of altering $VGpO_2 - PvO_2$ on the PaO_2 is examined, then the venous blood O_2 content, Hb concentration, t and l must be judiciously controlled and reported on the O_2 transfer curve.

The distance O_2 has to diffuse to reach a red blood cell (l) is difficult to control, however, the range of l may be minimized by not changing the hematocrit and maintaining the membrane blood path resistance (cross sectional area) constant. Alteration in the Sci-Med membrane blood path resistance occurs with changes in gas sweep flow, blood flow and blood path outlet pressure.

Protocol

Normothermic left heart bypass was established from the left atrial appendage to the left femoral artery in a canine model. Right heart C.O. was assured by maintaining a normal right atrial filling pressure. The left ventricle ejected the remainder of the cardiac output that was not diverted to the extracorporeal circuit by the left atrial cannula. Blood return to the circuit's collapsible reservoir was by gravity. Cricuit blood was then pumped through a heat exchanger and a spiral-wound silicone membrane by a twin roller pump to the left femoral artery.

The pulmonary circuit was intact and was ventilated with a mixture of N_2, CO_2 and O_2 to control the O_2 and CO_2 content of the left atrial blood to serve as a source of constant "venous" blood for the circuit and O_2 transfer studies.

The gas path of the membrane oxygenator was ventilated with a mixture of O_2, CO_2 and room air drawn by a vacuum source.

Figure One depicts the circuit and the instrumentation employed to retrieve the data in Table One. The $VGpO_2$ was dropped in 50 mmHg increments from 100% O_2 and measurements taken after equilibrium (5–10 minutes) at each value of $VGpO_2$. Table Two lists the calculated variables.

The protocol isolates the effect of alterations in SvO_2, Hct and t on the $VGpO_2$, oxygenator function curve during vacuum ventilation. Four clinically simulated phases will be studied and are outlined in Table Three.

Blood residence times of 5.07 and 5.13 sec/m^2 represent a C.O. = 1500 ml/min and, 6.56 and 7.14 sec/m^2, 2000 ml/min. SaO_2, PaO_2, and $\dot{V}O_2$ plotted against ventilating gas pO_2 and % O_2 for each phase and the effect of different values of SvO_2, t and hematocrit on O_2 transfer are evaluated.

Results and Discussion

Figures Two, Three and Four plot the affect of altering $VGpO_2$ and % O_2 on PaO_2, SaO_2 and $\dot{V}O_2$ respectfully for each phase of the protocol (refer to Table Two).

In general, decreasing $VGpO_2$ decreased measurements of blood oxygenation in an exponential manner. The twelve function curves fit an exponential decay model with correlation coefficients ranging from .85 to .99. Although some point scattering is evident, the plotted lines are from the exponential equations derived

