(2) On a personal computer (PC), PC-DOS is started, a drive program is launched, and, with pulsations [beats] set at 72 bpm, the cardiac ventricle assistance apparatus is driven.

(3) Measured data is taken into the PC as polygraphs (Nihon Kohden Corp., VG-185G) via an AD conversion board (National Instruments Corp., DaqPad-MIO-16XE-50), and is sampled (sampling time. 2 ms) at 500 Hz.

(4) Steps (1)-(3) were repeated for each artificial myocardium with differing diaphragm membrane thicknesses of the cardiac ventricle assistance apparatus at single-time output amounts, and data was measured accordingly.

(Ethical considerations)

Animal tests performed in connection with the present research were performed in conformance with the stipulations of the Ethical Committee of the Tohoku University School of Medicine's Institute for Animal Experimentation and the Tohoku University Institute of Development, Aging and Cancer, and no problems exist in terms of ethical aspects.

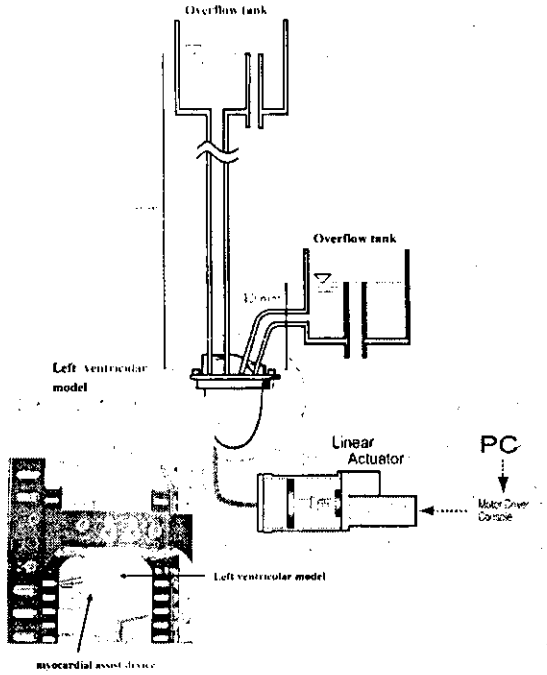

Fig. 12 Hydraulic simulated circulation apparatus. A water-head difference was set for the inflow and outflow portion sites, and left ventricle model performance capabilities were evaluated.

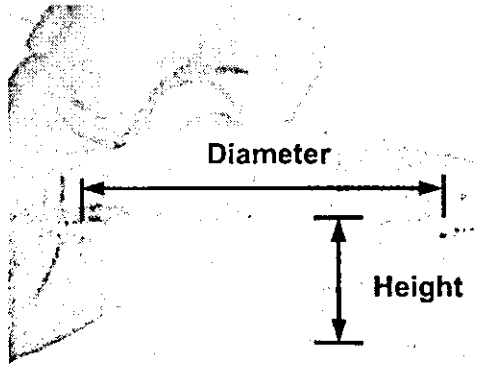

Fig. 13 High-volume type (advanced) cardiac ventricle assistance apparatus diaphragm. Maximum contraction performance two (2) times that of the conventional model was realized, and evaluations of effects given to organic hearts were attempted using a hydraulic model.

C. Research results

(1) Driving of cardiac ventricle assistance apparatus via electrocardiogram synchronization

As shown in Fig. 16, pressure given to the ventricular wall by the cardiac ventricle assistance apparatus is, at its maximum value, 50 N/cm2; thus, a value was obtained near to the 52 N/cm2 which is the value when ventricular assistance was performed in animal tests. Also, the following values were obtained: mean aortic flow rate, 1.6 L/min, and end-systolic left ventricle intraventricular pressure, 174 mmHg.

Figs. 14 and 15 show, respectively, mean aortic flow rates and end-systolic left ventricle intraventricular pressures for each membrane thickness, for the conventional type (single-time output amount: 40 mL), and for the novel type (single-time output amount: 56 mL).

