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Evaluation of Quadrox-i® Adult Hollow Fiber Oxygenator with Integrated Arterial Filter

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Abstract: Gaseous microemboli (GME) remain a challenge for cardiopulmonary bypass procedures in adult as well as pediatric cardiac surgery patients. The present study tested the effectiveness of a new adult membrane oxygenator in models both with and without an integrated arterial filter to evaluate GME trapping capability and determine membrane pressure drops at various flow rates and temperatures. The experimental circuit included a RotaFlow centrifugal blood pump, Quadrox-i® ($n = 8$) or Quadrox® ($n = 8$) adult microporous membrane oxygenator, and Sorin adult tubing package. A Sorin Cardiovascular® VVR® 4000i venous reservoir served as pseudo-patient. The circuit was primed with 900 mL heparinized human red blood cells and 300 mL Lactated Ringer's solution. The final hematocrit was 36%. Tests were performed at different flow rates (4 L/min, 5 L/min, and 6 L/min) and temperatures (35° and 30°). Five mL of bolus air was injected into the venous line over 15 seconds using a syringe connected to a 3/8 × 1/2 luer connector. The Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter had a similar pressure drop at 4 L/min and 35°C compared with Quadrox® membrane oxygenator whereas it had higher pressure drops at 5 L/min and 6 L/min ($p < .001$). Quadrox-i® adult microporous membrane oxygenator reduced the total emboli count and total emboli volume delivered to the pseudo-patient at all flow rates ($p < .001$). The emboli handling of Quadrox-i® adult microporous membrane oxygenator was not affected by flow rate and temperature. Compared with the traditional Quadrox® oxygenator, Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter and Softline coating has improved GME handling capacity.
Keywords: gaseous microemboli, membrane oxygenator, integrated arterial filter, cardiopulmonary bypass, neurological complication. *JECT. 2010;42:134–138*

A prominent strategy aimed at avoiding brain injury during open heart surgery is to reduce emboli load (1–3). The sources of gaseous or particulate emboli during cardiopulmonary bypass (CPB) are diverse, but primarily relate to specific surgical techniques as well as components of the extracorporeal circuit (4–6). Improvement of circuit design and CPB procedures is directed in part toward minimizing the delivery of gaseous microemboli (GME) to patients. In clinical CPB, GME trapping depends on three separate components within the circuit: reservoir, oxygenator, and arterial filter. Different oxygenators incorporate varying reservoir designs with special filter and defoamer materials (7). There are also differences in the pore size of filter materials. Quadrox® membrane oxygenator (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) has minimal priming volume and defoamer material incorporating polypropylene, polyurethane, and antifoam C. Our previous studies demonstrated Quadrox® membrane oxygenator reservoir has the best gaseous emboli capture capability as reflected by the lowest post-pump total emboli count and membrane pressure drop (7). With special filter and defoamer materials emboli may be trapped inside of the oxygenator. Additionally, the spatial configuration of fibers within the oxygenator affects air handling capability and pressure drop in the membrane compartment.

Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter and Softline coating (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) is comparable to Quadrox® hollow fiber membrane oxygenator with Safeline coating with regards to intended use, design, principals of operation, biocompatibility, and performance in terms of the oxygenator and heat exchanger components; and is comparable to the Quart Arterial Filter in similar measures in terms of the filter component.

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In this experiment, GME handling capability and transmembrane pressure drop of Quadrox-i® adult microporous membrane oxygenator were compared to Quadrox® oxygenator without an arterial filter in a simulated adult extracorporeal circuit.

MATERIALS AND METHODS

Experimental Circuit Design

The experimental circuit was designed to evaluate different oxygenators in terms of pressure drops and GME entrapment using an adult extracorporeal model (seeFigure 1). The experimental circuit included a RotaFlow centrifugal blood pump, Quadrox-i® or Quadrox® adult microporous membrane oxygenator, and Sorin adult tubing package (Sorin S.p.A., Milano, Italy). A Sorin Cardiovascular® VVR® 4000i venous reservoir served as pseudo-patient. The circuit was primed with 900 mL heparinized human red blood cells and 300 mL Lactated Ringer's solution. Pseudo-patient level was maintained at 500 mL. Total priming volume was 1200 mL and final hematocrit was 36%. Five thousand units of heparin were added to the circuit. A Hoffman clamp was placed at the end of the arterial line to maintain a target arterial line pressure of 200 mmHg. De-airing port of both oxygenators was closed in all experiments.

