

Is There Any Possibility that Heart Transplantation Can Be Replaced by an Artificial Heart?

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Abstract— EVAHEART is one of the Japanese-made implantable ventricular assist device (VAD) which was produced by a multi-institutional project. The pilot study of clinical implantation was started in May, 2005 and satisfactory performance has been exhibited in initial three cases which are running for three years. Prior to the clinical application, in-vitro test (hemodynamic, durability, and biocompatibility) and animal experiments were performed in parallel, because many break-through technologies are included in the EVAHEART system, such as cool seal circulatory system. Throughout the clinical postoperative care with EVAHEART, it was proved that this EVAHEART system exhibited an excellent performance. Although artificial heart is recognized as an expensive device, the first patient has found a full-time job, while paying a tax. Moreover, the safety is confirmed, showing a possibility that the EVAHEART can be replaced from cardiac transplantation in the near future.

I. INTRODUCTION

Japanese implantable centrifugal type ventricular assist device project was organized by Dr. Kenji Yamazaki of Tokyo Women's Medical University in 1990 and Sun Medical Technology Research Co., Waseda University and University of Pittsburgh Medical Center have been

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contributed for the development of clinical quality ventricular assist system, called EVAHEART[1][2]. They were implanted into 18 human cases in Japan up to now. The first three cases were all discharged and alive for three years. The first patient received EVAHEART in May, 2005 at Tokyo Women's Medical University has a full-time job. To achieve this present successful level, huge number of *in vitro* experiments and animal experiments were performed. Throughout the project, roles of biomedical engineers become more important. Bioengineers have been establishing a methodology of various types of *in vitro* tests to eliminate considerable risk factors, through a development of hydrodynamic performance tests, fatigue tests and biocompatibility tests. As *in vitro* tests have been proved effective, some typical fundamental tests and clinical data are briefly introduced in this paper.

II. MATERIALS, METHODS AND FUNDAMENTAL RESULTS

A. Hydrodynamic performance of the EVAHEART

Six times of the EVAHEART design modification was performed towards a final prototype system which is shown in Fig.1.

The *in vitro* data have been obtained from Waseda-original mock circulatory system as indicated in Fig.2. Special features of the mock system are as follows:

- 1) Anatomically identical shaped silicone left ventricle and atrium.
- 2) Similar pressure-volume curves in one cardiac cycle driven by linear actuator.

The EVAHEART was installed into the mock loop between LV apex and ascending aorta. This location is just simulated to the animal model. Fig.3 shows one of the fundamental flow characteristics represented as a "Head-Flow" relationship. 9L/min of blood pump flow was achieved against 100mmHg at the pump speed of 2400 rpm, which exhibited a satisfactory bypass flow for the patient of profound heart failure.



