Artificial Heart Research by the Use of Micromachines

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Good morning, everybody. My name is Nitta. I have long been vice-chairman of the Medical Application Working Group of the Micromachine Center. Naturally I have been closely related to micromachines. I specialize in cardiosurgery, and am working in a boundary area now popular, specifically in the area of biomedical engineering.

Today I have been requested to talk about micromachines and artificial organs, so will talk about what comes to mind. However, I am not confident about how to relate micromachines to this lecture.

[Kinds of Artificial Organs and the Current Situation]

The artificial organs are now applied systemically. For example, blood is pumped from the heart in the circulatory system to circulate through the whole body. Every organ related to it falls under this category.

The use of heart pacemakers is now a well-established practice for the circulatory system. It was formerly as big as 10 cm in diameter and 3 cm in thickness, but is now miniaturized to a weight of only 20 g. Its battery lasts as long as 10 years. It drives the heart by emitting electricity periodically. As a cardiac surgeon, I often have a look at the heart by inching an optical instrument through the chest. When I touch the heart lightly, it readily reacts to this mechanical stimulus. It also reacts to a flow of electricity. The heart shrinks when electricity passes through it. The heart pacemaker is based on this principle. If this device is rendered much smaller, it will sooner or later be incorporated into the heart and energized wirelessly from a device in or near the heart. This will also depend on how micromachine systems advances in the future.

Next comes an artificial valve. The heart is driven by a pulsation. Naturally, valves are required at every inlet. This valve is also manufactured artificially. It lasts 20 to 30 years in the human body.

Next, let me explain about an artificial heart in which I specialize. An artificial heart is to be embedded after the original heart has been removed from the human body. How long do you think it will last? May I ask this gentleman sitting in the front. Two years? Great! You are worthy of being at the top. The artificial heart we made works for about two to two and a half years. However, there are several problems to be solved. One is the formation of a thrombus. When blood touches an artificial material, it judges whether the material is friend or foe. On finding it is a foe, blood coagulates to concentrate on attacking it. This is what we call the formation of a thrombus. This should be prevented. The human heart works by a pulsation. It is known now that a man can live with a steady-flow pump, such as a centrifugal pump. However, what God gave us is a pulse pump. This pulse pump is subjected to a fatigue test, a pulsation of 100,000 times a day. No material on the earth can withstand a fatigue test of 100,000 operations a day for over five years. This means that no artificial heart is available that can last over five years. This is a task imposed upon us to find an answer to this problem. We are now getting various kinds of materials of a living body through gene manipulation, including cell engineering and tissue engineering. So eventually, we will be able to manufacture an artificial heart that will last over five years or over ten years if cell engineering, tissue engineering, and organ engineering work to cover an artificially-made one, moving parts, and the parts to withstand a fatigue test. The current heart transplantation has attained a five-year survival rate of 70 to 80%. If an artificial heart surpasses the transplanted heart, which lasts five years, we will be able to manage without relying on the human heart. The general ethical view prevailing in Japan is hindering the progress of heart transplantation. We researchers who are now developing artificial organs think it is ideal that God forgives us if we succeed in managing without relying on the organs of others by manufacturing a heart more excellent than the one God gave us with God-blessed wisdom.

This circulatory system is directly connected to life. For example, a man dies if his heart stops. This system is very important, because a man dies if oxygen is not supplied to the brain for three minutes. Another factor to be considered is the contact with blood. This is very specific, because artificial hearts will not work well unless a more advanced form is devised than other artificial organs.

Next, the respiratory system, where gases are exchanged. An artificial lung dominates this area. An example of lung transplantation survival was reported for the first time in Japan by Tohoku University the other day. We make this artificial lung. We are researching into an artificial lung even now. At present, a heart-lung machine is used clinically, which can be used as long as seven hours for heart operation with almost total safety. However, an artificial lung poses a problem if the operation lasts longer. It is very difficult to make this unit last longer. Our research into a built-in artificial lung are already under way. However, another factor we should consider after the removal of the lung is that the lung is used for speaking. The lung is used for uttering words. This mechanism of speaking should also be manufactured separately. The lung itself is very important, because it functions in various ways, such as the production of hormones. It is utterly impossible for us to copy the lung. What we can do well is only to exchanges gases. The current situation governing an artificial lung is that no artificial lung has been made available that can be used for a prolonged period of time because of its contact with blood.

