1. Introduction

Pulsatility of the circulatory system had been believed to be essential in the living body before Nose et al. succeeded in keeping a calf alive for 90 days under the continuous flow condition with the centrifugal blood pump in 1978. Moreover, many kinds of continuous flow ventricular assist devices (VAD), the axial flow pump and the centrifugal pump have begun to be used clinically as a bridge to heart transplantation since 2000. Although many patients with the implanted continuous flow VAD can survive for more than a few years, their aortic flow has pulsatility by their own residual heart beat. So it is still an important controversial issue whether the pulsatility is essential or not for the living body in normal survival.

It would be very important to observe the micro-circulation to evaluate the necessity of pulsatility. However, there is no way to continuously observe the microcirculation without anesthesia in the animal model. We have been developing an implantable probe for a long-term observation of microcirculation since 1987. In this article, the authors would like to introduce the historic and the present status of the probe.

2. Materials and Methods

2.1. CCD Probe for the Contact Observation of Microcirculation [2–5]

The first idea to develop a probe was based on the following principle. As the integration of the CCD (charge coupled device) has been increasing due to the development of micro- and nano-technology, the authors thought that microcirculation could be observed without the lens like a contact photograph by direct contacting the living tissue with the CCD surface and lighting it from the back side of the tissue (Fig. 1). The micro-vasculature was projected on the TV screen by putting the rat mesentery on the CCD enveloped with a thin transparent film for electrical insulation. Then the first probe was developed in the following manner. A 0.5-inch CCD with 250 K or 400 K pixels was used in this study. As the CCD surface is 1.5 mm below the edge of the ceramic package after removal of its cover glass, a fiber optic plate (FOP), which is a 2 mm long integrated hexagonal core glass rod that could conduct an image from one end to another without distortion, was adhered onto the CCD surface to ensure a good contact between the tissue and the CCD surface. The residual gap in the ceramic package was filled up with room temperature vulcanized (RTV) silicone adhesive or epoxy resin, and the outside of the package, including the lead wires, was molded with epoxy resin to provide electrical insulation. A LED was fixed into the center of the CCD, 10 mm above the FOP with a specially designed micro-stand. Figure 2 shows a scheme of the probe. Figure 3 shows a photograph of subcutaneous connective tissue of a rabbit taken by this probe. An arteriole and venule with a diameter as small as 20–30 μm could be observed.

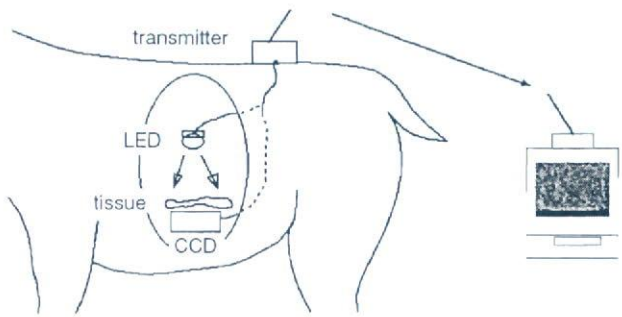

Fig. 1. The principle of the implanted probe to observe the microcirculation

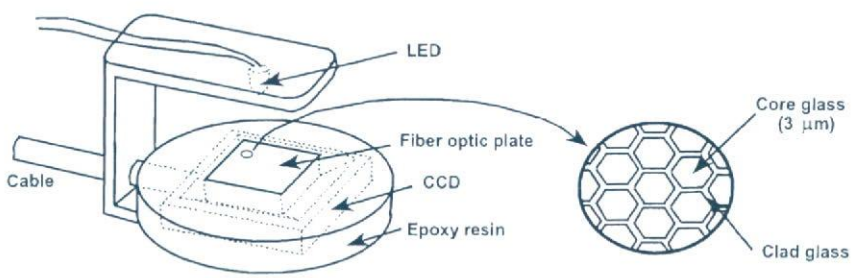

Fig. 2. Fabrication of the implantable probe using FOP

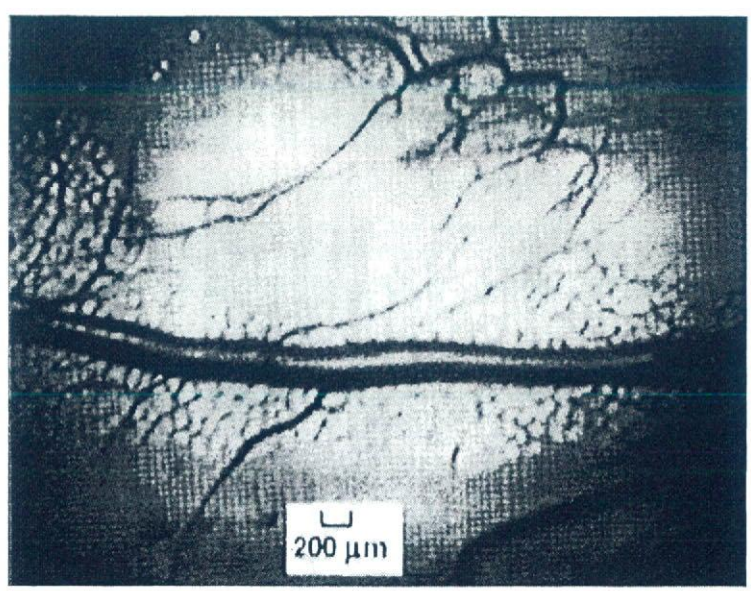

Fig. 3. Microvasculature of connective tissue in rabbit

A higher degree of magnification was required to observe the capillary circulation. A new probe used the tapered FOP, which could magnify the image 3 times, was designed as shown in Fig. 4. The tissue on the probe was magnified 165 times on the 14 inches TV screen. Figure 6 is a photograph of rat mesentery taken by this probe. The capillary vessels could be recognized with their circulation.

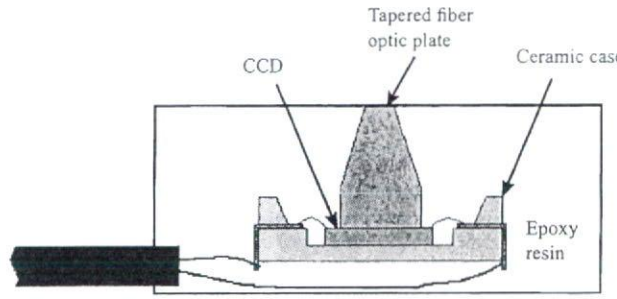

Fig. 4. Probe with a tapered FOP having 3 times magnification

2.2. Implantable Probe with a Micro-lens

One of the problems of the contact observation probe using the tapered FOP was a difficulty in getting a finely focused image in the case of the thickened tissue, such as omentum and fascia. A micro-lens system with a focus mechanism was required to be developed.

A single micro-lens with 4 mm in diameter and 4.2 mm long was made from acrylic resin. It is aspheric and has 3 times magnification. The lens was fabricated with the CCD camera as shown in Fig. 5. The distance between the objective and the lens and the lens and the CCD surface was 3 and 9 mm, respectively. The real magnification on the 14 inch TV screen was 165 times in the *in-vitro* experiment.

