

## Reduction of Microemboli Count in the Priming Fluid of Cardiopulmonary Bypass Circuits

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**Abstract:** Microemboli may impair cognitive function in patients undergoing heart surgery. Prebypass filtration has been shown to reduce particle load in the cardiopulmonary bypass (CPB) priming fluid. This study was performed to detect the embolic load of CPB priming fluid, to determine the efficacy of a 0.2  $\mu\text{m}$  prebypass filter (PBF) in reducing emboli in the range of 0.1–5  $\mu\text{m}$  and to provide guidelines for the handling of the device. A total of 12 CPB circuits were tested in two groups, using a laser light scattering particle counter, sensitive to microemboli in the range of 0.1–5  $\mu\text{m}$ . In control group A, priming fluid before administration to the CPB circuit was analyzed. Group B circuits contained microporous membrane oxygenators ( $N = 5$ ); group C consisted of CPB circuits with excluded membrane oxygenators ( $N = 7$ ). When group A was compared to groups B and C, significantly more microemboli were found in the categories 0.2  $\mu\text{m}$ , 0.5  $\mu\text{m}$ ,

0.8  $\mu\text{m}$  for both groups B and C ( $p < .05$ ). Group C circuits had higher microemboli counts in the categories 1.5  $\mu\text{m}$  and 3  $\mu\text{m}$  ( $p < .05$ ) when compared to group B. Microemboli bigger than 0.2  $\mu\text{m}$  could be eliminated after 2 min of prebypass filtration with a CPB flow of 5 L/min. The number of microemboli smaller than 0.2  $\mu\text{m}$  was reduced substantially. Small microemboli with a size of 0.1  $\mu\text{m}$  originate mainly from the priming solution. Microemboli in the range of 0.2  $\mu\text{m}$ , 0.5  $\mu\text{m}$ , and 0.8  $\mu\text{m}$  originate mainly from the CBP circuit. In circuits with bypassed membrane oxygenators, a higher microemboli count in the range of 1.5  $\mu\text{m}$  and 3  $\mu\text{m}$  may be explained by a possible filtering capacity of membrane oxygenators. The 0.2  $\mu\text{m}$  PBF is an effective tool to reduce the particle load in the CPB priming fluid. **Keywords:** heart surgery, cardiopulmonary bypass, emboli, particle, prebypass filtration, oxygenator. *JECT. 2003;35:133–138*

Cognitive decline complicates early recovery after coronary artery bypass grafting. In a recent prospective investigation, the effect of perioperative cognitive deterioration on longer-term cognitive function was determined. Cardiac patients were followed up for 5 years after coronary artery bypass grafting. Cognitive decline was evident in up to 75% of patients at the time of discharge from the hospital, and still detectable in a third of these patients after 6 months. Preventing perioperative cognitive decline may help to preserve long-term cognitive function and quality of life in elderly patients undergoing cardiac surgery (1).

Cognitive deficits in patients undergoing coronary surgery have been attributed to arterial emboli and hypoperfusion. Most of the emboli were detected by transcranial Doppler examination upon initiation of bypass, when

the heart was defibrillated, when clamps were manipulated, and when aortic cannulation was performed (2).

Arterial embolizations during cardiopulmonary bypass (CPB) are caused by either particulate or gaseous emboli. Particulate emboli may consist of inorganic material or biological aggregates. These emboli will not dissolve easily, especially if they are of nonorganic material. Blood vessels will be occluded (3). Sources of particulate emboli originating from the CPB circuit are residual debris from the fabrication of disposable equipment, particles in priming solutions, and tubing spallation attributable to wear of arterial pump boot tubing (3–5). Particles were also found to be generated from centrifugal pumps (6). Small gaseous emboli during CPB might be introduced by perfusionist interventions (7), use of vacuum assisted drainage (8), or by inadequate CPB circuit design (9). Small gaseous emboli may dissolve, depending on their size, temperature, and type of gas (3). CPB-derived emboli may also be generated by transfusion of stored banked blood, use of a cardiomy reservoir, and use of a bubble oxygenator (10).

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Particles smaller than 2  $\mu\text{m}$  might form aggregates with thrombocytes and fibrin, causing formation of thrombi and thromboembolization of the microcirculation (11).