1) It was confirmed that, in regards to the values for both mean aortic flow rates and end-systolic left ventricle intraventricular pressures for the novel artificial myocardium, compared with the values for convention artificial myocardium, for all diaphragm membrane thicknesses of 0.3 mm, 0.5 mm, and 1.0 mm, high values were shown. Thus, it was demonstrated that increasing the single-time cardiac output amount for the cardiac ventricle assistance apparatus artificial myocardium is effective in increasing cardiac output.

2) Diaphragm membrane thickness

One can confirm that, for conventional artificial myocardium, in regards to values for mean aortic flow rate and end-systolic left ventricle intraventricular pressure, maximum values are also obtained at diaphragm membrane thicknesses in the vicinity of 0.5 mm. It can also be confirmed that, for the novel artificial myocardium, as diaphragm membrane thickness becomes thicker, values for mean aortic flow rate and end-systolic left ventricle intraventricular pressure also increase. Thus, one can state that, in terms of diaphragm membrane thickness, for each of the values of single-time cardiac output amounts, it will be necessary to perform investigations of [respective] optimal membrane thicknesses.

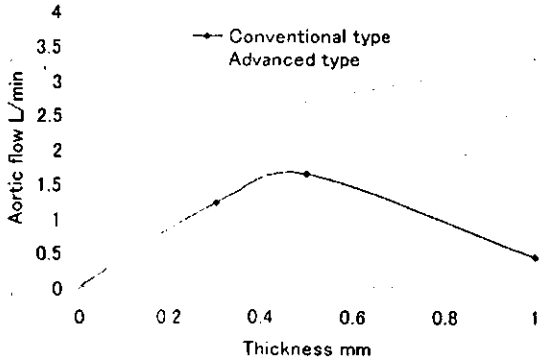

Fig. 14 Changes in output amounts (assisted flow amounts) for three types of diaphragm thicknesses (0.3 mm, 0.5 mm, 1 mm).

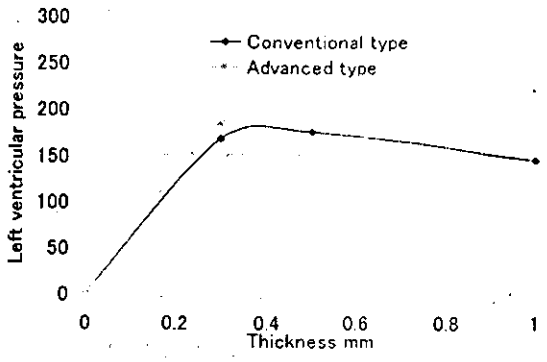

Fig. 15 Differences in internal pressures at left ventricle model contraction (systolic) phases for three types of diaphragm thicknesses (0.3 mm, 0.5 mm, 1 mm).

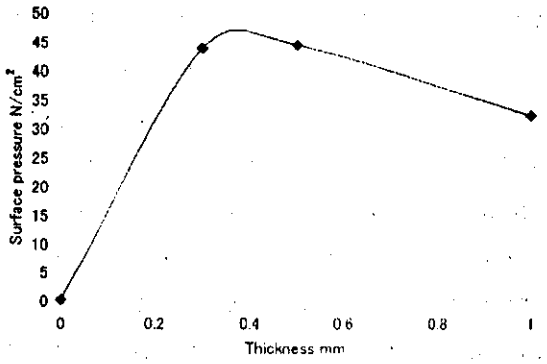

Fig. 16 Pressures applied to the cardiac wall surface at left ventricle model contraction (systolic) phases for three types of diaphragm thicknesses (0.3 mm, 0.5 mm, 1 mm).

D. Discussions and concluding summary

(1) Evaluations in animal tests and validity of comparative investigation

Below are shown the differences obtained for pressure given to the ventricular wall by the cardiac ventricle assistance apparatus, cardiac output, and left ventricle intraventricular pressure between the case of performing ventricular assistance for an organic heart and the case where the cardiac ventricle assistance apparatus was driven with the cardiac ventricle assistance apparatus evaluation circuit as performed within the present paper.

