Hitachi Review
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HITACHI
Inspire the Next

Healthcare Innovation

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From the Editor

Innovation in medical technology has made a major contribution to the advance of healthcare. Nevertheless, in order to control the ongoing rise in medical costs in developed economies, we are now entering a new era in which there is a need to combine the maximization of healthcare outcomes with cost reduction. Meanwhile, there is also a need to overcome challenges such as infectious disease that face emerging economies in ways that are compatible with the state of the local infrastructure and economic circumstances. As they become increasingly diverse, finding the best responses to individual healthcare problems is emerging as an important global challenge.

Hitachi has been contributing to the advance of healthcare ever since it first began supplying diagnostic imaging systems using technologies such as X-rays and ultrasound around 1950. In the 2000s, Hitachi's activities expanded into such fields as particle beam therapy systems and the use of information technology (IT) in disease prevention. Through its work with a wide range of stakeholders, including hospitals and local government, Hitachi is using technology to respond to the diverse challenges facing the healthcare sector in partnership with customers. In April 2014, Hitachi consolidated its healthcare businesses into a new Healthcare Group, making it the seventh of its business groups.

This issue of *Hitachi Review* presents examples of what Hitachi is doing to respond to the various challenges described above through its global ambitions for healthcare innovation (Global One Healthcare), which combine care cycle innovation (bringing innovation to the care cycle through collaborative creation with customers and advanced technology) with medical innovation that draws on the comprehensive capabilities of Hitachi with its extensive experience in IT and social infrastructure.

In this issue's Expert Insights, Dr. Makoto Suematsu, President of the Japan Agency for Medical Research and Development, which has taken on a central role in medical research and development and establishing the environment for such work, contributes an article expressing his expectations for healthcare innovation. In Technotalk, Dr. Gary L. Gottlieb, a past CEO of Partners HealthCare who has an ongoing leadership role in healthcare innovation around the world through his current position as CEO of Partners In Health, describes work on innovation in the USA and emerging economies as well as expectations of Hitachi in a discussion with Masaya Watanabe, Vice President and Executive Officer of Hitachi, Ltd. (President & CEO of the Healthcare Group and Healthcare Company).

Other articles present examples of care cycle innovation in which devices such as diagnostic ultrasound systems and open magnetic resonance imaging (MRI) systems are deployed in applications ranging from diagnostic testing to treatment, examples of medical innovations that use techniques such as IT and simulation to respond to diverse needs around the world for things like hospital management and health insurance measures, and the advanced core technologies that underpin these innovations.

I hope that this issue of *Hitachi Review* will provide you with a better understanding of Hitachi's healthcare activities, and that the products and services we have to offer will also play a role in achieving better healthcare.

Editorial Coordinator,
"Healthcare Innovation" Issue

Nobuyuki Osakabe
CTO
Healthcare Company
Hitachi, Ltd.

Healthcare Innovation

Contents

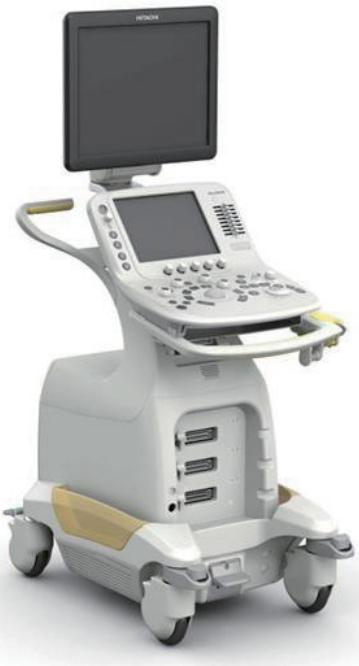
Healthcare Innovation

Medical technologies have made major progress around the world toward fulfilling the aim of achieving long and healthy lives.
Meanwhile, the circumstances surrounding the healthcare sector have undergone major changes in recent years, including the urgent need to deal with aging populations in developed economies and to provide healthcare infrastructure in emerging and developing economies, raising the importance of healthcare for preventing illness as well as for its treatment.
Recognizing that healthcare is an essential part of the infrastructure that underpins society, Hitachi supplies innovative technologies that draw on its comprehensive capabilities, along with the associated systems, solutions, and services.
Hitachi aims to contribute through healthcare innovation to the creation of a society in which everyone can live safely, enjoying a healthy life and peace of mind.

Laboratory automation system designed for speed and efficiency using single holders with RFID tags

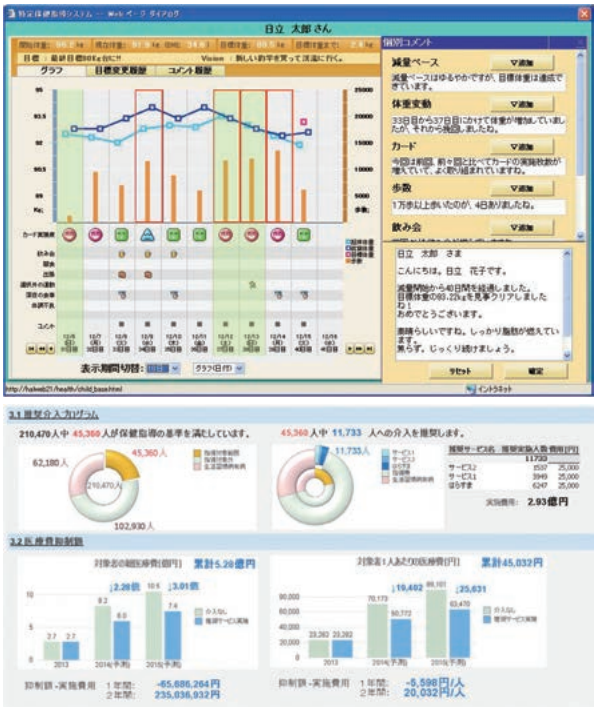
Artist's impression of an operating theater in which an open MRI has been installed as an intraoperative imaging system

Therapy room for particle therapy system
(Proton Beam Therapy Center, Hokkaido University Hospital)

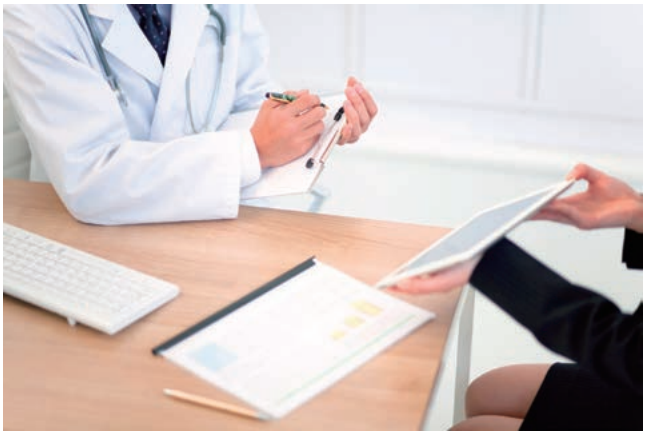


Diagnostic ultrasound system
"ARIETTA 70"* and a variety of special-purpose probes

* ARIETTA is a trademark of Hitachi Aloka Medical, Ltd.



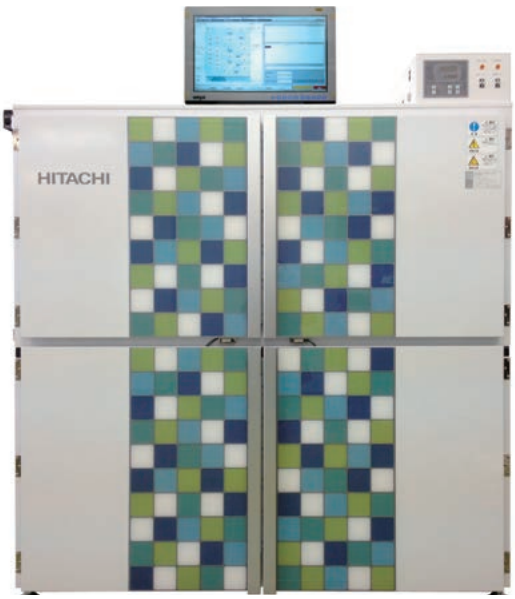
Disease prevention support technology for effective health insurance business



Hospital management solution

Plant solutions for biopharmaceuticals and regenerative medicine
High-volume cell culture system (top) and layout of cell processing center (CPC) (bottom)

Development of brain disease solutions using MRI measurement techniques and optical topography



Automated cell culture equipment for cell sheets that is helping regenerative medicine become more widely adopted

Expert Insights

Promoting Medical Innovations to Make Them Available to Patients as Soon as Possible

Makoto Suematsu, MD, PhD

President
Japan Agency for Medical Research and Development

Graduated in 1983 from the Keio University School of Medicine. After working as an Instructor, Department of Internal Medicine, Keio University School of Medicine, he took up a post as Bioengineer Step IV, Institute for Biomedical Engineering, University of California San Diego.
His appointments include Professor and Chair, Department of Biochemistry, Keio University School of Medicine in 2001, Dean, Keio University School of Medicine in 2007, and Leader, Global Center of Excellence for Life Sciences, Human Metabolomic Systems Biology from the Ministry of Education, Culture, Sports, Science and Technology.
He took up his current position in April 2015. He is also Leader, Japan Science and Technology Agency (JST), Exploratory Research for Advanced Technology (ERATO), Suematsu Gas Biology Project.
His main fields of study are biochemistry and gas biology.

The Japan Agency for Medical Research and Development (AMED) was established in April 2015 to take on a central role in medical research and development and in establishing the environment for such work.

AMED's mission is to bring basic and clinical research in the medical field into practical use so that it can be made available to patients as soon as possible. To achieve this, it will combine the medical research and development budgets of the Ministry of Education, Culture, Sports, Science and Technology; Ministry of Economy, Trade and Industry; and Ministry of Health, Labour and Welfare, and undertake seamless management extending from basic to applied research and development by allocating funding in a targeted and strategic manner based on "expert" reviews.

The government's "Healthcare Policy" aims to create a "society of health and longevity," by establishing world-leading medical technology and services, and by encouraging the creation and overseas expansion of healthcare industries. While the global market for medical devices is expected to continue expanding in response to factors such as the advanced aging of populations around the world and the growth in demand for healthcare in emerging economies, imports continue to exceed exports in the Japanese market, resulting in a trade deficit that has risen to approximately 800 billion yen. While Japan has capabilities in basic research and technology that are amongst the best in the world, it has lagged on practical applications. If it is to transform the medical device sector into a leading industry supporting its growth, Japan needs to press ahead with innovation in research and development and produce innovative Japanese-made devices and other systems that are internationally competitive.

To achieve this, AMED is embarking on an "all-Japan medical device development" campaign comprised of a wide range of initiatives involving collaboration between industry, academia, and government, and with the healthcare and engineering sectors working together. One such example is ongoing consultancy with seamless support through all phases, the effective identification of the needs of the clinical workplace; offering a full range of facilitation functions from basic research at universities to clinical research at companies, medical institutions, and elsewhere; clinical research and trials; and practical applications. While expanding sales channels by making full use of Japan's strengths in robotics and information technology (IT) and the manufacturing skills of small and medium-sized companies to achieve medical devices, system development, and product packaging that anticipate the future of medicine is not a simple objective, shifting to a "21st century model" for how to approach medical research and development should necessarily be expected to maximize the pace of research and development. I believe that the practical realization of world-renowned Japanese quality can do a lot to advance healthcare innovation.

By enhancing the quality and efficiency of healthcare, extending the healthy life expectancy of the Japanese people, and making innovative developments available to patients as soon as possible, AMED hopes to continuously provide a driving force behind the growth of Japan.

Technotalk

Providing Everyone with Better Healthcare through Practical Innovations

Gary L. Gottlieb, M.D., M.B.A. CEO of Partners In Health
Masaya Watanabe Vice President and Executive Officer, President & CEO, Healthcare Group and Healthcare Company, Hitachi, Ltd.
Harry Reddy, MS, MEng., MBA, Ph.D. (cont.) Deputy General Manager & Strategist, Healthcare Group, Hitachi, Ltd.

Healthcare faces numerous challenges that vary between countries and regions. While the requirement in developed economies is for the use of IT to provide more sophisticated medical services and greater efficiency to control rising medical costs, emerging and developing economies need simple and low-cost medical devices and services and the provision of healthcare infrastructure. Hitachi is involved in all aspects of the healthcare business, including diagnosis and treatment, testing and reagents, and informatics. By supplying a wide range of products, services, and solutions, and delivering innovations through collaborative creation with customers, Hitachi is responding to the challenges of healthcare both in Japan and elsewhere.

Healthcare Transformation in the USA

Reddy: Recent years have seen many changes in healthcare, including the use of information technology (IT) for disease prevention and medical safety. In the USA, in particular, a healthcare transformation is underway in the form of changes to the medical insurance system. Can you give us some background on these developments?

Gottlieb: The starting point for these recent healthcare changes came around the beginning of this new century with two major reports from the Institute of Medicine that focused on medical mistakes. While this focused many people's attention on safety, and led to a search for IT-based solutions, it was hampered at the time by a lack of investment.

Watanabe: Safety has become a major issue for healthcare in Japan. Hitachi's series of hospital information solutions use IT to assist with safety management activities such as incident management.

Gottlieb: That is certainly important work. In the USA, meanwhile, the inauguration of President Obama in January 2009 gave a boost to moves toward healthcare reform. This included a large funding allocation for medical IT in economic stimulus measures aimed at restoring the economy. This was reinforced by an emphasis on population health management (PHM) in the Affordable Care Act (ACA), a way of using data to reduce the risk of chronic illnesses, and adopting a long-term perspective extending from prevention to recuperation.

In the case of Medicare (the US healthcare insurance scheme for the elderly), 10% of recipients account for about 70% of total medical expenditures. A similar calculation for the entire USA finds that 50% of expenditures are used for just 5% of the population. In other words, appropriate medical intervention directed at the small number of patients at high risk of chronic illnesses is vital to controlling overall healthcare expenditures.

Watanabe: Appropriate medical intervention to prevent the deterioration of chronic illness is also a major concern within the Japanese health insurance industry. This has led to moves to provide better healthcare by coordinating medical data from the community. Because IT holds the key to healthcare reforms like this, Hitachi is drawing on its strengths in IT and data analytics to focus on solutions for healthcare reform. One example is a lifestyle guidance program aimed at tackling lifestyle diseases such as diabetes that launched in the UK in collaboration with the National Health Service Greater Manchester (NHS GM). It utilizes people's healthcare data and combines the clinical knowledge of NHS GM with Hitachi's data analytics to support personalized care.

Advances in Medicine Facilitated by Partners HealthCare

Reddy: Dr. Gottlieb, as President and Chief Executive Officer (CEO) of Partners HealthCare, a non-profit organization, you have taken the initiative and invested heavily in the healthcare transformation in the USA.

Gottlieb: Partners HealthCare was established in 1994 based on a vision of building a healthcare system

Gary L. Gottlieb, M.D., M.B.A.

CEO of Partners In Health

From 2010 until February of 2015, he served as President and CEO of Partners HealthCare, the parent of the Brigham and Women's and Massachusetts General Hospitals, operating the largest health care delivery organization in New England and among the nation's largest nonprofit biomedical research and training enterprises.
Dr. Gottlieb is a professor of psychiatry at Harvard Medical School and a member of the National Academy of Medicine. He served as president of Brigham and Women's/Faulkner Hospitals, as president of North Shore Medical Center, and as chairman of Partners Psychiatry.

that combines patient care, education, research, and community service. It includes community and specialty hospitals, a managed care organization, a physician network, community health centers, home care and other health-related entities, and employs a total of approximately 60,000 doctors, nurses, and other staff.

Partners' precious mission is to take really extraordinary people and have them take care of the sickest patient populations. Partners aims to cut medical costs by improving the quality and efficiency of care for the people among our population who are at the highest risk of serious illness. One such strategy is to use data and science to drive advances in medicine.

Watanabe: I understand that Partners HealthCare developed some of its own hospital information systems.

Gottlieb: Over the last 20 years, Partners and its hospitals developed a decision support based order entry system to make hospital operations safer and more efficient, an outpatient electronic medical record, an electronic medication administration system and several other best in breed solutions. As research and development in health IT progressed, Partners recognized there are limits to what we could do by ourselves and that we needed to call on the resources of an IT company.

Watanabe: I understand. For a company such as ourselves with the capabilities to build information systems, we see the potential for having ideas from the workplace taken on board by society and used to transform healthcare through IT.

Gottlieb: This concept of transforming healthcare through IT carries a very strong message. The reform of the healthcare system is something that involves a long-term perspective, looking ahead to the next decade or the next century. Partners HealthCare is currently undergoing a major change in our culture to adopt an IT-based clinical administration system. I launched this one billion-dollar project with the intention of it being used across the system and to enable our patients to have the safest possible care and rapid access to their own data and communication with their physicians and other providers. The system will change workflows dramatically.

Watanabe: You have been responsible for major investment in healthcare transformation in your role as CEO of Partners HealthCare, and I believe this is a wonderful example of leadership that looks to the future. As an IT vendor, Hitachi intends to press ahead with the use of IT in healthcare by working with customers led by people like you.

Partners In Health: Improving Healthcare in the Developing World

Reddy: Dr. Gottlieb, your recent appointment in March 2015 as CEO of Partners In Health, a non-governmental organization, expands your field of activities from the USA to the rest of the world. Please tell us about this new challenge.

Gottlieb: Partners In Health (PIH) was established in 1987 with the aim of providing healthcare to communities outside the reach of existing services. The organization has a staff of around 15,000, and provides healthcare to 3 million people in about 10 countries. It works in collaboration with local governments, multilateral agencies, corporate partners, foundations, and others on building sustainable health care systems in severely resource-constrained settings. Areas of great focus include treatment of tuberculosis and human immunodeficiency virus (HIV), improvement of maternal and child health, and malnutrition. PIH is also very invested in building pipelines of human resources for health in the countries where we serve. This includes sustainable education and training, including a new project to establish a University for Global Health Equity in rural Rwanda.

Watanabe: Does this include a focus on preventive

medicine?

Gottlieb: Very much so. There are four areas of particular importance when it comes to preventive medicine for the poor. These are the elimination of maternal mortality, death of children under five due to malnutrition, maternal-fetal transmission of HIV, and death from tuberculosis. To reduce maternal mortality, we are working on providing adequate facility based settings for care to complement primary and community based care. We are working collaboratively on a variety of point-of-care diagnostic techniques that can be deployed in the field at relatively low cost.

I see great potential for partnering with great companies like Hitachi. Partnerships have an important part to play in providing high-quality medical services.

Looking more widely, there are opportunities for genuine transformation and innovation, and we still have much to learn. Recent years have seen a rise in interest in "reverse innovation," whereby technologies or business models developed for developing and emerging economies are deployed in the developed world, and we hope to invest in fostering new innovations like this. Innovators like Hitachi are well placed to develop flexible technologies with potential for use both in the industrial world and in more constrained situations.

One example is the need for a means of unique patient identification in places that lack a system of residential registration. Providing healthcare infrastructure like this also boosts economic growth in the countries and regions concerned.

Watanabe: That is valuable advice. Hitachi is taking a one-step-at-a-time approach to emerging markets. For example, technology developed by Hitachi for identifying people from their finger veins is being used in research aimed at improving the accuracy of personal identification in census-taking in developing nations. We believe that increasing the accuracy of identification leads to advances not only in healthcare but also right across public services.

We are also doing what we can to aid economic development in places like Myanmar and Vietnam through activities such as the construction of data centers, training of IT personnel, and providing IT infrastructure. I too look forward to opportunities for working alongside Partners In Health to promote healthcare in emerging and developing economies.

Hitachi's Healthcare Business Targeting Growth through One Global Healthcare

Reddy: Next I would like to talk about our healthcare business. Hitachi has been developing and marketing medical equipment such as diagnostic X-ray, magnetic resonance imaging (MRI), and diagnostic ultrasound systems since around 1950. In recent years, this business has also expanded into therapy systems and medical IT, leading to its consolidation in April 2014 through the establishment of the Healthcare Group. Under new leadership, this approximately 6,000-strong organization is targeting growth based on a concept of "One Global Healthcare."

Watanabe: The operations of the Healthcare Group can be broadly divided into a diagnostic and clinical business that handles such products as diagnostic imaging systems, a testing and reagents business that deals with analyzers and similar, and an informatics business that includes medical information platforms. Rather than selling standalone machines, this involves solutions that combine diagnosis and treatment and that integrate technologies and services such as IT from other parts of the Hitachi Group. The business is contributing to quality improvements and efficiencies in healthcare through the implementation of healthcare innovations in response to needs such as support for the care cycle all the way from disease prevention to care during recuperation; providing

Masaya Watanabe

Vice President and Executive Officer, President & CEO, Healthcare Group and Healthcare Company, Hitachi, Ltd.

Joined Hitachi, Ltd. in 1982 and was appointed President of the Enterprise Server Division, Information & Telecommunication Systems Group in 2007; Vice President and Executive Officer, and Chief Strategy Officer of Information Telecommunication Systems Company in 2012; Vice President and Executive Officer, President and CEO of Hitachi America, Ltd., Chairman & CEO of Hitachi Information & Telecommunication Systems Global Holding Corporation, and Chairman of Hitachi Consulting Corporation in 2014. He was appointed to his current position in 2015.

medical information infrastructure for community-wide healthcare integration; and improvements to hospital administration.

As in other businesses, Hitachi is continually striving to develop leading-edge technologies for healthcare. In the case of diagnostic ultrasound systems, for example, Hitachi has been a leader in the field ever since the first model was released by Hitachi Aloka Medical, Ltd. (a Hitachi Group company) in 1960, including the development of a series of new technologies such as a convex probe with a curved tip, realtime ultrasound blood flow imaging, and cardiovascular color Doppler imaging. We also successfully commercialized an ultrasonic transducer in 2009 that works using semiconductor technology. We respond to the challenges of the medical workplace by supplying solutions derived from this portfolio of superior technologies.

Gottlieb: That is impressive. I look forward to seeing more technologies and tools for improving healthcare in the future.

Watanabe: In the clinical sector, we are devoting a lot of effort to proton beam cancer therapy systems that draw on technologies and know-how built up in the power systems business. We have made further enhancements to the system and developed various new technologies through joint research with customers at the forefront of this technology. For example, we are able to provide therapy that combines the spot scanning technique for precision targeting of the proton beam, which we worked on together with the MD Anderson Cancer Center in the USA, and the tumor tracking technique from Hokkaido University in Japan that enables the precise treatment of cancerous tissue even when it is moving inside the body.

Our involvement with the MD Anderson Cancer Center dates back to a 2002 order for a proton beam cancer therapy system, and recognition of its success from elsewhere in the USA has led to further orders for two systems from the Mayo Clinic in 2011 and one from St. Jude Children's Research Hospital in 2012.

Gottlieb: Both of these are superb high-profile institutions.

Watanabe: In the field of informatics, we are focusing on using data analytics to deliver innovations in the care cycle that extend from disease prevention to care during recuperation. The demonstration project being undertaken in collaboration with NHS GM in the UK provides a practical example of this.

The intelligent operating theater is another area of activity, and we have provided surgeons with the ability to view images from an open MRI system as they perform neurosurgical procedures. The system has already been installed at more than 10 facilities in Japan, and we plan to market it in the USA also.

Seeking to Achieve Social Innovation through Collaborative Creation

Gottlieb: When Hitachi talks about its Social Innovation Business, what do you mean by that?

Watanabe: Hitachi's existing businesses deal with products, services, and solutions that underpin such social infrastructure as power systems, water and sewage systems, and railways. Our Social Innovation Business seeks to enhance social infrastructure by combining IT with the knowledge obtained from these activities so that we can provide the public with new forms of value in terms of convenience and comfort. It aims to overcome the societal challenges facing particular countries and regions through collaborative creation with the customers who work with us as partners in this business.

Naturally, medicine is an important part of the social infrastructure and healthcare is one of the pillars of our Social Innovation Business. In the case of our positron emission tomography (PET) support solution, for example, we are creating value through the early detection of cancer and consequent healthcare savings by supplying not only PET scanners, but also support for everything from finance to the construction and operation of PET clinics. Based on existing projects and other experience from Japan, we are also contributing to healthcare innovation in places like China and India by supporting the provision of hospital infrastructure and improved management through collaborative creation with partners.

In other words, our Social Innovation Business can be thought of as manifesting our Mission of "contributing to society through the development of superior, original technology and products" achieved by seeking commonality between business objectives and the resolution of societal challenges.

Perhaps you can offer some advice to me and the other 3,000 or so researchers at Hitachi who are seeking to discover and develop innovative and effective ideas about what areas we should be focusing on in the future if we are to realize this vision?

Gottlieb: The need in developing and emerging economies is for healthcare technologies that are effective and economical. Given things like diagnostic imaging solutions that are easier to use, point-of-care diagnostics, portable medical devices, and flexible IT platforms that are simple to use, great progress should be possible in the healthcare infrastructures of these nations. Some of the innovations at Partners In Health derive from the knowledge of community health workers and the challenges they face. These people have taught us which

technologies and other innovations are needed over the long term. This is an approach that can also be put to work in industrialized countries. The availability of testing and screening systems that are simple to use even by people without specialist skills should be of benefit to home healthcare in developed economies also.

Reddy: This shift in healthcare services from hospitals to the home is a common trend in both Japan and the USA.

Gottlieb: That's right. Advances in home healthcare cut medical costs and play a useful role in disease prevention. The use of IT to put healthcare data to work should assist with diagnosis. However, as we touched on earlier, the lack of compatibility between the devices and other information systems makes it difficult to share information. This is a major drag on healthcare efficiency, and there is a need to think about standardization throughout the healthcare industry. This is because it will expand our options and lead to greater innovation.

Watanabe: Because standardization is not something one company can achieve on its own, we hope to work on this in collaboration with strong partners such as your organization. We have gained an appreciation of how much there is we need to work on together if we are to realize the great vision of progress in medicine throughout the world. Thank you for your time today.

Moderator

Harry Reddy, MS, MEng., MBA, Ph.D. (cont.)

Deputy General Manager & Strategist, Healthcare Group, Hitachi, Ltd.

Harry Reddy is a successful business executive and an accomplished corporate director in healthcare and technology industries. His leadership & focus has been on business management, corporate development, strategy formulation, business growth, innovation management, corporate entrepreneurship and business transformation, and has extensive experience in the USA, EU, Japanese and emerging markets.

Overview

Healthcare Innovation: Industry Challenges Being Addressed by Global One Hitachi

Harry Reddy, MS, MEng.,
MBA, Ph.D. (cont.)
Tomoyoshi Takeo

CHANGES SOUGHT IN HEALTHCARE

HEALTHCARE costs are increasing, but care delivery is not necessarily centered on patients' final outcomes and has too much variation from one hospital to another and from one region to another. One explanation for such a situation is that healthcare is too complex and fragmented, so to solve this problem it is necessary to adopt an industrial approach to innovate new solutions not only to improve care quality and patient outcomes, but also to reduce healthcare costs by "systems thinking."

Healthcare systems are different in different countries, and instead of focusing on which country's system is good or bad the focus needs to be on learning from different systems to improve healthcare systems. For example, the healthcare systems in the USA, UK, and Japan are all different, and not just in cost. What it means for Hitachi is that it should leverage its global competencies and innovate toward a next generation of healthcare that drives both effectiveness and efficiency in care delivery.

The healthcare industry is undergoing major changes, which are remarkable in the USA, with some of the key changes including: 1) the accountable care organization (ACO) concept whereby hospitals not only provide care but are also accountable for total cost and patient outcomes, 2) incentives for better care and cost control with new payment models, 3) engaged patients or consumerism, 4) medical home, 5) personalized medicine, and 6) growth opportunities with care consolidation, an aging society, and a growing middle class.

