**Original Articles**

**Effects of Purge-Flow Rate on Microbubble Capture in Radial Arterial-Line Filters**

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**Abstract:** The process of microbubble filtration from blood is complex and highly dependent on the forces of flow and buoyancy. To protect the patient from air emboli, arterial-line filters commonly use a micropore screen, a large volume housing with purpose-built shape, and a purge port to trap, separate, and remove circulating microbubbles. Although it has been proposed that an insufficient buoyancy force renders the purge port ineffective at removing microbubbles smaller than 500 μm, this research attempts to investigate the purge flow of an arterial-line filter to better understand the microbubble removal function in a typical radial filter design. As its primary objective, the study aims to determine the effect of purge-flow rate on bubble capture using air bolus injections from a syringe pump with 22-gauge needle and Doppler ultrasound bubble detection. The measureable bubble size generated in the test circuit ranged between 30 and 500 μm, while purge flow was varied between .1 and .5 L/min for testing. Statistical analysis of the test data was handled using a repeated measures design with significance set at $p < .05$ level. Outcomes demonstrated that higher purge flows yielded higher bubble counts, but the effect of purge-flow rate on bubble capture decreased as bubble size increased. Results also showed that purge flow from the test filter was capable of capturing all bubble sizes being generated over the entire flow range tested, and confirms utility of the purge port in removing microbubbles smaller than 500 μm. By analyzing bubble counts in the purge flow of a typical radial-filter design, this study demonstrates that currently available micropore filter technology is capable of removing the size range of bubbles that commonly pass through modern pump-oxygenator systems and should continue to be considered during extracorporeal circulation as a measure to improve patient safety. **Keywords:** micropore, arterial-line, filtration, microbubble, cardiopulmonary bypass equipment, patient safety, Doppler ultrasound, bubble counter. *J Extra Corp Technol. 2016;48:105–112*

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The filtration of microbubbles from the high rate of blood flow needed to maintain adequate tissue perfusion is a complex process influenced by numerous factors. Laminar flow vs. turbulent flow, viscous drag forces vs. buoyancy forces, changes in fluid velocity, pressure differential, and differences in filter design all play off each other as factors that can affect the removal of gaseous microemboli (GME) from the pump-oxygenator system. From a historical perspective, devices used to clean the blood in the early days of extracorporeal circulation (ECC) consisted mainly of two types, blood filters and bubble traps. Blood filters were commonly used to remove fibrin strands and other formed tissue debris, while bubble traps were designed specifically for clearing gross foam and free gas particles from the extracorporeal circuit (1). It wasn’t until the late 1950’s that the two functions were really combined into a single device (1). However, most early devices that included bubble filtration as an intended function, relied principally on a large volume to increase blood flow transit time and aid the buoyancy of microbubbles to affect their removal (1). In their treatise on the principles and techniques of extracorporeal circulation, Galletti and Brecher determine the maximum ascent velocity of a 500 μm bubble in whole blood to be 0.2 mm/sec, and suggest this to be the “minimum speed for removal” when considering the volume and fluid transit time through the devices available in that era (1, p. 157). More recent progress in bubble filtration has seen industry advance the use of depth filters, micropore screen filters, and the bubble absorbing capabilities of hollow-fibre oxygenators with a recent increased
interest in the latter (2–16). Current arterial-line filters usually include in addition to a large volume housing with purpose-built shape and purge port, a micropore screen mesh that incorporates several technological advancements in design. Where filter pore size once ranged between 70 to 100 μm with an open area between 34% and 66%, modern filter screens have reduced pore size below 40 μm while maintaining as much as 40% open area with improved biocompatible surfaces (1,17). Altogether, these features promote the principal arterial-line filter functions of trapping, separating, and removing microbubbles from the higher blood flow velocities commonly found in modern pump-oxygenator systems. Although the filtration rates of an arterial-line filter are ultimately derived from the combined effect of its various features, each feature remains distinct in the importance of its contribution to the filter’s overall performance.

