

An In Vitro Comparison Of Bubble Elimination In Quadrox And Capiox Oxygenators

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ABSTRACT

The generation of gaseous microemboli still remains an issue in cardiopulmonary bypass. We report the testing of the air handling capacity of the Capiox FX25, the Quadrox i (both with integrated arterial filter) and the Quadrox D plus separate Quart arterial filter. Therefore we introduce air in an extracorporeal circuit in a water filled laboratory setup. Number of emboli, bubble size and the total volume of air are measured with the GAMPT BCC200. In a first test we measure bubbles after introduction of a 50 ml bolus of air just prior to the oxygenator. In a second test we apply a subtle stream of micro emboli in a reproducible way. In the first test we find a total volume of 0.041, 0.173 and 4.215 µl measured distal to the arterial filter for the Capiox, Quadrox i and Quadrox D respectively. In Test 2 we compare bubble counts, air volume reduction, reduction in number of emboli and mean diameter index for the oxygenator/filter combinations. We find volume reductions of 99.8%, 88.5% and 93% respectively. Therefore we conclude that the Capiox may be superior to the Quadrox D and Quadrox i concerning air handling. Clinical testing and greater data collection are required to prove the significance of our findings.

INTRODUCTION

Gaseous microemboli (GME) have always been an issue in cardiopulmonary bypass. Their correlation with organ dysfunction after cardiac surgery has been widely studied and discussed^{1,2,3}. Although GME are often undistinguishable from other factors as a cause of worse patient outcome, its contribution is assumed to be significant and most likely based on ischaemia caused by partial occlusion of blood ves-

sels and endothelial damage⁴. The extracorporeal circuit (ECC) may contribute to the generation of GME^{5,6} as well as surgical interventions⁷. Since decades, efforts have been made to minimize the amount of air entering the patient's bloodstream, by the use of certain ECC components and by changing their design. When considering removal of GME from the ECC, the arterial filter and the oxygenator appear to be components of great interest⁸. The venous reservoir removes most visible air, but still allows GME to enter the arterial side of the circuit. Although an oxygenator is not designed for air removal, its characteristics play an important role in their capability to remove air⁹. The last obstacle for air before reaching the aorta is, in most cases, the arterial line filter. The filters used today are screen filters. Their capability to remove air depends mainly on a critical bubble point pressure, in its turn depending on the pore size of the filter. Smaller pore sizes increase their effectiveness¹⁰, eventually limited by the size of cellular components of the blood.

Besides generation of microemboli, massive air embolism remains a point of concern, although its incidence has fallen from once every 2500 cases in 1970 to once every 30,000 cases according to the most recent national survey in the USA¹¹. Massive air embolization is mainly caused by operator error.

When altering ECC components and perfusion practice, development has not always been focussed on their influence on GME generation and removal. Nevertheless, some new techniques may introduce new sources of emboli. Vacuum assisted venous drainage (VAVD) has shown to be a significant source of gaseous microemboli in the arterial line during extracorporeal circulation¹². It also re-introduces

the possibility of massive air emboli^{13,14}. Recently Terumo developed an oxygenator with integrated screen filter. The company states that this product handles air efficiently, even though the screen filter exists of only one layer wrapped around the oxygenation fibres. It is said to remove air via the microporous polypropylene hollow fibres of the oxygenator. We tested the air handling capacity of this product in comparison with an oxygenator and filter we use in our daily routine and an oxygenator with integrated filter.

METHODS

Three oxygenator/filter combinations (1: Capiox FX 25 microporous polypropylene hollow fibre oxygenator with integrated 32 µm polyester screen filter (Terumo^a), 2: Quadrox-i microporous polypropylene hollow fibre oxygenator with integrated 40 µm arterial filter (BE-HMO 71000, Maquet^b) and 3: Quadrox-D polypentene diffusion membrane oxygenator (Maquet^b) and Quart 40 µm arterial filter (BE-HMOD 2000, Maquet^b), respectively called CAP, Qi and QD in this article, are tested in a laboratory setup for their air handling capacity. Therefore the oxygenator/filter combinations are built into a closed ECC system, connected to a pseudo patient (50 liter container, filled with water at room temperature). The extracorporeal circuit (ECC), customized and sterilized by Maquet^b consists of a tubing set (Raumedic^c), collapsible reservoir (JVR 1900, Maquet^b), centrifugal pump (Rotaflow-RF32, Maquet^b) and hard shell cardiomy reservoir (HC 2821, Maquet^b). The Capiox FX 25 has an Xcoating (Terumo^a), the collapsible reservoir has a Safeline coating (Maquet^b) and all other components are Bioline coated (Maquet^b). Figure 1 shows a schematic picture of the ECC.

