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Establishment of Collaborative Research Centers for Medical Engineering in Japan

Cooperative Program "Biomedical Engineering" between Engineering and Medicine in Japan

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Introduction

1. What is biomedical engineering?

On the website of the Whitaker Foundation [1], biomedical engineering is defined as follows:"Biomedical engineering is a discipline that advances knowledge in engineering, biology and medicine, and improves human health through cross-disciplinary activities that integrate the engineering sciences with the biomedical sciences and clinical practice. It includes:

1) The acquisition of new knowledge and understanding of living Continued on page 2

Waseda University was a pioneer in the collaboration between the engineering and medical fields in Japan

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Introduction

1. Waseda's history of collaboration between the engineering and medical fields

Collaboration between Waseda's mechanical engineering department and the medical filed started over 40 years ago. These initial collaborations were as follows. Prof. Ichiro Kato developed the human interaction robot, the world's first practical myoelectric prosthetic hand and lower limb, with the Tokyo Metropolitan Prosthetic and Orthotic Research Institute, which was located next to Waseda University Continued on page 4

AIST as an M-E collaboration platform for R&D of medical devices

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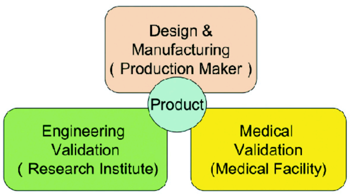
Introduction

In the field of artificial heart Dr. Tetsuzo Akutsu, who developed the world's second clinical artificial heart, said that three essential factors for development of artificial heart are materials, design and manufacturing. In the development of medical devices, M-E (Medical and Engineering) collaboration is important between design and manufacturing (production maker),engineering validation (engineering research institute), and medical validation (medical institution) as Fig.1. Before approval of products, a manufacturing/sales Continued on page 6



Global-COE Program for *in silico* Medicine at the Center for Advanced Medical Engineering and Informatics

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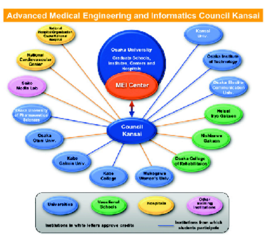
Introduction

The Center for Advanced Medical Engineering and Informatics

Osaka University has a long history of collaborative research between medicine and engineering. The center for advanced Medical Engineering and Informatics (MEI center: http://www.mei.osaka-u.ac.jp/) was established in 2004 in order to systematically promote research and education in inter-disciplinary field of medical engineering and informatics, as the first center founded at Osaka University after the reformation of National University to National University Corporation in Japan. Professors are jointly appointed from Graduate Continued on page 8



Cooperative Program "Biomedical Engineering" between Engineering and Medicine in Japan

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Continued from page 1 systems through the innovative and substantive application of experimental and analytical techniques based on the engineering sciences.

2) The development of new devices, algorithms, processes and systems that advance biology and medicine and improve medical practice and health care delivery."

In the United States of America, this field has been developing since 1970's, dramatically. More than 87 universities have bioengineering programs in undergraduate and/or graduate schools [2]. The numbers of students in undergraduate and graduate schools in biomedical engineering are approximately 12,000 and 4,000, respectively, as of the data of 2003. In Japan, some universities have started the programs related to biomedical engineering in a recent decade as shown in Table 1.

2. A Case of Tohoku University

On April 1st, 2008, we founded the first graduate school of biomedical engineering in Japan (Fig. 1). One of the primary mission objectives of the new graduate school is to contribute to human social welfare by defining the enigmatic mechanisms of life using engineering expertise, knowledge, and technology. The school was founded in accordance with a criterion set by the Ministry of Education, Culture, Sports, Science and Technology to develop the field that was called as an interdisciplinary one into a new and large disciplinary field of biomedical engineering. Over 80 years ago at Tohoku University, collaboration between the engineering and medical departments yielded the invention of the electric stethoscope. This is well known as a pioneering work of biomedical engineering in Japan, and much other collaborative work between the engineering and medical departments has since been performed at Tohoku University. The birth of the new graduate school was based on the traditional foundation of education and research established by our forward-thinking predecessors. Our school comprises 10 divisions with 31 laboratories conducting cutting-edge and strategic biomedical researches. The educational system is shown in Fig. 2. The aim is to educate researchers and engineers who have creativity, strong research skills, and expert