In a practical sense, the purge port offers the clinician some control over the ability to influence filter performance, as all other features are by necessity fixed and inaccessible to end-user manipulation. To effect filtration of the blood and to prevent exsanguination of the patient, the clinical perfusionist assumes the important responsibility of timing the opening and closing of the purge port, usually reserving the closed position for periods of little or no flow. Although it has been suggested that the purge port is mainly effective at clearing bubbles larger than 500 μm (18), increased efforts are still needed to help better understand the separate functions of arterial-line filters, especially the bubble removing capabilities of the side stream escaping through the filter’s purge port. To test whether or not utility of the purge port is limited to capturing predominately larger sized GME, this study explores the microbubble size range carried in the purge flow of a typical radial arterial-line filter design. The aim of the study is to determine the effect of purge-flow rate on bubble capture, and whether non-integrated arterial-line filters can complement emerging technologies in next-generation oxygenator designs.

METHODS

Circuit Design and Setup

The test circuit consisted of two CAPS single roller-head pumps calibrated for 1/2-inch tubing (Stockert Instrument GmbH, Munich, Germany), two Capiox RX25R filtered venous-cardiotomy reservoirs (Terumo, Ann Arbor, MI), two 1/2-inch polyvinyl chloride (PVC) raceway tubings, 3/8-inch PVC tubing (total length 420 cm), two 3/8-inch polycarbonate “Y” connectors, two 3/8 × 3/8-inch luered polycarbonate connectors, a Dideco D732 arterial-line filter with bypass loop and pressure monitoring port (Sorin Group, Mirandola, Italy), filter purge line without one-way valve (total length 100 cm), syringe pump (Terumo), 60-ml syringe with pressure tubing and 22-gauge needle, pre-bypass filter, YSI 400 temperature probe, dual-port Digitron 2088p pressure manometer (Digitron, Torquay, England, UK), 3/8-inch flow transducer (Transonic, Ithaca, NY), and a BC100 Doppler ultrasound bubble counter calibrated with 3/8-inch probes and set to record bubble sizes between 10 and 500 μm (GAMPT mbH, Merseburg, Germany).

As shown in Figure 1, two 3/8-inch PVC lines labeled A (air bolus injection arm) and B (test arm) are configured so that the inlet of two single roller-head pumps labeled P1 and P2 join to the venous outlet of reservoir R1 using a 3/8-inch “Y” connector. The two lines A and B rejoin again before terminating at the cardiotomy inlet port of reservoir R2 using a second 3/8-inch “Y” connector. Pump P1 generates flow in line A, delivering fluid from reservoir R1 through the test filter and into the cardiotomy inlet of reservoir R2, while pump P2 provides flow in line B from reservoir R1 to the cardiotomy inlet of reservoir R2. A filter purge line without one-way valve joins the test filter in line A to a 3/8-inch luered connector in line B. To complete the circuit, a 3/8-inch PVC tubing of 160 cm length connects the venous outlet of reservoir R2 to the cardiotomy inlet of reservoir R1. Height differences between the two reservoirs were adjusted to balance the infusion and drainage flow rate during recirculation.

The circuit with test filter was first primed with saline .9% solution (5.0 L) at room temperature (23.3°C) for initial de-bubbling with pumps P1 and P2 set at 4.5 and 1.5 L/min, respectively. Both pumps were adjusted to be occlusive at 350 mmHg for 1/2-inch raceway tubing, and the test filter was handled until visibly free of any gas particles, with the purge port open and the bypass loop clamped. To simulate the viscosity of whole blood for testing, glycerol (2.0 L) was added to the test circuit to approximate a clear blood analog using a 30–70% glycerol-saline mixture similar to that previously described (17). After
initial priming, the two color-coded BC100 probes were first attached to line A, pre- (blue) and post-filter (red), to verify the bubble size range generated by the air bolus delivery system using a syringe-pump infusion rate of 150 mL/h for 30 seconds (Figure 2). Before testing started, the two BC100 probes were then removed from line A and reattached to line B so that the blue probe was placed 25 cm before the filter purge line to 3/8-inch luered port connection, and the red probe was positioned 25 cm after. The 3/8-inch Transonic flow probe was attached to line B at a point 10 cm before it rejoins again with line A.

**Performance Testing: Purge-Line Resistance vs. Flow**

With both pumps stopped, the Digitron 2088p pressure manometer was zeroed, and the filter bypass loop clamped so that pre-filter pressures would be recorded during testing. To isolate flow in the purge line and measure the peak pressures due to its resistance, additional full clamps were placed at the test filter outlet in line A, and just before the filter purge line to 3/8-inch connection in line B. With pump P2 off, pump P1 was set at .1 L/min and adjusted in increments of .1 L/min to a maximum flow of .5 L/min with peak pressures recorded at each flow setting. The Transonic flow probe attached to line B was used to confirm flow output from pump P1 through the filter purge line and into the cardiotomy inlet of reservoir R2. The peak pressure readings measured at each flow setting will be used as reference points to adjust the pre-filter pressures needed to generate purge flows between .1 and .5 L/min during microbubble testing.

