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Original article

Artificial myocardium with an artificial baroreflex system using nano technology

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Abstract

Where is the place which should be helped in a patient with congestive heart failure? The answer may be contraction of the heart. At Tohoku University, development research of "the artificial myocardium" has been conducted, using a ball screw type electromagnetic motor. Furthermore, super-miniaturization is being attempted at present. Thus, a system with shape memory alloy is being developed. The cooling speed problem was solved by the application of the Peltier element. A drive at a speed equal to that of a heartbeat was realized by the application of this system. At present, a ventricular assist device is used for patients waiting for a heart transplant in Japan. An air driven type system disturbs a patient's QOL remarkably because it is connected to the drive device. With our concept, energy is provided by using the electromagnetic force from outside of the body by the use of transcutaneous energy transmission system. Magnetic shielding by amorphous fibers was used at Tohoku University to improve the total efficiency. A natural heart can alter the cardiac output corresponding to the demand. Artificial internal organs must participate in the system of the living body, too. Tohoku University has developed a resistance based artificial heart control algorithm, which simulated a baroreflex system to cope with every demand. Nano level sensing equipment is now under development at Tohoku University. At present, development is being conducted aiming at an "intelligent artificial myocardium".

1. Introduction

Heart transplant facilities have recently been expanded in Japan. Everybody hopes transplant procedures in this country will reach a satisfactory level [1–4]. However, the shortage donor hearts is a serious problem. A ventricular assist device is used as a bridge to transplantation [5,6].

Pneumatic driven ventricular assist devices such as Xemex and Toyobo have been playing a very important role [2–6]. According to the increase in the waiting period for a donor heart, the realization of a totally implantable artificial heart is becoming increasingly important. After going back to basics, reconsideration was given to the principles [7–11].

Where can most assistance be given to a patient suffering from congestive heart failure?

The answer may be the contraction of the heart.

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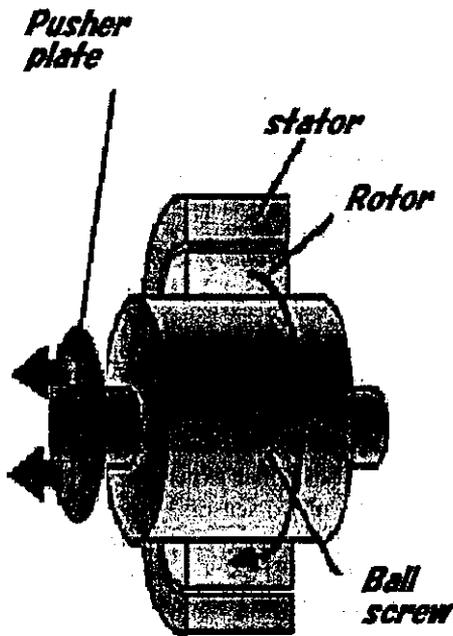E-mail address: yambe@idac.tohoku.ac.jp (T. Yambe).

Fig. 1. Schematic drawing of the ball screw magnetic motor for implantable artificial myocardium.

Fig. 2. Photograph of an example of a candidate for an implantable artificial myocardium using shape memory alloy with the Peltier element.

If we consider the principle of heart massage, cardiac output is supported by pushing a ventricle. Based on this idea, a system was devised by which the ventricle was pushed. This system is sewn onto the ventricle and assists the contraction power of the natural heart.

Development research of "the artificial myocardium" has been conducted in Tohoku University for many years. Air pressure drive type artificial myocardium research in chronic animal experiments had already proven successful and the supporting effect of the artificial myocardium was confirmed in chronic animal experiments over 3 months.

So, from this, obtaining an improved implantable artificial myocardium in QOL was planned. This year, with a Grant in aid for scientific research, and Science research-funds from the Ministry of Welfare, Labor, a new development project was commenced. The most advanced sensor and actuator nano technology was applied, aiming for the development of a super-miniature device, which exceeds retrogenerative medicine.

2. Actuator for an artificial myocardium

The challenge was to find a miniature motor with high torque from among all the miniature motors available throughout the world. A ball screw type electromagnetic motor, which was adopted in the robot arm in the space shuttle, was used [12–16] (Fig. 1). This motor was applied to the animal experiment, and at present, its effect on heart assistance is being confirmed.

Furthermore, as super-miniaturization is also a goal, a system with shape memory alloy is also being developed at present. Regarding the shape memory alloy, the rise in tem-

perature by the thrown energy is directly related to the drive [17,18]. Therefore, the energy efficiency is high. However, an important problem is the drive speed. Cooling down the shape memory alloy is difficult. This problem was solved at Tohoku University by the application of the Peltier element (Fig. 2). The Peltier element is a semiconductor element, which moves heat. The settlement side is refrigerated due to the movement. A drive at a speed equal to a heartbeat was realized by the application of this system and currently, research aiming at the improvement of the durability is being conducted.

This system also aims at the development of a super-miniature micro system. The development of a micro actuator for holding nano level structure development is indispensable. Various kinds of nano actuators are now under development at Tohoku University. These nano–micro systems are expected to become the key technology for artificial myocardium.
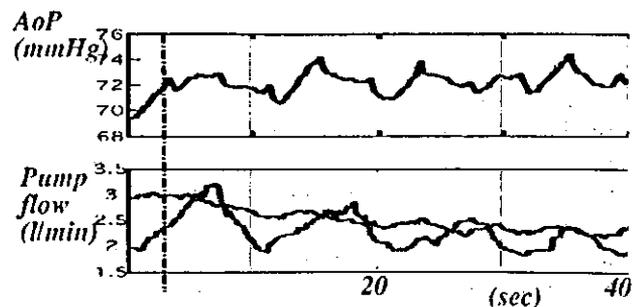

Fig. 3. Time series data of an artificial baroreflex system with biventricular rotary blood pump assistance with ventricular fibrillation. During increase of the blood pressure by drug administration, the drive speed of RP was automatically controlled to be decreased. This control algorithm can be used in the artificial myocardium system.
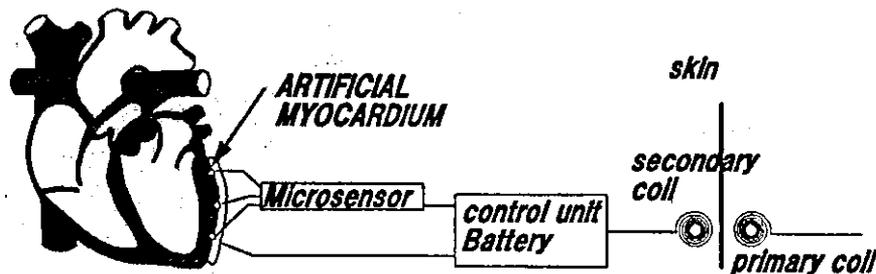
Fig. 4. Schematic illustration of the total system of an implantable artificial myocardium.

3. Energy supply system

At present, an assistant mechanical heart is used for patients waiting for a heart transplant. Only an air pressure drive type system is covered by insurance in Japan. An air driven type system disturbs a patient's QOL remarkably because it is connected to the drive device. So, a totally implantable system is necessary to improve the patient's QOL.

With our concept, energy is provided to the artificial myocardium using the electromagnetic force from outside the body. Such a system has been developed all over the world. Magnetic shielding by amorphous fibers was used in Tohoku University to improve the total efficiency [9,10]. Amorphous fibers are attached outside the coil, which is placed on the skin to prevent the leakage of magnetic power. Therefore, the efficiency of the energy transmission between the coils is improved.

Power generation equipment, to which nano technology was applied, is currently being developed at Tohoku University. This system can improve the efficiency of the energy use. As a comparison, this system resembles that of a hybrid car. The energy of the actuation part is used, and the generation of electricity is achieved.