Table 1 Biomedical engineering related programs in undergraduate and graduate schools in Japan. (Courtesy of Dr. K. Imachi)

as of January, 2008

	Before 2003	2004	2005	2006	2007	2008
	・1998 Hiroshima International University Faculty of Engineering Department of Medical Engineering ・1997 Kagoshima University Faculty of Engineering Department of Bioengineering ・1994 Kitasato University, School of Allied Health Sciences Medical Engineering ・1991 Suzuka University of Medical Science Faculty of Biomedical Engineering	・Chiba University Facuity of Engineering Medical System Engineering ・University of East Asia Faculty of Medical Technology ・Chiba Institute of Science Faculty of Risk and Management Department of Risk and Management	・Toin University of Yokohama Faculty of Biomedical Engineering	・Himeji Dokkyo University Faculty of Health Care Sciences Department of Medical Engineering ・Kyorin University Faculty of Health Sciences Department of Clinical Engineering	・Maebashi Institute of Technology Faculty of Engineering System Bioengineering ・Osaka Institute of Technology Faculty of Engineering Department of Biomedical Engineering ・Okayama University of Science Faculty of Engineering Department of Biomedical Engineering ・Kawasaki University of Medical Welfare Faculty of Health Science and Technolory Department of Medical Engineering ・Kyushu University of Health and Welfare School of Health Science Department of Medical Engineering ・Saitama Medical Science University Faculty of Health and Medical Care School of Biomedical Engineering ・Tokushima Bunri University Department of Science and Engineering School of Medical Engineering ・Musashi Institute of Technology Faculty of Engineering Department of Biomedical Engineering	・Tokai University School of Biological Science and Engineering Department of Human Science and Informatics ・Doshisha University Faculty of Life and Medical Sciences Department of Biomedical Engineering ・Shibaura Institute of Technology College of System Engineering Bioscience and Engineering
	・2003 Hiroshima International University Graduate School of Integrated Human Science Major in Medical Engineering ・2001 Yamaguchi University Graduate School of Medicine Major in Applied Medical Engineering Science ・2001 Kagoshima University Graduate School of Science and Engineering Major in Bioengineering ・1993 The University of Tokyo Graduate School of Medicine Department of Biomedical Engineering			・The University of Tokyo Gradute School of Engineering Department of Bioengineering	・Osaka Institute of Technology Graduate School of Engineering Major in Biomedical Engineering	・Tohoku University Graduate School of Biomedical Engineering ・Kyorin University Gradute School of Health Sciences Clinical Engineering ・Doshisha University Graduate School of Life and Medical Sciences Major in Life and Medical Sciences Biomedical Engineering

Figure 1 Graduate school of biomedical engineering, Tohoku University, first established on April 1st, 2008, in Japan.

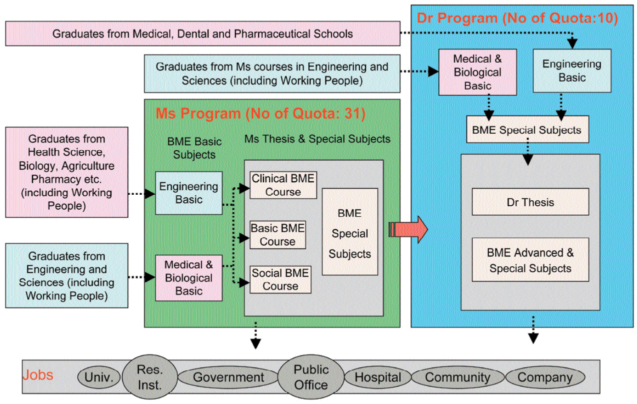

Figure 2 An overview of educational system in the graduate school of biomedical engineering, Tohoku University.

knowledge in the integrated field of biomedical engineering. These researchers and engineers will pursue their own research and development to promote evolution and innovation in science for the improvement of medicine and social welfare in order to realize a truly affluent society. We expect the students entering our new graduate school and exploring this new frontier to be leaders with high ideals and a zest for education and research in biomedical engineering.

Before the establishment of the graduate school of biomedical engineering, the 21st century COE program "Future Medical Engineering based on Bio-nanotechnology" (Leader: Masaaki Sato, FY2002 - 2006) was adopted and the main concept was taken over to the global COE program "Global Nano-Biomedical Engineering Education and Research Network Centre" (Leader: Takami Yamaguchi, FY2007 - 2011). The mission of the 21st century program was to form a global center of excellence in biomedical engineering. For this aim, we were uniting various technologies in order to develop the ultimate prophylactic measures for age-dependent diseases, using tailor-made diagnostic and therapeutic procedures and fostering young researchers through advanced research activities and education. As our unique education system we adopted two different ones: nomadic education system and itinerant education system. In the nomadic education system, through competition, students were selected to participate in cooperative research at universities abroad. Students from universities overseas were selected and invited to our program. In the itinerant education system, self-reliant students were selected and trained individually under special apprenticeship program with individual professors. Our advanced research in the field of biomedical engineering was taken in four areas: 1. Cell Function and Biomolecular Technology, 2. Nanomedicine, 3. Imaging and the Structure of Biomolecules, and 4. Medical Informatics.

The "Tohoku University Biomedical and Engineering Research Organization (TUBERO)" was established after our university was awarded a research grant from the "Special Coordination Funds for Promoting Science and Technology" for 2003 as part of the government's "Center of Excellence" program (Director: Makoto Tamai, FY2003 - 2007). We realized that one of the major objectives of this program was to produce successful results and led a new era in research and development. Moreover, the program of "Recurrent Education for the Development of Engineering Enhanced Medicine" has been performed from the view point of cultivation of human resources on the research grant of the "Special Coordination Funds for Promoting Science and Technology" (Leader: Takami Yamaguchi, FY2004 - 2008).