With the onset of CPB, rapid arterial infusion of a large volume of priming fluid occurs within a short time. Typically, 1600–2000 mL of CPB priming fluid are pumped into the adult patient within 30–60 sec. A possible gaseous and particulate embolic load of the CPB circuit may lead to arterial microembolization.

A prebypass filter (PBF) with a pore size of 0.2  $\mu\text{m}$  was found to be effective in reducing particles larger than 1  $\mu\text{m}$  contained in the priming solution of clinically used CPB circuits (12). However, until recently, it was not possible to measure emboli in the 0.1–5  $\mu\text{m}$  range online with a particle counter. An *in vitro* study was performed to determine the quantity and sizes of possible microemboli in the crystalloid priming fluid of our routine adult CPB circuits, and whether these microemboli could be effectively eliminated by use of a PBF with a pore size of 0.2  $\mu\text{m}$  before connection of the circuit to the patient. Because oxygenators have been found to eliminate gaseous emboli partially from CPB circuits (9,13), and because the effect of an oxygenator on small emboli had yet to be determined, one group of analyzed circuits contained no oxygenator, while the other group of circuits included a membrane oxygenator for adult patients.

## METHOD

The setup consisted of a Stoeckert S3 CPB console with arterial and sucker roller pump heads (Stoeckert, Munich, Germany) and custom-made adult CPB tubing packs with 1/2" arterial silicon pump boot, hollow fiber membrane oxygenator, collapsible venous reservoir (Affinity 321 VR, Medtronic, Duesseldorf, Germany), separate cardiomy reservoir (CR), 40  $\mu\text{m}$  Pall Auto-Vent SV arterial line filter (ALF), and a 0.2  $\mu\text{m}$  Pall R3802 prebypass filter (PBF, both Pall Medical, Dreieich, Germany). The design was identical in all CPB circuits. System 1 was composed of a Sorin Monolyth oxygenator, Sorin CRF 40 cardiomy reservoir, and a Sorin tubing set (all Sorin Biomedica, Puchheim, Germany). System 2 included a Medos Hilite oxygenator, Medos MC 440 cardiomy reservoir, and Medos tubing set (all Medos AG, Stolberg, Germany).

In group B, a membrane oxygenator was included in the setup and five circuits (three Sorin and two Medos) were analyzed. In group C, the oxygenator was excluded from the circulation before administration of priming fluid. In this group, seven circuits (four Sorin and three Medos without oxygenators) were tested. A total of 12 CPB circuits were studied.

The circuits were flushed with medical grade filtered CO<sub>2</sub> for 5 min. A Surgimedics/TMP 0.2  $\mu\text{m}$  gas filter was used for this purpose (HMT, Fuerstenfeldbruck, Ger-

many). The arterial line filter and the PBF were clamped and excluded from the flow after CO<sub>2</sub> flush before administration of priming fluid. The circuits were primed with 3000 mL pH-balanced full electrolyte solution (Thomaejonin, Delta-Pharma, Pfullingen, Germany). The normal priming volume of the CPB circuits is 1600 mL, the extra volume was administered to account for the loss of priming fluid attributable to the particle counts.

The system was primed according to our departmental standard, using the field sucker line aspirating the solution out of the infusion bag and pumping it into the cardiomy reservoir at maximum speed (250 rpm) to create a thorough washout of the cardiomy reservoir. The arterial pump head occlusion was set near occlusive to 400 mmHg (drop to 350 mmHg within 1 min). The PBF was excluded from recirculation immediately after the retrograde priming and deairing procedure. The cardiomy reservoir was excluded from recirculation after the initial priming. The CPB system was recirculated through the arteriovenous shunt for 5 min at a flow rate of 5 L/min at room temperature. A venous occluder (Stoekert, Munich, Germany) was adjusted to create a pressure head of 350 mmHg, measured at arterial pump boot outlet.