**Performance Testing: Purge-Flow Bubble Capture in a Radial-Filter Design**

To analyze the size range of bubbles removed in the purge flow, pumps P1 and P2 were set at 3.5 and 1.5 L/min, respectively, while a partial clamp placed on line A distal to the test filter was used to adjust the pre-filter pressures that correspond with purge-flow rates between .1 and .5 L/min as determined in the “Performance Testing: Purge-Line Resistance vs. Flow” section. To aid a more uniform recording of bubble size and number at all purge-flow rate settings, pump P2 was adjusted during testing to account for the changes in purge flow being added so that measurements taken at the Transonic flow probe in line B were maintained at 1.5 L/min. Also shown in Figure 1, a syringe pump and 22-gauge needle labeled SPair was used to deliver intermittent air bolus injections at a rate of 150 mL/h for 30 seconds in line A, while a pre-bypass filter placed before the filter purge line to 3/8-inch luered port connection in line B restricted the re-circulation of GME in the test arm. Data collection with the BC100 monitor was started in advance of each bolus injection to confirm a zero baseline before testing started. After each bolus injection, data collection was stopped, and the test circuit was de-bubbled in preparation for the next trial. The testing cycle of bolus injection, data collection, and de-bubbling was repeated three times for each purge-flow rate setting.

**Statistical Analysis**

PASW Statistics Version 18 (SPSS Inc., Chicago, IL) was used to analyze the collected test data. Inferential
statistics comparing the effect of purge-flow rate on GME capture was carried out using an analysis of variance (ANOVA) with Bonferroni post hoc tests in a repeated measures design. To further assess the impact of varying purge flows and whether bubble size itself has any effect on capture rates, the ANOVA was repeated by separating bubble counts into five size groups of roughly 100 μm each. The first group consisted of bubbles ranging in size from 30 to 100 μm, with each subsequent group covering a 100 μm size range in 10 μm increments. As an additional step to determine if the effects of purge-flow rate and bubble size could be further isolated and whether this would support findings from the ANOVA, a multivariate analysis of variance (MANOVA) for the 30 and 500 μm bubble counts was also performed using the same post hoc corrections. Results were considered significant at $p < .05$.

**RESULTS**

Table 1 details the peak purge-line pressures measured for flow rates between .1 and .5 L/min, showing a range of 22.1–288.4 mmHg. Figure 2 illustrates the bubble generating capabilities of the bolus delivery system when used under test conditions with both BC100 probes attached pre- and post-filter in line A. In addition to the over range events recorded pre-filter, both probes recorded 30-μm bubble counts as the smallest GME detected. Table 2 outlines demographic data for total bubble counts across all five purge-flow settings. Table 3 demonstrates the effect of purge-flow rate on bubble capture when all GME counts were included in a repeated measures ANOVA using Bonferroni post hoc corrections. As shown, the bubble capture for purge-flow rates above .3 L/min was significantly greater than the bubble capture measured for purge flows below .3 L/min ($p < .05$). When bubble counts were organized into groups of approximately 100 μm each, repeating the ANOVA showed that the effect of purge-flow rate on bubble capture decreased as bubble size increased for all groups except the 110–200 μm size range where no significant difference was detected (Table 4). As seen with the 30–100 μm bubble counts (Table 5), purge flow rates above .2 L/min yielded a significant increase in

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<tr>
<th>Table 1. Peak purge-line pressure measured in mmHg using 30–70% glycerol-saline prime at 23.3°C.</th>
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<th>Table 2. Showing total bubble counts for five purge-flow rate settings.</th>
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<th>Table 3. Effect of purge-flow rate on microbubble capture (30–500 μm) using one-way repeated measures ANOVA with Bonferroni post hoc tests.</th>
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*Significant at $p = .05$ level.

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Table 5. Effect of purge-flow rate on microbubble capture (30–100 μm) using one-way repeated measures ANOVA with Bonferroni post hoc tests.

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<th>(a) Purge Flow</th>
<th>(b) Purge Flow</th>
<th>Mean Difference (a - b)</th>
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<th>95% Confidence Interval</th>
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*Significant at p = .05 level.

