

Original Article

Laboratory Evaluation of a New Membrane Oxygenator with a Built-In Hemoconcentrator

Hiroshi Nishida, MD; Susumu Suzuki*, CE; Masahiro Endo, MD; Hitoshi Koyanagi, MD; Katsuyuki Kuwana**; Hikaru Nakanishi**; Masato Aoki**

Department of Cardiovascular Surgery and Cardiopulmonary Bypass*, The Heart Institute of Japan, Tokyo Women's Medical College, and Senko Medical Instruments Manufacturing**, Tokyo, Japan

Keywords: membrane oxygenator, hemofiltration, hollow fiber

Presented at the American Society of Extra-Corporeal Technology 34th International Conference, March 8-11, 1996, Dallas, Texas.

ABSTRACT

In order to facilitate the handling of cardiopulmonary bypass (CPB) and simplify the circuit, we have developed a new membrane oxygenator with a hemofiltration function. The hollow fiber units for gas exchange and hemofiltration were combined in concentric circles in a cylindrical housing. The total priming volume was 190 ml. Because we used a silicon-coated hollow fiber membrane for gas exchange, this oxygenator was completely resistant to serum leakage. The gas exchange and hemofiltration sections both have a blood-outside flow configuration. All blood flows in a radial direction from around the central core to the surrounding hollow fiber units, first to the hemofiltration portion and then to the gas exchange section. Filtered fluid was easily collected through a stopcock mechanism. The oxygen transfer rate was 312 ml/min at a blood flow rate of 6 L/min, and the ultrafiltration rate was 3.5 L/hour at a blood flow rate of 4 L/min with 25% hematocrit and 200 mmHg transmembrane pressure in an in vitro study. The pressure drop was 62 mmHg at a blood flow rate of 4 L/min. We found no adverse effects in an in vivo study using a mongrel dog. In conclusion, this durable combined device could achieve excellent and simplified hemoconcentration by having all the blood in the unit flow through the hemofiltration portion, and may be useful not only in CPB during open heart surgery, but also in extracorporeal membrane oxygenation.

Address correspondence to:
Hiroshi Nishida, MD
Department of Cardiovascular Surgery
The Heart Institute of Japan
Tokyo Women's Medical College
8-1 Kawadacho, Shinjuku-ku, Tokyo 162, Japan

INTRODUCTION

Although screening methods for homologous blood used during surgery have significantly improved, the danger of various blood-related infectious diseases has not been completely overcome. Therefore, there is still a great demand for open heart surgery without the need for homologous blood transfusion. A hemoconcentrator is one of the most important devices to achieve this goal and has been widely used to raise the hematocrit of blood diluted with priming solution and crystalloid cardioplegic solution. Because both the membrane oxygenator and hemoconcentrator are devices made of hollow fibers, we have been developing a combined device: an oxygenator with a hemofiltration function (1, 2). In this article, we will describe the specifications and the *in vitro* and *in vivo* performance of the final prototype, together with a brief description of the development process and the various advantages of this new device and concept.

MATERIALS AND METHODS

We have developed four prototypes, each improving and solving the problems of the previous design. We believe the performance of Prototype 4 is satisfactory for clinical application (Table 1).

The hollow fiber units for gas exchange (effective membrane surface area: 2.23 m²) and hemofiltration (0.61 m²) were combined in concentric circles in a cylindrical housing (outer diameter 95 mm, length 140 mm). The total priming volume is only 190 ml. In Prototype 4, we combined a longitudinal flow direction and radial direction by making a small gap between the central core and the surrounding hollow fiber bundle. All blood entering into this combined device first flows in a longitudinal direction to the small gap between the central core and surrounding hollow fibers for hemofiltration (Figure 1). The blood simultaneously radiates centrifugally into the adjacent hollow fiber units. This unique blood path enables the coexistence of excellent performance and a small pressure drop.

IN VITRO EVALUATION OF PERFORMANCE

In vitro performance was evaluated in a mock circulation using bovine blood. During the measurement of the oxygen transfer rate and pressure drop, which lasted for three hours, the hemoglobin concentration was maintained at 12 g/dl and the temperature was maintained at 37°C. Oxygen saturation of the venous blood was main-

tained at 65%. The ultrafiltration rate was measured at a hematocrit of 25% and 35%, while altering the blood flow rate from 2 L/min to 4 L/min.

