Removal of Particle Contamination in the Extracorporeal Circuit Detected by an In-Line Particle Counter

M Ueda, Y Kondo, K Fuse, H Makuuchi, T Konishi

Abstract

We investigated the number and size of the particles (diameter:> 1 μm) in the extracorporeal circuit by means of a particle counter. We also evaluated the efficacy of pre-bypass filters in the extracorporeal circuit. During in vitro tests, the removal efficiency of the Pall PP3802 and the Harvey H-600 were 99.3% and 63.8% respectively after recirculating for 5 minutes. In clinical cases, the mean number of particles in the cardiopulmonary circuit after a 5 minute recirculation was 4287 ± 836 particles/ml (pcs/ml). After using the PP3802, it dropped to 52 ± 11 pcs/ml. It is desirable to use a .2 μm pre-bypass filter for recirculating all cardiopulmonary products before operation.

Introduction

It has been reported that cardiopulmonary products and the extracorporeal circuit, etc., are contaminated by massive particles (1,2). However, by conventional measurement methods (microscopic observation), it is extremely difficult to determine the size distribution of particles suspended in the recirculating fluid and the number simultaneously (in a short period of time).

Hence, recirculation of priming fluid through disposable prebypass filters is used in a majority of procedures nowadays. Notwithstanding this trend, effective removal of these particles, which are the potential risk factor in vivo, has not been thoroughly confirmed.

In our hospital, the extracorporeal circuit typically contains a 5 μm recirculation filter. We decided to evaluate a 0.2 μm pre-bypass filter. We determined the particle contamination in the extracorporeal circuit using an in-line particle counter (a), and the removal efficiency of both these filters during in vitro tests and clinical cases.

Material and Particle Measuring Apparatus

Pre-Bypass Filter

The Pall PP3802 Prebypass Plus filter (b) (PP) with a pore-size of 0.2 μm and Harvey H-600 (c) (H-600) with a pore-size of 5 μm were used.

PP is a membrane type filter with Nylon 66 used as membrane material, having a surface area of 900 cm^2 and a dynamic priming volume of 190 ml. The H-600 is a membrane type filter with Nylon 66 over which acrylonitrile vinyl chloride copolymer is coated, having a surface area of 75 cm^2 and a dynamic priming volume of 125 ml.

In Line Particle Counter

A KL-01 particle counter was used to measure the particles. The KL-01 is capable of measuring the number and size of particles by a light block system sensor (KS-61) and by classifying particle diameters in 6 ranges which are digitally displayed. In these measurements, a continuous trace volume injection pump was used to classify the particle diameter in 5 different steps of 2, 5, 10, 20, and 50 μm using an in-line system.

In addition, while the measurement by the light block system sensor will cause a coincidental loss corresponding to an increase in number of particles, the true number of particles was derived from the following equation against the numeric value attributable to these losses on the basis of KS-61 count loss table.

The coincidence loss is less than 5% at 800 particles per ml.

$$C = N \times \mathrm{Exp}(-6.25 \times 10^{-5} \times N)$$

N: True number of particles (pc/ml)

C: Count value by particle counter (pc/ml)

Direct Communications to: M Ueda, Toranomon Hospital Cardiopulmonary Section in the Cardiovascular Division 2-2-2, Toranomon, Minato-Ku, Tokyo 105, Japan Telephone: Japan 81 Tokyo 3-588-1111

a *RION Particle Counter, Model KL 01, Kokubung City, Tokyo, Japan 185*

b *Pall Biomedical Products Corp., Glen Cove, NY 11542*

c *CR Bard, Billerica, MA 01822*

Article available at https://ject.edpsciences.org or https://doi.org/10.1051/ject/198921124

Method

A. In vitro tests

1) The level of particulate contamination of oxygenator (d), blood circuit (e) and cardiotomy reservoir (c), which constitutes our extracorporeal circuit, was investigated, using distilled water.

The particles initially contained in the priming fluid used for clinical cases were also measured (Figure 1).

The particles in the oxygenator and blood circuit were measured after recirculating for 5 minutes at a flow rate of 5 L/min. The recirculation was retained initially in the cardiotomy reservoir and thereafter collected in a glass bottle and measured. The priming fluid was measured after filling the glass bottle with injected additives followed by gentle stirring, using the Pall blood transfusion filter SQ40S. Meanwhile, the number of particles, exclusive of the priming fluid, was calculated by subtracting the number of particles in distilled water from the number of particles in the recirculation fluid.