1) Pressure given to the ventricular wall by the cardiac ventricle assistance apparatus

At systolic phase end, closely similar values were obtained: values of 52 N/cm2 in the animal tests, and of 50 N/cm2 in the tests using the evaluation circuit.

2) Cardiac output

Within the animal tests, in the case where ventricular assistance was not performed, cardiac output was 3.1 L/min, while in the case where ventricular assistance was performed, this was 4.0 L/min; thus, results were obtained such that cardiac output assistance of 0.9 L/min was possible. In the tests using the evaluation circuit, results were obtained such that cardiac output assistance of 1.6 L/min was possible. The value obtained in the animal tests was lower than the value obtained in the tests using the evaluation circuit.

3) Left ventricle intraventricular pressure

Within the animal tests, end-systolic left ventricle intraventricular pressure at time of driving the cardiac ventricle

assistance apparatus was 113 mmHg. This was a low value compared with the end-systolic left ventricle intraventricular pressure of 174 mmHg obtained in tests using the evaluation circuit.

As for reasons why, for cardiac output, the value obtained in the animal tests for left intraventricular pressure was lower than the value obtained with the cardiac ventricle assistance apparatus evaluation circuit, it is thought that two items had a major impact, namely:

(1) As for the neural regulation mechanisms of heart functions of an organic heart, the automatic nervous system performs the major work. However, when an increase of blood pressure has occurred, vagus nerve impulses increase, causing a reduction in the number of beats. Also, sympathetic nerve impulses to the myocardium restrain the contraction force of the myocardium; thus, the increase in cardiac output is restrained.

(2) An organic heart is self-beating. However, within the tests described in the present paper, since a left ventricle model which did not cause active contractions was used, myocardial wall displacement due to diaphragm displacement had a larger value in the left ventricle model than in the organic heart.

In item (1), in a state cut off from the nervous system, the fact that it was possible to measure hemodynamics when performing cardiac assistance ensured was effective. However, in item (2), it was shown that a left ventricle model must be created so as to perform self-pulsation [beating] and so as to have the maximum increase in left ventricular elastance (i.e., the left ventricular wall becomes its hardest) at the end of a systole, and that a revaluation of the cardiac ventricle assistance apparatus is necessary.

(2) Load given to ventricular wall for each different diaphragm membrane thickness

From the test results, with the conventional model (single-time output amount: 40 mL), values for mean aortic flow rate and end-systolic left ventricle intraventricular pressure did not increase as the diaphragm membrane thickness became thicker; rather, it was confirmed that both reached maximum values in the vicinity of 0.5 mm. Fig. 16 shows, within a conventional model, pressure given to the ventricular wall by the diaphragm of the cardiac ventricle assistance apparatus when the horizontal axis is taken as the diaphragm thickness. It can be confirmed that pressure given to the ventricular wall by the diaphragm also shows similar tendencies to the values for mean aortic flow rate and end-systolic left ventricle intraventricular pressure.

As for the artificial myocardium portion

of the cardiac ventricle assistance apparatus developed within the present research, water—an incompressible fluid—is made to flow in from the inflow port and then flow out repeatedly by the mechanical-drive actuator, and this serves as the specification for changing the diaphragm displacement.

(3) Summary

To clarify the dynamic consistency [compatibility] of the cardiac ventricle assistance apparatus and cardiac ventricles, and with the goal of determining guidelines for performing redesign and improvements of the shape of the cardiac ventricle assistance apparatus, a hydraulics circuit simulating the circulatory system was created, and tests of the fundamental characteristics of the cardiac ventricle assistance apparatus were performed. The following results were obtained.

(1) With artificial myocardium having the same specifications as that used for performing evaluations in animal tests, under the conditions of a preload of 10 mmHg, an afterload of 100 mmHg, and heartbeat of 72 bpm, obtained values were a mean aortic flow rate of1.6 L/min, and an end-systolic left ventricle intraventricular pressure of 174 mmHg.

