Toward Human-oriented Life

Minoru Sakairi, Dr. Sci.
Keiji Kobashi, Dr. Eng.
Yasutaka Hasegawa
Kazutoshi Kan

OVERVIEW: So that people can live healthy and happy lives, human-oriented technologies in the lifetime domain will become even more sought-after in the future as we face an unprecedented era with an aging population and fewer children. Hitachi views the lifetime domain from the three perspectives of prevention, diagnosis, and treatment and contributes to this field by offering solutions that take advantage of the characteristics of the group. Major examples of this work include positron emission tomography using semiconductor detectors in the field of diagnostics where Hitachi can call on a strong portfolio of individual technologies, a visceral fat simulation technique which represents an example of using large databases for preventive medicine, and an infrastructure technology for regenerative medicine which involves the use of infrastructure technology for therapeutic applications.

INTRODUCTION

THE aim of bringing about a healthy society through the very early diagnosis and treatment of cancer, heart disease, and brain disease in particular is becoming an increasingly important issue in Japan which leads the world in the aging of its population and where lifestyle-related disorders are on the rise. There are many ways of approaching the medical and health services that will be demanded by society in the future and one of these is to look at these issues from the perspectives of prevention, diagnosis, and treatment[1]. Put another way, this is about making a reality of disease prevention through the use of techniques like personalized risk prediction and

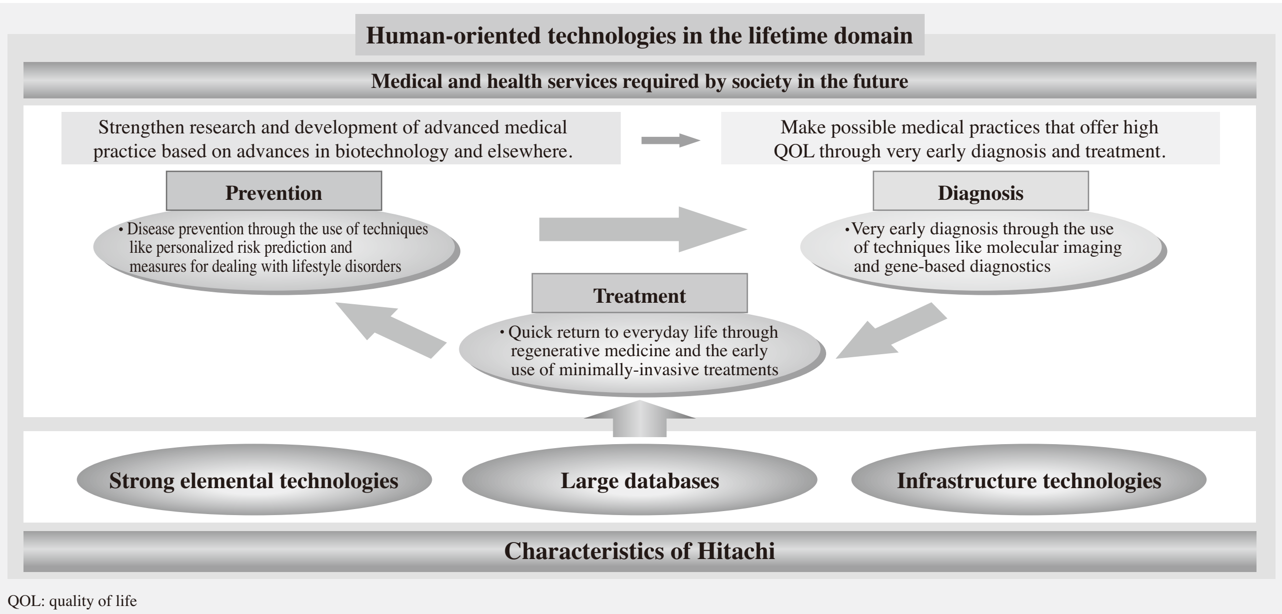


Fig. 1—Human-oriented Concepts in the Lifetime Domain.
The lifetime domain triangle of disease prevention through the use of techniques like personalized risk prediction and measures for dealing with lifestyle disorders, very early diagnosis through the use of techniques like molecular imaging and gene-based diagnostics, and a quick return to everyday life through regenerative medicine and the early use of minimally-invasive treatments will be essential in the future. This is supported by Hitachi's strong elemental technologies, large databases, and infrastructure technologies.

