表2　補助人工心臓

1．空気圧駆動型体外設置補助人工心臓
2．埋め込み型補助人工心臓
　2-1．拍動型補助人工心臓
　　　ノバコア
　　　ハートメイト
　　　ライオンハート
　2-2．無拍動型補助人工心臓
　　2-2-1．遠心ポンプ
　　2-2-2．軸流ポンプ

半永久的な補助人工心臓の応用においても，超長期の埋め込みが前提になる以上，現在本邦で汎用される体外設置型の空気圧駆動型補助人工心臓だけでなく，完全埋め込み型の，感染の危険がなく，自宅へ帰れるシステムの開発へ向かうのは時代の趨勢である．

完全埋め込み型の補助人工心臓システムとしては，アメリカで開発されたノバコア(World Heart)とハートメイト(Thoratec)が先行しており(**表2**)，日本でも臨床試験に供されたが，ともに日本人の平均の体格の成人に埋め込むにはやや大きく，70kg以下の体格の症例には推奨されない19)．

そこで，より小柄な体格の症例のために，遠心ポンプや軸流ポンプなどの無拍動ロータリーポンプが臨床に供されて注目されている．最初に臨床応用されたのは，小型のスクリューをもつ軸流ポンプのマイクロメドポンプ(Micromed)で，その後，ジャービック2000(Jarvik Heart)，ハートメイト2(Thoratec)，インコア(Berlin Heart)などの軸流ポンプが次々に臨床に供され，世界中で競争されている．現在，ジャービック2000の最長の生存例は5年を超え，2005年の米国人工内臓学会では，最長生存の患者自らが，自分の症例の症例報告を，自ら行って注目を浴びた20)．

遠心ポンプはスクリュータイプの軸流ポンプと比較して，回転数が少なくてすむので，耐久性や溶血の観点で有利であり，世界中で開発が進められつつある．最初の臨床応用は，オーストラリアからベントラコア(Micromedical)の報告が行われ，クリーブランドからコアエイド(Arrow)，日本のテルモもヨーロッパでデュラハート(Terumo)の臨床試験を開始した．2005年に入り，ついに日本でもエバハート(Sun Medical)臨床試験が開始され，マスコミをにぎわせたのは記憶に新しい．

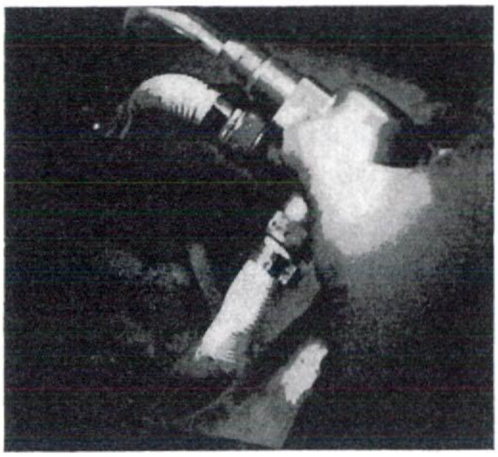

図1　動物実験中のエバハート

図1に，動物実験におけるエバハートの写真を提示する．体重50kgの山羊の胸腔内に容易に埋め込み可能であった．とくに送脱血カニューラがキンキングしないよう工夫が凝らされており，外科医の開発者ならではの手術の容易さが印象的なシステムである．東北大学では1年の長期生存実験を目指して，現在4か月目の山羊がオンゴーイングで生存中である18)．

人工心臓は重症末期心不全の治療方法として着実に進歩しており，歴史を顧みると，米国でも日本でも，創成期から現在に至るまで多くの日本人研究者がかかわっており，日本の功績が大きい分野である．今後日本でのますますの発展が期待される．

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ARTIFICIAL ORGAN RESEARCHIN 21ST COE PROGRAM OF TOHOKU UNIVERSITY

T. Yambe*, Y. Shiraishi*, S. Nitta*,S. Maruyama**, T.Takagi**,
K.Imachi***, Y. Luo***, K. Tabayashi****, S. Amae****, M.Sato*****
*Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
**Institute of Fluid Science, Tohoku University, Sendai, Japan
***Tohoku University Biomedical Engineering Reseacr Organization
****Tohoku University Hospital, Sendai, Japan
*****Graduate School of Engineering, Tohoku University, Sendai, Japan

E-MAIL: yambe@idac.tohoku.ac.jp

Abstract: Tohoku University was chosen as the first COE research institution in the 21st century. Various artificial organs, such as an artificial heart, an artificial myocardium, an artificial esophagus, and an artificial sphincter muscle, are now under development. There are common technologies for various internal artificial organs. The Nano sensing device, transcutaneous energy transimission system (TETS) and surface materials are common in various kinds of the artificial internal organs. So, it may be convenient to develop various kinds of artificial organs in one University。

Introduction

As for an implantable type artificial organ, a space for implantation is restricted. Therefore, micro device development is indispensable (1-11). Nanotechnology and micromachining technology development are very important. In Tohoku University, various artificial organ development is furthered according to the tradition of Nano machine micro machine development. In this paper, progress in various artificial internal organ projects were described

Artificial myocardium with Nano Technology .

The purpose of this research is developing nano artificial myocardium. Therefore, nano actuator, nano sensor, nano-microtip PC, nano fluid dynamics, nano TETS were studied in this project.

Especially, control-objectives value setup which imitated baroreflex system is tried using a nano sensor and a nano micro control chip. As a nano sensor, by this research, the nano thin film sensor adapting diamond-like carbon (DLC) was developed, and it applied for the patent (application for patent 2003-317956). The outstanding biocompatibility can be expected and the application to the artificial organ of all fields can be expected. Furthermore, the nano sensor adapting an optical fiber was also developed and it succeeded in the animal experiments. Since information, such as each ventricle, can be evaluated simultaneously, the optimal drive of artificial myocardium is possible.

A hemodynamics is checked by the nano sensor and it is expected that a patient's life prognosis is sharply improvable by controlling an artificial myocardium optimally. The actuator in which nano micro-machining is also possible is used for the artificial myocardium which this research develops.

An artificial myocardium is a system with which the pulsation of the heart is assisted. The external surface of the heart is equipped with an artificial myocardium. Therefore, like the conventional artificial heart, there is no risk of a thrombus and it does not have the problem of the durability of an artificial valve. When there is no necessity, an artificial myocardium does not operate, and since circulation is performed only with the heart, improvement in the durability of an artificial-myocardium system is expected.

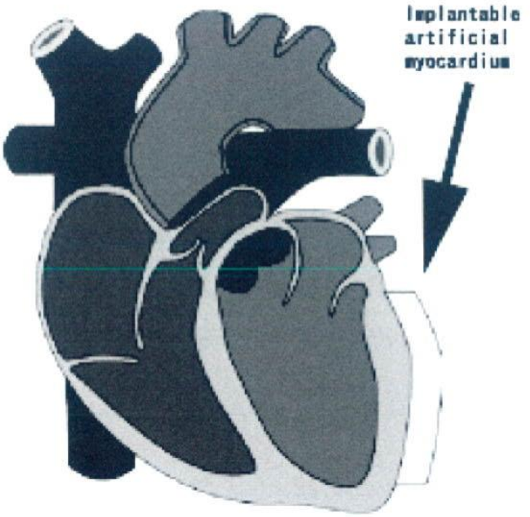

Fig.1 Schematic illustration of the implantable artificial myocardium

Development of an artificial esophagus which can drink by the use of Nanotechnology .

An about 10,000 Japanese per year died with an esophagus cancer. Everybody know that an operation of an esophagus cancer is difficult, because the reconstruction of an esophagus is needed. An operation will become easy if there is an artificial esophagus. An esophagus moves food by peristalsis. An simple pipe is not enough as an esophagus.

We invented the esophagus in which a peristalsis is possible. The developed artificial esophagus consists of a macromolecule material and artificial peristalsis muscles. Human's esophagus can swallow a thing by peristalsis. In order to realize a peristalsis, the shape memory alloy ring was used. The coil was made from the fiber of the shape memory alloy which improved durability by nanotechnology molecular crystal arrangement (Biometal, Toki Co., Tokyo, Japan).