The number of bubbles being captured. This contrasts with results for bubbles measured in the 210–300 and 310–400 μm size ranges (Tables 6 and 7), where purge-flow rates above .3 L/min were required to detect a significant increase in bubble counts. As shown in Tables 6 and 7, statistical differences detected at a purge flow of .3 L/min for the 210–300 μm range disappear for the 310–400 μm range.

Table 6. Effect of purge-flow rate on microbubble capture (210–300 μm) using one-way repeated measures ANOVA with Bonferroni post hoc tests.

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<th>(a) Purge Flow</th>
<th>(b) Purge Flow</th>
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*Significant at p = .05 level.

Table 7. Effect of purge-flow rate on microbubble capture (310–400 μm) using one-way repeated measures ANOVA with Bonferroni post hoc tests.

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<td>.084</td>
<td>–5.7053 2.619</td>
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<td>1.8169 4.6953</td>
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<td>.038</td>
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<tr>
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<td>.084</td>
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<td>.770</td>
<td>–1.3619 4.6953</td>
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</table>

*Significant at p = .05 level.

The effect of increasing bubble size appears to be further amplified in the 410–500 μm range where a purge flow of .5 L/min was needed to detect a significant difference in GME counts (Table 8). Tables 9 and 10 detail outcomes from the MANOVA that demonstrate that while purge flows above .3 L/min showed a significant increase in bubble capture at the same flow rate setting. Again, the effect of increasing bubble size appears to be further amplified in the 410–500 μm range where a purge flow of .5 L/min was needed to detect a significant difference in GME counts (Table 8). Tables 9 and 10 detail outcomes from the MANOVA that demonstrate that while purge flows above .3 L/min showed a significant increase in bubble capture.
for the 30 μm GME, no significant differences in bubble capture between the five purge-flow rate settings were detected for the 500-μm bubble size.

**DISCUSSION**

Although it is more common to assess filtration performance based on measurements taken at the filter outlet, measurements taken from the purge port in this study were used to explore the GME removal function of a typical radial arterial-line filter design, and whether its purge flow is limited to capturing predominately larger size bubbles (>500 μm). Concerning the latter objective, results from this study demonstrated that flow exiting the purge port was capable of capturing all sizes of GME being generated at all flow rates tested. This not only confirms effectiveness of the test filter’s purge flow at removing bubbles smaller than 500 μm, but also highlights flow as a principle factor in GME filtration. In answer to the study’s primary objective of assessing the effects of varying purge-flow rate on GME capture, outcomes showed that higher purge flows were associated with higher bubble counts, but the interrelated dependence on purge-flow rate decreased as bubble size increased. Even though this is consistent with the known flow-driven nature of GME capture, it also suggests

**Table 9.** Effect of purge-flow rate on microbubble capture (30 μm) using MANOVA with Bonferroni post hoc tests.

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>(a) Purge Flow</th>
<th>(b) Purge Flow</th>
<th>Mean Difference (a − b)</th>
<th>Significance</th>
<th>95% Confidence Interval</th>
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<td>.264</td>
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<td>200</td>
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<td>.015</td>
<td>−27.3834</td>
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<td>300</td>
<td>8.3333</td>
<td>.367</td>
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<td>1.000</td>
<td>−11.7167</td>
</tr>
</tbody>
</table>

*Significant at p = .05 level.

**Table 10.** Effect of purge-flow rate on microbubble capture (500 μm) using MANOVA with Bonferroni post hoc tests.

<table>
<thead>
<tr>
<th>Dependent Variable</th>
<th>(a) Purge Flow</th>
<th>(b) Purge Flow</th>
<th>Mean Difference (a − b)</th>
<th>Significance</th>
<th>95% Confidence Interval</th>
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</tbody>
</table>

that increasing bubble size within the sub-500 μm range may play a role in purge-flow capture rates of arterial-line filters with a radial design. Although the complexities of studying free gases in a fluid flow and limitations in the technology used for measuring it make interpretation of these results difficult, the theoretical influences of volume, flow, and buoyancy can offer possible explanations to the outcomes presented here.