measures for dealing with lifestyle disorders, very early diagnosis through the use of techniques like molecular imaging and gene-based diagnostics, and a quick return to everyday life through regenerative medicine and the early use of minimally-invasive treatments.

On the other hand, measured by things like life expectancy and hygiene standards, the quality of Japan's healthcare and insurance are world-class, and Japan's medical equipment technology and associated manufacturing technology are at a very high level. Despite this, the rapid expansion of large European and American corporations in the healthcare industry through international acquisitions in recent years has had a major impact on the international competitiveness of Japan's medical equipment industry. Further, aging populations, particularly in Japan but also in America and Europe, the economic development and expanding populations of China and India, and the integration into global markets of Russia and South America mean that the medical equipment industry is expected to grow further in each of these regions. To strengthen its international competitiveness in this developing global market, Japan's medical equipment industry needs to come up with distinctive products underpinned by advanced technologies such as biotechnology, nanotechnology, medical IT (information technology), and molecular imaging, and get them to market quickly.

For Hitachi, this means pursuing a development strategy for medical equipment technology based on the group's characteristics, which include (1) utilization of strong elemental technologies, (2) utilization of large databases held by the group, and (3) utilization of infrastructure technologies.

Fig. 1 shows the concepts behind human-oriented technologies in the lifetime domain from the two viewpoints of future social tends and the characteristics of Hitachi. That is, the application of Hitachi's characteristics to provide solutions for prevention, diagnosis, and treatment can be interpreted as what is meant by Hitachi's human-oriented technologies in the lifetime domain. Numerous projects based on these approaches are currently underway, primarily in research and development departments.

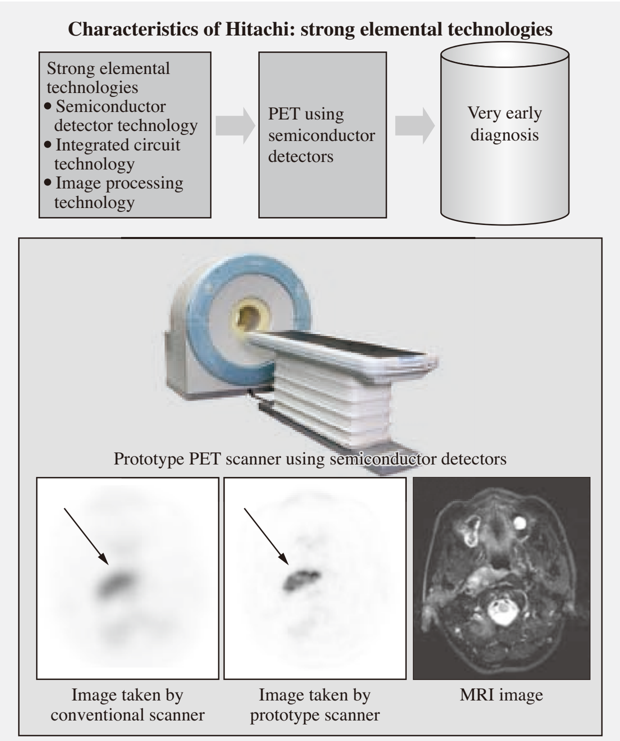
This article describes some representative examples of this work. Specifically, these are positron emission tomography using semiconductor detectors from the field of diagnostics, a visceral fat simulation technique from the field of preventive medicine, and infrastructure technology for regenerative medicine from the field of therapeutic applications.