One by one the Cap, Qi and QD are built

a Terumo, Leuven, Belgium

b Maquet, Hirrlingen, Germany

c Raumedic MÜNCHBERG, Germany

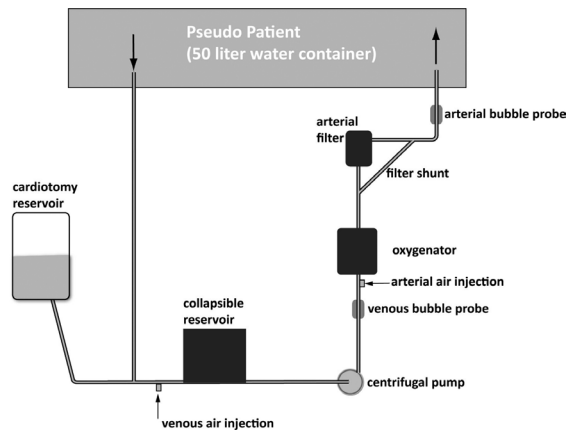


Figure 1. Extracorporeal circuit connected to the pseudo patient.

in between the centrifugal pump and the Quart arterial filter. During measurements with the Cap and Qi the Quart filter is clamped at both the inlet and outlet and the shunt bypassing the Quart filter is opened. During measurements with the Quadrox D the shunt is closed and the water is led through the Quart arterial filter. So, as CAP and Qi contain an integrated filter, all measurements are performed using one oxygenator and one filter.

The arterial probe of the bubble counter is positioned 8 cm distal to the filter, and the venous probe is located just between the centrifugal pump and the oxygenator, following the instructions of the manual¹⁵. The scale of the bubble counter is set to 20-500 µm. Pressure (measured at the top of the Quart arterial filter) and flow are maintained at 150 mmHg and 5 l/min respectively, running the pump at 3000 rpm's and partially clamping the arterial side 15 cm distal to the arterial bubble counter probe. The water level is kept at 300 ml in the cardiomy reservoir, which is positioned higher than the collapsible reservoir. Venous flow from the pseudo patient into the venous line was controlled by siphon drainage.

TEST 1

In Test 1 a 50 ml bolus of air is rapidly injected, just before the oxygenator ('arterial air injection' in figure 1). During four minutes thereafter, bubbles are counted

distal to the arterial filter ('arterial bubble probe' in figure 1) and at the point just prior to the air injection site ('venous bubble probe' in figure 1).

TEST 2:

In Test 2 the same amount of air is slowly introduced just before the venous reservoir ('venous air injection' in figure 1), during a period of 150 seconds, using a syringe pump (Perfusor® fm B.Braun^d). In this test, emboli are counted between the centrifugal pump and oxygenator, as well as after the arterial filter, during a four minutes time period.

Each test is performed twice for every oxygenator/filter combination. Between measurements the circuit is de-aired until no emboli are detected by the bubble counter (BCC200, GAMPT^e).

RESULTS

For each testing method (Test 1 (acute arterial) and Test 2 (continuous venous introduction of air) the results are displayed in tables 1 and 2 respectively.

For Test 1 we display the total amount of air passing through the oxygenator/filter combination (Vol out) and the maximum embolic load (max emboli/s). Furthermore the total number of emboli (Num Out) and their size (Diameter Out) is shown.

For Test 2 the amount of air entering the oxygenator is displayed as well (Vol

^d B.Braun, Germany

^e GAMPT, Zappendorf, Germany

In, Num In and Mean emboli/s). Mean number of emboli/s are displayed instead of the maximum. Volume reduction (VolRed), number reduction (NumRed) and mean diameter index (MDI) are parameters calculated from the measured data of Test 2.

Results of TEST 1

Re-entry effect:

In Test 1 we measured bubbles proximal to the air injection site. After air injection we found some bubble activity that could only be explained as a re-entry effect. The air passing the oxygenator and filter was not entirely removed by the pseudo patient and the venous reservoir. The bubbles detected at the venous site were therefore considered 'extra'. This re-entry effect was 1-6% of the total arterial bubble volume, increasing with larger arterial bubble volumes. As most of this re-introduced air will be removed by the oxygenator and the filter (88.5%-99.8% as shown in the results of Test 2), the arterial bubble measurements will be influenced by this effect in only a minor way (up to 0,7%). As the precise influence of this effect per test is not known, and the effect is not of major influence it is not corrected for.