Fig. 1. EVAHEART system for final prototype (clinical) model

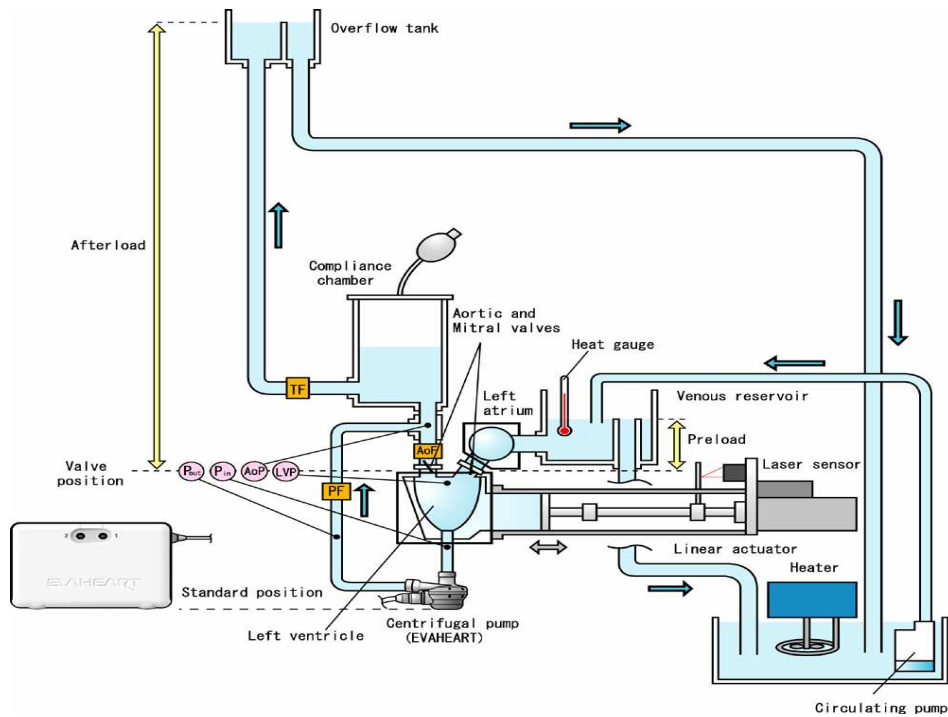


Fig. 2. Schematic drawing of mock circulatory system with EVAHEART

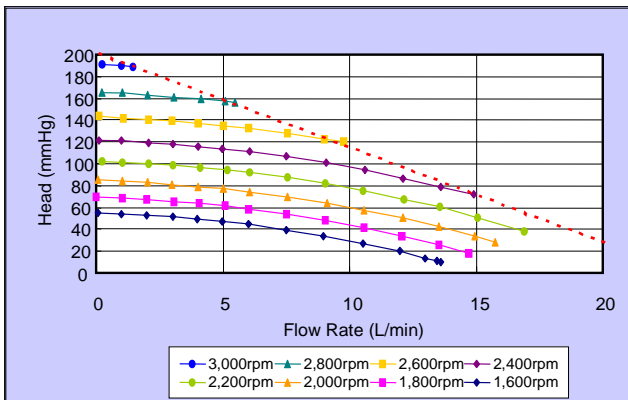


Fig. 3. Fundamental flow characteristics of EVAHEART

It is also essential to know the most reliable bypass flow at any time for the safe postoperative care. Therefore, software was designed to estimate the bypass flow. The estimated flow by motor current and rotational speed was continuously compared with that measured by electromagnetic flow probe which is installed in the previously-described mock circulatory system. A typical display of the flow monitor used for the clinical application can be seen in Fig.4. When a normal circulating condition (awake) was simulated in the mock circuit, the estimated flow was 5.84L/min, whereas the flow measured by the electromagnetic flow meter was 5.67L/min. Even if the pump flow was increased by twice as a simulation of exercise state, a difference between two flow values was also small and permissible. Therefore, it was confirmed that non-invasive flow measurement system can be used clinically.

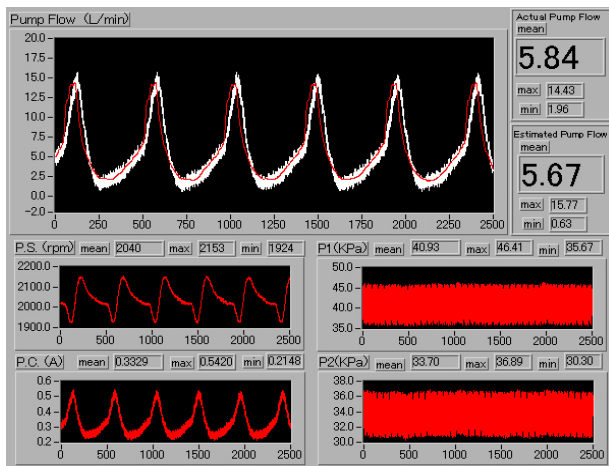


Fig. 4. Example of monitor display of EVAHEART flow estimated by motor current and rotational speed