TAKING ADVANTAGE OF STRONG ELEMENTAL TECHNOLOGIES —POSITRON EMISSION TOMOGRAPHY USING SEMICONDUCTOR DETECTORS

PET (positron emission tomography) is a nuclear medicine imaging technology. By detecting gamma rays emitted from radio-labeled pharmaceuticals injected into a living body, PET can obtain an image of the volumetric distribution of disease-related molecules. These images offer significant functional information for the diagnosis of various diseases. Because of its ability to detect biological changes before detectable morphological changes appear on a lesion, PET is seen as a promising molecular imaging technique that facilitates both very early detection of diseases and optimization of therapy management.

In a conventional PET scanner, gamma rays are detected and converted into photons by scintillation crystals and then the photons are converted into electrical signals by photomultiplier tubes. Since this two-step conversion process limits the energy and spatial resolution, these PET images do not provide sufficient quality for expected future medical uses. Hitachi drew on its accumulated know-how in the fields of radiation measurement, semiconductor technology, and information technology to develop a new PET scanner that uses semiconductor radiation detectors(2).

Because it uses direct signal conversion, energy resolution of semiconductor detectors is superior to that of conventional detectors. In addition, spatial resolution can be increased simply by miniaturizing the detector. Hitachi also developed a number of related technologies to realize semiconductor PET, including an ASIC (application-specific integrated circuit) to process very weak signals at high speed, and a tomographic image reconstruction technique utilizing high energy resolution of the PET scanner (see Fig.2). The new scanner features very accurate measurement with an energy resolution of less than 5% FWHM (full width at half maximum) and spatial resolution of less than 3-mm FWHM. This allows the identification of small lesions that are difficult to detect by conventional scanners. Ongoing clinical research results suggest that this new technology can open up new ways of performing quantitative diagnosis and therapy management. Hitachi plans to continue enhancing this technology while also



PET: positron emission tomography MRI: magnetic resonance imaging

Fig. 2—Positron Emission Tomography with Semiconductor Detectors and Comparison of Images Obtained (Nasopharyngeal Cancer).
Non-invasive assessment of the inhomogeneous distribution of metabolic activity and therapy resistance inside tumors is becoming very important as a means of optimizing therapy management. The newly developed PET scanner demonstrated its ability to delineate clearly the metabolic distribution inside a tumor.

conducting clinical research to identify new medical benefits provided by the technology.

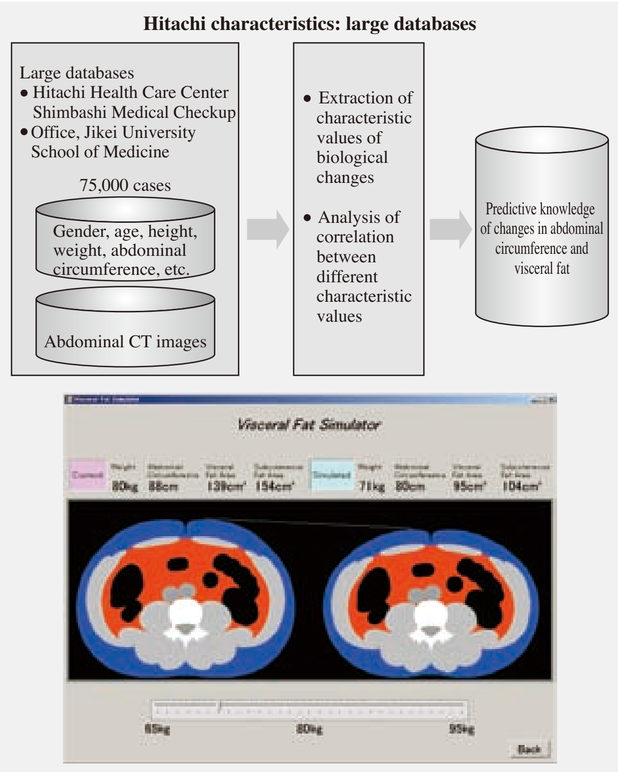
This research is one of the results of "The Matching Program for Innovations in Future Drug Discovery and Medical Care" scheme set up jointly by Hokkaido University, Shionogi & Co., Ltd. and Hitachi, Ltd. through the Ministry of Education, Culture, Sports, Science and Technology's "Creation of Innovation Centers for Advanced Interdisciplinary Research Areas" program.