Figure 2 shows how the GAMPT bubble counter presents its results after acute introduction of 50 ml of air (Test 1) directly before the Capiox oxygenator. The red line (arterial probe) in figure 2 presents the bubbles measured distal to the Capiox. It shows a reduction of emboli in the first minute after air introduction, down

	cap	Qi	QD
Vol Out (nl)	41 (28-55)	173 (121-225)	4215 (1850-6580)
Max emboli/s	118 (110-135)	107 (99-114)	321 (310-332)
Num Out	1243 (893-1592)	2044 (1440-2648)	8738 (8076-9400)
Mean Diameter Out (µm)	35 (35-36)	48 (48-48)	69 (60-77)
Max Diameter Out (µm)	98 (92-103)	178 (157-200)	394 (305-482)

Table 1. Results of Test 1.

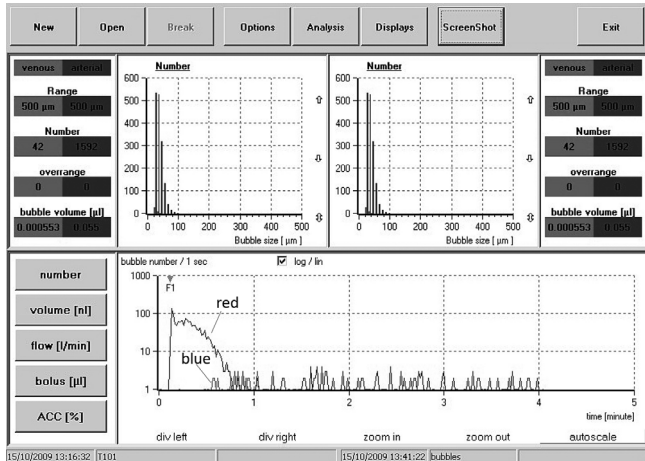


Figure 2. Test 1. Example of the bubble counter results after acute introduction of 50 ml of air, just before the oxygenator. Blue = venous air, measured before the Capiox FX 25, red = arterial air measured after the Capiox FX 25. F1 = moment of air introduction.

to a minimum of approximately 1 bubble per second. For Qi and QD we found the arterial emboli generation to remain at a higher level (approx. 10 bubbles per second) during the four minutes of measurement (figure 3). The blue lines in figures 2 and 3 represent the emboli measured before the oxygenator. These emboli originate from the 50 l container as a re-entry effect. This re-entry effect is 2%, 1% and 6% of the total air volume measured at the arterial site for Cap, Qi and QD respectively.

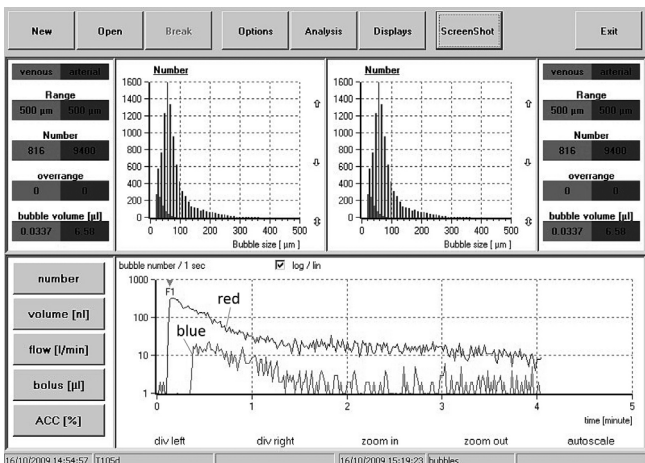


Figure 3. Test 1. Example of the bubble counter results after acute introduction of 50 ml of air, just before the oxygenator. Blue = venous air, measured before the Quadrox D, red = arterial air measured after the Quadrox D. F1 = moment of air introduction.

The total volume of air passing the oxygenator and the filter is different in all three tested oxygenator/filter combinations. This is clearly visible in figure 4. We found 41 nl (Cap), 173 nl (Qi) and 4215 nl (QD) passing oxygenator and filter. Worth mentioning is the big difference between

duplo's of QD (as shown in table 1). The test has been repeated, showing the same divergence (results not shown in this article). The total number of bubbles, measured at the arterial side is 1243, 2044 and 8738, for Cap, Qi and QD respectively. The average bubble size passing the oxygenator and filter is 35, 48 and 69 µm for Cap, Qi and QD respectively. The diagram in figure 5 expresses the number and size of the bubbles per oxygenator/filter combination. No bubbles >500 µm (presented as 'over range') were detected.