Experimental Design

Per study design, the experiment was performed at normothermia (35°C) and mild hypothermia (30°C) maintained via Heater-Cooler Unit HCU 30 (MAQUET Cardiopulmonary AG, Hirrlingen, Germany) throughout the whole procedure. Flow rates were monitored using TS410 transit-time tubing flow meters (Transonic Systems Inc., Ithaca, NY) at the pre-oxygenator site. An Emboli Detection and Classification (EDAC) Quantifier (Luna Innovations, Hampton, VA) was used to simultaneously record microemboli counts and total microemboli volume. Three transducers from the EDAC Quantifier were attached to EDAC connectors which were inserted into the circuit at venous, pre-oxygenator, and post-oxygenator sites. De-airing port of the oxygenators was closed during all experiments. Non-pulsatile perfusion was used in all experiments.

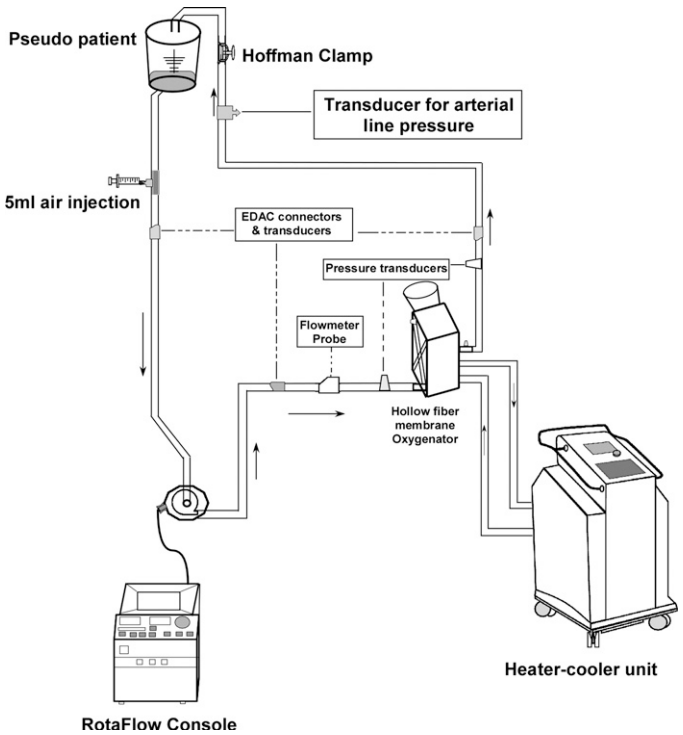

Figure 1. Schematic layout of experimental circuit.

Pressure was monitored at pre-oxygenator and post-oxygenator sites. To avoid confounds from the air injection, protocol pressure tests were conducted before air injection at every specified blood flow rate and temperature. Pressure data was collected using signal conditioning configurable connectors (SC-2345, National Instruments, Austin, TX) linked with a data acquisition device (NI USB-6251, National Instruments, USA, Austin, TX), which was connected to a computer via universal serial bus port. National Instruments LabView 7.1 software was used to quantify and display collected data. A 20-second segment of pressure readings (1000 samples per second) was recorded at each site. Trans-membrane pressure drop between pre-oxygenator and post-oxygenator sites was calculated at different flow rates and temperatures.

To introduce and detect gaseous microemboli 5 mL of air was injected into the venous line over 15 seconds using a syringe connected to a 3/8 × 1/2 luer connector. For each trial, 5-minute segments of data were recorded simultaneously at venous, pre-oxygenator, and post-oxygenator sites after the injection. Eight trials were conducted for each unique combination of flow rate (4 L/min, 5 L/min, and 6 L/min), temperature (35°C, 30°C), and oxygenator for a total of 96 trials (3 flow rates × 2 temperature × 2 oxygenator × 8 trials each). During the experiment, there was a 2-minute period between different injections at the same flow rate to allow the system to achieve full equilibrium, a 10-minute equilibrium period between different flow rates, and a 60-minute equilibrium period between different temperatures. With the exception of switching oxygenators ($n = 8$ for each group) all tests were conducted using identical protocols with all other components unchanged.