4. Artificial myocardium control algorithm

A natural heart can alter the cardiac output corresponding to the demand. Artificial internal organs must participate in the system of the living body, too. Therefore, artificial internal organs must maintain pace with the actions of the living body, and must cope with the total system. Tohoku University developed a resistance based artificial heart control algorithm, which had a simulated baroreflex system to cope with every demand [19,20]. A total artificial heart, a ventricular assist device, cardiopulmonary bypass, percutaneous cardiopulmonary support system (PCPS) and a rotary blood pump can be controlled with this automatic control system [19–21]. Fig. 3 shows time series data of biventricular total nonpulsatile artificial circulation with resistance based control algorithm simulating the baroreflex function. According to the increase of blood pressure with drug administration, the drive speed of the rotary pump was automatically controlled to be decreased. Since it can be calculated at the microchip level, it can be implanted in the control microchip for an artificial myocardium (Fig. 4).

The sensing device is, of course, important in the automatic control system. Nano level sensing equipment is now under development in Tohoku University. It can sense hemodynamic pressure, blood flow and several hormonal factors. A chronic durability animal experiment has already been completed with the micro sensors. More miniaturization is planned to build this into the nano level structure.

Development aiming at an "intelligent artificial myocardium" is being conducted at present.

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ORIGINAL ARTICLE

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Correlation dimension analysis of the artificial circulation

Abstract Artificial circulation has been analyzed by decomposing it into parts. However, the sum of the decomposed parts is not equal to the whole system, especially in nonlinear dynamic systems such as biological systems. To evaluate prosthetic circulation as an entity, not as decomposed parts, nonlinear mathematical analytic techniques, including fractal dimension analyzing theory, were used. Two pneumatically actuated ventricular assist devices were implanted as biventricular bypasses (BVB) in chronic animal experiments using four healthy adult goats. For comparison between natural and prosthetic circulation in the same experimental animals, the BVB-type complete prosthetic circulation model with ventricular fibrillation was adopted. All hemodynamic parameters with natural and prosthetic circulation were recorded under awake conditions and calculated by a personal computer system. By the use of nonlinear mathematical techniques, time-series data of the hemodynamics were embedded into the phase space, and correlation dimension analysis was performed to evaluate the reconstructed attractor. Our results suggest that the correlation dimension of the arterial blood pressure does not linearly increase according to the increase of the embedding dimension, even during artificial circulation, suggesting those are the fractal time series data. Dimensional analysis of the hemodynamics revealed that lower dimensional fractal dynamics were observed during prosthetic circulation. Fractal time series data are suggested to have robustness and error resistance. Thus, our results suggest that the circulatory regulatory system with the artificial heart may have these desirable characteristics.

Key words Chaos · Fractal · Fractal dimension · Total artificial heart · Correlation dimension

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Introduction

In 1981, Guevara et al. first reported that the cellular and subcellular mechanisms that produce the cardiac action potential were characterized by a chaotic attractor.[1] Other investigators reported that nonoscillatory cardiac tissues also manifested nonlinear dynamics.[2–4] Furthermore, the physiological function of the natural heart is characterized by a complex interaction of many control mechanisms that enable it to adapt to the changing environment.[5–7] This complexity, derived from the field of nonlinear dynamics, made it difficult to analyze the circulatory regulatory system quantitatively.[8,9] Analysis of nonlinear dynamics is currently an active field of research.[10,11] Its application to the cardiovascular system may aid our understanding of many physiological phenomena.[11]

Chaotic motion arises in nonlinear dynamic systems and can generate random-like time series, which closer analysis reveals to be highly ordered and critically dependent on the initial conditions.[2,12] Mathematically, all nonlinear dynamic systems with more than two degrees of freedom can generate deterministic chaos, becoming unpredictable.[2–4] To

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describe periodic, aperiodic, or even chaotic behavior of nonlinear systems arbitrarily with more degrees of freedom, several approaches have been applied.[2,13]

The concept of the *fractal* was developed by Mandelbrot to deal with complex geometric forms.[10,11,14] A fractal structure is not smooth and homogeneous. Instead, fractals are irregular, but their irregularity has an underlying pattern.[15,16] The more closely a fractal object is inspected, the more structure is revealed. Furthermore, the smaller-scale structure is similar to the larger-scale form.[15,16] Of physiological interest is the fractal-like branching structure of many anatomical structures, such as the central nervous system, vascular system, His-Purkinje fibers, and so on.[10]

Chaotic behavior in phase space generally has a *fractal dimension*,[10,14] a feature that allows its recognition. Periodic and quasiperiodic motions possess integer values;[2,10] however, chaotic motions have fractional values. The topological properties of the attractors and their quantification by dimensionality analysis may be an appropriate tool in the classification of circulatory dynamics and, thus, a possible diagnostic tool.[10,11] During the past decades, several investigators have undertaken nonlinear analysis using Grassberger and Procaccia's algorithm to evaluate the correlation dimension of time-series data.[17]

The use of the artificial heart has increased for the treatment of patients with severe heart failure following cardiac surgery and acute myocardial infarction. Thus, it is important to analyze the physiological effect of the artificial heart on the circulatory regulatory system.[18] In this study, to analyze the circulatory regulatory system with the artificial heart on an entity, not as decomposed into parts, the hemodynamic parameters of the artificial heart were analyzed by the correlation dimension analyzing technique that has been useful in the study of nonlinear dynamics coincident with deterministic chaos. Nonlinear behavior, such as chaotic dynamics, shows sensitive dependence on initial conditions; thus, use of the same experimental animals in the

same conditions is desirable. For comparison between natural and artificial circulation in the same experimental animals, the biventricular assist-type total artificial circulation model under ventricular fibrillation in chronic animal experiments was adopted.

Materials and methods

Animal experiments

The experimental goats weighed 60 to 70kg, with a mean of 65kg. They were fasted for 2 days before the experiments. Three goats were anesthetized by halothane inhalation. After tracheal tube intubation by tracheotomy, they were placed on a respirator. Electrodes for the electrocardiogram (ECG) were attached to the legs and later implanted into the pericardium.

· The left pleural cavity was opened by left fifth rib resection. Arterial blood pressure was monitored continuously with catheters inserted into the aorta through the left internal thoracic artery. Central venous pressure was measured by the fluid-filled catheter through the internal thoracic vein. For left artificial heart implantation, the intercostal arteries were separated to free the descending aorta. A polyvinyl chloride (PVC) outflow cannula was sutured to the descending aorta. A PVC inflow cannula was inserted into the left atrium through the left atrial appendage. Both cannulae were connected to our TH-7 pneumatically driven sac-type blood pump by the built-in valve connectors.[7] The PVC outflow cannula and the inflow cannulae were inserted into the pulmonary artery and the right atrium, respectively. Then, both cannulae were connected to the right pump. Pump output was measured by the electromagnetic flowmeter attached to the outflow-side cannulae.