Total arterial bubble volume after acute arterial introduction of 50 ml of air

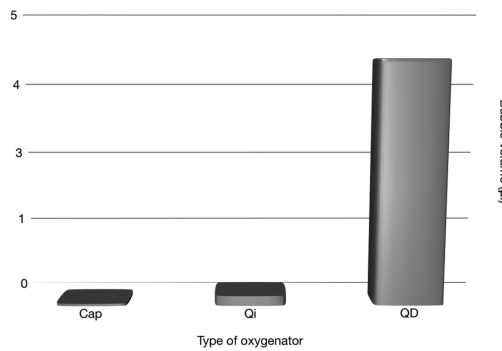


Figure 4. Total amount of air measured after the oxygenator and filter after acute introduction of 50 ml of air just before the oxygenator (Cap = Capiox FX 25, Qi = Quadrox i and QD = Quadrox D + Quart arterial filter).

Arterial bubble count after arterial introduction of air

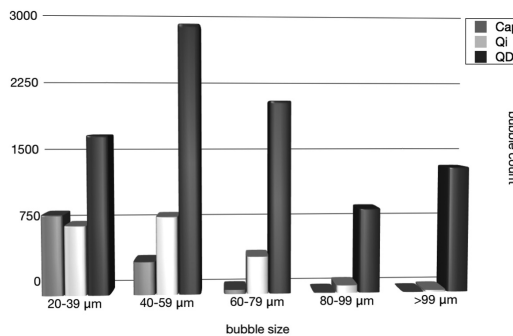


Figure 5. Bubble counts indexed to bubble size measured after the oxygenator and filter after acute introduction of 50 ml of air just before the oxygenator (Cap = Capiox FX 25, Qi = Quadrox i and QD = Quadrox D + Quart arterial filter).

RESULTS OF TEST 2

In Test 2 the slow introduction of 50 ml of air before the venous reservoir provides a continuous supply of small air emboli to the inlet of the oxygenator. The mean total amount of air supplied per test period is 555 ml. The mean embolic load is 30

	cap	Qi	QD
Vol Out (nl)	530 (524-536)	570 (531-619)	565 (561-569)
Max emboli/s In	31 (31-31)	32 (32-32)	30 (28-31)
Num In	4686 (4683-4689)	4840 (4813-4867)	4478 (4274-4681)
Mean Diameter In (µm)	46 (46-45)	46 (47-45)	48 (47-48)
Max Diameter In (µm)	259 (219-299)	224 (218-230)	226 (223-229)
Vol Out (nl)	0.9 (0.8-0.9)	65.4 (58.7-72.0)	39.6 (39.8-39.3)
VolRed (%)	99.8%	88.5%	93.0%
Mean emboli/s out	0.5 (0.4-0.5)	8.6 (8.0-9.1)	5.6 (5.3-5.9)
Num Out	70 (78.62)	1288 (1207-1369)	834 (788-880)
NumRed (%)	98.5%	73.4%	81.4%
Mean Diameter Out (µm)	26 (26-26)	39 (40-38)	39 (28-40)
MDI (%)	42%	15%	17%
Max Diameter Out (µm)	58 (48-68)	166 (180-151)	112 (107-116)

Table 2. Results of Test 2.

Vol in = total volume of air measured before the oxygenator inlet;

Mean emboli/s in = mean number of emboli measured per second before the oxygenator inlet;

Num In = total number of emboli measured before the oxygenator inlet;

Vol Out = total volume of air measured after the arterial filter outlet;

VolRed = $(1 - (\text{Vol Out} / \text{Vol In})) * 100\%$;

Mean emboli/s Out = mean number of emboli measured in one second after the arterial outlet;

Num Out = total number of emboli measured after the arterial filter outlet;

Num Red = $(1 - (\text{Num Out} / \text{Num In})) * 100\%$;

MDI = $(1 - (\text{Mean Diameter Out} / \text{Mean Diameter In})) * 100\%$

emboli/s (max 76), with an average bubble size of 46 µm (max 299). Ninety percent of the bubbles are between 20 and 80 µm, as shown by the blue lines in the diagram called 'Number' in figure 6.

