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# Filtration of Recirculating Cardioplegia Systems

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## Abstract

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*(J. Extra-Corpor. Technol. 20[1]: p. 30-34 Spring 1988)* Two recirculating cardioplegia delivery systems were examined to measure their particulate contamination level and the rate of particulate removal using an 0.8 micron Capture Membrane with standard housing assembly. Capture Membranes were changed at 5, 10, 20, and 30 minute time periods with the cardioplegia recirculating at 400 ml/min. A logarithmic equation was derived from the particulate counts measured. The extrapolated points demonstrated that 98% of particulate contaminates were removed from these systems after 60 minutes of recirculating.

## Introduction

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In 1955 Melrose introduced the use of cardioplegic solution to arrest the heart and create a quiet surgical field.<sup>1</sup> Today, cardioplegia is regularly used in 95% of the centers performing cardiac surgery.<sup>2</sup> The benefits of the use of cold cardioplegia include preservation of myocardial energy stores and protection of the myocardium from ischemic damage by decreasing the metabolic demands of the heart. The disadvantages of cold cardioplegia infusion into the aortic root include complications due to poor myocardial distribution, vessel perforation, vascular damage and air embolism.<sup>3</sup> A recent study by Robinson indicates that particulate contamination in cardioplegia solutions may also contribute to myocardial injury during cardiopulmonary bypass.<sup>4</sup> This study was designed to investigate the amount of particulate contamination and the length of recirculation necessary to remove 98% of this contamination from cardioplegia systems.

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Garven, Brooks and others have documented particulate contamination in intravenous and extracorporeal systems.<sup>5-12</sup> Particulate contamination from cardioplegic solutions and delivery systems may produce vessel blockage or vasoconstriction secondary to the vascular endothelium trauma.<sup>4,13</sup> Robinson's study found that administration of unfiltered cardioplegia into rat hearts "resulted in a progressive reduction in the coronary vascular flow due to a higher coronary vascular resistance and produced significantly higher levels of creatine kinase leakage."<sup>4</sup> His results suggest filtration could reduce vascular injury and enhance myocardial protection.

There are two possible locations for a filter in a cardioplegia administration system. These locations are as a final filter, and in a recirculation position. The best location is where the filter acts as a final filter and is interposed in the line carrying cardioplegic solution to the coronary arteries. In this position, the filter intercepts all particles that enter and blocks them from reaching the patient. The pore size of the filter is directly related to the size of the particle removed, thus a 0.2 micron pore filter can retain particles down to the size of the bacteria. While filter location in the patient line is best, it is only possible when the pore size of the cardioplegia filter is compatible with the components of the cardioplegic fluid. In the case where blood is to be added, an in-line sub-micron filter would intercept the red cells along with the solid particulates.

Robinson et al. leave no doubt that it is important to remove sub-micron particles present in the clear carrier solution, and yet, formed red cells must be allowed to pass to the patient in systems where blood is later added.

To resolve this conflict, a filter can be positioned in the recirculation line of the cardioplegia administration system, then later bypassed when blood is added. Thus, with each passing minute of recirculation of the clear solution, more and more particles are filtered from the reservoir and cardioplegic solution. (Solution cleared by the filter mixes with the solution in the system). In

effect, a filter in this location functions much as a prebypass filter would for the remainder of the extra-corporeal circuit. This is the approach that was taken in the present study.

## Methods and Materials

A total of six recirculating cardioplegia systems were evaluated in this study. These systems included three Cobe 027-801 Recirculating Cardioplegia Delivery Systems<sup>a</sup> and three Bentley Blood Recirculating Cardioplegia Systems.<sup>b</sup> Figure 1 shows the Cobe system which incorporates silicone tubing through the roller head. Figure 2 shows the Bentley system with the line connection for access to arterial blood when blood cardioplegia is requested. An 0.8 micron gridded Millipore Capture Membrane (MFM)<sup>c</sup> in Figure 3, was secured in a housing assembly as described by Brooks.<sup>5</sup> The MFM assembly was placed between the bubble trap and the recirculation line as depicted in Figures 1 and 2. The function of the MFM was twofold, to act as the filtering device in the system and to capture the particulates for counting.