A TH-7 pneumatically driven sac-type blood pump[7] was used to constitute a biventricular bypass (BVB)-type artifi-

Fig. 1. Photograph of the goat with biventricular bypass type total prosthetic circulation model
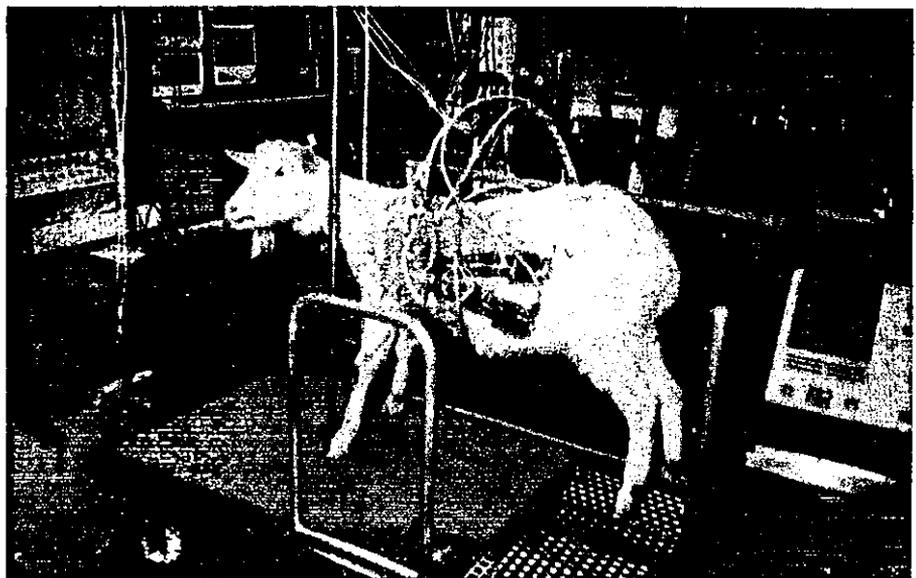
cial heart model (Fig. 1). The inner sac of the pump was coated with polyurethane, and the outer casing of the pump was made of polycarbonate. Silicone ball values were affixed to the inflow and outflow connectors. Both blood pumps were driven by our newly developed pneumatic driving console.

After the chest was closed, these pumps were placed paracorporeally on the chest wall, and then the goat was placed in a cage and extubated after waking. After the influence of the anesthesia was thought to be terminated (2–3 days after the operation), the goat was intravenously heparinized (100 U/kg) to record the control time-series data without biventricular assist device driving. Data recording was performed under the awake condition, when the goat was standing and in preparandial condition. Time-series data of the hemodynamic variables were recorded with an ink-jet recorder and on magnetic tape, after stabilization of all hemodynamic derivatives without driving by the artificial heart (20–30 min after the biventricular assist devices were stopped).

After the recording of control data, bilateral ventricular assistance was started and ventricular fibrillation was induced electrically. Between 20 and 30 min after confirmation of stabilization of the hemodynamics during operation of the total artificial heart, time-series data of the hemodynamic variables were recorded. The driving condition of both pumps was manually operated to maintain a satisfactory pump output (80–100 ml/min/kg) and to maintain the hemodynamic parameters within normal limits. The driving conditions of both pumps were fixed when the time-series data of the hemodynamic parameters were recorded.

Dimensional analysis

The oldest concept of dimension is that of the topological dimension Dt. Dt is 0 for a point, 1 for a line, and 2 for a plane.[17] A first generalization is the fractal dimension or Hausdorff dimension. Chaotic dynamics in phase space generally has a fractal dimension, which allows its recognition. To discriminate between deterministic and random activity, one evaluates the dimension D of the attractors that have been constructed in the phase space. If we use the simple sets, for example, a limit cycle or torus, the fractal dimension is an integer and is equal to the topological dimension. Many physically feasible methods of defining dimension have been devised. They are classified into five categories[10]: changing coarse graining level, using the fractal measure relations, using the correlation function, using the distribution function, and using the power spectrum.

In this study, we used the correlation dimension analyzing technique by the Grassberger-Procaccia method, which is useful for the evaluation of high-dimensional complex systems.[19] By the use of these nonlinear mathematical methods, time-series data of the hemodynamic derivatives with the natural and artificial heart were reconstructed in the phase space.[2,20] The phase space is a useful concept for visualization of the system's dynamic behavior.[2-4] It is an abstract space whose coordinates are the degrees of free-
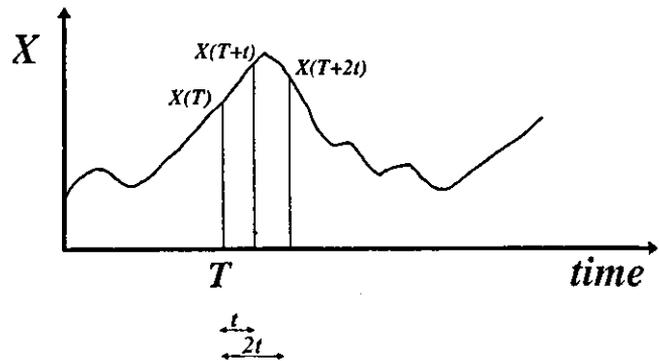

Fig. 2. Reconstruction methodology of the time-series data into phase space. The delayed values then define a single point in a multidimensional phase space and thus a vector (details shown in the text)

dom of the system being considered, i.e., the number of independent variables.[2,3,17] However, we cannot directly construct such a phase space for the circulatory regulatory system, which generates the hemodynamic time series data.

The first step is to find the phase space description of the digitized data. We had followed Taken's proposal and used the time-shift method.[20] In 1980s, Takens et al. proposed reconstructing the phase space by means of the time delay t. The values measured at fixed time delays $x(T)$, $x(T + t)$, $x(T + 2t)$ . . . are treated as though they characterized new variables. The delayed values then define a single point in a multidimensional phase space and thus a vector (Fig. 2). If trajectories starting from different initial values are attached to a discrete region within the phase space with a lower dimension, this region is called an *attractor*. An attractor may have fractal dimension and is then called chaotic or strange.

To give a geometric explanation of the computation of the dimension, we will illustrate schematically a proposal made by Grassberger and Procaccia to compute the so-called correlation dimension $D2$. After reconstruction of the attractor in the phase space, the number of data points lying inside the circle that have a radius of r^0, $2r^0$, $3r^0$, . . . etc. is counted. When $\log (r)$ versus $\log N(r)$, is plotted, a straight line is obtained. The slope of this line is exactly the dimension of the attractor.

By the use of these nonlinear mathematical methods, we calculated the correlation dimension of the hemodynamics during artificial circulation generated by the biventricular bypass pump under ventricular fibrillation, and compared it with that during natural heartbeat.

Results

A photograph of the complete artificial circulation model in the awake condition during the chronic animal experiment is shown in Fig. 1. After recording of control data without pump driving, ventricular fibrillation was electrically induced and the systemic circulation was maintained with the artificial heart.
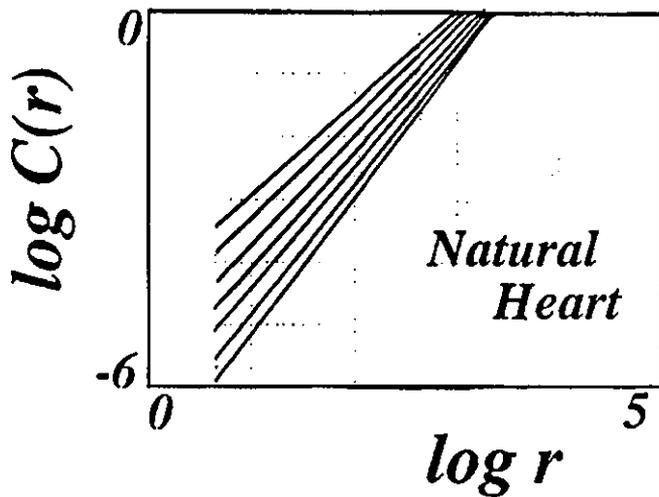
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Fig. 3. Correlation dimension analysis of arterial blood pressure during natural heart beat without biventricular assistance (details shown in the text)
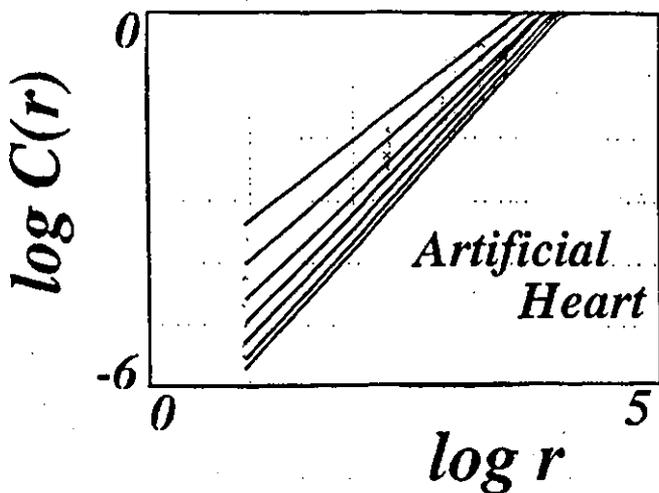