The differences in total volume of air measured at the arterial side are pointed out in Figure 7. Respectively 0.9 vs 65.4 vs 39.6 nl of air passed Cap, Qi and QD (Vol out, table 2). As the amount of air presented at the oxygenator inlet is comparable in all tests, the air reduction follows the same, but inversed, pattern (99.8% vs 88.5% vs 93.0% for Cap, Qi and QD resp.).

Figure 8 shows the number and size of the bubbles measured after the filter. Again the Capiox handles the air more efficiently. This accounts for the total number of bubbles as well as the average size and the maximum size of the bubbles passing oxygenator and filter. Numbers are displayed in table 2.

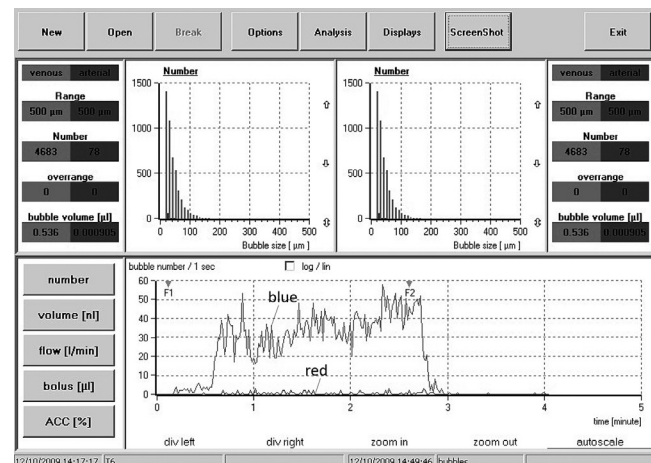


Figure 6. Test 2. Example of the bubble counter results after venous introduction of air. Blue = venous air, measured before the Capiox FX 25, red = arterial air measured after the Capiox FX 25. F1 = start air introduction, F2 = stop air introduction.

DISCUSSION

In this experiment we searched for possible differences in air handling capacity of the Capiox FX 25, compared to the Quadrox i and Quadrox D with Quart arterial filter. Our results show the Capiox FX 25 to remove air more efficiently than the Quadrox oxygenators with Quart filter.

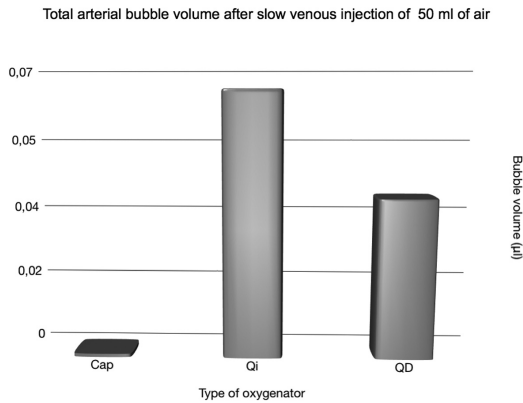


Figure 7. Total bubble volume passing the oxygenator and filter after slowly introducing 50 ml of air just before the venous collapsible reservoir (Cap = Capiiox FX 25, Qi = Quadrox i and QD = Quadrox D + Quart arterial filter).

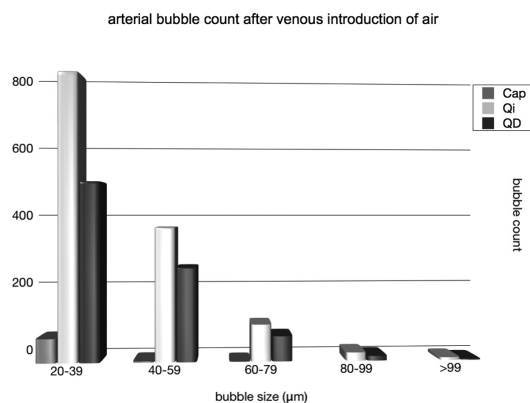


Figure 8. Bubble counts indexed to bubble size measured after the oxygenator and filter after introduction of 50 ml of air just before the venous collapsible reservoir during a time period of 2 minutes (Cap = Capiiox FX 25, Qi = Quadrox i and QD = Quadrox D + Quart arterial filter).

When searching for an explanation for the relatively big differences, we found first of all the pore size of the filters used. The fact that the Capiiox FX 25 has a filter with 32 µm pores, while the Quart and the Quadrox i have 40 µm pores may be considered a significant difference⁹.