The ring of a coil contracted in order and the peristalsis took shape. The animal experiment using the goat of the same weight as Japanese people was tried. The developed artificial esophagus was replaced with the excised esophagus. It was confirmed that the peristalsis had been realized in the body of a goat.

By the artificial esophagus, an operation of an esophagus cancer becomes easy. In the future, we can undergo an operation using an endoscope with artificial esophagus. Since there is little invasion, an operation of an old man will become possible. It is expected that invention of the artificial esophagus with peristalsis brings big progress to esophagus cancer surgical therapy.

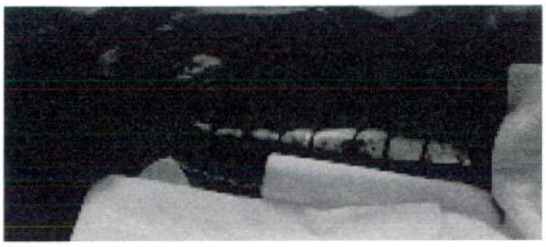

Fig.2 A photograph of an Artificial Esophagus, which can drink, after implantation

Project: Artificial Sphincter

Tohoku University invented the completely new artificial organ named artificial sphincter muscle as a completely implantable artificial organ.

Several patients must have Stoma following an operation of cancer of the Colon. An ostomy patient cannot control defecation . The artificial sphincter that we invented makes it possible for a patient to control defecation.

Fig.3 A Photrgaph of an animal experiment of the Artificial Sphincter during opening.

Therefore, we used the shape memory alloy. Two boards of a shape memory alloy were combined. A cushion was placed on the internal surface of a board to prevent tissue injury. Energy was transmitted by the transcutaneous energy transmission system (TETS). When a patient goes to a toilet, a patient brings TETS. TETS will be used, if a patient goes to a toilet and prepares(20-22) An artificial sphincter muscle opens and enables a patient to defecate. A patient can control defecation if this system is used. Thus, a patient's quality of life (QOL) will be improved greatly.

We wish to supply to a medical market soon.

Conclusion

Based upon various basic technologies, a lot of kinds of artificial internal organs can be carried out in Tohoku University. Further expansion of research theme can be expected in near future.

Acknowledgements

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Support Mechanism of a Newly-Designed Mechanical Artificial Myocardium using Shape Memory Alloy Fibres

Y. Shiraishi[1], T. Yambe[1], S. Itoh[2], R. Sakata[2], Y. Wada[2], K. Sekine[1], Y. Saijo[1], S. Konno[1], S. Nitta[1], Q. Wang[1], H. Liu[1], M. Higa[3], Y. Luo[3], D. Ogawa[4], A. Tanaka[5], M. Yoshizawa[6], Y. Kakubari[4], H. Miura[4], F. Sato[4], H. Matsuki[4], M. Uematsu[2], Y. Park[2], T. Tanaka[2], M. Umezu[2], T. Fujimoto[7], N. Masumoto[8], Y. Hori[3], H. Sasada[9], K. Tabayashi[10], E. Okamoto[11] and D. Homma[12]

[1] Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[2] Graduate School of Science and Engineering, Waseda University, Sendai, Japan
[3] Tohoku University Biomedical Engineering Research Organization (TUBERO), Sendai, Japan
[4] Graduate School of Engineering, Tohoku University, Sendai, Japan
[5] Faculty of Symbiotic Systems Science, Fukushima University, Fukushima, Japan
[6] Information Synergy Center, Tohoku University, Sendai Japan
[7] Shibaura Institute of Technology, Tokyo, Japan
[8] Nippon Institute of Technology, Saitama, Japan
[9] Graduate School of Agriculture, Tohoku University, Sendai, Japan
[10] Department of Cardiovascular Surgery, Graduate School of Medicine, Tohoku University, Sendai, Japan
[11] Graduate School of Engineering, Hokkaido-Tokai University, Sapporo, Japan
[12] Toki Corporation, Tokyo, Japan

Abstract— **As the heart failure is caused by the decrease in the myocardial contraction, the direct mechanical myocardial assistance in response to physiological demand, that is, the synchronous support of the contractile function from outside of the heart, might be effective. The purpose of this study was to develop an artificial myocardium which was capable of supporting the cardiac contraction directly by using the shape memory alloy fibres based on nanotechnology. Some methodologies using novel devices other than the artificial hearts are proposed so far with severe heart disease. However, it was also anticipated that the decrease in cardiac functions owing to the diastolic disability might be caused by using those 'static' devices. Then, this study was focused on an artificial myocardium using shape memory alloy fibres with a diameter of 100 – 150 um, and the authors examined its mechanism in a mock circulatory system as well as in animal experiments using goats. Basic characteristics of the material were evaluated prior to the hydrodynamic or hemodynamic examination using a mock ventricular model. The results were as follows: a) The length of the structure was able to be adjusted so that the system could wrap the whole heart effectively. b) In the hydrodynamic study using the mock circulatory system, the myocardial system was able to pump a flow against the afterload of arterial pressure level. c) In the animal experiments, aortic pressure and flow rate were elevated by 7 and 15% respectively by the mechanical assistance of the artificial myocardium, which was driven synchronising with the electrocardiogram, and also, d) The anatomically-identical shape of the artificial myocardium might be more effective for the assistance. In conclusion, it was indicated that this controllable artificial myocardial support system was effective for the mechanical cardiac support for the chronic heart failure.**

Keywords— **Artificial myocardium, Shape memory alloy fibre, goat experiment, mock ventricular model, hemodynamic effect**

I. INTRODUCTION

In general, the artificial ventricular assist systems, such as artificial hearts, were employed for the treatment of the severe heart failure in order to increase the circulation volume. However the complications caused by the hemolysis or thrombosis on the surface of the artificial materials are still outstanding problems in the application of those devices to patients. Heart transplantation has also been widely performed as destination therapy for the severe heart failure. But it is limited by donor organ shortages, selection criteria, as well as the cost [1]. And recently, cell transplantation to repair or supplement impaired heart tissue has been reported as an alternative therapy for that [2]. The authors assumed that the essence of the pathophysiological development of severe heart failure was in the decrease in the cardiac contractility. Then an artificial myocardium has been developed using a covalent nano-tech shape memory alloy fibre, which is capable of assisting natural cardiac contraction from outside of the ventricular wall as shown in Fig. 1. The purpose of this study was to develop a sophisticated artificial myocardium unit, and also to have examined the hemodynamic effects of the myocardial assist system on cardiac function.

The authors have been developing a totally-implantable artificial myocardial assist device [3]-[6]. The methodologies of the direct ventricular support systems were already reported as direct mechanical ventricular assistance (DVMA) by Anstadt's or other groups, as well as the right ventricular assist device which was invented and reported at IDAC, Tohoku University [7]-[9]. In this study, a design to surround the total heart has been established in order to refrain from the stress concentration by the mechanical assistance, and the hemodynamic performance of the artificial myocardial assist system were examined in a mock circulatory system as well as on animal experiments using goats.

II. MATERIALS AND METHODS

A. Basic constuctions of a newly-developed artificial myocardium using shape memory alloy fibres

The myocardial assist system, as shown in Figure 2, consists of a covalent type shape memory alloy fibre (Biometal®). The diameter of the fibre is 100 microns, and it is contracted by the Joule heating. In general, Ti-Ni alloy is well known as a material with the shape-memory effect[10]-[12]. The fibre material is able to be covered with a silicone –tubing (diameter: 150um). The configuration of the material was basically constructed by covalent bond, so that it indicated a big strain change by 5 to 10% in length. The linearity of the recovery strain and the changes in electric resistance could be adjusted through the fabrication process, so that the strain of the fibre could be easily controlled by using the digital-servo system without potentiometers.

B. Mock circulatory examination and animal experiments

Contractile function of the device developed was examined onto the originally-designed silicone mock left ventricle (Figure 3). Hydrodynamic evaluation was conducted against the afterload of 80 to 100mmHg without mock ventricular contraction.

