A Comparison of a Heparin Coated and a Non-Coated ECC Arterial Line Blood Filter

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Abstract

Two groups of five heparin coated (American Bentley AF 1040C) and non-coated (Gish Biomedical, Inc. AFS 40) ECC arterial line filters were compared In Vitro for pressure drop, debubbling time, air separating ability and clinically for blood handling ability.

After CO₂ flush and following Directions for Use, the debubbling time for the AF 1040C was 178 ± 11 sec. (1 S.D.) and 183 ± 29 sec. for the AFS 40. The preparation times were not significantly different and were confirmed by doppler. The AFS 40 exhibited a resistance to blood flow approximately 68% of the AF 1040C resistance. In the 11-40 micron range, the AFS 40 performed as a significantly better bubble trap during crystalloid recirculation after debubbling. With blood prime, the AFS 40 appeared to be a better bubble trap. However, both filters pass equal numbers of 80 micron bubbles when challenged with a 200 ml·min⁻¹ stream of air at 5 L·min⁻¹ blood flow. Platelet loss, hemolysis index, and white cell counts showed no significant difference in the clinical comparison.

Other studies have suggested that heparin coating facilitates filter preparation and have demonstrated clinical equivalency with non-coated filters. The AFS 40 and the AF 1040C appear to be clinically equivalent. The AFS 40 is a better bubble trap under normal ECC blood flow conditions.

Introduction

The extracorporeal circuit produces and infuses gaseous microemboli (GME) into the CPB patient arterial tree and possibly the cerebral microcirculation.¹ Transient neurological deficits and cerebral infarction occur less frequently with the use of arterial line filtration but are nonetheless a problem associated with embolic events generated by replacement of the heart and lungs with artificial organs during CPB.⁹⁻¹² Modern ECC components are being designed to minimize the amount and risk of GME produced. Conduct of perfusion has been demonstrated to affect the release of GME from the ECC.³⁻⁸⁻¹¹ Arterial line filtration has gained widespread popularity as an insurance against potential gross embolic events generated within the ECC.

The recent design trends for arterial line filters have included the incorporation of improved bubble trapping ability filter media housings and the bonding of heparin complexes to the filter media to attempt to improve blood handling ability and safety in use.¹⁻⁴⁻⁷⁻⁸

In this method a heparin-bonded screen filter (AF 1040C) design is compared to a non-coated screen filter with a housing designed to enhance bubble entrapment and that includes a bypass polycarbonate tube attached to the housing base (AFS 40). See Figure 1.

Controversy still exists concerning platelet aggregate removal and GME entrapping capability between filter designs.⁵ Recently, Kurusz in 1982 and Hill in 1985 have presented reasonable methods for clinical filter comparison.¹⁻⁴ Kurusz found no significant clinical or hematological difference between two forty micron filter designs. Rice, et al.⁵ found no clinical statistically significant differences in platelet loss, coagulation parameters or blood loss and usage between three patient/filter groups.

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⁵ American Bentley, Irvine, CA 92714
⁶ Gish Biomedical, Inc., Santa Ana, CA 92705
Hill demonstrated lower gross GME counts and no difference in the degree of blood/foreign surface interaction and cellular adhesion between a heparin coated twenty micron filter and a non-coated forty micron filter. Hill stated that the presence of the bound heparin complex appeared to facilitate priming and may allow quicker debubbling because of better surface wetting.

The present study employs an ECC A-V loop that incorporates a membrane oxygenator, closed venous reservoir and an isolated cardiotomy suction system to increase the opportunity to find measurable differences in the arterial filter designs in a clinical model. A rigid In Vitro timed debubbling method that features doppler confirmation of complete debubbling is employed to attempt to find a difference in debubbling times between the AFS 40 and AF 1040C.

Materials and Method

In Vitro Test

Figure 2 presents the In Vitro test circuit employed to calibrate the doppler probes and evaluate the debubbling time and gross air removal ability of the test filters. The micro-bubble detection system was indirectly calibrated by hyperventilating the bubble oxygenator at a low arterial reservoir level. The crystalloid perfusate had a high GME count and was passed through the forty micron, the twenty-five micron, and the five micron recirculation filters to discover the peak cut-off voltages for the reflected doppler signals for the GME that each pore size filter would allow to pass. A linear calibration curve was created.

