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Micromachining Technology and Biomedical Engineering

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ABSTRACT

Medical science and clinical medicine include many microscopic environments. Recent micromachining techniques fit the microscopic environments and are applied to microsurgery, fiberscopic operation, micromanipulation, artificial organs, and drug delivery systems. Microactuators, microsensors, and micro mechanical parts will be prepared for such medical devices and techniques. Virtual reality, stereovision, and fiber imaging support handling of cells and small targets of living body. The paper reports some perspectives of microtechnologies in biomedical engineering.

Index Entries: Micromachining; biomedical engineering; microteleoperation; virtual reality fiberscopic surgery; micromanipulation; microactuator; laser angioplasty; laparoscopic surgery; fiber sensor; drug delivery system; stereoscopic imaging.

INTRODUCTION

Medical science includes many microscopic environments. These environments fit in very well with the physical environment and dimensions used in the study of cells, organs, and bodily fluids. Still, the field has lacked the perspective of mechanical systems common in engineering. Research has concentrated on analyzing the behavior of single protein molecules and organelles or the macrolevel functions of tissue systems. It must be remembered that living organisms have up to now not been considered machines.

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In modern industrial fields, machines can only be built in mass production when there is a large supply of a wide variety of interchangeable components. Thus, there are machines available at the present time that contain components of 1 mm or less, but they are not so much modern machines as they are holdovers from handicrafts of the past. Examples would include many micromanipulation tools in medicine. These small mechanical components may sometimes reach a precision of 1 μm or so, but they all require large machine tools to produce. This is not the kind of technology that micromachines is concerned with. Micromachines require standardized groups of components that include micromechanisms. In this sense, they are more closely modeled on the system components produced in semiconductor technology.

Even if small components are available, the technology to bring them together must also be there. This will only become possible through the development of batch preassembly (like the silicon process) and molecular auto-assembly (like protein technology) technologies, and the microprocessing machinery and software to assemble them.

MEDICAL MICROMACHINES FOR MEDICAL HISTORY

Micromachines are well-suited to the production of machines on medical applications: machines that act on the body or its cells. This technology is concerned with nothing less than the creation of components able to work on the structure and functions of systems, cells, and other units far smaller than bodily organs. Medicine already makes use of machines that have dimensions in the sub millimeter range, but these do not work inside cells, tissue systems, or fine blood vessels. They may be small, but completely new production methods and concepts are still needed.

The two most common treatments currently used are surgery and pharmaceuticals. Micromachines will mean a drastic shakeup in the medical industry. Already the world of "old medicine" is seeing a shift, as micromachines, virtual realities, teleoperation, and intervention changes traditional surgical techniques toward those used in internal medicine. Physicians, meanwhile, are developing new treatment methods—surgical techniques and internal robots—in an effort to promote localized drug delivery systems, but these goals will not be achieved without the development of micromachine technology. This market accounts for over 1/3 of total medicine expenditure. It is vital that micromachines be utilized in this area first.

As a practical consideration, microsystems technologies would be applied following six categories of future biomedical engineering fields (Table 1). Micromachining technology is applied to some of these applica-

Table 1
Micromachine Technology Applications in Future Biomedical Engineering Fields

Medical applications	Future technological seeds
Microscopic surgery	Televised micro operation, virtual reality, microrobotics, laparoscopic surgery
Fiberscopic surgery	Stereo vision, remote microsensing systems, remote operations systems, microrobotics
Laser angioplasty	Fine fiber optics, microactuators, submicron sensing systems, virtual reality
Micromanipulation technology	Submicron mechanical probes, cell handling technology, integrated fluid circuits
Implantable artificial organs	Microactuators, microenergy sources, microparts, microsensors, nanoactuators,
Drug delivery system	Artificial membrane technologies, remote control technologies for microparticles

tions but ordinal microsize production technology remains in the status of a handicraft. Some of these technologies belong to microelectro-mechanical systems, but major parts are for mechanical, chemical, and optical systems in the microscopic domain.