Plegisol Cardioplegic Solution<sup>d</sup> was used as the test solution in this study. Ten milliequivalents of sodium bicarbonate were added to each bag using sterile technique per the recommendation of the manufacturer. As a control, two separate bags of Plegisol were passed through a MFM. Each MFM was rinsed with hot 0.2 micron filtered distilled water prior to drying, this avoided mistaking dried electrolytes for particles. Each membrane was dried and the particulates were counted using a 100x microscope. The MFM was carefully handled with forceps and was covered in a petri type slide dish to insure a valid counting index. Using a reticle scale in the microscope eye piece, the particulate counts on each MFM were sized in ranges 5-15 micron, 15-25 micron, 25-50 micron, 50-100 micron, >100 micron, and fibers. A high intensity light was required to visualize the particles under the microscope. To avoid extraneous contamination the sampling equipment was washing, rinsed with Freon and control test levels were done between each cardioplegic set.

Each cardioplegia system was then primed and recirculated through the MFM at a flow rate of 400 ml/min. This flow rate produced a pressure of 300 mmHg proximal to the MFM. This line pressure was chosen as the maximum acceptable line pressure. The membrane was replaced at recirculation times of five, ten, twenty and thirty minutes. After thirty minutes of recircula-

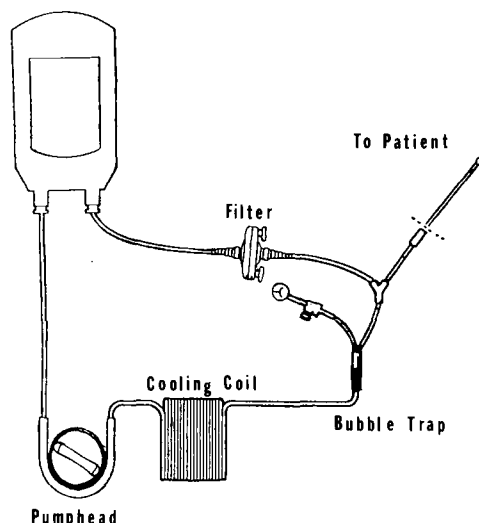


Figure 1: Illustration of the Cobe System with filter housing placed in-line.

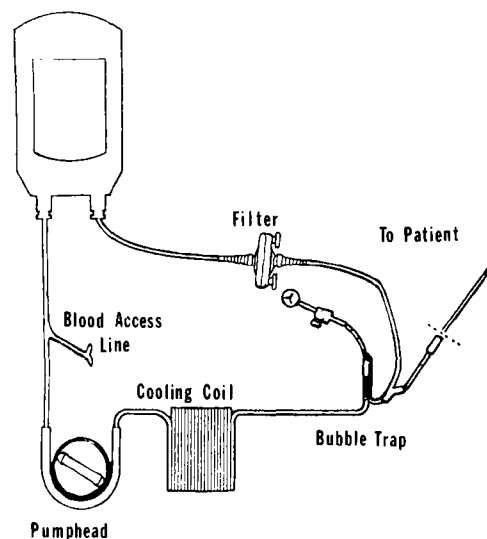


Figure 2: Illustration of Bentley Blood Cardioplegia system with the filter housing placed in-line.

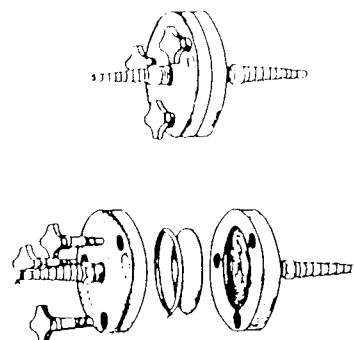


Figure 3: Illustration of Millipore Membrane Filter and housing assembly, from Brooks<sup>5</sup>. Top. Millipore filter and membrane assembled. Bottom, The disengaged view shows (A) inlet, (B) inlet end plate, (C) O ring, (D) disposable filter membrane, and (E) outlet.

a Cobe Corporation, Lakewood, CO 80215

b American Bentley Corporation, Irvine, CA 92714

c Millipore Company, Bedford, MA 01730

d Abbott Laboratory, North Chicago, IL 60064

tion, the cardioplegia system was drained through a MFM. The membranes were then processed and the particles counted as described above.

