Deevelopment of an Artificial Internal Organs and the New Diagnosis Tool of Pulse Wave

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1. Introduction

The Aim of the research in the Medical Engineering field is the development of the new diagnosis tool and therapeutic tools for the medical fields. One example of the research theme is an artificial internal organs based on Nano-technology. As for an implantable type artificial organ, a space for implantation is restricted. Therefore, micro device development is indispensable. 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. Various artificial organ project in Tohoku University are introduced.

2. Artificial Internal Organs for Digestive Tracts

2.1. Totally implantable artificial sphincter

After the surgery of Colon Cancer, several patients must have Stoma.. And they cannot control the defecation by themselves. So, it is not so good for their quality of Lofe(QOL). The artificial sphincter that we invented makes it possible for a patient to control defecation. Therefore, we used the shape memory alloy. Two boards of a shape memory alloy were combined. Energy was transmitted by the transcutaneous energy transmission system (TETS). Figure 1 is a photograph of the animal model of the stoma. When a patient goes to a toilet, a patient brings TETS. An artificial sphincter opens and enables a patient to defecate. A patient can control defecation if this system is used. Thus, a patient's QOL will be improved greatly.

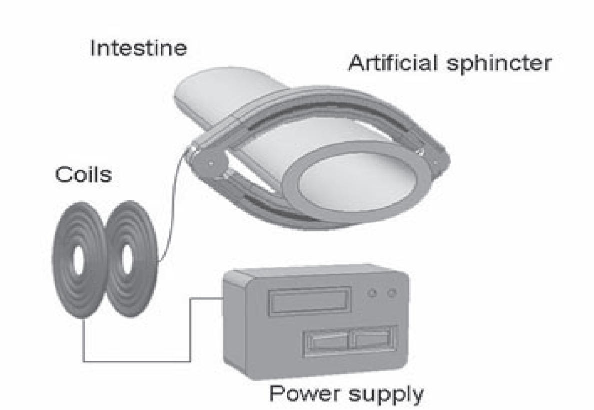

Fig. 1. Schematic illustration of an artificial sphincter

2.2. Artificial esophagus

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. The Gore Tex artificial vascular graft was used as a material which suits a living body. Man'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. 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 movement brings big progress to esophagus cancer surgical therapy.

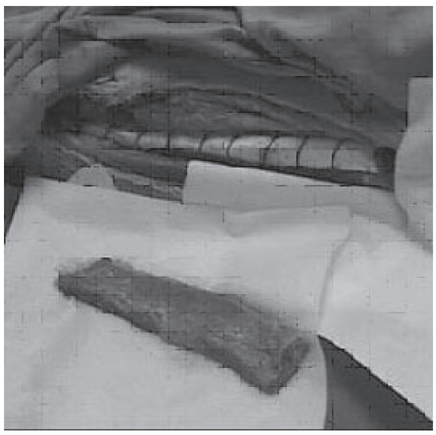

Fig. 2. Photograph of an artificial esophagus system

2.3. Peristalsis stent with hyperthermia function

An operation of an esophagus cancer is one of the most difficult operations even now, when medicine progressed. One of the most important points is the difficulties of esophagus reconstruction. In an operation, since the stomach and intestines are used as a substitute, an invasion becomes large and an operation of elderly people becomes difficult. Although the improvement in a life prognosis is expectable if cancer is resectable, there are a lot of cases, who were too late for surgery of the esophageal cancer at the time of diagnosis. Then, a Peristalsis Stent with Hyperthermia function for the terminal esophageal cancer patients, for whom an operation cannot be conducted, was invented. The Peristalsis Stent with Hyperthermia function has three characteristics. 1. Completely noninvasive, 2. Hyperthermia on the carcinoma tissue. 3. Peristalsis function. Possibilities are expected as one of the alternative candidates for a terminal esophagus cancer therapy.

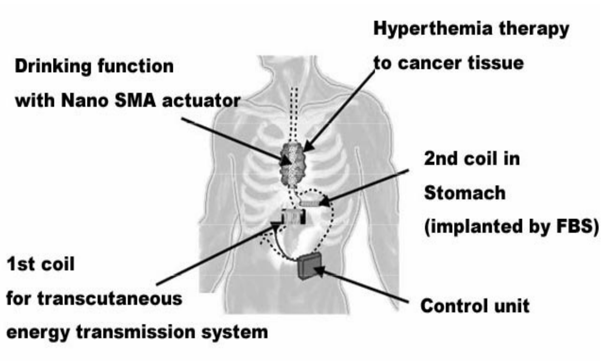

Fig. 3. Super stent system

3. Undulatrion Pump VAD Project

Rotary blood pumps (RP) are effective as small ventricular assist devices. They may be still more effective if pulsation is possible. We have studied an undulation pump (UP), which is a small RP, which can produce pulsation. In Japan, a development project of an implantable-type UP ventricular assist device (UPVAD) and UP total artificial heart (UPTAH) are underway. Six universities and some companies are together in charge of this five-year development project.