Major healthcare players such as General Electric Company (GE), Philips, and Siemens are investing in both internal innovation (biotech, mobility, services, clinical decision support, etc.) and external acquisitions. Major electronic companies such as Samsung and Sony are entering healthcare. Even focused non-healthcare companies such as Asahi Kasei and Bosch are entering healthcare. And, interestingly, Chinese companies such as Mindray are focusing on global growth by acquiring global companies.

Medical standardization, scale-up, evidence-based medicine, and access to remote areas are key issues in developing countries to meet the rising population. In developed countries, cost containment is a key issue because of the significant healthcare cost involved as a percentage of national gross domestic product (GDP)—for example 17.5% in the USA.

NEXT-GENERATION HEALTHCARE

The current healthcare system is in fact a sickcare system, which attempts to cure patients who are sick, but not to prevent their sickness! Next-generation healthcare (NGH) focuses on all three key components of healthcare—improving patient outcomes, improving quality of care, and reducing the cost of care—which is different from traditional healthcare in which neither patient outcome nor cost reduction is addressed. The three components are not just to be optimized but also simultaneously to be improved in NGH, which demands a systemic focus on disease prevention and management through continuums of care.

In this concept, prevention and total care management through the care cycle are the most important drivers of reducing the overall cost, which achieves true "health care," not just "sick care."

HITACHI'S INNOVATION FOR VALUE-BASED HEALTHCARE

Five Pillars Holding Up NGH

The three-component objective of next-generation healthcare is fulfilled by innovating and implementing

the five pillars—(1) patient-centric, (2) productivity improvement, (3) preventative care, (4) precision diagnosis & treatment, and (5) personalized medicine (see Fig. 1).

Building these five pillars will require advanced solutions—the first three being the information-and-communications-technology- (ICT) based technologies while the last two are medical-based technologies.

In this new NGH, the role of doctors will change, and new doctors will be introduced to not only enhance healthcare delivery, but also transform it for better efficiency and effectiveness.

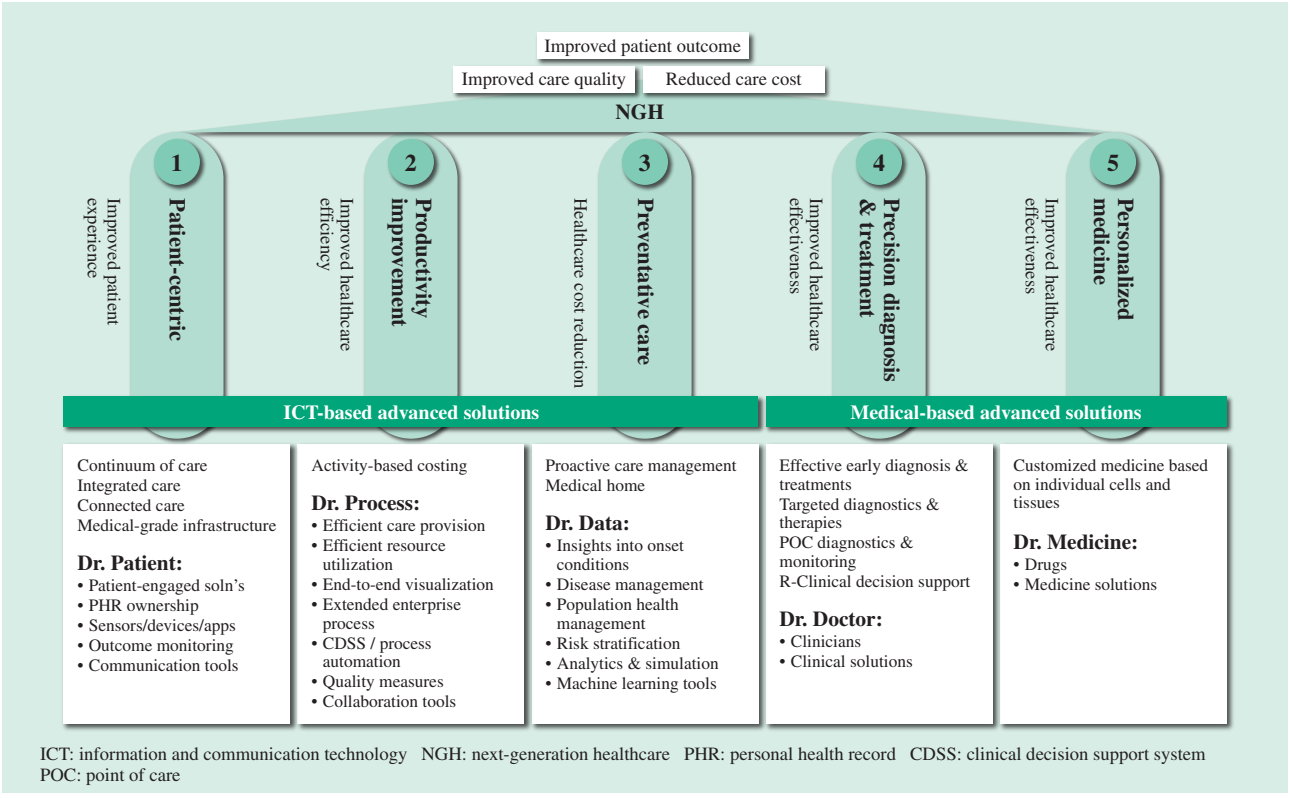
While even the best conventional healthcare is focused on two types of doctors—Dr. Doctor (medical doctors—checkups, diagnoses, procedures and treatments) and Dr. Medicine (medicine/drugs and therapies), the next-generation healthcare focus is on three additional types of doctors—Dr. Patient (patients serving as doctors in taking care of their own care, thereby increasing the patient experience), Dr. Process (processes serving as doctors in improving productivity, thereby increasing healthcare efficiency), and Dr. Data (data serving as doctors in offering insights and preventive care management, thereby decreasing healthcare costs).

What Should Hitachi Address and Why?

The innovations of conventional technologies have a good impact on quality of care, but little impact on healthcare cost reduction, so in order to reduce the cost of healthcare, the focus of innovation should also be on net-value-adding technologies that not only have a good impact on quality of care, but also have an impact on healthcare cost reduction and improved patient outcomes. Therefore, to lead into next-generation healthcare, it is also necessary to provide net-value-adding solutions in the areas of preventative care, disease management, data analytics, and process improvement.

New Categories of Healthcare Innovation

By considering the trends of next-generation healthcare, Hitachi is innovating in strategic areas such as: 1) data-based and process-based solutions to improve the efficiency of care and reduce healthcare



ICT: information and communication technology NGH: next-generation healthcare PHR: personal health record CDSS: clinical decision support system
POC: point of care

Fig. 1—Five Pillars of NGH.
Hitachi is implementing NGH by using ICT and medical technologies to establish five pillars. NGH differs significantly from the focus of existing healthcare on treating illness by instead adopting value-based healthcare that simultaneously improves the three critical elements of outcome, quality, and cost.

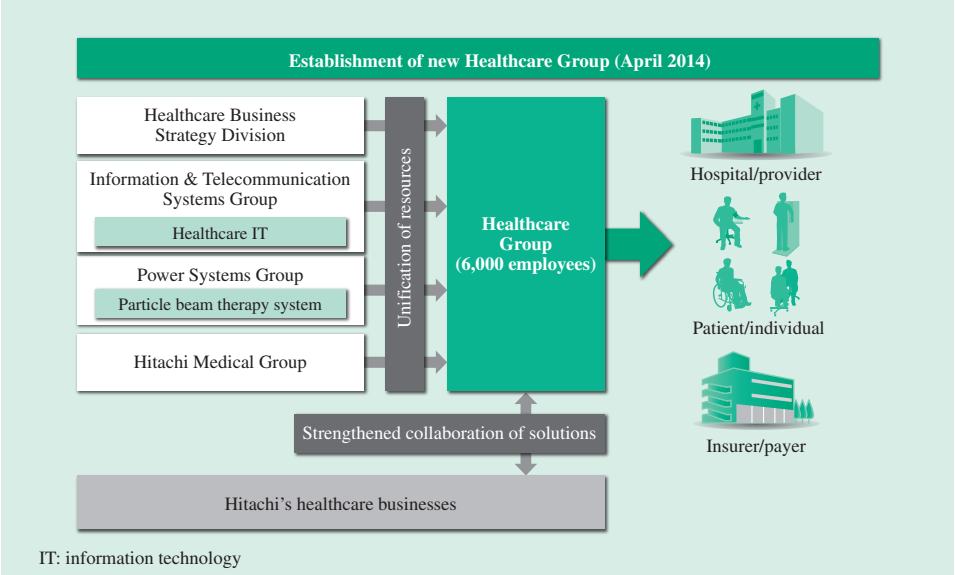


Fig. 2—Establishment of Healthcare Group. Hitachi established its new Healthcare Group by consolidating four existing businesses.

costs, 2) point-of-care diagnostics and monitoring to improve both the effectiveness and efficiency of care, and 3) targeted therapy and personalized medicine to improve the effectiveness of care.

These innovations are carried out in healthcare businesses, medical areas, and care cycles, and their value is further enhanced by the Social Innovation Business, as described in the next section.

HITACHI'S HEALTHCARE BUSINESS TRANSFORMATION

Hitachi has re-organized its healthcare businesses, which were scattered around within Hitachi Group, and created a new Healthcare Group effective April 2014. The new Healthcare Group is the integrated formation of four previously existing businesses in different divisions, and has about 6,000 employees. The purpose of the new group is twofold—1) integrate resources and establish unified strategies, and 2) strengthen collaboration with related Hitachi divisions. The target customers are of three types: hospitals/providers, patients/individuals, and insurers (private and governmental) (see Fig. 2).

Hitachi's existing healthcare solutions are mainly grouped into three categories: diagnostics and therapy solutions, in vitro diagnostics (IVD), and healthcare informatics, with annual total revenue of $3.2B.

In diagnostics, it offers imaging equipment, such as X-ray, computed tomography (CT), magnetic resonance imaging (MRI), ultrasound, and optical topography.

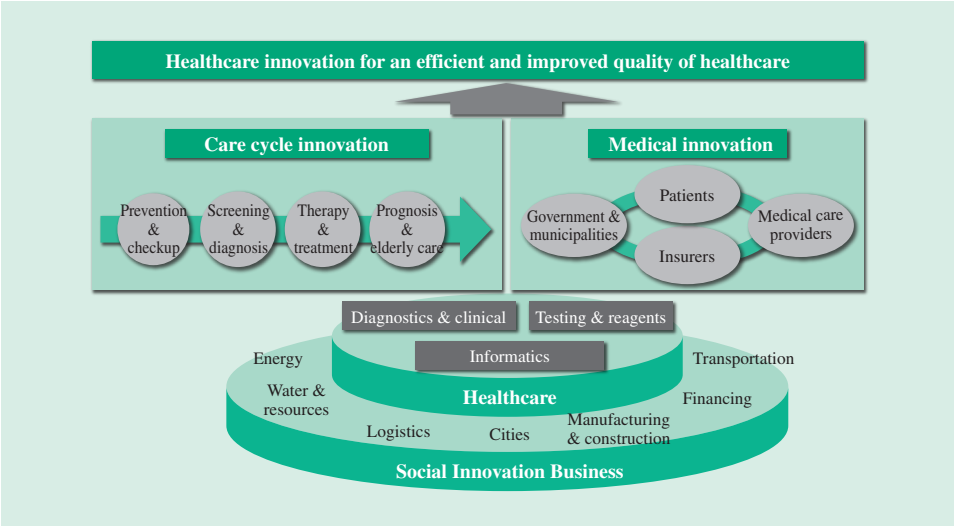


Fig. 3—Hitachi's Concept of Healthcare Innovation. Hitachi intends to deliver healthcare innovation to hospitals, health insurers, and others through care cycle innovation and medical innovation.

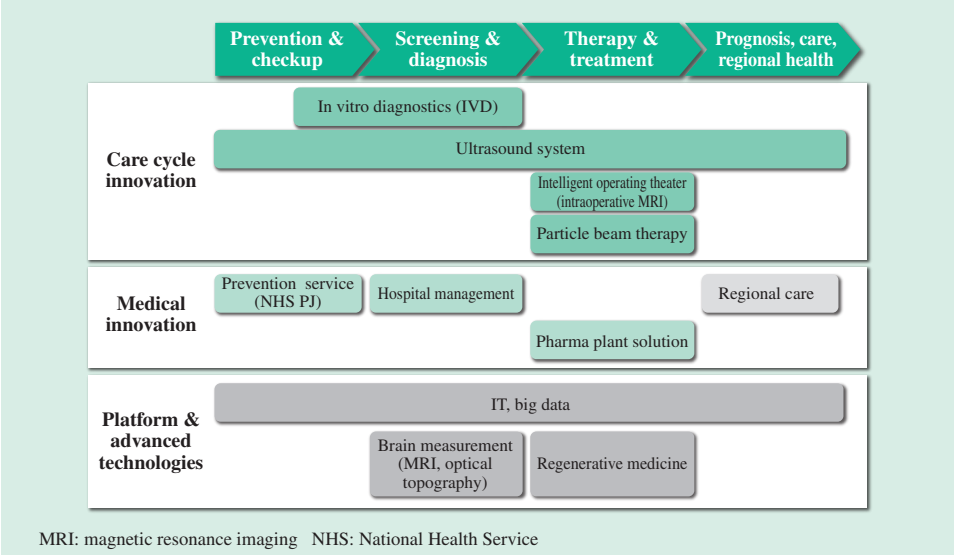


Fig. 4—Summary of this Issue of Hitachi Review.
The 10 articles in this issue of Hitachi Review cover care cycle innovation, medical innovation, and the platforms and advanced technologies that support them.

In the therapy category, it offers particle therapy equipment(a). This equipment includes very advanced cancer tumor irradiation systems that do not cause many side effects on healthy tissue.

In the IVD category, it offers a diversified product portfolio, including clinical analyzers, sample preparation, and DNA sequencers(b).

In the healthcare informatics category, it offers several solutions and services, mainly in Japan, and data storage and clinical repository solutions available world-wide.

These transformations are further augmented by innovating and offering new solutions (see Figs. 3 and 4).

Care Cycle Innovation

In order to improve care quality and efficiency, it is important to provide seamless healthcare services through care continuums, both horizontally (among disparate care settings) and vertically (among disparate care providers), for example, a connection between diagnostic imaging and therapy, and data re-utilization in various care settings. Hitachi offers an intelligent operation system that provides image guidance from permanent MRI for brain surgery operations to contribute to the accuracy of operations.

Medical Innovation

Hitachi offers a total solution that provides total hospital management improvement and total healthcare system management, including payers (private and public sector). As a total solution for one hospital, Hitachi has been working with Kurume University Hospital for a long time and began to build up a diabetes prevention system with the NHS(c) in Manchester, UK.

Platform and Advanced Technologies

Hitachi has recently acquired Pentaho, which specializes in big data analytics and visualization, and has been leveraging several internal technologies to offer platforms and advanced technologies such as a clinical semantic linker for clinical contextualization, natural language processer for capturing notes and voice, disease progression models, cost simulations, clinical content repository, and disease management cloud models.

CONCLUSIONS

In summary, Hitachi healthcare delivers value-based healthcare, resulting in integrated care for individuals and holistic value for society. It intends to fulfill its mission of innovating and offering healthcare solutions in two dimensions: care cycle innovation and medical innovation. Hitachi is also innovating

(a) Particle therapy equipment
A form of radiotherapy that directs a beam of high energy particles (heavy ions or protons) produced by an accelerator at cancerous tissue with pin-point accuracy to treat the cancer with minimal effects on healthy tissue.

(b) DNA sequencer
A device for automatically determining the sequence of bases in deoxyribonucleic acid (DNA). Reading the base sequence of DNA provides genetic information about the organism. In addition to their important role in human genome analysis, DNA sequencers are also used for DNA profiling and genetic diagnosis.

(c) NHS
Abbreviation of National Health Service, the UK public health system. Although not all general practitioners are covered, the NHS is government-funded and provides free access (with some exceptions) to services such as treatment of illness or injury, emergency medical centers, and use of ambulances.

in "value co-creation" with customers by using new business models for a sustainable future.

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Featured Articles

Diagnostic Ultrasound System for Care Cycle Innovation

Kinji Kuriyama
Kazufumi Tanaka
Naohiro Yoshida
Hiroaki Wakabayashi
Shinji Nishino

OVERVIEW: Diagnostic ultrasound systems play an important role in all four stages of the healthcare cycle, namely prevention and checkup, screening and diagnosis, therapy and treatment, and prognosis and elderly care. Hitachi is working on new initiatives for all of these stages. These include the diagnosis of hardening of the arteries in the prevention and checkup stage; increasing the throughput of prevention, checkup, screening, and diagnosis and providing probes to assist with this aim; functions and special probes designed to facilitate treatment procedures; and devices for both primary treatment and in-home healthcare for the prognosis and elderly care stage.

INTRODUCTION

THANKS to their small size, low cost, and portability, diagnostic ultrasound systems are used in a variety of different healthcare fields across the care cycle, with their use of ultrasound making them a very safe and non-invasive method for realtime medical imaging.

These characteristics have led to their use primarily for abdominal and cardiovascular applications and obstetrics, however with recent improvements in performance and function they have also come to be used often for applications like orthopedics, the treatment of rheumatism, and first aid.

Diagnostic ultrasound systems are also recognized for their potential use as small and inexpensive basic diagnostic tools, playing a role in policies of nations around the world that seek to control increases in healthcare expenditures driven by the growth and aging of the population and increased prevalence of lifestyle diseases.

This article describes how diagnostic ultrasound systems are being used in the care cycle, including new initiatives in this field being undertaken by Hitachi.

DIAGNOSTIC ULTRASOUND SYSTEMS AND THE CARE CYCLE

Principles and Components of Diagnostic Ultrasound Systems

Diagnostic ultrasound systems transmit an ultrasound signal into the body and generate images from the amplitude, phase, frequency shift, and other features of the signal reflected back from internal tissue. A system consists of a diagnostic unit that controls ultrasound transmission and reception, performs image processing, and houses the video monitor, and a probe that is held in direct contact with the body being scanned and acts as a transducer (it converts an electrical signal into ultrasound and converts the reflected ultrasound signal back into an electrical signal) (see Fig. 1).

Diagnostic ultrasound systems generate ultrasound in frequencies that range between about 1 and 18 MHz. While ultrasound is good at passing through and imaging body tissue, it is not as effective on bone or air, making it important when imaging to

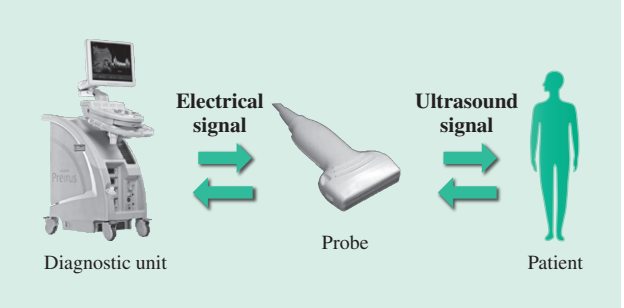
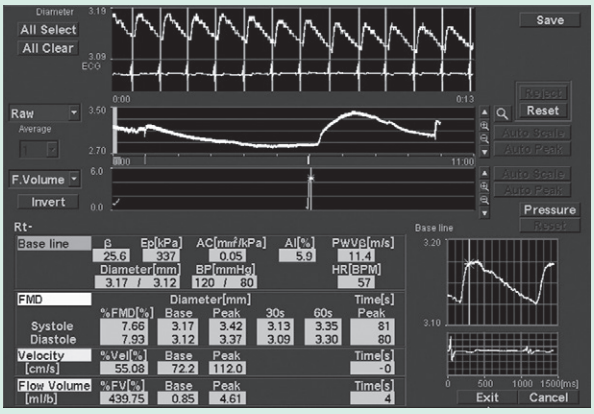


Fig. 1—Principles and Components of Diagnostic Ultrasound Systems.
Diagnostic ultrasound systems consist of a diagnostic unit that controls ultrasound transmission and reception and performs image processing, and a probe that converts between electrical and ultrasound signals.

avoid areas like the ribs or lungs. The frequency is selected based on factors such as the location being scanned or the characteristics of the tissue. High-frequency ultrasound, for example, has high resolution but is strongly attenuated, and therefore it is used for imaging tissue that is close to the surface. Low-frequency ultrasound, on the other hand, is less attenuated and so is used when imaging deeper tissue.

A wide range of probes are available for imaging different parts of the body. Examples include the phased array probes with a small end piece that are used to image the heart from between the ribs, convex probes (so called because of their convex end piece) used to push aside bodily gases to perform abdominal imaging, and linear probes that provide excellent adhesion for imaging superficial tissue. There are also numerous special purpose probes such as the internal probes used in obstetrics and urology and those fitted with a needle for taking biopsies (tissue samples).



FMD: flow mediated dilatation

Fig. 2—FMD Analysis.
FMD can detect arteriosclerosis at an early stage by assessing the function of the inner linings of blood vessels.

Role of Diagnostic Ultrasound Systems at Each Stage of the Care Cycle

This section describes the role of diagnostic ultrasound systems at each stage of the care cycle (prevention and checkup, screening and diagnosis, therapy and treatment, and prognosis and elderly care), and their potential enhancements. Being a form of diagnostic imaging system, naturally there is also strong demand for improvements in image quality.

The public is familiar with diagnostic ultrasound systems in the prevention and checkup stage through their use in complete medical checkups. The normal practice is for a specialist technician to operate the system and record the imaging data, and for a doctor to then use this data for diagnosis. As this involves scanning large numbers of patients and handling large quantities of data, throughput is an important issue.

There is also a high degree of familiarity with their use in screening and diagnosis, which includes the specific tests ordered after a complete medical checkup or progress checks during pregnancy. The former require higher image quality to improve diagnostic performance and support functions for such procedures as elastography, which displays tissue stiffness, and as with the prevention and checkup stage, there is also a need for throughput because of the large number of patients that are scanned. The latter, pregnancy progress checks, require measurement functions for checking fetal development.

While the use of diagnostic ultrasound systems in the treatment stage may seem unlikely, they are in fact used in supporting roles such as when placing a probe directly on the affected organ during open surgery to verify the location of a tumor. This requires probes with various different shapes and features to suit specific uses.

Uses in the prognosis and elderly care stage including post-operative checks and in-home care. For use by practitioners involved in primary healthcare who are unfamiliar with diagnostic ultrasound, the requirements for this phase include small, lightweight devices that are highly portable and simple to operate.

INITIATIVES FOR PREVENTION & CHECKUP —EARLY DIAGNOSIS OF HARDENING OF THE ARTERIES—

As diagnostic ultrasound is mainly used for the morphological imaging of tissue, it can be difficult to identify lesions that do not produce morphological changes.

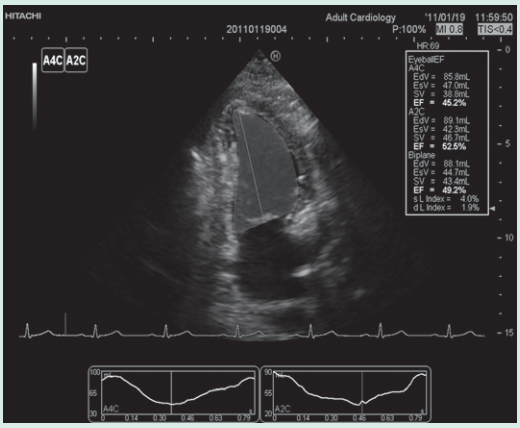
In arteriosclerotic disease (hardening of the arteries), for example, the usual means of diagnosis is to identify the morphological changes associated with the hypertrophy of arterial walls due to the buildup of plaque. However, arteries harden and lose their elasticity before hypertrophy is present. If this loss of elasticity can be identified, then earlier diagnosis will become possible.

Assessing the elasticity of arterial walls requires highly accurate measurement of the contraction of arteries in time with the heartbeat, a feat that is achieved by a technique that tracks the phase of the high-frequency ultrasound signal. Hitachi has utilized

this technique to develop flow-mediated dilatation (FMD) analysis, which can assess the function of the inner linings of blood vessels even before the arterial wall loses its elasticity (see Fig. 2). This technique is recognized as having the potential to contribute to preventive medicine through the early diagnosis of arteriosclerosis.

INITIATIVES FOR PREVENTION & CHECKUP AND SCREENING & DIAGNOSIS —IMPROVING THROUGHPUT—

The functional support provided by diagnostic ultrasound systems plays an important role in increasing their throughput when used for examinations. The main steps in an ultrasound examination are scanning with the probe (hereinafter, "scanning") to obtain a cross-sectional image of the area of interest and performing measurements on this image. As many aspects of ultrasound examination images are patient-dependent, there are also difficulties in interpretation, including such things as not being able to correctly identify lesions unless the image quality is adjusted properly during scanning. While recent systems offer an extensive range of image adjustment parameters that can compensate for individual differences between patients, adjusting these parameters takes a lot of work. Automatic optimization functions have been provided to minimize this workload by making the appropriate adjustments automatically based on the signal reflected back from the patient.



EF: ejection fraction

Fig. 3—Automatic EF Measurement Function.
This function can calculate cardiac output in realtime by using a realtime analysis of the shape of the heart chamber to perform precise tracing.

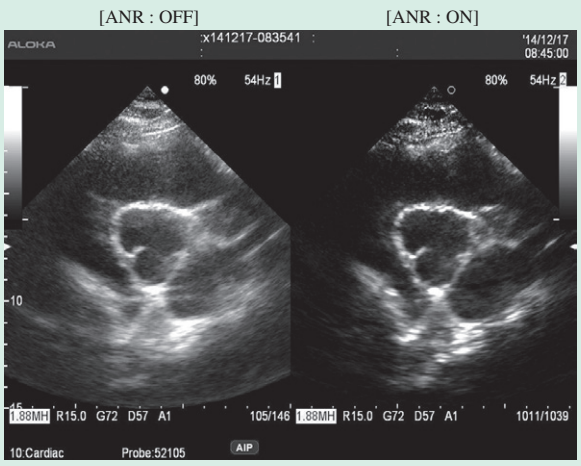
Automatic optimization functions include automatically compensating for patient differences in factors such as attenuation or the amplitude of the reflected signal, and making it possible to observe blood flow rates by setting the appropriate velocity range based on the condition of the patient and the location being imaged when using Doppler mode. These functions can reduce the amount of effort the operator needs to put into adjusting the image.

While diagnostic ultrasound systems resolve images by focusing the ultrasound in accordance with the depth below the skin, this assumes that the speed of sound in tissue is a constant value. However, because the actual speed of sound varies between patients and in different parts of the body, it is not uncommon for the spatial resolution of images to decline due to an inability to correctly focus the ultrasound. Accordingly, improved resolution can be achieved by estimating the speed of sound in the tissue being scanned and using this as a basis for automatic optimization.

Another important aspect of automation that Hitachi is working on is automatic measurement. For example, manually tracing the borders of cardiac blood vessels on images to estimate heart capacity places a heavy workload on the operator. However, when considering how to automate this tracing process, one problem is that it is not possible to identify blood vessel borders from variations in image brightness alone because of the difficulty of tracing out the entire heart at once. Automatic measurement functions for calculating cardiac output in realtime are capable of highly accurate tracing because they perform a realtime analysis of the shape of the heart chamber (see Fig. 3).