Fig. 4. Correlation dimension analysis of arterial blood pressure during complete prosthetic circulation with biventricular bypass pump
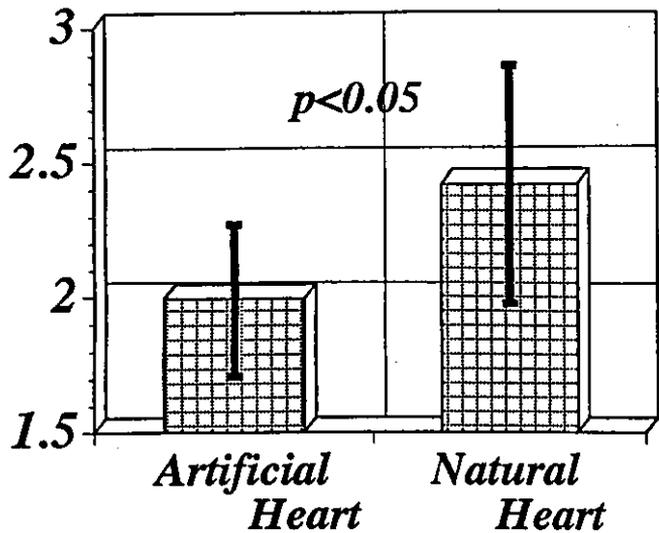

Fig. 5. Comparison of the correlation dimension (y axis) of arterial blood pressure during natural and prosthetic circulation in the same subjects by the use of the Grassberger-Procaccia dimensional analyzing algorithm

Satisfactory pump outputs (80–100 ml/kg/min) were easily obtained in this system, and all hemodynamic derivatives were easily controlled within normal values by manual control of positive pressure, negative pressure, systolic duration, and driving rate with the pneumatic drive console.

Fractal dimension analysis of arterial blood pressure was calculated in the computer by the correlation dimension analysis method using the Grassberger-Procaccia algorithm. For the dimensional analysis, time-series data of the hemodynamic parameters were embedded into the phase space by the nonlinear mathematical analyzing technique. As shown in Figs. 3 and 4, the slope was increased according to the increase of the embedding dimension from three to nine. However, increase of the slope showed the sigmoid pattern at its peak values. By the use of these peak values, we calculated the correlation dimension.

During natural heartbeat without assistance, the correlation dimension of the arterial blood pressure was 2.41 ± 0.44. Thus, the fractal dimension was significantly smaller than the embedding dimension and larger than 1, which is the dimension of the limit cycle attractor of a periodic system, suggesting that arterial blood pressure is the fractal time-series data. During operation of the artificial heart, the correlation dimension was 1.99 ± 0.28, significantly smaller than that obtained with time-series data of the hemodynamics with the natural heart ($P < 0.05$). The fractal dimension of arterial blood pressure during artificial circulation showed that time-series data of the hemodynamics had characteristics of fractals, even during prosthetic circulation.

Discussion

One of the major findings of this study is that the hemodynamics derivative was the fractal time-series data even during the artificial circulation produced by the pneumatically driven artificial heart. With the fractal time-series data, the slope of the relationship between log r and $N(r)$ does not linearly increase according to the increase in the embedding dimension.[19-21] The convergent values of this slope indicate the correlation dimension of the attractor.[19] With the random time-series data, the reconstructed attractor showed a nonstructured pattern, and the fractal dimension of this pattern is equal to the embedding dimension.[2-4] With the periodic data, the reconstructed attractor showed the characteristics of a limit cycle attractor, and its fractal dimension is 1.[2-4] Both the random and the periodic series are not fractal time-series data. The dimension of the fractal time-

series data is a fraction and is significantly different from the dimension of both the random and the periodic time-series data.[10,14]

In summary, our data suggest that the time-series data of the hemodyamics during both natural and artificial circulation are fractal time-series data, because, first, the reconstructed attractor of the data plotting distribution in the phase space had fraction fractal dimension, and, second, their fractal dimensions were significantly different from that with a limit cycle attractor in a periodic system and that with a random distribution attractor. Several investigators have shown the robustness and error resistance of the fractal time-series data.[10,11,14] Thus, our results suggest that artificial circulation may show these desirable characteristics like those of natural circulation. Another finding of this study is that the fractal dimension of the hemodynamic derivatives with artificial circulation was significantly smaller than that with natural heart circulation. Our results show the possibility that the lower dimensional attractor was shown in the reconstructed attractor of the artificial circulation. A recent report from our team showed that rhythmic fluctuations of the hemodynamics were significantly changed during artificial circulation compared with natural circulation.[13] These phenomena must contribute to the fractal dimension of the hemodynamics with prosthetic circulation.

The fractal dimension revealed further information concerning the whole nonlinear dynamic system compared with conventional spectral analyzing methodology,[10,14] because power spectral analysis of the hemodynamics shows us the decomposed components of the circulatory regulatory systems, such as the sympathetic and parasympathetic nervous systems.[13] Deterministic analyses of the electrical signals appear to be more sensitive to changes in biological generators during normal function and abnormal pathology than the more common stochastic analyses.[21,22] These nonlinear mathematical analyzing techniques give us information concerning the whole circulatory regulatory system, and thus we can estimate the information entropy of the cardiovascular control system. From the viewpoint of the whole system, artificial circulation is mediated by the lower non-linear dynamic systems.

In conclusion, arterial blood pressure was fractal time-series data even during artificial circulation, and the fractal dimension of the hemodynamics during artificial circulation is smaller than that during natural circulation. These results suggest that artificial circulation has the characteristics of robustness and error resistance, and these nonlinear mathematical analyzing techniques give us information concerning the whole circulatory regulatory system, including the artificial heart.

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Can personality traits predict pathological responses to audiovisual stimulation?

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Abstract

The "Pockemon shock" is the most famous accident in the history of the broadcasting industry in Japan. Based on the experiences of this unfortunate accident from famous animation program "Pocket Monster", this study focused on the psychology and psychosomatics of the patients. A head-mounted display was used as the three-dimensional image presentation device and "Descent", a free software shooting game, was used as the software. Ten healthy adult male volunteers were used in this experiment after obtaining their informed consent. The oxygen metabolic change in the anterior lobe of the brain was measured by near infrared spectroscopy and recorded on an electrocardiogram. The mental scaling tendency of the object was analyzed using the type A behavior pattern and the hostility scaling. The Cook and Medley hostility (HO) scale from the Minnesota multiphasic personality inventory (MMPI) was also used in this experiment. From this scaling methodology, the paranoid scale, cynicism scale, lie scale, social support quality and social support quantity were calculated. All measured time series data were kept in the normal range, and no fatal arrhythmia or epilepsy were observed during experiments. In some cases, the brain oxygen metabolism may completely differ for the objects of Type A and Type B behavior patterns. On the whole, correlation did not become significant in type A scaling and hostility scaling. In a comparison of the percent changes of the HF in HRV with lie scaling, significant negative correlation was observed. The social support quantity was calculated from Cook and Medley, and significant negative correlations were observed with percent changes of LF/HF in HRV. The lie scale and social support quantity are opposite scaling. The sympathetic nervous system and parasympathetic nervous system have an opposite function also. Therefore, our results showed an interesting phenomenon, when considering the relationship between the autonomic function and the pathophysiological reaction to the audiovisual stimulations. As for the photo sensitive epilepsy, it was reported to be only 5–10% for all patients. Therefore, 90% or more of the cause could not be determined in patients who started a morbid response. The results in this study suggest that the autonomic function was connected to the mental tendency of the objects. By examining such directivity, it is expected that subjects, which show morbid reaction to an audiovisual stimulation, can be screened beforehand.

