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Letters to the Editor

Working toward Best Practice: Microbubble Filtration and Patient Safety During Extracorporeal Circulation

To the Editor,

I have read with great interest the article from Potger et al. (1), and commend the authors for the contribution they make in this investigation. While congratulating them on their work, I also raise the following points to continue what I believe is much needed discussion on the very important topic of gas-bubble transmission during extracorporeal circulation (ECC).

To build an appropriate context for the discussion as it relates to the present study, we should first consider what happens to a bolus of air traveling down the venous line in an ECC circuit. As a bolus of air enters the venous reservoir, it passes through a venous filter usually consisting of a large micron-pore screen (>60 μm). Although a portion of the air volume entering may become trapped inside the reservoir, the relatively small numbers of large bubbles that make up the original air bolus are transformed into a much larger number of smaller bubbles as they traverse the venous filter. The large cluster of smaller microbubbles now pass through the membrane oxygenator where they are either absorbed into the oxygenator's gas phase, or undergo another transformation in size as they are forced through the tightly wound fiber-bundle and then expelled into the oxygenator's outlet. Next, the well-refined cluster makes its way to the arterial-line filter where bubbles are either purged out, or escape and pass through the filter toward the patient. The main point here being the stepwise reduction in bubble size that an air bolus passing through the venous reservoir undergoes before reaching the arterial-line filter. It follows then that to maximize the benefit of arterial-line filtration, the rational for the rated pore size used should consider the size range of bubbles being emitted from the oxygenator system.

Although Potger's group suggests that the integrated system of the Fusion oxygenator is more efficient at capturing microbubbles than a 38-μm stand-alone Affinity filter with NT oxygenator, an alternate perspective given in a review of the data presented from their original work may help expand on this interpretation. As shown in Tables 1 and 2, data taken from the Potger et al. article (1) are used to show the percent increase in median bubble volume and count for each system between the 3-L/min and 5-L/min tests. Although both systems exhibit an increase in transmitted bubble volume and count at higher flow rate settings, the Fusion oxygenator displayed a larger percent increase over the Affinity NT system with 2.4 times the measured volume and nearly a two-fold increase in bubble count at 5 L/min as compared to 3 L/min. This suggests that air-handling performance of the Fusion oxygenator is affected more by increasing flow rate, which could have a significant clinical impact. And while blood flow rates of 5 L/min may be common during adult ECC procedures, flow rates above 5 L/min are not uncommon. Given the implications, this finding warrants further investigation to better determine air-handling capabilities of the Fusion oxygenator at higher flow rate settings. To continue, results from the Potger et al. paper (1) also presented in Table 3 show the percent increase in median bubble size measured above the rated pore size of each system in the first and third minute of testing at each flow setting in the study. Although it is not surprising that bigger bubbles were shown to pass through the larger pore diameter of the 38-μm Affinity filter, the Fusion oxygenator again showed a higher percent increase in emitted bubble size over its rated pore size at both periods and at both flow rate settings. When considering the differences in volume between a 25-μm bubble (.007 nL) and a 38-μm bubble (.028 nL), results derived from the cumulative volume measured at the outlet of each system might be more predictable then they prove to be remarkable. But what is remarkable in my opinion is the degree of stability in performance that the stand-alone filter displayed over the integrated system of the Fusion oxygenator under increasing levels of stress. Even with a larger pore diameter, the 38-μm Affinity filter with NT oxygenator still showed more consistent behavior in filtration performance over the Fusion oxygenator as flow rate increased.

Another point for discussion is the noted increase in bubble volume measured at the inlet of the affinity NT system while conducting the tests at 3 L/min. The authors

Table 1. Microbubble transmission (volume): Percent increase in total median microbubble volume (nL/min) at the outflow of the two oxygenator-arterial filter systems from 3 L/min to 5 L/min.

	Total Volume at 3 L/min	Total Volume at 5 L/min	Percent Increase (%)
Affinity system (38 μm)	81.6	157	192
Fusion (25 μm)	35.4	86.3	244

Table 2. Microbubble transmission (count): Percent increase in total median microbubble count in the outflow of the two oxygenator-arterial filter systems between 3 L/min and 5 L/min.