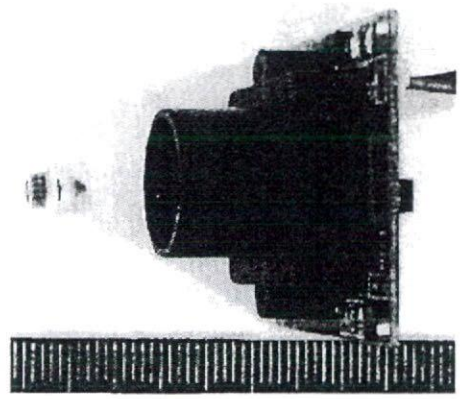

Fig. 5. The micro-lens and the CCD camera

Three types of focusing mechanisms, the screw type, the gear and cam type and the air bag type were tested. Figure 6 shows the screw type probe, in which the focus was adjusted by turning the stage. It was implanted into a goat as shown in Fig. 7. This goat was the first animal observing its own microcirculation. However, in this system, the focus could not be adjusted from outside the body after implantation. A gear train and a cam focus adjust system, in which the revolution number of the

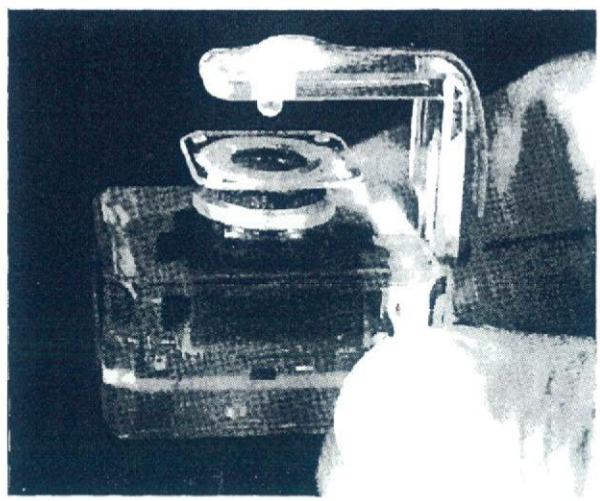

Fig. 6. The implantable probe with the screw type focus adjust system

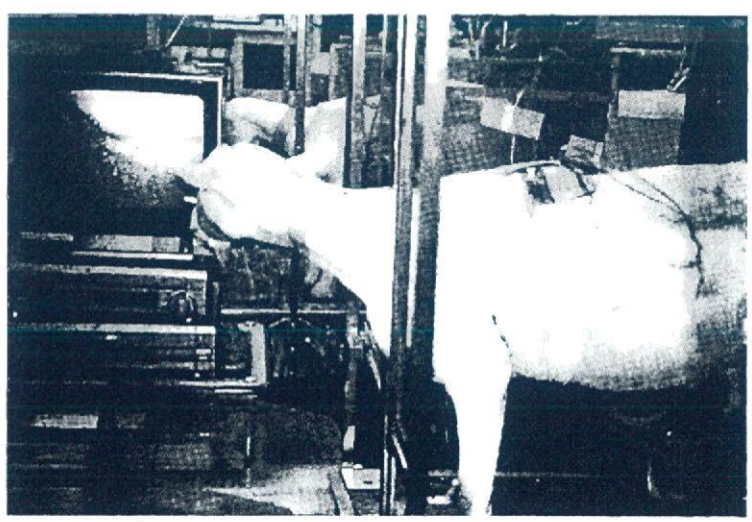

Fig. 7. The first goat observed its own microcirculation

micro-motor was reduced by the gear train and the cam control the focus position, was difficult to precisely adjust to the focus, and the size of the probe became big. The air bag type focus adjust system, in which the focus could move precisely by inflation and deflation of the air in the bag from outside the body, was the best from the view points of its accuracy and dimensions. The CCD with a driver and micro-lens was packed into an acrylic resin case (37x37x38 mm) with a thin transparent stage to put a living tissue on it. The air bag placed at the back side of the CCD unit, could inflate and deflate from the outer side and precisely change the distance between the lens and the stage for focusing. The probe was implanted into a rabbit, and subcutaneous connective tissue and/or fascia was fixed on the stage. A weak light from LED was projected from the backside of the tissue. The CCD image was sent out to the TV by a transmitter fixed on the skin. The flow of erythrocytes and leukocytes in the capillaries as well as in the arteriole and venula could be observed on the TV screen as shown in Fig. 8.

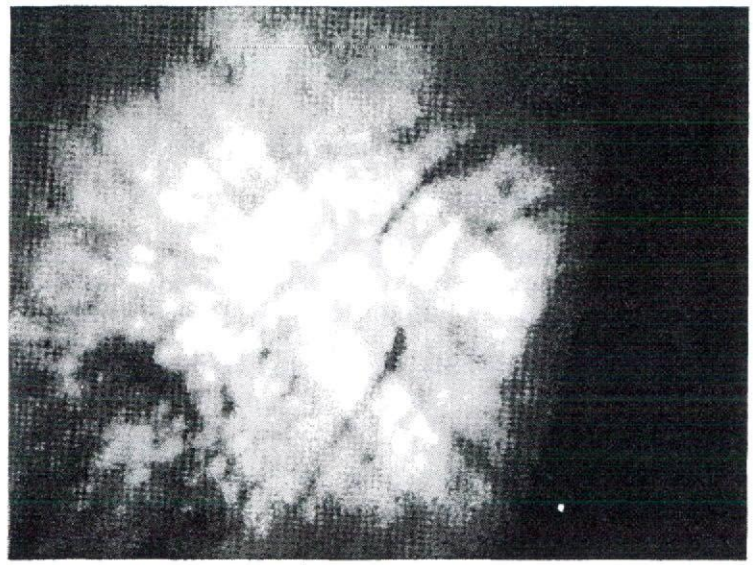

Fig. 8. Microcirculation in the fascia of the rabbit

2.3. Development of an Implantable Probe with a High Degree of Magnification

Although the capillary flow could be observed in the last model, its magnification and resolution were insufficient to analyze the erythrocyte speed, the diameter change in the arteriole. The size reduction of the probe is another important problem to be addressed in the long-term implantation in the animal model. A new probe with high magnification and of a smaller size was designed. A micro-lens having 2 mm in diameter, 2 mm long and 6 times magnification was designed, and it was made

of acrylic resin. The lens was installed into a CCD camera with 8 mm in diameter and 60 mm long (Fig. 9). The probe could magnify the image on the stage about 650 times on the 14 inch TV screen. An acute experiment was performed with a rabbit. The probe could be easily inserted. A distinct microcirculation image including the capillary flow could be observed when the camera was inserted into the subcutaneous connective tissue (Fig. 10).