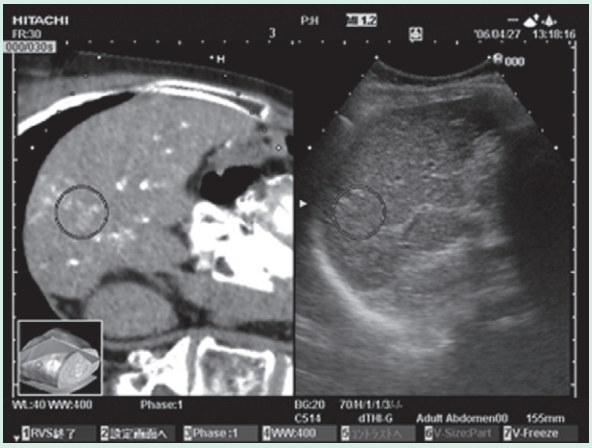
As the quick and accurate identification of lesions is also important for improving the throughput of ultrasound examinations, along with making image adjustment faster (as described above), there is a need to provide images in which lesions are easily visible. Internal organs imaged by diagnostic ultrasound systems frequently have speckle (ultrasound interference) patterns. As this hinders the identification of edges or structures, it has led to the adoption in recent years of adaptive image processing techniques such as HI REZ (high-resolution imaging) with functions that include identifying and highlighting edges or structures and reducing speckle patterns.

There are many artifacts in ultrasound images, such as those caused by multiple reflections or side lobes, and these are also a major factor in poor visibility. One



ANR: acoustic noise reduction

Fig. 4—ANR Function.
The ANR function suppresses artifacts to provide clear images of the aortic valve and surrounding structures.



RVS: Real-time Virtual Sonography CT: computed tomography

Fig. 5—RVS Function.
The RVS function displays marks to indicate the location of the tumor in the CT image on the left and the matching location on the ultrasound image on the right.

way of improving visibility is acoustic noise reduction (ANR), a technique for analyzing the signal received back from the body to selectively minimize artifact signals (see Fig. 4).

INITIATIVES FOR THERAPY AND TREATMENT

In the therapy and treatment stage of the care cycle, diagnostic ultrasound systems are frequently used in supporting roles such as when placing a probe directly on the affected organ during open surgery to verify the location of a tumor. This section describes Real-time Virtual Sonography*1 (RVS), a treatment support function that Hitachi was the first in the world to commercialize*2, and also special-purpose probes.

Treatment Support Functions

Uses for diagnostic ultrasound systems in treatment take advantage of their simplicity of operation and realtime performance, with applications that include checking the location and direction of movement of the needle used for radiofrequency ablation (RFA) treatment for liver cancer, and identifying where to implant the radioactive seed used in brachytherapy for prostate cancer.

To simplify these uses even further, Hitachi has led the world in developing the RVS function, which combines realtime ultrasound images with a simultaneous image of the same cross section using a different modality, such as computed tomography (CT) or magnetic resonance imaging (MRI) (see Fig. 5).

RFA treatment uses an ultrasound probe to image the liver from between the ribs as a needle is inserted into the tumor to destroy it using heat. Because RFA positions the probe between the ribs, bone or air can get in the way and prevent the location of the tumor from being identified by ultrasound alone. The RVS function makes the tumor easy to find by augmenting the ultrasound with a CT image.

In addition to CT or MRI images, further improvements to the technique are also being made by incorporating the display of three-dimensional ultrasound data, or by using it in conjunction with a contrast agent. Meanwhile, clinical research is proceeding on expanding its uses to other parts of the body such as breasts, kidneys, and the prostate. The market for the technique is expected to grow in the future.

Special Probes for Assisting Treatment

The section describes surgical probes developed to assist treatment.

In the case of surgery for the removal of a region of tissue designated by pre-surgical planning, a surgical probe provides a realtime view of the designated region to ensure that the tissue removal is performed accurately and also to detect any lesions that were not identified prior to surgery. Probes are available in a wide variety of shapes to suit different surgical

*1 Real-time Virtual Sonography is a trademark of Hitachi Medical Corporation.
*2 Based on research by Hitachi Aloka Medical, Ltd.

techniques and locations. Examples include micro-convex probes that can be held between the fingers, T-shaped linear probes that provide a good cross-section image and can make perforations, and hockey stick probes that can be inserted into narrow locations that are otherwise difficult to access (see Fig. 6).

Another technique of recent years is minimally invasive laparoscopic surgery, which seeks to minimize incisions in the skin and to enable patients to return quickly to a normal life. This involves opening a number of small incisions in the body through which a laparoscope can be inserted by way of a trocar (a pipe that holds the incision open). Hitachi has developed extremely small probes for the specific purpose of imaging organs through a trocar. These include a laparo probe with a transducer (oscillator) in the probe tip that can be manipulated externally to bend in four different directions, and a drop-in probe fitted with fins that can be grasped by forceps (see Fig. 7).

Through the commercialization of these various different surgical probes, Hitachi is helping support the therapy and treatment stage of the care cycle.

INITIATIVES FOR PROGNOSIS AND ELDERLY CARE

As noted earlier, nations around the world are variously taking steps to improve the quality and efficiency of healthcare as part of policies for controlling increasing medical expenditures. Primary and in-home healthcare play major roles in these measures, areas that operate under different conditions to previous purchasers of diagnostic ultrasound systems, in different environments with different experiences and needs.

In addition to considerations of cost and ease-of-use, diagnostic ultrasound systems are recognized for their potential uses in primary and in-home healthcare, which are called on to deal with a wide range of medical conditions under the constraints of limited time and information, by acting as diagnostic imaging systems that provide considerable assistance with diagnosis by augmenting the information obtained by medical practitioners from physical examinations.

To achieve this, systems must be able to deliver imaging performance with simple operation. As noted above, the nature of diagnostic ultrasound systems means they are more influenced than other diagnostic imaging modalities (such as MRI or CT) by the characteristics of the patient and the skill of the operator, often requiring detailed adjustment to obtain good quality images.

Ease of installation is another important consideration for primary healthcare, where the availability of space for a consultation is often limited. While existing hand carried units (HCUs) include small models similar in size to a laptop computer, for various different reasons these still tend to require a dedicated trolley, meaning that the space requirements in practice are little different from a conventional diagnostic ultrasound system.

Hitachi's own Noblus[*3] diagnostic ultrasound system is a compact model that features high image quality and advanced functions. In terms of ease of use and installation, however, it cannot really be described as suitable for primary and in-home healthcare.

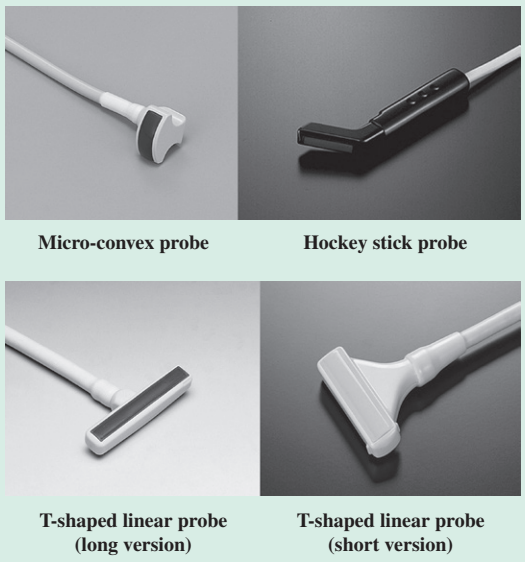


Fig. 6—Special-purpose Probes.
Probes are available in a wide variety of shapes to suit different surgical techniques and locations.

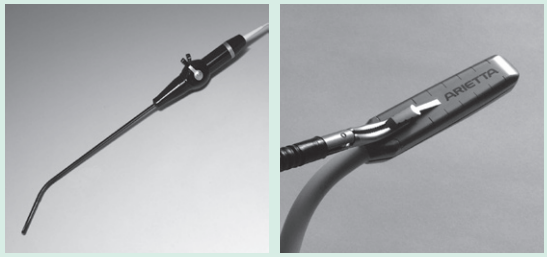


Fig. 7—Probes Designed Specifically for Laparoscopic Surgery.
The probes have a slim design to allow for insertion into the trocars used with laparoscopes and a movable tip.

*3 Noblus is a trademark of Hitachi Aloka Medical, Ltd.

Hitachi is currently proceeding with development aimed at entering this market and releasing models that can gain a high market share. By utilizing automatic techniques for optimizing imaging to suit individual patients based on know-how built up over many years in how to obtain images suitable for diagnostic use, the resulting systems will deliver solutions to the challenge of combining imaging performance with simple operation, two objectives that at first sight may appear to conflict. Hitachi is also working on design features such as seeking to ensure that systems are available for use when needed but do not get in the way during consultations that may take place in a limited space, such as outpatient healthcare.

FUTURE OUTLOOK—HEALTHCARE IT—

The ability to work with and utilize information technology (IT) will be a major challenge for diagnostic ultrasound systems in the future. Healthcare IT has the potential to dramatically transform the quality and efficiency of medical practice. A survey conducted in the USA found that approximately 72% of the country's doctors made routine use of smartphones and similar devices in their work, a percentage that continues to rise[(1)].

At a macro level, meanwhile, progress is being made in areas such as the introduction of electronic health records (EHRs) by governments and initiatives for the medical use of artificial intelligence. In order to make the most of diagnostic ultrasound systems in routine healthcare under these changing market conditions, Hitachi believes in the need to consider product development that takes account of systems' affinity with digital tools and allows for future workflow integration with EHRs and other systems, and integration with such technologies as artificial intelligence and the cloud to support diagnosis and other activities.

CONCLUSIONS

This article has described new initiatives Hitachi is pursuing for each stage of the care cycle. Many of these initiatives will help make life easier not only for patients but also for the medical practitioners who use the systems.

Along with improvements in throughput and quality of life (QoL), Hitachi intends in the future to develop and supply customers with products for use in a wide variety of applications at each stage of the care cycle.

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Featured Articles

Improving Laboratory Reliability through Visualization of Medical Testing Process

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Kumiko Kamihara
Tomonori Mimura

OVERVIEW: Recent years have seen demand for a higher level of quality management in the field of in vitro diagnostics for medical testing. Among the requirements for certification under the latest ISO 15189 standard is the collection and management of records for all testing processes. When Hitachi High-Technologies Corporation conducted a survey of all processes that take place at a testing laboratory, it found that management of the materials used with test equipment and management of measurement processes were of particular importance to laboratory-wide management. To achieve this, Hitachi High-Technologies developed a laboratory automation system, which uses single holders with RFID tags, and the reaction curve fitting method, a technique for determining the characteristics of the chemical reactions that take place during sample analysis.

INTRODUCTION

MEDICAL testing, the analysis of blood or other samples from a patient, plays an important role in diagnosing disease and in deciding how best to treat it. Along with performing large numbers of analyses in a short timeframe to cope with the increasing number of tests and samples, medical laboratories also need to provide doctors with accurate and highly reliable data. To achieve this, laboratories have installed automated sample transportation lines and a variety of automatic analyzers. Along with progress in the automation of medical testing comes a strong demand for reliability, with a variety of practices having been developed for this purpose.

Meanwhile, the ISO 15189:2003 standard has been published for quality management in medical laboratories, with implementation starting in Japan in 2005. The main method used in the past for the management of laboratory accuracy has been to conduct quality control using regular measurements of selected patient samples (quality control samples). This was also augmented by quality control of equipment and materials, including patient sample handling, reagents and other consumables, and devices.

The ISO 15189 standard certifies laboratory quality in terms of the results of the information required for laboratory-wide quality control, techniques for quality control of equipment and materials, testing accuracy control data, and the verification of reliability improvements.

This article describes techniques for the quality control of laboratory automation systems and analyzers.

MOVEMENT OF SAMPLES THROUGH A MEDICAL LABORATORY

After patient interview and the collection of samples in an examining room, samples are taken to a medical laboratory for testing. The route followed by a sample depends on its type (blood serum, plasma, urine, etc.) and the tests to be performed (biochemistry, immune serum, hematology, etc.). It may pass through preparatory processes such a centrifugation, etc. via laboratory automation equipment and a variety of analyzers (biochemistry and immunoassay analyzers, blood analyzers, etc.) in order to generate the output results as data that help facilitate patient treatment back in the examining room (see Fig. 1).

Laboratories collate and combine results from a variety of measurements that are passed back to the doctor in a patient examination report. The Information & Telecommunication Systems Company of Hitachi, Ltd. markets an information system for managing multiple analyzers and supporting operations from ordering tests to performing them and reporting the results.

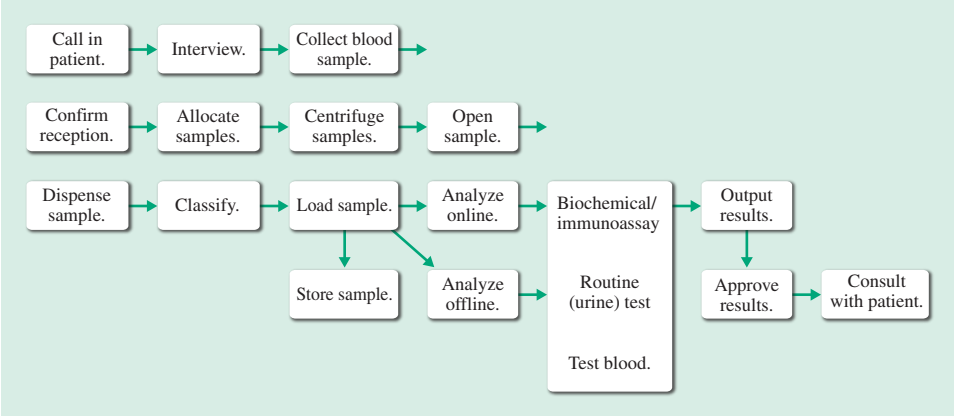

Fig. 1—Laboratory Sample Flowchart.
After sample preparation, which depending on the sample type may include centrifugation, labeling, and dispensing, a blood sample is transported to the analyzer where the specified measurements are performed.

A subject attracting considerable interest at present is the digitization of clinical data and the use of electronic medical records and big data analytics for purposes such as preventive medicine.

At the same time, there has been less progress on systematizing the handling of materials in the laboratory, such as quality control samples and reagents. While identification barcodes are attached to patient samples at the time of collection, and the collected samples then move through the sample preparation steps prior to loading into the analyzer and performing measurements, because the number and type of samples and the tests to be performed vary from patient to patient, difficulties have included the efficient tracking of multiple samples in realtime and backtracking the actual route that samples have taken.

LABORATORY MANAGEMENT

Comprehensive management techniques are important for laboratory-wide quality control, including not only sample test results but also the management of equipment (analyzer operation, maintenance and inspection, etc.) and materials (samples, reagents, etc.).
(1) The interconnection and operation of preparation and analysis processes in the laboratory must be managed.
(2) Practices are needed for the monitoring and quality control of analytical testing processes of patient samples in the various types of analyzers.
(3) It is necessary to manage equipment and materials, such as reagents, quality control materials, and maintenance.

When a fishbone diagram (cause and effect diagram) is used to represent the requirements of laboratory management, these can be broadly divided into requirements that relate to equipment and requirements that relate to the people who use the equipment and their operating practices (see Fig. 2).

The equipment-related requirements can be further divided into managing equipment condition, managing consumables, and managing equipment operation.

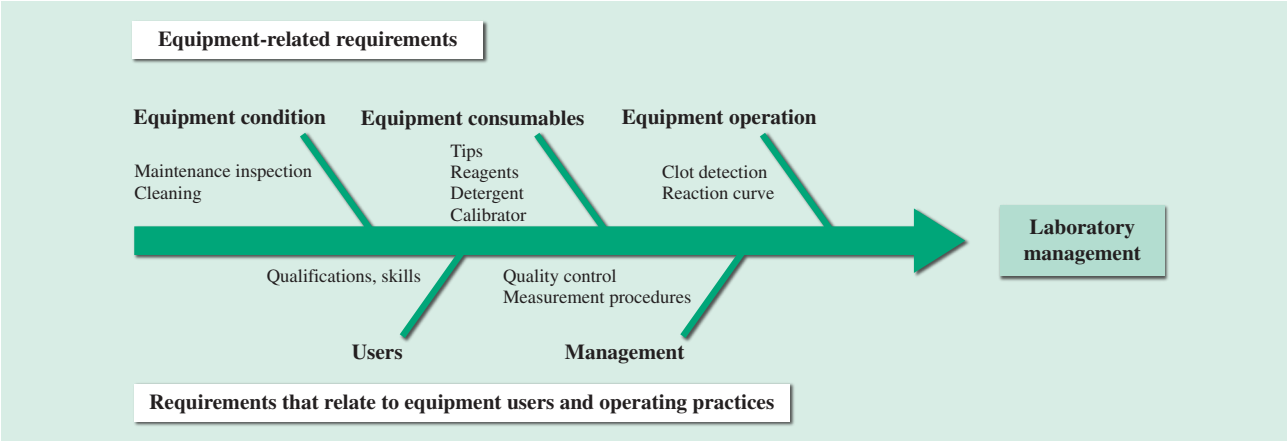

Fig. 2—Laboratory Management.
Laboratory management can be broadly divided into requirements that relate to equipment and requirements that relate to the people who use the equipment and their operating practices.

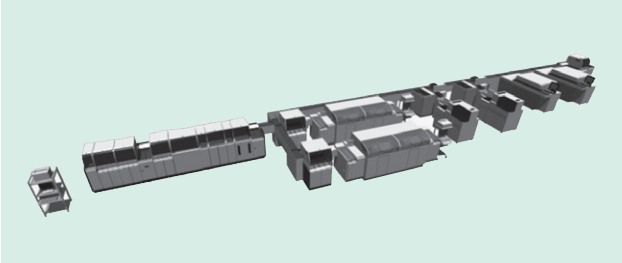

Fig. 3—Example Layout of Laboratory Automation System.
Efficiency improvements and the elimination of errors can be achieved by combining Hitachi High-Technologies' laboratory automation system with its automatic biochemical analyzers.

(a) Managing equipment condition
This includes maintenance inspections, parts replacement, cleaning, and so on.
(b) Managing consumables
These include cuvettes, lamps, reagents and calibrators (lot, expiry date), electrodes, detergents, sample tubes (test tubes), and tips.
(c) Managing equipment operation
This includes detecting shortages of samples or shortages of reagents, detecting fibrin clots, calibration curve sensitivity, and reaction curve management.

In regard to requirements that relate to the people who use the equipment and their operating practices, quality control and measurement procedures can be improved by enhancing the user interfaces of equipment and systems to make it easier for staff to perform checks quickly and determine equipment status prior to use. Similarly, the more that the screens used on sample preparation equipment and analyzers are based on similar concepts, the less time it takes for medical testing technicians to check the status of sample preparation equipment or learn how to operate the analyzers.

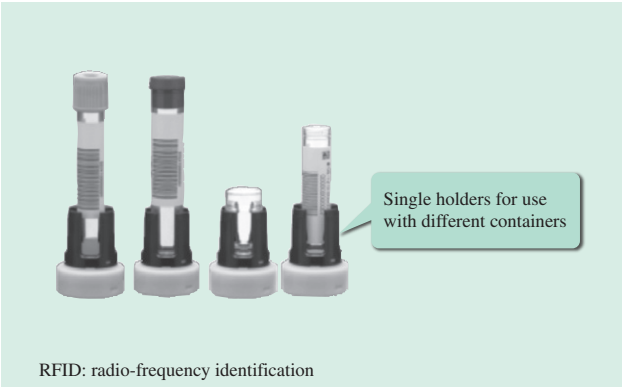

Fig. 4—Single Holder with RFID Tag.
High-speed transportation is achieved by taking advantage of the faster reading time possible when using RFID. This facilitates the tracking of samples to ensure that each one is transported to the required analyzers.

SAMPLE MANAGEMENT IN LABORATORY AUTOMATION SYSTEMS

Single sample carriers are a useful way to speed up the transportation of samples in the laboratory and to make this process more efficient. Similarly, the double identification of samples is necessary to verify that the controlled laboratory has performed measurements on all of the collected samples. This means attaching radio-frequency identification (RFID) tags to new single holders, and sample barcodes to test tubes that contain samples. Hitachi High-Technologies Corporation has developed a laboratory automation system that tracks the location of samples on the transportation line and prevents misidentification (see Fig. 3).

The laboratory automation system uses single holders with RFID tags to identify samples on the transportation line (see Fig. 4).

Because of the need to halt and rotate samples to read the sample information when using barcode labels, this takes approximately 5 s. RFID tags, in contrast, do not require this halt and rotate step and can be read in just 0.2 s. Accordingly, the use of RFID has increased transportation speed.

Furthermore, enhancements to user interfaces have made it easy to determine where individual samples

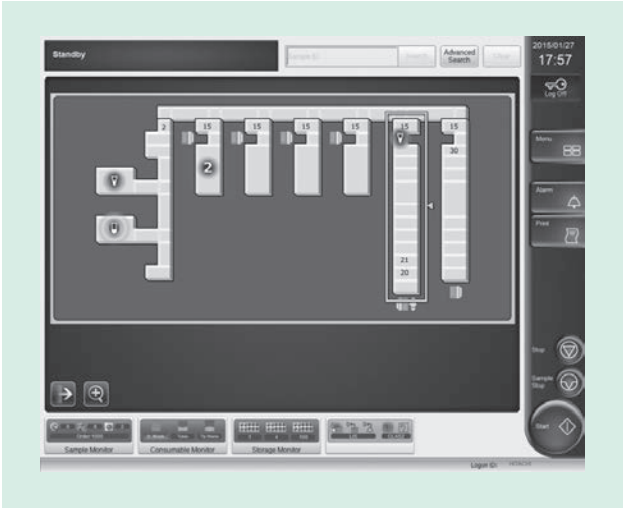

Fig. 5—The Laboratory Automation System Sample Monitor Screen.
The screen is used to check the location and progress of specific samples.

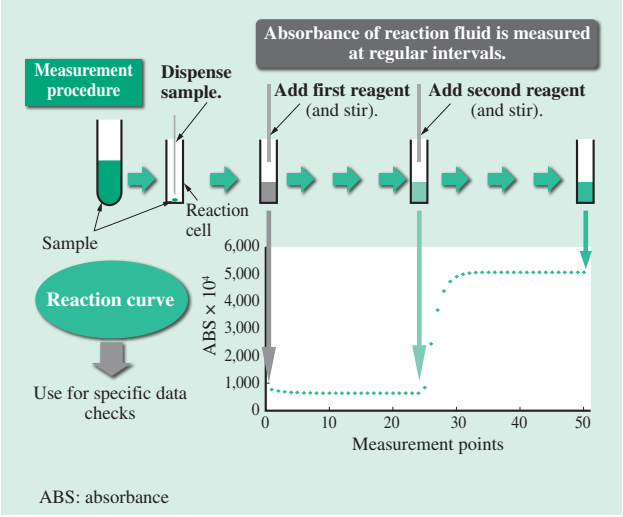

Fig. 6—Measurement Processes for Automatic Biochemical Analyzers.
Reagents are added to the blood serum, urine, or other sample and the sample is stirred to promote a reaction causing the optical absorbance to change. This changing absorbance value is measured at regular intervals.

are located in a large laboratory, making it possible to respond quickly to doctor inquiries about testing progress or conduct prompt retesting (see Fig. 5).

MANAGEMENT OF MEASUREMENT PROCESS FOR ANALYZERS

The sequence of operations performed by analyzers also needs to be managed. The following are some examples of such checks.

(1) Before measurement
Is the cuvette clean?

(2) Sample dispensing
Has the correct quantity of sample been pipetted?
Was any fibrin or other contaminating material pipetted along with the sample?

(3) Reagent dispensing
Has the correct quantity of reagent been pipetted?

Furthermore, management of the measurement process can ensure the reliability of measurement through the combined control of both the reaction process and equipment operation. In recent years, analyzers have also been fitted with mechanisms for detecting abnormal conditions during the analysis reaction, such as the use of a photometer to check for excess absorbance or clot detection in the sampling mechanism. The requirement is to achieve a higher level of reliability by trying to detect abnormalities not just in the measurement results but also during the reaction.

In an automatic biochemical analyzer, this is achieved by taking periodic photometer absorbance measurements after the sample and reagent have been added to the cuvette (see Fig. 6).

The sequence of absorbance values obtained by these measurements is called the "reaction curve." The end-point assay and rate assay are two types of reaction curves. In an end-point assay, the reaction reaches equilibrium during the measurement period, whereas a rate assay measures how the reaction changes.

Hitachi High-Technologies is working on use of the reaction curve fitting method to monitor ("visualize") the reaction process as a check.

The reaction curve fitting method is a technique for producing numeric indicators (parameters) for the measured reaction curve by using a model function derived from chemical kinetics to approximate it in accordance with the reaction pattern based on factors such as lipid quantity or enzyme activity.

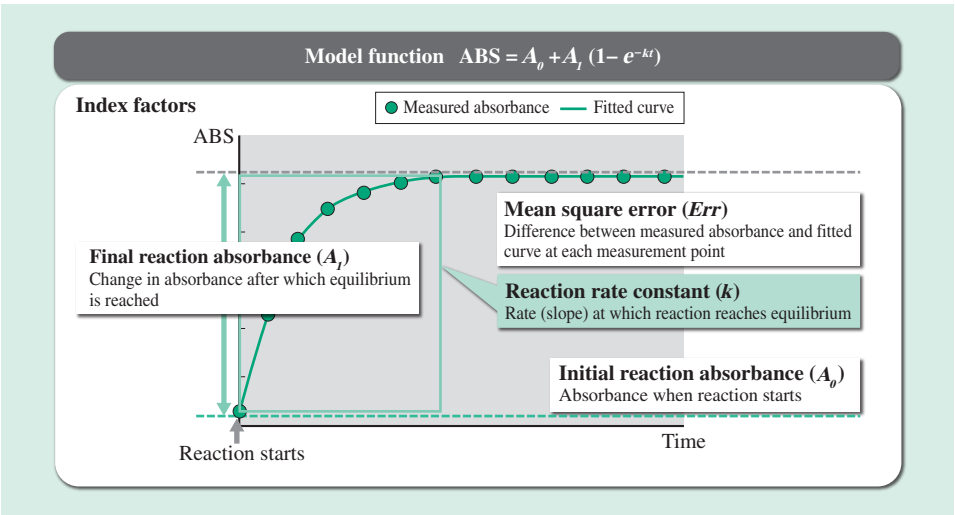

Fig. 7—Reaction Curve Fitting for End-point Analysis.
Four "index factors" that characterize the pattern are calculated using a model function derived from chemical kinetics.

The approximation function is calculated as follows.

In the case of an end-point assay, the absorbance starts changing when the reaction is initiated then settles to a constant value after a certain period of time. Accordingly, the reaction is approximated by a model function that replicates the start of the reaction and its final level of absorbance (see Fig. 7).

In the case of a rate assay, the approximation uses a model function that replicates the lag phase immediately after the reaction is initiated during which it has yet to reach a steady rate (see Fig. 8).

Hitachi High-Technologies has used the reaction curve fitting method to obtain numeric parameters for a variety of reaction curve patterns so that abnormalities caused by the sample, reagent, or equipment during the reaction process can be detected by monitoring the value of these parameters.

FUTURE MEDICAL LABORATORIES

In the future, the development of the Internet of things (IoT) will increasingly change the laboratory, including an increase in the number of sensors fitted in analyzers to help determine the location of patient samples, and the embedding of integrated circuit (IC) chips in consumables to enable the realtime management of equipment and materials where required. Amid this flood of information, laboratory administrators will be called on to respond appropriately depending on the circumstances, whether it is the morning rush during the day or emergencies during the night. This requires the collation and interpretation of a variety of information and the provision of information that is appropriate.

Continuous Improvement of Laboratories

Laboratories are continually changing in step with advances in medicine. The use of experience design for analysis is an effective way to make ongoing improvements in the laboratory, such as further shortening the time taken to provide test reports, analyzer integration, and changes to testing routes along with the expanding range of measurements to be performed due to advances in personalized medicine such as genetic diagnosis and the addition of new biomarkers. Also of importance will be integrated management systems that enable the incorporation of new analyzers and flexible changes to laboratory layout through the use of IoT technology with various sensors.