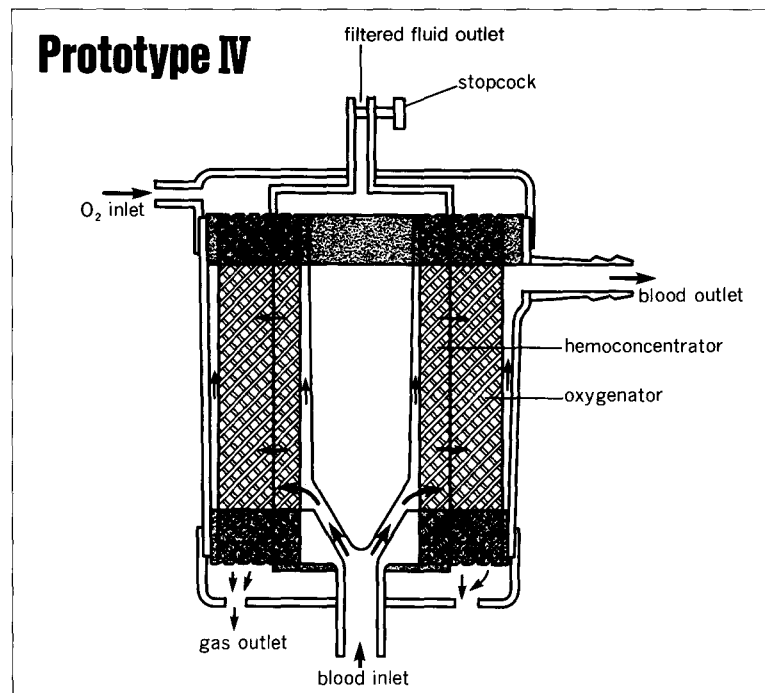
IN VIVO ASSESSMENT OF PERFORMANCE

After completing the developmental stage and *in vitro* evaluation, we conducted a preclinical *in vivo* assessment in a canine model. A mongrel dog weighing 14 kg underwent cardiopulmonary bypass with a closed circuit containing Prototype 4 for three

Table 1: Specifications of Prototype 4

[Housing] Outer diameter: 95 mm; Length: 140 mm		
[Hollow Fiber Bundle] Outer diameter: 80 mm; Length: 85 mm		
[Central Core] Diameter: 35 mm		
[Priming Volume] 190 ml		
Module	Oxygenator	Hemoconcentrator
Material	Cross-Wind Polypropylene (silicone coated)	Cross-Wind Polypropylene
Outer Diameter	300 μm	300 μm
Wall Thickness	30 μm	30 μm
Porosity	30%	40%
Surface Area	2.23 m ²	0.61 m ²
Packing Density	55%	50%

Figure 1: Diagram of Prototype 4



hours. A perfusion cannula was inserted into the ascending aorta, and a single stage drainage cannula was inserted into the right atrium. The hematocrit was maintained at 26% during the experiment.

IN VITRO PERFORMANCE

1. Oxygen transfer rate (Figure 2): The oxygen transfer rate was 312 ml/min at a blood flow rate of 6 L/min with hematocrit of 35%, and 250 ml/min at a blood flow rate of 4 L/min.

2. Ultrafiltration rate (Figure 3): The ultrafiltration rate was 3.5 L/hour at a blood flow rate of 4 L/min with 25% hematocrit and 200 mmHg transmembrane pressure, and 2.0 L/hour with 100 mmHg transmembrane pressure.

3. Pressure drop: The pressure drop was 62 mmHg at a blood flow rate of 4 L/min and 99 mmHg at a blood flow rate of 6 L/min (Figure 4).

The sieving coefficient for albumin in the hemofiltration portion was 0.35. In the hemofiltration portion, porosity of the hollow fibers was 40%.