MICROSCOPIC SURGERY

Microsurgery is the most typical application of micromechanical systems. Microsurgery is a short form of "microscopic surgery" and means the finest operation under a stereo-microscope of 60 × magnification maximum. An artery or a nerve of 600 μm diameter can be anastomosed by a well trained operator, who stitches them up with sutures of 20-μm diameter needles and strings. Ophthalmology, otology, peripheral vascular surgery, neurosurgery, and plastic surgery mainly use this operation method. The thinnest limit of operable arteries and nerves depends upon working gaps between the object lens and objects for operation. If the gap is < 15 cm, surgical tools cannot be manipulated. Another limitation is training difficulty, because microsurgery depends on the accuracy of the moving human hand. Therefore, the technical improvements of microsurgery have slowed down in the 30 y since the stereo-microscopic operation system was announced in 1957.

To make the operation technique easier and finer to fit in smaller gaps than the human hand can work in, the micromanipulator or a microrobot hand driven remotely by microactuators could be applied to microscopic surgery. Human hand movement is proportionally reduced and transfered to the robot hands and resistance from the object is sensed by the microsensors in the robot hands and fed back to the human hand. Visual information obtained by a stereo microscope transfers video signal to a stereoscopic television display or to a head-mount display. These techniques are generally called "virtual reality" or "artificial reality".

LAPAROSCOPIC SURGERY AND FIBERSCOPIC SURGERY

One of the modern trends in surgical procedures is less invasive operating techniques. Instead of conventional surgical methods, remote operations using an endoscope or intervention techniques have been gradually but more frequently applied in surgical operations. The key technology is the optical endoscope system, which is usually used for observing abdominal organs through a hard and straight tube (called a laparascope) penetrated through the abdominal wall. One typical example of this surgery is laparoscopic cholecystectomy.

Since late in 1980s televised operations using a hard laparoscope and a laser scalpel have been realized. Laparoscopic surgery to the myoma of the uterus was first the major application, but the technique was diverted to cholecystectomy (*1–3*). Advantages of the operation methods are as follows:

1. low invasiveness;
2. few postoperative complications, especially low adhesion of the peritoneal membrane;
3. earlier release from the hospital; and
4. almost no scarring on the abdominal wall.

The most important innovation of the laparoscopic cholecystectomy might be that this method introduced systematically microdisposable parts into surgery. The mechanical parts were developed and composed of staplers and their applicators, trocars, which are guiding pipes of mamipulators into the abdominal cavity, a lapaloscope, a laser scalpel, and interchangeable operating tips for micromanipulations. These parts are systemically arranged and mass-produced as microdisposable units.

This system suggests to us the future image of surgery. Most future operations will be performed from inside the body cavity through narrow channels of the body wall. New types of remote microoperation techniques will inevitably appear in the surgical world. What is the next technological breakthrough?

Current laparoscopic operations use four or five trocars penetrated through the abdominal wall at one time to guide many straight instruments. A trocar is a hard straight hollow tube with an outer diameter of almost 6 mm. The endoscope is a hard and straight laparoscope that allows an image of the abdominal cavity to be sent by a lens system to a television camera with charge coupled devices (CCD). Almost all inserted instruments for the operation are hard and have a rod-like shape. Because the operator inserted those instruments from different directions to hold and pull organs and tissues, many trocars are essentially used to support these instruments.

If instruments were developed with soft materials and were able to bend, and they could work as a robot's hand does, operations would be changed completely. The operation would be performed with fewer trocars. But nowadays, many operators who performed laparoscopic surgery using soft fiberscopes said that the orientation of direction is very difficult to adjust to compared with the hard laparoscopes. The direction of the patient's head and legs was missed frequently when they used the bending endoscope. To prevent such problems, we must develop some micronavigation systems and positioning sensors such as a microgyroscope or microaccelerometer, on top of the endoscope.

Stereo-vision application will improve the system. The anastomoses of the intestine have been already tried in clinical cases under stereo-vision using a new stereo-laparoscope that has an assembled double optical system in a trocar (*4*). The technique will inevitably cause the development of remote-controlled small operation equipment, which will be used for almost all small abdominal operations.

For such remote operations, many sensing transducers will be requested to detect tissue characteristics of physical and chemical properties instead of human fingers and many off-line sensors. A miniaturized electric sector scanning ultrasonic detector has been developed and is used to differentiate string-like tissues into choleduct, artery, vein, nerve, or connective tissue instead of using human fingers (*4*).