Innovation in Information Delivery —Greater Use of Mobile Devices—

Systems have already been implemented for sending things like equipment alarms or emergency test results to mobile devices. These devices are a useful way of monitoring and checking information in realtime. In the future, bidirectional practices such as the issuing of instructions to laboratory staff by administrators and communicating with equipment maintenance companies to share information will lead to quicker responses. In addition to their use in laboratories, the standardization of mobile devices as part of hospital infrastructure is also anticipated.

It is extremely important for staff that the screens used by mobile and other IT devices, sample preparation systems, and the different types of analyzers be based on the same concepts so that anyone can intuitively know how to use them, thereby helping shorten the time it takes to learn how to

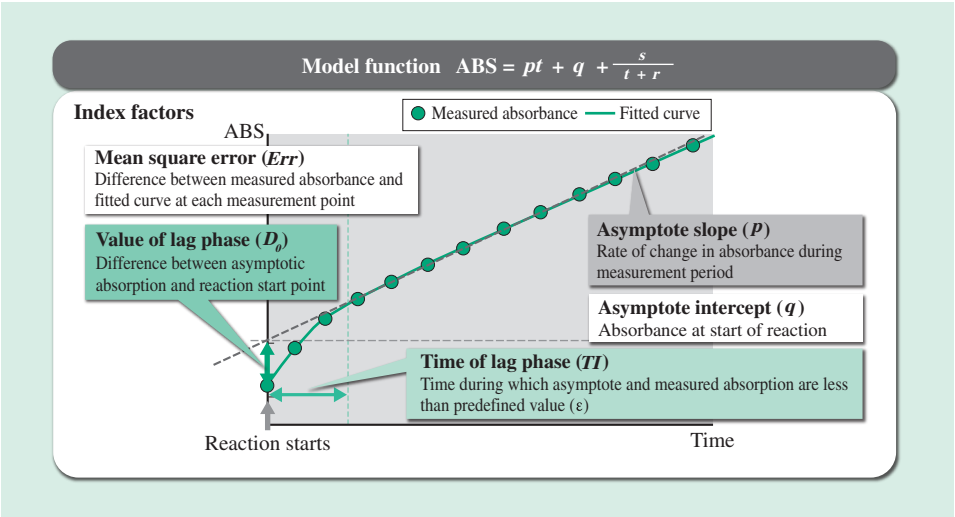

Fig. 8—Reaction Curve Fitting for Rate Analysis.
Five characteristic "index factors" are calculated using a model function that replicates the lag phase.

operate these systems. It is also essential that staff members are provided with appropriate instructions.

CONCLUSIONS

Thanks to user interface enhancements, the use of single sample carriers with RFID tags, and the reaction curve fitting technique, it is now possible to visualize the complex processes that take place at medical laboratories, which combine medical testing information with such equipment and materials as analyzers, samples, and reagents. In addition to improving productivity, this visualization of the medical testing process is also leading to improved laboratory reliability through process management. In the future, Hitachi High-Technologies intends to provide appropriate operational information in realtime and support the adoption of IoT technologies.

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Featured Articles

Open MRI for Neurosurgery

Yukihiro Yasugi
Kazunori Waragayu

OVERVIEW: An open MRI system is one in which the gantry does not enclose the patient, with models in the 0.2-T to 0.4-T range being widely used, particularly for diagnostic imaging. The features of open MRI include a high level of safety, being able to perform imaging without exposure to radiation and featuring spaciousness, low magnetic field intensity, and a low level of magnetic field leakage. By checking for brain tissue deformation after the skull is opened and providing imaging data updates to the neurosurgery navigation system, the installation of a Hitachi open MRI system in a neurosurgery theater provides a system that helps achieve precision in neurosurgical procedures. Furthermore, the low level of magnetic field leakage means conventional surgical instruments can still be used.

INTRODUCTION

RECENT years have seen an increasing number of advanced neurosurgical procedures performed in Japan and elsewhere. Because of the precision these procedures require, it is common practice to use a navigation (guidance) system. Among the challenges of removing a brain tumor in particular is to complete the procedure without damaging the motor nerves and other critical brain functions. This has led to widespread use of intraoperative navigation systems that use magnetic resonance imaging (MRI) images captured pre-operatively. One of the problems with this approach, however, is when the surgical procedure results in brain shift[*1].

This article describes an operating theater system that can capture intraoperative MRI images using an in-theater MRI system.

CURRENT SITUATION AND CHALLENGES FOR NEUROSURGERY

Past brain tumor surgery has involved supplying magnetic resonance (MR) image data taken prior to the operation to the navigation system and removing the tumor with the aid of a microscope. The problems with this are as follows:

(1) The problem of the brain shifting after the skull is opened or brain tissue being deformed during the process of removing a tumor has meant that experienced surgeons have had to make allowances for these phenomena during surgery.

(2) Highly malignant glioblastomas in particular occur in the cerebrum and spread into (infiltrate) the surrounding brain, making the distinction between diseased and normal tissue unclear to the naked eye.

(3) As the removal of excessive brain cell tissue can result in a loss of function, the practice has been to remove small amounts at a time and perform pathology testing during surgery to identify whether the removed material contains normal or cancerous cells. This takes a long time and involves a lot of work.

(4) The only way to check whether a tumor has been fully removed without any remaining cancer tissue has been to perform a post-operative MR scan.

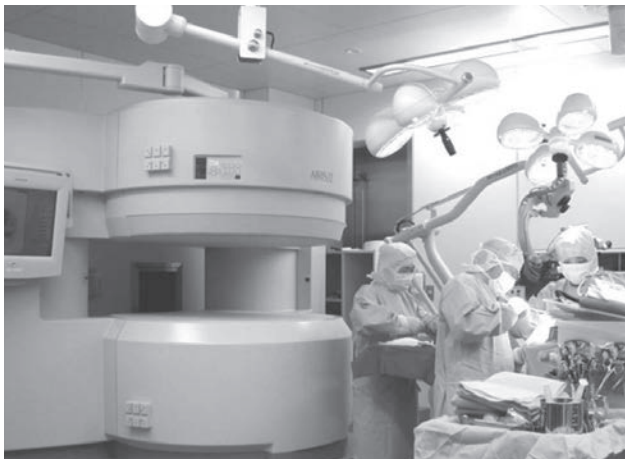
(5) Because of the very high risk of relapse if the malignant tumor is not fully removed, five-year survival rates have been remarkably poor.

USE OF OPEN MRI CONSTRUCTED IN THEATER

To overcome these problems, an open MRI system was constructed in an operating theater at Tokyo Women's Medical University Hospital in 1999 to improve the neurosurgical treatment of malignant tumors by enabling intraoperative MRI (see Fig. 1).

However, because operating theaters contain a lot of other equipment, surgical instruments, and special systems that are not present in a normal diagnostic

*1 The physical movement or deformation of the brain. The significant deformation of brain tissue that occurs when the brain is exposed.



MRI: magnetic resonance imaging

Fig. 1—Operating Theater MRI System (Source: Tokyo Women's Medical University Hospital).
By using a permanent magnet MRI that features minimal magnetic leakage, it is possible to perform neurosurgery adjacent to the MRI system.

MRI room, special measures needed to be taken based on the following two considerations.
(1) Prevent the magnetic field and high-frequency electromagnetic radiation from the MRI system from interfering with theater equipment.
(2) Prevent electromagnetic interference (EMI) from the theater equipment (such as noise or changes in the ambient magnetic field) from interfering with the MRI system.

Through its involvement in installing the system at Tokyo Women's Medical University Hospital, Hitachi was able to build up system implementation engineering know-how, including consulting with doctors, nurses, technicians, information technology (IT) staff, and other users about their requirements and establishing working arrangements and quality control with the other companies involved in the project, such as peripheral and other equipment suppliers.

The system at Tokyo Women's Medical University Hospital was a major success, quickly collecting evidence on treatment performance that was presented at academic conferences (see Table 1). It routinely achieves a 90% or better tumor removal rate, and has demonstrated its ability to attract brain tumor patients from around Japan, with an increasing number asking to be treated at a hospital where the operating theater is equipped with an MRI system[(1)].

TABLE 1. Five-year Survival Rates for Different Grades of Brain Tumor (Source: 66th Annual Meeting of the Japan Neurosurgical Society)
The malignancy of a brain tumor is indicated by a grade, with grade 4 being the most malignant. Surgical success is typically assessed by five-year survival rates, with Tokyo Women's Medical University achieving roughly three times the average for this measure in Japan.

Tumor malignancy	Five-year survival rate	
	Average for Japan	Tokyo Women's Medical University
Grade 2	69%	90%
Grade 3	25%	75%
Grade 4	7%	19%

INTRAOPERATIVE IMAGING OF NERVE FIBERS IN BRAIN

The two ways in which MRI images are used in neurosurgery are pre-operative use for planning and intraoperative use for monitoring. The concept behind equipping an operating theater with an MRI system is to achieve the following four key expectations (see Fig. 2).
(1) To be able to obtain imaging data in a timely manner in an operating theater equipped with an MRI system and use it to update three-dimensional data for image-guided surgery ("navigation").
(2) To be able to use conventional practices and instruments without requiring special surgical instruments by adopting open MRI.
(3) To achieve a high rate of full recovery.
(4) To enable evidence-based treatment while reducing the risk of medical error and law suits.

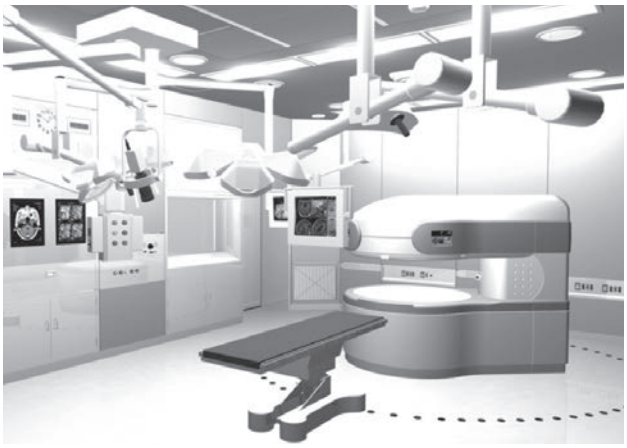


Fig. 2—Use of MRI as an Intraoperative Imaging System.
A neurosurgery operating theater equipped with an open MRI system. The dotted line on the floor indicates the magnetic field safety zone with a threshold of 0.5 mT (approximately 10 times the Earth's magnetic field). Conventional surgical instruments can be used outside this zone.

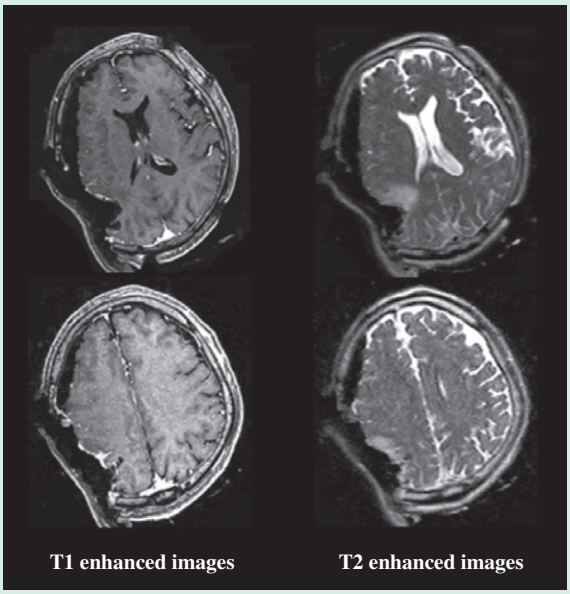


Fig. 3—Images Captured by Intraoperative MRI Imaging (Source: Kagoshima University Medical and Dental Hospital). The photograph shows two sets of cross-section cranial images with different contrast. Image data is captured in three dimensions and sent to the surgery navigation system.

Improving the five-year survival rate for brain tumor removal requires both maximizing the proportion of tumors removed and preserving brain function to minimize post-operative complications. MRI imaging is an effective way to identify the relative locations of a tumor and normal tissue. Similarly, surgery navigation systems are able to provide surgeons with accurate information about the site of the surgery by using an optical or other measurement device to detect the location of surgical instruments and display the location of the instrument tip on the brain image.

Furthermore, diffusion-weighted imaging (DWI) is a non-invasive MRI imaging technique that can provide information about the orientation of nerve fibers in the brain. This technique provides a way to determine the orientation of nerve fibers associated with particularly important motor functions in the vicinity of the tumorous lesion. Because the physical shape of the brain changes during the process of an operation, it is desirable to provide data updates through the use of intraoperative DWI. This use of intraoperative DWI images to determine nerve locations for surgery navigation helps avoid damage to patient motor functions. This helps make open brain surgery possible while minimizing brain nerve damage[(2)].

Fig. 3 shows cranial images captured during neurosurgery. Images captured while the skull is open show how the removal procedure causes the repositioning of brain tissue.

WIDER ADOPTION OF SYSTEM AND GUIDELINES ON ITS USE

Following the installation of the Tokyo Women's Medical University system, in parallel with seeking to deploy the system at the neurosurgery departments of other major university hospitals, Hitachi also took the lead in establishing a society for intraoperative imaging based around neurosurgeons in Japan who are recognized as key opinion leaders (KOLs)[*2]. This led to similar systems being installed at a total of 10 hospitals in Japan, including at Nagoya University and Kagoshima University.

The society for intraoperative imaging has since been upgraded to a full academic society under the title, Japan Society of Intraoperative Imaging, with its 15th conference being held in 2015.

A committee of the Japan Society of Intraoperative Imaging set up to formulate guidelines for intraoperative MRI published its draft Guidelines for Intraoperative Use of MRI in July 2014[(3)].

These guidelines divide MRI installations into two types depending on whether the system is in the operating theater (a "dedicated system") or an adjacent room (a "2-room system").

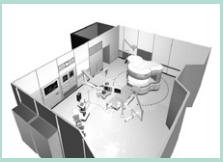
Table 2 compares the two configurations.

The limited magnetic field leakage from open MRI systems that use permanent magnets means they can be installed in-theater. This should reduce safety incidents by shortening the distance that patients undergoing open brain surgery need to be moved. Hitachi is also working on measures that minimize the durations of interruptions to surgery by developing functions such as a rotating operating table that facilitates the repositioning of patients when they are moved between the surgery and imaging positions. Surgeons recognize that it is important to minimize any additional burden imposed on surgical personnel by the MRI imaging process, and that any problems with safety or with the effort and time required will lead to less frequent use of the MRI imaging that the equipment is there to perform.

Accordingly, it is recognized that dedicated systems are necessary if extensive use is to be made of MRI systems.

*2 Medical practitioners with extensive influence in the healthcare industry.

TABLE 2. Comparison of "Dedicated" and "2-room" Operating Theater MRI Systems
Dedicated systems can be located in the operating theater because they use open MRI, which has a low level of magnetic field leakage, thereby enabling more extensive use of MRI systems, with less time and effort required for imaging, and fewer safety problems.

		Open MRI (low level of magnetic field leakage)	Cylindrical MRI (high magnetic field strength)
Dedicated system (MRI in operating theater) 		Advantages: Short patient movement distance (either using a rotating configuration or a movement of less than 2 m), convenient for taking multiple images Disadvantages: Not suitable for use as a diagnostic MRI	Measures need to be taken to deal with magnetic field leakage. Poor return on investment
2-room system (MRI in adjacent room) 	Movable MRI system		Advantages: No need to move patient Disadvantages: Expensive, difficult to manage problems associated with magnetic field (leakage field movement)
	Movable operating table		Advantages: Can be used for diagnostics as well as surgery Disadvantages: Safety problems associated with large amount of patient movement

CONCLUSIONS

The demands placed on the intraoperative use of MRI in neurosurgery are high and the market is a dynamic one. The advantages of MRI for intraoperative monitoring include the lack of exposure to radiation and the high-contrast images it provides of tumors, meaning that precise surgical navigation is possible using MRI image data that can be updated during surgery by taking advantage of these features.

There is a demand for precise surgery navigation systems that use intraoperative MRI systems as a way of achieving reliable tumor removal without damaging healthy brain tissue.

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Featured Articles

Particle Therapy that is Easy on Patients

Hiroshi Akiyama, Ph.D.
Kenta Mochizuki
Masumi Umezawa

OVERVIEW: Hitachi has drawn on the beam control technology it built up through its participation in large accelerator projects to enter the market for particle therapy systems, with five facilities currently in operation and five more in commissioning or under construction. Current marketing focuses on systems that use the spot scanning technique developed at the MD Anderson Cancer Center. On individual projects, Hitachi also works through collaborative creation with customers to develop and supply the latest technologies, including spot scanning, tumor tracking, and CBCT. Along with taking on the ongoing challenge of new technology in order to offer it to the market in a timely manner, Hitachi also intends to continue developing technology so that it can supply particle therapy systems as integrated solutions.

INTRODUCTION

RECENT years have seen growing demand for radiotherapy for cancer treatment. Particle therapy techniques such as those that use proton beams or carbon ion beams have attracted attention in the field of radiotherapy because of their ability to focus the beam on the affected area only and thereby keep damage to healthy tissue to a minimum.

Hitachi has built up skills in accelerators and related beam technologies through its participation in national projects that involve building large particle accelerators for physics experiments. Having utilized these technologies in the development of particle therapy systems, Hitachi entered the market for this equipment by supplying a proton beam therapy system to the Proton Beam Therapy Center, University of Tsukuba Hospital. This system commenced operation in September 2001, and has since treated more than 3,300 patients.

This article describes Hitachi's expansion into the market for particle therapy systems, its product range, and the development of advanced technologies through collaborative creation with customers.

EXPANSION INTO THE MARKET FOR PARTICLE THERAPY SYSTEMS AND PRODUCT FEATURES

Expansion into the Market for Particle Therapy Systems

Hitachi is actively expanding into overseas markets as well as in Japan.

Hitachi became the first Japanese supplier[*1] to enter the US market for particle therapy systems in December 2002 when it received an order for a proton beam therapy system from The University of Texas MD Anderson Cancer Center (MDACC). Hitachi was also the first supplier of particle therapy systems in the world[*1] to successfully implement a spot scanning system. Spot scanning is a new technique that minimizes unintended irradiation of healthy tissue by targeting the dose on the affected area. As of August 2015, of the more than 6,200 patients who had received treatment at MDACC, more than 1,400 were treated using spot scanning.

The proton therapy system at the Nagoya Proton Therapy Center in Nagoya in Aichi Prefecture commenced operation in February 2013. This system also supports spot scanning, making it the first in Asia[*1] to use proton beam scanning. The Nagoya system has treated about 900 patients in the two years and five months since it opened, treating about 500 over a one year period in 2014. The three systems at Tsukuba, MDACC, and Nagoya have already treated a total of more than 10,000 people.

The molecular tracking proton therapy system installed at the Proton Beam Therapy Center at Hokkaido University Hospital incorporates a variety of new technologies, including Real-time Image Gated Particle Therapy, robotic couch, and cone beam computed tomography (CBCT). It commenced operation in March 2014.

*1 Based on research by Hitachi, Ltd.

Orders for two proton beam therapy systems were received from the Mayo Clinic in May 2011 for their Rochester, Minnesota and Phoenix, Arizona campuses in the USA. The Rochester system commenced treatment in June 2015.

Another order for a proton beam therapy system was received in February 2012 from St. Jude Children's Research Hospital in the USA. This system commenced treatment in November 2015.

In 2014, a project got underway to supply Hitachi's first heavy ion particle therapy system to the provisionally named Osaka Heavy Ion Particle Cancer Therapy Clinic. Further orders for proton beam therapy systems were received for the Sibley Memorial Hospital, a member of Johns Hopkins Medicine in the USA in June 2015 and for the Nagamori Memorial Center of Innovative Cancer Therapy and Research at the University Hospital of the Kyoto Prefectural University of Medicine in July 2015.

Features of Hitachi Particle Therapy Systems

Hitachi supplies systems based on scanning technology. Compared to broad beam techniques used in the past, scanning can target the beam at the affected area and results in less generation of secondary particles. By eliminating the need for patient-specific components like the range compensators and apertures, scanning also has lower running costs and can shorten treatment times.

For its proton beam therapy systems, Hitachi uses the compact synchrotron accelerators developed for Hokkaido University Hospital. It is also developing an accelerator that is designed for small size for use in heavy ion therapy systems. Hitachi offers three different rotating gantries to suit customer needs: a standard 360º model, a small 360º model, and a 190º rotating model. The options for the imaging system used for positioning are a standard dual-axis X-ray imaging system, and CBCT, CT on Rails in treatment room. The options for image registration are a 2D/2D mode that works with dual-axis X-ray imaging; a 2D/3D mode, which uses a large number of digitally reconstructed radiography (DRR) images created from the computed tomography (CT) image used for treatment planning and compares these to the X-ray images during positioning to calculate any deviation automatically; and a 3D/3D mode that works with CBCT and an in-room CT system.

Hitachi has also developed its own particle treatment planning system. The version for proton therapy is already in use at three facilities in Japan.

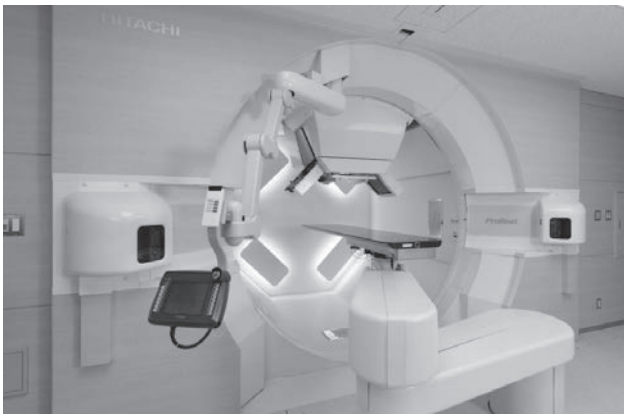

Fig. 1—Example Treatment Room Design.
The photograph shows the Proton Beam Therapy Center at Hokkaido University Hospital.

Another version of heavy ion therapy is currently under development. While it is one thing to develop the latest particle therapy techniques, to be released on the market they must be supported by a treatment planning system. By developing its own particle treatment planning system, Hitachi is able to bring new technology to market in a timely manner.

Easy-to-use Systems that are Conscious of People and Environment

Previous accelerator systems operated non-stop to ensure stability. For the University of Tsukuba Hospital system that entered service in 2001, Hitachi implemented a system that saved energy by only operating when needed. The MDACC system that started operation in 2006, meanwhile, featured operator-less operation with all of the parameters for the accelerator and radiotherapy system set automatically. This provides an efficient system in which the beam generation system function operates automatically in response to therapist requesting the beam after positioning is complete.

Furthermore, the design division of Hitachi designed the interior of the therapy room to provide a relaxing treatment space with soft lines (see Fig. 1).

Compact System

Growing demand is anticipated in the future for proton beam therapy systems, not only from major hospitals, but also from smaller facilities and urban clinics where space is limited. In response, Hitachi is developing a system with a single-room gantry that has a much smaller installation footprint thanks to use of the small gantry and the compact accelerator developed for the Hokkaido University Hospital system (see Fig. 2).

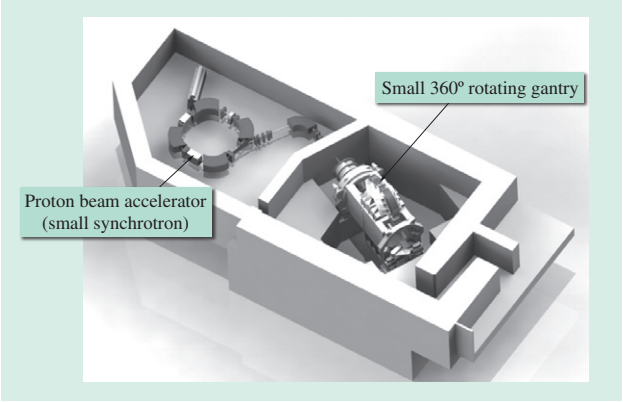

Fig. 2—Overview of Single-room Proton Beam Therapy System.
The system achieves a smaller installation footprint by combining a proton beam accelerator with a single therapy room with a rotating gantry.

DEVELOPMENT OF NEW TECHNOLOGY THROUGH COLLABORATIVE CREATION WITH CUSTOMERS

Hitachi has been developing and implementing world-leading particle therapy technologies in collaboration with worldwide customers. Examples include the development and implementation of the scanning technique with MDACC[1], and the combination of real-time image gated technique and scanning irradiation developed in collaboration with Hokkaido University Hospital through the "Advanced Radiation Therapy Project: Real-time Tumor-tracking with Molecular Imaging Technique" project of the Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program)[2]. The following sections describe notable examples of this work along with the plans for the future.

Improvements in Radiotherapy Accuracy

Work on improving image-guided radiotherapy (IGRT) is ongoing in all areas of radiotherapy with the aim of achieving greater accuracy, with tumor tracking and CBCT imaging having already been implemented for proton beam therapy systems through joint development with Hokkaido University Hospital.

Fig. 3 shows a control screen for tumor tracking in which the current marker position is displayed both in numeric format and as a radiography image. The system operates such that the proton beam is only delivered when the marker is within a designated tolerance of the location determined during treatment planning. Approval for manufacture and sale of the system that combines tumor tracking and proton beam scanning

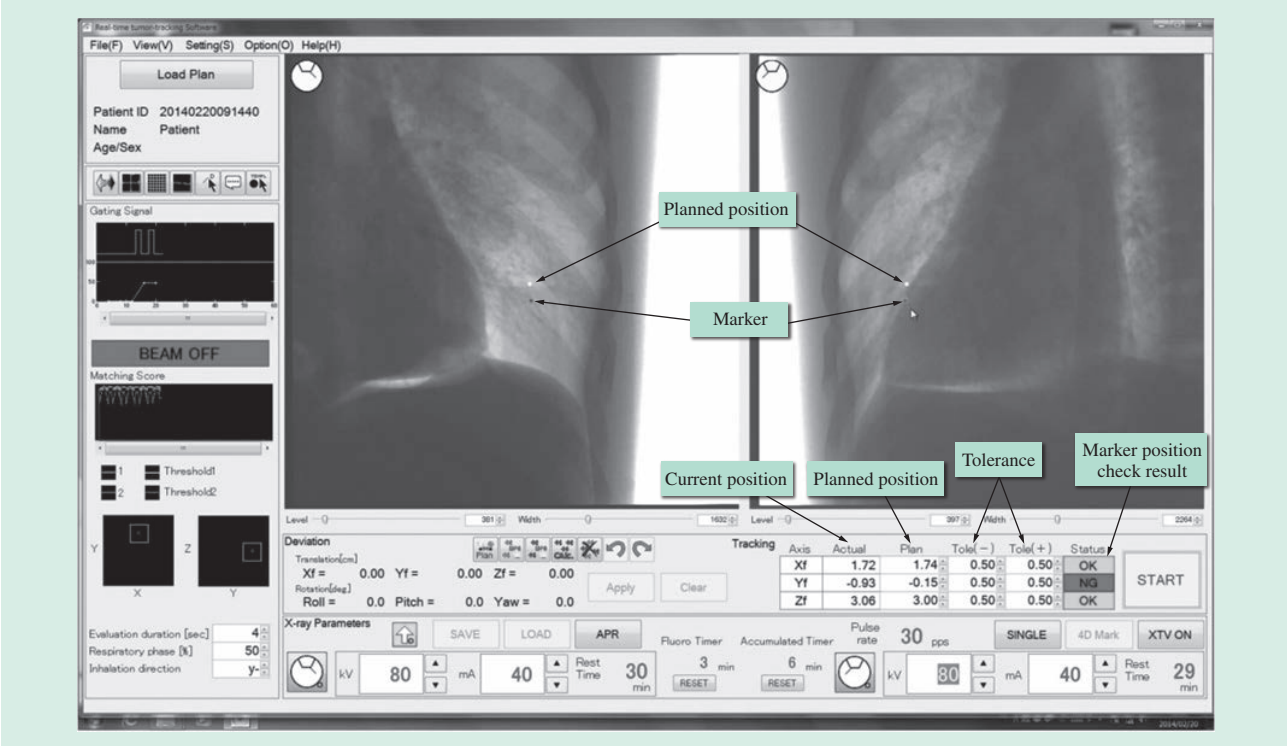

Fig. 3—Control Screen for Tumor Tracking.
The proton beam is only output when the marker position, determined from the radiography image refreshed 30 times per second, is within a designated tolerance of the planned position. The radiography images shown here are from a test run conducted using a phantom (a simulated human body) in which a marker has been inserted for testing purposes.