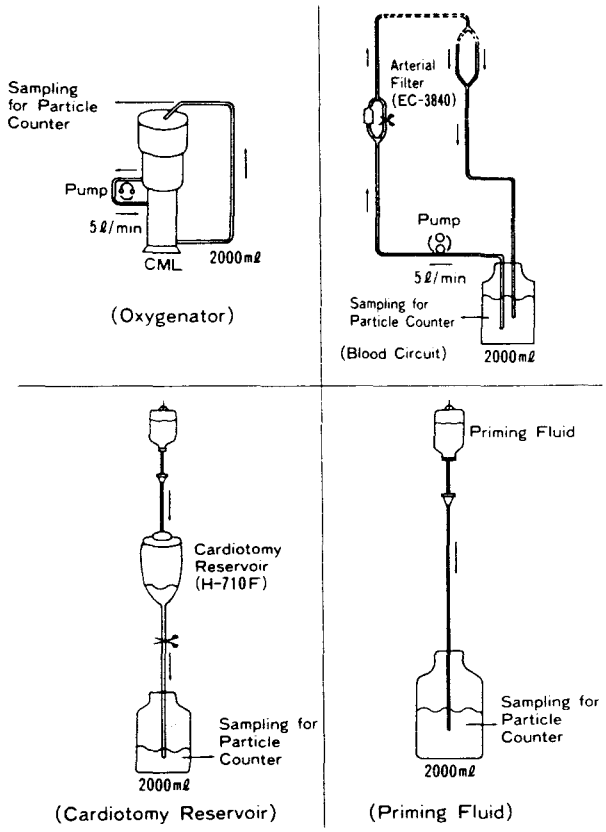

Figure 1. In Vitro Circuit for Counting Contaminating Particulate Matter in the Priming Solution and each Cardiopulmonary Product.

d *Coke Laboratories, Inc. Lakewood, CO 80215*
e *Tyson tubing, Senko Medical Inst. Co., Ltd. Bunkyo-Ku, Tokyo, Japan 113*

2) The particle removal performance of PP and H-600 was investigated (Figure 2).

Two liters of mock priming fluid (1400 ml of 5% glucose solution, 300 ml of mannitol and 300 ml of Hespan) was primed into the closed circuit, and circulated initially through the bypass line for 5 minutes at a flow rate of 5 L/min. Then, it was recirculated for 15 minutes through the filter line.

3) The internal resistances of PP and H-600 were investigated at each flow rate, using 2 kinds of solutions having different viscosities.

B. Clinical cases

PP was applied to 10 different cases of open heart surgery for adults using the CML. The filter was mounted in between the arterial line and venous line at the surgeon's site and measurement was made at the venous return entry port of the CML (Figure 3).

1) 2.2 liters of loading fluid were bypassed initially without going through the PP. After recirculating the circuit (sucker and vent lines are excluded) for 5 minutes at a circulating flow rate of 5 L/min, particles were measured. Then, circulation was performed under the same conditions but included passing through the PP, and the effect was investigated. The priming fluid of 5% glucose solution and 20% mannitol (5 ml/kg), Hespan (95 ml/kg), 7% $NaHCO_3$ (2 ml/kg), 100 ml of 25% albumin, and 100 ml of Exocorpol was used and instilled in the circuit via a blood transfusion filter.

2) After recirculating, PP was withdrawn and investigated by scanning electron microscopic observation and X-ray diffraction analysis.

Results

A. In vitro tests

1) Table 1 illustrates the number of particles present in each component of the extracorporeal circuit priming fluid. The number of particles larger than 1 μm adhering to the oxygenator, blood circuit, and cardiotomy reser-