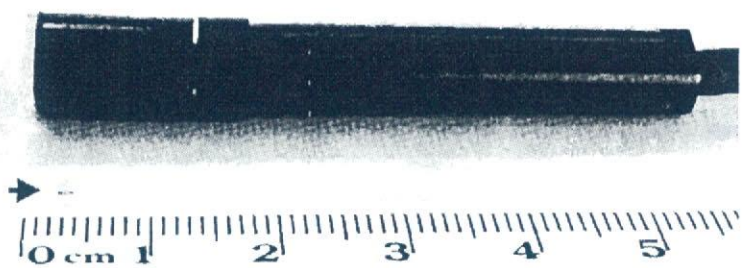

Fig. 9. The newly developed micro-lens (arrow) and the probe

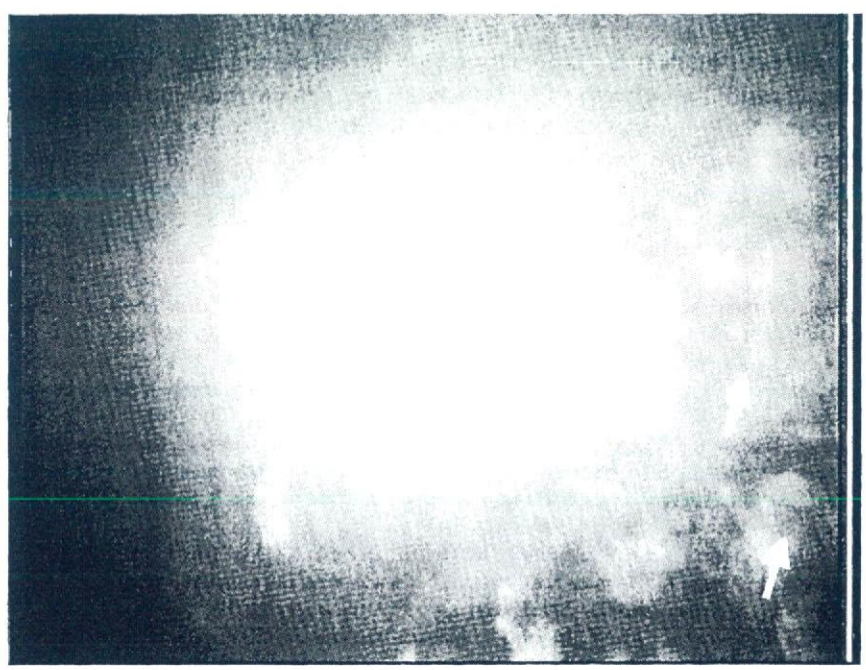

Fig. 10. Microvasculature of the rabbit subcutaneous connective tissue (Arrows shows a capillary vessel)

3. Discussion

It would be very important to clarify whether pulsatility of the blood flow is essential for the living body or not, because it would be the keypoint to develop the future artificial heart. One of the effective methods to prove it is to observe the microcirculation chronically and continuously without restriction of the behavior such as anesthesia. The authors have been developing an implantable probe to observe the microcirculation using a CCD camera. However, many obstacles such as pixel number of CCD, magnification and resolution of the micro-lens, focusing mechanism, light source and the total size of the probe had to be overcome. Magnification and the probe size were almost satisfactory to be implanted. The problems are associated with development of the micro focus mechanism and the illumination method. The micro-focus mechanism is being developed using a shape memory alloy. Our final goal is to observe the microcirculation not only at the thin and soft tissue like connective tissue but also at the parenchymatous organs such as the lung, kidney, liver, etc. For this purpose, it would be important to find out what kind of light (wave length, brightness, transmission or reflect, etc) should be projected.

4. Conclusions

Many types of implantable probes to observe the microcirculation were designed and evaluated. Although several problems such as the micro focus mechanism, light source and the resolution remain unsolved, its possibility to be completed in the nearest future has been proved.

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Nanotechnology in Artificial Organ Development and its Application in Diagnosis Methodology in Baroreflex Sensitivity of Patients with Hypertension

T. YAMBE[1,*], M. YOSHIZAWA[2], N. SUGITA[2], A. TANAKA[3], K. IMACHI[4]

[1] *Institute of Development, Aging and Cancer, Tohoku University, Sendai, Japan*
[2] *Information Synergy Center, Tohoku University, Sendai, Japan*
[3] *Faculty of Engineering, Fukushima University, Japan*
[4] *Tohoku University Biomedical Engineering Research Organization, Sendai, Japan*

Space in the human body is so limited that nanotechnology and micromachining technology are important for development of the internal artificial organs. Based on nanotechnology, development of various kinds of artificial organ has been conducted in Tohoku University, including artificial myocardium, artificial heart, rotary blood pump, artificial esophagus and artificial sphincter. Furthermore, automatic control algorithm for the artificial heart and assisted circulation was applied in the invention of the new diagnosis methodology for the baroreflex sensitivity of patients with hypertension. A successful clinical application of this new invention was made. Technical application of the large range of the developments is expectable in artificial internal-organs development.

K e y w o r d s: nanotechnology, artificial myocardium, rotary blood pump, baroreflex sensitivity, hypertension

1. Introduction

From the historical point of view, miniaturization of artificial internal organs has been one of the most important factors until now. Space in the human body is so limited that nanotechnology and micromachining technology are important in development of the internal artificial organs. Based on nanotechnology, various artificial organs have been p developed in Tohoku University, the including artificial myocardium, the artificial heart, the rotary blood pump, the artificial esophagus and artificial sphincter. These various artificial internal organs are based on the common base technology. Biocompatible nano materials are important. Transcutaneous energy transmission

* Correspondence to: Tomoyuki Yambe, 4-1 Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan, e-mail. yambe@idac.tohoku.ac.jp

systems using nanotechnology are also an important factor. In this paper, the recent progress of the artificial internal organ development is reported. Furthermore, automatic control algorithm for the artificial heart and assisted circulation was applied to the invention of the new diagnosis methodology for the baroreflex sensitivity of patients with hypertension. A successful clinical application of this new invention was performed. Technical application of the artificial internal-organ developments is expectable.

2. Artificial Internal Organs Using Nanotechnology

Based on nanotechnology, development various artificial organs has been performed in Tohoku University, the including artificial myocardium, the artificial heart, the rotary blood pump, the artificial esophagus and artificial sphincter.

2.1. Artificial Esophagus

Everybody knows that surgery of esophageal cancer is difficult because of the reconstruction of the esophagus after the resection of the carcinoma tissue. If there is an artificial esophagus, surgery will be simple and easy. Surgery with artificial esophagus will be feasible with only fiberscope.

In Tohoku University, the project on the artificial esophagus is ongoing [1]. Based on the achievements of the project, invention of the therapeutic stent, which has a therapeutic effect on the carcinoma tissue and the drinking function, is now under development. This therapeutic and drinking stent is easily inserted into the esophagus without any invasion. So this therapeutic and drinking stent was easily used for patients with the end stage esophageal cancer, which is not respectable.

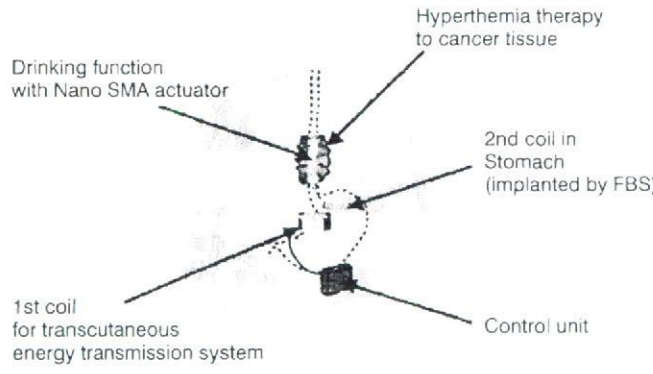

Fig. 1. Therapeutic and drinking stent for the end stage esophageal cancer

2.2. Artificial Myocardium

The final place which should be assisted is the myocardial contraction after a complete surgical repair. Even after complete revascularization of the coronary artery and a complete repair of the heart valve, cardiac output cannot be maintained when the contraction power is insufficient. An artificial myocardium system was invented in Tohoku University by the use of nanotechnology [2]. This system consists of various kinds of nanotechnology units, including the surface finishing technology, several kinds of nano sensors, .nano mictotip PC, and TETS with nano tech.