Tohoku University is investigating the influence that the UP under development has on internal-organ circulation. Goats with the same weight as Orientals were used for the experiment. The UP was implanted using the left-heart bypass system. As a result of the animal experiments, the blood circulation dynamic state was stabilized, and a sufficient left-heart-supporting effect was observed. We observed a tendency in which myocardial blood flow, and kidney blood flow changed due to UP various mode support. The problem of multiple organ failure is important during the clinical application of a ventricular assist device. Assistance for internal-organ circulation is important in preventing multiple organ failure. It is concluded that UP may be useful in preventing multiple organ failure. It was concluded that UP might be useful to prevention of multiple organ failure.

Fig. 4. Undulation Pump

4. Artificial Myocardium Using Nano Technology

The purpose of this research is developing nano artificial myocardium. Therefore, nano sensor development is performed. And nano control chip development is performed. An artificial myocardium actuator is also developed by nanotechnology. A control-objectives value setup which imitated baroreflex system is tried using a nano sensor and a 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 organism affinity 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 experiment. Since information, such as each ventricle, can be evaluated simultaneously, the optimal drive of artificial myocardium is possible.

Sunagawa et al. had reported the new bionic medical treatment method which can raise a heart failure patient's probability of survival by applying a biological information and performing circulation dynamic state control. The heart failure medical treatment by carrying out pacing of both the ventricles is the established methodology. A hypothesis is drawn from these two reasons. 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 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.

Currently, artificial-myocardium research is under promotion using an electro-hydraulic system. N chronic animal experiments.

Furthermore, the molecular crystal arrangement of a shape memory alloy is prepared by application of nanotechnology. Development of the artificial muscles which have improved durability and the speed of response is progressing by reducing a hysteresis. Now, cultivation of a heart muscle cell attracts attention with reproduction medical treatment. Although it is easy to create a cell sheet, 3-dimensional construction is very difficult. Of course, reconstruction of the coronary arteries is needed, and it is apprehensive also about thrombus formation.

On the other hand, the nano level actuator by nanotechnology is important. If it succeeds in this development, it is expected that it becomes applicable to various artificial organs.

Transcutaneous energy transmission system using nanotechnology enables us the embodiment of the smaller totally implantable device.

Animal experiments were performed and the supporting effect was obtained by the mechanical assistance.

Artificial myocardium may become one of the candidates for mechanical assistance in future.

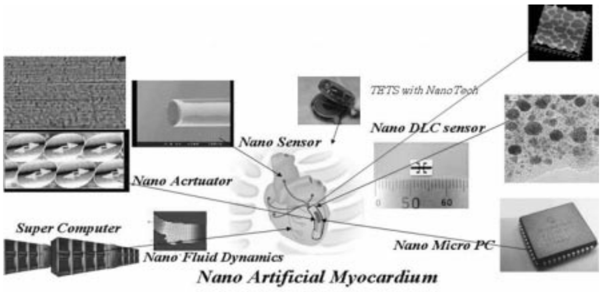

Fig. 5. Artificial Myocardium

5. Brain Function Control Units

0.5-1% of the general population have the epilepsy (NIH Consensus Panel, 1990). Seizures cannot be controlled by medications in 20% of epilepsy patients. A third of these patients need the surgical resection of epileptic focus for the control of the attacks. However, surgical resection of a part of brain have a risk of complications. There is a patient who feels a sign before the convulsions of epilepsy. When feeling a sign, there is a treatment, which performs a vagal nerve stimulus. However, a stimulus of a vagal nerve is not a trustworthy treatment.

We had invented the method of cerebral partial cooling and applied for the patent (2004-304964).

By this method, if a patient feels the sign of the attack of epilepsy, a switch will be pushed. Control switch was implanted under the skin. By switch on, the focus of epilepsy is cooled and a convulsion attack is prevented beforehand. A battery is used in a patient with few attacks. Transcutaneous energy transmission system (TETS) is used in a patient with a frequent attack. In this system, if a patient feels a sign, TETS will be used. Outer coil will be attached to the inner coil under the skin. Energy is supplied and a focus is cooled. Now, we are studying the prediction algorithm of epilepsy. If prediction is possible, the automatic control of epilepsy will become possible. It is expected that it becomes good news for the patient of epilepsy.

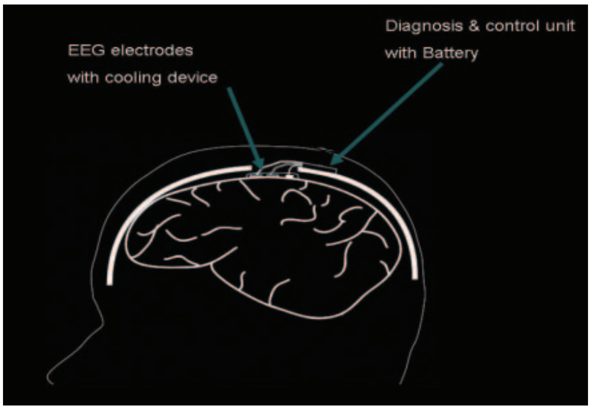

Fig. 6. Epilepsy attack control machine

6. Baroreflex Sensitivity of an Artery

A baroreflex function is the one of the most important factor in the patients with hypertension. Heart rate falls reflectively at the time of a blood-pressure rise. And, an artery is extended reflectively, when blood pressure goes up. Blood pressure returns to a normal value because of heartbeat reduction and blood vessel extension.

