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NONPULSATILE FLOW: REVIEW

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Development of Terumo implantable left ventricular assist system (T-ILVAS) with a magnetically suspended centrifugal pump

Abstract The research group of Terumo, NTN, and the Setsunan University have been developing an implantable left ventricular assist system (T-ILVAS) featuring a centrifugal blood pump with a magnetically suspended impeller (MSCP). The present study describes recent progress in the development of the T-ILVAS, focusing on ex vivo and in vivo evaluations of the prototype MSCP. The MSCP is composed of four parts: a magnetic bearing, an impeller, a housing, and a DC burshless motor. The impeller is suspended by a magnetic bearing, thus providing contact-free rotation of the impeller inside the pump. The prototype MSCP was placed paracorporeally in three sheep and implanted intrathoracically in two sheep to evaluate its long-term durability and nonthrombogenicity. One sheep implanted ex vivo with the paracorporeal MSCP (Model I) survived for 864 days without any mechanical failure or thromboembolic complications, and with negligible hemolysis. The implantable Model II pump was evaluated ex vivo in two sheep and intrathoracically implanted in one sheep. These experiments were terminated 70, 79, and 17 days after implantation due to mechanical failure caused by blood leakage through the intrahousing connector of the Model II pump. However, there was no intradevice thrombus formation in any of the retrieved pumps. The dual connector system was then introduced to the Model II pump (the modified Model II), and the pump was intrathoracically implanted in a sheep. The sheep survived for more than 14 months without major complications, and the study is being continued. The preliminary chronic animal experiments demonstrated improved durability and nonthrombogenicity of the MSCP, with a low hemolysis rate for up to 864 days. Thus, the MSCP has significant potential for long-term application as an implantable circulatory assist system. Further developments toward a totally implantable system, including an implantable controller and a transcutaneous energy/information transfer system, are under way.

Key words Implantable left ventricular assist system · Magnetic bearing · Centrifugal pump

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Introduction

Rotary blood pumps, such as the axial flow pump and the centrifugal pump, are being developed worldwide as implantable ventricular assist systems (VAS). The advantages of the rotary blood pump are its compactness, simplicity, and low cost. The pump can be implanted in both men and women, even those of small body size, with better quality of life and cost-effectiveness.

Since 1995, the research group of Terumo, NTN, and Setsunan University (Dr. Akamatsu) have been developing a totally implantable left ventricular assist system (T-ILVAS), using a centrifugal pump with a magnetically suspended impeller (MSCP) (Fig. 1).[1,2] Because the MSCP is a sealless rotor pump providing contact-free rotation of the impeller without any material wear, it is expected to be one of the most durable blood pumps. In vitro studies have demonstrated that the MSCP has excellent hydrodynamic performance with a low rate of hemolysis.[2] We have devised three prototype MSCPs: the paracorporeal Model I, the implantable model II, and the modified Model II.

The present study describes ex vivo and in vivo evaluations of the prototype MSCP using a chronic sheep left heart bypass model.

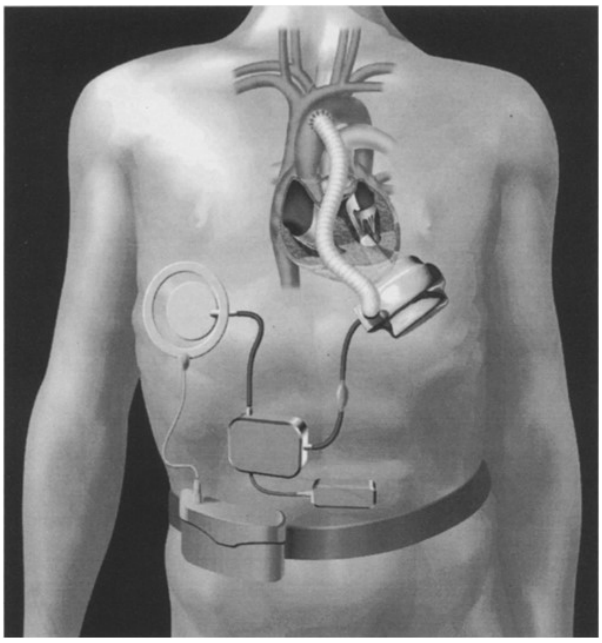

Fig. 1. Schematic illustration of the Terumo Implantable Left Ventricular Assist System (T-ILVAS)