B. Durability test for EVAHEART

Because of a new design and function in the EVAHEART, such as cool seal system, durability test protocol, including a design of the test machine, was discussed with US Food and Drug Administration (FDA). Whole view and schematic drawing are indicate in Fig. 5.[3] Major circulatory loop of the durability test machine is compared of motor-driven left ventricle with two valves, elastic tubes for afterload compliance, screwclamp for peripheral resistance and overflow-type preload chamber. The pulsatile flow is circulated in the mock circuit, where EVAHEART is also driven in between LV and aorta, which is the same way as the clinical implantation. To ensure a practical durability for a long-time usage, general cycle of three activity levels, these are “sleep”, “awake” and

“exercise”, are sequentially shifted one after the other everyday. For example, normal cardiac function (awake) was set at 70 BPM with a total flow (sum of the cardiac output and the bypass flow) of 6.6 L/min and bypass flow from EVAHEART was automatically sent at 6.3 L/min, if the rpm was fixed at 1900 rpm.

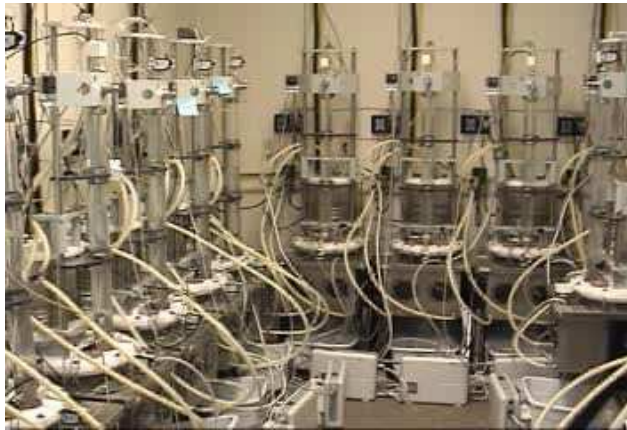


Fig. 5. Durability test for EVAHEART

18 EVAHEARTs were evaluated by 18 identical durability mock loops for over one year. It is fortunate that no injured surface was observed on the surface of impeller and inner housing. Moreover, there was no termination of the test due to the mechanical failure of the pump system. It was statistically proved that this EVAHEART system was successfully passed the reliability of 80% and the confidence level of 90%, even if one system had a problem.

C. Biocompatibility test for EVAHEART

Biocompatibility is one of the most important items to be considered for long-term usage of the blood pump. Test protocol of biocompatibility using our circuit [4] is as follows:

- 1) Heparinized fresh porcine blood harvested from the same animal should be used for comparative study.
- 2) Therefore, identical two circuits should be always prepared for comparative study.
- 3) Pulsatile circulation to simulate hemodynamic pressure / flow condition is preferable to obtain practical data.

Fig. 6 is one of the test results after one hour circulation of fresh bovine blood. Anticoagulant agent (heparin) was used to maintain the ACT of around 300sec. The same amount of blood was divided and injected into two identical circuits. As can be seen on the upper photographs of Fig. 6, fibrin network was observed and some blood cells were captured on the miractran surface of the LV pump. On the contrary, MPC surface was clean.[6] Although both coating materials are polyurethane, biocompatibility was clearly differentiated. Fig.7 is one of the mechanical hemolysis test results. Instead of the pulsatile pump at the LV portion, non-pulsatile pumps (Biopump and EVAHEART) were installed in each circuit. Hemoglobin level was represented as N.I.H (Hemolytic Index) which was derived from the

equation in Fig. 7. It was found that the hemolysis level data were reproducible and hemolysis by EVAHEART was much lower than that by Biopump®.