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Waseda University was a pioneer in the collaboration between the engineering and medical fields in Japan

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Continued from page 1 in the 1960's. In conjunction with medical doctors from the National Cancer Center Research Institute, Prof. Kato also authored a paper on a palpation robot for breast cancer [1] - by pressing on the breast, the robot could identify the location of the cancer; this paper is referenced in many papers on minimally invasive surgery, especially robot-assisted breast cancer surgery, which currently is one of the hot research topics in advanced countries. Finally, Prof. Kiichi Tuchiya was involved in collaborative research with Tokyo Women's Medical University on the artificial heart. In fact, the implant of an artificial heart was demonstrated during one of Waseda's annual science and engineering festival around that time. Prof. Fujie, who is one of the authors, remembers the smell of electrical knife after the demonstration.

2. Robot-centered collaboration between the engineering and medical fields

It is well-known that Waseda does not have a medical school. So, after the 1960's, a lot of Prof. Kato's disciples collaborated with the medical departments of other universities and with national research institutes in research on medical-assistive robots, and they achieved remarkable results and even breakthroughs, which at the time were less well known worldwide than Waseda's research on biped robots and intelligent robots. In addition, one of Prof. Tsuchiya's disciples achieved the first practical use of the artificial heart.

Furthermore, in 2001, the bioscience and biomedical engineering course was established as an interdisciplinary major at Waseda University, thanks to the efforts of Prof. Tsuchiya. In addition, the Tokyo Women's Medical University‐Waseda University Joint Institute for Advanced Biomedical Sciences (TWIns) was established in 2008, and Prof. Umezu, Prof. Takanishi and Prof. Fujie became faculty members for the major in modern mechanical engineering.

3. Current state and vision of collaboration between the robotic and medical fields

In the 21st century Center of Excellence (21COE) program “Innovative research on symbiotic technologies for humans and robots in the elderly dominated society,” medical-assistive robots were established as the core technology that utilized the infrastructure of the university introduced above. Based on the achievements of the 21COE program, Waseda has established one of the most innovative education and research institutes in the world;

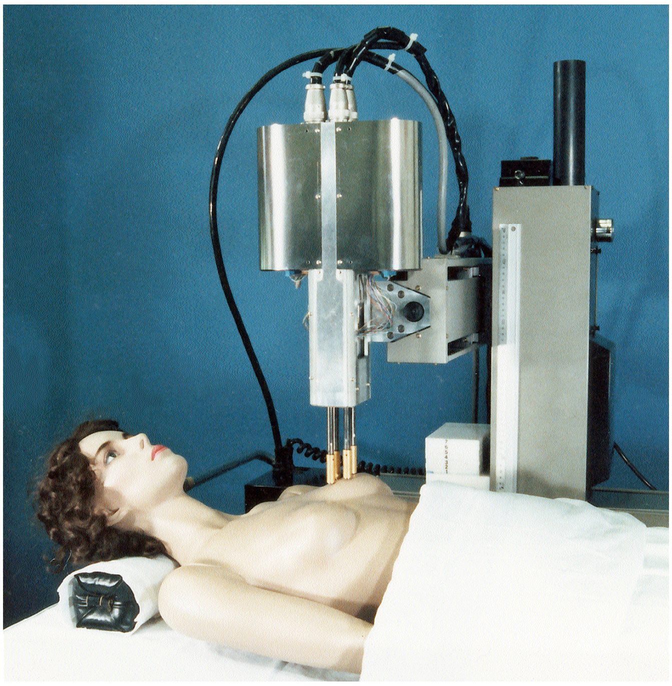

Fig. 1 palpation robot of breast cancer (WAPRO-4R)[1]

Fig. 2 TWIns

called “Global Robot Academia,” the institute aims not only to develop application robots but also to systematize the field of robotics.

Representative results of our two COE programs in the robotic and medical fields follow.

In the surgical field, a dexterous master-slave surgical robot with heartbeat canceller for endoscopic off-pump coronary artery bypass has been developed with Prof. Takemura of Gifu University (Fig. 3)[2], and a needle-insertion robot based on a physical properties model has been developed with Prof. Hashizume of Kyusyu University[3].

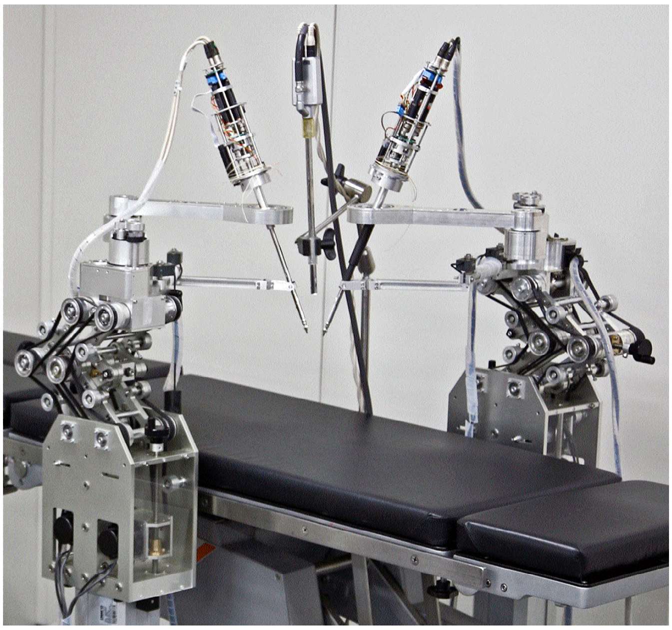

Fig. 3 Heartbeat canceller surgical robot [2]