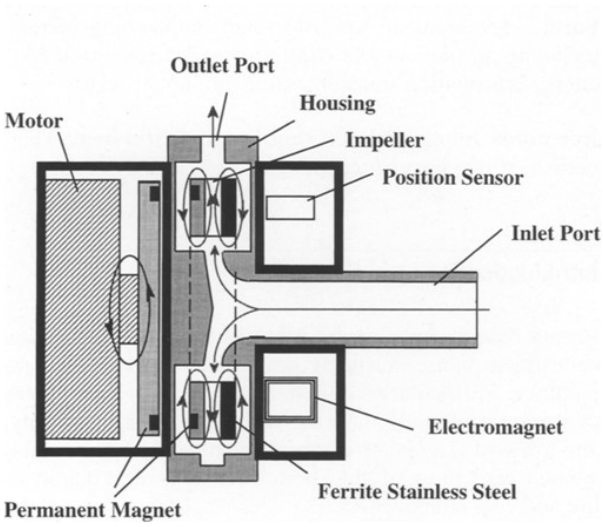

Fig. 2. Schematic cross section of the MSCP

Materials and methods

Description of the device

The MSCP is composed of four parts: a magnetic bearing, an impeller, a housing, and a DC brushless motor (Fig. 2). The impeller rotates by a magnetic coupling between the impeller and the motor, and is suspended magnetically by the three electromagnets. The electric current of the electromagnet is controlled by using three position sensors to maintain the impeller free-floating at the center of the pump housing. Up to now, we have devised three prototype models: the paracorporeal Model I, the implantable Model II (Fig. 3), and the modified Model II. The sizes of the blood chamber and the impeller were identical in these three prototype models. The implantable Model II and the modified Model II had a displacement volume of 196 ml and a weight of 400 g. The Model I and the modified Model II had dual electric wires separately connected to the motor and the electromagnets. The Model II had a single electric wire, with the intrahousing connectors between the motor and the electromagnets. The sensorless motor was also introduced to the modified Model II pump.

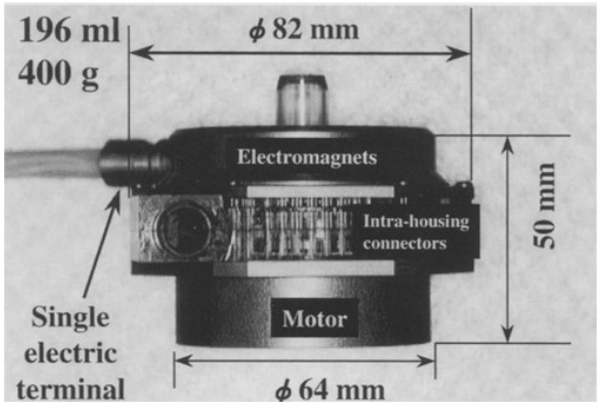

Fig. 3. Implantable Model II MSCP with intrahousing connectors

The blood-contacting surfaces of the pump and the inflow and outflow conduit were entirely modified with a heparin immobilization technique (Hepaface).[3] Both the Model II and the modified Model II pumps were entirely covered with silicone rubber 0.5 mm in thickness for in vivo studies.

Ex vivo study

The MSCP was evaluated pracorporeally for long-term durability and nonthrombogenicity in a chronic sheep left heart bypass model. Three sheep (sheep 1–3) were anesthetized with ketamine, intubated, and mechanically ventilated. Anesthesia was maintained with enflurane (Ethrene, Abbott Laboratories, Chicago, IL, USA). The Dacron outflow graft (C.R. Bard, Haverhill, MA, USA) was sutured to the descending aorta and the inflow conduit was inserted into the left ventricle through a cuff sutured to the left ventricular apex. The sheep recuperated from surgery and were allowed free access to a standard sheep diet and water. Institutional guidelines for the care and use of laboratory animals were observed. The pump was operated at a fixed rotational speed. Model I was evaluated in one sheep and Model II in two sheep. Aortic pressure and pump flow rate were continuously measured throughout the experiments. The hematological values of the animals were periodically monitored throughout the experiments. Hematocrit, platelet counts, leukocyte counts, activated clotting time, pro-

thrombin time, and plasma free hemoglobin levels were measured. Additional values, such as plasma protein, electrolytes, liver enzymes, creatinine, and blood urea nitrogen, were also measured. Coumadin was given orally after the chest drainage tubing had been removed (usually 3–5 days postoperatively) to maintain prothrombin time at an international normalized ratio (INR) of 1.5–2.0. No other anticoagulant or antiplatelet agent was used.

Intrathoracic implantation of the MSCP

The Model II and modified Model II pumps were intrathoracically implanted in sheep 4 (45 kg) and sheep 5 (80 kg). The pump was percutaneously driven. The surgical procedure, postoperative monitoring, and anticoagulant regimen were the same as in the ex vivo experiments.