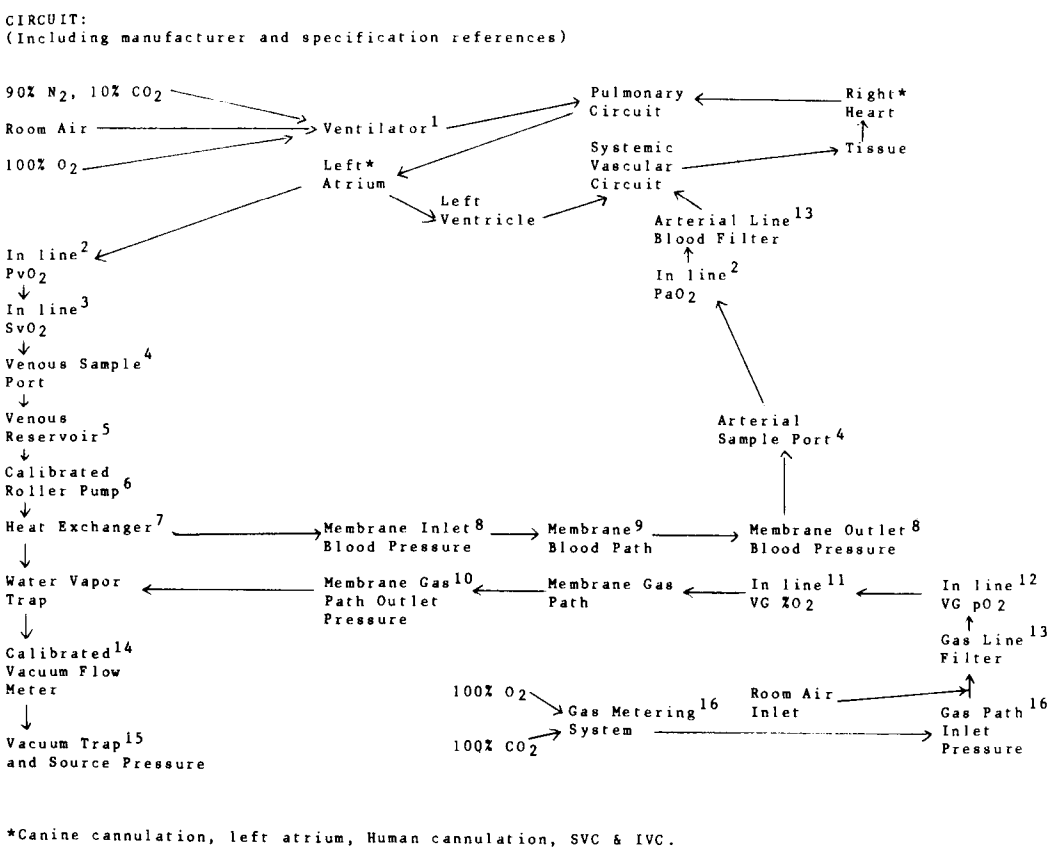

FIGURE 1. *In Vivo* circuit employed to study vacuum ventilation mixture of room air and oxygen to control the PaO_2.

from the linear regression of the $VGpO_2$ versus the natural logarithm of PaO_2, SaO_2 or $\dot{V}O_2$.

Phases I and IV showed little difference in affecting the three function curves. C.O. and blood residence time were similar in Phase I and IV, therefore the drop in hematocrit from 34.5 to 23.4% from Phase I to IV and the increase in the SvO_2 from 74.6 to 80.2% from Phase IV to I had equal offsetting effects on the O_2 transfer curves.

Substantially less oxygen was transferred at each

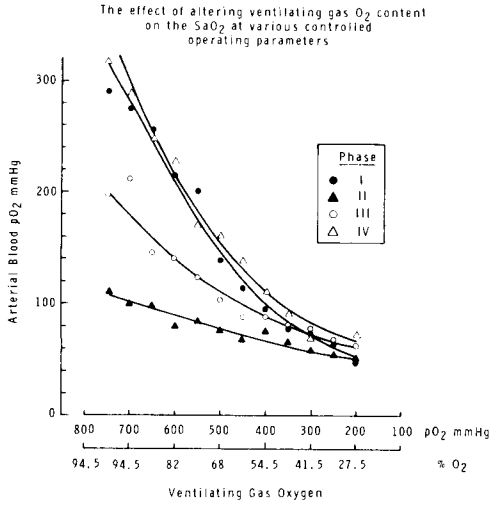

FIGURE 2. The effect of altering ventilating gas O_2 content on the PaO_2 at various controlled operating parameters.

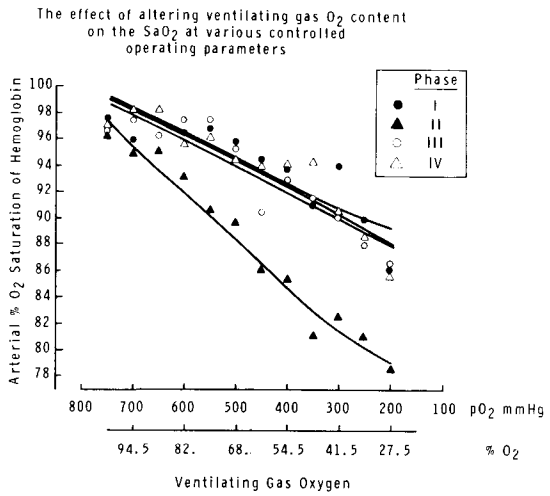

FIGURE 3. The effect of altering ventilating gas O_2 content on the SaO_2 at various controlled operating parameters.

TABLE I

Figure One manufacturer and parameter references and specifications.