Hemodyamic data were also obtained from normal adult healthy goats, the mean weight of which was 50kg. Prior to the measurement, the artificial myocardial assist device with parallel-linked shape memory alloy fibres was covered with silicone rubber, and it was attached onto the ventricular wall. Left ventricular (LV) pressure was measured by a catheter tip transducer (Millar, SVPC-664A), The sensor was inserted at the left atrial portion through the mitral valve. These hemodynamic data were recorded by a digital recording unit (TEAC, LX-10) and the sampling frequency was 1.5kHz.

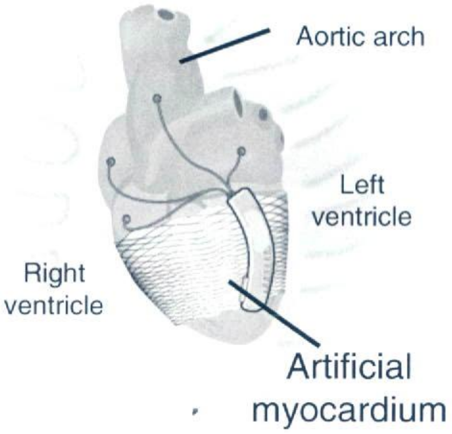

Fig. 1 Schematic illustration of an artificial myocardium attached on the ventricular wall; the synchronous contraction can be achieved according to the natural physiological demand.

Fig. 2 Whole view of the mechanical artificial myocardium developed; the ventricle was covered by the band-shaped device and it was able to support the contractile function synchoronising with natural heart beat.

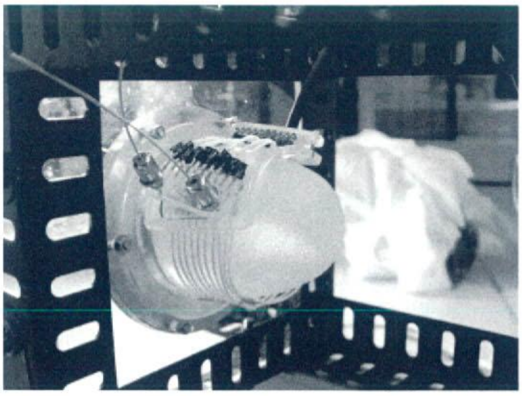

Fig. 3 Hydrodynamic examination of the artificial myocardium; the device was attached onto the silicone mock left ventricular model.

III. RESULTS AND DISCUSSION

A. Hydrodynamic function in the mock circulatory system

The several mechanisms were examined in the mock circulatory system, which was attached onto the silicone left ventricle. An example of the hydrodynamic test was shown in Figure 4. The length of the structure of the myocardial assist device was adjusted to fit the ventricular model so that the system could wrap the whole heart effectively. And as shown in Figure 4, the elevation of the pressure and flow rate measured at the outflow portion of the ventricular model were around 10mmHg and 1L/min, respectively. The it was indicated that the myocardial system was able to pump a flow against the afterload of arterial pressure level.

B. Hemodynamic effects on animal experiments

The myocardial device developed was successfully installed into the goats' thoracic cavity. Prior to the installation of the device, it was covered with silicone tubings and sheets as shown in Figure 2. For the installation of the former electrohydraulic myocardial assist device which was developed by the authors [6], it was necessary to remove at least the fifth costa to make enough room to be fitted in the thoracic cavity. But in this study by using shape memory fibres, the actuator itself was so small that it would be enough in less capacity for it in the thoracic cavity. Moreover, the procedure of the closed chest was found to be much simpler.

Hemodynamic waveforms were changed by the mechanical assistance as shown in Figure 5. The aortic flow rate as mean cardiac output was increased by 23% and the systolic left ventricular pressure was elevated by 6% under the low cardiac output condition at 2.5L/min by the mechanical assistance as shown in Figure 6. Therefore it was indicated that the effective assistance might be achieved by using the Biometal shape-memory alloy fibre.

IV. CONCLUSIONS

A myocardial assistive device has been developed and it was suggested that the effective assistance could be achieved in goats. When it is attached onto the ventricular wall, it should be considered the forced refrigerant effect by blood circulation such as coronary perfusion. It consisted of shape memory alloy fibres, which was capable to be totally installed into the thoracic cavity. It was easy to attach the device onto the ventricular wall. The elevation of the cardiac functions followed the changes in vascular hemodynamics were investigated by the mechanical assist.

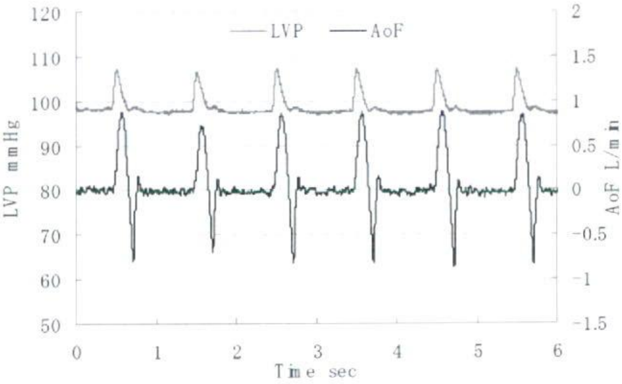

Fig. 4 Changes in pressure and flowrate derived at the outflow portion of the mock left ventricular model by the assistance of the artificial myocardium. These hydrodynamic data were obtained from the mock circulatory system with the afterload of 100mmHg.

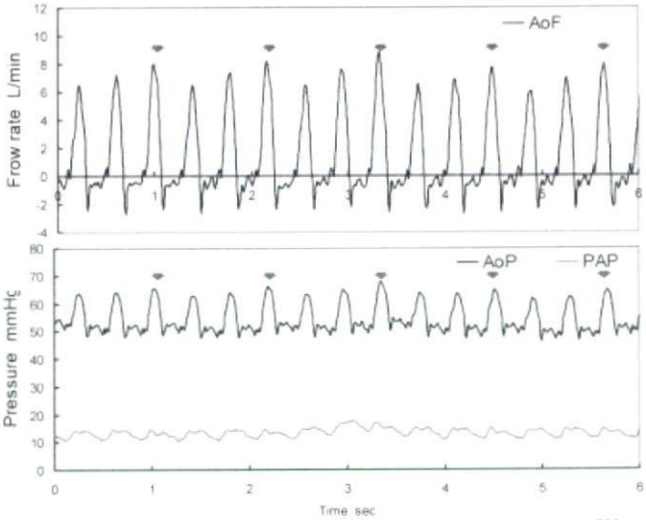

Fig. 5 Changes in the hemodynamics obtained from a goat (50kg); AoP: aortic pressure, AoF: aortic flow measured at the root, PAP: pulmonary arterial pressure. The arrows indicated the mechanical support aspects by the artificial myocardium, and each assistance was synchronising with natural electrocardiograms.

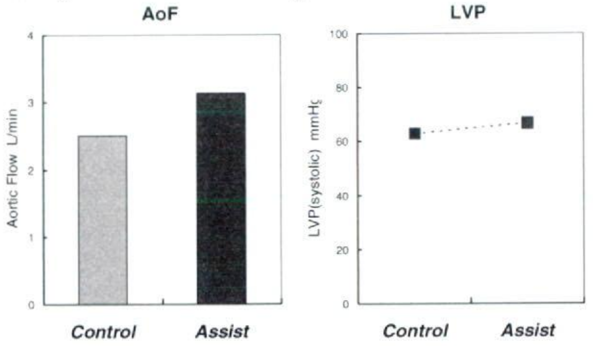

Fig. 6 Changes in the left ventricular pressure (LVP) and mean cardiac output calculated by aortic flow volume; 'control': without assistance, 'assist': mechanical assistance by the artificial myocardium.

As our system could assist natural ventricular functions with physiological demand, it might be applied in patients with angina of effort or for the artificial circulatory support for the patients with chronic heart failure, as well as the cardiac massage at lifesaving emergency for the recovery from ventricular fibrillation.

Therefore, it was indicated that this controllable artificial myocardial support system was effective for the mechanical cardiac support for the chronic heart failure.

All the animal experiments related to this study were scrutinised and approved by the ethical committee on the animal experiment of the Department of Medicine, Tohoku University, and also the Institute of Development, Aging and Cancer, Tohoku University, 2004-2006.