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1. Introduction

The "Pockemon shock" is the most famous accident in the history of the broadcasting industry and audiovisual equipment society in Japan [1]. After it happened, the Japanese people started countermeasures immediately. A project team was inaugurated in the several agencies. In Japan, Animation and Television games are progressing at the world's fastest rate. The performance of audiovisual equipment is also No. 1 in the world. The Japanese people regarded the problem to be so serious that they supported the research work on the study for evaluating the responses to audiovisual stimulation such as TV, game machines and newly developed virtual reality (VR) machines [1–4]. In Tohoku University, the autonomic nervous system responding to VR was evaluated [2].

Among the large number of people watching the TV program "Pocket monster", only a small number showed a pathological reaction, but it is necessary to determine the factors for such pathological reaction. This paper focused on the psychology and psychosomatics of the patients [5–8].

2. Materials and methods

An analysis method from the perspective of multiple dimensions is required to analyze a living body response toward VR. A head-mounted display was used as the three-dimensional image presentation device for VR and "Descent", a free software shooting game, was used as the software for the virtual three-dimensional game. In the game, the game player flies in the three-dimensional virtual space, striking down one enemy one after another through movement. The movement of the head does not correspond with the rotation of the view in the three-dimensional image.

An unpleasant sensation is thus created because input to the central nervous system does not correspond with the three-dimensional images. It is well known that a pathological response is started by this game.

Ten healthy adult male volunteers were used in this experiment after obtaining their informed consent approved by the Ethical committee in Tohoku University Graduate School of Medicine.

During the three-dimensional game with VR, the oxygen metabolic change in the anterior lobe of the brain was measured by near infrared spectroscopy (NIRO-300, Hamamatsu Photonics) [9,10]. An electrocardiogram was recorded at the same time to evaluate the heart rate variability (HRV).

The time series data were recorded in the digital data recorder. After the experiments, recorded data were inputted into the personal computer system through the AD converter. Quantified evaluation and statistical handling were performed in the personal computer system. Spectral analysis was performed with fast Fourier transform to evaluate the fluctuations in the time series data.

The mental scaling tendency of the object was analyzed using the type A behavior pattern and the hostility scaling. The Cook and Medley hostility (HO) scale from the Minne-

sota multiphasic personality inventory (MMPI) was used in this experiment. From this scaling methodology, the paranoid scale, cynicism scale, lie scale, social support quality and social support quantity were calculated.

Responses to the three-dimensional shooting game were compared with the mentality tendency by the quantified value of scaling.

3. Results

All measured time series data were kept in the normal range, and no fatal arrhythmia or epilepsy were observed during experiments. Satisfactory measurements were obtained during experiments in 10 subjects.

Examples of the time series data of a volunteer, who showed a type A behavior pattern, is presented in Fig. 1. Examples of the time series data of a volunteer, who showed a type B behavior pattern, are presented in Fig. 2.

A volunteer with type A behavior showed stable time series data during the three-dimensional VR shooting game in oxygen metabolism of the anterior lobe of the brain. However, the example of a volunteer with type B behavior showed significant alteration in the time series data of oxygen metabolism in the brain.

Responses to the three-dimensional VR game were calculated with percent changes of the heart rate and tissue oxygenation index (TOI) measures with near infrared spectroscopy. Type A behavior scaling and hostility scaling were
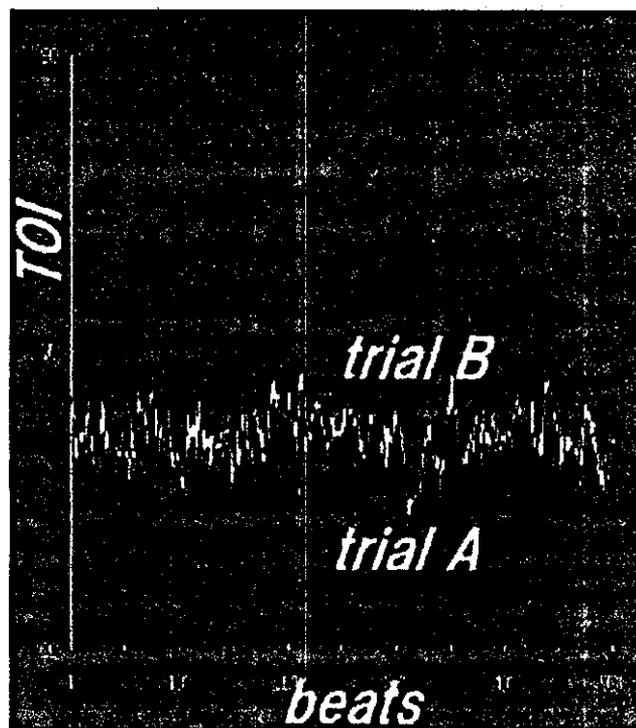

Fig. 1. An example of the time series data of a volunteer, who showed a type A behavior pattern during resting condition and VR game immersion. Trial A showed the data from first experience of this game and trial B showed the second.
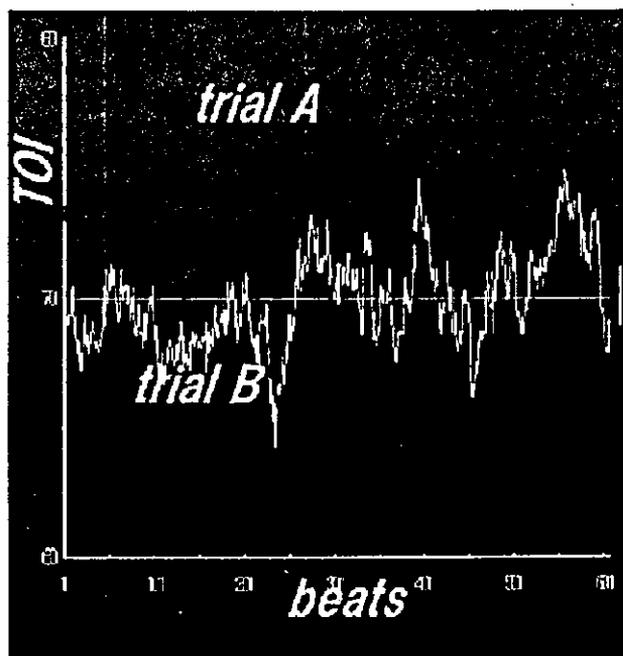
Fig. 2. An example of the time series data of a volunteer, who showed a type B behavior pattern during resting condition and VR game immersion. Trial A showed the data from first experience of this game and trial B showed the second.
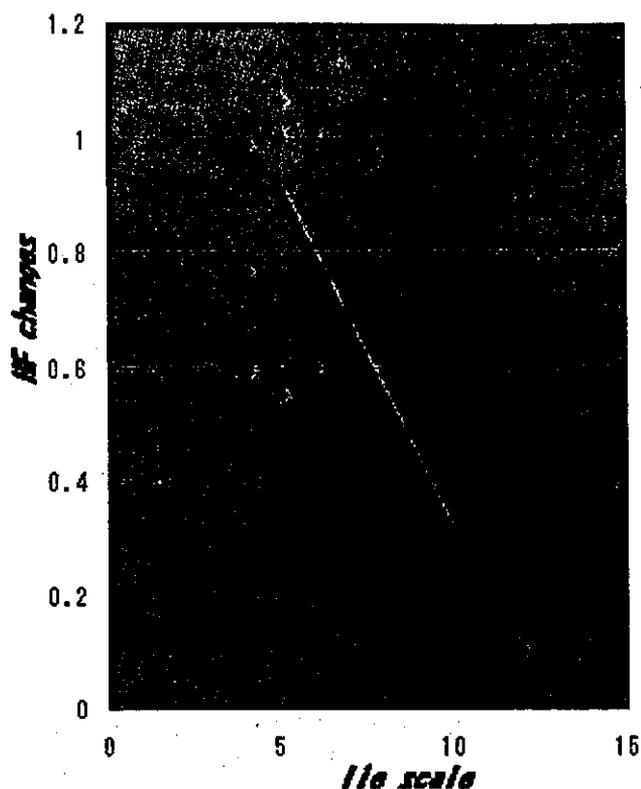