As depicted in Figure 3, the large volume housing causes laminar blood flow at the filter inlet to break down as it disperses into the filter housing proper, giving way to a turbulent transition flow that develops as the incoming fluid decelerates. This is in sharp contrast to blood flow in the areas around the filter’s outlet and purge port, which approximates a return to near laminar flow again with a build up of higher exit velocities. Although internal volume affects flow velocity, increasing flow rate augments the force responsible for trapping GME within the blood and the effective influence it has at each filter port. This helps explain the increase in bubble counts observed in this study with increasing purge-flow rates. As purge flow increases, its drag force also increases and extends to affect a larger area around the purge port opening. This allows an increasing number of GME held within the slower turbulent transition flow to pass into and be more aptly captured in the competing drag forces of the higher velocity purge flow. And while the drag effects of flow can be easily seen even unaided, such as during priming or when air gets carried down the venous line over the course of a clinical ECC procedure, a force other than flow must be present that can help explain the effects of increasing bubble size also detected in this study.

The discovery and initial use of buoyancy as a force is credited to Archimedes, the 3rd-century BCE Greek mathematician and astronomer. In terms of force, Archimedes' principle states that when an object is immersed in a fluid, the amount of buoyancy force acting on the object is equal to the weight of the fluid it displaces. If an object is lighter than the weight of the fluid being displaced, the object rises. If the object is heavier, it sinks. If on the other hand the objects weight is equal to the weight of its displaced fluid, then it is neutrally buoyant and the object will float at depth. When differences in density between air and any liquid are considered, it seems reasonable to expect, according to Archimedes principle, that even a 30-μm air bubble would be propelled upward when contained in a non-moving fluid. This principle however becomes largely muted in relation to ECC circuitry as the buoyancy forces of even large size bubbles are overtaken by drag forces in the blood flow. And yet, differences in the volume of blood displaced between a 30-μm (0.014 nL) and a 500-μm (65.45 nL) bubble seem too great to be of no consequence. This raises the query whether it is possible that the reduced drag and pattern of the transition flow in radially designed filters allows buoyancy to influence bubble position enough so that increasing GME size has a potentiating effect on drag forces in the purge flow. Unless this outcome is due to a characteristic of the air bolus delivery system itself, limitations in the measuring instrument used, or some other unknown random effect, buoyancy could help explain why higher purge flows were needed to detect significant increases in bubble counts as GME size increased. The contrasting results between bubble sizes observed in this study as purge-flow rate varied do suggest that there are differences in bubble position within the transition flow that are related to their size, and that these differences can result in more effective removal of larger microbubbles. Although more work is needed to confirm this observation, one important relevance to this finding if proven to be reproducible could be that the flow pattern in radial-filter designs enables buoyancy forces to aid the removal of larger size microbubbles, even in the sub-500 μm range. This could have implications for perfusion practice as it firmly resonates with the rational that filter purge lines should remain open during periods of flow to ensure effective microbubble removal.

Aside from known issues related to the current available technology used to measure microbubbles in ECC circuits (17), interpretation of the results being presented here are severely dampened by the low sample size and the bolus delivery system selected to generate the microbubble counts. Although the issue of sample size can be easily overcome with increased effort, the bolus delivery method used was
specifically chosen to address a fundamental question underlying the research: When exposed to a wide range of bubble sizes, is the purge port limited to capturing bubbles larger than 500 μm? To improve both reliability and validity of microbubble counts, future work should consider a more refined bubble delivery system that could ideally affect control over the size range being generated.

Although the extent that buoyancy forces aid bubble removal from arterial-line filters is left unresolved, results from this study highlight purge flow as a determinant factor in micropore filter performance. The path GME follow as they course through a filter is closely linked to the path of the fluid trapping them. Microbubbles carried in the blood flow crossing the filter screen are either held in place against the micropore mesh, or pass through toward the patient as they get swept away in the high velocity flow developing at the filter’s outlet. Meanwhile, microbubbles that circulate upward in the transition flow are filtered out as they make contact with the rapidly accelerating side stream exiting the filter’s purge port. And while buoyancy forces likely aid the filtering process, the removal of GME from blood as it relates to micropore arterial-line filters is more a function of flow. This is especially true as bubble size decreases and buoyancy becomes negligible in comparison to the viscous drag forces contained in flowing blood. At risk of overstating the obvious, the size and quantity of GME removed through a filter’s purge port is not determined by an sufficient buoyancy force, but by the number of GME carried in the transition flow that make contact with the higher velocity purge flow. The purge runoff from the 27-μm test filter was capable of removing the smallest bubble sizes being generated at all flow rates tested, demonstrating that current commercially available filters remain an effective compliment to emerging concepts in next-generation oxygenators and should continue to be considered as a standard of care for improved patient safety.

REFERENCES