Another difference is the type of fibres. The Capiiox FX 25 and the Quadrox i both have micro porous oxygenation fibres, but the Quadrox D has a diffusion membrane consisting of polypentene (closed) fibres. This may account for the great difference found in Test 1, where massive air is introduced into the oxygenator. Inside the Capiiox FX25 or the Quadrox i the air may purge through the porous fibres. The Quadrox D has a deairing membrane at the top of the oxygenator where massive

air should be removed. The efficiency of this membrane may be less than the efficiency of microporous fibres. The air inside the oxygenator may disperse bubbles for a longer period of time after air injection, as seen in figure 3 compared to figure 2. The Quadrox i does have porous fibres but seems not as effective at removing air as the Capiiox. The incorporation of the one layer screen filter close to the hollow fibres seems to create a situation where bubbles are easily led through the porous fibres of the oxygenator.

Despite the fact that only a single oxygenator per test setup has been used, homogeneity of the product is presumed sufficient to trust our conclusions to be useful. However, we tested under non clinical conditions, using water instead of blood, 20 instead of 37 °C, and a 50 liter container instead of a patient. These factors are of significant influence when measuring gaseous emboli⁸, so clinical performance may not correlate with the results from our experiment. Especially the use of water instead of blood may be of significant impact. Blood has a lower surface tension, diminishing bubble point pressure and thereby reducing the capability of screen filters to trap air. Furthermore when using blood, membrane surfaces will be coated with proteins, affecting the air handling capacity of the oxygenators and filters.

F. de Somer and colleagues¹⁶ tested the accuracy of the GAMPT BC200. They concluded the maximal measurable bubble count to be ± 200 counts/s, as the minimum time interval between bubbles is 5000 µs. In Test 1 we find maximum bubble counts of 135, 114, 332 counts/s for Cap, Qi, QD resp. The fact that we did find 332 counts/s may be explained by difference in software versions. According to F. de Somer the measurements of the GAMPT BC200 may underestimate the real embolic load. In this view Test 1 shows bubble counts that may be underestimated, especially for the higher embolic

load using the Quadrox D with separate arterial filter.

The technique we used to introduce bubbles in Test 2 creates a slow stream (30 counts/s) of relatively small (46 μm) bubbles with good reproducibility. Maximum arterial bubble counts are between 3-27 counts/s. Measurements by the GAMPT BCC200 of this kind of embolic load are expected to be accurate.

M. Jirschik and colleagues¹⁷ found the Quadrox i to reduce 75% of the total volume of air during clinical application with 76 patients. In our non clinical setting we found a volume reduction of 88.5%. Jirschik concluded the Quadrox i to be superior to the Polystan Safe Maxi with a volume reduction of 46%. Weitkemper and colleagues found the Quadrox i to be the best of six, when testing oxygenators for their air handling capacity¹⁸. Although conditions in our experiment are different, the volume reduction of the Capiox being 99.8% is striking. A study with clinical setup and greater data collection is required to prove practical and statistical significance of our findings.

We tested only air handling, so these results represent only one aspect of the performance of the oxygenators and filters. Pressure drop, compliance, oxygen- and carbon dioxide transfer rate or other important characteristics were not tested.

This experiment focuses on the removal of air by oxygenators and filters only. Jones and colleagues have shown that other components may also play a significant role in the removal of air from the ECC⁸. They showed that components from different companies have very different characteristics, concerning air removal. For optimal air removal venous air filtration¹⁹ or an arterial bubble trap²⁰ could be used, but this will of course, increase complexity of the circuit.

In this experiment, the equipment we

used did not entirely remove all of the air from the extracorporeal circuit. Furthermore Test 2 imitated a possible clinical situation (air entering the venous line) for only 4 minutes. During the longer time period of an operation the total amount of air presented to the ECC may be higher. This means that professionals should still focus on the prevention of air entering the ECC.

CONCLUSION

The air handling capacity of the Capiox FX25 is superior when introducing a large bolus of air, as well as after slow introduction of micro-emboli, compared to Quadrox i and the Quadrox D/Quart oxygenator/filter combinations.

When comparing the Quadrox i with a Quadrox D with a separate Quart arterial filter, we find the Quadrox i to handle massive air in a better way than the Quadrox D. On the contrary the Quadrox D may handle micro bubbles somewhat better than the Quadrox i.

The tested materials may not perform in the same manner in a clinical setting, therefore further testing is required.

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