Statistical Analysis

Analysis of variance models, allowing for heterogeneous variance components, were fit to the pre- to post-oxygenator pressure drop to compare oxygenators (Quadrox® versus Quadrox-i®), temperature (30°C or 35°C), and blood flow rates (4 L/min, 5 L/min, and 6 L/min). Linear mixed-effects models were fit to the continuous outcomes (i.e., total volume and emboli count) to compare oxygenators (Quadrox®

versus Quadrox-i®), temperature (30°C or 35°C), blood flow rates (4 L/min, 5 L/min, and 6 L/min), and location (venous, pre-oxygenator, and post-oxygenator). The linear mixed-effects model is an extension of linear regression that accounts for the within-subject variability inherent in repeated measures designs. In this study, the repeated factor is the location (venous, pre-oxygenator, and post-oxygenator). Residual diagnostics were used to evaluate model fit. *P*-values were adjusted for multiple comparisons testing using the Tukey-Kramer procedure. All hypotheses tests were two-sided and all analyses were performed using version 9.1 of the SAS System for Windows (SAS Institute Inc., Cary, NC).

RESULTS

Trans-Membrane Pressure Drop

Table 1 summarizes trans-membrane pressure drops for the respective oxygenators between pre-oxygenator and post-oxygenator sites under different flow rates and temperatures. Comparison demonstrates consistent trends among the respective oxygenators. For the same temperature, pressure drop was highest at 6 L/min and lowest at 4 L/min. For the same flow rate, there was a slight increase in pressure drop when the temperature decreased from 35°C to 30°C due to increase in blood viscosity.

Table 1. Trans-membrane pressure drop (mmHg) between pre-oxygenator and post-oxygenator sites at different temperatures (35°C, 30°C) ($n = 8$).

	35°C		30°C	
Flow Rate	Quadrox®	Quadrox-i®	Quadrox®	Quadrox-i®
4 L/min	55.33 ± .64	54.19 ± .53†	56.25 ± .33	57.32 ± .19*
5 L/min	66.98 ± .39†	69.45 ± .18*†	68.23 ± .27	74.04 ± .17*
6 L/min	79.89 ± .53†	86.35 ± .33*†	81.52 ± .42	92.01 ± .43*

*$p < .001$ Quadrox® versus Quadrox-i® adult microporous membrane oxygenator at same temperature.
†$p < .001$ comparison between 35°C and 30°C for the same type of oxygenator.

Oxygenators and Emboli Capture

Tables 2 and 3 summarize total GME count and emboli volume (mL) as well as classification and quantification of microemboli by size at the three respective sites measured by the EDAC quantifier. Lower total emboli count and volume was recorded for Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter at every flow rate and temperature ($p < .001$). Total post-oxygenator emboli count for Quadrox-i® adult microporous membrane oxygenator was about 50% less (53,304 ± 1462 versus 27,398 ± 1256) and total volume was about 90% less (.27 ± .01 versus .03 ± .00) compared with Quadrox® membrane oxygenator at the 4 L/min flow rate. More detailed classification of emboli counts by size (μm) indicates that Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter has better gaseous emboli trapping capacity compared with Quadrox® membrane oxygenator ($p < .001$) (Table 3).

Influence of Temperature and Flow Rate on Emboli Load

When the temperature decreased from 35°C to 30°C minimal changes in total emboli count and volume were recorded at the respective sites and flow rates. Classification of microemboli was not significantly changed by temperature. When flow rate increased, significantly fewer emboli

Table 2. Total emboli count and total emboli volume (mL) at venous, pre-oxygenator, and post-oxygenator sites at different flow rates and temperatures ($n = 8$ for each group).