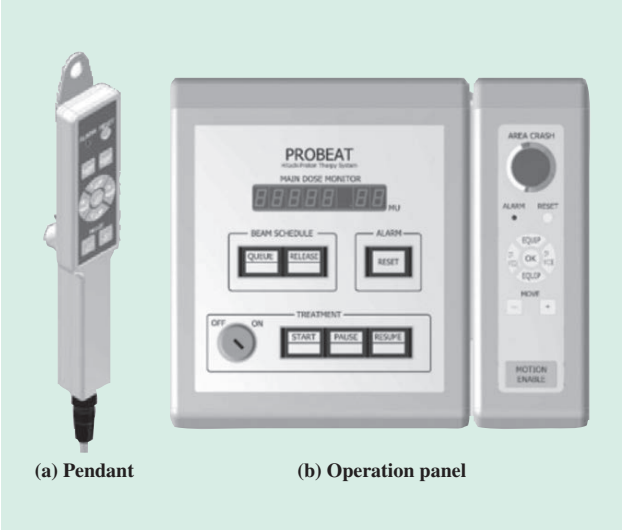

Fig. 4—New Control Unit Design.
(a) shows the pendant used to operate the gantry, couch, laser marker, and other therapy room equipment.
(b) shows the operation panel used to perform operations such as turning the beam on or off.

was obtained under the Pharmaceutical Affairs Act in August 2014, with treatment commencing in December of that year.

To provide regular assessments of the condition of the patient's tumor and perform more accurate positioning, Hitachi has developed a CBCT imaging technique that utilizes the X-ray imaging system housed in the rotating gantry. The technique obtains a CBCT image by rotating the gantry, using the same imaging system as that used by conventional positioning and the tumor tracking technique described above.

Improvements in Ease-of-use

In addition to technical performance enhancements, wider adoption of particle therapy systems will also require that they be made easier to use from the customer's perspective. Hitachi is consulting with customers to improve the design of its control units and other components with which users come into contact. Notably, as part of the discussions following the order from Mayo Clinic, the therapists planning to operate the system were invited to the design section at Hitachi where the design was being undertaken to talk to the engineers face-to-face. Fig. 4 shows the designs of the mechanical control unit called the pendant and the operation panel used for particle therapy, which were the outcomes of this work. These features have also been offered to subsequent customers and adopted for their simplicity and ease-of-use.

Future Development Plans

The market for particle therapy systems is shifting toward demand for systems that are suitable for a wider range of customers, such as the compact single-room system described above. Accordingly, in addition to the ongoing development of leading-edge technologies through collaborative creation with customers, it is also essential to develop systems that deploy these technologies in ways that are easier and simpler. To achieve this, Hitachi intends to go beyond the development of the therapy systems themselves to collaborate with partners both internal and external on the development of comprehensive systems that also consider things like the process before and after therapy and the movements of patients and staff.

CONCLUSIONS

Hitachi operates its particle therapy business globally, based on leading-edge technologies developed through collaborative creation with major hospitals in the world. While its particle therapy systems are currently ranked in the top three in terms of market share and sales[*2], Hitachi aims to increase this ranking to number one through initiatives such as increasing sales of heavy ion therapy systems and offering packages that provide compact single-room systems suitable for installation at mid-sized private hospitals. Hitachi also aims to operate an information technology (IT) service business in the healthcare sector by utilizing joint research with the major US hospitals that are customers for particle therapy systems to establish techniques that utilize IT platforms to provide things like more sophisticated treatment planning and shorter treatment times.

In the future, Hitachi intends to contribute to healthcare around the world by improving the quality and efficiency of medical practice in its role as a leading supplier of healthcare innovation.

*2 As of August 2015, based on research by Hitachi, Ltd.

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Featured Articles

Innovative Disease Prevention Support Involving Collaborative Creation with Customers

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OVERVIEW: One of the major challenges facing the healthcare field is the pursuit of measures for strengthening disease prevention in Japan and elsewhere in order to control healthcare costs. To achieve this, it is important to provide highly effective prevention measures to large numbers of people, particularly intervention in groups. Accordingly, developing the associated technology involves field work and data that is coordinated with customers. Hitachi is working with the Hitachi Health Care Center and Hitachi Health Insurance Society to develop techniques for assisting the prevention of chronic diseases and for the analysis of medical costs. Drawing on the results of this work, it is also verifying the benefits that these measures deliver in practice.

INTRODUCTION

CURRENTLY, with rising medical costs having become a major social issue particularly in developed economies, one of the measures being adopted to overcome this challenge is improvement of disease prevention, especially focusing on chronic diseases[(1)]. The USA is proceeding with its Population Health Management measures for getting the right mix of healthcare services, including disease prevention, while the UK has introduced free health checks through the National Health Service (NHS) and in certain regions is offering lifestyle improvement programs that seek to prevent conditions such as diabetes and hypertension. Similarly, Japan has its "specific medical checkup" and "specific health guidance" programs that target metabolic syndrome, a precursor of chronic diseases.

One of the challenges for implementing these initiatives is the need to deliver highly effective measures to large numbers of people. Healthcare services provided by medical institutions involve examining and correctly diagnosing individual patients, providing them with treatment, and assessing the results individually. Disease prevention, on the other hand, is a public health measure that offers the same prevention services to groups of people and assesses performance across the entire group. The use of healthcare information in electronic form is important to achieving this because of the need to understand people's state of health and the benefits of services at the group level.

In response, Hitachi has been looking at electronic consultation results and medical claims and working on the development of healthcare information processing techniques with the aim of providing highly effective disease prevention measures. In particular, this has involved technology development in collaboration with customers based on Hitachi's belief that the use of large amounts of actual data to verify performance in the field helps develop technologies that are genuinely useful. Specifically, Hitachi has worked with the Hitachi Health Care Center, which is responsible for the health management of staff and the Hitachi Health Insurance Society, which staff are able to join to conduct analyses of healthcare data from several hundred thousand people, utilizing the findings to promote overall staff health and verifying the effectiveness of the measures adopted.

This article considers the health management activities undertaken by insurers such as health insurance unions, and describes technology development that has been undertaken with the aim of making these activities more effective. Note that the data used in this research was collected subject to auditing based on the ethics rules set by Central Research Laboratory of Hitachi, Ltd. All data was used in an anonymized form.

EFFECTIVE HEALTH MANAGEMENT AND TECHNOLOGY DEVELOPMENT

Insurers often deal with health management by contracting a service provider to deliver health guidance (see Fig. 1). The following three factors are considered important for making this sort of health management more effective.

(1) Health guidance that is both effective and efficient

Even if the health guidance delivered by a guidance service provider is effective in itself, it will not be able to be provided to large numbers of people or at a reasonable cost if it requires too much work. It is important that guidance be provided in a way that is both effective and efficient.

(2) Selecting participants who will benefit from health guidance

Health guidance is unlikely to deliver significant benefits if it is provided to people who already have a healthy lifestyle or to people in whom disease has progressed to a point where other treatments are more important. Accordingly, it is essential to select participants who will benefit from health guidance. Providing guidance to people who are unlikely to benefit from it is a waste of funds and it is not uncommon for participants to lose interest in trying to make lifestyle improvements a second time.

(3) Having the understanding of others associated with health guidance

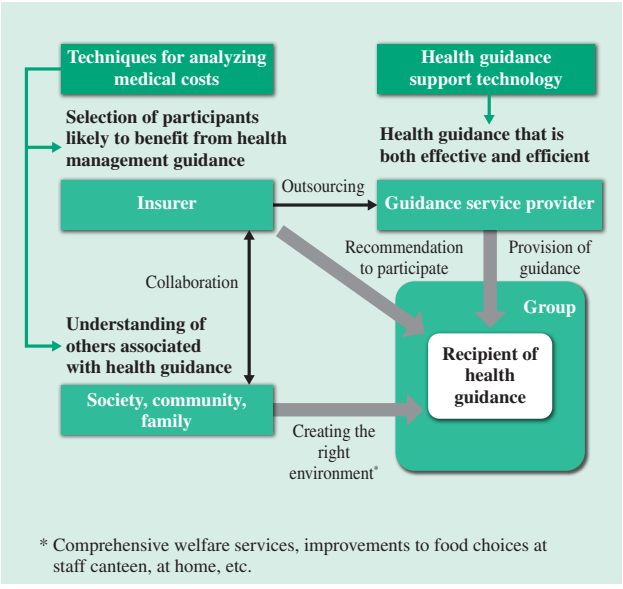

Fig. 1—Structure of Insurance Business and Technologies being Developed.
After first selecting the participants, the insurer contracts a guidance service provider to provide health guidance.

The environment around a person who is trying to make lifestyle improvements is important to their success. This means it is important that the entity paying for the health guidance (typically the insurer), and also the other people involved, such as the employer or family, appreciate the need for the guidance and help provide a supportive environment.

In response to the first of these objectives, Hitachi has developed health guidance support technology that can efficiently generate effective health advice. For the second and third objectives, Hitachi is working on developing techniques for analyzing medical costs in ways that demonstrate, in terms of medical costs, the prevalence of chronic diseases and the benefits of prevention achieved by health guidance.

TECHNOLOGIES THAT SUPPORT DISEASE PREVENTION

This chapter describes the health guidance support technology and the techniques for analyzing medical costs that enable effective health management, as described above.

Health Guidance Support Technology

Overview of Hitachi's Lifestyle Change Program

Hitachi devised a lifestyle change program that focuses on metabolic syndrome. The program aims to reduce visceral fat by a gradual weight loss of 5% (or 7% for those weighing over 90 kg) over a 90-day period (see Fig. 2). Participants first set specific behavior targets using cards that each represent 100 kcal of exercise or food and then record their weight and daily activity (number of steps walked, use of 100-kcal cards, etc.). The participants then receive health management advice from healthcare professionals ("Advisors") via e-mail, typically at 10-day intervals. The idea is that they will reach their weight loss target by continuing this pattern of 90 days of weight loss and 90 days of weight maintenance[(2)].

Health Guidance Support Technology that Generates Advice Options

One of the challenges of giving health management guidance is how to make the preparation of the advice included in the e-mails sent to participants by Advisors more efficient. Because Advisors send health guidance to a large number of participants, they have a heavy workload that requires them to prepare a large amount of advice every day. When this work was analyzed in detail, it was found that Advisors prepare this advice based on an appraisal of each participant's weight and

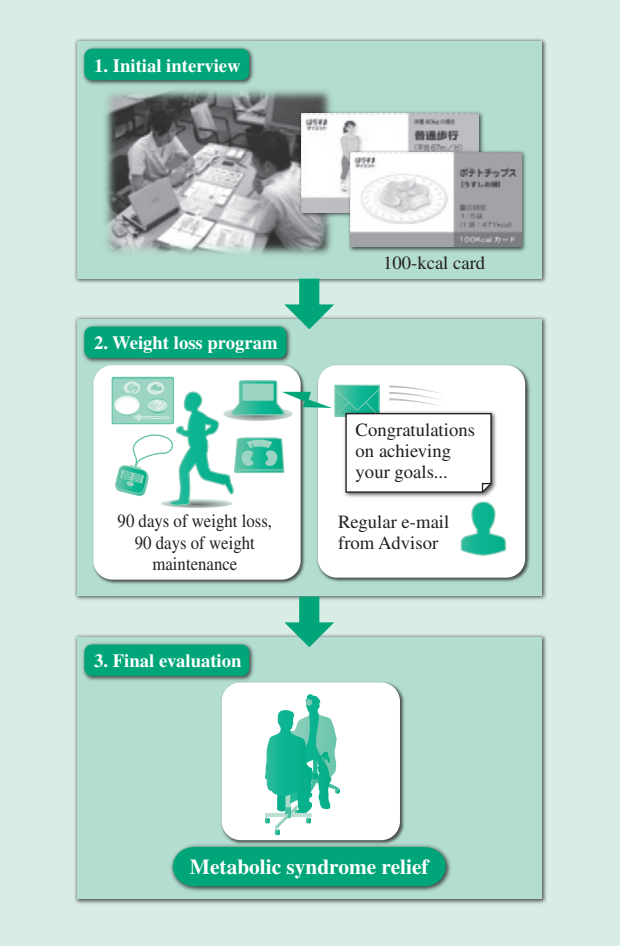

Fig. 2—Hitachi's Lifestyle Change Program.
Reduce weight by 5% (or 7% for those weighing over 90 kg) over a 90-day period by using 100-kcal cards to set behavior targets.

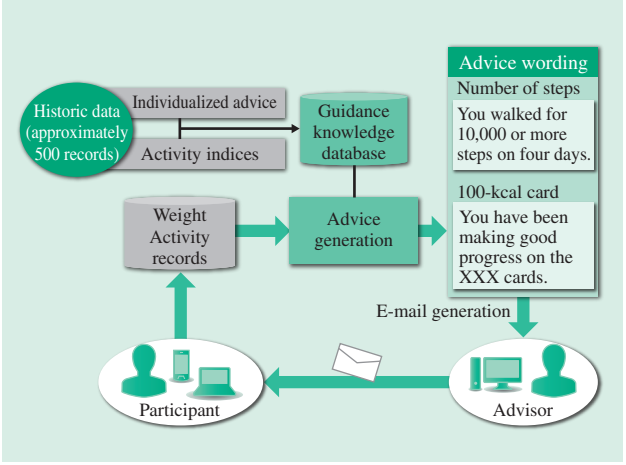

Fig. 3—Health Guidance Support Technology for Auto-generation of Advice Options.
Advice options are generated automatically based on factors such as the participant's weight and activity records.

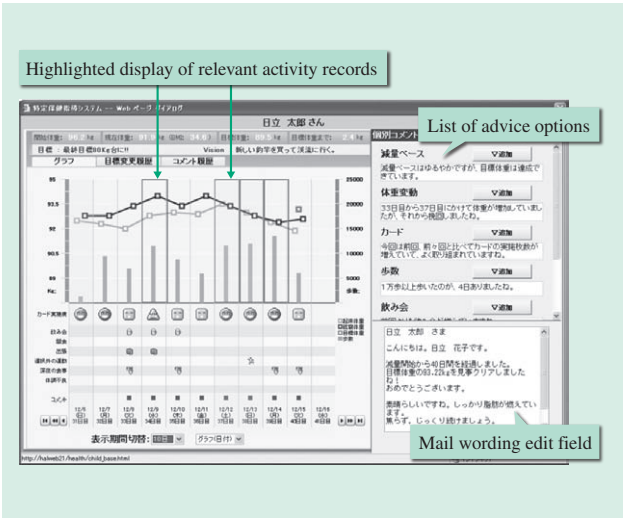

Fig. 4—Advisor Screen in Guidance Support System.
Advisors can prepare e-mails by selecting the appropriate advice from a list of options.

activity records, and that this takes a lot of their time.

In response, in collaboration with the Hitachi Health Care Center, a detailed analysis that included use of natural language processing techniques was conducted on approximately 500 sets of written advice sent out by Advisors in the past. The results indicated that most of the advice contained praise for participants' activities and that the advice could be categorized into a number of patterns. Based on these findings, Hitachi established a knowledge database for health management guidance and developed health guidance support technology that automatically generates advice options based on participants' weight and activity records (see Fig. 3)[3].

Fig. 4 shows the screen provided for Advisors by the support system built using this technology. The participant's weight and activity records are displayed on the left and a list of possible advice options praising their activities is displayed on the right. Also, because it takes time to identify praiseworthy activity records in text format, moving the mouse cursor over candidate advice options highlights the corresponding activity records in a red frame. When the Advisor uses the mouse to click the add button for the most suitable advice, an e-mail is generated automatically with that advice inserted into the message.

This health guidance support technology was incorporated into an information system for improving the efficiency of health management guidance using Hitachi's lifestyle change program. The system handles the input and browsing of weight and activity records as well as generating advice and transmitting e-mail, enabling both participants and Advisors to

access these records via an Internet server. Advisor work times were evaluated after the system was installed at the Hitachi Health Care Center. The results confirmed that tasks that previously took about 25 minutes could now be completed in about 5 minutes[4].

Techniques for Analyzing Medical Costs

Medical Cost Analysis and Challenges for Health Management

To demonstrate the prevalence of chronic diseases and the effectiveness of health management guidance, Hitachi is developing techniques for analyzing medical costs that model the progress of illness from deterioration in lifestyle practices to the emergence and subsequent worsening of symptoms by utilizing health check records and claims data held by an insurer. Chronic diseases progress through the interaction between diabetes, hypertension, hyperlipidemia (abnormal cholesterol, etc.), and their associated complications. This creates a challenge because it means that it is not easy to model the progress of illness in ways that consider these interactions using past techniques for the detailed analysis of things like incidence rates and medical costs that focused on individual diseases.

Disease Progression Model Using Bayesian Network

Accordingly, Hitachi is working in collaboration with Hitachi Health Insurance Society to construct a disease progression model that represents the detailed relationships between multiple diseases and contributing factors by utilizing a machine learning technique called a Bayesian network. A Bayesian network is a way of modeling the probability dependencies between data items.

Fig. 5 shows the relationships between the main contributing factors determined based on this disease progression model for chronic diseases. Factors between which dependencies are greater than a certain probability are indicated by lines. The data used to build the model consisted of Hitachi Health Insurance Society health check records and claims for approximately 110,000 people. Fig. 5 also shows how the model represents the interrelationships between diabetes, hypertension, and hyperlipidemia, and the relationships with complications such as nephropathy or cardiovascular disease. In this way, the complex interrelationships between contributing factors can be modeled.

To determine whether this disease progression model expresses the progress of chronic diseases from the initial appearance of symptoms and their subsequent worsening, the model was used to predict the following year's medical costs for 20,000 people based on their health check records and claims, with the difference between actual and predicted costs being calculated as a standard deviation. The results demonstrated that the following year's medical costs for the 20,000 people could be predicted with a margin of error for accuracy of about 5% or less[5].

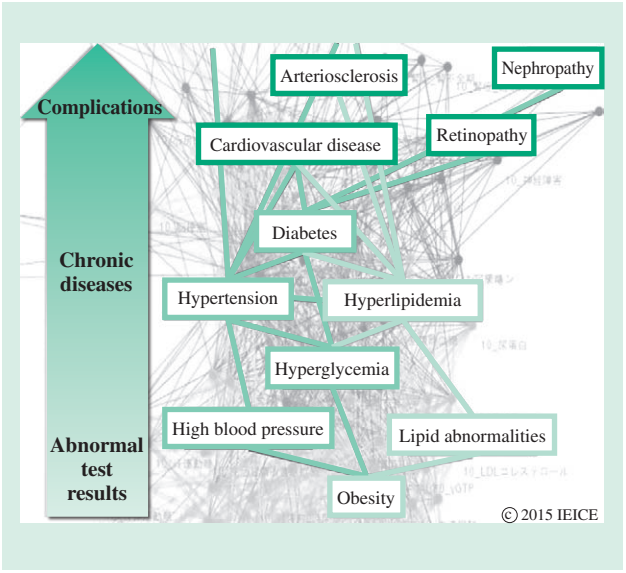

Fig. 5—Interrelationships between Contributing Factors to Chronic Disease[5].
A model represents the interrelationships between conditions such as diabetes, hypertension, and hyperlipidemia (abnormal cholesterol, etc.).

USE FOR HEALTH MANAGEMENT AT HITACHI HEALTH INSURANCE SOCIETY

The technology developed together with Hitachi Health Insurance Society is being deployed in practice and its performance is being assessed. This chapter describes some of this work.

Savings on Medical Costs Associated with Hitachi's Lifestyle Change Program

Hitachi Health Insurance Society has been providing specific health guidance (active support) using Hitachi's lifestyle change program since 2008. A survey was conducted in 2008 using claims data held by Hitachi Health Insurance Society that tracked 312 participants in the lifestyle change program and compared them to 2,358 non-participants. The results indicated a significant drop in the number of visits to a medical institution by participants compared to non-

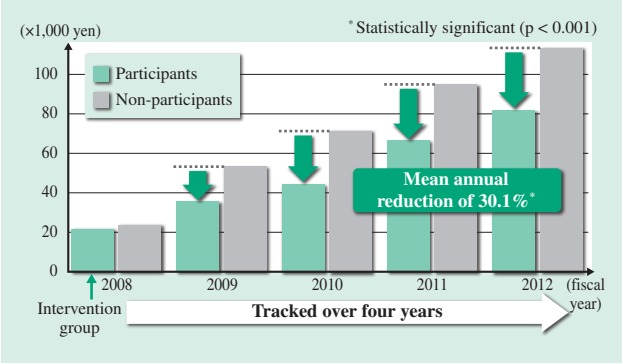

Fig. 6—Annual Per-person Medical Costs.
Participants in Hitachi's lifestyle change program have medical costs that are approximately 30% lower than non-participants.

participants (see Table 1). Fig. 6 shows a comparison of the annual per-patient medical costs. This indicates that medical costs for participants are approximately 30% lower than for non-participants[5]. Together with the shortening of work times for Advisors (as described above), Hitachi's lifestyle change program is able to provide health management guidance that is both effective and efficient.

Note, however, that participation in specific health guidance is voluntary, meaning that selection bias is possible.

TABLE 1. Number of Health Checks per Person per Year
The number of visits per year to medical institutions by Hitachi's lifestyle change program participants is less than those of non-participants by a statistically significant margin.

Survey fiscal year	Participants	Non-participants
FY2008	2.1 times	2.2 times
FY2009–FY2012	3.3 times*	3.8 times

* Statistically significant (p < 0.01)

Selection of Recipients of Health Management Guidance Based on Benefits

The selection process for receiving health management guidance is based on the level of disease risk as indicated by test results and other predetermined criteria, similar to the specific health guidance (active support) program, for example, which is available to those not on medication who have a fasting blood sugar level of 100 mg/dL or above, a neutral fat level of 150 mg/dL or above, and a systolic blood pressure level of 130 mmHg or above. However, the criteria are generally set broadly and the benefits of guidance may vary between individuals, even if they are on the same active support program, or depending on the nature of the health management guidance offered. Essentially, rather than risk of disease, the selection of participants should be based on who will benefit from health management guidance. Accordingly, Hitachi has used the disease progression model it created using the techniques for analyzing medical costs to develop

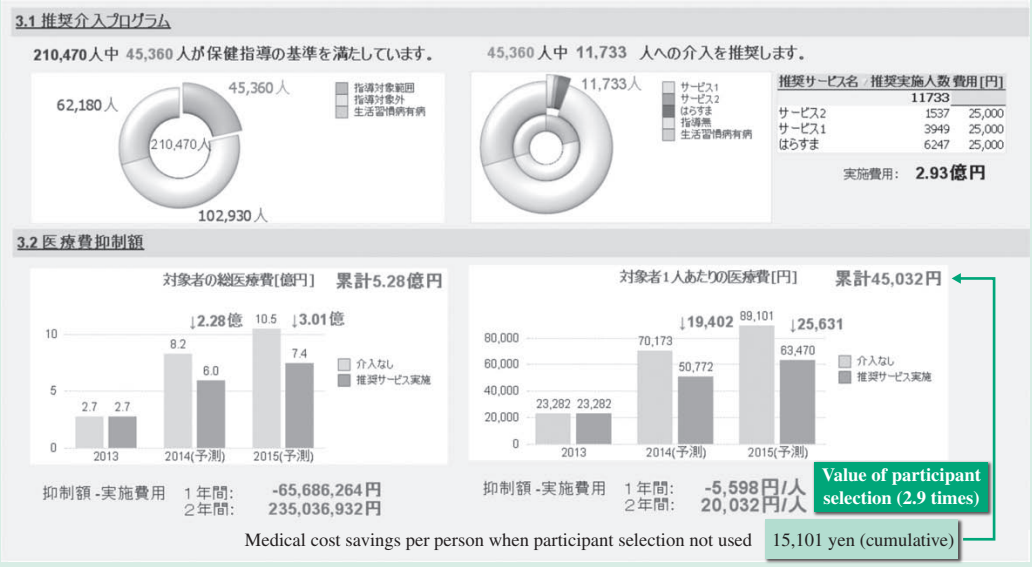

Fig. 7—Functional Prototype of Participant Selection Method for Health Management Guidance.
The method can select who should receive health management guidance and predict the resulting savings in medical cost.

a method for selecting participants that is based on the benefits of health management guidance.

Fig. 7 shows part of a screen from a functional prototype that uses this selection method. The pie chart at the top left indicates the number of participants eligible for the health management guidance program and the chart at the top right indicates the number of participants who are likely to benefit. The bar charts in the bottom part of the screen show the medical costs of chronic diseases predicted by the disease progression model. They show the predicted one-year and two-year costs with and without the program. The total medical cost is displayed at the bottom left and the cost-per-individual at the bottom right. The predicted medical cost savings over two years are 45,032 yen per person, roughly three times greater than the savings achieved if the selection process is not used (if participants are instead randomly selected from those eligible).

Claims data was used to determine the benefits in the case of 50 people currently involved in a health management guidance program run by Hitachi Health Insurance Society, and who were chosen using this benefits-based selection process. While monitoring of these participants has so far only been going on for half a year, the medical cost savings have already been approximately six times those for conventional health management guidance. Hitachi intends to continue monitoring progress closely.