Then, the digestive system and artificial intestines come next. Organs for the urological area should also be considered. We are working to make artificial valves for patients who are finding it difficult to urinate. Since an artificial valve should open and close, we are using shape memory alloys for the manufacture of artificial valves for patients suffering from dysuria, and confirming whether they serve the purpose by using laboratory animals. The test of laboratory animals is going on successfully.

Next, motor-related organs.

And the sensory system, which should desirably be studied in preference to other areas. We have sensory organs with which we can see, hear, and touch. We are trying to replace this sensory system with a sensor system, which, for example, resembles the eyes of a robo cop such as we see in the movies. However, the information those eyes are actually collecting is different from what our eyes collect. We may copy a human system when we think of a sensor system. It is desirable, however, that, if a microsensor system, for example, is capable of collecting the volume of information beyond the reach of a human system, this function should be utilized to the full. This should be a well-developed area. For example, our brain thinks various things, issues commands, and controls in various ways. The brain issues various commands through the neural system, such as moving hands, raising blood pressure, and secreting hormones. If we can intercept the commands midway to obtain the information and convert it to electric signals, we will be able to do what the brain intends to do next while thinking to do something. We are now doing this by varying the quantity of electricity. The subject of this interface will come up later. I think this will be a main area in which micromachines take part in the future.

Then, the ear, the nose, the intestines, the esophagus, the windpipe, the lung, the liver, the ovaries, joints, and artificial blood vessels. The artificial blood vessel is nearly perfected among the artificial organs in the circulatory system. The aorta and a blood vessel with a large diameter are in the stage of nearly ideal perfection. What is left unsolved is that an artificial blood vessel does not expand as desired when it should expand because of the difference between the properties of the human blood vessel and those of an artificial one. We refer to this as the mismatching of a living body. Such a thing has not yet been solved, but an artificial blood vessel that lasts for a considerably long time has been made available. However, an obstacle has not yet been removed in the case of a slender blood vessel, say, with a diameter of 1 mm, an obstacle in which, when blood takes a slender blood vessel as a foe, it coagulates there. I think this may be a situation in which micromachines will play an active part.

In addition, an eye, a tooth, an artificial heart, a valve, a pacemaker, an artificial kidney, the bladder, the urethra, the skin, and an artificial leg are the subjects of study.

[The Artificial Heart]

Please allow me to dwell on the artificial heart in which I specialize. The artificial heart beats 100,000 times a day with a discharge volume of about 70 cc each time. A displacement of about 70 cc is therefore required if we are to make a pulse pump. Its size is determined in this way. A steady-flow pump and a centrifugal pump have come to be used for men as well. When I started studying artificial hearts, it was believed that a man would not survive with a steady-flow pump. However, a man was found to survive. What makes the difference is that, if a man is required to have 100 cc of blood per kg of his weight for living, a steady-flow pump should have a capacity of 100 cc plus 20 cc. Conditioned as such, however, it is quite intriguing for us in that it can be miniaturized. A man has two pumps for the right and left ventricles. God combined the two together, but the two look like one. Actually, however, there are two pumps. One is a low-pressure pump for sending blood to the lung, a low pressure equivalent to about 20 mm/Hg. The other, the left pump, sends blood systemically with a pressure equal to blood pressure. It therefore follows that the pump should have a power as great as four to five times. Since the right heart sends blood to the lung, it pulsates by breathing. When air is inhaled, the pressure in the lung becomes negative to allow blood to return with a rush. When the heart is checked, it stops sometimes, for example, when struck with a catheter. The patient is conscious, so he keeps breathing. Then, the breathing pressure only comes out in arterial pressure. When the patient is conscious, I tell him, “Cough a little”, while his heart isn’t beating. He coughs, then his heart begins beating again in some case in response to this mechanical stimulus of coughing. Just coughing raises the pressure to about 120. Such a thing occurs at a place just outside the right heart. Therefore, I think a steady-flow pump will do for the right heart in the future, because it makes such pulses, though slow. As for the left heart, a pulsating flow is better than a steady one for making men and laboratory animals vivid. I dare say vivid. If I am allowed to say so, a steady-flow pump is very small, easy to make, and inexpensive. In the future, I believe, a steady-flow pump will be used for the right and a pulsating-flow pump for the left.