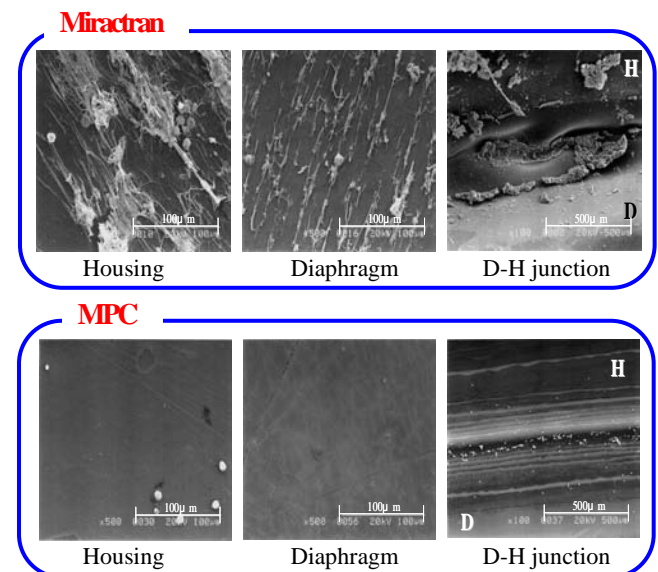
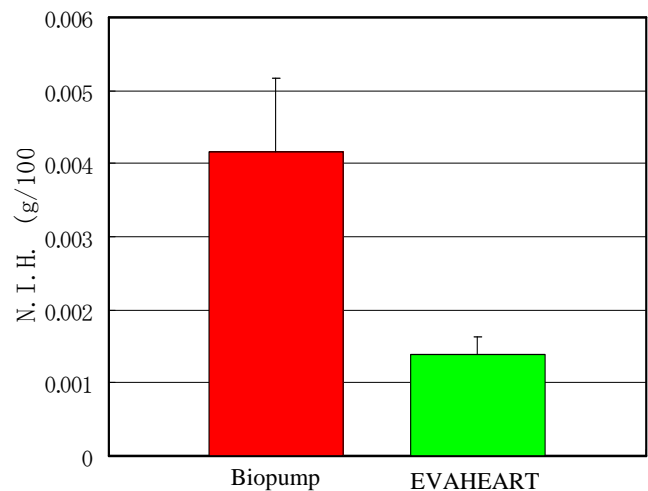


Fig. 6. Example of the biocompatibility test results obtained from our in vitro circuit (Comparison of biocompatibility between Mirastran and MPC)



$$N.I.H = \frac{\Delta PFH \times V \times (100 - Ht)}{Q \times T}$$

- ΔPFH : Increase in Plasma Free Hemoglobin
- V : Circulation blood volume
- Ht : Hematrit
- Q : Pump flow
- T : Circulation time

Fig. 7. Comparison of mechanical hemolysis between Biopump and EVAHEART obtained from our in vitro testing for blood hemolysis

III. CLINICAL RESULTS AND DISCUSSION

A. Clinical trails of EVAHEART as a pilot study

The first clinical implantation of EVAHEART was performed at Tokyo Women's Medical University in 2005 under the guideline for next-generation ventricular assist device [7]. The Japanese government organized a committee to set up a protocol for new implantable devices and it was suggested that two-staged clinical trials were favorable: pilot (Feasibility) study and pivotal study.

Table 1 is a patient summary of EVAHEART for pilot study. The first three patients were suffered from DCM (Dilated Cardio-Myopathy), but after implantation, all patients discharged and high quality of life with EVAHEART can be maintained for over 1000days.

B. Hemodynamic performance with EVAHEART

Fig.8 shows an improvement of hemodynamics after implantation of EVAHEART. Dramatically decrease in pulmonary arterial pressure and PC wedge pressure, and increase in cardiac index were noticeable.

Fig 9 is a typical bed-side monitoring screen which indicated hemodynamic waveforms during EVAHEART pumping. Although pump revolution number is constant around 2000 rpm, pulsatile pump flow is generated, because of a contraction of the natural heart; a pressure difference between inlet and outlet of the pump is varied for systolic and diastolic phases. Then, operating point is shifted in turn on the head-flow chart. In the first case, the amplitude of the bypass flow was 15 L/min as shown in the third column of the screen in Fig.9.