	Total Count at 3 L/min	Total Count at 5 L/min	Percent Increase (%)
Affinity system (38 μm)	1,030	1,458	142
Fusion (25 μm)	542	1,047	193

propose that this may be the result of bubble recirculation coming from the cardiotomy reservoir, but are unable to confirm this. Because a similar increase in measured volume was not observed during the 5 L/min tests, I suggest that it may still be possible to confirm or discount the proposed theory using the data collected with the GAMPT BC100 monitor (GAMPT mbH, Zappendorf, Germany). By reviewing the graphs for bubble number and volume of each trial, the authors could compare the results for any differences in shape of the graphs themselves. When both arms of the study have been controlled equally for unwanted effect, the shape of the graphs generated with the pre-oxygenator Doppler probe during bolus delivery should be very reproducible. If the increase in volume noted is due to recirculating bubbles, then the graphs for the affected trials should show a steady increase or build-up of bubble number and volume that is representative of the time delay required for the microbubbles to recirculate through the pre-oxygenator probe. If all graphs have a similar shape, then alternate possibilities should be explored as the increase in volume observed is less likely due to the recirculation of bubbles. For example, because the air-bolus delivery system chosen is passive in that the rate and volume of air delivered is in part dependent on the system pressure of the ECC circuit itself, extra efforts to maintain a constant line pressure between trials would be a requirement to ensure that volume delivery remained the same for each test. Even small differences in line pressure could be responsible for variations in delivered volume. This aspect may be even more important in the Potger et al. study due to expected differences between the two systems as the Fusion oxygenator is purported to incorporate a tighter fiber-bundle and increased resistance as one of its design features. Moreover, because it is implied that the Fusion system generates a higher-pressure drop as a feature of normal operation, it is presumed that the line pressure had to be artificially raised during testing with the Affinity NT system to reproduce the bolus volume delivered between trials. This could open an unwanted potential for complicating the study with bias against the affinity NT oxygenator as the net effect would be to compress microbubbles more than they would naturally occur when using this system in a clinical setting (2). Although the Fusion oxygenator is designed to benefit from its integrated system with tighter fiber-bundle, imposing the same line pressure on the looser fiber-bundle of the Affinity NT oxygenator would appear to be counterproductive in achieving a balanced outcome.

Although the original study might fulfill its purpose as an aid to considering the Fusion oxygenator as a replacement system, it would be helpful for future work to consider expanding the boundaries of study design to better inform the broader interests of best practice. For example, it might prove useful to add a third arm that combines the Fusion oxygenator with a 20-μm stand-alone filter to compare outcomes that can offer more insight on best practice issues related to microbubble filtration and patient safety. With the advent of next generation oxygenators and other associated technologies (3,4), there is bound to be an increase in the number of researchers interested in establishing a comparison of the clinical effectiveness between such devices, which emphasizes the reason I feel the present discussion is so important to this readership. The rational for keeping line pressure constant when pressure differential itself becomes part of the intervention needs to be rethought. In line with this would be a review of the bolus delivery system used, whether passive or active, and how this might impact outcomes of these critical studies. When considering the complexities that can arise from the variable nature that gas in solution can assume (2), it is easy to reason that there is probably

Table 3. Microbubble transmission (size): Percent increase in median microbubble size (μm) above system rated pore size as measured in the first and third minute during both 3 L/min and 5 L/min tests.

	Median Bubble Size (μm) at 3 L/min				Median Bubble Size (μm) at 5 L/min			
	First minute	Increase (%)	Third minute	Increase (%)	First minute	Increase (%)	Third minute	Increase (%)
Affinity (38 μm)	41	108	37	97	44	116	40	105
Fusion (25 μm)	35	140	26	104	39	156	33	132

no perfect way to quantify the impact air delivery has on ECC systems in the clinical setting. And it should be just as easy to reason that there is likely no single way to make an attempt at quantifying it either. The Potger et al. study opens up yet another window from which we can view the complex mosaic of this most difficult clinical equation, and I hope their efforts in this area of perfusion science do not stop here. I also hope that this renews interest and encourages others to continue researching the multifaceted problem of microbubble transmission during ECC as a means of strengthening this profession through improved patient safety. In a more personal note, the present work from Potger and coworkers also helps confirm for me at least what I have already concluded from investigations of my own. Given their popularity and widespread use, 38-μm arterial-line filters may be overrated as the size range of bubbles that pass through hollow-fiber oxygenators could limit the protection they offer.

Daniel P. Herbst, MSc, CCP, CPC
Department of Cardiac Surgery
Centre Hospitalier Universitaire de Sherbrooke
Sherbrooke, Quebec, Canada

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