(2) Increasing the single-time output amount of the cardiac ventricle assistance apparatus artificial myocardium portion is effective in increasing cardiac output.

(3) In regards to the values of respective single-time output amounts according to the diaphragm membrane thickness of the cardiac ventricle assistance apparatus artificial myocardium portion, there is a necessity to perform investigations of optimal membrane thicknesses.

(4) When performing fundamental characteristics evaluations of cardiac ventricle assistance apparatus using a hydraulics circuit simulating the circulatory system, it was shown that, in a state cut off from the nervous system, it is possible to evaluate the dynamic interactions between artificial cardiac assistance and an organic heart.

As developments for the future, on the basis of results obtained in the present paper, design is to be made of a cardiac ventricle assistance apparatus having a high dynamic consistency [compatibility] with an organic heart. Also, for a hydraulics circuit that is to be used to perform evaluations of the cardiac ventricle assistance apparatus, it has been shown that a left ventricle model must be created so as to perform self-pulsation [beating] and so as to have the maximum increase in left ventricular elastance (i.e., the left ventricular wall becomes its hardest) at the end of a systole, and that a

revaluation of the cardiac ventricle assistance apparatus is necessary.

From the next fiscal year on, progress shall be made on further research of capabilities evaluations of other types of cardiac ventricle assistance apparatuses, including models applying shape memory alloys, etc., and towards a unified system creation incorporating each type of sensor.

Research concerning Optimal Design of a Cardiac Ventricle Assistance Apparatus through Measurement Fusion Simulation

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Summary of Research

As fundamental research for the optimal design of a cardiac ventricle assistance apparatus through measurement fusion simulation, which, here, is the fusion of numerical computations with ultrasonic measurements, for measurement fusion simulation that includes errors at upstream speed boundary conditions as well as ordinary simulations, comparison was made of computational accuracy vis-à-vis a baseline solution. Here it became clear that, through the application of feedback, there is a major improvement in computational accuracy.

A. Purpose of research

The purpose was to, through the performance of measurement fusion simulation through the fusion of numerical computations with ultrasonic measurements, establish analysis methods for the performance of optimal design of a cardiac ventricle assistance apparatus.

B. Research methods

Within the present research, unification was made of blood flow measurements using an ultrasonic diagnostic apparatus and numerical simulations made using a computer. The aim is the realization of measurement fusion simulation that merges the characteristics of each of these methods. As fundamental research for such, we investigated the serviceability of measurement fusion simulation for errors arising from upstream speed boundary conditions using three types of numerical computation.

C. Research results

For the comparison of computation results, used were the results for the 17th cycle, where it can be determined that all results have converged. Within the measurement fusion simulation, an optimum gain of K=20 was found through trial and error. The error between the ordinary simulation and the baseline solution occurred with the reason being differences in upstream boundary

conditions. Conversely, since with the measurement fusion simulation, computation is performed while feeding back the baseline solution, the computation results almost nearly match with the baseline solution. Also, as for the comparison of color Doppler images of the vicinity of the aneurysm, with the measurement fusion simulation, results closely resembling the baseline solution were obtained.

D. Disucussions

It was made clear that, through measurement fusion simulation, blood flow within a living organism could be reproduced in real time. It is expected that, through the use of such, it will become possible to perform optimal design of a cardiac ventricle assistance apparatus.

E. Concluding words

The serviceability of measurement fusion simulation within the optimal design of a cardiac ventricle assistance apparatus was clarified. Into the future, the present method will be applied in the optimal design of a cardiac ventricle assistance apparatus.