This is an artificial heart developed for the first time in the U.S. by Dr. Akutsu, now honorary chairman of TERMO CORPORATION if I remember right. Since it was made in 1957, its history is very short. Generally, an artificial heart has only a short history usually less than half a century. At that time, a laboratory animal could survive only 1.5 hours.

This was also made by Dr. Akutsu in 1975. In this manner, we now have two artificial pumps. This pump served to help a calf survive experimentally 268 days. However, when an artificial pump is embedded in a calf for 268 days, the calf grows two times heavier. This makes it impossible for this heart to answer the purpose.

[Current Problems Related to Artificial Organs]

The artificial organs we are now confronted with are under study by researchers including myself who are currently researching into an artificial heart nearly as long as its history. The points at issue are how deftly we can make very small artificial organs and how we can make them serviceable for a long time without problems. I am thinking of having as many researchers as possible participate in studying the extent to which micromachines can answer the needs so that ideal artificial organs can be made.

Therefore, we have summarized the defects and points at issue with the artificial organs now available. They are too heavy and too big. These problems are indisputably the ones micromachines can answer. The sensors do not work as desired, either. Micromachines are also good at this point. Moreover, they are not well controlled automatically. There are two kinds of controls: one type of control is to have the unit fit the body itself when embedded, and the other, to have the unit last longer such as with an artificial heart, the durability of which poses a problem. However, micromachines enable the processing and control of information, thus dominating this sphere of activity.

They are not energy-effective, either. For example, I am now developing an engine for medical treatment using a shape memory alloy. The shape memory alloy I am now using is a commercially available large-diameter unit. I believe that if the alloy can be divided into very small elements and then re-assembled, it will be easier to control and be energy-effective. I am proposing this concept to the industry, but to no avail.

The engine has been completed in my head, but the industry is quite reluctant in complying with my request. Further, it does not last long. To make matterÇì worse, unpleasant things occur one after another, such as noise and vibration, accompanied by thrombus as a by-product. Since an artificial heart is a foreign body, it can also become a source of infection. The human body reacts to foreign bodies in various ways. Bleeding also poses a problem.

[Characteristics Desired for Upcoming Artificial Organs]

Desirable characteristics for newly developed artificial organs are, first, miniaturization, second, to interface with nerves for automatic control, third, to have a control system that is acceptable for both the living body and the embedded artificial organs, and fourth, to harmonize with the living body in various ways. Many issues have come up in the past, such as noise. Another desirable characteristic for artificial organs is to last several years. The artificial hearts now available last a little over two years, but should desirably last longer.

Now, we have two large national projects in Japan, led by the Ministry of Health and Welfare and NEDO. We are setting about dealing with an artificial heart. The project by the Ministry of Health and Welfare has lasted five years and will come to an end this year. We hope it continues longer. As one of the members participating in the NEDO project, I am glad to know of the decision to continue this project one more time.

Recent Research of Artificial Organs

This is an artificial heart we developed. It is still large, but it has two pumps, right and left, in this form. This shows how it was embedded in the thoracic cavity.

And this is an artificial heart equipped with a microsensor, undoubtedly related to micromachines. I think it is the first product in the world into which a chip was inserted directly. It is a result of the work I did about fifteen years ago together with Professor Esashi at Tohoku University. Frankly, I was also a student of Professor Matsuo for one and half years, who was Professor Esashi's teacher. So I started this work.

This is an auxiliary artificial heart. Pressure sensors are attached to the outlet and inlet, where they are connected to the living body. This is an artificial blood vessel leading to the aorta, and this is a duct. This is a cannula with which to draw blood from the heart. Attached at the top in this manner is a microsensor. Here is another. It is made in this manner, and its surface is covered with an antithrombotic material so that blood can hardly perceive it as a foreign body. It is about 20 microns thick, covering the sensor surface.

This is a diagram of the sensor itself. I am not a specialist in this field, but, according to Professor Esashi, it is very difficult to connect a lead wire to a sensor. I think the solution to this can be found by integrated molding. Actually, it is being perfected. This is the surface of a pressure sensor to be pressured. This is the rear side. This is a connecting part. This is an experiment using a goat. This is a system to assist the left ventricle. This is a sensor. This is a trace of the micro-sensor after two weeks.

We also have to measure the flow. This is a blood flow meter using ultrasonic waves, developed jointly with Cornell University. This is its trace, which is almost the same as that of the conventional electromagnetic flowmeter.