Five each of the two groups of test filters were CO₂ flushed for five minutes and then retrograde filled at 1 L·min⁻¹ of 37°C crystalloid flow. Antegrade filter flow was begun immediately at 5 L·min⁻¹. The bleed line with one-way valve was always left open and allowed about 175 mls. per minute flow to the cardiotomy reservoir as the filter afterload was held at 100 mmHg constantly. Every thirty to forty seconds, the filter was inverted and the bypass line opened and the filter exit was observed for rising bubbles. The filters received only gentle percussion by hand every ten seconds. The debubbling process was timed from the beginning of retrograde priming to the end when the doppler computer screen no longer showed GME showers with percussion by hand in the upright or inverted position and no bubbles were visible to the eye with the filter in the holder. The perfusate was replaced in the In Vitro test circuit after every manufacturer pair was tested to simulate clinical routine and to not allow silicon antifoam agent dissolving in the prime to depress the GME counts as time proceeded in the tests. Doppler GME profiles at the filter inlet and outlet were collected and averaged for each filter type.

The perfusate was replaced with 22% bovine blood, the micro-bubble detector recalibrated as above and GME profiles recorded for the last filter pair. The filters were challenged with a 200 ml/min continuous stream of room air with the bleed line open and the blood flow at 5 L·min⁻¹. GME profiles at the filter outlet were recorded during the stress of continuous stream of room air.

Blood flow was varied in the In Vitro test circuit and the pressure drop across the AF 1040Cs and the AFS 40s were evaluated for resistance to blood flow.

Clinical Comparison

Two well matched groups of five male coronary artery bypass graft patients were randomly assigned to either the AFS 40 or the AF 1040C arterial line filter. The patient’s ECC arterial venous loop included the Shiley M-2000 membrane oxygenator and SVR collapsible venous reservoir. A 22 French aortic cannula

c Shiley, Inc., Irvine, CA 92714
AFS-40 vs. HEPARIN COATED AF-1040C: GME SIZE FREQUENCY DISTRIBUTION
PLASMALYTE

![Graph showing GME counts distribution](image1)

**Figure 3:** The mean values of the test filter (n = 5) inlet and outlet GME counts for a crystalloid prime. Both filter designs cut off GME at forty micron limits.

AFS-40 vs. HEPARIN COATED AF-1040C: GME SIZE FREQUENCY DISTRIBUTION
BLOOD

![Graph showing GME counts distribution](image2)

**Figure 4:** The mean values of the test filter (n = 5) inlet and outlet GME counts for a bovine blood prime.

was employed with a CPB cardiac index of 2.1 to 2.6 L·min·M⁻². Moderate systemic hypothermia was employed. The cardiectomy suction return was isolated from the arterial venous loop and not mixed with the patient’s circulating blood volume. If cell transfusion were required, the cardiectomy return blood was processed by the cell saver. The cardiectomy return blood was not returned to the patient’s circulating blood volume until the “termination of CPB” blood samples were drawn for analysis.

Blood was collected and laboratory tests were performed immediately pre-CPB, on CPB, post-hemodilution, and on termination of CPB. The blood samples were analyzed for hematocrit, platelet count, white blood cell count, and plasma free hemoglobin.

The In Vitro laboratory measurements and the clinical performance measurements were grouped for the test filters and analyzed employing a student’s t-test. Statistically significant difference was assigned to p values less than .05.

**Results**

**In Vitro Comparison**

Figures 3 and 4 illustrate the average test filter inlet and outlet GME profiles. Generally, the AFS 40 averaged lower GME counts per minute within the same micron size limits. The GME counts at the larger micron

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d Microstat, Ecosoft, Inc., Indianapolis, IN 46220
size limits decreased dramatically when the perfusate was changed from crystalloid to blood. Figure 4 suggests that the AFS 40 is a better bubble trap in the twenty to forty micron range under normal blood flow conditions.