LASER ANGIOPLASTY

All tissues and organs are supplied with energy and oxygen by their arterioles and dispose their produced or wasted materials and carbon dioxide through the venulous. Therefore, if we guide a fine endoscope through the arterioles or venulous, we can approach and treat almost all organs and tissues.

From arterioles, since 1974, many vascular surgeons and physicans have developed many kinds of angioplasty tools (*5*). The transluminal coronary angioplasty (PTCA) is one of the most successful invention technologies applied to coronary occlusive diseases today. The method widens narrowed coronary arteries using a balloon catheter, but this balloon catheter is not applicable when the artery is completely clotted or the patency of vessel cavity is very thin. Laser antioplasty without an imaging system has been developed for such cases (*6–8*). These blind laser angioplasty methods have been criticized for their risk of perforating the vascular wall. Hence, the laser angioplasty with an ultra-thin image fiber has been developed. As the outer diameter is limited at the utmost to 1.5 mm, many technological demands exist for micromechanical technology.

Improvement of images coarseness would be the first target of microsystems technology. As angioscopic images are obtained through narrow communication channels, the number of picture elements has been 5000 pixels at most. For example, the outer diameter of a modern finest image fiber reaches only 200 μm, but the number of image elements is only 1600 pixels if we use glass fibers. When clinicians diagnose the pathophysical abnormality with endoscopic images, this number of pixels seems inadequate. Therefore, we must develop some image enhancement systems. One resolution would be optical scanning methodology and another would be stereo-vision systems. These techniques would provide some supplementary images to the original pixels and cause a human optical illusion, which is also the same principle produced in the dynamic vision applied to movie and television images (*9*).

Remote operability of a bending catheter tip is a great target of microtechnology. Current angioplasty catheters are usually bend using thin long cables. If we can use microactuators on the tip of the catheter, it will be adequate for decreasing the cannula diameter and bending remotely. Recently, a micromotor with an outside diameter of <1 mm, and a tube of a few micrometers outer diameter that is able to be bent pneumatically have been developed by Toshiba. These actuators may be applicable for microcatheter techniques.

Sensing by using catheter-immersed transducers is also one good example of microtechnologies. In cardiac catheter testing, pressure, blood flow rate, blood gas information, and blood chemical analysis data are collected by transducer systems outside the body. When we collect such data on-line, we must develop catheter-tip type transducers. The size of ordinal electronic transducers are not smaller than 1 mm and, more importantly, the electric current through the vessels sometime causes microshock to the heart. From that point of view, optical fiber sensing systems will provide better solutions (*10*). Today, glucose sensors using thin optical fibers that are coated with immuno-fluorescent materials have been developed, and such a pH sensor was reported (*11*). The technology goes to futuristic cellular sensing devices that were developed as single fiber systems (*12*).

MICROMANIPULATION TECHNOLOGY

Micromanipulation technology is familiar to biotechnology, especially cell handling techniques. Cell sorting, cell fusion, DNA fragment injection in a cell, and organelle handling are techniques used with many kinds of microscopes and stereo microscopes. With ordinal microscopes, we can manipulate a cell, fuse cells, and inject DNA fragments or other materials into a cell with micropipet of 1 μm external diameter. For measuring cell function, patch clamp methodology for analyzing the function of a single ion channel developed by Neher and Sackmann in 1976 is also supported by the micropipet and micromanipulation technique (*13*).

In those technical fields, some microelectromechanical systems have been applied. Instead of many microsize glass tools, especially micropipets and microknives, which are conventionally made by microforge methods, molded micropipets are made by microelectrodischarge fabrication technology. Instead of manual cell-manipulation, optical cell trapping systems have already produced noncontact micromanipulation of microscopic particles, living cells, or chromosomes. Microinjection methods have also improved by nano-precise positioning techniques actuated by micropiezoelectric elements (*14*). Micromanipulation methods using electrostatic forces have been applied in integrated microfluidic circuits that are made by lithographic techniques. The target of the system application is cell fusion and chromosome handling (*15*). All these products have incentives to produce a desktop biotechnological factory using micromachining technology.

Measuring physical parameters of live materials with atomic precise scales can be pursued by many types of scanning probe microscopes and near field microscopes. These instruments will unveil many secrets of cell structures and functions. Using such technology, the ultramicrosurgical techniques will open new domains, such as remote micro operation, organ operations, and molecular treatment in a cell.