A laser light scattering method was used to evaluate microemboli counts in the circulating priming fluid of the CPB circuit. An HIAC Royco 8000A particle counter with eight channels (Pacific Scientific HIAC Royco, Silver Spring, MD) was installed. For this study, the particle sensor MC 100 (Pacific Scientific HIAC Royco) with a range of 0.1–5  $\mu\text{m}$  was used. The sensor operates at a flow rate of 100 mL/min. The sensor was flushed during measurements with medical microfiltered CO<sub>2</sub> (Surgimedics/TMP 0.2  $\mu\text{m}$  gas filter) according to the manufacturer's recommendation at 1 L/min. A calibrated Sho-Rate 1355 flow meter (Brooks Instrument, Veenendaal, NL) was introduced into the sampling line after the particle sensor to ensure the appropriate flow rate through the device. The particle sensor was calibrated before measurements by the manufacturer with defined polystyrene spheres in distilled water. The results of the microemboli counts were printed in a tabular format.

Before measurements, the particle counting system was flushed with sterile Thomaejonin solution for 30 min. This solution was also analyzed to provide a baseline measurement of the priming fluid and served as control group A.

At a turbulent flow site, a part of the recirculating CPB volume was branched off. The particle count run took 30 seconds, with a flow rate of 100 mL/min for the MC 100 sensor. The analyzed priming fluid was discarded from the circuit. Baseline count with sensor MC 100 was performed after 5 minutes of recirculation with a flow rate of 5 L/min. After inclusion of the PBF, microemboli counts were repeated after 1, 2, 3, 4, and 5 minutes of recirculation (Figure 1).

When PBF was excluded, the PBF loop was clamped and flow instituted via A-V shunt. When PBF was included, the A-V shunt was clamped and the PBF loop opened. When the oxygenator was excluded, the roller pump outlet was connected to the ALF inlet and the oxygenator thus bypassed.

Statistical analysis was performed using SPSS for Windows, version 9.0. For comparison of the three groups, priming fluid (A), CPB with oxygenator (B), and CPB

without oxygenator (C), the Kruskal–Wallis test for non-normal distribution of parameters in independent groups were used. Differences between the groups were tested in ranks of scores. For comparison of groups A versus B, B versus C, and A versus C, the two-tailed Mann–Whitney U test was used. Differences were regarded as significant when  $p$  was  $< .05$ .

**RESULTS**

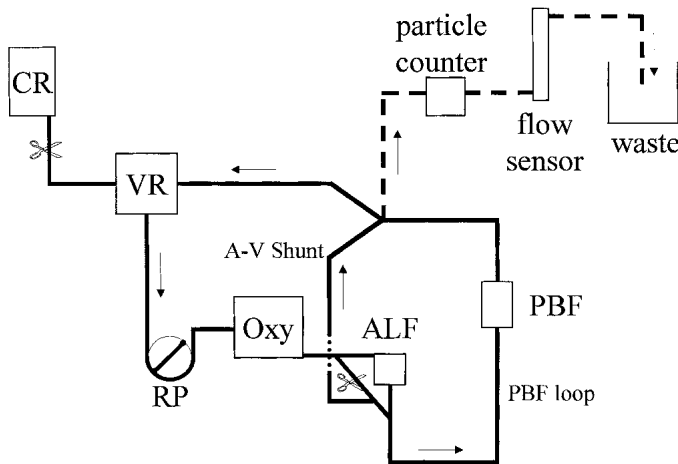
All values are given as mean particle counts per mL priming fluid with standard deviations (SD) and range. To determine possible microembolic load of the priming fluid before administration to the circuit, the same particle counting system was used (group A). The results were then compared to the microemboli count of the primed CPB circuits with oxygenator (group B) and without oxygenator (group C) (Table 1).

When the mean microembolic counts of the priming fluid per category are subtracted from the values of the circuits, the microembolic load generated by the circuits can be determined (Table 2).

Differences in microemboli count were found when the priming solution (group A) was compared to either group B or group C. In the categories 0.2  $\mu\text{m}$ , 0.5  $\mu\text{m}$ , and 0.8  $\mu\text{m}$ , more microemboli appeared in the CPB circuits than were introduced by the priming solution.

When the two circuit groups B and C were compared directly, a slight difference, which gained statistical significance, was found in the categories 1.5  $\mu\text{m}$  and 3  $\mu\text{m}$ . Further analysis of the raw data revealed that these differences were mainly caused by two circuits in group C (one Medos, one Sorin). A higher number of microemboli per mL priming fluid were detected in these two circuits for the categories 1.5 and 3  $\mu\text{m}$  (Figure 2).

The effect of a PBF on microembolic activity was studied in groups B and C. Microembolic load was measured at baseline without PBF and after 1, 2, 3, 4, and 5 min of prebypass filtration at a flow of 5 L/min through the PBF (Tables 3 and 4).