DATABASE UTILIZATION —VISCERAL FAT SIMULATION TECHNIQUE USING LARGE DATABASE

Measures to counter metabolic syndrome have gained attention in recent years from the perspective of preventing lifestyle disorders such as high blood pressure and diabetes. From April 2008, the Ministry of Health, Labor and Welfare of Japan introduced a system of specific health checkups and specific health guidance with a focus on metabolic syndrome. As part of the specific health guidance, selected patients were shown images of visceral fat accumulation taken using X-ray CT (computed tomography) at their initial consultation. Showing patients these images while offering advice is believed to be an effective method. As a result, this has created a demand for technologies that can provide effective support for the use of images when giving advice at small clinics without a scanning machine or at consultations when the patient's weight has changed such as after undergoing a weight-loss program.

Hitachi analyzed its own store of more than 75,000 health examination data samples to develop a technique for estimating visceral fat accumulation from the patient's weight and abdominal circumference. The group also developed a technique for displaying the estimated extent of fat accumulation as a simulated cross-section of the abdomen by analyzing the anatomical structure of the abdominal region and devising a shape-change model that characterizes this structure. This not only shows the current extent of visceral fat accumulation, it can also estimate how things like the abdominal circumference and visceral fat accumulation will change in the future in response to weight changes and display this as a cross-sectional image. Some of this technology was developed jointly with the Shimbashi Medical Checkup Office, Jikei University School of Medicine.

Two major features of the visceral fat simulation developed by this work are the very accurate visceral fat estimation algorithm based on the analysis of a very large set of health examination data samples held by Hitachi, and the use of visualization technology to show the accumulation of visceral fat as a simulated cross-sectional image. The relationship between weight, abdominal circumference, and visceral fat area was analyzed from the 75,000 health examination data samples and an algorithm developed that can estimate visceral fat accumulation from weight and abdominal circumference. Analysis of this huge volume of health examination data samples showed that people with small abdominal circumferences and people with large abdominal circumferences may experience different changes in abdominal circumference following a similar level of weight loss(3). These results also made it possible to estimate the future values of parameters such as abdominal circumference and visceral fat accumulation after the patient reaches their



CT: computed tomography

Fig. 3—Prototype System Fitted with Technology for Simulating Visceral Fat.
The system provides a visual representation of the estimated accumulation of visceral fat in a form similar to an image taken using X-ray CT.

target weight. The system was designed to be able to present the estimated extent of visceral fat accumulation in visual form using a format similar to the images produced by X-ray CT and can provide personalized feedback about the patient's future risk by entering the desired target weight and displaying the future extent of visceral fat accumulation as an image by modifying the simulated cross-sectional image in accordance with the change from the patient's current weight (see Fig. 3). It is expected that the system will be adopted as a tool to support specific health guidance in the future.

INFRASTRUCTURE TECHNOLOGY UTILIZATION —INFRASTRUCTURE TECHNOLOGY FOR REGENERATIVE MEDICINE

The field of regenerative medicine, which uses cells, tissue, and similar for treatment, is making progress on techniques for human clinical practice aimed at treating a wide range of different disorders. Currently, regenerative tissue is grown using manual processes that satisfy the standards of GMP (good manufacturing practice) and concerns that wider adoption of regenerative medicine would increase manpower costs, labor, and operating expenses have made the establishment of an infrastructure that can support the industrialization of regenerative medicine an important issue. Against this background, Hitachi is working on research and development into the establishment of an infrastructure business for regenerative medicine centered on automatic cell culture systems, cellular transport technology, and CPCs (cell processing centers).