Figure 5 depicts the outlet filter GME profiles that result when both filter designs are challenged with a continuous stream of 200 ml/min of room air in 5 L-min of blood flow. Both filter designs passed GME up to eighty microns.

Clinical Comparison
Table 1 compares the filter test group patient morphology, the test filter prime volumes, and the In Vitro laboratory and clinical debubbling times. There were no significant differences in test filter patient group morphology, CPB time, depth of hypothermia, and the number of coronary artery bypass grafts performed. The priming volume of the AFS 40 is significantly less than the priming volume of the AF 1040C. There were no significant differences between filter groups in the clinical or In Vitro laboratory debubbling times. However, the laboratory debubbling times, as confirmed by doppler count, were significantly longer (p < .05).

Figure 6 depicts the pressure drop versus blood flow for the AF 1040C and AFS 40 arterial line blood filters.

The AFS 40 has approximately 70% the resistance to blood flow of the AF 1040C. Previous clinical data is included for the Pall and Bard heparin coated filters for comparison.

Table 1
Patient group morphology, filter prime volumes and filter debubbling times

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age ±10</th>
<th>Weight ±10</th>
<th>BSA ±17</th>
<th>Clinical Time ±11</th>
<th>Prime Volume ±5</th>
<th>Number of Graphs ±2</th>
<th>CPB Time ±41</th>
<th>Depth of Hypothermia ±1.1</th>
</tr>
</thead>
<tbody>
<tr>
<td>AF 1040C</td>
<td>63 Years</td>
<td>71.5 kg</td>
<td>1.84 m²</td>
<td>145 sec</td>
<td>275 mL</td>
<td>2.8</td>
<td>93 min</td>
<td>33.4°C</td>
</tr>
<tr>
<td>AFS 40</td>
<td>64</td>
<td>74.9</td>
<td>1.87</td>
<td>138 sec</td>
<td>224 mL</td>
<td>3.2</td>
<td>102</td>
<td>33.4</td>
</tr>
<tr>
<td>p Value</td>
<td>.4739</td>
<td>.3074</td>
<td>.3580</td>
<td>.2714</td>
<td>.0001</td>
<td>.2357</td>
<td>.3306</td>
<td>.5000</td>
</tr>
</tbody>
</table>

AFS-40 vs. HEPARIN COATED AF-1040C:
GME COUNTS WITH 200 mL·min⁻¹ AIR CHALLENGE AT 5 L·min⁻¹ BLOOD FLOW

Figure 5: The outlet filter GME profiles that result when the filter is challenged with a 200 mL·min⁻¹ stream of room air in 5 L·min⁻¹ of blood flow.

Figure 6: The average resistance to bovine blood flow for the two test filters compared to previous clinical data by Hill, et al.
Table 2 lists the mean and standard deviation (± numbers) for he blood handling parameters versus CPB events. The only statistically significant differences were in the pre-bypass and terminating bypass plasma free hemoglobin values. The AFS 40 patient group started with significantly greater plasma free hemoglobin and ended with the same.

Figure 7 illustrates the change in platelet count between the two filter groups. The platelet change profile was not significantly different between the two filter groups.

Figure 8 plots the change in plasma free hemoglobin versus bypass event. Figure 8 reports the hemolysis index, the milligrams of hemoglobin freed per hundred liters of blood pump per blood hemoglobin concentration of 8 Gm%. The hemolysis index was not significantly different even though the absolute values of the plasma free hemoglobin in the AFS 40 test group pre- and postbypass were greater than the AF 1040C patient group.