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Address of the corresponding author:

Author: Yasuyuki Shiraishi, D.Eng
Institute: Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University
Street: 4-1 Seiryo-machi, Aoba-ku
City: Sendai (ZIP: 980-8575)
Country: Japan
Email: shiraishi@idac.tohoku.ac.jp

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Preliminary Study on the functional reproduction of an Artificial Myocardium using Covalent Shape Memory Alloy Fibre Based on Control Engineering

Yasuyuki Shiraishi[1], Tomoyuki Yambe[1], Kazumitsu Sekine[1], Yoshifumi Saijo[1], Satoshi Konno[1], Shin-ichi Nitta[1], Qingtian Wang[1], Hongjian Liu[1], Masaru Higa[2], Daisuke Ogawa[3], Akira Tanaka[4], Makoto Yoshizawa[5], Yasuyuki Kakubari[3], Hidekazu Miura[3], Fumihiro Sato[3], Hidetoshi Matsuki[3], Shinji Itoh[6], Akinori Kamoda[6], Ryo Sakata[6], Yumiko Wada[6], Miyuki Uematsu[6], Youngkwang Park[6], Takashi Tanaka[6], Mitsuo Umezu[6], Tetsuo Fujimoto[7], Noriyasu Masumoto[8], Hiroshi Sasada[9], Koichi Tabayashi[10], Eiji Okamoto[11] and Dai Homma[12]

[1] Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
(Tel : +81-22-717-8517; E-mail: shiraishi@idac.tohoku.ac.jp)
[2] Tohoku University Biomedical Engineering Research Organization (TUBERO), Sendai, Japan, [3] Graduate School of Engineering, Tohoku University, Sendai, Japan, [4] Symbiotic Systems Science, Fukushima University, Fukushima, Japan, [5] Information Synergy Center, Tohoku University, Sendai, Japan, [6] Graduate School of Science and Engineering, Waseda University, Tokyo, Japan, [7] Shibraura Institute of Technology, Tokyo, Japan, [8] Nippon Institute of Technology, Saitama, Japan, [9] Graduate School of Agriculture, Tohoku University, Sendai, Japan, [10] Graduate School of Medicine, Tohoku University, Sendai, Japan, [11] Hokkaido-Tokai University, Sappro, Japan,
[11] Toki Corporation, Tokyo, Japan

Abstract: The authors have been developing an artificial myocardium using a sophisticated covalent shape memory alloy fibre, which is capable of assisting natural cardiac contraction from the outside of the ventricular wall. We applied engineering method based on robotics control and constructed the artificial myocardial assist system which might be able to regulate derangement and regenerative tensile force on the surface of heart. In this study, a design to surround the total heart has been established in order to refrain from the stress concentration by the mechanical assistance, and the hemodynamic performance of the artificial myocardial assist system were examined in a mock circulatory system as well as on animal experiments using goats. Basic characteristics of the shape memory alloy fibre unit were examined and the displacement control could be achieved under the condition of the different external temperature by feedback using the PID control. And also the increase of the external work of the goats left ventricular pressure-volume relationship were obtained by the assistance using an artificial myocardium with parallel-linked configuration, and therefore it was indicated that the effective ventricular mechanical support could be performed by the device.

Keywords: Artificial myocardium, hemodynamic assistance, pressure-volume relation, shape memory alloy fibre

1. INTRODUCTION

In general, the artificial ventricular assist systems, such as artificial hearts, were employed for the treatment of the severe heart failure in order to increase the circulation volume[1-10]. However the complications caused by the hemolysis or thrombosis on the surface of the artificial materials are still outstanding problems in the application of those devices to patients. The authors assumed that the essence of the pathophysiological development of severe heart failure was in the decrease in the cardiac contractility. Then an artificial myocardium has been developed using a covalent nano-tech shape memory alloy fibre, which is capable of assisting natural cardiac contraction from outside of the ventricular wall without any blood contact surfaces of the device[11-16]. The purpose of this study was to develop a sophisticated artificial myocardium unit, and also to have examined the hemodynamic effects of the myocardial assist system on cardiac function.

2. MATERIALS AND METHODS

2.1 Basic characteristic of myocardial unit

The myocardial assist system consists of a covalent type shape memory alloy fibre, 'Biometal'. The material of the shape memory alloy fibre was structured as covalent shape, so that it had long durability of periodic contraction over 800 million cycles. The relationship between the temperature and the strain of the fibre was shown in Figure 1. The diameter of each fibre employed for the ventricular supporting girdle is 100-150 microns, and it is contracted by the Joule heating by 5 to 10% of the total length. The artificial myocardium has been constructed to be parallel link structure by using those fibres. Firstly, the electric resistance of a fibre in the length of 200mm, which was suitable unit length for the circumferential girdle of the ventricle, was obtained with different percent shortening.

And secondly, in order to achieve the accurate settlement of the displacement of the shape memory alloy fibre unit, the authors applied the PID control

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against the electric resistance of the fibre. Each electric resistance value of the fibre was obtained and converted to electric voltage through a bridge circuit, and those values were imported into the originally-designed microcomputer by using SH2-7044 for the control of PID. The control algorithm was configured to generate sequential pulse with pulse width modulation in order to change the wattage, which was input into each fibre.

The changes in displacement were obtained by the laser meter (Keyence, LB-01) as well as the mechanical load by the load cell (Kyowa, LVS-1KA) under the conditions as shown in Table 1: a) different ambient heat transmission in the room temperature air and water, and b) different bias tensile force.

2.2 Hemodynamic changes in goat

Hemodyamic data were obtained from normal adult healty goats, the mean weight of which was 50kg. Prior to the measurement, the artificial myocardial assist device with parallel-linked shape memory alloy fibres was covered with silicone rubber, and it was attached onto the ventricular wall as shown in Fig. 2 and 3. For the first stage evaluation of the myocardial assist girdle system, the actuation of the device was regulated by

Table 1 An example of the experimental condition for the comparison of the characteristics of the biometal fibre

Items	Values
Voltage applied	36VDC
Length of fibre	200mm
Frequency	0.5Hz
Duration energised	200msec
Ambient heat transmission	$2.4\mathrm{x}10^{-2}$,$6.0\mathrm{x}10^{-1}$ J/(m sec K)
Bias tensile force	$5.0\mathrm{x}10^{-2}$, $1.7\mathrm{x}10^{-1}$ N/mm

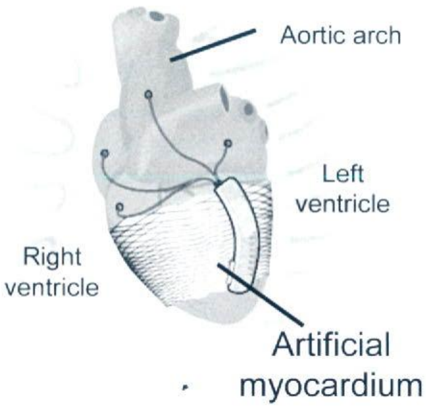


Fig. 3 Schematic illustration of an artificial myocardium attached on the ventricular wall; the synchronous contraction can be achieved according to the natural physiological demand.

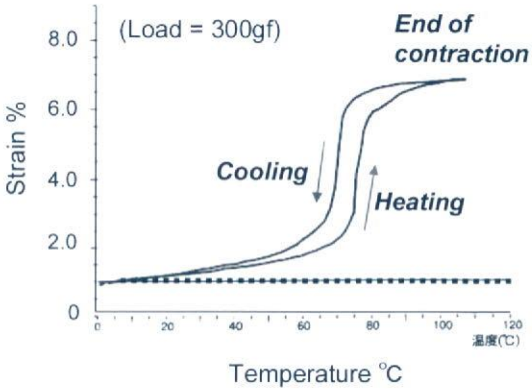


Fig. 1 Schematic illustration of the temperature-strain curve obtained from the Biometal Fiber.