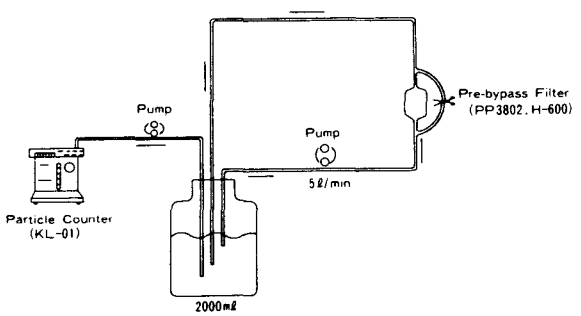

Figure 2. In Vitro Circuit for Performance Test of Prebypass Filter

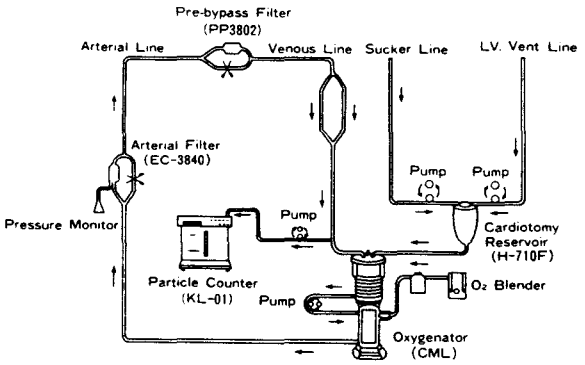

Figure 3. Extracorporeal Circuit for Counting Contaminated Particle Matter during Clinical Operation.

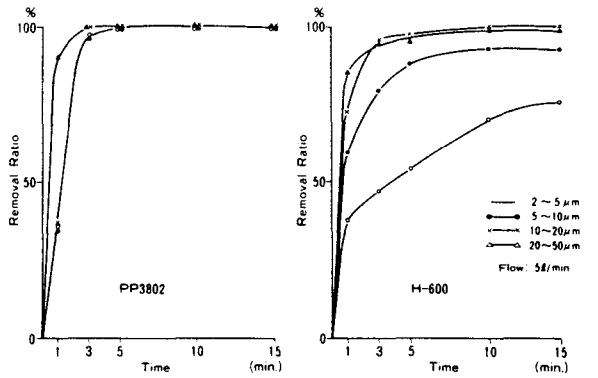

Figure 4. Contaminated Particle Removal Performance of the pp3802 and the H-600.

voir were 823.0 pcs/ml, 317.5 pcs/ml, and 341.5 pcs/ml respectively. In addition, the number of particles present in the priming fluid was 1251.5 pcs/ml, far more than the number of particles in the 3 circuit components.

2) The results of the particle removal performance by the PP and H-600 are illustrated in Figure 4.

The particle content of the recirculating fluid at the point of sampling (see Figure 3) was reduced when filters were incorporated into the system. By 5 minutes, the Pall PP3802 reduced the presence of 2–5 μm particles by 97.5%, 5–10 μm by 96.9%, and completely removed 10 μm and larger particles. On the other hand, H-600 demonstrated removal efficiency of 2–5 μm particles by 37.9%, 5–10 μm by 79.0%, and 10 μm and larger by 95.0% after 3 minutes.

In addition, the H-600's removal efficiency was 54.1% for 2–5 μm after 5 minutes and showed a trend toward increasing thereafter. Its removal efficiency for 5–10 μm was 88.0% after 5 minutes and equilibrium reached over 90% after 10 minutes.

3) The internal resistances of PP and H-600 are illustrated in Figure 5.

PP resistance values when Lactated Ringer's solution was used were 30 mmHg at one l/min 94 mmHg at 3 l/min, and 164 mmHg at 5 l/min, while H-600 values were 8 mmHg, 22 mmHg, and 45 mmHg respectively. On the other hand, when priming fluid prepared by our hospital was used, PP values were 61 mmHg at 1 l/min, 183 mmHg at 3 l/min, and 310 mmHg at 5 l/min, while H-600 values were 9 mmHg, 28 mmHg, and 52 mmHg—very low compared to PP.

Table 1

Number of Particle Matter in the Priming Solution and each Cardiopulmonary Product.

	Particle Size (μm)					
	2 ~ 5	5 ~ 10	10~20	20~50	>50	Total
Oxygenator	563.0	219.2	39.0	1.8	0	823.0
Blood Circuit	240.4	68.7	7.8	0.3	0.3	317.5
Cardiotomy Reservoir	245.7	78.6	15.3	1.9	0	341.5
Priming Fluid	826.8	304.0	108.4	11.7	0.6	1251.5

(pcs/mℓ)

Oxygenator: Cobe CML
Cardiotomy Reservoir: Harvey H-710F
Blood Circuit: Tygon tubing circuit
Senko Medical Inst., Co., Ltd.

B. Clinical cases

1) The results obtained on the application of PP to clinical cases are illustrated in Table 2.