		35°C		30°C	
Flow Rate	Site	Quadrox® ($n = 8$)	Quadrox-i® ($n = 8$)	Quadrox® ($n = 8$)	Quadrox-i® ($n = 8$)
4 L/min					
	Venous	119,306 ± 1699 (1.03 ± .09)	41,156 ± 969* (.54 ± .06†)	111,265 ± 2203 (1.06 ± .06)	39,406 ± 775* (.54 ± .05†)
	Pre-Oxygenator	85,871 ± 1451 (.77 ± .07)	35,697 ± 503* (.74 ± .05)	86,361 ± 2803 (.74 ± .04)	33,658 ± 654* (.66 ± .02†)
	Post-Oxygenator	53,304 ± 1462 (.27 ± .01)	27,398 ± 1256* (.03 ± .00†)	53,667 ± 3117 (.23 ± .01)	27,749 ± 387* (.02 ± .00†)
5 L/min					
	Venous	83,537 ± 982 (.61 ± .03)	29,023 ± 961* (.12 ± .02†)	85,484 ± 251 (.63 ± .03)	29,374 ± 503* (.16 ± .04†)
	Pre-Oxygenator	77,650 ± 856 (.89 ± .06)	29411 ± 679* (.60 ± .04†)	71753 ± 700 (.70 ± .02)	28756 ± 311* (.59 ± .03†)
	Post-Oxygenator	51,470 ± 1021 (.28 ± .02)	20562 ± 284* (.03 ± .00†)	47626 ± 721 (.25 ± .01)	21405 ± 354* (.02 ± .00†)
6 L/min					
	Venous	65,007 ± 466 (.57 ± .02)	23,941 ± 876* (.08 ± .02†)	60,649 ± 1142 (.58 ± .03)	25,520 ± 560* (.07 ± .01†)
	Pre-Oxygenator	64,438 ± 561 (.76 ± .05)	25,718 ± 824* (.46 ± .01†)	54,568 ± 1230 (.62 ± .02)	28,182 ± 681* (.50 ± .03†)
	Post-Oxygenator	39,913 ± 466 (.29 ± .02)	17,320 ± 503* (.03 ± .00†)	35,131 ± 695 (.26 ± .01)	20,329 ± 440* (.02 ± .00†)

(Numbers in parentheses represent total emboli volume).
*$p < .001$ comparison of total emboli count between Quadrox® and Quadrox-i® adult microporous membrane oxygenator at same flow rate and temperature.
†$p < .001$ comparison of total emboli volume between Quadrox® and Quadrox-i® adult microporous membrane oxygenator at same flow rate and temperature.

Table 3. The classification and quantification of microemboli by size class (μm) detected at post-oxygenator site at different flow rates and temperatures ($n = 8$ for each trial).

		35°C		30°C	
Flow Rate	Size	Quadrox® ($n = 8$)	Quadrox-i® ($n = 8$)	Quadrox® ($n = 8$)	Quadrox-i® ($n = 8$)
4 L/min					
	0–20 microns	23,755 ± 557 (45% ± 0%)	11,570 ± 770* (42% ± 1%)	23,959 ± 1311 (45% ± 0%)	11,953 ± 313* (43% ± 1%)
	20–40 microns	14,450 ± 530 (27% ± 0%)	7,763 ± 322* (28% ± 0%)	14,336 ± 1081 (27% ± 1%)	7,470 ± 91* (27% ± 0%)
	Over 40 microns	15,099 ± 560 (28% ± 1%)	8,065 ± 208* (29% ± 1%)	15,372 ± 835 (29% ± 1%)	8,326 ± 112* (30% ± 0%)
5 L/min					
	0–20 microns	22,242 ± 467 (43% ± 0%)	7,452 ± 193* (36% ± 1%)	20,601 ± 378 (43% ± 0%)	8,057 ± 175* (38% ± 0%)
	20–40 microns	13,811 ± 375 (27% ± 0%)	5,255 ± 119* (26% ± 0%)	12,684 ± 233 (27% ± 0%)	5,415 ± 87* (25% ± 0%)
	Over 40 microns	15,417 ± 311 (30% ± 0%)	7,856 ± 172* (38% ± 1%)	14,340 ± 206 (30% ± 0%)	7,933 ± 131* (37% ± 0%)
6 L/min					
	0–20 microns	18,531 ± 309 (48% ± 0%)	5,658 ± 346* (33% ± 1%)	15,169 ± 398 (43% ± 1%)	7,746 ± 212* (38% ± 0%)
	20–40 microns	9,417 ± 157 (23% ± 0%)	4,129 ± 143* (24% ± 0%)	8,450 ± 230 (24% ± 0%)	4,904 ± 126* (24% ± 0%)
	Over 40 microns	11,965 ± 203 (30% ± 0%)	7,533 ± 111* (44% ± 1%)	11,512 ± 263 (33% ± 1%)	7,679 ± 133* (38% ± 0%)

(Numbers in parentheses are percentages relative to the total emboli count at post-oxygenator site).
*$p < .001$ comparison of emboli count at post-oxygenator site between Quadrox® and Quadrox-i® at same flow rate and temperature.

were delivered at each site recorded regardless of oxygenator and temperature ($p < .001$).