**Figure 1.** Circuit layout. ALF = arterial line filter; CR = cardiotomy reservoir; Oxy = membrane-oxygenator; PBF = prebypass filter; RP = roller pump; VR = venous reservoir.

**Table 1.** Mean microemboli count per mL priming fluid after 5 min of recirculation without PBF.

Group	A Mean	A SD	B Mean	B SD	C Mean	C SD
0.1 $\mu\text{m}$	3251.2	$\pm 533.0$	3888.2	$\pm 812.2$	3275.5	$\pm 734.8$
0.2 $\mu\text{m}$	513.1	$\pm 133.6$	1832.8	$\pm 284.2$	2112.2	$\pm 210.4$
0.3 $\mu\text{m}$	166.8	$\pm 105.8$	106.0	$\pm 45.0$	172.2	$\pm 59.5$
0.5 $\mu\text{m}$	31.1	$\pm 26.9$	262.0	$\pm 142.2$	462.4	$\pm 312.2$
0.8 $\mu\text{m}$	15.6	$\pm 16.5$	107.6	$\pm 59.1$	233.6	$\pm 178.2$
1.5 $\mu\text{m}$	0.5	$\pm 0.7$	0.2	$\pm 0.1$	1.3	$\pm 0.8$
3 $\mu\text{m}$	0.7	$\pm 0.9$	0.2	$\pm 0.0$	1.4	$\pm 1.3$
5 $\mu\text{m}$	0.1	$\pm 0.1$	0.0	$\pm 0.0$	0.1	$\pm 0.2$

Mean = mean values of microemboli count.  
SD = standard deviation.

**Table 2.** Comparison of groups A, B, and C after 5 min of recirculation without PBF.

Groups	B-A Mean	A vs. B $p$ Value	C-A Mean	A vs. C $p$ Value	C-B Mean	B vs. C $p$ Value	A vs. B vs. C $p$ Value
	0.1 $\mu\text{m}$	637.03	ns	24.3	ns	-612.7	ns
0.2 $\mu\text{m}$	1319.68	.002	1599.1	.001	279.4	ns	.000
0.3 $\mu\text{m}$	-60.85	ns	5.4	ns	66.2	ns	ns
0.5 $\mu\text{m}$	230.93	.002	431.4	.001	200.4	ns	.000
0.8 $\mu\text{m}$	92.01	.002	218.0	.001	126.0	ns	.000
1.5 $\mu\text{m}$	-0.32	ns	0.8	ns	1.1	.004	.028
3 $\mu\text{m}$	-0.54	ns	0.7	ns	1.2	.004	.035
5 $\mu\text{m}$	-0.12	ns	0.0	ns	0.1	ns	ns

Mean = mean values of microemboli count.  
ns = not significant ( $p$  value  $> 0.5$ ).

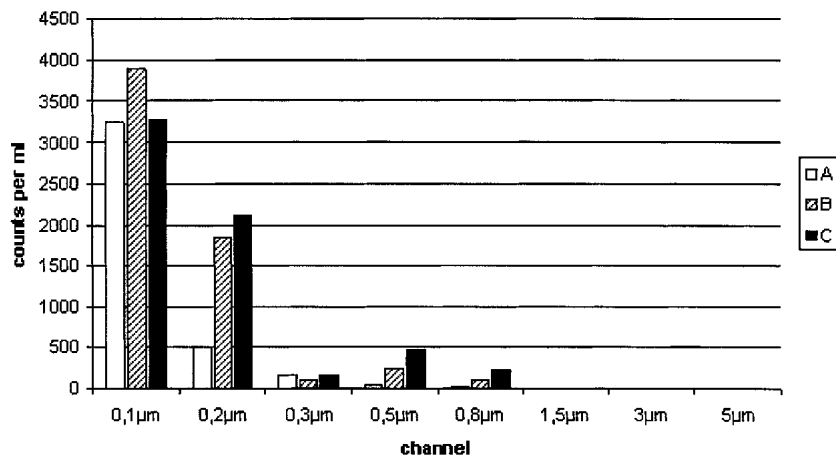


Figure 2. Mean microemboli counts in groups A, B, and C before prebypass filtration. Group a = white column; group b = hatched column; group C = black column.