## Results

The particulate counts of the cardioplegic control solutions can be found in Table 1. These counts were compared with the governmental particle limits for large parenteral solutions as listed in Robinson's study.<sup>4</sup>

**Table 1**  
Comparison of Particle Contamination Per Liter of Cardioplegia Control Solutions with United States and British Pharmacopoeia Limits

Particle Size (diameter)	United States and British Pharmacopoeia		Plegisol	
	Pharmacopoeia		Bag #1	Bag #2
5 µm	80,000		277	355
10 µm	50,000		193	247
25 µm	5,000		46	66

**Table 2**  
Particle Counts in Six Recirculating Cardioplegia Systems

Time	Mean			SD		
	Both	Cobe	Bentley	Both	Cobe	Bentley
5 min.	244	247	240	68	96	48
10 min.	410	447	373	102	146	26
20 min.	567	635	499	128	164	7
30 min.	689	763	615	127	148	56
Drain	124	127	121	59	31	88
<b>Total</b>	<b>813</b>	<b>890</b>	<b>736</b>	<b>202</b>	<b>178</b>	<b>144</b>

**Table 3**  
Percent of Particulates Remaining After Specific Time Period

Time	Cobe			Bentley			Average
	#1	#2	#3	#1	#2	#3	
5 min	81%	68%	70%	72%	73%	54%	70%
10 min	58%	49%	45%	61%	43%	40%	49%
20 min	29%	34%	25%	43%	29%	20%	30%
30 min	14%	13%	15%	25%	13%	8%	14%

**Table 4**  
Particle Counts in Size Ranges After 30 Minutes Recirculating

	5-15 µm	15-25µm	25-50µm	50-100µm	100	fibers	total
<b>Cobe 1</b>	445	141	93	44	21	9	753
<b>Cobe 2</b>	355	223	156	54	25	14	827
<b>Cobe 3</b>	450	297	235	53	41	16	1092
<b>Bentley 1</b>	390	231	160	57	42	15	895
<b>Bentley 2</b>	335	158	96	59	37	14	699
<b>Bentley 3</b>	286	128	102	39	33	27	615

These values are also listed in Table 1. The cardioplegic solution counts were well within the governmental limits. No particles greater than 100 microns were found in the cardioplegia controls. Also no fibers, which are defined as particles having a length to width ratio of ten to one, were found.

Table 2 shows the average number of particles, recovered from each system at different recirculation time periods and the total for all six systems. The total count was derived by summing each time period plus the drain value.

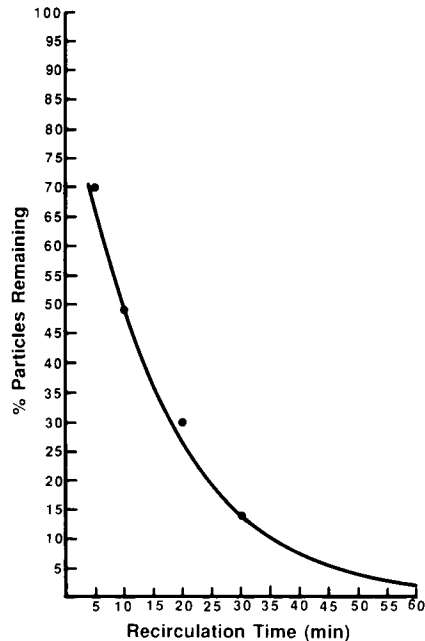
To evaluate these particle counts, a calculation was performed to determine the percent of the total number of particles remaining after each time period. The equation used to calculate this percentage is:

$$\% \text{ particles remaining} = \frac{\text{total count} - \text{timed particle count}}{\text{total count}} \times 100$$

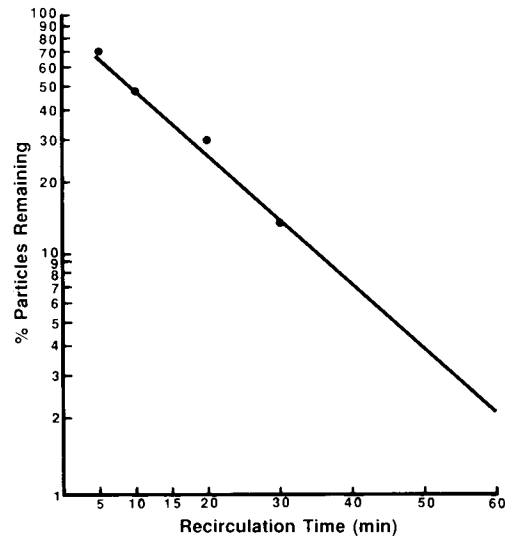
The calculated values for each system and the average of all six systems are listed in Table 3. Plotting these percent values forms an exponential decay curve as shown in Figure 4. To determine the recirculation time required to remove 98% of the particles present, an equation was derived to extrapolate the curve past the 30 minute measured value. The derived equation is:

$$y = 90 e^{-0.0623x}$$

In this equation, y is equal to the percent of particles remaining, x equals the recirculation time. The correla-



**Figure 4:** Graphic representation of the extrapolated curve with the average obtained points plotted of the percentage of particles remaining after recirculation at each time period.