The sensitivity of the baroreflex system is calculated at the heartbeat reaction to blood-pressure change. However, even if the reaction of a heartbeat is measured, the baroreflex function of an artery is not known. Then, we invented the new method of diagnosing the baroreflex sensitivity of an artery, using the pulse wave velocity (PWV).

Since PWV correlates with the elasticity of an artery, PWV has been used for atherosclerosis diagnosis until now. Therefore, if PWV is used, change of the elasticity of an artery can be diagnosed. The reaction of an artery can be measured if the elasticity of an artery can be diagnosed. Therefore, if PWV is measured, the baroreflex function of an artery can be diagnosed. However, even if it refers to medline and searches a patent, there is no report of a method which measures a baroreflex sensitivity by PWV, until now.

Therefore, this report is the first in the world. By ten healthy objects, the time series of a heart rate variability, fingertip pulse change, and blood pressure was recorded. The obtained data were inputted into PC through the AD converter.

Preventive medicine is a priority for most governments because of increasing medical and health care expenses [1-7]. In Japan, the concept of metabolic syndrome has recently been identified to play an important role in the pathophysiology of many diseases [3-7]. Hypertension, hyper-lipidemia, diabetes mellitus, and obesity are important consequences of metabolic syndromes. Among these, hypertension is paramount when considering disruption of organ function [8,9]. Thus, prevention of hypertension is very important.

The baroreflex system is a key indicator of hypertensive pathophysiology [10,11]. When blood pressure (BP) increases, heart rate (HR) decreases, and there is peripheral arterial dilation [12,13]. By decreasing the cardiac output and peripheral arterial resistance, BP returns to normal. Hypertension is a concern in the young as well as the elderly [14,15]. Baroreflex sensitivity is reduced in younger hypertensive patients [14-16]. However, currently there is no simple and sensitive diagnostic method to measure the arterial behaviour in the baroreflex system.

This study describes the development and clinical application of a novel baroreflex diagnosis machine and offers a preliminary consideration of its clinical applicability.

6.1. Diagnosis of arterial baroreflex sensitivity

Every medical student studies the baroreflex system as a typical example of homeostasis [12-16]. When blood pressure increases, baroreceptors in the carotid arteries and aortic arch sense the increase in the baroreflex sensitivity. When this information was transmitted to the central nervous system, the HR lowers and arteries dilate. These reactions restore the normal BP (Fig. 7).

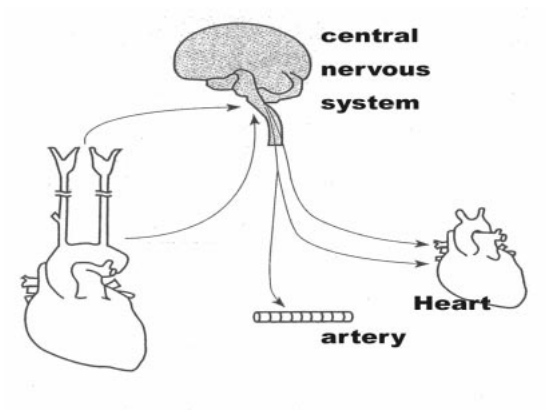

Fig. 7. Schematic diagram of the baroreflex system

Baroreflex sensitivity was evaluated by measuring the HR response to the BP changes (Fig. 8). The slope of the linear regression line demonstrated the sensitivity of the baroreflex system of the heart.

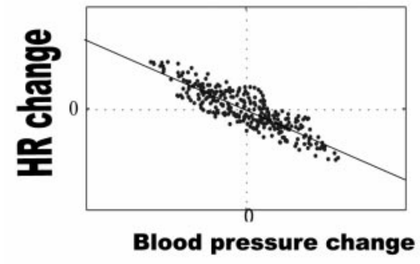

Fig. 8. Baroreflex sensitivity of the heart.

While HR response in the baroreflex system can be monitored, no method currently exists to evaluate arterial baroreflex function, possibly because of the difficulty in evaluating vascular tone during wakefulness.

Recently, new methodologies — brachial ankle pulse wave velocity (baPWV) and cardio-ankle vascular index (CAVI) - have been developed to evaluate human arterial stiffness [17-20]. These methodologies non-invasively evaluate arterial wall stiffness using the pulse waveform of the brachial and ankle arteries. These methodologies are based on the premise that pulse wave velocity (PWV) is correlated with arterial wall stiffness. Thus, PWV increases when the arterial wall becomes harder and decreases when the arterial wall softens.