別紙5

研究成果の刊行に関する一覧表

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Recent Progress in Artificial Organ Research at Tohoku University

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Abstract: Tohoku University has developed various artificial organs over the last 30 years. Pneumatic driven ventricular assist devices with a silicone ball valve have been designed by the flow visualization method, and clinical trials have been performed in Tohoku University Hospital. On the basis of these developments, a pneumatic driven total artificial heart has been developed and an animal experimental evaluation was conducted. The development of artificial organs in Tohoku University has now progressed to the totally implantable type using the transcutaneous energy transmission system with amorphous fibers for magnetic shielding. Examples of implantable systems include a vibrating flow pump for ventricular assist device, an artificial myocardium by the use of shape memory alloy with Peltier elements, and an artificial sphincter for patients with a stoma. An automatic control system for artificial organs had been developed for the ventricular assist devices including a rotary blood pump to avoid suction and to maintain left and right heart balance. Based upon the technology of automatic control algorithm, a new diagnostic tool for evaluating autonomic nerve function has been developed as a branch of artificial organ research and this new machine has been tested in Tohoku University Hospital. Tohoku University is following a variety of approaches aimed at innovation in artificial organs and medical engineering fields. **Key Words:** Vibrating flow pump—Artificial sphincter—Transcutaneous energy transmission system—Shape memory alloy—Artificial myocardium.

Tohoku University has been involved in artificial organ research for over 30 years. The first case discharged from a hospital in Japan wearing a ventricular assist device (VAD) was achieved by Tohoku University Hospital in 1985. Various artificial organs are currently under development at Tohoku University.

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PNEUMATICALLY ACTUATED VENTRICULAR ASSIST DEVICE

Circulatory support devices are necessary in some patients with severe congestive heart failure. However, some ventricular assist devices are too expensive, especially for patients in developing countries. We succeeded in reducing the cost by adopting silicone ball valves. Clinical application of our pneumatic ventricular assist device was performed, and about 30% of patients were discharged from the hospital after weaning. Figure 1 shows the Tohoku University type pneumatic VAD.

PNEUMATIC TOTAL ARTIFICIAL HEART

Development of the pneumatic total artificial heart (TAH) was carried out in our laboratory based

FIG. 1. The Tohoku University type pneumatic ventricular assist device is shown.

FIG. 2. The Tohoku University type pneumatic total artificial heart is shown.

on the development experiences with the VAD. To reduce cost and improve durability, silicone ball valves were adopted in our TAH system. The basic material of this TAH was designed using a polyvinyl chloride paste, and the inner surface of the inner sac was coated with polyurethane to prevent thrombus formation. To test this pneumatic TAH, a fitting study into the chest cavity of adult goats was conducted (Fig. 2).

VIBRATING FLOW PUMP

Small size implantable ventricular assist device

The size and weight of implantable devices is so important that various investigators have taken various developmental approaches. We aimed to solve the problem by increasing the drive frequency of the ventricular assist device. A vibrating flow pump, and small stroke volume with high driving frequency enabled us to realize a small and lightweight implantable ventricular assist device.

The weight of actuators has recently been lessened by adopting a cross-slider mechanism. Miniaturization was successful compared with a linear motor drive (Fig. 3).

High frequency oscillated blood flow made by vibrating flow pump (VFP) is so unique that influences on the cardiovascular system might be needed. We evaluated the effect of oscillated assist flow with VFP upon renal circulation using near infrared spectroscopy in animal experiments on adult goats. During oscillated assist flow, oxygenated hemoglobin in the kidney tended to increase. This finding will be useful when considering the clinical application of VFP.

TRANSCUTANEOUS ENERGY TRANSMISSION SYSTEM

Energy transmission is an important issue in the development of internal artificial organs. To maximize energy transmission we developed a transcutaneous energy transmission system applying amorphous fibers for magnetic shielding, and achieved over 90% energy transmission efficiency (Fig. 4).

APPLICATION OF THE SHAPE MEMORY ALLOY FOR ARTIFICIAL INTERNAL ORGANS

Development of a small, lightweight actuator is the most difficult challenge for totally implantable artificial organs because space in the body is limited.