Figure One Reference	Device, Parameter or Specification	Device Manufacturer
1.	Respiratory rate % O_2, % CO_2	Harvard Animal Respirator, Harvard Apparatus Co. 150 S. Dover Road, Millis, MA 02054
2.	In line PaO_2, PvO_2	Critikon Oximeter, Divison of McNeil Laboratories 2602 McGaw Avenue, Irvine, California 92714
3.	In SvO_2, 40-100% line	Industrial Inventions, Inc., Model 1400, RD2-463, US Route 1, Monmouth Junction, New Jersey 08852
4.	PaO_2, $PaCO_2$, PaH PvO_2, $PvCO_2$, PvH SaO_2, SvO_2	Instrumentation Laboratories, 313 Blood Gas and pH Analyzer, 113 Hartwell Ave., Lexington, Mass. 02173 American Optics Oximeter, Model #10800, Eggert and Sugar Roads, Buffalo, NY 14215
5.	RV500-1 Venous Reservoir	Sci-Med Life Systems, Inc., 13010 County Road, Minneapolis, MN 55441
6.	Cardiac Output (C.O.)	Travenol Modular Calibrated Twin Roller Pump, Travenol Laboratories Inc., 1 Baxter Pkwy, Deerfield, IL 60015
7.	Omnitherm Heat Exchanger	Sci-Med Life Systems, Inc.
8.	Membrane Blood Path pressure in and out (PM_I, PM_O)	Calibrated Hewlett-Packard strain gauge transducer, 175 Wyman Street, Waltham, Mass. 02154
9.	Spiral Wound Silicon Membrane Oxygenator	Sci-Med Life Systems, Inc.
10.	Negative pressure gauge 0 to -760 mmHg Membrane gas path pressure out (PG_O)	Sarns, Inc., 6200 Jackson Road, Ann Arbor, MI 48103
11.	Ventilating Gas % O_2, 0-100% ($VGpO_2$)	Ohio Medical Products, Model 201, Arco Inc., Madison, WI 53701
12.	Ventilating gas pO_2, p-800 mmHg ($VGpO_2$)	Beckman Instrument, Model OM-15, Corporate, 2500 Harbor Drive, Fullerton, CA 92634
13.	Gas and blood line microfilters	Pall Corporation, Geen Cove, NY 11542
14.	Vacuum Flow Meter (calibrated O_2 flow meter), 0-15 L/min (GQ)	Sarns, Inc.
15.	Vacuum Source and Trap, Set at -200 mmHg	Oxequip, Inc., Chicago, IL 60658, Mackbeck Sales, Murray Hill, NJ 07974
16.	Gas Flow Metering System, Membrane gas path pressure in (PG_I)	Olson Medical Products, Ashland, Mass. 01721

$VGpO_2$ during Phase II than Phase III. Phases II and III had identical hematocrits and t values, yet the decreased SvO_2 in Phase II compromised the oxygenator's ability to attain acceptable PaO_2 and SaO_2 values at $VGpO_2$s less than 600 mmHg (82% O_2). Inadequate blood oxygenation would occur when values of SvO_2 became too low for the perfusionist selected variables of blood residence time and the ventilating gas O_2

TABLE II

Equations for and units of measure of protocol calculated parameters.

Calculated Parameter	Equation	Units of Measure
Membrane gas path resistance	$(PG_I-PG_O)/GQ$	mmHg/L/min
Membrane blood path resistance	$(PM_I-PM_O)/C.O.$	mmHg/ml/sec
$\dot{V}O_2$	Equation 2 (text)	mlO_2/min
t	Equation 8 (text)	seconds
Average membrane blood path pressure	$(PM_I-PM_O)/2$	mmHg

TABLE III

Protocol phase control parameters of hematocrit, SvO_2, PvO_2, blood residence time and blood path resistance in the membrane oxygenator.

CONTROL PARAMETERS:

Phase	Hematocrit %	Residence Time sec/M^2	Venous $\%O_2$ Saturation %	Venous pO_2 mmHg	Blood Path Resistance mmHg/ml/min
I mean	34.5	6.56	80.2	50.1	.087
S.D.	2.5		2.8	5.9	.003
II mean	41.	5.07	68.	51.	.053
S.D.			2.5	4.4	.008
III mean	41.	5.13	79.8	56.6	.06
S.D.			1.9	2.8	.002
IV mean	23.4	7.14	74.6	43.7	.081
S.D.	.2		2.3	2.5	.012

content. CO_2 transfer would be compromised if gas sweep rate were inadequate for the venous blood CO_2 content and blood residence time.

Phases I and III had higher values of hematocrit and similar SvO_2s yet the oxygenator was able to transfer substantially more O_2 at higher values of the $VGpO_2$ in Phase I due to the increased blood residence time at the lower cardiac output through the 1.5 m^2 membrane.

The greater the hematocrit and the lower the values of t and SvO_2, the greater the $VGpO_2$ needed to attain an arterial pO_2 and SO_2 acceptable for tissue perfusion. Conversely, lower hematocrits, longer values of t and high SvO_2s facilitate blood oxygenation at lower values of $VGpO_2$.

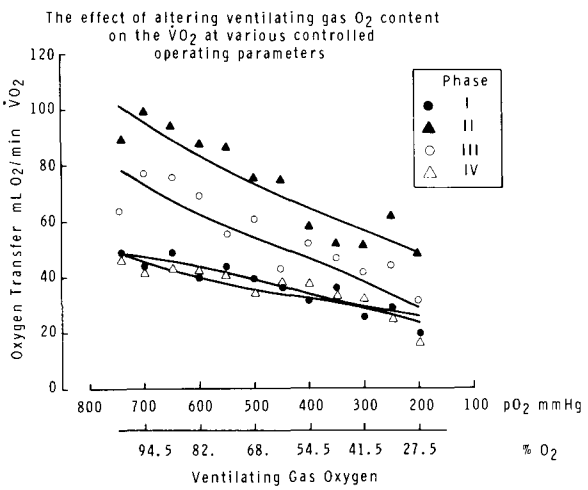

FIGURE 4. The effect of altering ventilating gas O_2 content on the $\dot{V}O_2$ at various controlled operating parameters.