Results

Ex vivo studies

Table 1 summarizes the results of the ex vivo and in vivo studies. All animals recovered well from the surgery. Sheep 1 (70 kg) implanted with the Model I pump survived for 864 days without any sign of mechanical failure or thromboembolic complications. However, the experiment was terminated because of massive bleeding caused by fracture of the polycarbonate inlet port. Plasma free hemoglobin levels remained normal throughout the experiments. Renal and hepatic function remained in the normal range throughout the experiments. Figure 4 shows the changes in plasma free hemoglobin levels and in renal and hepatic function of sheep 1. The retrieved pump from sheep 1 was completely free of intradevice thrombus formation (Fig. 5), and there was no detectable kidney infarction (Fig. 6). The experiment with sheep 2 was terminated at 70 days because of Hall sensor dysfunction of the motor. The experiment with sheep 3 was terminatd at 79 days because of a short circuit is a motor electric terminal. The retrieved pumps from these animals were free of intradevice thrombus formation.

Intrathoracic implantation of the MSCP

The implantable Model II had a good anatomical fit in the chest cavity of a small sheep weighing 45 kg (sheep 4). However, the experiment was terminated 17 days after implantation because of mechanical failure of the Model II pump. Although the blood-contacting surfaces of the retrieved pump were completely free of thrombus formation, there was massive leakage of blood into the electromagnets and the motor through the intrahousing connectors. The mechanical failures of the Model II observed in sheep 2 and 3 may be caused by a small amount of blood leakage through the intrahousing connectors. The connector system of the Model II pump was changed to a dual-wired system, and a sensorless motor was also introduced in the modified Model II pump. Sheep 5 was then intrathoracically implanted with the modified Model II pump. The sheep has survived for more than 14 months, and the experiment is ongoing without major complications. Plasma free hemo-

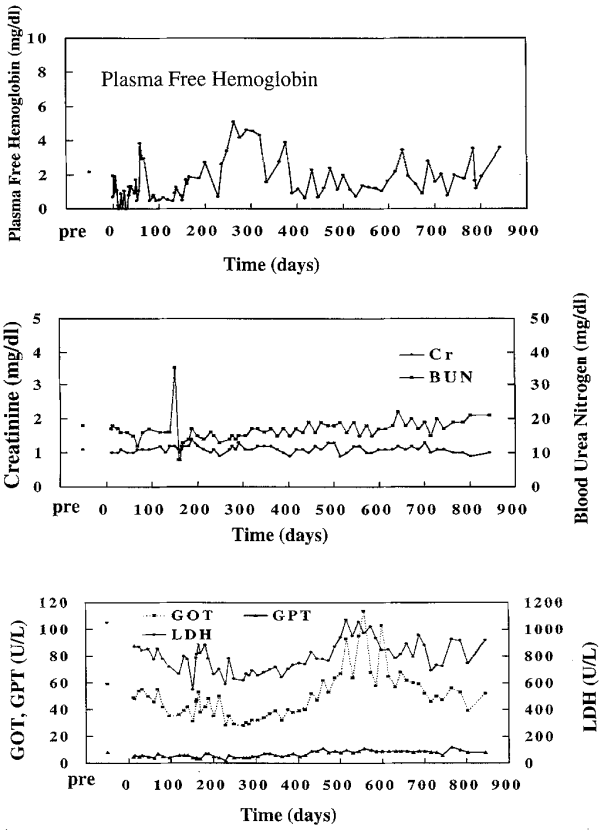

Fig. 4. Changes in plasma free hemoglobin level (*upper*) and renal (*middle*) and hepatic (*lower*) functions over time in sheep 1

Table 1. Summary of chronic animal study

Sheep no.	Body weight (kg)	Location of pump	Duration (days)	Cause of termination
1	70	Ex vivo	864	Bleeding
2	60	Ex vivo	70	Hall sensor dysfunction
3	60	Ex vivo	79	Short circuit in a motor electric terminal
4	45	Intrathoracic	17	Blood leakage through the connector
5	80	Intrathoracic	>430	Ongoing