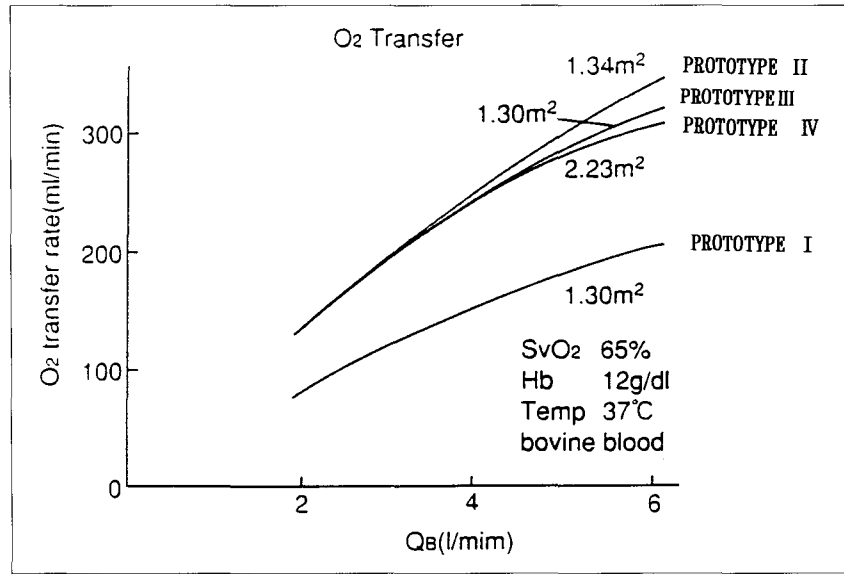
IN VIVO ASSESSMENT

The oxygen transfer rate was 26.7 ml/min at a blood flow rate of 0.9 L/min when SVO_2 was 90.1%. Ultrafiltration was 1.8 L/hour.

DISCUSSION

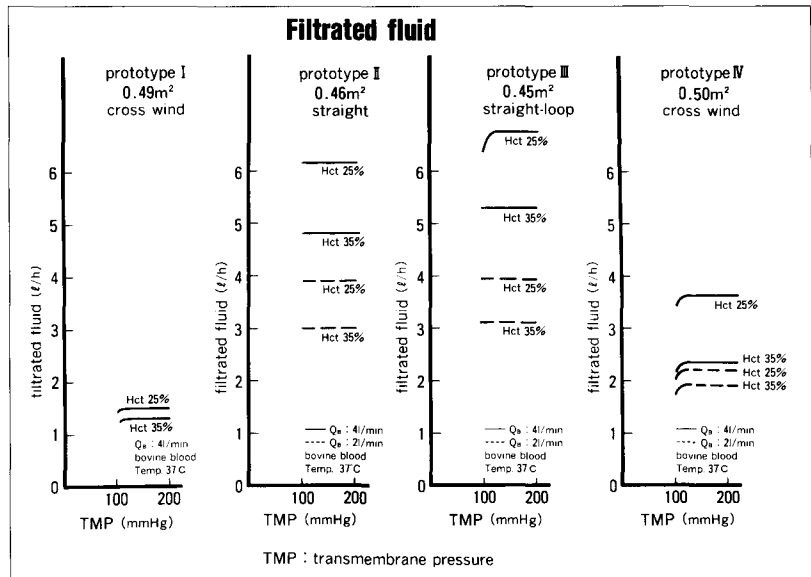
To avoid various bloodborne infections such as hepatitis and AIDS, and to avoid homologous blood transfusion-related complications such as graft versus host disease, there has been a great demand to decrease or abolish the use of homologous blood transfusion in open heart surgery. To remove excessive fluid from blood diluted with priming solution and crystalloid cardioplegic solution, a hemoconcentrator with a hemofiltration function is a simple and useful device. Although the hemoconcentrator is structurally very similar to a membrane oxygenator, the conventional hemoconcentrator has traditionally been separate from the membrane oxygenator. This makes the extracorporeal circuit unnecessarily complex. With this background, we came up

Figure 2: Oxygen transfer rate.



O₂ = oxygen; SvO₂ = oxygen saturation of the blood on the venous side; Hb = hemoglobin; Temp = temperature

Figure 3: Ultrafiltration rate



Hct = hematocrit; Q_B = blood flow rate

with the idea to combine these two hollow fiber units into a single housing.