Clinical Example

Figure Five plots the bypass course for a 41 year old male redo coronary artery bypass graft patient. The circuit in Figure One was employed with a 3.5 m^2 membrane.

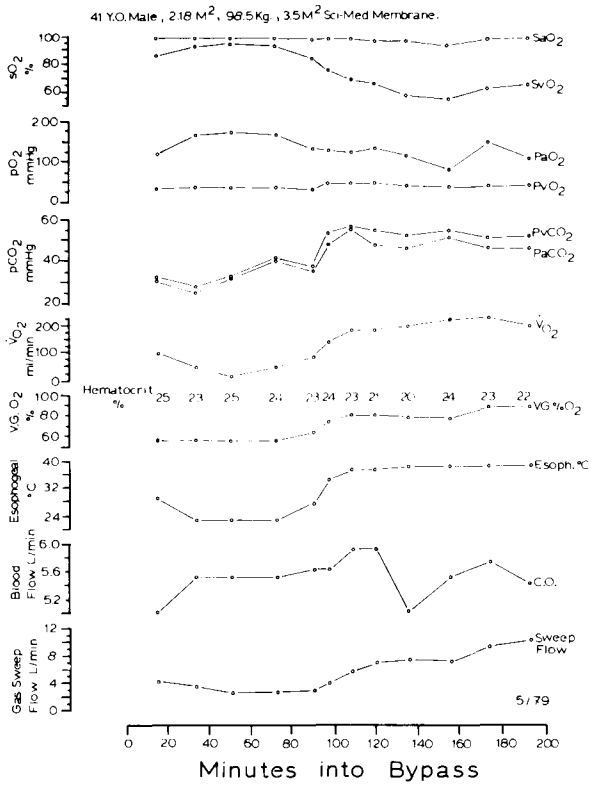

FIGURE 5. The bypass course for a 41 year old male, redo coronary bypass graft patient employing vacuum ventilation and a 3.5 m^2 Sci-Med Membrane System.

Vacuum ventilation was employed to mix room air and 100% oxygen to vary $VGpO_2$ to control the PaO_2. The vacuum flow rate was adjusted to alter the gas sweep rate to control the $PaCO_2$.

The patient was cooled to 22°C esophogeal. The $\dot{V}O_2$ reflects the decreased metabolism at 22°C and the resulting elevated SvO_2 and PvO_2 in the face of a Cardiac Index of 2.5 L/min/m^2. The high venous O_2 content allowed ventilation with 55% O_2 in the sweep gas and the low production of CO_2 by the patient facilitated the respiratory alkalosis experienced at a sweep rate of 2.7 to 4 L/min at 30–50 minutes into bypass. Efforts to decrease the sweep rate to retain CO_2 were not successful until patient warming began. CO_2 addition to the ventilating gas was justifiable at 0–40 minutes but not carried out.

Warming to 34°C brought a substantial increase in $\dot{V}O_2$ and concurrent drop in SvO_2 and PvO_2 despite the increase in C.O. at 100 minutes. The increase in CO_2 production was not responded to by an increase in sweep rate before CO_2 retention and an increase in total CO_2 content of the blood was realized (respiratory acidosis). The gas sweep rate should have been increased at the beginning of warming (50 minutes) and to a greater magnitude at 35–38°C to blow off the CO_2 accumulation with warming.

Blood oxygenation and PaO_2 control were easily and safely controlled by altering the $VGpO_2$. CO_2 control by altering the gas sweep rate in this example was tedious but a function of the perfusionist mastering the technique of predicting CO_2 dynamics with rapid warming with the Sci-Med membrane in specific patient populations.

Conclusions

1. Blood oxygenation with a vacuum drawn mixture of room air and oxygen through the Sci-Med membrane is a safe and predictable clinical modality.

2. Arterial blood pO_2 is adjusted by alterations in the % O_2 in the ventilating gas and arterial pCO_2 is controlled by the total vacuum gas sweep rate.

3. Blood/membrane residence time, venous blood O_2 content, hemoglobin concentration and membrane blood path thickness affect the oxygen transfer rate in the Sci-Med Membrane System. If the ventilating gas % O_2 is decreased, these variables and arterial blood gases must be carefully monitored to avoid O_2 debts and CO_2 retention in changing patient situations such as rapid warming.

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