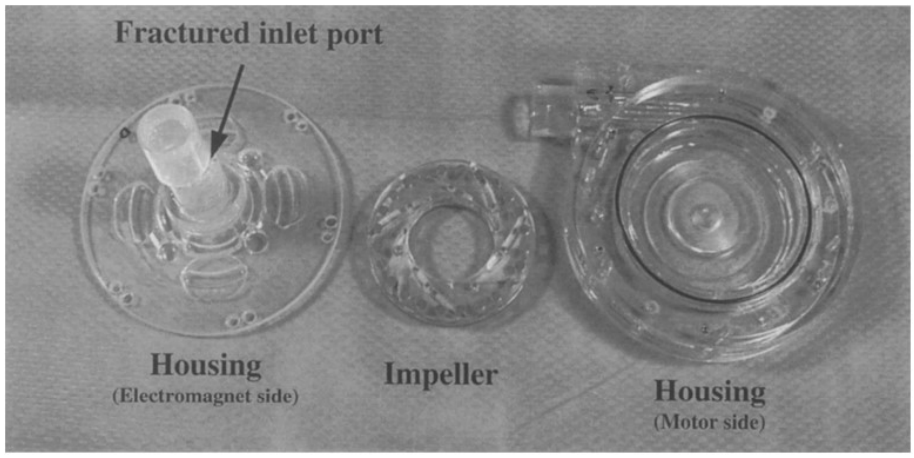

Fig. 5. Photograph of the retrieved pump from sheep 1 after 864 days

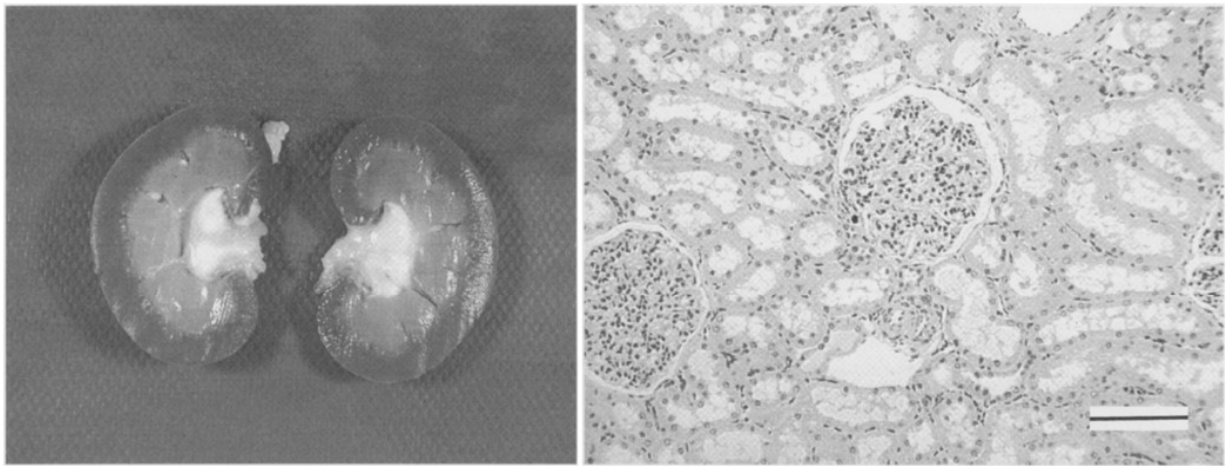

Fig. 6. Cross-section (*left*) and light photomicrograph (*right*, hematoxylin and eosin stain; *bar*, 100 μm) of the kidney retrieved from sheep 1 after 864 days of implantation

globin levels have remained within the normal range except for perioperative periods in sheep 5. The temperature of the tissue adjacent to the pump casing became normal 10 days postoperatively.

Discussion

There have been a number of approaches to the development of a rotary blood pump for use as an implantable VAS. However, the conventional rotary blood pumps have had limited durability and nonthrombogenicity because of problems associated with the bearings and the seal. In order to avoid these problems, continuous purge systems have been implemented in the pump system by several gropus,[4,5] and other groups have employed blood-immersed bearings.[6–9] However, all of these pumps are subject to mechanical wear. Among these, the use of a magnetic suspension system has been one of the most promising approaches to obtain mechanical reliability as well as nonthrombogenicity of a rotary blood pump.[10,11] We have developed a sealless centrifugal pump with a magnetically suspended impeller (MSCP), which operates completely contact-free without any material wear. The MSCP theoretically would lost for years. We have demonstrated that the Model I MSCP can operate for more than 2 years in ex vivo animal model. In vivo evaluation using intrathoracic implantation of Model II demonstrated excellent anatomical fit in a small animal weighing 45 kg. All experiments in animals with the Model II pump were terminated because of mechanical failures caused by blood leakage through the intrahousing connector. However, no intradevice thrombus formation or thromboembolism in major organs was encountered in any of these studies. After the introduction of a dual connector system and sensorless motor, the modified Model II pump was able to operate in vivo for more than 14 months without any sign of mechanical failure or thromboembolic