The basic concepts of the design are as follows:

1. To combine a hemoconcentrator and oxygenator in one housing.
2. To adopt a blood-outside flow pattern, not only in an oxy-

oxygenator, but also in a hemoconcentrator.

Although most of the currently available oxygenators utilize blood-outside configurations, hemoconcentrators use a blood-inside design. The relatively low flow rate is the reason for the blood-inside design of the hemoconcentrator. To facilitate increasing the blood flow rate in the hemoconcentrator and to make combination easier, we adopted a blood-outside flow pattern for the hemoconcentrator.

3. To adopt a stopcock mechanism to facilitate the collection of filtrated fluid.

When the stopcock is opened, hemo-filtration commences and the filtrated fluid comes out through the stopcock. Hemoconcentration can be easily stopped by simply closing the stopcock. Manipulation of the roller pump, which sends the blood to the hemoconcentrator, is not required.

The principal goal of the design was the maximum utilization of all the hollow fibers in both the oxygenator and the hemoconcentrator without creating any significant dead space. For this purpose, it was essential to obtain an even and effective distribution of the total blood flow to the entire device. A low pressure drop was another important requirement because the combined device has a long blood path.

The various advantages of this newly conceptualized device are summarized as follows:

1. Advantages in handling

- a. Simple circuit: An additional parallel circuit for the hemoconcentrator is unnecessary.
- b. Fewer pumps: A separate pump for the hemoconcentration circuit can be abandoned.
- c. Less priming volume
- d. Easy collection of filtrated fluid
- e. Fewer personnel to handle cardiopulmonary bypass: The perfusionist can concentrate on the oxygenator and the blood level in the reservoir.

2. Theoretical advantages in performance

Because the blood flow rate through the hemoconcentrator portion is the same as the systemic blood flow rate, flow rates of 4 to 6 L/min are used, which are significantly greater than

Figure 4: Pressure drop

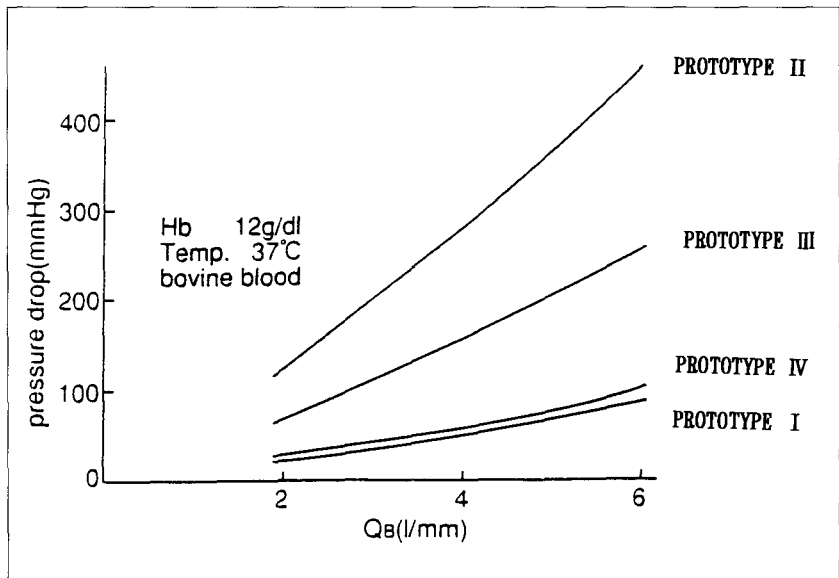
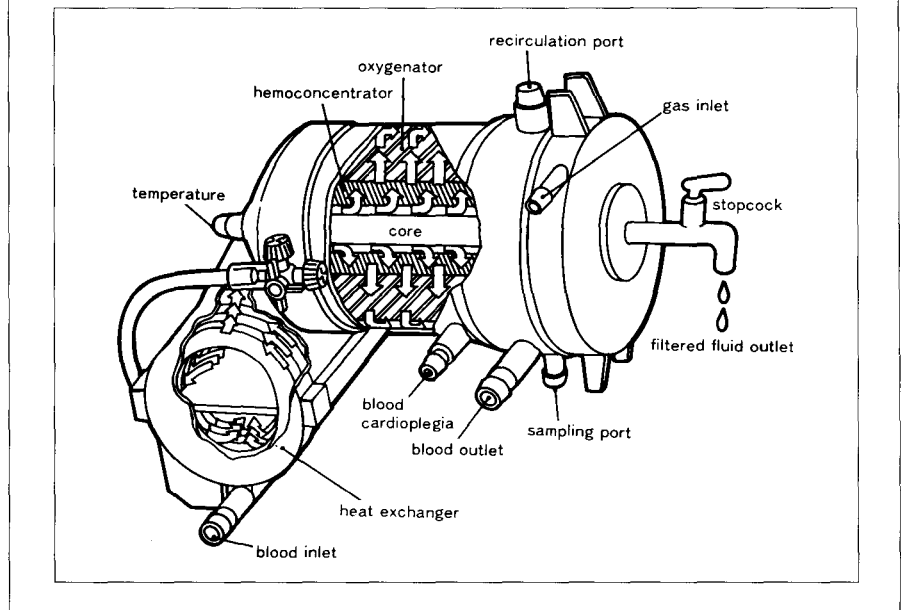