In the rehabilitation and assistive technology fields, the Takanishi Lab. has collaborated with Asahi University to develop a new rehabilitation robot, known as "Waseda Asahi Oral-Rehabilitation Robot No.1"(WAO-1) [4] to provide massage therapy of the maxillofacial region (Fig. 4). In addition, the Fujie Lab. has developed with the Shizuoka Cancer Center a rollover support system, called “Intelligent Corset, [5]” for cancer bone metastasis patients (Fig. 5).

Moreover, the Takanashi Lab. is working on a bipedal humanoid robot, “WABIAN-2R” (WAseda BIpedal humANoid-No.2 Refined) [6], as a human motion simulator, which allows the testing of welfare apparatuses in the development stage on a humanoid in place of a human being such as a hemiplegic patient, as well as the feedback of quantitative data for further development of the welfare apparatuses (Fig. 6).

Our laboratories also have developed new mobility-aid devices that can enhance personal mobility of the elderly and/or infirm. For example, the Takanashi Laboratory has developed a multi purpose biped loco-motor called “WL-16RV” (Waseda Leg-No.16 Refined V) as an independent leg module that is sufficient for practical use, such as in a wheelchair that is able to walk up and down stairs carrying or assisting a human (Fig. 7)[7]. In addition, the Fujie Laobratory has developed a walking-enhancement vehicle called “Tread-Walk” that not only expands the activity area of the user but also helps to maintain his or her body functions (Fig. 8)[8].

From now on, collaboration between the robotic and medical fields will be one of the most important missions in the “Global Robot Academia.” We will develop many kinds of robots to support patients, as well as disabled and elderly people, from the view point of physical assistance but also with a focus on mental support, safety, and ethics. Finally, we aim to construct M-Robotics (Methodical

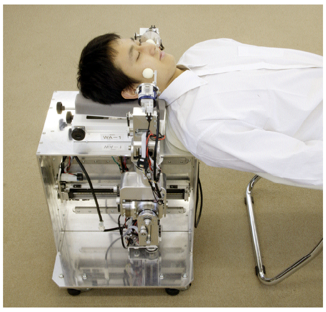

Fig. 4 WAO-1 [4]

Fig. 5 Intelligent corset [5]

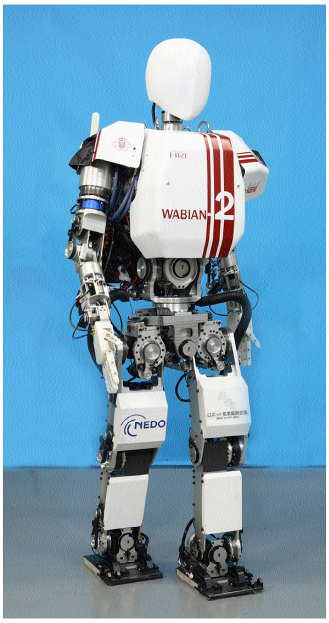

Fig. 6 WABIAN-2R [6]

Fig. 7 WL-16RV [7]

Fig. 8 Tread-Walk 1 [8]

Robotics) by applying solutions to the various pragmatic problems of daily living. M-Robotics, which is based on the principles and systems of robot technology that already have been developed, will provide significant support for future generations.

4. Challenges to the vision of collaboration between the engineering and medical fields in Japan

To improve collaboration between the engineering and medical fields so that innovative and intelligent machines such as robots may be developed, many academic engineering and medical societies need to cooperate closely. Currently, some engineers collaborate with medical doctors in only the evaluation phase of machine development. In future, it will be important for engineers to collaborate with medical doctors from the initial phase of machine research and development. In addition to the cooperative alignment of professional societies in the engineering and medical fields, opinions and information also should be exchanged and stored regularly between engineers and medical doctors. As a result of this alignment and exchange, an important information platform will be established to develop medical devices, machines, and systems. Furthermore, an education and training system should be established to bring about the smooth collaboration between engineers and medical doctors. Finally, a joint society representing the engineering and medical fields should recommend science and technology policy for Japan.

The Japan Society of Mechanical Engineering already is planning to conduct unit meetings as soon as possible on medical and engineering technology, similar to the meetings already being conducted by the engineering and medical fusion system unit, System Integration (SI) section, Society of Instrument and Control Engineers (SICE) and by the Japan Society of Computer Aided Surgery (JSCAS).

5. Conclusion

Beginning in the 1960s, Waseda University's Mechanical Engineering groups have collaborated with representatives of the medical field to develop numerous medical, surgical, and medical-assistive systems.