Use of Workplace Health Maps

It is recognized that the benefits of health management guidance are compounded when the insurer and employer work together on its implementation, and the Ministry of Health, Labour and Welfare is proceeding with collaborative activities it calls “collabo health.” The sharing of information about employee health

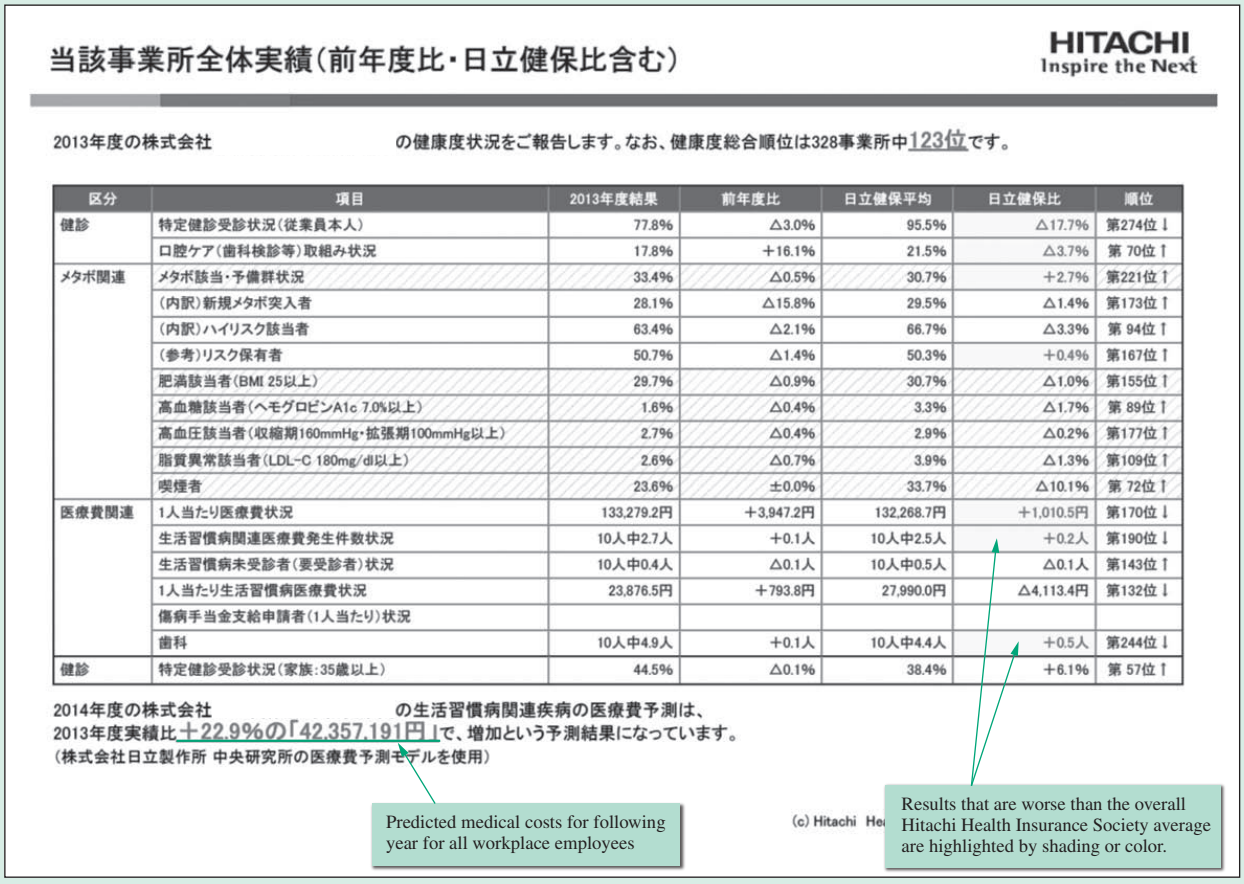

Fig. 8—Workplace Health Maps (Data for Entire Workplace).
The map is used to assess the health of employees at the workplace by showing their state of health and the predicted medical costs associated with chronic diseases.

problems between insurer and employer is crucial to this initiative. Accordingly, Hitachi is working on the development of "workplace health maps" that can assess the health of employees at a workplace through a comparison with the overall state of health of all employees.

Fig. 8 shows part of a workplace health map (data for entire workplace) being used in practice by Hitachi Health Insurance Society. The indices selected based on health check, metabolic syndrome, and medical cost criteria are compared to the mean values for all of Hitachi Health Insurance Society to compare the healthiness of workplace employees. The map also shows the predicted medical costs for the coming fiscal year for all employees at the workplace, which are determined using the techniques for analyzing medical costs developed by Hitachi. In addition to the overall totals shown in the figure, detailed documents are also produced showing things like health check results and medical costs that are used by Hitachi Health Insurance Society when requesting the cooperation of particular workplaces. The workplace health map is a useful resource for implementing "collabo health."

CONCLUSIONS

Drawing on actual data and practical know-how held by Hitachi Health Care Center and Hitachi Health Insurance Society, Hitachi has been working on the development of health guidance support technology and techniques for analyzing medical costs, and the evaluation of their effectiveness in practice. In doing so, it has established techniques for controlling the prevalence of chronic diseases and rising medical costs.

This new ability to collect and analyze large volumes of diverse information on people's health is shedding light and providing quantitative data on areas that were previously hidden. Meanwhile, knowledge and skills previously restricted to those with expertise or experience are now becoming widely available. By making active use of healthcare information through collaborative creation with customers, this is facilitating the development of innovative technologies for reducing the incidence of chronic diseases and the supply of highly practical products and services.

The increased prevalence of chronic diseases is also a major social issue outside Japan. In an initiative involving collaborative creation with a customer, Hitachi is developing a new healthcare service for preventing chronic diseases in Manchester in the UK. The techniques and knowledge resulting from the customer collaborative creation activities described in this article will also be deployed in this UK project. Similarly, Hitachi intends also to deploy techniques and knowledge from the UK in Japan and other countries or regions.

Once you lose your good health it is too late. Hitachi is seeking to create a world in which, by learning from data and the knowledge of those who have gone before, people can recognize the importance of health and take steps to maintain it before it is lost.

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Featured Articles

Hospital Management Solutions Implemented in Partnership

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Kazuaki Mukai
Asuka Kihana
Yuta Miyakawa
Hiromitsu Negishi

OVERVIEW: Hospital management solutions from Hitachi constitute a service business that helps improve operational efficiency at hospitals by Hitachi acting as a partner engaged in comprehensive and ongoing activities that relate to the various management challenges that hospitals need to deal with, including optimizing the operation of hospital infrastructure such as diagnostic imaging systems and operating theaters, improving the efficiency of hospital workflows, and managing patients in ways that include working with the community to manage hospital admissions. One of the core elements of this is a service business launched a few years ago that focuses on supporting the operation of diagnostic imaging centers. For hospitals in Japan and elsewhere, Hitachi is seeking to establish relationships with administrators, clinical departments, and radiology departments, and to identify and overcome the challenges facing hospital administration, through efficient hospital administration, particularly in radiology departments.

INTRODUCTION

IT was in the late 1980s that debate got underway at a national level in Japan about the need to take steps to deal with changes in the conditions under which hospitals operate, including the aging of the population, changing patterns of ill health, and wider use of advanced medical equipment.

Studies into the modernization and regularization of hospital management conducted by Japan's then Ministry of Health and Welfare with the aim of improving hospital functions and patient service led to the establishment in 1986 of a discussion group on the modernization and regularization of medical administration, which published a report of its findings the following year[(1)]. This report identified three requirements for future medical administration: (1) Improve the managerial skills of hospital managers, (2) Rationalize practices and improve efficiency, and (3) Tailor management to the needs of the community. In 1988, a report from the Medical Business Review Committee noted the importance of consulting to hospital management.

Now, 30 years after these developments, the scope of the hospital management consulting market has expanded such that the value that consultants can provide to hospitals and the value that hospitals seek from consultants have both become more diverse, encompassing things like finance, organizational management, and recruitment, and this has resulted in the market growing into one that requires an even greater level of differentiation.

The vision underpinning Hitachi's healthcare business strategy is to build a society in which everyone can live in good health, safety and security. To realize this vision, Hitachi is pursuing a healthcare innovation business in which patients, medical institutions, insurers, and local government play a role as stakeholders. Its aim is to improve the quality and efficiency of healthcare by operating service businesses that optimize all stages of the care cycle at hospitals and in community healthcare (see Fig. 1).

PROGRESS ON HOSPITAL MANAGEMENT SOLUTION SERVICES INVOLVING COLLABORATIVE CREATION WITH CUSTOMERS

Hospital management solution services from Hitachi constitute a service business based on collaborative creation with customers that helps improve operational efficiency at hospitals by Hitachi acting as a partner and engaging in comprehensive activities that relate to the various management challenges that hospitals

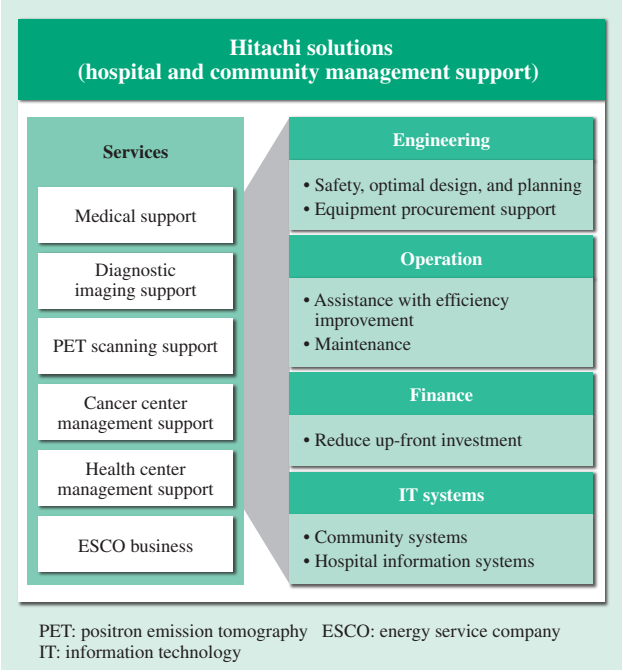

Fig. 1—Hospital and Community Healthcare Solutions Targeted by Hitachi.
Hitachi supplies services for hospital and community healthcare that optimize all stages of the care cycle.

need to deal with, including optimizing the operation of hospital infrastructure such as diagnostic imaging systems and operating theaters, improving the efficiency of hospital workflows, and managing patients in ways that include working with the community to manage hospital admissions.

Hitachi sees these activities as part of the consulting services it offers for medical administration, with the aim being to work with customers to deliver improvements in three particular areas, namely (1) hospital management, (2) the quality of healthcare, and (3) patient satisfaction.

The following sections describe examples of these activities.

Ways of Improving Hospital Administration

At a hospital where it provided a positron emission tomography (PET) support service[(2)], Hitachi started work in early FY2000 on suggesting and implementing improvements aimed at hospital-wide optimization by liaising between managerial and clinical staff.

Initially, to proceed with improvements in hospital administration in accordance with policies set by the hospital manager, improving clinical efficiency in ways that lead to higher profitability was set as the goal of the administrative improvement activities, meaning the implementation of an environment in which clinical staff could focus on their core medical duties. Accordingly, top priority was given to hospital-wide optimization in accordance with policies set by the hospital manager.

While the project adopted performance-related payment as the basis for charging for services relating to administrative improvement activities, a feature of Hitachi's approach is that it also involved priming administrative improvements through up-front investment in manpower costs and resources such as information technology (IT). This approach was intended to provide greater clarity in the sharing of risks and benefits between Hitachi and the hospital and is seen as a useful way to keep both parties motivated to work together on administrative improvements. Furthermore, another feature of Hitachi's involvement was that it went beyond merely suggesting and proposing improvements to hospital administration and included continuing to work with the hospital on the joint implementation of initiatives until the actual improvements to hospital administration became clearly evident. This included working at the hospital to support these actions and ongoing work with clinical staff after actions had been implemented to assess their effectiveness (see Fig. 2).

Hitachi worked with the hospital's stakeholders on measures for dealing with a number of challenges. This article describes two such examples involving establishing practices for facilitating early discharge and supporting hospital admissions, and initiatives for making better use of available surgery slots.

(1) Establishment of practices for facilitating early discharge and supporting hospital admissions

An inability to properly coordinate patient discharges meant that a surgical ward was unable to increase the number of new admissions it could accept, leading to an ongoing problem with poor ward turnover. Following consultations with doctors, nurses, and other staff, Hitachi identified the current practice of placing busy doctors in charge of determining where patients were to be transferred and of coordinating the transfer process, and the small number of candidate hospitals to which patients could be transferred, as being among the potential reasons for this poor coordination of patient discharges. In the case of the admission of new patients, in addition to these problems with coordinating hospital transfers, the investigation also uncovered a new problem whereby the ward admissions process was taking too long due to increases in the number of patients transferred from other wards and the number of pre- and post-operative patients.

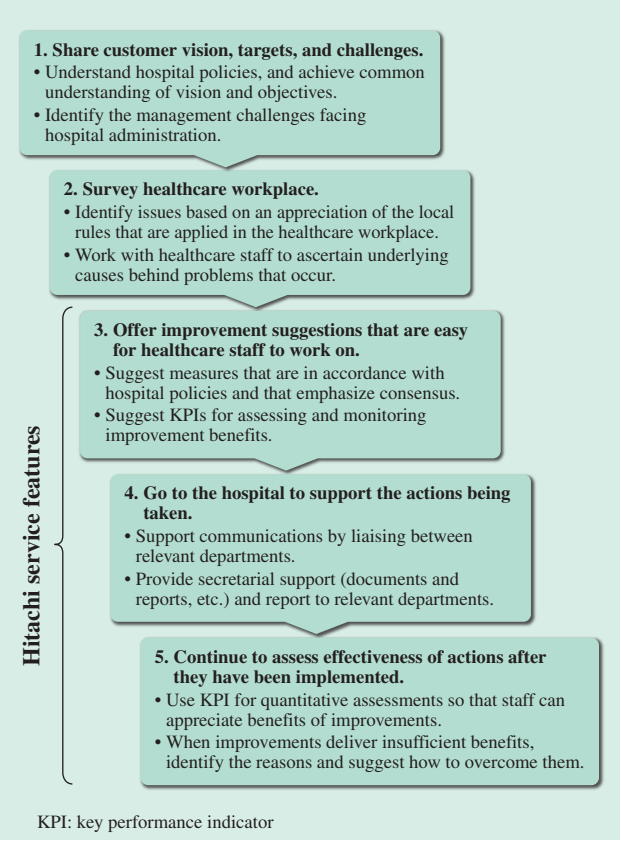

Fig. 2—Features and Flowchart of Hitachi's Hospital Management Solution Service.
In addition to surveys and advice, Hitachi's hospital management solution service features ongoing support.

To take on the problem of poor coordination of patient discharges, a nine-month trial was conducted during which authority for the job of coordinating transfers, previously the responsibility of doctors, was reassigned to the ward's medical social worker who works for the community healthcare liaison department. The trial achieved an increase in the number of transfer coordination cases from 43 prior to the reassignment of the social worker to 111 after they became involved. In addition to demonstrating that early intervention by the social worker can reduce the workload for doctors, these results also led to faster transfer coordination processing. With regard to making additional hospitals available as potential transfer destinations, a number of candidates chosen jointly by the community healthcare liaison department and Hitachi were visited to make new destinations available for patient transfers. Similarly, to deal with the inability to increase the number of new admissions, a seven-month trial was conducted in which the community healthcare liaison department took on some of the work of processing admissions that was previously administered by ward nurses. The trial demonstrated that this led to faster admissions processing, with the number of admissions increasing from 309 prior to community healthcare liaison department involvement to 358 afterwards. Furthermore, collating information on the above transfer coordination and admissions processing in the community healthcare liaison department enabled the management of admission and discharge for each patient to be consolidated.

(2) Making better use of available surgery slots

It goes without saying that the more operations a hospital performs the better it is for hospital revenue. Accordingly, with the aim of increasing the number of operations performed at the hospital described above, a study was launched to look at changes aimed at optimizing surgery slots and encouraging the use of free slots based on a proposed target for the number of operations.

Hitachi consulted with ward medical directors for 23 clinical departments and 28 departments that use operating theaters and collated the number of doctors, patients waiting for surgery, and duration of wait for each department, whether they wanted to increase or decrease the number of surgery slots, and their comments and suggestions for surgery departments.

When Hitachi analyzed the information collected on the number of doctors, patients waiting for surgery, and duration of wait for each department, and whether they wanted to increase or decrease the number of surgery slots, those clinical departments (including orthopedics, neurosurgery, gastrointestinal, and cardiovascular) with a large number of doctors, patients waiting for surgery, and long wait times tended to have a higher demand for increasing the number of surgery slots, indicating that they should be given priority for increasing the number of surgery slots. On the other hand, those clinical departments that tended to have a comparatively smaller number of patients waiting for surgery and shorter wait times, and those where the scheduled surgery times are less than the available surgery slots, in other words those departments that have a low key performance indicator (KPI) for planned utilization (for the purposes of this article: scheduled surgery time/available surgery time) (otolaryngology 15%; ophthalmology 18%; plastic surgery 25%), tended not to have a strong need for additional surgery slots, and consideration was given to whether it would be desirable to combine the available surgery slots in these departments with the available surgery slots in other departments with a similar tendency so that they operate as shared slots.

Based on suggestions derived from the results from the actual data collected and analyzed by Hitachi, hospital administrators undertook a revision of surgery slots for the first time in about a decade.

The feedback from clinical departments also indicated problems such as the difficulty of obtaining informed consent from patients and coordinating surgery schedules due to the short time between making a provisional reservation for an operating theater and its actual use for surgery, which is only seven days under current operational rules, and issues such as lack of clarity as to whether or not slots are genuinely available when viewing electronic medical records from IT terminals in clinical departments because the information on the availability of free surgery slots does not match the information for slots available in the surgery department itself. In response, Hitachi looked at how to encourage the use of free slots by making it easier to book surgery from a clinical department. This led to a change in practice whereby the time between a provisional reservation being made for an operating theater and its actual use was doubled to 14 days to provide an environment in which it is easy to book a free operating theater slot. They also established an environment in which the date for surgery can be decided between the patient and doctor face-to-face by giving doctors in clinical departments the ability to check the availability of free slots in realtime during patient consultations by making a specification change so that the availability of anesthesiologists can be understood from electronic medical records in a way that can indicate free operating theater slots. These initiatives succeeded in improving the utilization of surgery slots.

OPERATIONAL SUPPORT SERVICE FOR DIAGNOSTIC IMAGING CENTERS

Whereas the hospital management solution service described above is an all-encompassing initiative that undertakes improvements in a strategic manner by taking a broad view of all hospital activities, the operational support service described in this section is targeted specifically at diagnostic imaging centers.

The operational support service for diagnostic imaging centers incorporates know-how and experience gained in the hospital management solution business and has the following three features.

(1) Installation of diagnostic imaging systems

Hitachi installs diagnostic imaging systems from the hospital's vendor of choice. Hitachi provides engineering support to ensure that the latest equipment operates at the time of installation together with other added value such as formulating a 10-year business plan. The latest equipment is installed under Hitachi ownership, which has the advantage of reducing the hospital's high property tax burden.

(2) Support for overcoming hospital problems

Hitachi helps overcome problems that hospital staff are unable or find difficult to deal with, including coordinating the different hospital departments, promotional work, and setting operating targets for the diagnostic imaging center that include indicators of the ability to attract patients.

(3) Risk sharing

The use of performance-based service fees means that Hitachi takes on a level of risk similar to the hospital, providing a mechanism for support over a long period of time until operating targets are achieved.

The operational support service for diagnostic imaging centers is based on the assumption that support for the hospital will typically continue for 10 years and involves three steps until the results are achieved (see Fig. 3).

In the first step, Hitachi spends three months proposing operating targets and plans for the diagnostic imaging center to the hospital. To set targets that can be agreed to by both hospital administrators and frontline staff, a project team is set up with members from both the hospital and Hitachi to first identify the operational issues by analyzing data on current circumstances and to set targets that the hospital can achieve. Meanwhile, Hitachi also consults with everyone from hospital administrators to frontline staff to identify workplace issues. Once all of this information has been collated by the project team, 10-year operating targets and plans are prepared for the diagnostic imaging center.

Once agreement on these operating targets and plans has been reached between the hospital and Hitachi, the second step is for the two partners to work together to achieve the operating targets, typically over a three-year timeframe. The focus during this stage is on increasing the number of outpatient tests performed. This involves providing ongoing support that includes improving test bookings, introducing support staff, installing the latest diagnostic imaging systems, and promotional advertising.

The third step is to support stable operation of the center over a seven-year period to keep achieving the operating targets. This provides long-term support for maintaining the practices that continue to deliver

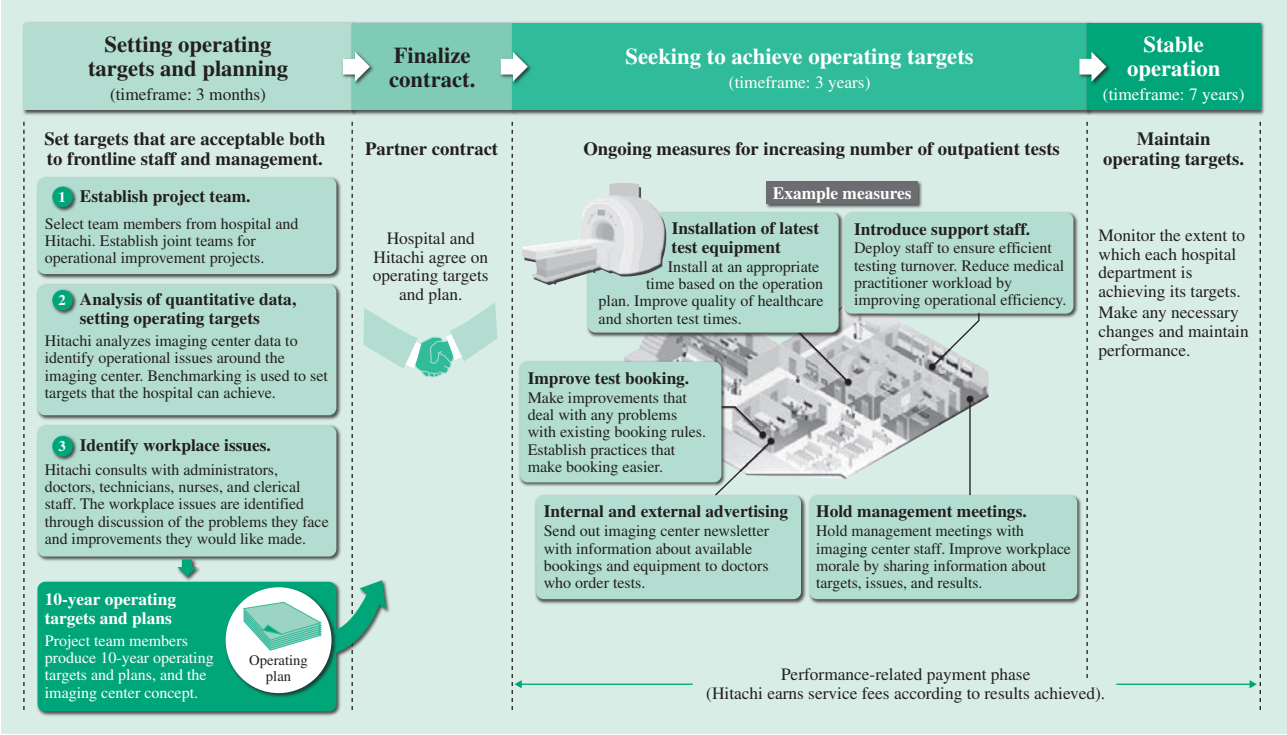

Fig. 3—Flowchart of Operational Support Service For Diagnostic Imaging Centers.
The figure shows an example of measures taken to achieve hospital operating targets. Hitachi works with the hospital to formulate solutions to healthcare workplace issues and supports both the initial and ongoing achievement of operating targets.

results while making course changes as needed by monitoring how well each of the hospital departments achieves its targets.

CONCLUSIONS

Hitachi is deploying its healthcare innovation business outside Japan as part of a strategy of accelerating the expansion of its overseas business. In accordance with this strategy, Hitachi is trialing a "market-in approach" in China and India in keeping with community needs based on business experience in Japan.

In China, Hitachi is seeking to market solutions for business efficiency improvement based on past experience to potential partner hospitals against a background of public hospitals being privatized at an accelerating rate in accordance with national policy.

In India, responding to the ongoing government-led provision of hospital infrastructure, Hitachi is seeking to investigate opportunities for healthcare solution services in that country by participating in an international demonstration project organized by Japan's New Energy and Industrial Technology Development Organization and working on a hospital energy efficiency project of the All India Institute of Medical Sciences.

In the future, Hitachi intends to expand these businesses as part of its Social Innovation Business, which is being promoted in accordance with its announced global community strategy.

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Featured Articles

Plant Solutions for Next Generation Biopharmaceuticals and Regenerative Medicine

Haruo Suzuki
Yukio Fukushima
Tadatoshi Iwabuchi
Yoshinori Momota

OVERVIEW: There has been an increase in plans for new facilities in the pharmaceutical manufacturing industry over recent years in anticipation of developments such as the rising level of capital investment prompted by ongoing technical innovation and rapid growth in the market for biopharmaceuticals, and the introduction of regenerative medicine using iPS cells and similar on a commercial scale. Hitachi is contributing to the supply of equipment that delivers a high level of safety and security, having gained many years of experience in optimizing and enhancing the efficiency of such facilities and improving their productivity and quality.

INTRODUCTION

BIOPHARMACEUTICALS with more sophisticated functions than low-molecular-weight drugs have been an active area of development in recent years, accounting for the largest share of per-drug sales by value. Regenerative medicine, meanwhile, which uses cells directly, is being put to a wider range of uses and the field is recognized for its potential applications in treating illnesses that do not respond well to drugs.

Hitachi's plant solutions business has a large share of the market for biopharmaceutical and regenerative medicine plants in Japan, with these being the mainstays of Hitachi's pharmaceutical plant business.

This article gives an overview of the equipment used in these plants and describes Hitachi's activities in the field.

PLANT SOLUTIONS FOR HEALTHCARE SECTOR

Hitachi's industrial equipment business has experience supplying a wide variety of equipment for chemical, chemical synthesis, food, gas, and other plants. The pharmaceutical plant business supplies important solutions by building the equipment used to produce pharmaceuticals that account for a large part of the healthcare market. The pharmaceutical market is valued at 10 trillion yen in Japan and 100 trillion yen globally, with the manufacture and sale of pharmaceuticals continuing to rise in both markets, and with further growth anticipated.

The pharmaceutical plants supplied by Hitachi include plants for biopharmaceuticals, synthetic pharmaceuticals, solid preparations, aseptic pharmaceutical production, and regenerative medicine. Among these, Hitachi has held a large share of the Japanese market for biopharmaceutical and regenerative medicine plants in recent years, both markets where further growth is anticipated, and it is in these types of pharmaceutical plants that Hitachi sees itself as having particular expertise. These plants have the following four characteristics.

(1) Even small variations in the production process or small deviations from standard conditions can influence the quality, yield, and level of impurities in the pharmaceuticals produced.

(2) Because many of the drugs have large molecular structures compared to the sort of pharmaceuticals produced by chemical synthesis, or a large degree of structural variability, there is a limit to how far consistency can be verified.

(3) Side effects or other problems may occur unless adequate measures are taken to prevent or eliminate impurities and contamination.

(4) A high level of investment in production equipment is needed to ensure high quality.

As a variety of technologies are needed to overcome these problems, considerable research, development, and other work is being undertaken.

Hitachi has been engaged for many years in research and development and in the acquisition of know-how about how to deal with these problems. The results of this work are incorporated into the plants it supplies, with many such examples in operation. Hitachi is also pressing ahead with further research and development to acquire new technologies. The following 10 technologies are past examples of such work:

(1) Technologies for achieving and maintaining sterile conditions
(2) Cleaning techniques
(3) Culture productivity improvement techniques
(4) Culture process simulation techniques
(5) Technologies for metabolic analysis of culture processes
(6) Technologies for virus inactivation
(7) Development of technology for improvements to purification equipment
(8) Development of technology for single-use equipment
(9) Technology for containment and maintaining a clean environment
(10) Modularized equipment configuration techniques

Hitachi is seeking to use these technologies for things like making enhancements and improving accuracy.

WORK ON BIOPHARMACEUTICAL PLANTS

Hitachi has supplied more than 200 pharmaceutical plants to date, including the fabrication of more than 500 fermenters, a key item of equipment in biopharmaceutical plants.

The production of biopharmaceuticals (antibody medicines and vaccines) consists of a culturing step that uses animal or other cells in which the desired product is produced by biological reactions, and a purification step during which the purity of the product is improved. Because the fermenter has a major influence on plant productivity, its design and manufacture is crucial.

The culturing step typically starts with the cells being cultured in flasks and then gradually scaled up to the scale of 5,000 to 10,000 L. As this up-scaling results in significant changes to the culture environment in the fermenter, when building commercial-level production equipment, it is essential that the design gives adequate consideration to the factors that influence productivity. Fig. 1 shows a high-volume cell culture system in the 10,000-L range.

Hitachi uses computational fluid dynamics (CFD) for fermenter simulation in order to design suitable fermenters. The simulation performs a predictive analysis of factors that influence cell multiplication, such as the stirrer shear force, uniformity of mixing, and the appropriate gas exchange in the fermenter, and compares the results against the flask-scale experimental data provided by the customer to determine the cell multiplication characteristics and appropriate culturing conditions so that this information can be incorporated into the equipment design to improve productivity.