Fig. 3. Relationship between the percent changes of the HF in HRV and lie scaling. Significant negative correlation was observed.
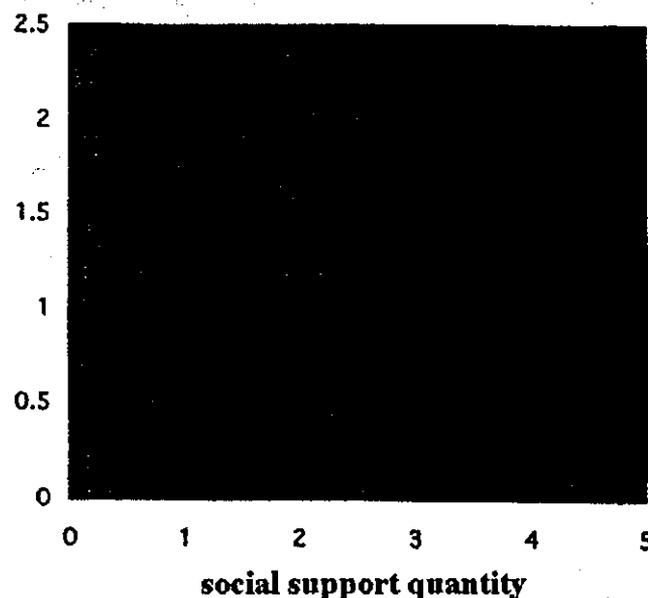

Fig. 4. Relationship between the percent changes of the LF/HF in HRV and social support scaling. Significant negative correlation was observed.

calculated and compared with the percent changes of these parameters. However, no significant correlation was observed.

HO scale showed the hostility scale, paranoid scale, cynicism subscale, lie scale and several kinds of social support scaling. These scalings were compared with the percent changes of the parameters, and the lie scale showed significant negative correlation with the percent changes of the heart rate during an experiment.

Spectral analysis was performed for the HRV, LF and HF, and LF/HF were calculated from the analyzed data. Fig. 3 shows the percent changes of the HF in HRV with lie scaling. Significant negative correlation was observed.

The social support quantity was calculated from Cook and Medley. Fig. 4 showed correlation with the percent changes of LF in HRV. Significant negative correlation was calculated.

4. Discussion

It is estimated that over 10 million people watched the Pocket Monster television program in 1997. Among these watchers, over 700 children were taken to hospital by ambulance with severe sickness. It is possible that more children went to hospital by car or on foot—the government does not know the exact number.

It is also possible that the occurrence rate of children, who felt nauseous during the Pocket Monster program, was not so large. Though the percentage may not have been so high, severe convulsions were reported in some patients; thus, the problem was regarded as serious.

As for the photo sensitive epilepsy, it was reported to be only 5–10% for all of the patients. Therefore, 90% or more of the cause could not be determined in patients who started a morbid response.

What divided the television viewers?

This paper focused on mental characteristics.

In this research, the technique of mental scaling was newly introduced. For mental scaling, the type A behavior pattern and the hostility scaling were used. Various experts have reported on the relevance of a type A behavior pattern and a hostility scaling.

In some cases, the brain oxygen metabolism may completely differ for the object of Type A and Type B behavior patterns. On the whole, correlation did not become significant in type A scaling and hostility scaling. There is argument regarding the relation of the hostility scale and the type A behavior pattern among Japanese people. This concerns the various kinds of low rank scaling in the hostility scaling. Various scaling, such as a cynicism scale, a paranoid scale, a lie scale and a social support quantity, have been reported. Generally, a paranoid scale, a cynicism scale, a lie scale, etc. suggest the directivity of a comparatively negative reaction. A social support quantity is a scale in which an opposite direction is shown.

Significant correlation was observed in the low rank measure of a hostility scaling. Correlation with the lie scale, which is a low rank measure of a hostility scaling, was suggested as the spectrum component of the HRV at the time of the VR game. As for the HRV, the social support quantity also showed significant correlation, too.

The lie scale in Cook and Medley showed a tendency for negative reaction to the responses. The HF component in HRV showed the parasympathetic function. So, the results in this study suggest that the object, which shows a negative reaction, has the high reactivity of a parasympathetic nervous system to the audiovisual stimulation.

The social support quantity is a scale in which an opposite reaction is shown. Generally, the social support quantity is low when the hostility scale is large. LF/HF in HRV showed the sympathetic nerve function. So, results in this study suggest that the object, which shows a positive reaction, has the high reactivity of a sympathetic nervous system to the audiovisual stimulation.

The lie scale and social support quantity are opposite scaling. The sympathetic nervous system and parasympathetic nervous system have the opposite function also. So, our results showed an interesting phenomenon, when considering the relationship between the autonomic function and the pathophysiological reaction to the audiovisual stimulations.

These results suggest that the autonomic function in the three-dimensional game by the VR was connected to the mental tendency of the objects. By examining such directiv-

ity, it is expected that subjects that show the morbid reaction to an audiovisual stimulation can be screened beforehand.

After establishing standard guidelines for audiovisual content risks, mental scaling of an object may become an important factor in the future.

Acknowledgements

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Original paper

Non-linear dynamic analysis of hemodynamic parameters in an undulation type artificial heart system

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Abstract

Undulation pump total artificial heart (UPTAH) is a unique total artificial heart implant (TAH) using an undulation pump that is a continuous blood flow pump. To evaluate the autonomic nerve function mediating the circulation system, we analyzed the hemodynamic parameters during animal experiments with UPTAH using the non-linear mathematical analyzing technique, including chaos and fractal theory. Adult female goats were used for the implantation of UPTAH. The natural heart was replaced with UPTAH under extra-corporal circulation. The conductance- and arterial pressure-based control method (1/R control) was applied on the 5th to 7th post-operative day as the influences of the cardiopulmonary bypass circulation were diagnosed to be terminated. Hemodynamic parameters were recorded on the data recorder, and non-linear mathematical analysis was performed. For the quantitative evaluation of the strange attractor, which was the characteristics of the deterministic chaos, the fractal dimension analysis was carried out. As a result, hemodynamic parameters fluctuated on the time axis and showed fractal characteristics, which were thought to be the characteristics of the deterministic chaos. The reconstructed attractor of the hemodynamics showed various behaviors according to changes in the situation of the goats. These results suggest that non-linear dynamical analysis might be useful in monitoring the circulatory regulatory system in artificial heart circulation. © 2002 Éditions scientifiques et médicales Elsevier SAS. All rights reserved.

Keywords: Undulation pump; Total artificial heart; Chaos; Fractal; UPTAH

1. Introduction

The undulation pump total artificial heart (UPTAH) [1], which was developed at the University of Tokyo, is a small size total artificial heart implant using an undulation pump that is a continuous blood flow pump (Fig. 1). The driving mechanism and flow pattern of UPTAH is so unique that we examine the circulatory regulatory system using UPTAH. In this paper, to evaluate the circulatory regulatory system including the artificial heart under various conditions, a non-linear mathematical analyzing technique including chaos and fractal theory [2-9] was used on the UPTAH implanted animal.