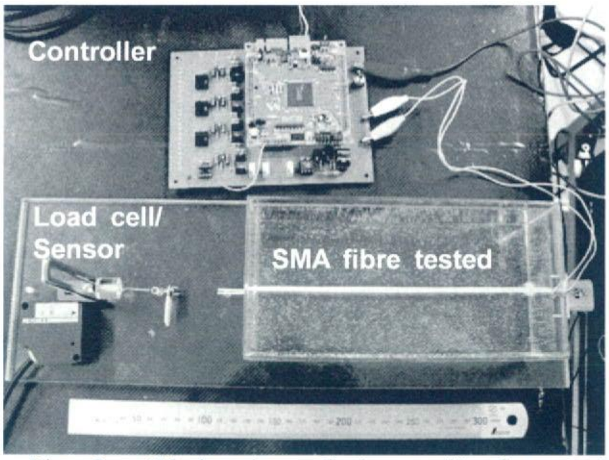


Fig. 2 Whole view of the tensile force and displacement test circuit for the examination with the PID control.

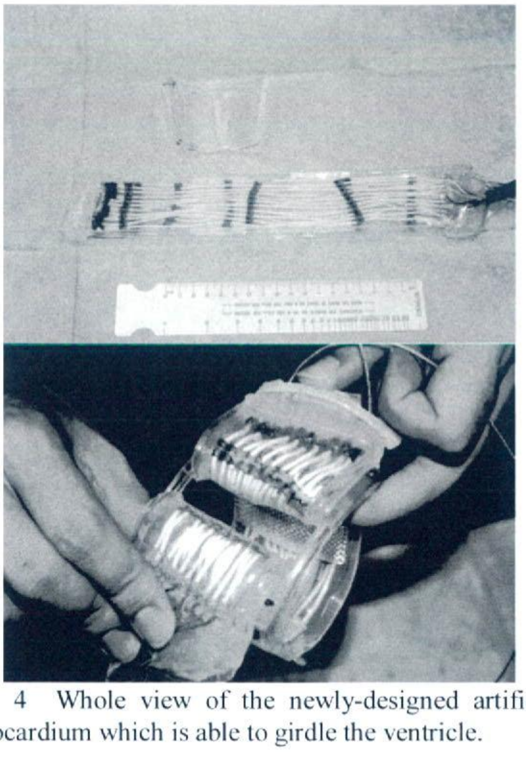


Fig. 4 Whole view of the newly-designed artificial myocardium which is able to girdle the ventricle.

on-off switching without PID control in order to examine the capability of supporting natural cardiac contractile function.

Left ventricular (LV) pressure was measured by a catheter tip transducer (Millar, SVPC-664A), and LV volume was obtained by a conductance catheter (Taisho-Ika, Sigma-5). Each sensor was inserted at the left atrial portion through the mitral valve. The data was recorded by a digital recording unit (TEAC, LX-10) and the sampling frequency was 1.5kHz.

3. RESULTS AND DISCUSSION

3.1 PID control for the displacement

As shown in Fig. 5 and 6, the accurate displacement control could be achieved in each shape memory alloy fibre by the PID control under the different tensile forced condition by using different bias spring, as well as the different ambient heat transfer condition, which was obtained from the test circuit as shown in Fig. 2.

3.2 Pressure-volume relationships in a goat

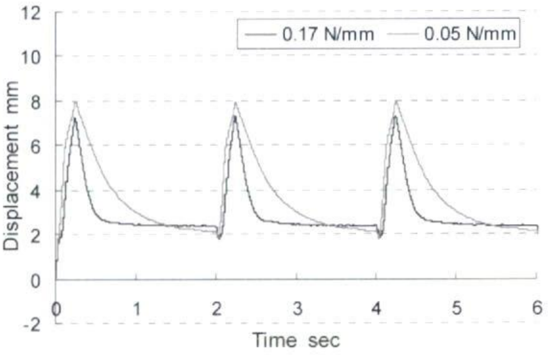
Fig. 4 shows that the external cardiac work was elevated by the mechanical assistance using a myocardial assist device. As a result, it was indicated that the synchronous mechanical assistance by using the system might be effective for the artificial circulatory support for the patients with chronic heart failure or angina of effort.

4. CONCLUSION

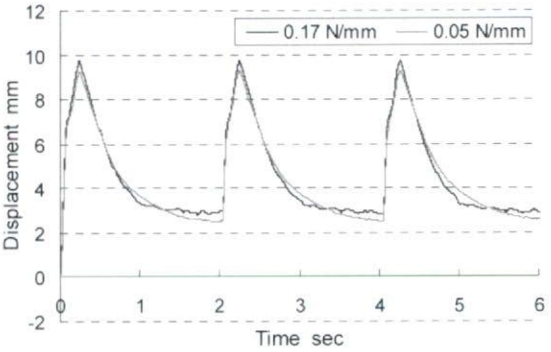
Functional changes of the covalent type shape memory alloy fibre were examined. And it was indicated that the capability of the sophisticated functional reproduction of natural myocardial contraction could be represented by using the PID control method.

As the contractile tensile force and shortening of myocardial tissues might be adopted to each hemodynamic condition, it was suggested that these methods for the control of the fibres might be useful to achieve more effective assistance by the artificial myocardium system.

And myocardial assistive device has been developed and it was suggested that the effective assistance could be achieved in goats. When it is attached onto the ventricular wall, it should be considered the forced refrigerant effect by blood circulation such as coronary perfusion during the PID control..

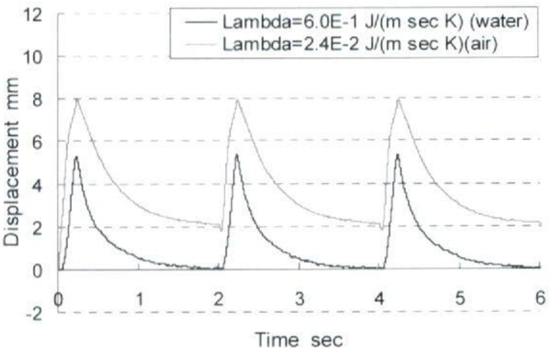


(a) Bias spring effect – open-loop control

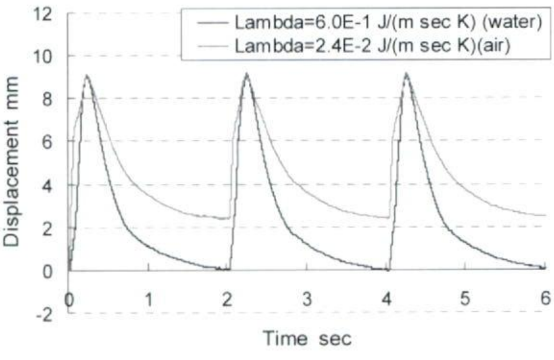


(b) Bias spring effect – PID control

Fig. 5 Changes in displacement obtained from the shape memory alloy fibre tested with the PID control under the different bias spring condition: a) open-loop, b) PID control.



(a) Heat transfer effect – open-loop control



(b) Heat transfer effect – PID control

Fig. 6 Changes in displacement obtained from the shape memory alloy fibre tested with the PID control under the different ambient heat transfer condition: a) open-loop, b) PID control.

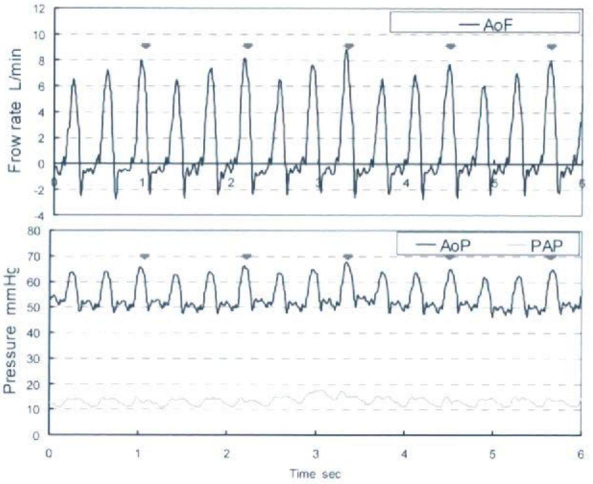


Fig. 7 Hemodynamic waveforms obtained from a goat; 'AoF': aortic flow at ascending aorta, 'AoP': aortic pressure measured at ascending aorta, 'PAP': pulmonary arterial pressure. The red arrows indicated the mechanical assistance by the artificial myocardial support.