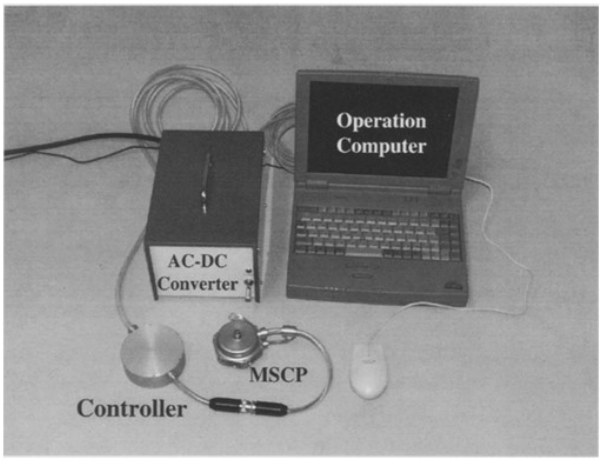

Fig. 7. Model III system with an implantable controller

complication. Plasma free hemoglobin levels were maintained within the normal range in all animals during experimental periods of 17 to 864 days.

For the next phase, we have developed the Model III system, consisting of a prototype MSCP with a sensorless motor and dual electric wires and an implantable controller 10 mm in diameter and 39 mm thick (Fig. 7). The input power of the Model III system was reduced to 13 W at a flow rate of 5 l/min and a pressure head of 100 mmHg. The implantable controller has different driving modes, including a fixed rotational speed mode, a fixed motor current mode, a controlled motor current mode, and a pulsatile mode.[12,13] Further developments toward a totally implantable LVAS, including a transcutaneous energy and information transfer system and internal/external batteries, are under way.

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References

1. Akamatsu T, Nakazeki T, Itoh H. Centrifugal pump with a magnetically suspended impeller. Artif Organs 1992;16:305–308
2. Akamatsu T, Tsukiya T, Nishimura K, Park CH, Nakazeki T. Recent studies of centrifugal blood pump with a magnetically suspended impeller. Artif Organs 1995;19:631–634
3. Nojiri C, Kido T, Sugiyama T, Horiuchi K, Kijima T, Hagiwara K, Kuribayashi E, Nogawa A, Ogiwara K, Akutsu T. Can heparin immobilized surfces maintain nonthrombogenic activity in in vivo long-term implantation? ASAIO J 1996;42:M468–M475
4. Frazier OH, Nakatani T, Duncan JM, Parnis SM, Fuqua JM. Clinical experience with the Hemopump. Trans ASAIO 1989;35:604–606
5. Yamazaki K, Litwak P, Kormos RL, Mori T, Tagusari O, Antaki JF, Kameneva M, Watach M, Gordon L, Umezu M, Tomioka J, Koyanagi H, Griffith BP. An implantable centrifugal pump for long term circulatory support. ASAIO J 1997;43:M686–M691
6. Butler K, Thomas D, Antaki J, Borovetz H, Griffith B, Kameneva M, Kormos R, Litwak P. Development of the Nimbus/ Pittsburgh axial flow left ventricular assist system. Artif Organs 1997;21:602–610
7. Jarvik RK. System consideration favoring rotary artificial heart with blood immersed-bearings. Artif Organs 1995;19:565–570
8. Kawahito K, Benkowski R, Otsubo S, Rosembaum B, Moreland R, Noon GP, Nose Y, DeBakey ME. Ex vivo evaluations of the NASA/DeBakey axial flow ventricular assist system. ASAIO J 1996;42:M754–M757
9. Makinouchi K, Nakazawa T, Takami Y, Takatani S, Nose Y. Evaluation of the wear of the pivot bearing in the Gyro C1E3 pump. Artif Organs 1996;20:523–528
10. Hilton EF, Allaire PE, Baloh MJ, Maslen E, Bearson G, Khanwilkar P, Olsen D. Magnetic suspension controls for a new continuous flow ventricular assist device. ASAIO J 1997;43:M598–M603
11. Okada Y, Ueno S, Ohishi T, Yamane T, Tan CC. Magnetically levitated motor for rotary blood pumps. Artif Organs 1997;21:739–745
12. Nishimura K, Tsukiya T, Akamatsu T, Kono S, Yamada T, Bam T. Control of the pressure flow relationship with a magnetically suspended pump in a chronic animal experiment. ASAIO J 1997;43: M553–M556
13. Kono S, Nishimura K, Yamada T, Oonishi T, Tsukiya T, Akamatsu T, Ban T. In vivo and in vitro evaluation of the pulsatile mode of a magnetically suspended centrifugal pump. ASAIO J 1997;43: M580–M584