To improve existing systems and develop new and innovative systems in the medical field, engineers and medical doctors need to cooperate. In addition, academic societies representing both the engineering and medical fields should provide the infrastructure for smooth cooperation. The ultimate result of these efforts will be significant improvement in the QoL (Quality of Life) of patients, as well as disabled and elderly people.

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AIST as an M-E collaboration platform for R&D of medical devices

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Continued from page 1 company should perform many kinds of safety/efficacy tests and clinical tests in collaboration with clinical facilities. These are the different process from other industrial products to deliver safe medical products. M-E collaborations in the stage of development for each device are exemplified here.

(1) Monopivot type centrifugal pump for circulatory assist

In the development of centrifugal pump with a monopivot (single pivot) bearing for open-heart surgery and circulatory assist for two weeks or more, we collaborate with University of Tsukuba and with Tohoku University in animal experiments. We design, fabricate, and sterilize the pump models. Medical doctors conduct operations and maintain animals with facility staffs. As shown in Fig. 2, a production maker, Senko Medical Instrument Mfg. Co., Ltd. in our case, performs design and manufacturing and then apply for approval of the product.

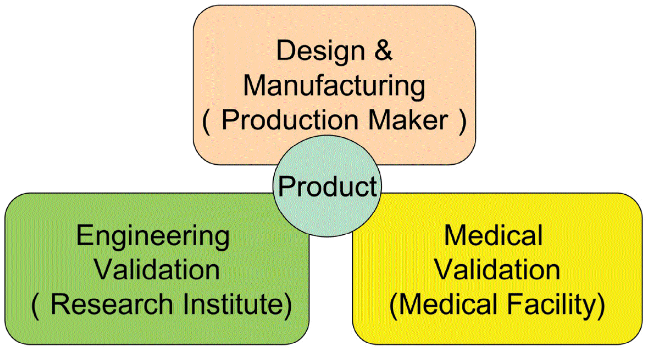

Fig. 1 M-E collaboration for a product

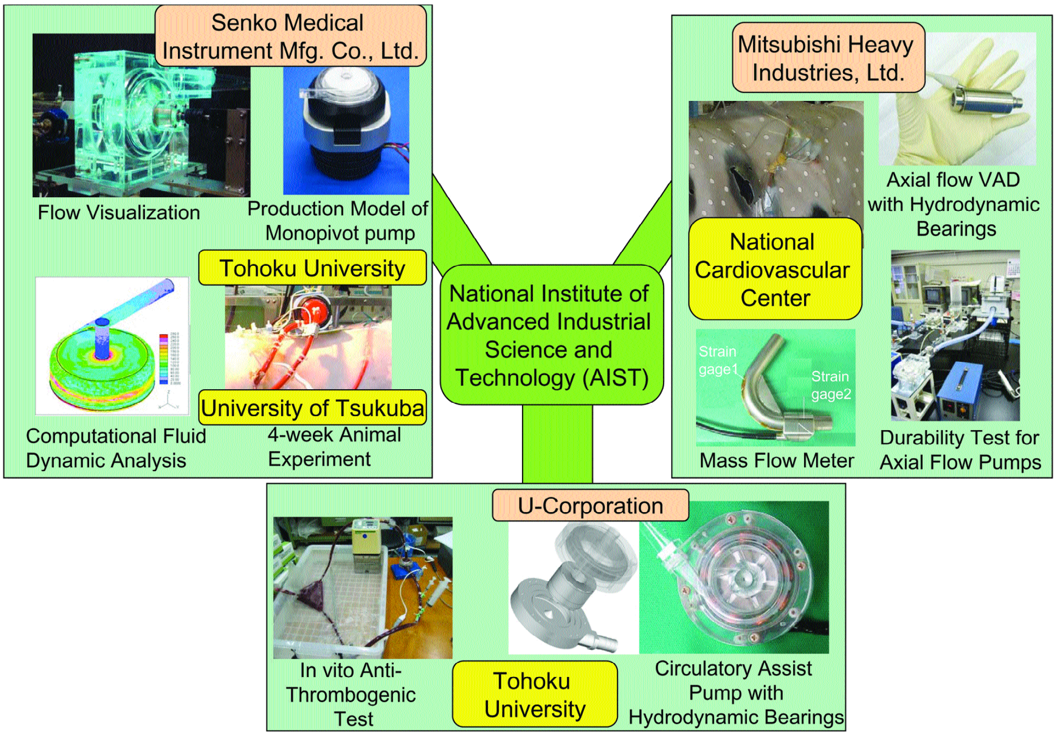

Fig. 2 M-E collaboration of AIST

Regarding the prototypes made of acrylic resin, the closed impeller, 50 mm in diameter, is supported by a monopivot bearing at the end and by a permanent magnet at the other end. The prototypes (DD1-DD10, MC1-MC5 models) were tested with sheep at University of Tsukuba for over 4 weeks and no significant complications were found[1)2)].

Regarding the production type made of polycarbonate, the impeller is 50 mm in diameter and has 4 straight paths, which is supported by a monopivot bearing through 4 ribs. The model was tested with goat at Tohoku University for 4 weeks and no significant complications were found.