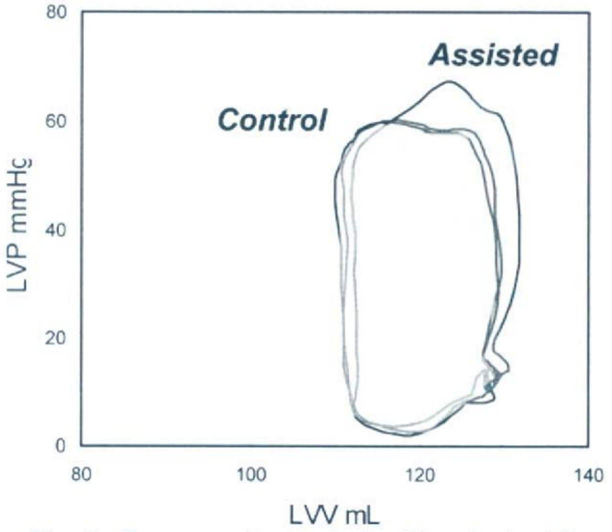


Fig. 8 Pressure-volume relationships obtained from a goat; 'Control': without assistance, 'Assisted': with mechanical assistance by the myocardial assist device developed.

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Evaluation of Cardiac Function of the Patients with Left Ventricular Assist Device by Transesophageal Echocardiography

Y. Saijo[1], Y. Saiki[2], A. Iguchi[2], K. Tabayashi[2], Y. Shiraishi[1], K. Sekine[1] and T. Yambe[1]

[1] Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan
[2] Department of Cardiovascular Surgery, Tohoku University Hospital, Sendai, Japan

Abstract— **The control of left ventricular assist device (LVAD) has been based on pressures of left ventricle (LV), aorta (AO) and pulmonary artery (PA) and flows in AO and PA. These parameters are one-dimensional and suitable for control of LVAD because they are numerical and quantitative. However, evaluation of the cardiac function by echocardiography is very useful in clinical settings because the cardiac function changes rapidly and dramatically. Transesophageal echocardiography is very useful for the assessment of cardiac function of the patients with LVAD implantation because it can detect and visualize what is happening in the heart immediately and directly.**

Keywords— **Transesophageal echocardiography, cardiac function, left ventricular assist device,**

I. INTRODUCTION

The control of left ventricular assist device (LVAD) has been based on pressures of left ventricle (LV), aorta (AO) and pulmonary artery (PA) and flows in AO and PA. These parameters are one-dimensional and suitable for control of LVAD because they are numerical and quantitative. However, evaluation of the cardiac function by echocardiography is very useful in clinical settings because the cardiac function changes rapidly and dramatically. For example, slight dilatation of LV may lead to large a mitral regurgitation due to tethering effect when the cardiac function is deteriorated and LV was enlarged.

The objectives of the present study are to observe LV volume and regurgitations and to evaluate cardiac function of the patients with LVAD by transesophageal echocardiography.

II. METHODS

A. Patients and Methods

522 consecutive cases of cardiovascular surgery were evaluated by intra-operative transesophageal echocardiography to assess cardiac function. The observation period is from May 2000 to April 2006. The transesophageal ultrasound probe (Omniplane II, Philips, Andover, USA) was inserted after induction of general anesthesia. The ultrasound device was SONOS 5500 (Philips, Andover, USA). The ejection fraction (EF) obtained with area-length method, assessment of grades of mitral, aortic and tricuspid valvular regurgitation, and dimensions of the aortic root were recorded. Among these cases, LVAD was implanted for 5 patients. In these 5 patients, right ventricular (RV) wall motion and RV volume were also measured.

The images and movies were recorded on a digital video recorder (DCR-TRV30, Sony, Tokyo, Japan). Images and movies were captured via IEEE1394 to a personal computer (VAIO-RZ 55, Sony, Tokyo, Japan) for further evaluation.

III. RESULTS

The condition of anesthesia, drug administration and volume infusion lead to LV enlargement. In some cases, mild mitral regurgitation (MR) worsened to severe MR.

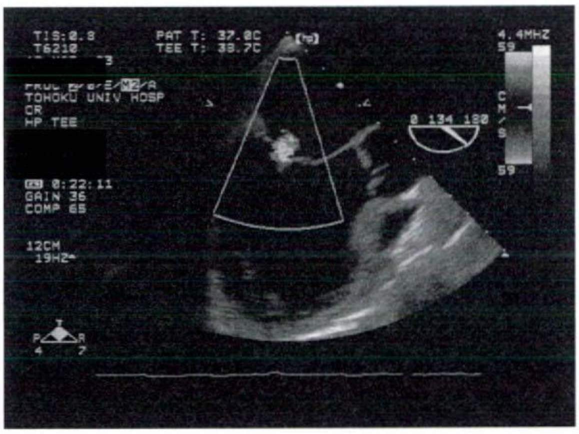

Fig. 1 Mild mitral regurgitation (MR) after induction of general anesthesia.

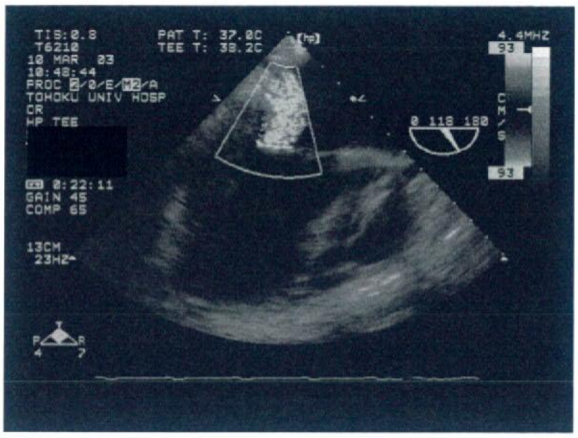

Fig. 2 Worsening of MR after infusion of volume.

We also experienced a case with severe "To and fro" tricuspid regurgitation without turbulent flow by rapid volume infusion.

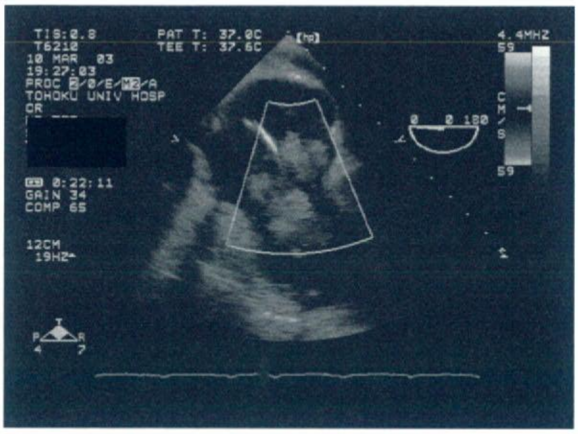

Fig. 3 Tricuspid regurgitation (TR) without turbulent flow

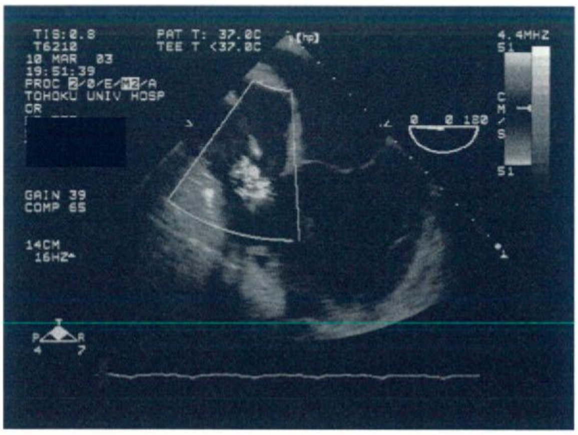

Fig. 4 Return to the mild TR

We also experienced a case with ventricular tachycardia immediately after the surgery was started. In the case, smoke-like-echo in LV was observed unless sufficient PCPS support.