LDH level is continuously monitored as an indication of biocompatibility. It was selected as one of the parameters for monitoring at the postoperative care. As shown in Fig.10, LDH level can be stabilized within one to three months in all three cases after implantation of the EVAHEART. It was found by both in vitro and clinical data that EVAHEART can maintain a low hemolysis level during pumping.

C. Quality of Life with EVAHEART

In the first case, before implantation of the EVAHEART, the patient always lay on bed and could not move due to a severe heart failure, however, he walked in the hospital only few days after receiving EVAHEART. He never felt an existence of 420g, silent – EVAHEART in the body. [8] He spent ten months for rehabilitation training, then, discharged from the hospital. At that time, his medical cost at home was only 1/100 as compared with that in the hospital. Moreover, he found a full-time job after 18 months later. Fig.11 is the first patient working in the company. His battery is located on his back.

As the pumping duration for the first three patients exceeds 1000 days without any major problems, survival rate with EVAHEART is much better than that with other devices. For example, survival rate with US pulsatile

Table 1. First three clinical cases of EVAHEART pilot study

No.	Age/sex	Diag	Institute	POD(2008.4.30)
1	46 / M	DCM	TWMU	1088+ (on going)
2	29 / M	DCM	TWMU	1028+ (on going)
3	40 / F	DCM	NCVC	1024+ (on going)

DCM: Dilated Cardio Myopathy

TWMU: Tokyo Women's Medical University, Tokyo

NCVC: National Cardiovascular center, Osaka

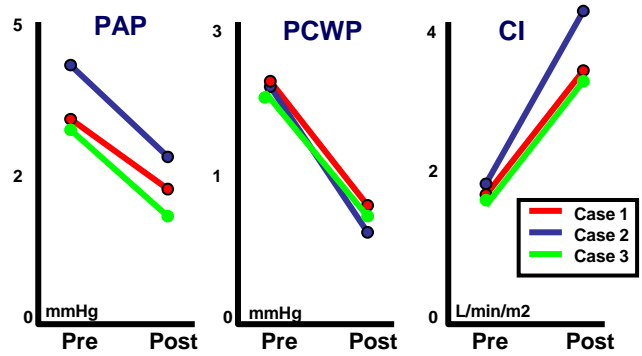


Fig. 8. Hemodynamic improvement of the first three clinical cases with EVAHEART



Fig. 9. Typical monitor screen of hemodynamic waveforms during EVAHEART pumping (case 1)

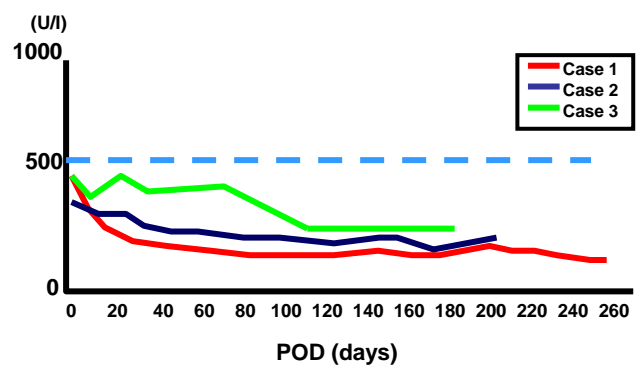


Fig. 10. Changes in LDH value (hemolysis rate) of the first three clinical cases with EVAHEART

implantable devices exhibited only 30 % after 18 months pumping. [9]

IV. CONCLUSION

The authors have been establishing a methodology to eliminate considerable risk factors through a development of practical *in vitro* test circuits. And, some typical clinical data were also introduced.

As mentioned above, it was confirmed that all *in vitro* tests are effective to ensure a safety toward clinical application. Therefore, clinical trials can be performed without any major problems. According to the comment by the first patient with EVAHEART, he does not wish to receive donor heart; he is satisfied with his present quality of life. Now, we should discuss a relationship of effective treatment between organ transplantation and artificial organs.

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Fig. 11. The first patient with EVAHEART: He has a full-time job