Furthermore, a high level of sterilization and cleaning are needed to ensure process stability during the culturing step. In the case of a large biopharmaceutical plant, there may be upwards of 1,000 valves that need to be operated correctly to perform sterilization and cleaning. To achieve this operation, Hitachi uses control techniques based on the use of a distributed control system (DCS). When developing the software, Hitachi automates the process and maintains product quality without cross contamination by ensuring it fully understands things like equipment characteristics and customer cleaning procedures, and offers operating practices that are based on sterilization and cleaning mechanisms that derive from scientific principles.

Given the innovative nature of biopharmaceuticals, they are increasingly becoming recognized throughout the world for their potential to protect people's health through benefits such as treating difficult diseases and preventing infection. Hitachi intends to continue contributing to the enhancement of plants through work on improving the productivity and quality of biopharmaceutical manufacturing technology.

Fig. 1—High-volume Cell Culture System.
This high-volume cell culture system (supplied by Hitachi, Ltd.) is used for the production of antibody drugs.

TECHNOLOGY DEVELOPMENT BY MAB

The Manufacturing Technology Association of Biologics (MAB) was established in September 2013. Initially made up of 29 organizations (24 companies, two associations, one independent administrative corporation, and two universities), another company has since joined, giving it a current make up of 25 companies, two associations, one national research and development agency, and two universities. Toshiaki Higashihara, President & COO of Hitachi, Ltd. has served as director since the association was formed.

MAB is an "all-Japan" organization that consolidates Japanese know-how for the manufacture of the next generation of biopharmaceuticals and other products. Its aims are to establish the industrial technology for the manufacture of the next generation of antibody drugs and other products in accordance with international standards and to deploy international business models for personalized medicine.

The main research topics being worked on by MAB fall into the following five categories.

(1) Development of technology for establishing production cell cultures

(2) Development of high-performance cell culturing techniques

(3) Development of advanced downstream technologies

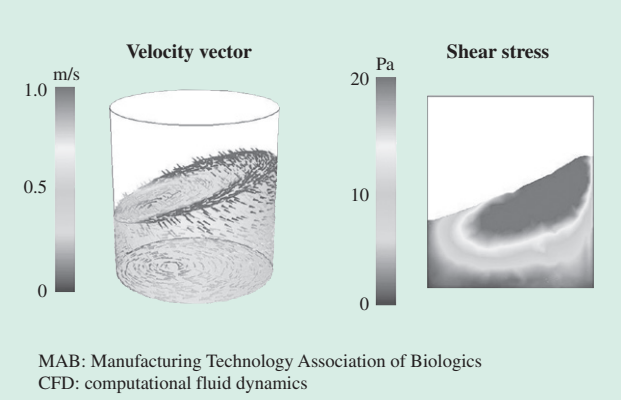
(4) Development of advanced quality assessment techniques

(5) Establishment of technologies for creating the next generation of platforms that comply with international standards

Hitachi plays a central role in the association, working on the second and third of these categories.

In the case of high-performance cell culturing techniques in particular, Hitachi is working in collaboration with its own Research & Development Group (previously the Hitachi Research Laboratory) to utilize its expertise in CFD analysis (see Fig. 2) to participate in the design stage of the next generation of single-use culturing systems being built by other association members for screening, process investigation, and production, making a major contribution to improving the performance and reliability of the products being developed.

MAB has set up the Kobe Good Manufacturing Practice (GMP) facility in an annex building at the Integrated Research Center of Kobe University, Kobe City, and is working on product developments that outperform products from overseas suppliers like "Company G," "Company M," and "Company Z" that are already on the market. Hitachi is the only member of MAB that is a pharmaceutical plant manufacturer and, through the provision of its know-how, is making a major contribution to these activities, which are being conducted under an "all-Japan" organizational structure. In the future, Hitachi aims to expand its plant solutions business by utilizing the various forms of knowledge acquired at MAB and the strong "pipes" that connect it with association members.



MAB: Manufacturing Technology Association of Biologics
CFD: computational fluid dynamics

Fig. 2—CFD Analysis of Production Fermenter.
As part of the development of the next generation of 200-L class single-use production fermenters in collaboration with other companies that belong to the MAB, Hitachi used CFD analysis to verify product performance and reliability improvements.

WORK ON REGENERATIVE MEDICINE PLANTS (CPCs)

Regenerative medicine involves the process of culturing cells or tissue for transplanting into a patient and is recognized for its potential to treat conditions that do not respond well to drugs. Until recently, regenerative medicine in Japan involved providing treatment under the Medical Practitioners Law and production under the Pharmaceutical Affairs Act, but the number of manufacturing facilities has been growing since the passing of the Act on the Safety of Regenerative Medicine and the Pharmaceutical and Medical Device Act in November 2014, establishing the conditions for cell and tissue production. While the market is a small one compared to that for pharmaceutical plants, Hitachi has been supplying plants and equipment for production and research use since 2004.

The plants that produce regenerative medicine products are called cell processing centers (CPCs). A CPC cultures harvested cells over a period of several weeks or months in an incubator kept at a temperature of around 37ºC. During this period,

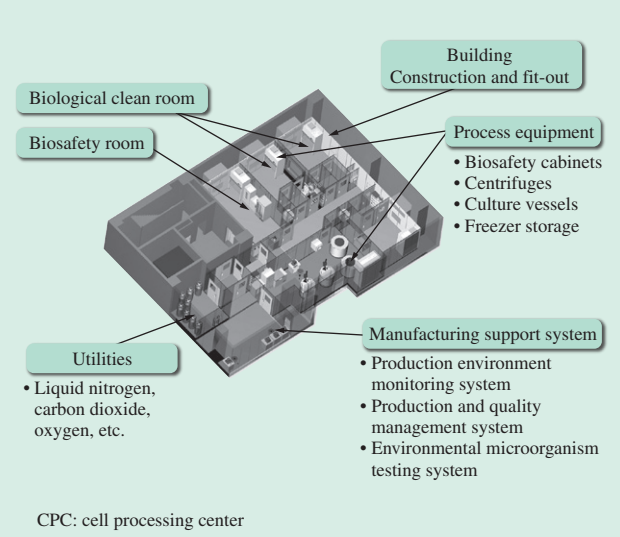


Fig. 3—Example CPC Layout.
CPCs have a large number of rooms. It is important to manage things like cleanliness and air pressure to maintain the environment in the cell handling laboratory (biological clean room).

Fig. 4—CPC Test Facility at Matsudo Research Center.
A variety of development work is conducted to reduce the risk of product contamination and improve staff work environments.

culture vessels are taken out of the incubator for cell processing operations such as replacing the culture medium, sub-culturing (transferring a portion of cells to a different vessel), or selection. The cells or tissue cultured by this process (in the form of tissue sheets, for example) are cleaned and then packaged in a sterile container for delivery. This end product is sent to a medical institution for transplanting into the patient. These processes need to be performed in a controlled environment to minimize the risk of contamination by microorganisms or other sources.

However, many cell processing operations depend on manual techniques such as the use of pipettes and are often performed inside a biosafety cabinet. Accordingly, cell handling laboratories fitted with biosafety cabinets are commonly set up as ISO 6 biological clean rooms. CPCs are made up of a number of rooms. In addition to the cell handling laboratory, these include a cell storage facility, a packaging room, a sterile room, a gowning room, and an airlock to prevent the entry of contaminated air. They are also augmented by utilities such as a carbon dioxide supply, for example (see Fig. 3). A key factor in the design of these facilities is to prevent staff, materials, and air from acting as carriers, bringing contaminants such as microorganisms into the cell handling laboratory.

Hitachi Plant Services Co., Ltd. has supplied numerous CPCs to universities, organizations, private companies, and medical institutions since delivering its first CPC to the Donated Blood Distribution Foundation in 2004. These customers include medical institutions that transplant cells cultured in a CPC into patients. With regenerative medicine having become a recognized industry over the last few years, there are examples of private companies conducting clinical trials of regenerative medicine and related products and obtaining preliminary approval for their use. Hitachi has provided support to companies that have purchased its equipment to help them obtain the approvals they need for production.

Technology development aimed at minimizing the risks associated with CPCs is also ongoing. Fig. 4 shows a CPC constructed at the Matsudo Research Center of the Infrastructure Systems Company of Hitachi, Ltd. This CPC is equipped with the ability to spray microbes or admit contaminated air, enabling its use for risk assessment in various different situations. One risk with a particularly large impact is the entry of contaminated air into the cell handling laboratory due to a fault in the air conditioning used to control the air pressure in various rooms. Disruption of air pressure can also occur due to switching over to the backup system in the event of a power outage. Hitachi is developing a pressure differential simulator that can consider a wide variety of situations, such as low external air pressure during a typhoon. This ensures that ducting, equipment, door interlocks, and so on are designed correctly.

While this article has focused on production facilities, Hitachi is active in a wide range of areas aimed at ensuring the success of customer businesses, supplying comprehensive solutions that include biosafety cabinets, isolators, and other production equipment; production management systems that minimize human error and facilitate management; and cell transportation.

CONCLUSIONS

The healthcare sector is anticipating significant growth in the market for biopharmaceutical and regenerative medicine plants, a field that can contribute to the safety and security of society through the supply of high quality products. Hitachi intends to continue paying close attention to the requirements for these plant solutions as it aspires to deliver the best possible equipment.

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Featured Articles

The Innovation Game

"How to Better Find It, Embrace It and Transform It into Explosive Growth"

William A. Burns

OVERVIEW: The term "innovation" seems to be spoken everywhere these days. In many new ventures, it is the sole "coin of the realm," the purest element of today's hyper-paced business environment. Learning to surf the innovation wave and the market with all the success it bears is a winning strategy; failing to embrace it means everything a company has worked for, no matter how long and how hard, can come crashing down. With so much at stake, why do so many companies experience difficulty in finding innovation, embracing it and leveraging it as part of the very growth engine needed to stay on top, not just for a brief span of time, but consistently year after year, decade after decade? This article explores some central themes related to innovation and answers some questions. What impact does the pace of change have on companies today? How and why are some players stumbling when seeking innovation? Finally, how are companies like Hitachi surfing the innovation wave to fuel growth, unlock markets, and pave the way for a better tomorrow?

IN THE AGE OF HYPER-INNOVATION, NO ONE IS SAFE:

DRIVING the pace of innovation in today's business encompasses a revolution in technology that leaves no aspect of an enterprise, from the factory floor to marketing, unaffected. Society is currently experiencing its very own industrial revolution, one that is every bit a match for what the world went through in the late 18th century. Innovation then gave rise to steam engines, power looms, canals, the factory system, mass production, paper money, stock and bond markets, and the corporation as the modern business organization. Today, innovation arises in developments in microelectronics, driverless cars, the Internet of things, instant communication, genetic engineering, sustainable materials, bio-engineering, electronic money, real-time payment to inventory systems, and the sharing economy.

The way in which business had been traditionally conducted turned upside down overnight. However, some of the best business executives continue to run their enterprises as if the real excitement is still to come. A word of advice: stay put too long and watch the enterprise become as obsolete as the horse and buggy, the vinyl record, or the mechanical watch. Each in its day dominated; each was abruptly done in by emerging technology.

Embracing a faster pace of innovation in today's business environment requires more nimble organizations than ever before. Companies must shift quickly in response to change, or they will simply fail, or even fail to be relevant. Innovation puts a premium on adapting; the faster the pace of change, the greater the premium. Take away change and there is no need to adapt. If it worked yesterday, there is every reason to believe it will work today. Unfortunately, change is one of the constants in life. What executives are now facing is change that transforms organizational vision, business models, and solutions. Today's business conditions give new meaning to the words of the Greek philosopher Heraclitus: "All is flux, nothing stays still—there is nothing permanent except change." In other words, if a company wants to stay afloat and prosper, it needs to change its approach to innovation.

CHANGING THE WAY INNOVATION IS MANAGED

If embracing innovation is the key to long-term corporate viability, why do so many companies struggle to embrace and harness it as a growth engine?

Frankly, business processes can limit evaluating innovation. For instance, the demand of keeping up with the current business environment simply doesn't allow for the time to focus on innovation. Chasing individual customer needs and wants can often leave organizations confused, frustrated, and burnt out when trying to identify where the market is heading. As a result, it is not surprising that innovation has gotten a bad reputation. But it doesn't have to be this way. When done properly, integrating innovation into a business model can be done with low risk and produce high returns. There is no other option—companies must innovate. When the pace of change outside an organization is faster than the pace inside the organization, it is going to find itself out of business. In fact, more and more businesses are gaining a competitive advantage solely on price and others are using technology to disrupt entrenched and leading market players.

Hitachi Data Systems Corporation (HDS) has developed a simple framework for creating, managing, and unlocking the potential of innovation. Its model leverages the power of markets, the rigorous definition of requirements and an evidence-based approach to determine success, coined by HDS CEO Jack Domme as "Market In" Innovation. HDS's Global Health and Life Sciences team has implemented this "Market In" approach to develop the company's first vertically-focused solution. This paves the way for subsequent vertical business units to innovate, succeed, and expand the volume and market reach of the business in the future.

HERE'S HOW IT WAS DONE

Innovate Where the Company Differentiates

Being different is not the same as being differentiated. Customers must value a company's differentiation and they must acknowledge its core value. In mid-2005, many companies were investing in platform and technology acquisitions to manage the quickly growing segment of unstructured data. While HDS made similar investments to remain on par with the industry, it differentiated itself by heavily investing in managing the content itself. This comprised the very files and pieces of information that HDS customers used to run their businesses on a daily basis. By developing a "One Platform for All Data" approach, the organization differentiated itself from its competition. Its key asset: providing the foundation of an information management infrastructure that the market valued far more than the next iteration of blazing fast hardware.

Ask Better Questions

In today's economy, most companies are obtaining useless or even damaging answers to their problems because they simply do not ask the right questions or rely on a select handful of customers to provide insight on how a market truly functions. This approach is dangerous because it leaves a huge blind spot as to the actual market. HDS's early efforts at innovating with its healthcare customers involved select or marquee customers clamoring to access and manage data more efficiently. Hence, it developed a number of outside-the-box solutions to solve this problem. It was only when these solutions failed in the context of non-HDS customers that it realized it was asking the wrong questions and needed to see the larger picture. HDS discovered several things. Many potential customers didn't want to better manage data, but actually use their data more effectively. They wanted to interact with it on a piece-by-piece basis, directly integrating it with their electronic medical record applications and mobile devices. Not only did HDS ask the wrong questions, but it compounded the problem by telling folks to think outside-the-box when generating solutions. This confined way of thinking reduced the number of solutions eligible to solve the problem and increased the number of bad ideas.

Why? Well, as it turned out, it wasn't necessary to think outside-the-box, what was actually needed was a new box to engage with real issues and solve problems.

Find Breakthroughs

Success in finding breakthroughs is often predetermined by the groups that are assigned to this critical task. In many cases, expertise is the enemy of innovation. In fact, solutions developed by experts are often incremental and only build on past experiences and versions of a solution. Experts might find themselves incrementally advancing the past and, due to this cognitive investment, become mentally or emotionally blocked from disrupting it. Breakthroughs require a fundamentally different perspective.

At HDS, it was only when it looked at how to enable customers' interaction with their data in a healthcare enterprise that it fully understood the nature of the problem. The challenge was never about aggregation or data storage. Rather it dealt with

ways to efficiently develop new paradigms for data interaction that allowed customers to pick and choose which portions of the data they wanted to use, how they wanted to use it, and where and when they wanted to use it. This customer-centric breakthrough formed the bedrock definitions of what eventually became the Hitachi Clinical Repository (HCR).

HOW TO PLAY THE INNOVATION GAME

The rules of this critical innovation game are simple and straightforward:
(1) Innovate Where the Company Differentiates
(2) Ask Better Questions
(3) Find Breakthroughs

HDS's success in approaching innovation required it to think differently, move quickly, and abandon some of the fundamental business processes that it had learned which had become obsolete. In addition to new fundamental rules, an organization must learn to measure itself differently, especially in embracing failure and redefining its definition of success. Another aspect of this new core innovation process, involves adapting to the current dynamically different business reality. HDS came up with new rules for this innovation game, ventured to play it in a whole new arena, and its success with this approach forced it to adapt to a few new realities:

Measure, Measure, Measure

(1) Measure the Market

In the past, the company only looked at how big the total market size was. In today's hyper-paced business environments, it analyzes the size of the market segment it is entering and how quickly it can establish revenue, market share, and a sustained presence.

(2) Measure the Requirements

Not all customers in a particular market segment will have an exact and common set of needs and requirements. That means the company needs to ask: "Does the company understand the differing customer pools in the segment that it is entering?" Also, "Have these requirements been measured against these divergent customer pools?

(3) Measure the Company's Success against Both

Correlating the company's exact market segments against its ability to define the exact requirements in each customer pool greatly enhances initial success rates and helps establish an initial "success trajectory" and then gain momentum.

Fail Fast

Companies not only need to embrace failure; they need to embrace it quickly. In the case of HDS, weeks and months spent defining and redefining the perfect set of requirements only slowed the pace of innovation. Objectively identifying a common set of features and requirements the customers DID NOT want allowed it to rapidly narrow its focus and increase its development speed on features it knew would succeed.

Invest in Discrete Steps

By discreetly dissecting the company's progress into smaller steps, it was able to timely act and react to what was unfolding in front of it. For example, rather than understanding the entire market segments, it successfully identified, understood, and validated the first eight to 10 customers in the discrete pool it was targeting. This dissected approach also allowed it to micro focus on all aspects of its new product, from features to pricing, services, support and delivery.

Not How Many, But How Much

This is perhaps the most crucial new metric to embrace when playing the innovation game. In many cases, companies misinterpret the early stages of innovation by asking themselves how many customers have bought a new product. Innovation can fail when impatient management teams quantify success in footprints and not in revenue. In the early out-of-the-gate stages of any innovative product or service, organizations are not fully tuned to sell or deliver at scale. The generation of revenue itself is really the core metric to seriously consider. If a company is generating a revenue stream from this new innovative product or service that has still yet to be integrated into its core business, then it is most likely looking at a success in innovation. Once other portions of the business can be integrated at scale, it will be discovered that revenue delivery scales with it.

CONCLUSIONS

Deep down, companies know innovation is vital to their businesses' continued success. Despite initial reservations, it doesn't have to be expensive, difficult, or stressful. It just takes three simple steps:
(1) **Differentiation** means not just making a company different for its own sake, but focusing its energies on what makes its business unique.
(2) **Question Framing** requires that before looking outside-the-box for solutions, a company carefully

considers whether it actually needs a completely different type of box.
(3) **Breakthroughs** arise when an organization gathers people with different points of view and levels of expertise.

These fundamental principles of defining and managing innovation can align to any business in any industry. Change is going to happen whether a company likes it or not. By skillfully playing the innovation game, it can make sure that change proves beneficial.

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Featured Articles

Dealing with Brain Disease

Atsushi Maki, Ph.D.
Hisaaki Ochi, Ph.D.
Masashi Kiguchi, Ph.D.

OVERVIEW: Brain disease has become a subject that can no longer be ignored when considering QoL in the modern context. While improvements in medical technology and living standards have helped tackle many forms of illness, humanity still lacks effective measures for dealing with diseases of the brain, the seat of consciousness. To take on this major societal challenge and contribute to global development, Hitachi is striving to develop solutions for dealing with brain disease. To achieve this, it is important to decode the meaning of complex neural circuits made up of more than 14 billion neurons each with thousands of interconnections to other neurons. In response to this challenge, Hitachi is working on ways of assessing clinical effectiveness by consolidating techniques for observing the function, structure, and behavior of cranial nerves and by understanding and modeling the processes that take place in the brain.

INTRODUCTION

ALONG with advances in medical technology, recent years have seen interest in ways of considering the state of ill health in the world based on use of disability-adjusted life-year (DALY) statistics[1, 2] that take account not only of disease incidence and mortality rates, but also the effect on a patient's life after contracting a disease. Fig. 1 shows DALY statistical data compiled from World Health Organization (WHO) statistics. The figure shows 2000 and 2012 data for middle-income countries experiencing rapid growth, and 2012 DALY statistics for high-income countries that are recognized as foreshadowing the future of the entire world.

The DALY statistic is also used in Japan, where it is generally calculated by the formula: (number of deaths × standard life expectancy at age of death in years) + (number of incident cases × disability weight of disease × average duration of case, in years, until remission or death), although certain corrections have also been added in recent years.

This DALY statistic can be thought of as a quality of life (QoL) indicator in the narrow sense of relating to health and gives an indication of how much mental disorders and other forms of brain disease (hereafter "brain disease") affect QoL. Also, from the trend in the DALY statistic, it is also known that the diseases that clearly increase in step with economic development are brain, neoplasm, heart, and musculoskeletal diseases. Based on data obtained by the analysis of direct medical costs, direct non-medical costs, and indirect costs[3], the economic cost of brain disease is in the order of 440 trillion yen when estimated in terms of national gross domestic product (GDP). This is approximately 5% of the total GDP.

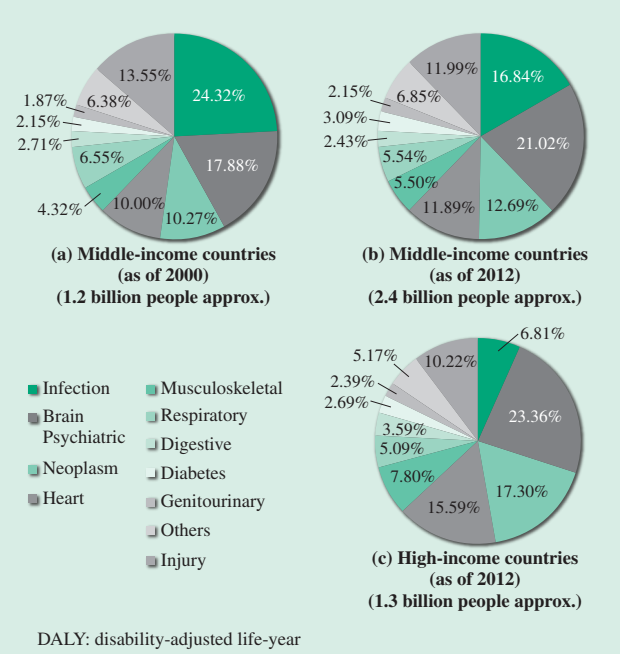

Fig. 1—International DALY Statistics.
The graph shows DALY statistics for different causes of health problems presented by income band (World Bank classification). Note, however, that stroke, which is usually classified as a heart condition, has been reclassified in the "brain psychiatric" category in this graph.

Techniques for the scientific understanding of the brain will be essential if prevention and treatment for this major societal challenge are to be established. This article describes the current progress and future plans for the development of technologies being undertaken by Hitachi to understand the brain in collaboration with clinical institutions.

MRI MEASUREMENT TECHNIQUES FOR EARLY DIAGNOSIS OF BRAIN DISEASE

MRI Measurement Techniques

Magnetic resonance imaging (MRI) is a diagnostic imaging technique that utilizes the principle of nuclear magnetic resonance. Compared to X-ray computed tomography (CT), features of MRI include that it does not expose subjects to radiation and that it can obtain information on biological function as well as morphological information. Typically, the signal-to-noise (SN) ratio of an MRI system is proportional to its static magnetic field strength, and the performance of MRI systems has improved rapidly in recent years with systems of 3 T or more having been developed to enable imaging with high resolution and contrast (see Fig. 2).

The aging of the populations in developed nations in particular has made dealing with the rapid increase in neurodegenerative diseases such as Parkinson's and Alzheimer's disease an issue of particular concern. As with other major diseases, the prognosis is significantly improved by early diagnosis and treatment. However, because the early physical symptoms are similar to many other diseases, neurodegenerative disease has to date been diagnosed from the presence of major morphological changes of the brain in MRI scans, meaning that differential diagnosis could not be performed until the disease was well advanced. This has created a need for early differential diagnosis techniques.

This chapter describes diffusion kurtosis imaging (DKI) and quantitative susceptibility mapping (QSM), two diagnostic applications of MRI developed for the early diagnosis of neurodegenerative disease.

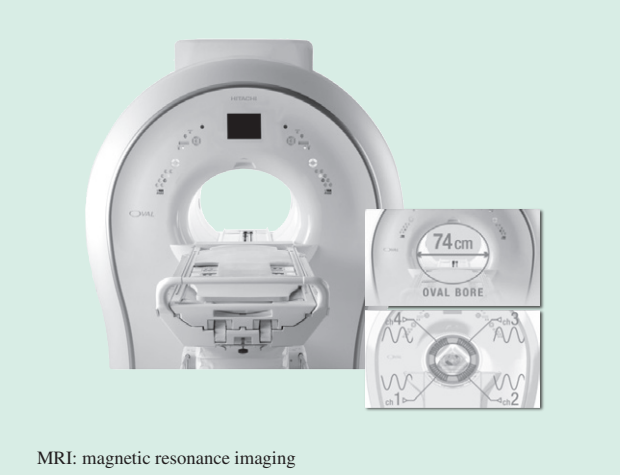

Fig. 2—3-T Superconducting MRI System.
The 3-T superconducting MRI system (Hitachi Medical Corporation) shown here combines a 74-cm oval bore with high image quality achieved using four independent transmission channels.

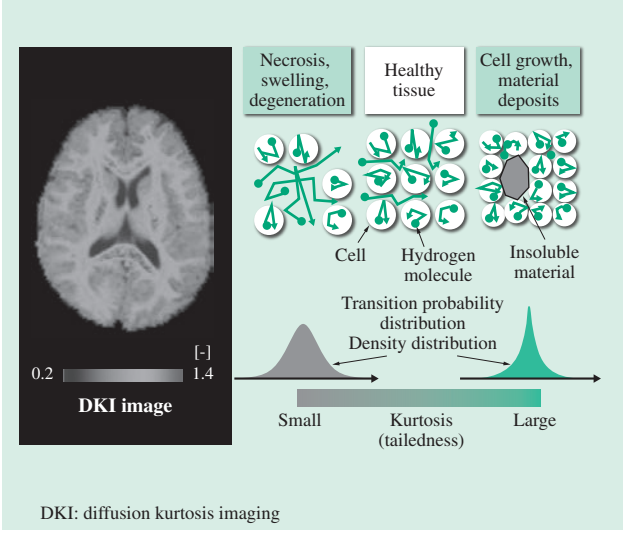

Fig. 3—Overview of DKI.
The figure shows an example DKI image. Hitachi is developing a technique for identifying the minute structural changes that occur in the early stages of neurodegenerative disease with the aim of enabling early diagnosis.

DKI

Diffusion weighted imaging (DWI), a diagnostic application of MRI that utilizes the diffusion of hydrogen molecules to image tissue characteristics, has already demonstrated its usefulness in the diagnosis of conditions such as brain infarctions and brain tumors. Whereas DWI uses the diffusion coefficient obtained by assuming that the transition probability distribution of molecular diffusion follows a normal distribution as its main diagnostic indicator, there has been growing interest in recent years in analytical methods that assume a non-normal distribution because of their ability to take full account of how the fine structure of tissue restricts diffusion. The reason for this interest is that these techniques have the potential to provide a sensitive means of identifying the minute changes in microstructure caused by disease.

DKI can image changes in the amount of insoluble material and density of tissue cells by using the kurtosis (tailedness) of the transition probability distribution as an indication of the extent to which the diffusion of hydrogen molecules is restricted by tissue structure (see Fig. 3). It can show the minute changes in white matter and gray matter structure that occur in the early stages of neurodegenerative disease. One of the challenges of DKI is that, while it dramatically increases the amount of diagnostic information that can be obtained, it takes longer to capture an image than DWI. However, this time has been shortened by using error propagation analysis to identify the imaging conditions that minimize measurement error[4]. Hitachi has led its competitors in the commercialization of this technology, making it available for routine clinical testing, with clinical research into the identification of Parkinson's disease symptoms currently underway in collaboration with Iwate Medical University[5].