Prebypass filtration reduced the number of measured microemboli in all categories. After 2 minutes of PBF with a CPB flow of 5 L/min, virtually no microemboli could be detected in the range of 0.2–5 µm, and the number of microemboli in the category 0.1 µm was reduced by the factor 10, approximately (Figure 3).

**DISCUSSION**

When discussing the findings of this study, it has to be remembered that the laser light scattering method cannot determine whether counts are caused by microparticles or by microbubbles. However, in clinical practice, this may not be of significance because both bubbles and particles in small capillaries have been shown to cause regional blood distribution problems (11,14–17). Microparticles in myocardial capillaries after administration of unfiltered crystalloid cardioplegia were associated with adverse effects on restoration of cardiac function during reperfusion (18).

In a pretest, the number of emboli present in the priming solution and CPB circuits in the categories of 2–400 µm was measured in the same circuit setup with a different

particle sensor (HRLD 400, HIAC Royco). A number of used PBFs were also evaluated by electron microscopy. Some large particles with sizes of 10–25 µm were found. Emboli of these sizes have been documented by other groups (12,19,20).

The differences in microemboli counts between groups A (priming solution) and groups B and C may be explained by different mechanisms. Although the priming solution seems to contain a very large number of small particles in the range of 0.1 µm, some microemboli are added by the circuits themselves. There are differences between group A and groups B and C in the categories 0.2, 0.5, and 0.8 µm. Obviously, these differences in microembolic activity originate from the CPB circuit components during recirculation. When groups B and C were being compared, a discretely higher number of microembolic counts, which reached statistical significance, were found in the categories 1.5 and 3 µm in the circuits without oxygenators. This phenomenon may be explained by a filtering effect of the membrane oxygenators. Some investigators have found such a filtering effect (13). This effect may not be true for the very small emboli because there are no differences between groups B and C in the categories 0.1–

Table 3. Effect of PBF on microemboli count in group B with oxygenator (N = 5).

	No PBF	SD	1 min		2 min		3 min		4 min		5 min	
			PBF	SD	PBF	SD	PBF	SD	PBF	SD	PBF	SD
0.1 µm	3888.2	±812.2	414.1	±68.3	372.8	±31.6	350.9	±42.6	348.8	±38.8	347.4	±41.1
0.2 µm	1832.8	±284.2	3.7	±7.4	1.5	±3.2	0.1	±0.1	0.0	—	0.0	—
0.3 µm	106.0	±45.0	0.2	±0.3	0.1	±0.1	0.0	—	0.0	—	0.0	—
0.5 µm	262.0	±142.2	0.4	±0.8	0.1	±0.3	0.0	—	0.0	—	0.0	—
0.8 µm	107.6	±59.1	0.1	±0.2	0.1	±0.1	0.0	—	0.0	—	0.0	—
1.5 µm	0.2	±0.1	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—
3 µm	0.2	—	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—
5 µm	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—

No PBF = mean microemboli count before use of PBF.  
 1 min PBF = mean microemboli count after 1 min of prebypass filtration.  
 SD = standard deviation.

**Table 4.** Effect of PBF on microemboli count in group C without oxygenator ( $N = 7$ ).

	No PBF		1 min		2 min		3 min		4 min		5 min	
	No PBF	SD	PBF	SD	PBF	SD	PBF	SD	PBF	SD	PBF	SD
0.1 $\mu\text{m}$	3275.5	$\pm 734.8$	411.0	$\pm 79.7$	367.3	$\pm 44.5$	363.5	$\pm 41.5$	361.9	$\pm 45.2$	362.4	$\pm 44.0$
0.2 $\mu\text{m}$	2112.2	$\pm 210.4$	1.9	$\pm 3.1$	0.1	$\pm 0.4$	0.1	$\pm 0.2$	0.0	$\pm 0.1$	0.0	—
0.3 $\mu\text{m}$	172.2	$\pm 59.5$	0.4	$\pm 0.9$	0.1	$\pm 0.1$	0.0	—	0.0	—	0.0	—
0.5 $\mu\text{m}$	462.4	$\pm 312.2$	0.2	$\pm 0.3$	0.2	$\pm 0.3$	0.0	—	0.0	—	0.0	—
0.8 $\mu\text{m}$	233.6	$\pm 178.2$	0.1	$\pm 0.1$	0.1	$\pm 0.1$	0.0	—	0.0	—	0.0	—
1.5 $\mu\text{m}$	1.3	$\pm 0.8$	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—
3 $\mu\text{m}$	1.4	$\pm 1.3$	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—
5 $\mu\text{m}$	0.1	$\pm 0.2$	0.0	—	0.0	—	0.0	—	0.0	—	0.0	—

No PBF = mean microemboli count before use of PBF.  
 1 min PBF = mean microemboli count after 1 min of prebypass filtration.  
 SD = standard deviation.