In the baroreflex system, the arterial wall softens in response to an increase in BP, thereby decreasing the vascular resistance (Fig. 9). BP will return to normal because of the decrease in resistance. The softness of an arterial wall can be measured by PWV.

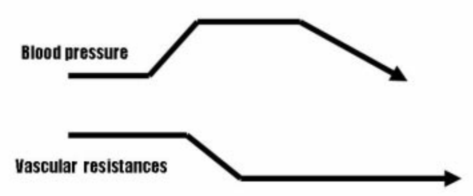

Fig. 9. Schematic representation of the time series response data for the vascular resistance of the baroreflex system.

The PWV value could possibly be used to quantitatively measure the baroreflex sensitivity of the arterial wall. PWV can be calculated from the pulse wave transmission time (PTT) and distance.

Thus, measurements of PTT and BP permit an evaluation of arterial baroreflex response.

6.2. Animal experiments

To evaluate the autonomic responses of the PTT or PWV, chronic animal experiments were carried out using healthy adult goats. The goats used in the experiment had weighed almost the same as an average Japanese person. All experiments were approved by the Ethical Committee of the Institute of Development, Aging and Cancer, Tohoku University. Under anaesthesia, the chest cavity was opened in the fourth intercostal space. Implants included an electromagnetic flow meter, electrodes for electrocardiogram (ECG), catheter-tip pressure sensor inserted into the femoral artery and fluid-filled catheter inserted into the left ventricle. After the chest was closed, the goats were moved to their cages. Measurements were taken when the goats were conscious in the chronic stage.

After intravenous injection with methoxamine, BP suddenly increased (Fig. 10). HR reduced in response to the increase in systolic pressure, and PTT increased in response to the BP change. Prolongation of the PTT indicated the softening of the artery. Therefore, PTT and PWV were thought to be indicative of the autonomic response of an artery.

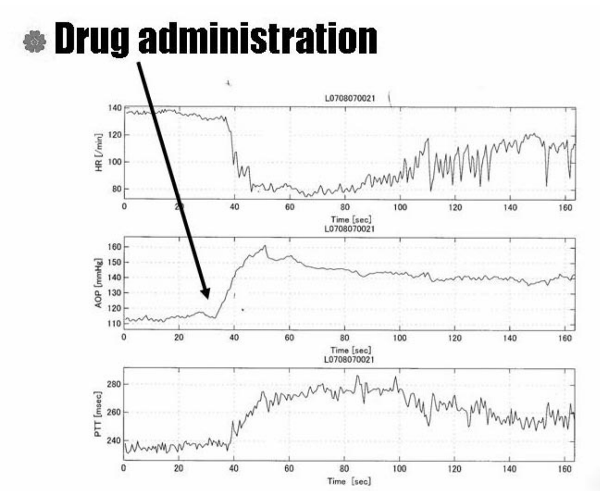

Fig. 10. Time series data of the HR, systolic BP and PTT in a healthy and conscious adult goat.

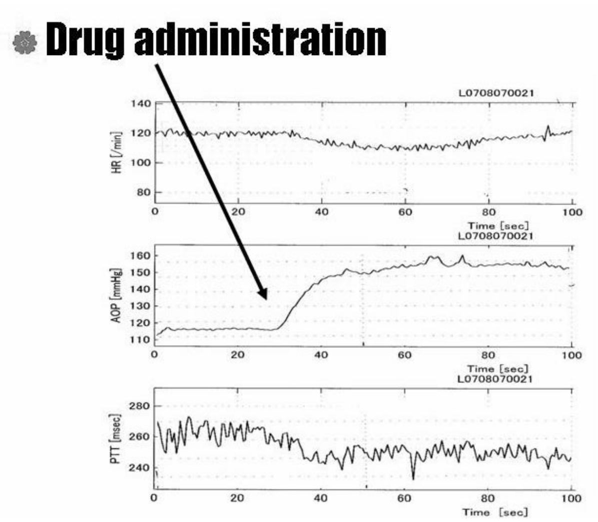

Fig. 11. Time series data of the HR, systolic BP, and PTT in a healthy and conscious adult goat after complete blockage of an autonomic nervous system using atropine and propranolol.

To demonstrate the autonomic nervous control of the HR and PTT, the autonomic nerves were blocked using atropine and propranolol [21,22]. During this blockage, the HR did not respond to the BP change; however, the PTT showed marginal decrease in response to the increase in systolic pressure (Fig. 11). This small decrease of the latter might have been due to hardening of the artery caused by methoxamine.

The results are consistent with HR and PTT being indicative of the autonomic response to BP changes in the baroreflex system.

6.3. Measurement equipment and analysis

PTT and PWV were easily measured by monitoring ECG and pulse wave. Figure 12 shows the equipments used for the measurement. The newly developed system used only an ECG and a pulse wave recorded from the radial artery or fingertip. These time series were inputted into a personal computer, and analyzed quantitatively using a custom-developed software.