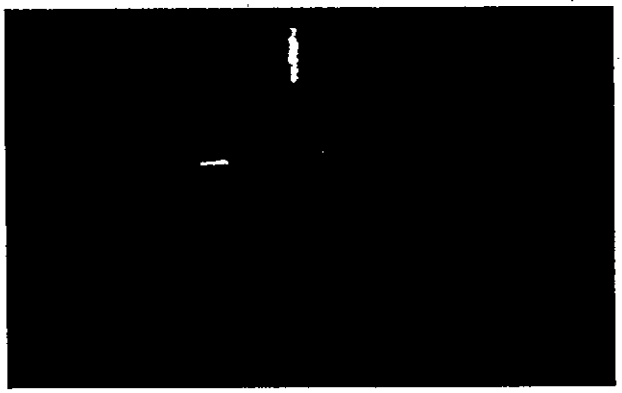

FIG. 3. The photograph shows a vibrating flow pump, implantable ventricular assist device.

FIG. 4. A transcutaneous energy transmission system using amorphous fibers is illustrated.

Shape memory alloy (SMA) is a high-efficiency material. Input energy into SMA becomes very efficient actuating power.

Saywer et al. reported on the development of an SMA actuator for a TAH (1). They attached a large quantity of SMA to an artificial ventricle, which added contraction power to the ventricle. However, the drive speed of SMA was too small compared with the heart rate. Nitta et al. and Hayashi et al. reported on a VAD actuated with SMA (2,3). However, the drive speed was insufficient for the heart rate. Other researchers proposed various applications that attracted the attention of some research teams, such as valves for the urinary tract and stoma (4,5).

Recently, we invented the Peltier-SMA actuator for assisted circulation. This article reports and discusses the feasibility of SMA in artificial organ research.

ARTIFICIAL MYOCARDIUM

Bridging use of ventricular assist systems in heart transplantation may become necessary for a long time because of the shortage of donated hearts. In this situation, the quality of life of the patients waiting for a donor heart becomes increasingly important, so development of a totally implantable system is highly desirable (6–11). Toward this end, miniaturization of actuators is fundamental, especially for people with small physiques such as average Japanese people (6–8). The blood chamber in a natural heart is formed by myocardium. Therefore, a chamber is equal to an actuator; however, it is not so with the artificial heart, unfortunately.

Constituting an artificial heart is not the final goal of our studies; in fact, we are aiming to develop artificial heart muscle. Artificial heart muscle would be sewn onto the ventricle to support the contraction power of the natural heart ventricle. Since SMA is a highly efficient material, an actuator made of SMA can be miniaturized. Furthermore, since the drive mechanism is simple, an SMA actuator is expected to be durable.

However, the most important limiting factor of an SMA actuator is its drive speed because of the cooling time (1–3). We focused our attention on Peltier elements, which are the most suitable for rapid cooling. Electric energy becomes the movement of the heat in Peltier elements, as we have shown in Fig. 5. In other words, heat is moved from one side to another side, thus one side is heated and the other side cools down rapidly.

We utilized these characteristics in this study. Peltier elements were attached to SMA and record-breaking rapid cooling of SMA was achieved (1–3). As shown in Fig. 6, Peltier-SMA can actuate both ventricles of an artificial heart if the Peltier-SMA is installed in the ventricular septum. The Peltier-SMA may be an ideal drive mechanism candidate for a total artificial heart.

First, we induced an electrical current into a Peltier element attached to the SMA. Electrical current induced the heat transfer from one side to the other side. Then, heat was moved from the heat sink to the SMA. Thus, the SMA was heated and driven. After that, the electrical current was inverted. Then, the heat was moved from the SMA to the heat sink. Thus, the SMA was cooled and driven to the opposite side.

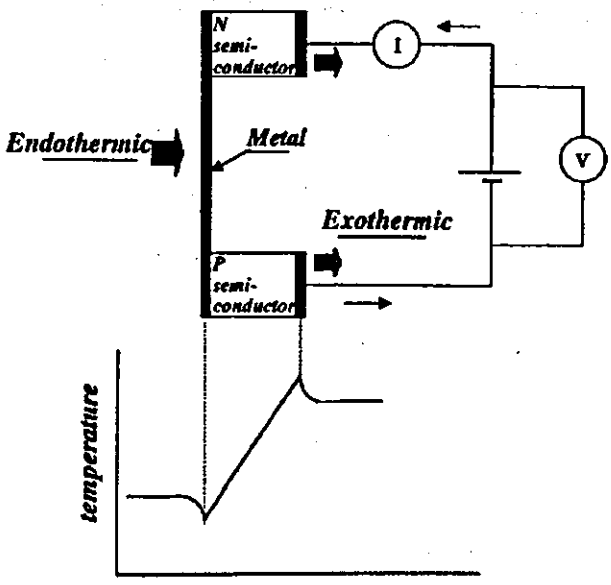

FIG. 5. Heat transfer in the Peltier element is shown.