Automatic cell culture systems use proprietary robotics technology to grow cells in a container called a cell cartridge that contains an enclosed space and perform operations such as seeding and replacing the culture medium automatically. In this way, a cell cartridge and the cells to be cultured are inserted into the machine which then automatically performs these operations such as seeding and replacing the culture medium. The cell cartridges have a two-layer structure with feeder cells in the lower layer and corneal epithelial cells on the top layer. Between these layers is a permeable membrane and the top surface consists of a temperature-responsive culture surface. Cells exhibit adhesion to this culture surface at the culture temperature of 37°C but lose this adhesiveness at 32°C and below and this provides a non-invasive way of recovering the cultured tissue as a cellular sheet simply by changing the temperature.

Further, the quality of regenerative tissue cultured on this temperature-responsive culture surface can be maintained during transport by retaining this adhesiveness. To achieve this, a constant-temperature transport container developed by Hitachi Transport System, Ltd. is used. The container is made of a thermal insulator and a heat storage material called n-eicosane which has a phase transition temperature between liquid and solid of 36.4°C, and it is designed such that the region around the heat storage material is filled with thermal insulator.

An experiment was conducted whereby rabbit corneal epithelial cells were incubated automatically in the automatic cell culture system for two weeks and then transported at constant temperature (37°C) to the transplant clinic where the corneal epithelium was transplanted into a rabbit with a damaged corneal epithelium (see Fig. 4). The experiment reduced the cartridge temperature to 20°C after transporting and the corneal epithelium sheet was then peeled off. Next, it was transplanted onto the eyeball and the survival of the graft monitored for a week. The

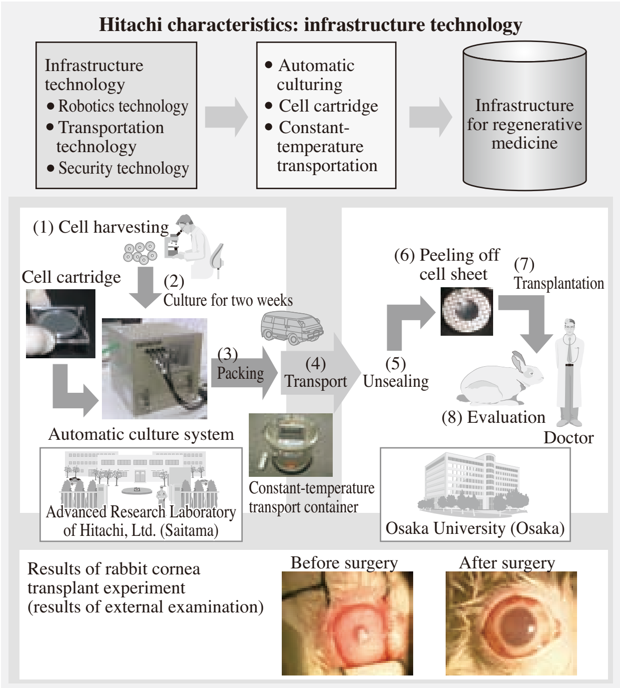


Fig. 4—Sequence of Steps in Transplant Experiment Using Automatic Culture Technology and Constant-temperature Transportation Technology.
An automatically cultured corneal epithelium sheet was transported at constant-temperature and successfully transplanted into a rabbit with a damaged corneal epithelium.

results confirmed that peeling off the cellular sheet and survival for one week after the transplant were both successful[4].

Although this experiment assumed transportation by land transport lasting eight hours, investigations into techniques for air transport in an airplane are also underway so that the tissue can be transported over a wider region. The introduction of traceability using electronic tags is also being considered to prevent mix-ups, and to improve information management.

The automatic cell culture system was a result of work carried out through a New Energy and Industrial Technology Development Organization (NEDO) fundamental technology research promotion program called “Development of Nano Biointerface Technology for Tissue Engineering.”