DISCUSSION

The Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter and Softline coating is a novel membrane oxygenator designed to enhance GME trapping capability. Results demonstrate trans-membrane pressure drop increased with higher flow rates and lower temperatures. The Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter had a similar pressure drop at 4 L/min compared with Quadrox® membrane oxygenator, however the Quadrox-i® exhibited slightly higher pressure drop at 5 L/min and 6 L/min.

EDAC results demonstrated temperature has little influence on GME generation, with minimal changes in total emboli count and volume recorded at various sites and flow rates given a change in temperature. Another notable finding is the effect of flow rate on emboli. When the flow rate increased, significantly fewer emboli were delivered at each of the three sites regardless of oxygenator and temperature. One possible explanation is increasing rotation speeds may trap more emboli inside the centrifugal blood pump. In addition, the centrifugal pump reduces or breaks up bubbles into much smaller bubbles, especially at higher revolutions per minute, such that they may not be counted by EDAC.

Limitations of this Study

We intentionally did not use an arterial filter in the Quadrox® group. Use of an arterial filter (Quart) with Quadrox® oxygenator (in line with clinical CPB procedures) would necessitate an open purge line with the net effect of lower actual flow rates in the Quadrox® group compared to the Quadrox-i® group despite similar target flow rates. Blood flow may be diverted from the pseudo patient depending on circuit pressure and pseudo patient resistance. We have already demonstrated this "stolen blood flow" in our pediatric models (8). Flow rates must be identical to make a direct and meaningful comparison between oxygenators. Additionally, based on our earlier experiments flow rate is one of the major determinants for emboli detection and classification (5).

Another limitation of the study is that we can only simultaneously detect and evaluate microemboli at three sites using this unique EDAC system (9). We preferred to place the first connector on the venous line (mirroring our clinical set-up) to determine if there were differences among injections (or any outliers) after 5 mL bolus air injection into the venous line. Second and third connectors were placed before and after the respective oxygenator to evaluate microemboli trapping capacity. This precluded a fourth connector before the Hoffman clamp because a maximum of three transducers were available. This contrasts with our clinical set-up which employs the first connector on the venous site and the second one after the arterial filter.

Although 5 mL of bolus air was introduced in both circuits over 15 seconds data was recorded for 5 minutes. This duration was selected due to results of pilot experiments demonstrating a 5 minute interval was adequate to detect all microemboli resulting from bolus air injection with no microemboli detected at the end of the 5 minute duration. Only after no further microemboli were detected followed by a waiting interval allowing the circuit to equilibrate was the next air bolus injected. In the Quadrox® group, however, more emboli in terms of counts and volume were recorded after first injection at the venous site because not all emboli can be trapped or detected in the first pass. In the Quadrox-i® group more emboli in terms of counts and volume was trapped in the first pass through the oxygenator

because of the integrated arterial filter, resulting in fewer microemboli recorded at the venous site over the five minute duration. For both circuits, the majority of microemboli were detected in the first 30 seconds after bolus air injection during the 5 minute duration. Another important consideration is that though we injected 5 mL bolus air we were able to record a maximum of 1 mL, presumably because EDAC cannot record volumes in excess of 0.5 mL or because most of the volume was trapped in the reservoir before rather than making second and third passes through the venous transducer. Results warrant further experimental evaluation with different bolus injections.

CONCLUSION

Compared with traditional Quadrox® adult microporous membrane oxygenator, Quadrox-i® adult microporous membrane oxygenator with integrated arterial filter and Softline coating has better GME handling capability with similar trans-membrane pressure drops. Based on these results obtained using membrane oxygenators with a closed de-airing port, further research employing an open de-airing port as well as including an arterial filter in the Quadrox® group are warranted.

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