Then, we use an artificial heart to assist the heart. To ensure that the heart can set up for itself, we draw two hysteresis curves of the left ventricle in this manner to connect them with a straight line. The more upright the inclination of the straight line, the more active is the heart. The more it declines, the worse is the heart. We therefore measure using a hysteresis curve to see how active is the left ventricle. This necessitates measuring pressure and the quantity of the discharge from the left ventricle. By measuring the two, we can measure how active the heart is.

[Neural Interface]

Let me explain about the neural interface we just talked about.

This shows the findings of the experiment using a goat. Above is aortic pressure. This is a neurogram, a measurement of the integrated action potential of a nerve. This is aortic flow.

Here, "stand up" is written. When a goat tries to stand up, we can obtain neural information in advance. This means that we can obtain neural information in advance when a goat stands up. With this method, we can manage well by accelerating the beat rate if we can judge whether various kinds of artificial hearts are in a state acceptable to the body and what should be done from that point. This means that we can get signals earlier than God. In the case of God, it sends signals in like manner to have an organ that raises blood pressure and secretes hormones, which in turn raises blood pressure. This takes dozen or so seconds. In the case of an artificial heart, however, we can control the above process in a few seconds instead of dozen or so seconds. This is welcome for us. This kind of work is carried out infrequently, and we are the first in the world to take the initiative.

This is a neural device for that purpose. It is made into a cuff containing a nerve so that the nerve is protected from damage when pierced directly. The cuff is also a kind of interface used, for instance, for applying electricity or stimulation. This is exactly the process by which the nerve is electrically converted to a control system or for use as information. A new trial like this has appeared. As I mentioned just before, this may explain the reason why a new trial like this to what we call a sensor system will be applied more and more frequently.

[Microsensors]

With microsensors, we can obtain a variety of information on vital signs, including blood pressure, blood flow, pulse rate, breathing condition, temperature, and chemical substances for artificial heart, such as glucose, insulin, CRP and ammonia. The microsensors also enable us to obtain information from a living body, such as the concentrations of oxygen and carbon dioxide in the blood, pH level, and electrocardiogram. Those microsensors are embedded in the body, and driven electromagnetically. Our system also has them. In short, a microsensor can send electricity into the body, a device with primary and secondary coils wound around it. Therefore, a microsensor can transmit power and information wirelessly without a cord piercing the skin even when embedded in the body. Its efficiency is such that it can send electricity with an efficiency of about 90% by increasing flux density with an amorphous material in our case. In the future, therefore, various devices will be embedded in, for instance, the body of a sick patient or a postoperative patient, to be controlled intensively at a given place. It is not necessary for those devices to pierce the body for communication. We therefore assume that, as with the artificial heart, we will eventually be able to go to an electric station after several decades when we are short of electric supply in our daily life as we now go to a gas station for gasoline.

At present, most of the microsensors are used for a catheter. It is desirable, however, that microsensors be embedded in artificial organs. If so, we can obtain a variety of information and use it for controlling.

This is a sensor that Esashi Laboratory is researching. This is a self-mobile active catheter, for insertion into a blood vessel in the brain, which is one of our projects we are doing our utmost to promote as members of the committee in the Micromachine Center. Since artificial blood vessels are considered a hard nut to crack, we are in the process of developing this, accompanied by the development of various element technologies.

As I am a cardiac surgeon, we are thinking of embedding sensors in various parts of the heart. By so doing, we can understand well how a pump works. And this is an artificial valve which stands for 20 to 30 years. Since its movement is actuated by a difference in pressure, it moves only passively. If a micromachine can be used skillfully, a valve will come to open spontaneously by controlling it with greater skill.

[Review of the Study of Artificial Organs in the 21st Century]

In 2018 such as, for instance, an artificial kidney, now used in vitro, will be made available for embedding in the body. Here is what we call a hybrid. It will become possible to make what an artificial thing cannot do by using various cells and tissues of the living body. We are also expecting the emergence of a bio-cell by around 2014 as researchers of artificial organs.

In this presentation today, we are looking forward to the realization of artificial organs that are durable, reliable, stable, miniaturized, and biocompatible along with energy transportation or a battery system by utilizing micromachine technology.

Thank you very much.

(This paper is a summary of Prof. Nitta's lecture, prepared by MMC.)