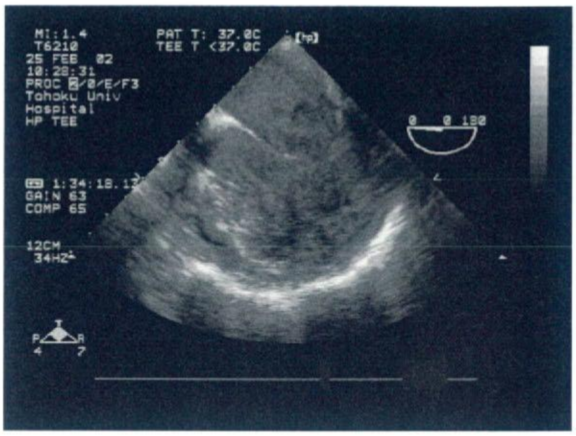

Fig. 5 Smoke-like echo in left atrium and ventricle at ventricular fibrillation

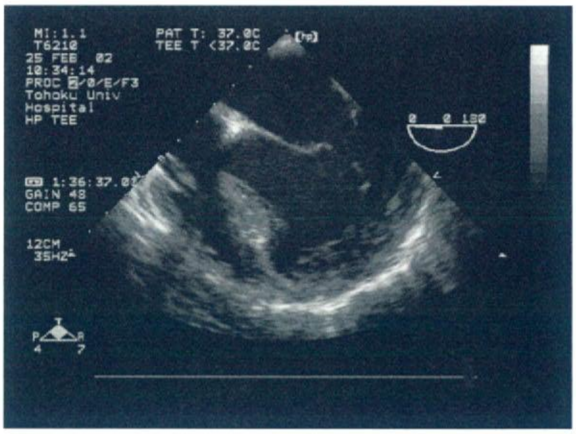

Fig. 6 Smoke-like echo disappeared after returning to sinus rhythm with DC conversion

One case with LVAD implantation showed dramatically improvement of LVEF (from 15% to 60%) at the three month but cardiac output of natural heart was almost zero at that time. One and half year after, the cardiac function was improved and LVAD exchange was operated without cardiopulmonary support.

One case which was successful for LVAD weaning, LV volume was fluctuated by the small difference of natural heart rate and LVAD heart rate.

IV. CONCLUSIONS

Transesophageal echocardiography is very useful for the assessment of cardiac function of the patients with LVAD implantation because it can detect and visualize what is happening in the heart immediately and directly.

Author: Yoshifumi Saijo
Institute: Department of Medical Engineering and Cardiology, Institute of Development, Aging and Cancer, Tohoku University
Street: 4-1 Seiryomachi, Aoba-ku
City: Sendai 980-8575
Country: Japan
Email: saijo@idac.tohoku.ac.jp

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Autonomic Nervous Activity Revealed by a New Physiological Index $\rho_{\max}$ Based on Cross-Correlation between Mayer-Wave Components of Blood Pressure and Heart Rate

Akira Tanaka[1], Norihiro Sugita[2], Makoto Yoshizawa[3], Yasuyuki Shiraishi[4],
Tomoyuki Yambe[4] and Shin-Ichi Nitta[4]

[1] Faculty of Symbiotic Systems Science, Fukushima University, Fukushima, Japan
(Tel : +81-24-548-8411; E-mail: a-tanaka@sss.fuskuhima-u.ac.jp)
[2] Graduate School of Engineering, Tohoku University, Sendai, Japan
(Tel : +81-22-795-7130; E-mail: sugita@yoshizawa.ecei.tohoku.ac.jp)
[3] Information Synergy Center, Tohoku University, Sendai, Japan
[4] Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan

Abstract: The authors have proposed a new physiological index $\rho_{\max}$ which is the maximum cross-correlation coefficient between blood pressure and heart rate whose frequency components are limited to the Mayer wave-band (0.04-0.15Hz). The advantages of this index are small individual difference and high reproducibility compared with other physiological indices which are calculated independently single cardiovascular measurements. The previous study showed that the index $\rho_{\max}$ is possible to assess visually-induced motion sickness. However, the relation between the proposed index and autonomic nervous activity has not been clarified yet. In this study, the change in $\rho_{\max}$ during sympathetic or parasympathetic blockage has been investigated in comparison with conventional indices in an animal experiment. The results have indicated that $\rho_{\max}$ does not have information on parasympathetic nerve activity but sympathetic one.

Keywords: heart rate, blood pressure, autonomic nerve function.

1. INTRODUCTION

In order to assess the biological effect of visual stimulation in terms of autonomic nervous activity, the authors have proposed a new physiological index $\rho_{\max}$ which is the maximum cross-correlation coefficient between blood pressure and heart rate whose frequency components are limited to the so-called Mayer wave-band (0.04-0.15Hz). The reason why only Mayer waves (10s period or 0.1Hz components; LF component) included in blood pressure and heart rate were used is the relationship between them can reflect the difference between the resting state and the exiting state caused by visual stimulation. The advantages of this index are small individual difference and high reproducibility compared with other physiological indices which are calculated independently from cardiovascular measurements [1]. Therefore the authors have introduced $\rho_{\max}$ for evaluation of the effect of visual stimulation. The previous study showed that the physiological index $\rho_{\max}$ is possible to assess visually-induced motion sickness more apparently than conventional indices such as the LF/HF of heart rate [1]-[3]. However, the relation between the proposed index and autonomic nervous activity has not been clarified yet. In this study, the change in $\rho_{\max}$ during sympathetic or parasympathetic blockage has been investigated and compared with conventional indices in an animal experiment.

2. METHODS

The proposed physiological index $\rho_{\max}$ was calculated as the following steps.

First, the beat-to-beat variables, heart rate *HR* [min^{-1}] and mean blood pressure *MBP* [mmHg], were interpolated by the cubic spline function to be time-continuous functions, and they were re-sampled every ΔT=0.2s. After that, each data was filtered through a band-pass filter with a bandwidth between 0.04Hz and 0.15Hz to extract the Mayer wave components.

Let k denotes the discrete time based on $t = k\Delta T$. For simple expression, let $x(k) = -MBP(k)$ and $y(k) = HR(k)$. The minus sign shown in $-MBP$ was introduced so that $x(k)$ and $y(k)$ might become as in-phase as possible for simple interpretation in depicted figures. The cross-correlation coefficient ($\rho_{xy}(\tau)$; the cross-correlation function normalized by root mean square values of input and output signals at lag time $\tau = k\Delta T$) from $x(k)$ to $y(k)$ was calculated time-discretely on the basis of 2min data (600samples) segmented by the Tukey window as follows:

$$\rho_{xy}(\tau) = \frac{\phi_{xy}(\tau)}{\sqrt{\phi_{xx}(0)\cdot\phi_{yy}(0)}} \tag{1}$$

where $\phi_{xx}(\tau)$ and $\phi_{yy}(\tau)$ are auto-correlation functions of $x(t)$ and $y(t)$, respectively, and $\phi_{xy}(\tau)$ is the cross-correlation function from $x(t)$ to $y(t)$. The maximum value of lag time τ was 10s (50samples). Furthermore, the maximum cross-correlation $\rho_{\max}$, i.e. the maximum value of $\rho_{xy}(\tau)$ for the positive τ, was obtained as

$$\rho_{\max} = \max_{0\mathrm{s}<\tau<10\mathrm{s}} \rho_{xy}(\tau) \tag{2}$$

3. EXPERIMENT

The goat used in the experiment weighted 50kg. The goat was anesthetized by halothane inhalation. After tracheal tube intubation by tracheotomy, the distal end was connected to a respirator. Electrodes for the electrocardiodiagram (ECG) were attached to the legs. Arterial blood pressure *BP* was measured with a catheter inserted into the artery through the left femoral artery. ECG and *BP* ware stored in a personal computer every 1ms.

After the control data was stored, atropine was injected in order to block parasympathetic nerve activity. Then propranolol was injected after physiological parameters returned to the same level as the control level.

HR was calculated from the reciprocal of the inter-R-wave interval of the ECG signal. *MBP* was obtained as the mean value of the pressure signal over one heartbeat .