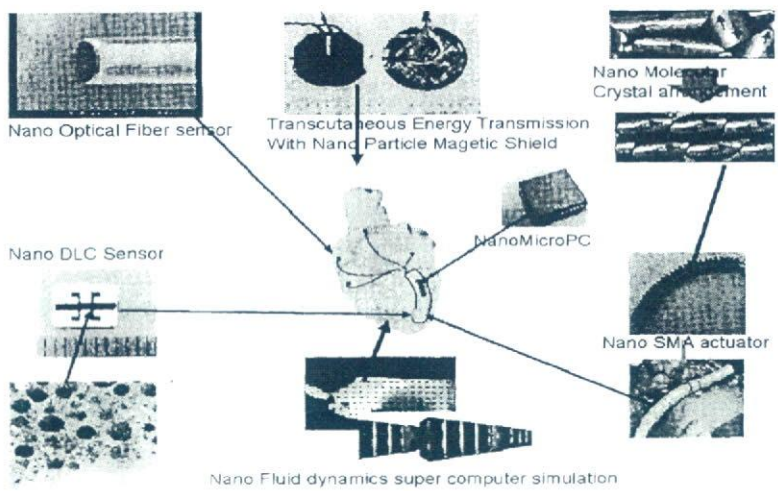

Fig. 2. Artificial myocardium

2.3. Artificial Heart

By the use of nanotechnology, an artificial heart system using the Undulation Pump system has been developed in Tohoku University. This system consists of various kinds of nanotechnology items, the including surface finishing technology, several kinds of nano sensors, .nano mictotip PC, and TETS with nano tech. The control logic for the artificial heart and the artificial myocardium needed the system identification, so this logic might be useful for the diagnosis of the circulatory condition of the patients.

3. Baroreflex Sensitivity of the Artery in the Patients with Hypertension

A system identification is required for the automatic control of the artificial heart and the artificial myocardium. The system identification is useful for the diagnosis of patients with circulatory diseases.

Metabolic syndrome attracts attention as an important pathophysiology item in Japan [3]. Hypertension is one of the important elements which constitute the Metabolic syndrome. In a healthy human body, even if the blood pressure rises, the heartbeat decreases reflectively, the blood vessel relaxes and the blood pressure is lowered. However, this reflective function fails in the hypertensive patient [4–5]. It is known that the baroreflex function is insufficient or weak especially in the case of youth hypertension [6–7].

In order to diagnose the function of baroreflex, there are some diagnostic methods. For example, there is the method of calculating from the reaction of the heartbeat to blood-pressure change. No method of diagnosing the baroreflex function of a blood vessel existed at all.

We invented the first method of diagnosing the baroreflex function of a blood vessel. This new diagnostic method is outlined in this paper. The equipment which diagnoses the baroreflex function of a blood vessel does not exist in all in the world. This is because the method of measuring the elasticity of a blood vessel by the noninvasive method is difficult. Then, we paid our attention to the pulse wave transmission time (PTT) and the pulse wave velocity (PWV).

PTT and PWV are dependent on the elasticity of the arterial wall. According to the increase of the arterial wall elasticity, PWV will become increased. This phenomenon was applied, and the methodology which measures the baroreflex function of a blood vessel was invented from PWV information. The conceptual diagram of the system is shown below.

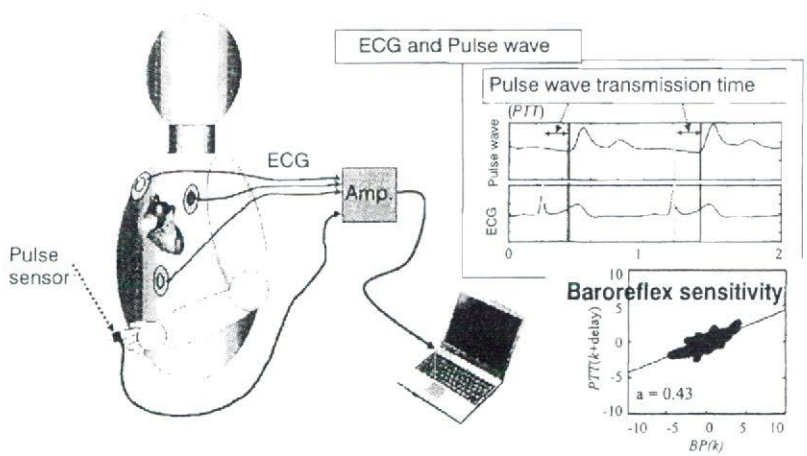

Fig. 3. Baroreflex sensitivity evaluating system

In this system, the measurement parts are only the pulse wave and the electrocardiogram. Cardiophonogram may be used for substitution of the electrocardiogram. The arm, the wrist, or the ankle are sufficient as the measurement part of the pulse wave. The data will become exact if loads, such as conversion of the posture and injection of the medicine, are added. Diagnostic measurement is possible even if there is no load.

The acquired time series information is input into a personal computer through an AD converter. Quantification and statistics processing are calculated. The time series of the cardiac contraction is measured from the R wave of the electrocardiogram or two sound of the cardiophonogram. The RR interval is changed into the Y-axis. The wave by which the smoothing was carried out by the Spline interpolation is re-sampled in 200 ms. As for the digital data, by which the discrete sampling was carried out, the frequency analysis is performed. Fluctuation of each time series curve is calculated. The delay time with the greatest correlation is calculated from the cross-correlation of the obtained time series. By this means, the influence that a change of blood pressure produces on the elasticity of the blood vessel will be calculated. The X axis is set as the change of the blood pressure, and the Y-axis is set as PWV or PTT after the delay time with the greatest correlation. The regression straight line is computed using the method of the least square. The methodology which adds a band pass filter to the time series curve and enables to observe the Mayer wave around 0.1 Hz is sufficient.

An example of the cross-correlation of the systolic blood pressure time series and the pulse wave transmission time series is shown in Fig.4.

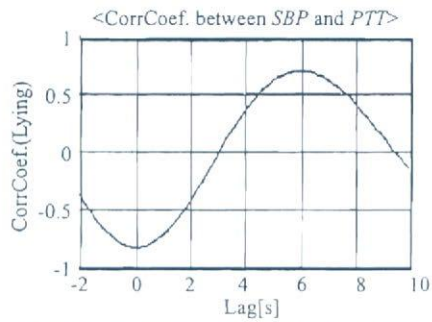

Fig. 4. Cross correlation of the SBP and PTT

In this example, the greatest cross-correlation in the delay time around about 6.0 seconds is observed. Then the pulse wave transmission time after the blood-pressure change and the delay time of the maximum correlation was plotted.

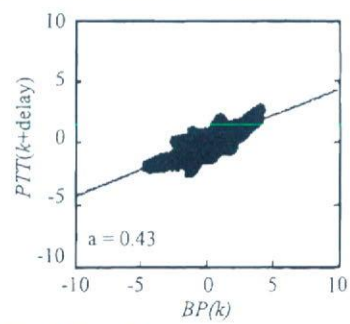

Fig. 5. Baroreflex sensitivity of the artery

The result by which a significant correlation was observed showed that blood-pressure change changed the blood vessel elasticity, reflectively. The regression straight line was calculated by the method of the least square. The sensitivity of the baroreflex function of the blood vessel can be calculated from this result. In the case in which the blood pressure is high, the baroreflex function of the blood vessel showed a falling tendency.

Previously the method of calculation of the baroreflex function of a blood vessel did not exist. We invented the method of calculation of the baroreflex function of the blood vessel from information processing of the blood pressure and the pulse-wave propagation time. The correlation analysis showed a changing PTT according to the blood-pressure change after several seconds.

From the regression straight line, it is expected that the sensitivity of the reflective function of the blood pressure is calculable. From now on, collection of cases can be performed after their examination by the Ethics Committee of the appropriate hospital.