CONCLUSIONS

This article has given examples of Hitachi’s human-oriented technologies in the lifetime domain.

With developments such as the emergence in recent times of GE Healthcare as a very large manufacturer of medical equipment following the purchase of Amersham Biosciences of the UK by GE of the USA, and the birth of mega-pharma businesses such as Pfizer Inc. of the USA associated with the restructuring of the international pharmaceutical industry, large corporations from around the world that see the healthcare industry as a growth engine for the next generation are investing huge sums.

Against this background, the authors of this article are working actively to visualize the future of the healthcare industry in the form of a technology road map and toward a fusion from the seeds (technology seeds) of Hitachi’s commercial resources and concepts from future market needs, while at the same time engaging in an iterative process of deciding the objectives for research and development of technologies judged to be important based on needs that are actualized and needs that are latent[5].

Amidst these concepts of technology commercialization, there is a deepening not only from the perspective of the measurement of molecules, DNA (deoxyribonucleic acid), tissue, organisms, and other biological entities, but also of concepts arising from research that takes account of people, in other words, from human-oriented research in the lifetime domain. The authors believe that the three research topics from the prevention, diagnosis, and treatment perspectives raised in this article truly provide good examples of the fusion of Hitachi’s strengths to meet the latent needs that emerge from these concepts.

The medical and healthcare industries look after people’s health in Japan and elsewhere and are part of the social infrastructure. The authors believe that supporting the expansion of these industries by further deepening human-oriented technology in the lifetime domain is one of Hitachi’s greatest duties.

REFERENCES

(1) Committee on Competitiveness of Key Technology Industries — Japan, COCJ Forum on International Competitiveness in Industry and Technology (Mar. 2006) in Japanese.

(2) T. Shiga et al., "A New PET Scanner with Semiconductor Detectors Enables Better Identification of Intratumoral Inhomogeneity," J. Nucl. Med. **50**, 1, pp.148-155 (2008).

(3) Y. Hasegawa et al., 29th Annual Meeting of Japan Society for the Study of Obesity, Summary Proceedings, p.245 (Oct. 2008) in Japanese.

(4) T. Nozaki et al., Second Meeting of the Regenerative Medicine Technology Innovation Workshop, Summary Proceedings, p.18 (Nov. 2008) in Japanese.

(5) M. Sakairi, "Research and Development of Bio-medical Instruments," Hitachi Hyoron **87**, pp.483 - 488 (May 2005) in Japanese.

ABOUT THE AUTHORS

Minoru Sakairi, Dr. Sci.

Joined Hitachi, Ltd. in 1981, and now works at the Central Research Laboratory. He is currently engaged in the development of bioinstrumentation and environmental analysis. Dr. Sakairi is a member of The Institute of Electronics, Information and Communication Engineers, The Chemical Society of Japan, and The Japan Society for Analytical Chemistry.

Keiji Kobashi, Dr. Eng.

Joined Hitachi, Ltd. in 1995, and now works at the Medical System Research Department, Central Research Laboratory. He is currently engaged in the development of positron emission tomography using semiconductor detectors. Dr. Kobashi is a member of The Japanese Society of Nuclear Medicine, The Atomic Energy Society of Japan and The Japan Society of Mechanical Engineers.

Yasutaka Hasegawa

Joined Hitachi, Ltd. in 2004, and now works at the Platform Systems Research Department, Central Research Laboratory. He is currently engaged in the development of healthcare information systems. Mr. Hasegawa is a member of the Japan Society for the Study of Obesity and the Japan Society of Ningen Dock.

Kazutoshi Kan

Joined Hitachi, Ltd. in 1981, and now works at the Bio and Measurement Systems Laboratory, Advanced Research Laboratory. He is currently engaged in the development of automatic culture systems. Mr. Kan is a member of The Robotics Society of Japan, The Society of Instrument and Control Engineers, and the Japanese Society for Medical and Biological Engineering.