CVRR, %RR50 which are known as the indices of parasympathetic nerve activity were calculated for each dataset which was segmented into 2min (600samples) 5min after infusion. %RR50 is defined as the percentage of normal R-R intervals that changed in absolute value by more than 50 msec from the previous interval. The CVRR is defined as the ratio of the standard deviation of the R-R intervals to their average value.

$\rho_{\max}$ was calculated time-discretely on the basis of 2min-long data segmented by the Hamming window from -1min to 1min.

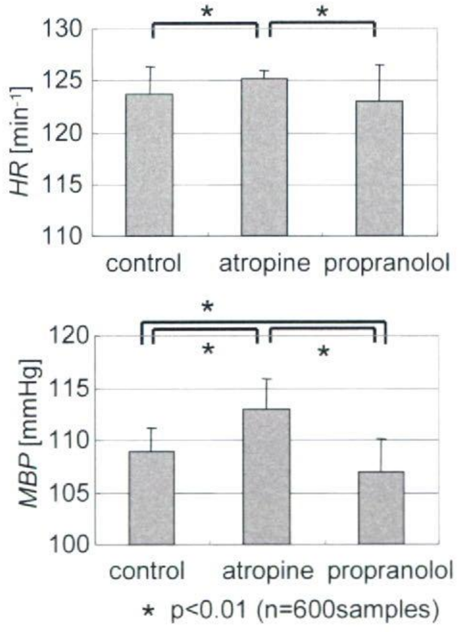

Fig. 1 Difference in physiological parameters within each condition.

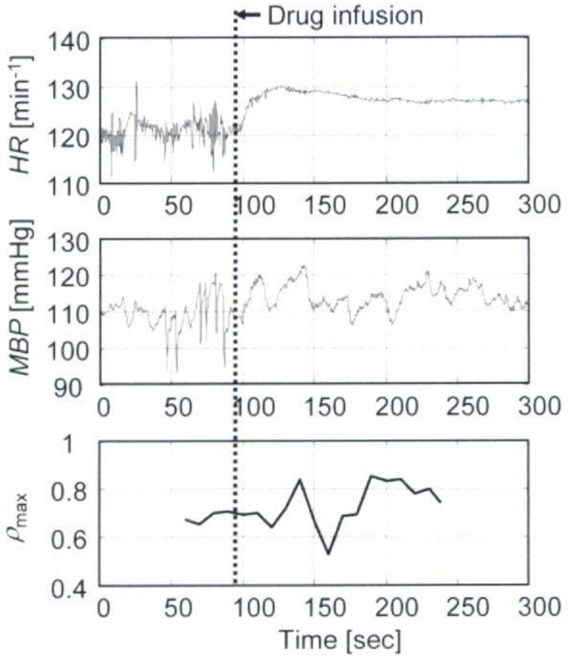

Fig. 2 Change in *HR*, *MBP and* ρ_{max} after atropine infusions.

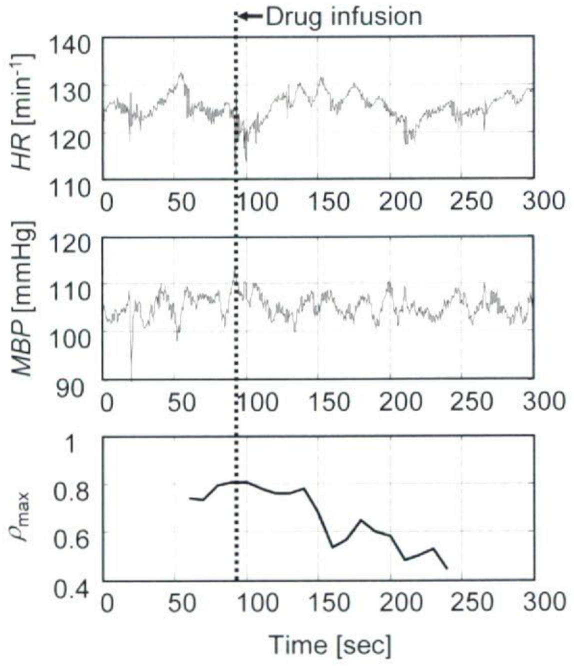

Fig. 3 Change in *HR*, *MBP* and ρ_{max} after propranolol infusions.

4. RESULT

Fig. 1 shows the changes in *HR* and *MBP* caused by drug infusions. *HR* and *MBP* increased significantly in atropine injection. On the other hand, *MBP* decreased

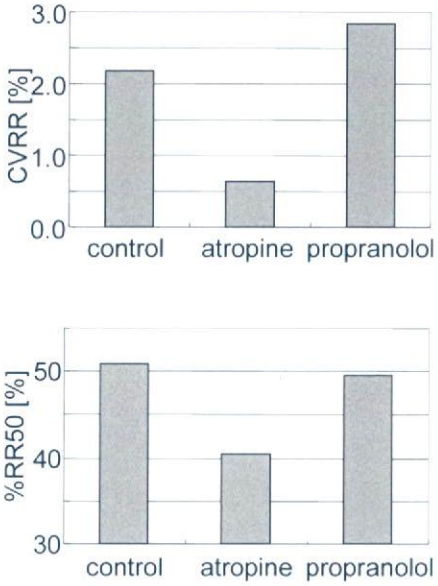

Fig. 4 Change in CVRR and %RR50 Difference in physiological parameters within each condition.

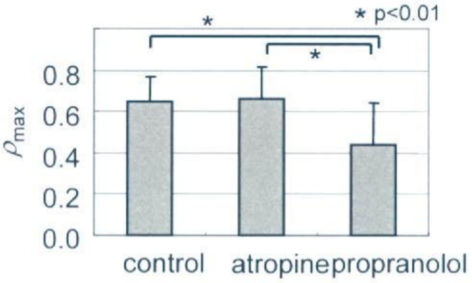

Fig. 5 Change in ρ_{max} after drug infusions.

significantly in propranolol injection. Fig. 2 and 3 show the transient response of *HR*, *MBP* and ρ_{max} to atropine and propranolol infusion, respectively. Atropine infusion makes *HR* increase and fluctuation of *HR* decrease. In atropine infusion, there is no specific tendency in ρ_{max}. On the other hand, it can be seen that ρ_{max} decreases after propranolol infusion.

Fig. 4 shows CVRR and %RR50 of each dataset segmented into 2min 5min after the drug infusions. CVRR and %RR50 decreased in atropine injection.

Fig. 5 shows the change in ρ_{max} after drug infusions. ρ_{max} significantly decreased in propranolol injection though there is no significant change in atropine injection.

5. DISCUSTION

The parasympathetic blockage caused decrease of CVRR and %RR50 which are known as the indices of parasympathetic nerve activity though there was no significant change in ρ_{max}. On the other hand, the sympathetic nerve blockage caused marked decrease in ρ_{max}. These results indicate that ρ_{max} represents the sympathetic nerve activity. In the authors' previous study, ρ_{max} and the LF/HF had different changes during visual stimulation though the LF/HF also represents sympathetic nerve activity. This seems to be because ρ_{max} includes the information on cardiovascular regulation via not only heart rate variability but also vascular regulation. Thus, it seems that vascular regulation mainly contributes to the change in ρ_{max} for physiological and/or psychological stimuli such as visual stimulation.

To clarify the effect of each of heart rate and vascular regulations upon ρ_{max}, the closed-loop identification using AR model [4] may be effective as well as the tifurther experiment using drugs which preferentially affect vascular regulation such as alpha blockers.

6. CONCLUSIONS

In this study, the basic characteristics of ρ_{max} previously proposed by the authors have been investigated by an animal experiment. It was shown that ρ_{max} is associated with the sympathetic nervous function.

Actually, the baroreflex system has multivariable feedback loops. However, analysis of ρ_{max} is based on the hypothesis that the system can be regarded as a single-input and single-output open-loop system. In further studies [5], therefore, we should compare the results of ρ_{max} with causal coherency functions used by Porta [6]. The causal coherency functions can divide linearity of the baroreflex system into two independent parts of linearity, i.e., the baroreflex arch and mechanical arch.

In further studies, it is necessary to evaluate the effect of each of heart rate and vascular regulations upon ρ_{max}.

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