Acknowledgments

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Restructuring of myocardium using shape memory alloy fibres

Yasuyuki Shiraishi[a], *Tomoyuki Yambe*[a], *Dai Homma*[b]
[a] Institute of Development, Aging and Cancer, Tohoku University
4-1 Seiryo-machi, Aoba-ku, Sendai 980-8575, Japan
shiraishi@idac.tohoku.ac.jp
[b] Toki Corporation, 3-43-15 Ohmori-kita, Ohta-ku 143-0016, Tokyo, Japan

Background and objectives

Recently, the ventricular assist devices are widely applied for a surgical treatment of the final stage of severe heart failure as the bridge to heart transplantation or the destination therapy. However, it was anticipated that the artificial components in the ventricular assist devices might cause the problems concerning thrombosis and infection. As heart failure involves the decrease in myocardial contractile function, the mechanical assistance by using an artificial myocardium might be effective. The authors have been developing a mechano-electric artificial myocardial assist system (artificial myocardium), which is capable of supporting natural contractile function from the outside of the ventricle. The system was originally designed by using sophisticated covalent shape memory alloy fibres (Toki Corp., Biometal®), and no special surface modification of the device was not applied for enhancing blood compatibility. The purpose of the project on the development of an 'intelligent artificial myocardium' was to design a sophisticated myocardial assist device, which could represent direct mechanical myocardial assistance in response to physiological demand.

Structural design for functional improvement

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 um, and moreover the structural design was examined for its functional improvement. The authors investigated the myocardial structure in native hearts, and fabricated several types of myocardial assist device based on these results; the circumferential type, and the oblique types which were three-dimensionally constructed. Their hydrodynamic or hemodynamic functions were also examined in a mock circulatory system as well as in animal experiments using goats.

Results

The structure of myocardial fibers of a goat's heart could be represented by a single muscular band [1]. The oblique design of the myocardial assist device was made to form the contractile streamlines from the apex to ascending aorta. Basic characteristics and hemodynamic effects of the circumferential or oblique types were examined in goat experiments (n=4) as well as in the mock circulatory system. The results were as follows:

a) In the hydrodynamic test using the mock circulatory system, the volume assisted which was elevated by 39% by morphological design.

b) Hemodynamic data obtained in goats indicated the more effective volumetric assistance by the oblique design, and on the other hand there was no significant difference in systolic assisted pressure.

Therefore, it was suggested that the morphological design of artificial myocardial support system could be more effective for the functional improvement of artificial myocardium as well as its control system design.

Figure: Oblique type of artificial myocardium (bottom right), which was girdling the goat's ventricle designed from the native myocardial structure (bottom left), might be more effective.

Reference:

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心室と心不全のメカニクスモデリングに基づく人工的心筋補助の試み

白石　泰之*　　山家　智之　　西條　芳文　　柴田　宗一（東北大学加齢医学研究所）
増田　信也　　田林　晄一（東北大学心臓血管外科）
梅津　光生（早稲田大学理工学術院）　本間　大（トキ・コーポレーション）

Artificial Myocardial Assistance using the Sophisticated Shape Memory Alloy Fibre Based on Engineering Approach for Cardiac Mechanics

Yasuyuki Shiraishi*, Tomoyuki Yambe, Yoshifumi Saijo, Muneichi Shibata,
Shinya Masuda, Koichi Tabayashi (Tohoku University)
Mitsuo Umezu, (Waseda University), Dai Homma, (Toki Corporation)

Abstract

The authors have been developing a mechano-electric artificial myocardial assist system (artificial myocardium), which is capable of supporting natural contractile function from the outside of the ventricle. 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 um, and moreover the structural design was examined for its functional improvement. The authors investigated the myocardial structure in native hearts, and fabricated several types of myocardial assist device based on these results; the circumferential type, and the oblique types which were three-dimensionally constructed. Their hydrodynamic or hemodynamic functions were also examined in a mock circulatory system as well as in animal experiments using goats.

キーワード：心筋構造，形状記憶合金線維，人工心筋，循環補助，血行動態
(Keywords: myocardial structure, shape memory alloy fibre, artificial myocardium, ventricular assist device, hemodynamics)

1. はじめに

心臓が全身の臓器の需要に見合う充分な血液量を駆出できない場合や、または血液拍出が充分であっても心室充満圧が上昇する場合、内科的にもしくは外科的に治療がなされる(1)。現在、このような心不全状態がとくに重篤であれば、心臓移植を最終手段として、補助人工心臓を用いた循環の補助が行われる。しかしながら医用アクチュエータとして人工的補助循環に用いられるシステムは、主として血液との直接的な接触によってポンプ機能を代替するものであり、自己化した組織でない人工物と接することによって促進される微小血栓による梗塞形成の問題が臨床応用時には懸念されている。

病的に心室壁の局所または心臓全体のサイズが拡張した心不全治療の外科的なアプローチの方法として、心臓の収縮形態を外科的に再形成し、正常な心室壁形状に構築し直

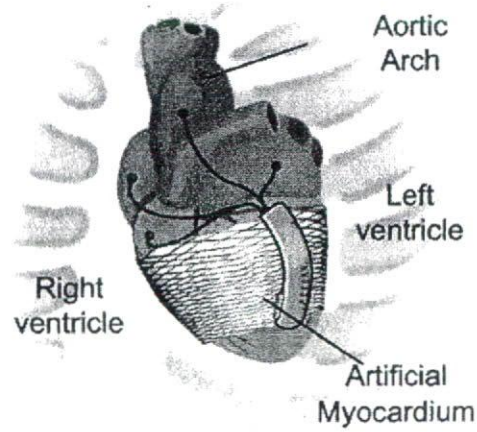


図1　微細径形状記憶合金線維を用いた人工心筋の構成
Fig. 1　Schematic drawing of the myocardial assist device developed

すことによって心室内腔容積を縫縮させる手技や、静的に心臓の過拡張を妨げる人工物によって心室壁の挙動範囲を制限する方法などがこれまでに開発され、臨床に応用されている。しかしながら、これらの手技や方法によって心室メカニクスの本態的な変化がどのように生じるのかは、未だ詳細は解明しておらず、臨床現場においても多くの検討がなされている[2]-[6]。

心不全によって引き起こされる血液拍出機能低下の本質は、心臓を構成する心筋の収縮能の低下であり、その治療メタコンセプトは心臓の収縮機能を改善させることにあると考えることができる。そこで筆者らは、これまで生体心筋の収縮を力学的にサポートする人工心筋開発を進めている[7]。このシステムは心臓の収縮を外部から力学的にサポートし、生体および機械の制御系とを統合することによって必要なときに必要なだけ血液拍出機能を支援するものである。現在開発中の装置では、微細形状記憶合金線維を用いたユニットを構成し、それらを組み合わせることによって自然心臓の収縮によく似た人工的補助を実現することを設計目標としている（図1）[8][9]。その駆動原理のため、血液と人工物との直接接触がなく、したがって溶血や血栓形成の問題がない。本研究では、これまでの開発研究の成果をふまえ、さらに生体との力学的親和性の高いシステムを設計するため、生体心臓の形態学的構造に似た収縮走行方向を有する装置の開発を試みた。

2. 方法

〈2·1〉 生体心臓の構造と心筋走行 ポンプ機能の異なる二つの心室から構成される生体心臓は、一つの心筋バンドに展開することができる[10]。図2は健常成山羊の心臓を摘出後、心臓壁層を心筋の走行に沿って剥離展開したものであるが、大動脈から肺動脈に至るまで複雑なねじれ構造を持ちながらほとんど単一の方向性を有するバンド状の心筋相から構成されていることがわかる。