Since the pivot undergoes concentrated exposure to the phenomena of wear, hemolysis, and thrombus formation, we conducted separately the engineering validations using flow visualization, durability test, hemolysis test, and in vitro antithrombogenic test.

In the in vitro antithrombogenic tests, the closed circuit was filled with bovine blood, and sodium citrate and $CaCl_2$ were used to maintain ACT value to be 200 s at 37°C for two hours. The pump was set at 200mmHg-4L/min with a rotational speed of 2800 rpm. Slight thrombus observed at a sharp corner was successfully removed by modifying sharp corners round and by designing male and female pivots in the same radius.

In the durability test the pump was set at 300mmHg-4L/min with a rotational speed of 3300 rpm in the closed circuit filled with 37°C saline. The female pivot was made of ultra high molecular weight polyethylene (UHMWPE). The steady wear rate was found to be 1.5 micrometer/day for the last 3 weeks.

(2) Non-contacting type axial flow pump with hydrodynamic bearings for ventricular assist

We are also developing a non-contacting type axial-flow pump with hydrodynamic bearing for an implantable left ventricular assist device in collaboration with Mitsubishi Heavy Industries, Ltd. and with the National Cardiovascular Center in animal experiments.

The impeller is supported with a hydrodynamic radial bearing and a hydrodynamic/ passive-magnetic thrust bearing. The pump is made of Titanium alloy and the size is 29 mm in diameter and 75 mm in length, and 10mL in priming volume, whose size is one of the world's smallest among non-contacting types. Pumping pressure 100 mmHg and flow 5 L/min can be attained at a rotational speed of 9000 rpm. We conducted hemolysis tests, in vitro anti-thrombogenic tests with nonpulsatile mock loops, and durability tests with pulsatile mock loops. The animal tests were conducted at the National Cardiovascular Center and attained 90-day implantation[3)].

Though a flow meter is important especially for patients discharged from hospital, the flow estimation for an axial flow pump is not so easy as a centrifugal pump since the axial flow pump has no linear relation between current and flow rate. We are developing a miniature mass flow meter which detects the fluid dynamic centrifugal force in a bending tube, which is not affected by blood viscosity. The prototype was verified the accuracy and the response characteristics in a mock circulatory loop[4)].

(3) Non-contacting type centrifugal pump with hydrodynamic bearings for circulatory assist

We are also developing a sensorless centrifugal blood pump (HH1-HH8, HH101-HH202) with hydrodynamic bearings for circulatory assist in collaboration with a manufacturing company, U-Corporation.

The impeller diameter is 36 mm and the priming volume is 13 mL. The hydrodynamic bearings are composed of a top thrust bearing in spiral groove type, a bottom thrust bearing in step type, and a radial bearing in herring bone type. Radial bearing is placed in the central plane of radial-flux motor to assure stability[5].

The impeller displacement, namely the hydrodynamic bearing gap, was modified to suppress the hemolysis level by balancing the hydrodynamic force and the motor magnetic force and by introducing a step hydrodynamic bearing. The hemolysis index, NIH<0.01 g/100L, was attained when the bearing gap reached more than 50 micrometers. After an in vitro thrombogenic test and an animal test at Tohoku University for 24 h, no complications were found.

Through these M-E collaborations we learned that it is important (1) to hear the other members' voice, (2) to try plural solutions before design modification, and (3) to isolate product information between companies.

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Global-COE Program for *in silico* Medicine at the Center for Advanced Medical Engineering and Informatics

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Continued from page 1 Schools of Medicine, Dentistry, Pharmaceutical Science, Frontier Bioscience, Engineering, Science, Engineering Science, and Information Science and Technology, Institutes for Protein Science, Institute of Scientific and Industrial Research, and Cybermedia Center. This center has two organizations for education: the division for open education of graduate students and the unit for recurrent education of engineers and researchers in business and industry (Fig.1).

The former division is organizing four education courses, i.e. Biomedical Informatics course, Biomaterial course, Advanced Diagnosis and Treatment course and Molecular Imaging Course for master's course students, and the latter unit is organizing problem-based and project-based learning for doctoral students in areas of Medical Database, Biomedical Engineering and Informatics Platform, and Advanced Biomedical Measurement and Diagnosis System. These programs are approved as Osaka University Graduate School Advanced Subprogram and are open for all graduate students of Osaka University, and more than hundred students completed these programs every academic year.

The latter units was started in 2006 and provides Advanced Diagnosis and Treatment Engineering consisting of Diagnosis/ Treatment Systems subcourse and Biomedical Imaging and Information subcourse; Biomedical Informatics consisting of Medical Informatics subcourse, Biosimulation subcourse and Bioinformatics subcourse; and Biomaterials for Advanced Biomaterials subcourse.