0.8  $\mu\text{m}$ . Moreover, a higher microembolic activity was only found in two of seven circuits, and these were made by two different manufacturers. However, because of the small sample size, it is difficult to reliably answer this question.

Interestingly, the number of counts in both groups for microemboli smaller than 0.1  $\mu\text{m}$  was also reduced. This phenomenon had been predicted in 1989, when a 5  $\mu\text{m}$  and a 0.2  $\mu\text{m}$  PBF were compared (12). The 5  $\mu\text{m}$  PBF was able to remove particles smaller than its actual indicated pore size. Because of similar material, it was postulated that the 0.2  $\mu\text{m}$  PBF would have the same capability. This hypothesis was confirmed with our study.

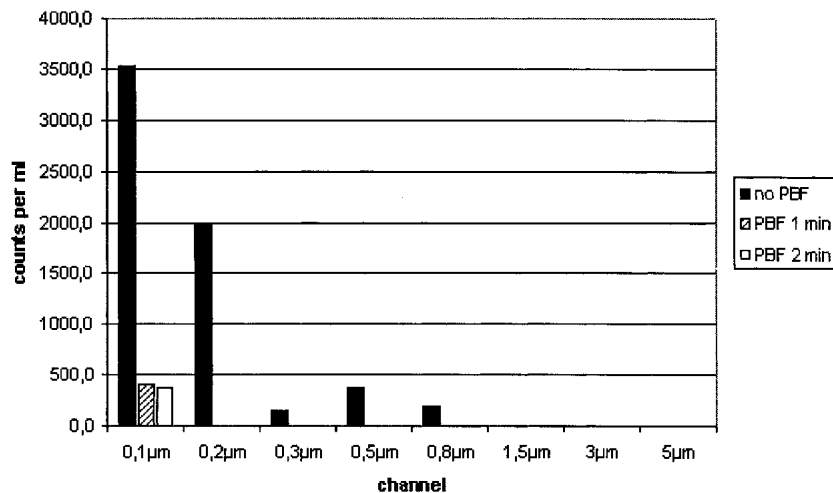
Recently, a novel device for the elimination of microbubbles during CPB has been investigated (21). However, removing bubbles smaller than 10  $\mu\text{m}$  has shown to be less efficient. Also, particles may not be removed as easily as bubbles because of their different weight and flow characteristics. Moreover, this system is designed for use during CPB to decrease microbubble content of the perfusate.

Prebypass filtration may be beneficial in the setup of

minimally invasive surgery, where CPB circuits are not used during the operation, but are set up as a backup safety precaution should cardiopulmonary support be needed. Possible bacterial contamination of unused circuits that will be needed for a different procedure and, therefore, remain filled with priming solution for several hours might be prevented.

Further studies are necessary on a larger number of CPB circuits to reinforce our results. Filtration of priming fluid with a 0.2- $\mu\text{m}$  filter before administration to the CPB circuit would give a more accurate idea of particle load of the CPB circuit alone.

We conclude that for routine and emergency preparation of a CPB circuit, it is recommended to filtrate the crystalloid perfusate through a 0.2- $\mu\text{m}$  PBF for a minimum time of 2 minutes at a flow of 5 L/min. This simple measure will reliably eliminate any microemboli bigger than 0.2  $\mu\text{m}$  and decrease the load of microemboli in the range from 0.1–0.2  $\mu\text{m}$ . Microembolic load of the CPB priming fluid contributing to neurocognitive decline of patients undergoing heart surgery with CPB may easily be reduced.



**Figure 3.** Effect of PBF on mean microemboli counts in averaged groups B and C. Before PBF = black column; PBF after 1 min = hatched column; PBF after 2 min = white column.

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