**Figure 5:** Logarithmic representation of the extrapolated line with the average obtained points plotted of the percentage of particles remaining after recirculation at each time period.

tion coefficient was calculated at .93 which is significant at  $p < .001$ . Analysis of variance performed on predicted versus residual (predicted—actual) revealed significance at  $p < .001$ . Plotting these points on logarithmic paper formed a straight line as shown in Figure 5. Both figures show that 98% of the particles are removed after recirculating the cardioplegia at 400 ml/min for 60 minutes.

Table 4 lists the particle counts, in specific size ranges, filtered from the systems after thirty minutes of recirculation. A large number of the particles were found to be in the 5 to 15 micron range.

## Discussion

In the early 1960s Gravan and Gunner conducted studies concerning particulate contamination of parenteral fluids. As a result of these findings, the pharmaceutical industries were encouraged to establish quality control standards.<sup>8,14</sup> These governmental standards, shown in Table 1, were established for parenteral solutions that would be administered into the venous side of the circulation. Cardioplegic solutions are introduced directly into the myocardial circulation. To date, no concrete evidence exists to document human cardiac tissue damage caused by particulate contamination of unfiltered cardioplegia systems. However, Robinson's

study which infused unfiltered and filtered cardioplegic solutions into the coronary ostia of rat hearts showed significant results. When infusing unfiltered cardioplegia, Robinson found an increase in creatine kinase leakage from the heart muscle, with decrease coronary vascular flow possibly due to vasospasm, and poor myocardial recovery. The filtered cardioplegia group had improved coronary flow rates and better myocardial recovery. This study clearly indicates that the governmental limits, designed for venous infusion, may not adequately protect patients from particulate induced coronary artery damage.<sup>4</sup>

Membrane filtration is a simple and effective method of removing particulate contamination in the recirculating system cleanup phase. There are several factors which determine how quickly the desired level of cleanliness is achieved. These factors include the initial level of contamination, the effectiveness of the filter, and the ratio of the recirculating flow rate to the total volume in the system. The time periods chosen for collection of particles in this study reflect the number of total passes through the MFM. An important factor in removing particles from the system was the number of times the total solution volume passed through the filter. At 400 ml/min, there is one system volume pass through every two and one-half minutes, therefore the total recirculation period of 30 minutes would result in twelve system volume pass throughs.

In this study the initial contamination level of 813 particles is low in comparison to the governmental limits on parenteral solutions. It is significant that there were no fibers found in the cardioplegia solution controls, but fibers were later found in the solutions after the cardioplegia delivery systems had been recirculated as shown in Table 4. Similarly, no particles greater than 100 microns were found in the control solutions, but particles of this size were found in the solutions after it had been recirculated. These larger particles may have been left in the cardioplegia system after manufacturing or from tubing spallation in the roller head.

Table 2 indicates that total particle count on the capture membrane increases as recirculation time increases. When these values are converted to a percent of particles remaining (Table 3), one can see the decrease in particulate count in the system with time. Graphing these values illustrates an exponential decay. (Figures 4 and 5) Since one goal of this study is to determine the recirculation time required to remove 98% of the particles present, it is necessary to extrapolate points past the thirty minute time period. This extrapolation is accurate as reflected by the 93% confidence coefficient of the derived equation. Both figures show 98% of the particles are removed after recirculating at 400 ml/min for 60 minutes or an equivalent of 24 system volume pass throughs.

The results of this study are important to the perfusionist. Cardioplegia particulate contamination may cause myocardial injury by vascular endothelial trauma. The heart may not recover as rapidly or as fully when unfiltered cardioplegia is used.<sup>4,13</sup> In these two types of recirculating cardioplegia systems, 98% of the particulate contaminates are removed in 60 minutes when recirculating at 400 ml/min through an 0.8 micron filter. Knowing this information, the perfusionist can act to effectively remove particulate contamination from entering the coronary vessels by using a filter designed for cardioplegia.

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