Figure 5: Diagram of the commercial version



that obtained with the conventional blood-inside perfusion-type hemoconcentrator, in which flows are typically 200 to 500 ml/min. This significantly higher blood flow rate assures improvement of performance of the hemoconcentrator.

3. Theoretical advantages in durability

- a. Durability of oxygenator: Because silicon-coated (0.2 micron thickness) polypropylene microporous hollow fibers were adopted in the oxygenator portion of this device, serum leakage cannot occur,

even with long-term usage.

- b. Durability of hemoconcentrator: Because of the higher blood flow through the hemoconcentrator, clogging of the micropores in the hollow fibers, which leads to a drop in the hemofiltration performance, is significantly less than with the blood-inside perfusion mode.

To accomplish these goals, we previously developed three prototypes (1). However, satisfactory performance could not be simultaneously obtained for both basic performance and pressure drop. In Prototype 1, pressure drop was satisfactory, but oxygenation and hemofiltration performance were poor, mainly due to an unacceptable amount of dead space. In Prototypes 2 and 3, oxygenation and hemofiltration performance were excellent, but the pressure drop was unacceptably high, due to an excessively long blood path. The relatively lower ultrafiltration rate of Prototype 4, as compared with those of Prototypes 2 and 3, was due to the lower porosity of the hollow fibers. On the other hand, a linear relation between ultrafiltration rate and transmembrane pressure was maintained even under the high transmembrane pressure in Prototype 4. We consider this phenomenon the result of the radial flow direction in Prototype 4. This characteristic may be beneficial when considering the situations under which this combined device will be used. In this combined device, transmembrane pressure will reach much higher levels because of the significantly greater blood flow through the device. To decrease the large pressure drop, we developed the fourth prototype with a unique blood path combining longitudinal and radial flow patterns. The pressure drop obtained in Prototype 4 was nearly the same as that with Prototype 1 and significantly lower than those observed with Prototypes 2 and 3. We consider this degree of pressure drop to be acceptable for clinical application. With these modifications, satisfactory performance was obtained. Excellent handling with no serious problems was also confirmed in *in vivo* assessment, and we believe the developmental stage has been completed. With the incorporation of a heat exchanger, the development of the commercial version has been completed (Figure 5). For actual clinical application, several small adjustments and modifications must be made, such as the establishment of a cost-effective and realistic manufacturing process, including the process for making the hollow fiber units for hemofiltration hydrophilic without affecting the performance of the oxygenator hollow fibers under sterile conditions.

In conclusion, the combined device is highly durable, and could be useful for assisted circulation requiring long-term oxygenation and management of circulating blood volume in patients with impaired urinary output.

REFERENCES

1. Nishida H, Endo M, Koyanagi H, Suzuki S, Kuwana K, Nakanishi H. Oxygenator with built-in hemoconcentrator: A new concept. *Artif Organs*. 1995; 19: 365-368.

2. Nishida H, Endo M, Koyanagi H, Suzuki S, Nakanishi H, Kuwana K. Development of an oxygenator with built-in hemoconcentrator. *Jpn J Artif Organs*. 1995; 24: 620-623.