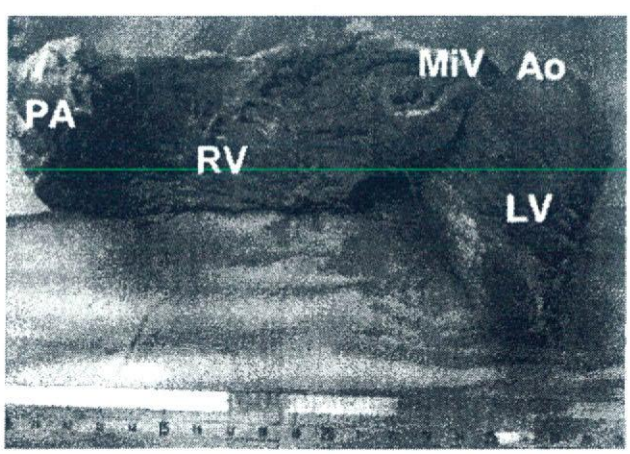


図2 健常成山羊摘出心の心筋バンド展開

Fig. 2 A goat's heart showing the ventricular myocardial band dissection which was unfolded by Torrent-Guasp's procedure

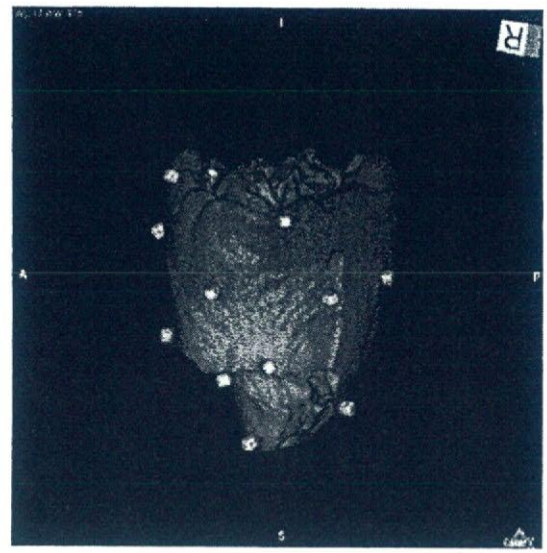


図3 MDCTを用いて3次元構成した摘出展開山羊心臓（白色の点は心筋層に縫合された樹脂製マーカで、心筋バンド中央及び端部をそれぞれ示したもの）

Fig. 3 Numerical reconstruction of the goat's heart from the data measured by MDCT; the white-coloured plastic markers indicated the centre and the edges at each portion of myocardial band unfolded.

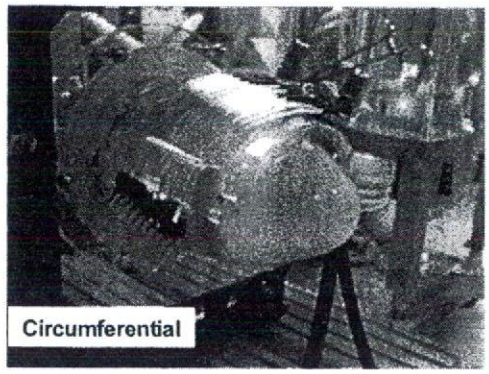
さらに、この摘出心の走行構造を明らかにするため、樹脂製のマーカを縫合し、再構成した心臓構造をMDCTを用いて計測した（図3）。

〈2·2〉 3次元的収縮を実現する人工心筋装置と基礎特性 上述の心筋走行に関する知見は、通常左開胸下で観察される心臓全体の収縮期の挙動と一致しており、人工心筋による補助時にもこれらの収縮方向を考慮することが有効であると考えられたため、(a)従来の左室短軸に沿った収縮装置、(b)左室の収縮方向に対して可変角をもたせた収縮装置、(c)左室壁の心筋走行に沿う人工心筋走行とした収縮装置の3種類を試作した。またこれらの装置による駆出性能を定圧負荷の水力学的試験回路を用いて計測し、駆出サポートによる収縮期の流量補助量の基礎データを取得し比較した。

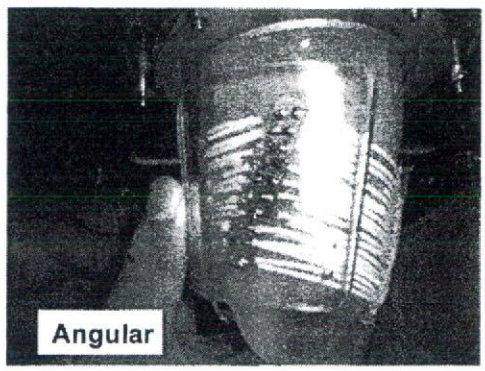
〈2·3〉 動物実験による生体心筋走行を模擬した人工心筋装置の血行力学的効果の基礎検討 試作した人工心筋装置について、健常成山羊（体重50kg）の心臓に装着し、心臓外部からの収縮支援による効果を血行力学的に調べた。なお、本研究で実施した動物実験はすべて東北大学加齢医学研究所および東北大学大学院医学系研究科の動物実験倫理委員会の審査を受け、定める規則に厳密に則って行われたものである。

3. 結果

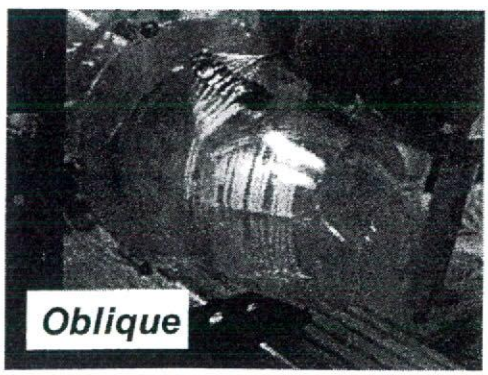
〈3·1〉 **試作した人工心筋装置**　CT などの計測結果に基づいて試作した人工心筋装置は図 4 に示すごとくである。シリコーン製左心室モデルに対して装着し、いずれも過度な変形など認められなかった。



(a) 従来型(circumferential-type)



(b) 可変角度型(angular-type)

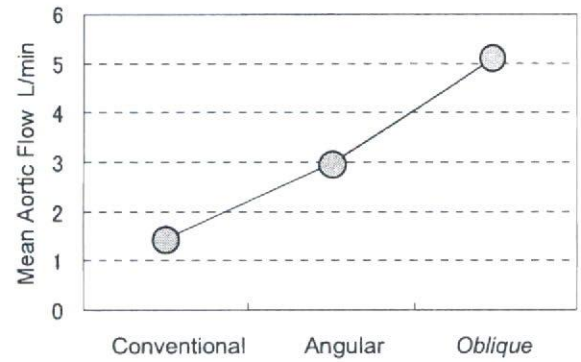


(c) 斜方収縮型(oblique-type)

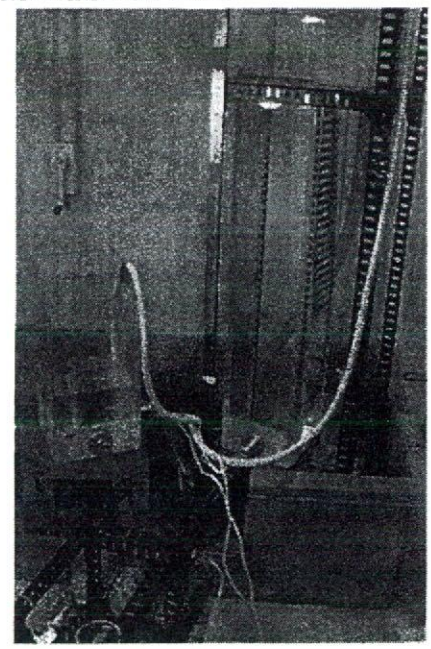
図 3　シリコーン製左心室モデルに装着された、試作した 3 種類の人工心筋装置

Fig. 3　Three different types of prototype models for the artificial myocardial support, which were attached on the silicone left ventricular model.