2. Material and methods

Adult female goats weighing between 40 and 79 kg were used for the implantation of UPTAH. Under general anesthesia, the left chest cavity was opened with a fifth rib resection. The natural heart was replaced with UPTAH under extra-corporal circulation [10]. After surgery, the cardiac output was maintained at 100 mL/kg/min by controlling the right pump manually. To prevent lung edema,

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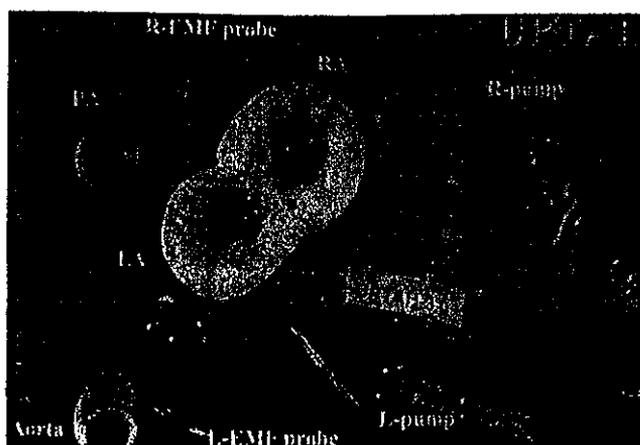*E-mail address:* yambe@idac.tohoku.ac.jp (T. Yambe).

Fig. 1. A photograph of an undulation pump total artificial heart (UPTAH). R-EMF probe: right electromagnetic flow probe; RA: right atrium; PA: pulmonary artery; LA: Left atrium; L-EMF probe: left electromagnetic flow probe; R pump: right pump; L pump: Left pump.
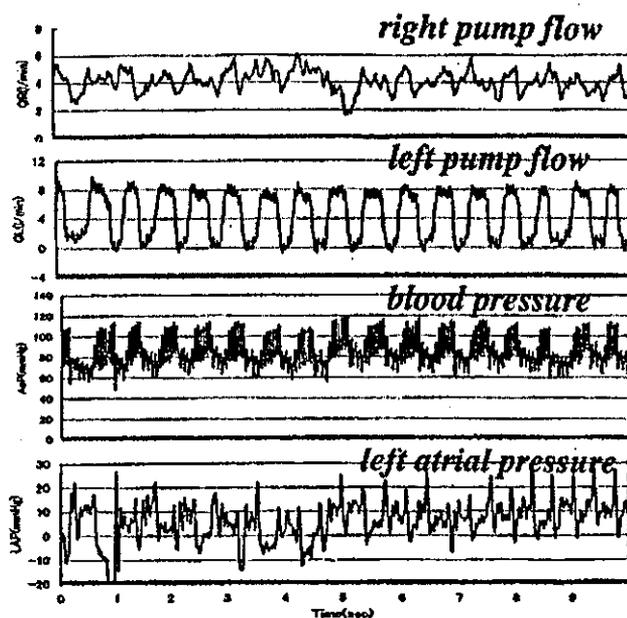

Fig. 2. Time series data of the hemodynamic parameters in a goat fitted with UPTAH.

QR: right pump outflow; QL: left pump outflow; AoP: aortic pressure. LAP: left atrial pressure.

the left atrial pressure was controlled automatically around 8mmHg. The arterial pressure-based control method (1/R control) [10,11] was applied on the 5th to 7th post-operative day.

During experiments, aortic blood pressure, pulmonary arterial pressure and left and right atrial pressures were continuously monitored via fluid filled catheters with pressure transducers (Nihon Koden, Tokyo, Japan). Left and right pump outputs were continuously measured with electromagnetic flow probes (Nihon Koden). Time series data of hemodynamic parameters were embedded into the phase space and projected into the three dimensional phase space. For the quantitative evaluation of the reconstructed attractor, fractal dimension analysis of the reconstructed attractor [2-5] was carried out using a personal computer system.

3. Results

To date, 47 cases of implantation have been performed on adult goats, and 1/R control has been applied in 10 cases. The longest survival of a UPTAH goat was 81 days. Recorded hemodynamic parameters were analyzed in the computer system once the conditions were stable. Time series data of pump output, blood pressure and left atrial pressure waveform are shown in Fig. 2. Unfortunately, some time series waveforms were significantly influenced by the body position of the experimental goats, and some spikes were observed in the blood pressure waveform, probably because of influences of the body motion to the fluid filled catheter. We therefore used the waveform of the left pump output in this study.

For example, the reconstructed attractor of the left pump output waveform, embedded into the four dimensional phase space and projected into the three dimensional phase space, is shown in Fig. 3. The larger shape attractors are shown during the sitting position compared to standing, although the band of the attractors did narrow a little.

As shown in the altered pattern in this figure, the shapes of the attractors were significantly altered with the behavior of the goats. Quantitative evaluation was attempted in this study using the fractal dimensional analysis of the reconstructed strange attractors, which had fractal characteristics. For example, the fractal dimension of the left pump output tended to decrease when the goats was standing, suggesting a change in the circulatory regulatory system. However, because of large standard deviations, no. significant tendency of the changes in the fractal dimension were observed with each behavior of the goats.

4. Discussion

In this study, UPTAH was implanted in normal adult goats and a normal circulation was obtained. Hemodynamic parameters with UPTAH showed various circulatory behaviors according to changes in the condition of the experimental goats. These changes may be due to the properties of peripheral vessels mediated by the autonomic nervous system and some hormonal mediators.

It was interesting to note that the shape of the strange attractors was altered during the sitting and standing positions. Some reports have showed that the parasympathetic nervous system tends to increase during sitting or resting [2-7]. These investigators reported the increase of the

Of course, further investigation is needed. We will continue these approaches aiming at the sensitive monitoring methodology of artificial circulation.
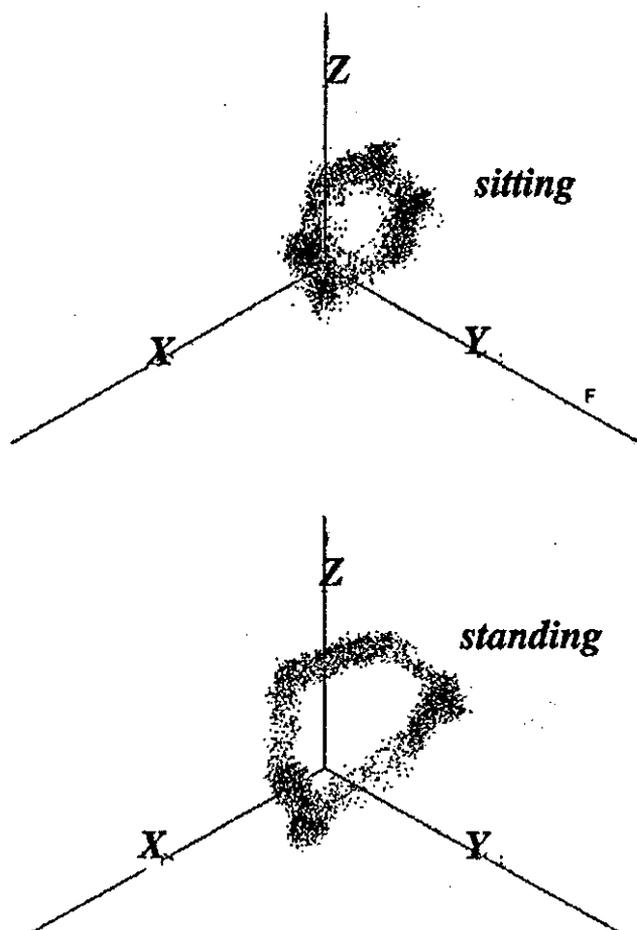
Fig. 3. Reconstructed attractor of the left pump outflow embedded in the four dimensional phase space and projected into the three dimensional phase space.

fluctuations in the hemodynamic parameters, such as heart rate or blood pressure. In our study, the band of the strange attractor became a little bit wider during sitting. However, this was not significant and additional experiments will be needed. Non-linear mathematical analyzing technology was very sensitive to the condition of the various parameters. It depended on an autonomic nervous system, hormonal factors, body motion, mental condition of the goats, and so on. A lot of parameters influenced the non-linear dynamics in the cardiovascular system and it was very difficult to evaluate the non-linear dynamic behavior quantitatively. However, this technique was so sensitive that it might be useful for the evaluation of cardiovascular dynamics in artificial heart circulation, including UPTAH.