As a result of the initial recirculation of priming fluid through the circuit for 5 minutes, massive numbers of particles, as much as 4287 ± 836 pcs/ml, were confirmed in the cardiopulmonary circuit. Among these particles,

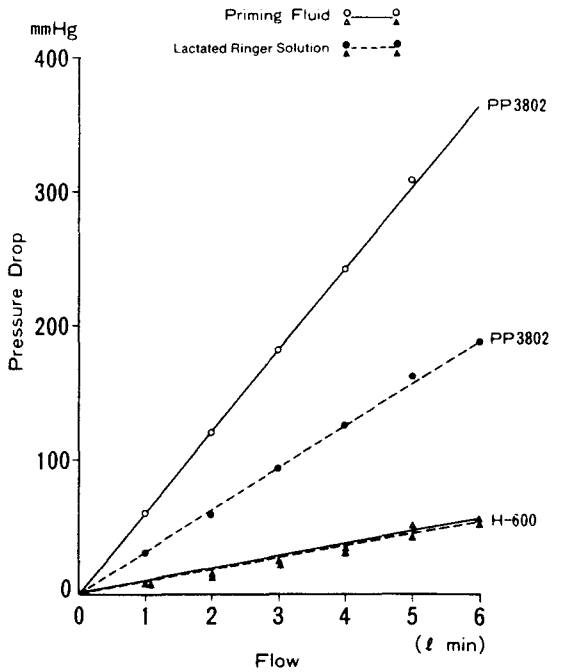

Figure 5. Typical Pressure Drops entire PP3802 and H-600.

Table 2

Removal Efficiency of the PP3802 during Clinical Operation.

(n = 10)

Particle Size (μm)	Unfiltered(pcs/mℓ)	Filtered(pcs/mℓ)	Removal Ratio (%)
2~5	3123.0±593.2	37.0±8.2	98.8
5~10	1058.5±238.8	13.8±3.8	98.6
10~20	104.8±22.5	1.5±0.8	98.5
20~50	1.0±1.7	0.3±0.3	—
>50	0	0	—
Total	4287.3±836.5	52.6±11.9	98.7

smaller diameters were present as 3123 ± 593 pcs/ml (2–5 μm and 1058 ± 238.8 pcs/ml (5–10 μm diameter) were in the majority. As a result of filtration with PP, the particles in the cardiopulmonary circuit were drastically reduced to a mean number of 52.6 ± 11.9 pcs/ml, representing a removal efficiency of 98.7%.

2) By means of a scanning electron microscopic observation, particles ranging in size from several μm to about 50 μm were confirmed on the surface of the filter. In addition, their composition was identified as Na, K, Cl, Ca, Si, Al, etc., by X-ray diffraction analysis.

Discussion

A particle in the circuit can become a foreign body in vivo, and many reports have been presented to date warning against harmful effects of such foreign matter (3). Foreign matter can move from one place to another depending upon its size. And it is presumed that the foreign matter of larger size (10–20 μm) may remain in the pulmonary blood vessels, while those of medium size (3–6 μm) may become lodged in the pancreas and liver. The object of preventive methods against the potential risk involved with these particles is to remove as many particles as possible before their entry in vivo. However, since it is impossible to remove micro-particles through a filter of 5 μm pore-size (the most common nowadays), it is considered most desirable to use a filter capable of removing particle size down to the size of bacteria. Hence, we have attempted to remove the particles suspending in rinsing fluid by using 0.2 μm recirculation prebypass filter. Kemna (4) and Kudo (5) have reported that numerous foreign matter was confirmed when they used a filter of pore size of 5 μm during recirculation prior to extracorporeal circulation. We have also confirmed during in vitro tests that there were voluminous particles contaminating the oxygenator, blood circuit, and cardiotomy reservoir. Of these, specifically a cardiotomy reservoir and membrane oxygenator combination contained many particles in diameter 2–20 μm. In addition, a far greater number of particles than originally expected were measured in the oxygenator.

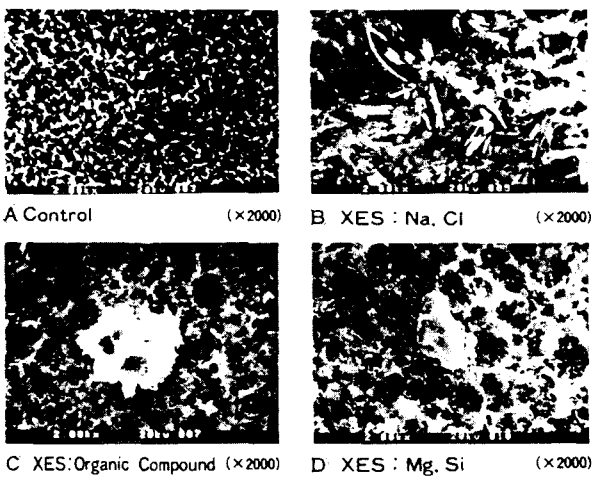

Figure 6. Scanning Electron Micrograph of Particulate Contamination.