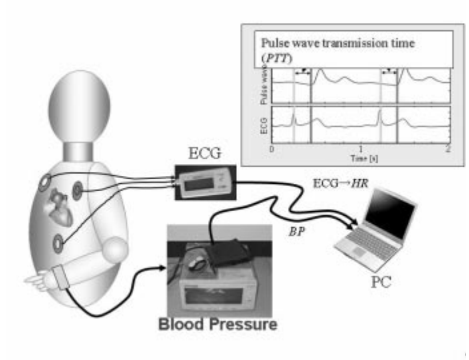

Fig. 12. A schematic illustration of the measurement equipment.

HR was calculated from the reciprocal of the inter-R-wave interval of the ECG signal. PTT was defined as the time interval from the peak of the R-wave to the point at which the pulse wave signal began to increase. HR and PTT were interpolated by cubic spline functions to continuous-time functions, and were resampled every 0.5 s.

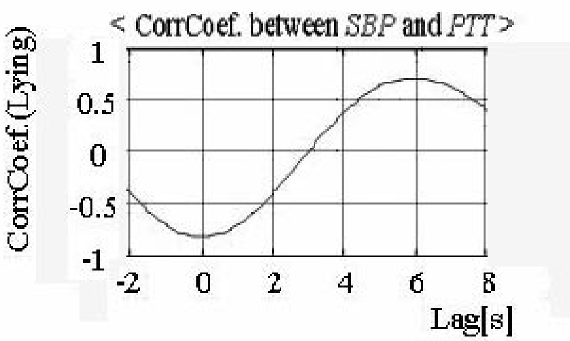

Fig. 13. An example of the cross-correlation function between the systolic BP and PTT.

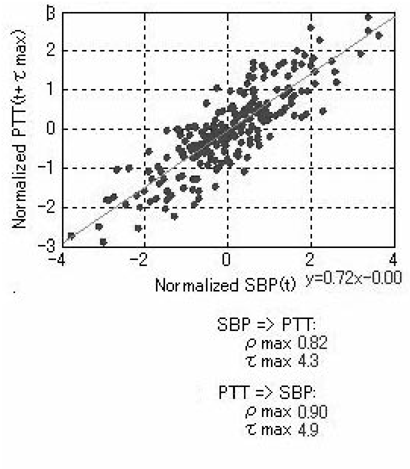

Fig. 14. An example of the correlation between the normalised systolic BP and normalised PTT in a patient.

Figure 13 displays an example of the cross-correlation function between the systolic BP and PTT. The strongest correlation was observed approximately 6.0 s later. Thus, band-pass filter was used in the analyses. Each data point was filtered through a band-pass filter with a bandwidth between 0.08–0.1 Hz to extract the Mayer wave component. Figure 14 displays an example of the correlation between the systolic BP and PTT. PTT was plotted after 6.0 s. Significant correlation was evident in the time sequence between BP change and PTT change after calculating the delay time by cross-correlation. The slope of these parameter changes was easily obtained, and it demonstrated the sensitivity of the baroreflex system of an artery.

The utility of this system for the quantitative diagnosis of the baroreflex sensitivity of an artery was recognized by the patent application.

6.4. Clinical evaluation

The arterial responses were measured in terms of the PWV calculated from the PTT from the heart to an artery. In this system, the HR change corresponding to the BP change in time series sequence was observed. Delay time was measured by the cross-correlation function. Slope of the changes in BP and HR indicates the sensitivity of the baroreflex system of heart. Furthermore, this system could also measure the sensitivity of the baroreflex system of an artery.

Clinical research of our study has begun after ethical committee allowance. So far, the results have shown that our system can successfully detect decreased sensitivity of the baroreflex system in hypertensive patients. We are now analyzing the various data of the patients with hypertension.

Further examination will be needed using more cases. This new method may be useful to follow up patients with hypertension.

7. Pulse Diagnosis Machine

There is the concept called "pulse diagnosis" in the Oriental medicine. Oriental doctor contacts three fingers in the radius artery of a left-hand wrist and a right-hand wrist as we shown in Fig. 15. And various pressure is applied to a finger and a pulse-wave form is sensed manually. The pulse diagnosis was made into the methodology which diagnoses various diseases. Arrhythmia information, a flow rate, pressure information from the heart, etc. are included in the pressure wave form of a pulse wave.

Furthermore, the arterial-elasticity change resulting from an atherosclerosis can be diagnosed. The information on the amount of circulation blood reflecting a renal function and the information on the liver function to participate in the viscosity of blood are also included in the wave of a pulse wave. The blood sugar level accompanying diabetes also influences viscosity. The information on the central nervous system function which controls blood vessel movement, and the information on change of the nutrition state accompanying an alimentary canal disease may also be included.

However, degradation of the information in the methodology of diagnosis is not avoided only by having told the follower the instruction by experience. If there is no objectivity even if it will talk, if it has the tradition for thousands of years in the Oriental medicine, persuasive power is completely missing medically and scientifically. Even if the pathological condition could be diagnosing with tradition medicine in the past, it becomes impossible to completely diagnose without transfer. Tradition maintenance of the methodology of diagnosis, and for generalization, quantification and informational sharing are indispensable.