As shown in Fig. 3, the shape of the attractors changed according to the condition of the goats, suggesting that these methodologies may be useful for the monitoring of the circulatory regulatory systems (including the autonomic nervous system), which are responsible for the chaotic dynamics of the hemodynamic parameters.

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Recent Progress in Artificial Organ Research at Tohoku University

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*Yuri A. Kovalev, *Dan X.D.Sha, *Shunsuke Nanka, *Yoshifumi Saijo, *Yoshiyuki Mibiki,
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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.

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

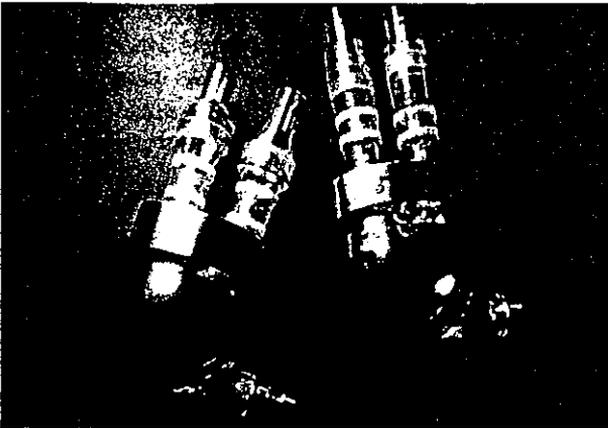Development of the pneumatic total artificial heart (TAH) was carried out in our laboratory based

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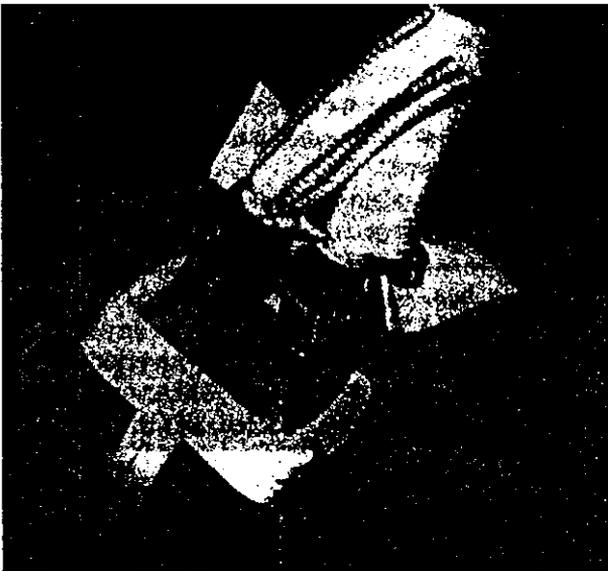FIG. 1. The Tohoku University type pneumatic ventricular assist device is shown.

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.
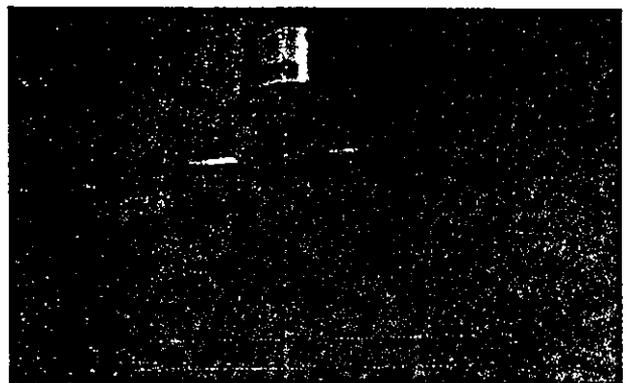

FIG. 3. The photograph shows a vibrating flow pump, implantable ventricular assist device.

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.
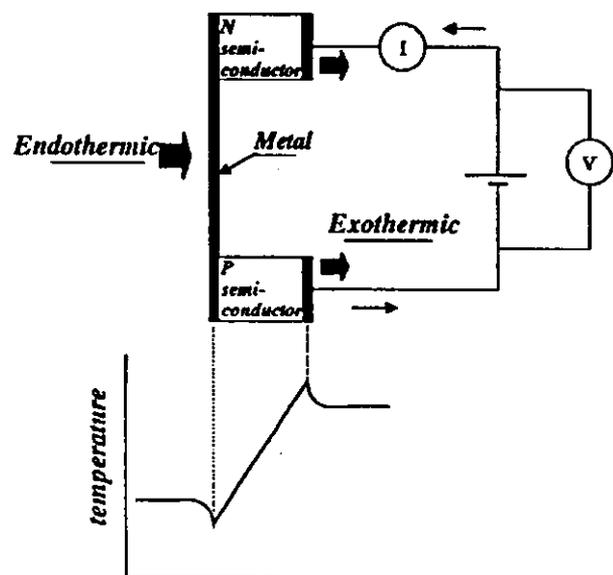

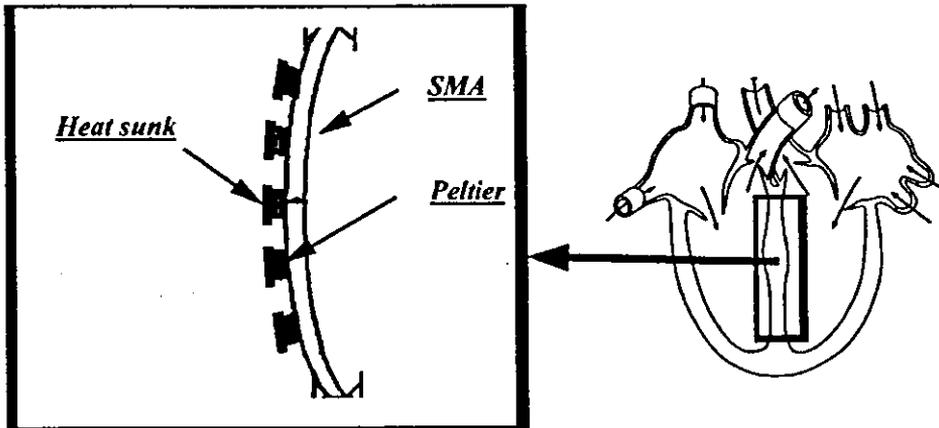FIG. 5. Heat transfer in the Peltier element is shown.

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.
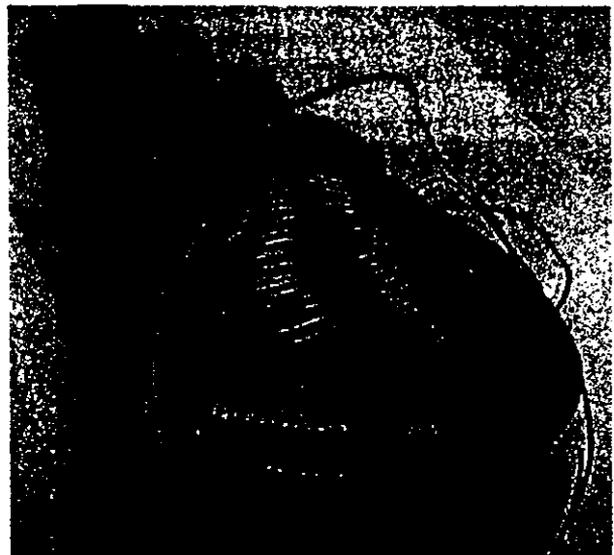

FIG. 8. Peltier-SMA artificial myocardium on a plastic model of a heart is shown.