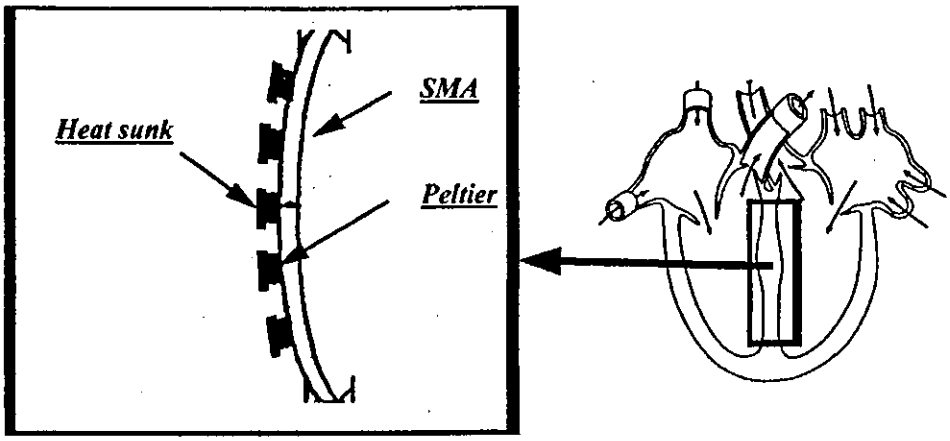

FIG. 6. Peltier-shape memory alloy (SMA) actuator for total artificial heart is shown.

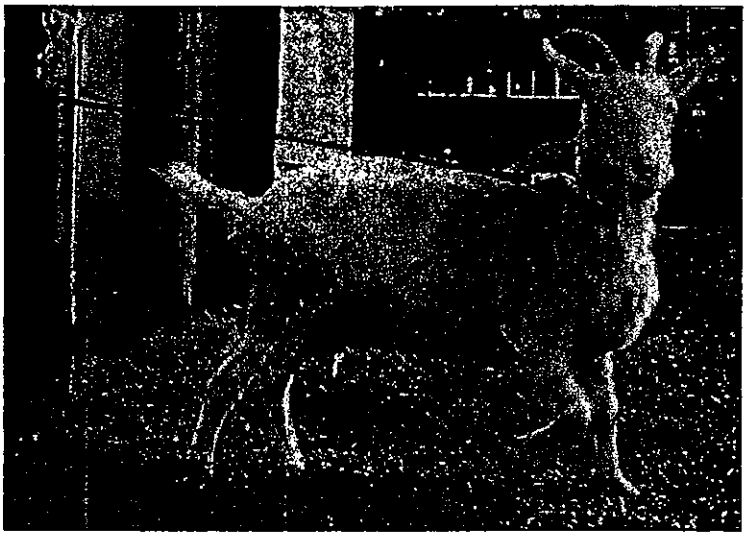

FIG. 7. A goat with pneumatic artificial myocardium is pictured.

We developed an artificial muscle to support the right ventricle that was pneumatically actuated. The moving patch actuator was sewn into the right ventricle. This device was designed to support patients with right heart failure such as pulmonary hypertension, several kinds of abnormalities, and so forth. We succeeded in prolonging the survival of goats for three months using right ventricular supporting artificial myocardium, as shown in Fig. 7.

The design of artificial myocardium for right heart support is based on our previous studies. Figure 8 shows our Peltier-SMA right heart supporting artificial myocardium on a plastic model of a heart. We are currently conducting the animal experiments.