Table 2  
<table>
<thead>
<tr>
<th>Event</th>
<th>Pre-CPB</th>
<th>Post Dilution</th>
<th>Terminating CPB</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hematocrit %</td>
<td>32.2</td>
<td>21.5</td>
<td>25.3 AF 1040C</td>
</tr>
<tr>
<td>±4.3</td>
<td>±4.0</td>
<td>±2.7</td>
<td></td>
</tr>
<tr>
<td>32.6</td>
<td>21.5</td>
<td>24.8 AF 40</td>
<td></td>
</tr>
<tr>
<td>±4.9</td>
<td>±3.2</td>
<td>±2.7</td>
<td></td>
</tr>
<tr>
<td>4523</td>
<td>4966</td>
<td>3875 p Value</td>
<td></td>
</tr>
<tr>
<td>Platelets x 10^12/mm³</td>
<td>221.2</td>
<td>144.0</td>
<td>172.3 AF 1040C</td>
</tr>
<tr>
<td>±85.0</td>
<td>±31.7</td>
<td>±39.9</td>
<td></td>
</tr>
<tr>
<td>272.4</td>
<td>123.0</td>
<td>166.4 AF 40</td>
<td></td>
</tr>
<tr>
<td>±71.8</td>
<td>±64.2</td>
<td>±38.7</td>
<td></td>
</tr>
<tr>
<td>1667</td>
<td>2652</td>
<td>3950 p Value</td>
<td></td>
</tr>
<tr>
<td>WBC x 10^12/mm³</td>
<td>5.98</td>
<td>3.5</td>
<td>8.62 AF 1040C</td>
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<tr>
<td>±8.2</td>
<td>±3.3</td>
<td>±2.82</td>
<td></td>
</tr>
<tr>
<td>7.52</td>
<td>3.52</td>
<td>8.8</td>
<td></td>
</tr>
<tr>
<td>±3.24</td>
<td>±1.47</td>
<td>±3.2</td>
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</tr>
<tr>
<td>1634</td>
<td>4885</td>
<td>4633 p Value</td>
<td></td>
</tr>
<tr>
<td>Plasma Free [Hb] mg%</td>
<td>8.6</td>
<td>7.3</td>
<td>14.8 AF 1040C</td>
</tr>
<tr>
<td>±2.2</td>
<td>±1.9</td>
<td>±5.1</td>
<td></td>
</tr>
<tr>
<td>15.0</td>
<td>11.4</td>
<td>28.3</td>
<td></td>
</tr>
<tr>
<td>±14.6</td>
<td>±5.4</td>
<td>±13.6</td>
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</tr>
<tr>
<td>0110</td>
<td>0757</td>
<td>0350 p Value</td>
<td></td>
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</table>

Figure 7: The change in platelet count during the course of CPB.

Discussion

Heparin bonding to screen arterial line filters does not significantly decrease the filter preparation and debubbling times. The fact that the well controlled In Vitro debubbling times as confirmed by doppler were significantly longer than the clinical debubbling times suggest that the arterial line filter user should spend more time debubbling the arterial line filter even though there are visual cues that the debubbling process has terminated.

There appears to be no significant difference in these two filters' abilities to separate gross continuous streams of air to the filter inlet. Even though the bleed lines were open and a constant afterload of 100 mmHg was applied to the filter outlet, GME up to eighty microns passed the filter media. Under normal blood flow conditions, the AFS 40 housing appears to be a better bubble trap in the fifteen to forty micron size limits. As Hill and co-workers found in their comparison of heparin coated versus non-coated screen filters, there were no significant differences measured in platelet
AF 1040C VS. AFS 40
HEMOLYSIS RATES

Figure 8: The change in plasma free hemoglobin levels during the course of CPB.

The use of an isolated arterial-venous loop that employs a closed membrane circuit with collapsible venous reservoir offered every opportunity to measure significant differences in blood handling ability between the heparin coated and non-coated screen arterial line filters.

References


Questions from the Audience

Question—Unknown: Do you heparinize the crystalloid prime? Does it make a difference?
Answer: Yes. I would only have to speculate. I believe not.

Question—Scott Bell: You debubbled your filters, using CO₂ flush. Did you by any chance do the same thing without CO₂ flush?
Answer: Yes. And the debubbling times are about 40 percent greater. They’re still the same between the two groups.

Question—Mary Williams: I was just wondering why you picked two filters that were so dissimilar. Why not pick one coated and one non-coated, basically the same filter to compare?
Answer: Very good. That’s the single biggest flaw in this method. We wanted to collect clinical data on a newly available filter—yet compare it to a large market standard, the AF1040C, that was heparin-coated.