〈3·2〉 **水力学的試験結果**　図 4 は、シリコーン製左心室モデルおよび水力学的試験によって得られた人工心筋装置収縮期の単位時間あたり駆出量を比較しまとめたものであるが、自然心臓の心筋走行の走行に沿った収縮補助形態の装置（Oblique-type）では、従来形状のもの(circumferential-type)に比べて約 3 倍の駆出効果を得ることが示された。



(a) 左心室モデルを用いた収縮期駆出量の比較, comparison of systolic output obtained in the hydrodynamic test circuit indicated in (b) by using the silicone left ventricular model.



(b) 定圧負荷駆出流量試験装置; hydrodynamic test circuit for the examination of output by the contraction of three types of myocardial assist devices

図 4　3 種の収縮補助装置の水力学的試験

Fig. 4　Hydrodynamic test circuit with the silicone left ventricular model which is capable of simulating arterial pressure loading.

〈3-3〉 動物実験による血行力学的効果の基礎検討　いずれの収縮補助形態を用いても心臓周囲の臓器に圧迫を起こすといった空間容積的な問題は観察されなかった。図5従来型(circumferential)と斜方型(oblique)は動脈圧および大動脈基部流量を比較したものであるが、心筋走行に沿う形態での収縮サポートを行うことにより、収縮補助率は約1割の増大が得られることが示された。一方、収縮支援による収縮期圧の人工心筋装置非駆動時に対する上昇率は大きな違いは見られず、斜方形態の収縮によって心室駆出容量補助が有効に行われたことが示された。

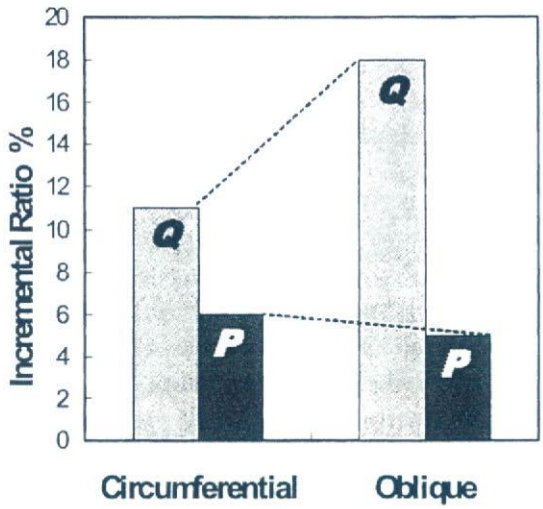


図5　収縮支援形態の違いと非駆動時と比較した圧流量駆出率変化

Fig. 5　Comparison of incremental ratios in cardiac output and systolic arterial pressure between the circumferential and oblique-type myocardial assistance obtained in a goat.

4.　まとめ

生体心臓の心筋の走行を解剖学的に調べ、有効な心筋収縮補助を行える人工心筋アクチュエータの設計を試みた。微細形状記憶合金線維を用いた人工心筋によって、充分な血液拍出をサポートしつつ生体心臓と力学的整合性の高いシステムを具現化するために、装置の形状と機能の制御のみならず、負荷側の生体心臓のメカニクスを考慮した設計が必要であることが示されつつある。多くの医用アクチュエータは、人工物の機能を強力かつ工学的に高機能にすることで、生体機能を超えた人工的なサポートを実現している。図6は左室形成術前の心室瘤をMRIデータを元に作成したものであるが、現実には、このような個別の病態に対応して外科治療戦略の一選択肢として有用なシステムの開発が望まれる。臨床現場でのシステム自体の柔軟性を保持しながら、生体－機械のアフォーダンスを具現化する人工

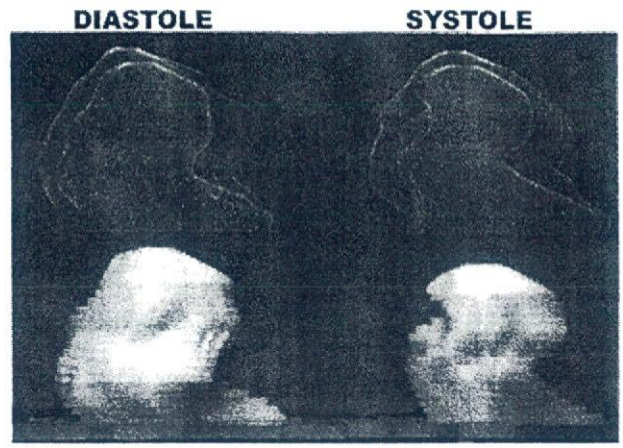


図6　左室瘤形状のモデリング例：術前評価データの数値再構築（上）および内腔形状モデル（下）

Fig. 6　An example of iastolic and systolic structure calculated from a patient's preoperative MRI measurement of ventricular aneurysm (upper) and their plastic modelling sculptured (bottom) for the preparation of ventriculoplasty.

心筋システム開発が必要であると考えられ、国産の微細機能材料成形加工技術を応用した新しい医用アクチュエータとして今後の設計開発の展開がおもしろいところである。

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心臓収縮を補助する新しいアクチュエータ

白石　泰之[1]，山家　智之[1]，西條　芳文[2]，梅津　光生[3]，馬場　敦[4]
羅　雲[1]，鄭　徳泳[1]，Telma Keiko Sugai[5]，吉澤　誠[6]，藤本　哲男[4]，本間　大[7]
東北大学加齢医学研究所[1]，東北大学大学院医工学研究科[2]，早稲田大学先端生命医科学センター[3]，芝浦工業大学[4]，東北大学大学院工学研究科[5]，東北大学サイバーサイエンスセンター[6]，トキ・コーポレーション[7]

A sophisticated mechanism for an artificial myocardial assist device

Yasuyuki SHIRAISHI[1], Tomoyuki YAMBE[1], Yoshifumi SAIJO[1], Mitsuo UMEZU[3], Atsushi BABA[3], Yun Luo[1], Dukyoung JUNG[1], Telma Keiko SUGAI[1], Makoto YOSHIZAWA[1], Tetsuo FUJIMOTO[3], Dai HOMMA[4]
Tohoku University[1], Waseda University[2], Shibaura Institute of Technology[3], Toki Corporation[4]

1. 緒言

これまでの重症心不全の治療に対する外科的治療方法には，左室形成術，補助人工心臓などがあり，近年では，組織工学的手法を応用した心筋再生も現実的な治療方法となりつつある．本研究では，心不全の本質が心筋自体の収縮機能の低下にあることに着目して，収縮拡張機能を力学的に心筋外部から補助するシステムの開発を進めている．これは，極細の形状記憶合金線維を応用したもので，アクチュエータ要素の線維はおおよそ 10 億回以上の収縮弛緩繰り返し耐久性をもち，100 マイクロメートルの直径の線材単体で生体心筋収縮に対して約 1000 倍のオーダの張力を発生することができる．要素機能は収縮のみであるが，モータなどのもつシステム微小化に関わる寸法効果の問題がなく，さらに高度な可制御性を有するため循環補助要素として種々の応用が可能であると考えている．