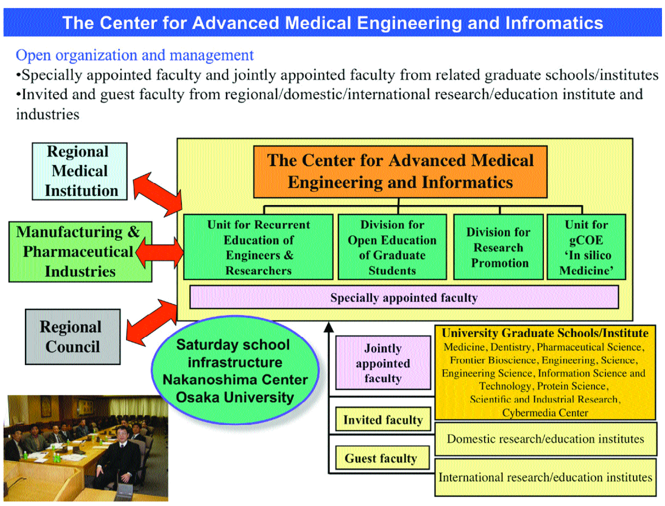

Figure 1

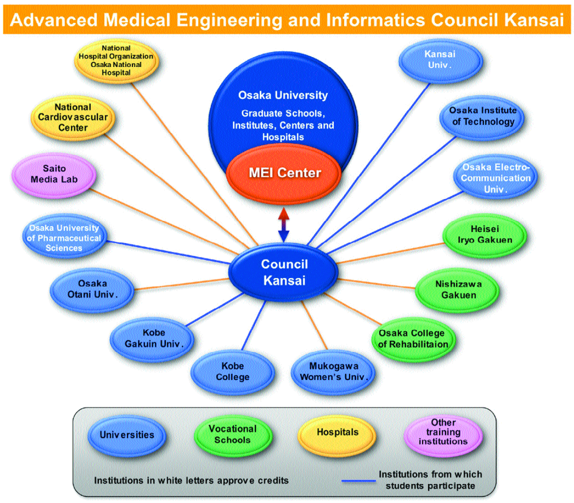

Figure 2

Provided also are subcourses for fundamentals on biomedical engineering and informatics of General Clinical Medicine, and Ethics and Intellectual Property; and for advanced course on Biomedical Statistics, PET Molecular Imaging, Computational Protein Dynamics and others. These subcourses are arranged as a Saturday school throughout the whole year mainly for continuing education purpose. These are also open for graduate students of member universities of Advanced Medical Engineering and Informatics Council in Kansai as well as Osaka University, and individual university approves each subcourse as the official subjects with credits (Fig. 2). Participated are four hundreds industry and business people and hundred students from member universities of the council per year in total person- subcourses, approximately.

The research promotion division works as the platform of collaborative research between medical, dental and pharmaceutical sciences; and engineering, engineering and information sciences and technology. Projects on the engineering for advanced measurement, diagnosis and treatment include trial to diagnose neurologic or psychiatric diseases based on sensing of brain activities; development of device and technology to quantify and diagnose the body motion dynamics, for instance, in Parkinson's, a chronic neurological disease; and development of kinetic modeling of drug distribution using PET. The major target of the database research projects is the development of multi-spatiotemporal scale / multi-levels / high variability learning database that connects the structure of various body organs and functions semantically and constructs the ontology of living systems based on the user's research / registered history. These technologies have applied to the advancement of database in disorder / medical treatment and development of a unification system. Biosimulation and network projects involve the *in silico* cardiology aiming the modeling of cardiac function and predicting the risk of arrhythmia from the chemical structure of the drugs, and the network-based automated implantation planning on virtual private network. Other topics include the development of artificial retina device and tempo-spatial biomedical imaging technology referring the biological mechanism; the development of high-performance computing technology for biomedical image processing and of middleware for grid computing-aided medical diagnosis. These activities are summarized in part in the series of MEI international symposium.

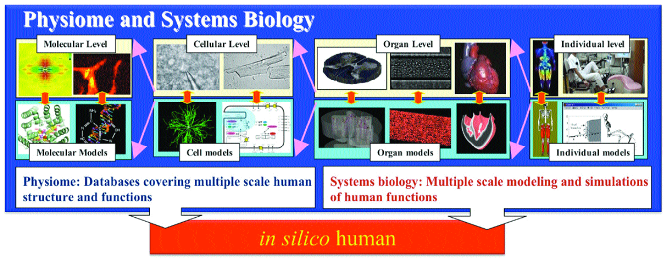

Figure 3

Concerning research projects on the physiome and system biology, a Center of Excellence program, so-called g-COE program, was started in the academic year of 2007.

Center of Excellence for an *in silico* Medicine Oriented Worldwide Open Platform

Physiome and systems biology are emerging and interdisciplinary research fields, arising in consequence of development of biological and medical sciences, engineering and information sciences and technology. For biosciences, complete sequencing of human genome was the epoch-making event liberating vast amounts of experimental data. Advanced engineering and technology allow us to measure human physiological functions with high resolution using PET and MRI among others. Information technology and applied mathematics continue remarkable development, enabling modeling and simulating human functions *in silico*, i.e., within the computer.