Aiming at new deployment of the methodology of a pulse diagnosis, the new pulse-wave diagnostic equipment "a pulse-diagnosis machine" which performs a "pulse diagnosis" was developed.

This study aimed at the contemporary deployment based on "taking a lesson from the past" of a pulse diagnosis. If a pulse-diagnosis machine is used, a scientific quantitative diagnostic method can be brought to the Oriental medicine only with empiricism for the first time in the world. An outline is described below and consideration was added to the results.

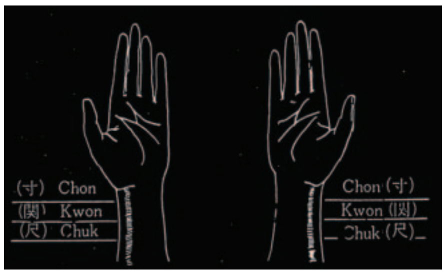

Fig. 15. Concept diagram of the Pulse diagnosis

7.1. Arterial pulse waveform

Before performing pulse-diagnosis machine development, the meaning which an arterial pulse wave form has was reconfirmed. Various information in human body is theoretically included in the pressure wave form of an artery. Therefore, theoretically, various kinds of quantitative diagnosis will be embodied from this wave form. The rise foot of an artery wave is generated after ECG Q wave about 100ms. It is known medically that this standup delay time will be applicable also as an index of the cardiac function. When the heart contracts, an aortic valve will open, and blood will flow into an ascending Aorta from the left ventricle. Intra aortic pressure will go up quickly simultaneously with blood inflow, and a pressure wave form will be formed. Therefore, the important information about a cardiac function is included in a rise foot.

It is the wave of the first peak in an artery pressure waveform, and Percussion wave in the first half of two waves near the pulse-wave peak, and they are mostly in agreement with the peak of a blood-flow wave. Although this wave is the highest score in a youth healthy person, the Tidal wave generated next becomes the highest score in elderly people and an atherosclerosis patient. Tidal wave (recoil wave) is called Second wave, Catacrotic wave, Elastic wave, Spatsystolisher Gipfel, etc. Main components are the reflected waves from a peripheral, and have a shallow valley (Midsystolic dip) between Percussion wave in many cases. This wave is small at a youth and increases by atherosclerosis progress, such as an aging and a blood-pressure rise. Moreover, it becomes small as a pulse wave proceeds in a peripheral artery.

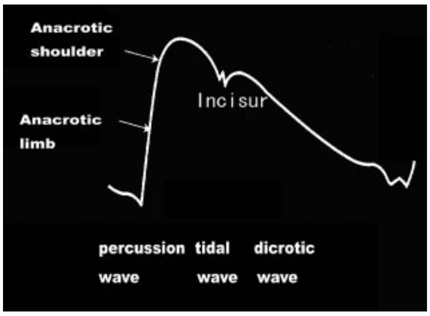

Fig. 16. Time series data of the Arterial pulse pressure waveform

As for Tidal wave, the Idiopathic Hypertrophic Subaortic Stenosis (IHSS), and aortic valve stenosis significantly influenced the waveform. The contraction dynamic state and the left ventricle outflow way are also participating in this wave formation..

The difference of the height of Percussion wave and Tidal wave and the ratio of full wave quantity are displayed in Augmentation Index AI= $\triangle p/A$. This is broadly applied as a parameter which shows the elastic modulus of a blood vessel system. Commercialization is also tried as an index called blood vessel age.

Formation of a notch is accepted in the downward foot of a main artery pressure waveform, and it is called the Incisor, dicrotic notch, etc. This is small vibration produced in a pulse wave simultaneously with closing of an aortic valve. This is a cut which is between a contraction phase and a diastolic phase. Since it is the index which shows closing of an aortic valve, there is a report of disappearing by aortic valve closing insufficiency (AR). By the aging and blood-pressure rise, when main artery compliance becomes small, there is a tendency to decrease.

The upheaval which appears at an extended early stage is called Dicrotic wave, and originates in reflection from the peripheral of an artery pulse wave. Generally Tidal wave and dicrotic wave are reverse-correlated. In a youth, Dicrotic wave is large. In arteriosclerosis with an early advance of a reflected wave, Tidal wave becomes large. This Dicrotic wave is important in order to maintain a coronary-arteries blood flow. The artery pressure waveform to which this wave becomes large is called Dicrotic Pulse. For example, in DCM, Tidal wave disappears and turns into only Dicrotic wave. On the contrary, in aortic valve closing insufficient AR, Dicrotic wave falls prominent.

The elasticity of such an artery is fluctuated in response to change of not only an atherosclerosis but an autonomic-nerves tonus. Therefore, in the wave of a pulse wave, the control factor of a central nervous system also becomes an important parameter. Furthermore, if the amount of circulation blood increases, theoretically, it will work in the tendency for the whole pressure-waveform time series curve to go up. Moreover, if blood viscosity changes, it will result in affecting the whole waveform. Thus, various parameters worked mutually and have formed the waveform of a pulse wave.