IMPLANTABLE ARTIFICIAL ORGANS

The artificial organ is one type of cybernetic system that includes many functions for measuring and controlling. Instead of almost all organs, we can apply prosthetic organs for those substitutes today. The finest and most successful artificial internal organ might be the cardiac pacemaker, which is fabricated as a microelectronic system. Some types of modern pacemakers have a signal detecting electrode to catch sinus potential, and an acceleration transducer that detects the exercise load of the patient. Those signals are processed by built-in microprocessors that are designed especially for low electric power consumption. Each component has been especially developed for the pacemaker, and today the pacemaker is one of the most miniaturized, reliable, and durable instruments in clinical medicine.

Similar examples are found in sensory prostheses, such as an internal ear substitute and functional electric stimulation system of muscles. These products are mainly composed of microelectronic circuits and have been developed to be made as small as possible. However, other large internal organs or extremity prostheses have not successfully been built as small as bodily organs. One reason is that the size of the mechanical parts is too large. There is thus an incentive to develop micromechanical parts applicable for such internal organs.

The most fundamental micromechanical inventions in this field exist in microactuator and energy converter technology. Live organs use chemical energy. In human-made systems, energy sources must be supplied externally as a substitute of chemical energy sources. If we build up tether-free internal organs, we must develop an energy transmitting system through skin or a high-density energy reservoir. Electromagnetic force, magnetic force, and ultrasonic force can be supplied from outside the body. Recent developments of microelectrostatic motors and ultrasonic motors are good key technologies in this field, but the most important products will be microsize linear actuator elements that can be integrated like the sarcomere of the muscle fiber. A film-type actuator powered by linear electrostatic actuator principles has already been developed and used (*16*). The electrostatic linear actuator has the potential to produce artificial muscle systems. A microlinear-actuator element that is able to use vibrational energy in the field has been reported, and this element can integrate itself with the muscle structure (*17*).

For developing endocrine organs, like pancreas, adrenal organs, and so on, we must prepare some macrodrug delivery systems, which I call artificial endocrine organs. To develop artificial microendocrine organs, such as an artificial pancreas or an artificial Langerhans island, we must develop ultra microsize glucose sensors, drug containers, and drug releasing systems. Instead of these systems, one substitute is the microinjection system, which resembles a mosquito needle. Recently an injector with a fine needle with saws has been developed (Togawa, 1992).

A microsecretorial gland that looks like a pill and is used for measurement and treatment in the intestinal tract usually called an endoradiosonde. The prototype was reported 30 years ago, but recently it revived the first proposal of medical micromachines (MITI of Japan, 1991).

DRUG DELIVERY SYSTEMS

Drug delivery systems (DDS) using microcapsule technology seem to be a final target of endosonde to use internally in humans. Today's microcapsule technology for DDS is mainly dependent on constructing liposome-coated drugs applied in vessels. Two important technolgoies are included: how to deliver the drug to target organs or tissues at the most beneficial time; and how to escape from phagocytes. We must develop capsules destructible by outside signals and detecting methods of capsules from outside of the body. One trial is microcapusulae made from some kind of polymer films that can detect and destroy by external ultrasonic power excitation (*18*), but this method has major limitations to delivering drugs outside of vessels or into cells. We must add some functions that enable us to release drugs outside of the vessels. This machine parts would become submicrometer in size.

IN FUTURE

Micromechanical systems technology will have a great impact on biomedical engineering. Technologies for the creation of sub-micro sensor elements will cause a great advance in developing micromachines in medical fields, but recent surveys related to the microsensor reported that the electronic transducer has great difficulty miniaturizing below 10 μm. We must find some other principles to detect chemical or physical parameters in the living body. Optoelectronics will supply us with some methodologies, such as photon technology and fiber optics. Remote sensing technologies also will give us much information about the internal body from outside. As shown in past 40 years, automated multichannel biochemical sample measurement systems (autoanalysers) have made great advances after the system components became miniaturized and the total system could sit on a desktop. Today, new machines for sorting cells, organelles, and DNA fragments have been requested as automatic desktop machines. In such machines, microsize measuring transducers is also requested.

There are no existing technologies that meet all these requirements. Even those that have potential are still in the experimental stage, in the development stage, or just on the drawing board, but many of them will be important, basic technologies in the near future.

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