The project promoted by this global Center of Excellence for *in silico* medicine aims at integrating these developments and contributing to moving the world towards a new generation of life science where physiological and pathological information from the living human body can be quantitatively described *in silico* across multiple scales of time and size and through diverse hierarchies of organization - from molecules to cells and organs to individuals (Fig. 3).

Promotion of physiome and systems biology requires development of mathematical models that are capable of describing structure and function of the human body across multiple scales, which will be integrated into databases of human physiology. Development of simulators is also performed. It enables us to quantitatively analyze the dynamics of physiological functions, eventually leading to the predictive medicine. *In silico* platforms established within internet- accessible computers play important roles to promote physiome and systems biology. US and EU countries have been aware of their importance and taking initiative. The *in silico* medicine project has got into the international concerted efforts as a Japanese contribution.

Databases of genes and proteins have been widely utilized. So far, these databases deal with static information. Databases establishing by the *in silico* medicine project try to archive more dynamic information, that is, human physiological functions represented by changes in "states" of proteins, cells and organs along time at multiple scales in time and space. The database of the *in silico* medicine at www.physiome.jp has just been open in the public domain with hundreds of peer-reviewed dynamic models of human physiological functions. Each model in the database is represented by its hierarchical and modular structure, allowing the user to investigate the model across multiple scales.

A promising research in the project is *in silico* cardiology, where an integrated system to evaluate quantitatively and even predict a potential risk of drug effect inducing cardiac arrhythmia based on the electrophysiological data and computer simulations of models. Dr. Kurachi, Director of MEI center said. "The platform development must be performed in coherent with targeted physiological functions. The quantitative risk evaluation and prediction of drug effect inducing cardiac arrhythmia are now going to be possible. This is because we could measure the dynamic changes in the membrane potential of cardiac cells and associated ionic channel current with very high accuracy, from which one could relate the cellular function to the microscopic molecular function such as interactions between drugs and channel proteins, and to the macroscopic tissue and organ level functions such as spatio-temporal conduction of cellular activations. The platform must be designed so that it can systematically support such processes across different levels and scales, leading to a scientific discovery and a new integrated understanding of the human physiological functions." The *in silico* medicine project includes a multiple of targets such as *in silico* lung project, *in silico* dentistry, *in silico* neurology among others.

The integrative approach for those varieties of human physiology and pathology will eventually allow us to understand the dynamic mechanisms underlying functions. This means that we will be able to explore the logics of proteins and cells through the modeling of nano and microscopic dynamics governed by the first principles of physics, the logics of cells, organs, and individuals through the phenomenological modeling of meso and macroscopic dynamics of systems as the aggregation of the nano and microscopic objects, and finally, the meta-logics that will bridge between the different scales and hierarchies.

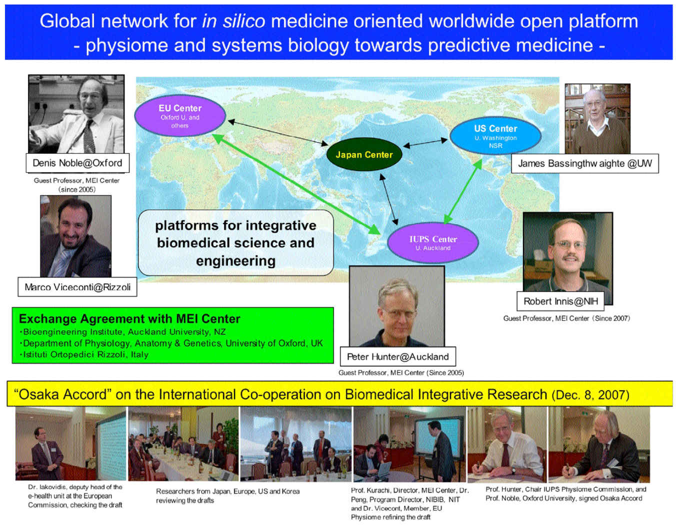

Figure 4

To promote *in silico* medicine oriented research, addressed are the two tasks: (i) to develop models that are capable of describing structure and function of the human body across multiple scales and hierarchies, leading to a database of human physiology and pursuing its sophistication, and (ii) to develop the simulator, *in silico* human, which will enable us to achieve quantitative analyses of the dynamics associated with human physiological functions. Toward this end, two teams are organized and working: the team for research and development of platform system for the projects on platform systems for simulations, on platform systems for databases, and on time series and imaging data analyses; and the team for research in human structure and physiological functions for the projects on human motor functions, on cardiovascular and pulmonary functions, and on pharmacokinetics.

The second MEI International Symposium held in Osaka in 2007 had participation of some of the key people in Integrative Research worldwide, from EuroPhysiome community, IUPS Physiome Project, European Commission, US-NIH, and the Japanese Ministry of Science and Technology. This event became a good opportunity to strengthen the international co-operation on Biomedical Integrative Research, pulling together as the "Osaka Accord" (Fig. 4).

You will find more details of the activities at MEI Center and the g-COE program at websites http://www.mei.osaka-u.ac.jp/english/index.html and http://www.mei.osaka-u.ac.jp/gCOE/english/index.html as well as http://www.physiome.jp/. We welcome your visit.

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