So, it becomes possible to diagnose medical information from the wave form of the arterial pulse wave.

7.2. Basic examination of the Pulse diagnosis machine

The pulse diagnosis in an Oriental Medicine contacts three fingers to the radius artery of both wrists, and is performed so that it may show Fig. 1. And it is carried out by carrying out a sensing pressing with a finger using various pressure. Therefore, it may be able to be embodied by applying theoretically three precise pressure sensors which Fig. 3 is shown.

Fig. 17. Sensors for the Pulse diagnosis machine

If this machine is used, the embodiment of an objective and high scientific quantitative diagnosis of Puls diagnosis with reproducibility is expectable. Then, the pressure sensor was contacted noninvasively from the radius artery skin surface based on the methodology of a pulse diagnosis so that it might show Figs. 17 and 18.

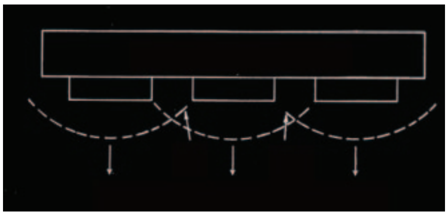

Fig. 18. Concept diagram of three pressure sensors and Pulse diagnosis

The whole sensor was pressed in the direction of a perpendicular from external surface by the air pressure in which the quantitative evaluation is possible. The system which digitizes the sensing pressure waveform of the pulse diagnosis in an Oriental Medicine, and records on a data recorder was developed using this method. Pressure information is detectable with the pressure transfer on the upper surface of a radius artery so that it may show Fig. 18. It is perfect to carry out, after checking the basic performance in the model circulation circuit and checking safety, validity, etc. by the animal experiment in the system development.

It is considered to be standard after a check to perform clinical application at the last. Then, the model circulation circuit by the WindKessel theory of the left-heart circulation equipped with pre load, after load, and compliance was created using the artificial heart, and the basic performance was checked. The photograph of the pulse-diagnosis sensor with which the Moc circulation circuit which imitated the left-heart circulatory system was equipped is shown to Fig. 19.

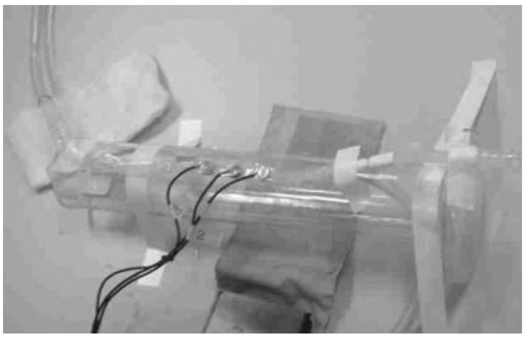

Fig. 19. A photograph of the pressure sensors for Pulse diagnosis and model circulation of a radial artery

Creation of the model circulation by the circulation medium which imitated blood in the model circulation circuit using an artificial heart was tried. The sensing by the pulse-diagnosis sensor was tried to the model artery of various elastics modulus which imitated the radius artery. Pressure by various air pressure was applied from sensor external surface, and reappearance of the scientific and quantitative pulse diagnosis using the pulse diagnosis of an Oriental Medicine was tried.

According to methodology with the reproducibility using such model circulation, the check of a measurement result which was good at scientific quantitative evaluation is attained.

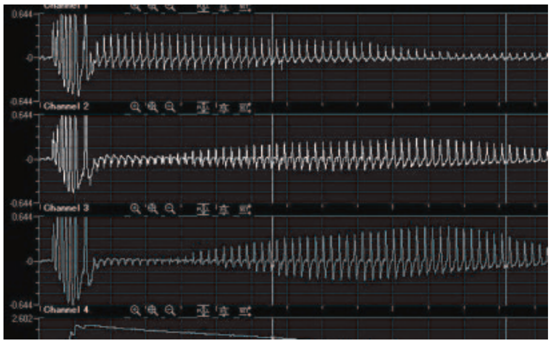

Fig. 20. Alteration of an external surface pressures and pulse diagnosis sensor waveform. From upper tracing, waveform of the sensors of proximal, mid, and peripheral were shown.

If model circulation is used, it is easy to change the contractility of left-heart circulation independently. It may be able to be also simple in changing peripheral blood vessel resistance. Moreover, we can also free in changing compliance. Therefore, the factor of a pulse diagnosis can be evaluated quantitatively in Moc circuit.

The sensing result of the pulse diagnosis at the time of decreasing outside pressure gradually is shown to Fig. 20. Sequentially from the upper side, proximal side, mid side, and peripheral pulse wave were shown.