ARTIFICIAL SPHINCTER

After an operation for rectal cancer or colon cancer, some patients require stoma and this adversely affects their quality of life.

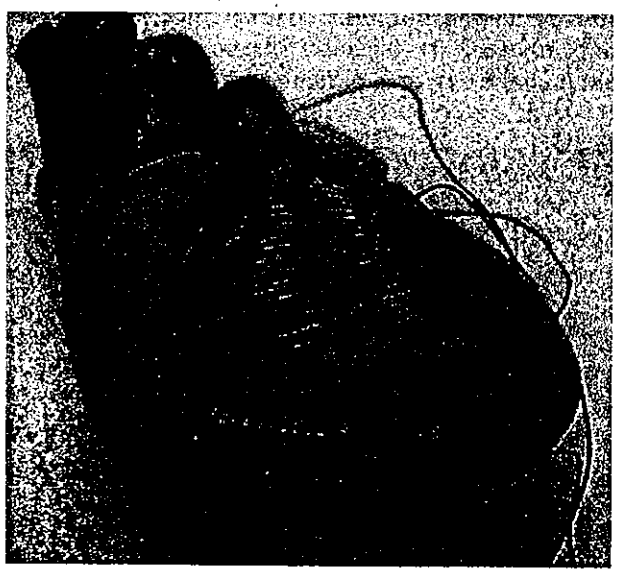

FIG. 8. Peltier-SMA artificial myocardium on a plastic model of a heart is shown.

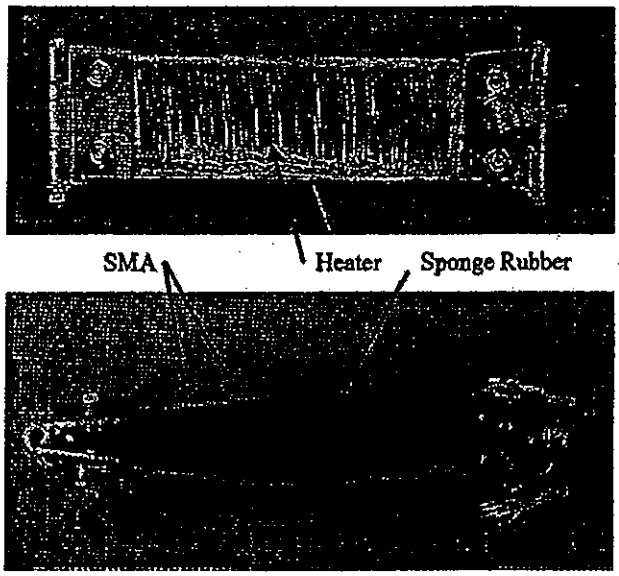

FIG. 9. Shown is a prototype artificial sphincter.

We developed an artificial sphincter to meet this need using an SMA to the stoma as shown in Fig. 9 (4). When the temperature is raised by electricity, the artificial sphincter opens, which allows patients to control their evacuations. A photograph of a prototype artificial sphincter is shown in Fig. 9. Long-term animal experiments are now being conducted on this device.

Electric power was supplied to the artificial sphincter by the use of the transcutaneous energy transmission system (TETS) as shown in Fig. 4.

Basic performance of this artificial implantable device is now under discussion. However, we are still evaluating different coating materials for the implantable part, because Silastic material for an implantable device is difficult to import.

FIG. 10. A pig with artificial sphincter is shown.

The objective of the design concept is to enable patients to go to the bathroom whenever they choose. And then, when ready, they would take the TETS and attach it to their abdomen so that they would be able to control the implanted sphincter easily.

At present, the development of an artificial sphincter is at the stage of long-term animal experiments. Figure 10 shows a pig with a stoma and artificial sphincter. We are currently conducting a long-term endurance test for an artificial sphincter with TETS. When this test is completed we aim to begin preclinical trials.

CONCLUSION

This article reports on various artificial organs developed by Tohoku University and evaluates them for clinical applications.

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