2. 人工心筋の構造と機能

ポンプ機能の異なる二つの心室から構成される生体の心臓は，一つの心筋バンドに展開することができる．図 2 は，健常成山羊の心臓を摘出後，心臓壁層を心筋の走行に沿って剥離し展開したものである．このように解剖学的には，大動脈から肺動脈に至る複雑なねじれ構造を持ちながらほぼ単一の収縮方向性を有する帯状の心筋層から構成されている．さらに，生体心臓では，図 3 に示すように，wall-thickening effect と呼ばれる収縮時の心筋層の厚みの増加が観察される．微細形状記憶合金線維をアクチュエータとして人工心筋を構成する際に，これらの生体心臓の構造と機能的特長を機械的に再現することを試みている．図 4 は，心筋層の走向の解析に基づく人工心筋による力学的支援を模擬循環回路において再現したものであるが，水力学的には，心筋走向と方向が合致した左心室収縮の補助によって，有効な血行力学的支援

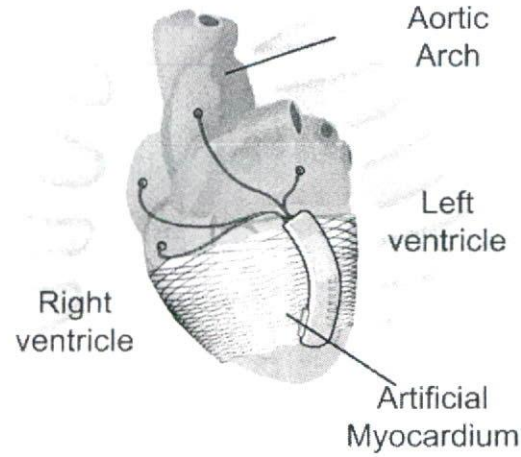

図 1　人工心筋バンドによる力学的循環補助の模式図；心臓の壁面外部に装着し，心筋収縮をサポートする．

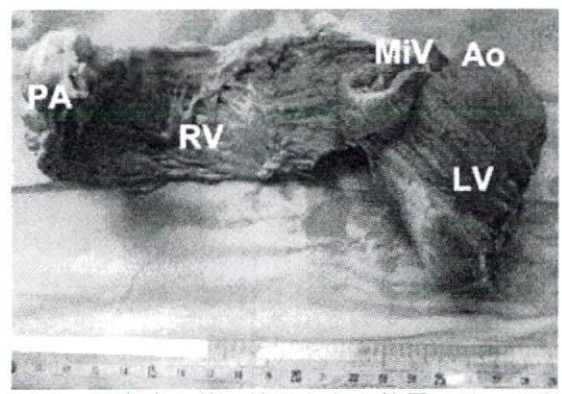

図 2　健常成山羊の摘出心を心筋層に沿って剥離展開したもの；左室心筋層が心尖部から大動脈基部に向かって約 45° で走向する．

が行えることが示唆されている．さらに，これらを機械的に再現することのできる新たな構造を開発し，図 5 に示すように人工心筋バンドに構造的に付加し，成山羊を用いた動物実験においてその効果を確認しつつある．

3. 結果及び考察

これらの人工心筋の形状と機能は，充分な血行力学的補助を実現するとともに，胸腔内の限られた空間の中に埋め込まれ，心臓及び他の臓器に対する障害となってならない．そのため，長期使用を前提とした動物実験を行い，開発した人工心筋による血行力学的補助効果の検討に加えて，組織病理学的検討も併せて進めている．図 4 に示した構造では，水力学的には最大約 5L/min の平均駆出が可能であり，急性動物実験では，補助時の心拍平均で約 18%の平均流量の増加が観察された．また，図 5 に示す構造を付加した人工心筋バンドでは，従来形状のものと比較して約 2.8 倍の補助増加率が得られている．

4. まとめ

医工学技術を駆使した人工心筋を構築することで，必要なときに制御可能で，血行力学的に有効な補助が行える機械式人工心筋のアクチュエータを開発した．これまで重症心不全の補助循環治療に用いられてきた人工心臓などに関わる血栓形成や微小梗塞の生成といった問題は少ない装置であるが，生体心臓を介して血流に有効な外力を伝達するメカニズムを応用するには，心臓の収縮拡張能を妨げることなく，また組織学的損傷を引き起こすことなく心臓外部に適正に装着されなければならない．さらに，これらの人工心筋による収縮機能は，自律神経系によって制御される心臓血管系の状態に影響を及ぼすことが考えられ，循環補助効果を得るだけではなく生体制御系との整合を詳細に検討するシステムの開発が必要である．現在，慢性実験によってこれらの評価を進めつつあるが，アクチュエータ自体の体積が小さく高効率で収縮を補助できる人工心筋システムによって，新たな補助循環に対するアプローチとなる可能性もあり，今後の研究の展開が楽しみなところである．

4. まとめ

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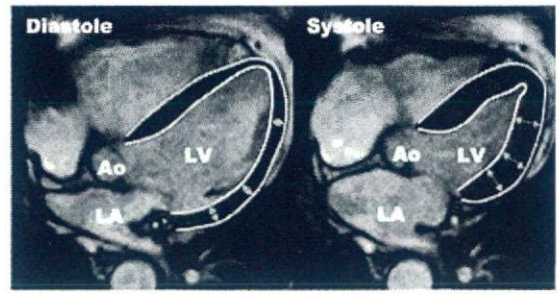

図 3　健常生体心臓で観察される心臓収縮時の壁厚増加（左：拡張期，右：収縮期）；収縮時には有効な血液拍出が行われる．

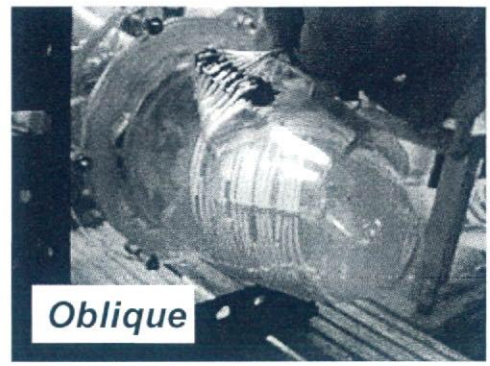

図 4　模擬循環回路のシリコーン製左心室モデルに装着された人工心筋バンド（Oblique 型）；心尖部を囲み心室壁長軸に対して斜方に固定設置される．

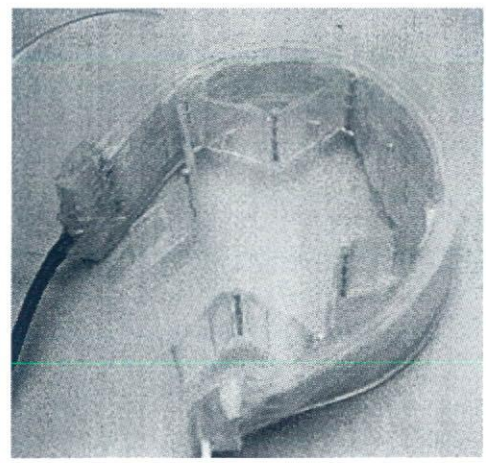

図 5　心筋バンドに付加された人工心筋の収縮による効果を増大させる構造

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