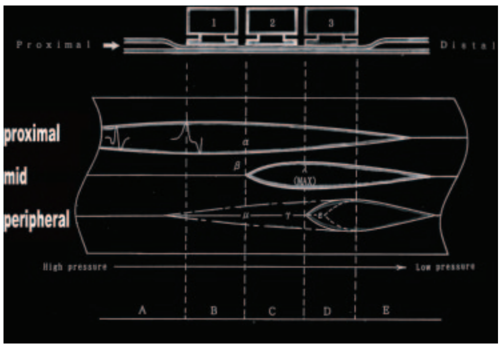

Fig. 21. Theoretical background of the three pressure sensors waveform were shown

If it presses from external surface by high pressure and a radius artery is made to blockade by external pressure, pressure is undetectable in peripheral sides. On the other hand, if external pressure is loosened gradually, a gradually big sensing wave will be detected a central-site and peripheral side.

A theoretical background is shown to Fig. 21. It is thought that the measurement result of having been good quantity has presented the height of the probability of scientific measurement like a theoretical background. It becomes indispensable experimenting after the scientific probate examination of a model circulation circuit according to a living body. Then, the quantitative examination of the pulse-diagnosis machine using the goat holding the almost same weight as Japanese people was tried.

Using the goat with a weight of about 60kg, the neck was cut open, the carotid artery was exposed, the sensor was contacted, and the pulse-wave sensing examination was tried.

Consequently, the almost same pulse-diagnosis measurement result as Moc circulation was obtained, and detection of the wave-like change by medication was also embodied as the still more interesting data. In an animal experiment, it is also possible to fluctuate the object for the strange laborious works of the heart, the compliance of a blood vessel, peripheral resistance, the amount of circulation blood, pre load, after load, etc. free unlike a human body.

Therefore, the quantitative experiment which can give a scientific basis can also be conducted to the concept of the Oriental Medicine in wave diagnosis of a pulse diagnosis from ancient times.

If this machine is used, the light of objective science can be applied to the world of an Oriental Medicine for the first time in the world.

Thus, first, the basic examination using Moc circuit was performed and the animal experiment was presented after that. After also fully checking safety, fixed quantity nature, and validity, finally the clinical test was tried.

8. Methodology of Time Series Data Analaysis

In the methodology of the pulse diagnosis in an Oriental Medicine, various pressure is applied and a radius artery is palpated in a fingertip. There is also the interesting side in this methodology hydro-dynamically. For example, a blood flow is first intercepted by pressure of the radius artery by the side of the heart. After that, little by little, a blood flow is made to resume and the pressure pulse-wave waveform by the side of the peripheral generated gradually is observed. Many information not only about circulation dynamic state information, such as a cardiac function, but each internal organs will be acquired from this waveform. It is theoretically considered that many information contains in the wave height and the waveform of a pulse-diagnosis wave so that it may be expressed in the principle figure of the blood-flow resumption shown to Fig. 7.

The viscous factor of blood also relates to the pulse-wave information on these pulse diagnosises. Furthermore, it is dependent also on factors in the skin in a blood vessel, such as NO, at the action of the blood vessel at the time of re-reflux of a transient ischemia, for example. Therefore, functional diagnosis of the inner skin which becomes important in atherosclerosis advance will also be embodied.

However, scientific evidence is completely missing only by the methodology only depending on experience which was performed by the Oriental Medicine until now. So, Pulse diagnosis machine was invented. And then, various pressure was applied from external surface and objective quantification of the wave information which a pulse diagnosis has was measured. By measuring a pulse wave scientifically, conversion in the science of the pulse diagnosis for which it depended only on experience until now embodied.

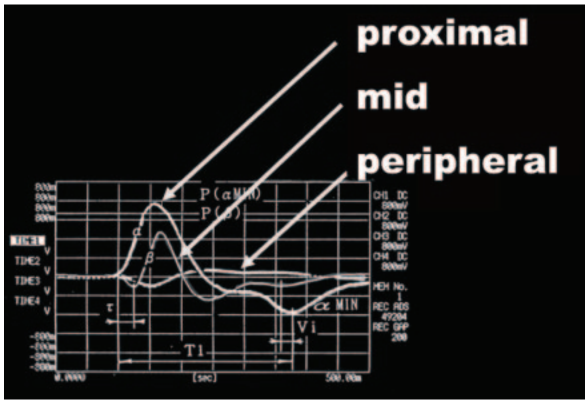

Fig. 22. Three waves of the sensors from the Pulse Diagnosis Machine

Three waves of a pulse-diagnosis sensor are shown to Fig. 22. Sequentially from the top Proximal side, and next is shown the center (Mid) side and lower pattern showed the peripheral side. The wave height declines, so that it is a peripheral, since pressure is applied from external surface .

As shown in Fig. 22, various parameters were calculated from this wave and scientific / quantitative analysis of a pulse diagnosis was embodied for the first time. Various fluctuation components exist on the time series information on the cardiovascular system, which is represented by the wave of a pulse diagnosis, and it is controlled by the autonomic nervous system. Therefore, autonomic-nerves information diagnosis will also be embodied from diagnosis of a pulse wave.

This system will be the good news when we consider the development of the non invasive measurement.

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