This perhaps stems from the mixing of various kinds of fluids in the prime causing variation in compatibility due to pH and composition (6), resulting in the separation of fine crystals. Together with this, there exists a possible presence of glass fragments (3) generated when breaking drug ampoules or particles present in disposable syringes (6) and blood transfusion sets (3). As a result of comparative evaluation performed on particle removal performance between PP and H-600, the PP has demonstrated its superb removal performance in a short recirculation time compared to H-600. When judging according to the relative pore-sizes, the values obtained were exactly what we would have originally expected. In addition, it was confirmed that H-600 has removal capability even for the particles in diameter of 2–5 μm. This was perhaps because of the structure of H-600 being a membrane type with Nylon 66 used as membrane material having absorptive capability. From the preceding we might assume that it is highly probable for PP to remove micro-particles of below 0.2 μm since PP has the same structure and membrane material as the H-600. When internal resistances were measured, H-600 showed little or no variation in pressure at each flow rate using solutions having different viscosities, and has shown a very low resistance compared to PP. As a result of having recirculated the cardiopulmonary circuit in clinical cases, a large number of particles with a mean of 4287 ± 836 pcs/ml were measured. This number was far more than the sum of individual numbers of particles determined during in vitro tests and far exceed the criterion set forth in the Japanese Pharmacopoeia.

This phenomenon perhaps originates in cardiopulmo-

nary product use during in vitro tests. It is anticipated that mixtures of fluid for injection fluid could have possibly been further activated while going through the cardiotomy reservoir and circulating in the oxygenator and blood circuit. However, it may be necessary to evaluate this point further in the future. Then, as a result of 5 minutes recirculation with PP, the number of particles in priming fluid was drastically reduced to as low as a mean of 52.6 ± 11.9 pcs/ml. Such values thoroughly satisfy the criterion of the Japanese Pharmacopoeia (8). Accordingly, there is every indication to believe that PP is a useful filter capable of removing as much as possible of these particles of potentially embolic nature once perfused. Upon investigation of particle contamination in the extracorporeal circuit using an in-line particle counter and evaluation of the efficiency of pre-bypass filters, the following conclusions were obtained:

1) We have confirmed that massive particles contaminate the oxygenator, blood circuit, and cardiotomy reservoir.
2) In clinical cases, massive particles far exceeding the criterion of the Japanese Pharmacopia were confirmed when recirculated perfusate had been measured.
3) As a result of recirculation with PP incorporated into the extracorporeal circuit, as much as 98.7% of particles were removed in a short period of time.
4) From the point of view of removing as many particles (potential emboli) as possible before CPB, it is desirable to use the PP pre-bypass filter for recirculating extracorporeal circuit components before operation.

Reference

1. Brooks JD, Beauchamp RA, et al. Efficacy of Particulate Removal by a Prebypass Filter With Different Oxygenation System. J Extra-Corpor Technol. 1979;11:175–182.
2. Araki T, Itoh K, Tabe T, et al. Evaluation of contaminated Particles in Extracorporeal Circuit. J Artificial Oranges (in Japanese). 1977;6:304–307.
3. Horioka M, Aoyama T. Particle Matter in IV Solution. J Modern Medicine (in Japanese). 1976;8:3–12.
4. Kemna GD, Docherty JP. Why filter the cardiopulmonary circuit Pre-bypass? J Extra-Corpor Technol. 1979;11:119–123.
5. Kudo K. Disposable Pre-bypass filter for rinse of the extracorporeal circulation circuit. J Artificial Organs (in Japanese). 1981;10:842–845.
6. Kohobo F. Incompatibility of IV Fluid III (in Japanese). 1987;11–13.
7. Aoyama T. Problem of Contamination of Particles and Bacterias. J Monthly Pharmaceutical Affair (in Japanese). 1979;21:45–52.
8. Standard of Japanese Pharmacopoeia, Item: Particulate Matter in Injection. 1986;11:A-107.