QSM

The variable magnetic susceptibility of tissue causes localized variations in the magnetic field inside a body that is exposed to the magnetic field of an MRI magnet. QSM measures the MRI signal phase difference due to this spatial variation in magnetic field inside the body and performs a quantitative calculation of the magnetic susceptibility distribution in the tissue to produce an image of the distribution of magnetic susceptibility due to the presence of things like proteins and iron (see Fig. 4). This can observe iron deposits in tissue affected by degenerative disease prior to the appearance of morphological changes.

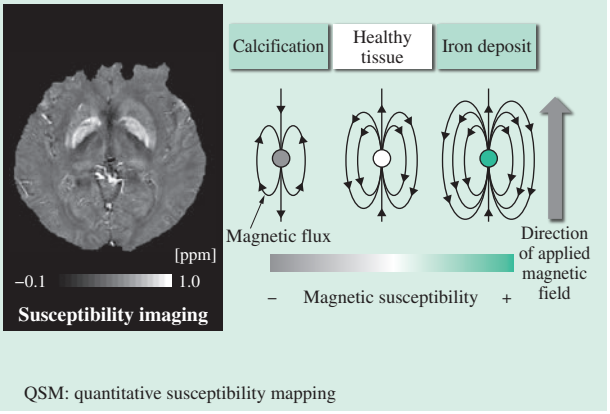

Fig. 4—Overview of QSM.
The figure shows an example magnetic susceptibility image. Hitachi is developing a technique for identifying abnormal iron deposits in neurodegenerative disease tissue.

While past measurement techniques have had problems with deterioration in estimation accuracy for microstructure, a technique has been developed that can detect minute changes by also performing estimation based on spatial frequency[6]. The effectiveness of this technique is currently being assessed through joint research with a university. In joint research with Iwate Medical University, research is underway on its use in conjunction with DKI for the early differential diagnosis of neurodegenerative disease[7], with the hope that achieving early identification will assist with the development of early-stage treatments.

APPLYING OPTICAL TOPOGRAPHY TO BRAIN DISEASE

Optical Topography

Optical topography is a technique developed for imaging brain function under everyday conditions[8]. It enables the topographic observation of brain activity by using two wavelengths of near-infrared light at which tissue is highly transparent to measure and image changes in blood flow due to neural activity on the surface of the brain (see Fig. 5). Research is being conducted into a variety of brain diseases, with optical topography systems developed based on this principle ranging from wearable units that target the frontal lobe to units that perform measurements of the entire head[9], [10], [11]. The technique is being used for an increasing range of clinical applications, with its use in assisting the differential diagnosis of depression symptoms approved for health insurance coverage in 2014. As a non-invasive technique that can perform measurements under everyday conditions, it is also being adopted for use in developmental neuroscience[12], [13], [14] and social neuroscience[15] (see Fig. 6).

Drug Efficacy Prediction Using Optical Topography

Chemical reactions underpin the functions of the brain. This makes drugs an important option for the treatment of brain disease. The safety and efficacy of drugs are determined by conducting large clinical trials, but just as everyone has a different personality, the neural circuits that are established during brain development differ from person to person. This means that the efficacy of drugs for brain disease varies from person to person. On the other hand, whereas the increasing prevalence of brain disease is leading to the increasing prescription of drugs, deciding whether to continue or halt the treatment involves observing the

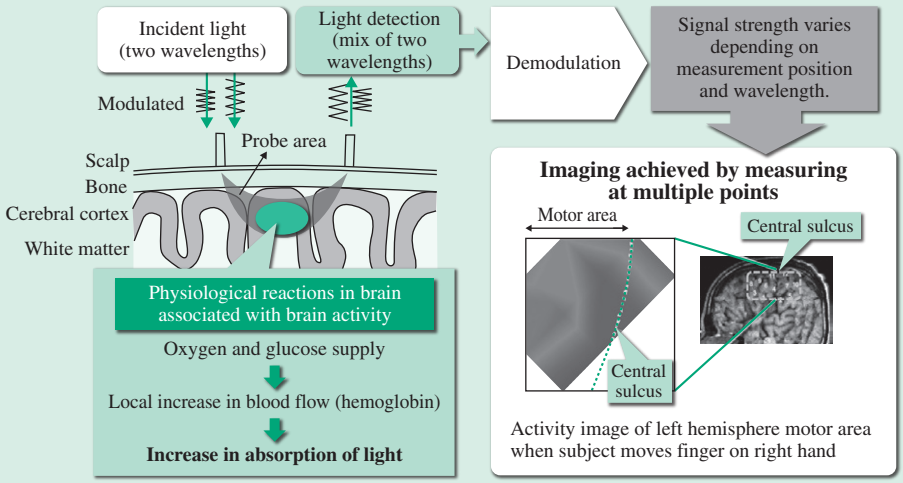

Fig. 5—Principles of Optical Topography.
Near-infrared light modulated at each wavelength and direction of incidence is shone through the scalp to measure changes in blood flow associated with brain activity.

patient for several months after the start of treatment to determine whether there is any sign of an alleviation of symptoms. If a technique were available for confirming the efficacy of drugs used to treat the brain, it would be possible to determine efficacy for each individual in more quantitative ways and to monitor the progress of the treatment.

For these common issues associated with brain disease, a technique has been devised that uses optical topography to provide information on the efficacy of drugs for the brain (joint research with Jichi Medical University and Chuo University) (see Fig. 7)[16), 17)].

The technique for assessing the efficacy of drugs for brain disease enables the efficacy of a drug to be predicted early in the treatment, and shortens the several months it subsequently takes to confirm efficacy. In cases where it is difficult for the patient to recognize the efficacy of a drug, it also helps prevent patients from abandoning treatment because it helps them see the benefits of the treatment for themselves. Based on the same idea, the technique can also be applied to new therapies such as neurofeedback and cognitive-behavioral therapy, which seek to (re) construct nerves. By making a biological record of the

	Clinical and research use	Wearable unit for research	
Series	ETG series (clinical use) OTR series (research use)	WOT series	HOT121B
Photograph	FDA-approved model: ETG-4000 		
Application	Clinical applications (insurance-approved) •Assistance with differential diagnosis of symptom of depression •Pre-surgical diagnosis of language dominant hemisphere •Testing for epileptic focus	Frontal lobe research	Research into 46 regions of frontal lobe
Features	Two wavelengths, 24 to 120 sites, standalone	Two wavelengths, 10 to 22 sites, wearable (wireless), simultaneous measurement of four subjects	One wavelength, two sites, reduced skin blood flow, wearable
Sold by	Hitachi Medical Corporation	Hitachi High-Technologies Corporation	Hitachi High-Technologies Corporation
Manufactured by		Hitachi Kokusai Yagi Solutions Inc.	

FDA: U.S. Food and Drug Administration

Fig. 6—Optical Topography System for Use in Research and Clinical Testing.
The figure shows the range of systems available, including a model for measuring the entire head and wearable units that target the frontal lobe. The systems can be used both to perform detailed measurements of a subject's brain and to study the brain activity associated with communication through the simultaneous measurement of multiple subjects.

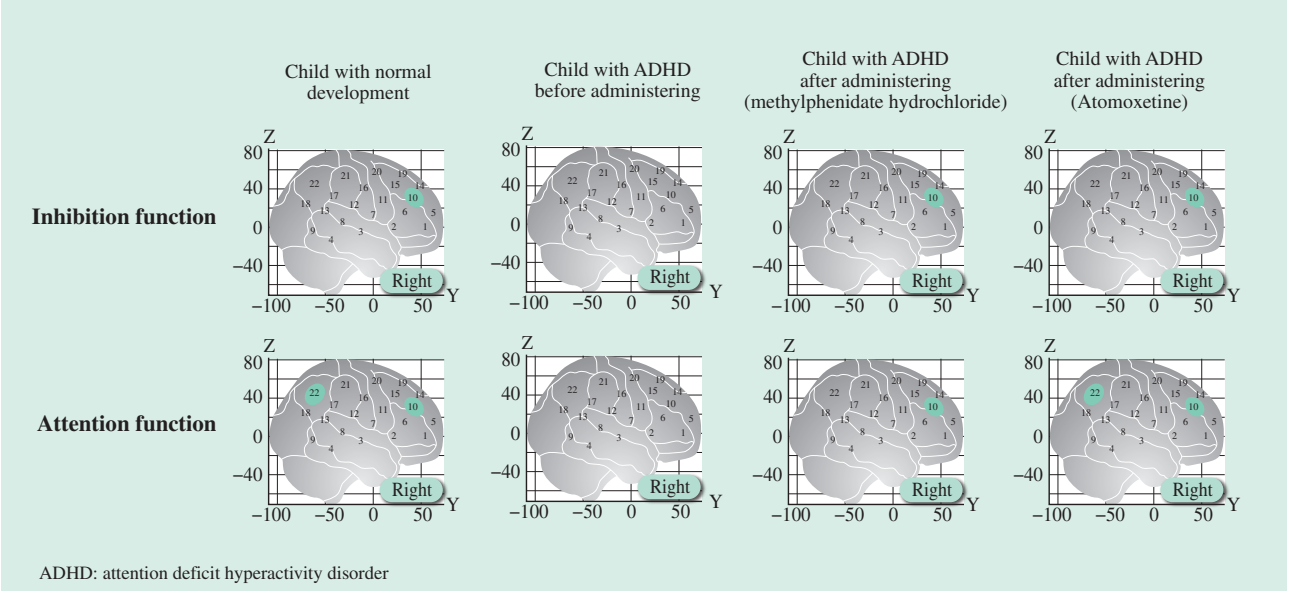

Fig. 7—Drug Efficacy Assessment for Children with ADHD.
Children who were administered methylphenidate hydrochloride sustained-release tablets and Atomoxetine showed the same response as a child with normal development when exercising the inhibition function and attention function (courtesy of Yukifumi Monden of Jichi Medical University).

condition of the brain, this enhances the patient's QoL by facilitating a shift from standardized to precision (personalized) medicine.

RE-WORK SUPPORT

When a mental illness such as depression causes a person to take a long-term leave of absence from work, it is not easy for them to resume employment soon after the illness goes into remission. Returning to work too soon frequently leads to taking more time off or being re-admitted to the hospital. Consequently, there is an emphasis on rehabilitative training prior to returning to work, with Hitachi providing a "re-work" (return to work) support program that is provided in the form of group training for employees who have taken time off. The objective is for such employees to establish patterns of daily activity, to recover the strength to resume normal work routines, and to avoid taking further time off by equipping them with resilience and the ability to deal effectively with stress in the workplace and elsewhere. This requires that individual employees develop the ability to control themselves by assessing their own state of mental and physical health.

The re-work support program uses factors such as depressive mood[18], stress, patterns of daily activity, quality of sleep, physical fitness, and ability to work (work capability assessment) as indicators of mental health. Typically, mental and physical health assessments involve things like self-evaluation questionnaires or interviews and observation by a clinical psychologist. However, subjective assessments often suffer from poor accuracy, such as an assessment that indicates the patient's condition is very good because the judgment is made in comparison with their experience of severe early-stage symptoms, or a patient pretending to be well in order to hasten a return to work, or, alternatively, deliberately claiming to be in poor health. In response, Hitachi has been developing measurement techniques for the objective assessment of mental and physical health.

Changes in brain function or physiology due to depressive mood, stress, or other factors are measured using brain function measurement systems (optical topography) and autonomic nerve measurement systems (fatigue and stress assessment systems) respectively. Factors like patterns of daily activity and quality of sleep are measured using accelerometers (life logs), and ability to work is measured by monitoring personal computer (PC) use (BM1). The aim is to augment the patient's self-assessment and advice from a clinical psychologist by collecting this data over time and presenting the state of recovery in a variety of visual forms (see Fig. 8), making the re-work support program more effective. This use of measurement-based mental healthcare is currently being trialed through use in the re-work support program described above.

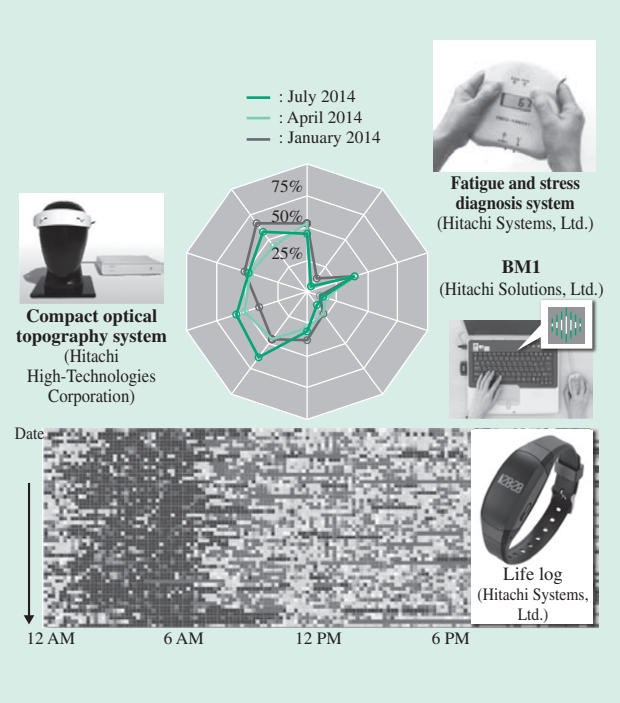

Fig. 8—Visualization of Mental Health.
The figure shows a radar chart that shows how measurements change over time (top) and a "life tapestry" that indicates the pattern of daily activity (bottom).

In the future, it is anticipated that this technology will be combined with information technology (IT) to reduce its cost, and that it will be deployed in comprehensive mental healthcare services that include patient self-assessment after returning to work and help prevent mental illness.

FUTURE OUTLOOK

The workings of the brain are extremely complex and develop over time as information is absorbed from the environment. This dynamic and complex circuitry makes it difficult to achieve a quantitative understanding of the cause and effect relationships that lead to brain disease. Techniques for obtaining a diagnosis have been developed by correlating symptoms with the signals observed using different measurement modalities. However, given the severe social effects of brain disease noted above, there is an urgent need to develop solutions that can genuinely deal with brain disease. While many techniques have been developed for the sake of prevention and treatment that provide results in isolation, as of this time they have yet to reverse the worsening in DALY statistics.

One of the key challenges in all this is to create "precision medicine" that can deal with the highly individual nature of brain disease. By providing consistent measurement indicators that cover everything from prevention to diagnosis and treatment, even if for only a single disease, it will be possible to adapt to individual diversity. To achieve this, it will be necessary to build systems and establish a foundation of knowledge for providing a quantitative understanding of gene expression and variation, and cranial nerve function, structure, and behavior in cranial nerve circuits that are built up over the course of a lifetime. This is because acquiring an understanding of ever-changing cranial nerve circuits will require the collation of systematized knowledge by first classifying brain states based on genes and behavior, and then determining the brain structure and function associated with each classification. In the future, it will be important to build a "development compass" by undertaking research and development of information theory and sensor technology that can integrate the three factors for understanding the brain in an informational sense and interpret them (see Fig. 9).

This integration of new technology platforms and the reconstruction of a foundation of knowledge will accelerate the development of nerve (re)construction techniques that utilize technologies, such as robotics

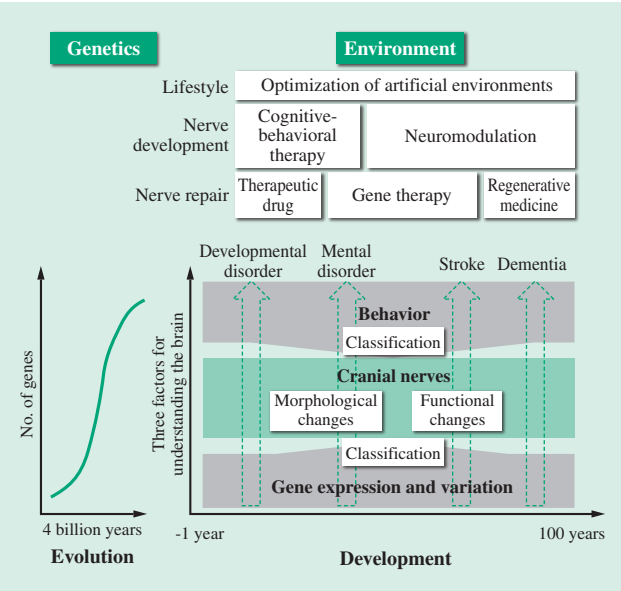

Fig. 9—"Development Compass" for Development of Brain Disease Solutions.
Brain disease can be understood by establishing a foundation of knowledge of the progress of brain development by conducting longitudinal measurements over each age range of the three factors for understanding the brain (indicated by the green dotted arrows). This makes it possible to diagnose and treat individuals and accelerates the development of new therapies.

and information and communication technology (ICT), and the development of techniques for nerve repair based on more biological indicators. Furthermore, the quantitative understanding of brain development will likely extend beyond the healthcare sector and encompass the construction of artificial environments that encourage healthy development. Hitachi intends to pioneer a new future through the pursuit of an understanding of the brain, which is the core of people and society.

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Featured Articles

Wider Adoption of Regenerative Medicine Driven by Open Innovation

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OVERVIEW: The large-scale and safe production of cells for medical use is the greatest challenge to the wider adoption of regenerative medicine. Although the culturing of cells for medical use is largely performed manually at present, the key to more widespread use of regenerative medicine lies in the use of techniques for automated cell culture for the up-scaling and rationalization of cell production and the reliable supply of high-quality cells. Hitachi is combining technology from medical engineering to develop closed systems for automated cell culture and cell transportation techniques. The automated cell culture equipment developed by Hitachi can produce cells with quality equivalent to that of manual culture. Hitachi is also working on the development of cell transportation vessels that prevent contamination and maintain constant temperature and pressure. Based on this research and development, Hitachi is seeking to facilitate the wider adoption of regenerative medicine by establishing a cell value chain that can deliver high-quality cells to patients around the world.

INTRODUCTION

HIGH hopes are being placed on regenerative medicine providing the next generation of therapies that can treat patients who do not respond well to conventional pharmaceuticals, with benefits that include improving the patient's quality of life (QoL) and reducing social insurance costs. Along with the development of processing techniques for induced pluripotent stem (iPS) cells and other types of cells, the urgent challenges facing the establishment and spread of regenerative medicine also include the rationalization of costs without compromising efficacy and safety. Hitachi is seeking to establish a new cell value chain for regenerative medicine by consolidating technology and know-how developed in related activities as well as through research and development work that takes advantage of open innovation to commercialize basic research undertaken by universities. In this way, it is helping create a healthy society with a better QoL in which every patient can receive treatment.

TRENDS IN REGENERATIVE MEDICINE

The market for regenerative medicine is forecast to expand rapidly after 2020 to reach 17 trillion yen by 2030[(1)]. Japan's Institute of Physical and Chemical Research (RIKEN) became the first in the world to commence clinical research into the use of iPS cells for retinal disease in September 2014. It is anticipated that treatments for numerous diseases will become available in the future through the use of iPS cells. There is also a trend toward such treatments involving allogenic rather than autologous transplantation, with the expectation that this will become a widespread practice. The enactment of a new law on regenerative medicine in November 2014 (the Act on the Safety of Regenerative Medicine) included the introduction of a system for the early approval of cell-based products and permission for the outsourcing of cell processing. It is anticipated that facilities for the safe and efficient production of cells will be established by specialist companies in the future. Whereas the market has been dominated by venture businesses in the past, major Japanese corporations among others have been active in acquiring or establishing alliances with regenerative medicine companies, indicating that regenerative medicine is well on the way to becoming a recognized industry.

ACTIVITIES BY HITACHI

The biggest challenge to be overcome if the wider adoption of regenerative medicine is to enable all patients to receive treatment with confidence is

the establishment of technology for the large-scale production of high-quality cells suitable for medical purposes at low cost. The high cost of regenerative medicine is also an obstacle to its wider adoption, with the current cost of cell production for each treatment being upward of one million yen.

By developing techniques for automated cell culture, Hitachi is seeking to encourage the wider adoption of regenerative medicine by making it possible to produce cells at high volumes and levels of reliable quality not possible when production is performed manually[2), 3), 4)]. In particular, development is proceeding on closed automated cell culture systems that provide the high degree of sterility needed for medical use, and on systems that incorporate techniques that culture multiple vessels at the same time. Also under development are large sub-culture systems that use large-scale surface culture vessels for volume production and techniques for air freighting live cells for medical use in ways that maintain their sterility and efficacy. The following sections describe these technical developments.

Automated Cell Culture Equipment for Cell Sheets

One feature of Hitachi's automated cell culture equipment is its use of fully enclosed culture vessels and circuits to prevent contamination by bacteria or other sources from the external environment. Based on this core technology for closed automated cell culture, Hitachi has developed automated cell culture equipment for cell sheets incorporating tissue engineering undertaken jointly with Tokyo Women's Medical University, which has clinical experience with regenerative medicine.

Fig. 1 (a) shows the Automated Cell Culture Equipment 3 (ACE3) system for culturing up to 10 cell sheets at a time[5), 6), 7)]. In addition to using γ radiation to sterilize the set of closed culture vessels and circuits prior to use, the system has a detachable design that allows the culture vessel and circuit modules to be replaced for each patient (single-use modules) to prevent cross-contamination between patients when performing autologous transplantation. While the environment inside the closed culture vessel and circuit is maintained at high humidity (95% or higher) during culture, the other internal parts of the system are kept dry. Along with maintaining the cleanliness of the environment where the system is located to minimize the amount of dust generated during operation, its comparatively small installed size (1.7 m wide × 0.795 m deep × 1.58 m high) makes it suitable for installation at existing cell processing facilities (CPFs).

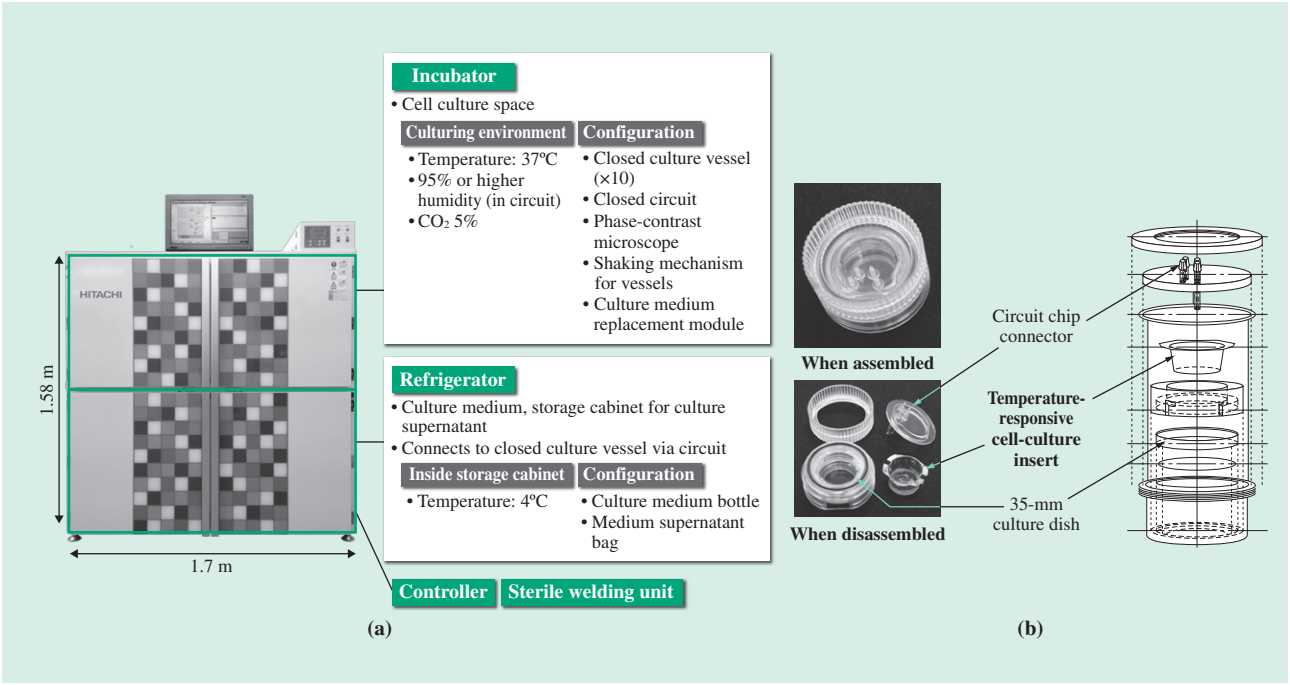

Fig. 1—ACE3 Automated Cell Culture Equipment for Cell Sheets and Closed Culture Vessel.
(a) shows external view and configuration of Automated Cell Culture Equipment 3 (ACE3) system for culturing up to 10 cell sheets at a time. (b) shows configuration of closed culture vessel for double-layered culture with temperature-responsive cell-culture insert.

The main features of the automated culture function of the ACE3 are cell seeding, maintenance of constant temperature and humidity, gas exchange, medium exchange, and observation using a phase-contrast microscope. The microscope can be used to automatically record images of designated points in each closed culture vessel at user-specified time intervals. The system also supports remote operation from outside the CPF, with a function that enables users to manually observe and photograph any location in the closed culture vessels whenever they want.

The closed culture vessels can be used for the double-layered culture of epithelial cells with a sealed structure enclosing a cell-culture insert [see Fig. 1(b)]. Furthermore, the permeable membrane that forms the culture surface of the cell-culture insert is grafted using a temperature-responsive polymer (by CellSeed Inc.). Varying the temperature from the culture temperature (37ºC) to room temperature (below the phase transition temperature of 32ºC) changes the culture surface treated with temperature-responsive polymer from hydrophobic to hydrophilic. This detaches the adhered cells, enabling the cell sheets to be harvested without the use of enzymes and without damaging the cells[8].

After the sterile removal of the closed culture vessels from the system, the cell sheets in the closed culture vessels in which they have been automatically cultured are transported at constant temperature to the operating theater or other point of use in the transportation vessels provided with the system. This maintains the quality of the cells or regenerated tissue at the completion of production.

An ACE3 has been installed at Tokyo Women's Medical University for use in restoring the esophagus after the removal of esophageal cancer by endoscopic surgery[9], and its performance in automated culture is being assessed. Automated culture tests performed on the ACE3 using commercially available human oral mucosal epithelial cells demonstrated its ability to perform sterile production of cell sheets that satisfy the same criteria as applied to cell sheets produced manually, namely cell morphology, stratification, sheet separation and harvesting, cell count, cell viability, and marker protein positive rate.

Hitachi has also developed a large automatic human myoblast sub-culture system using closed large-scale surface culture vessels (59 cm × 70 cm) specially designed for cardiomyocyte regeneration through participation in a Funding Program for World-Leading Innovative R&D on Science and Technology (FIRST Program) based at Tokyo Women's Medical University. This system can culture human myoblasts automatically with a yield in the range of 10^9 cells. As demand for mass culture applications such as cardiomyocyte regeneration and undifferentiated iPS cells is expected to grow in the future, Hitachi aims to use this system as a platform for developing mass culture production technology.

Cell Transportation Technology

The commercialization of regenerative medicine and its establishment as an industry in its own right requires technologies for transporting the cells and tissue from the facility where they are produced to the recipient medical institution. The transportation options include road, rail, and air, depending on the distance, and whichever method is used, ensuring the sterility and efficacy (cell viability, morphology, and so on) of the manufactured tissue transportation is just as vital as it is beforehand. Maintaining quality requires control of the factors that cause environmental changes during cell transportation, with parameters like temperature and pressure in particular needing to be kept constant just as in the manufacturing

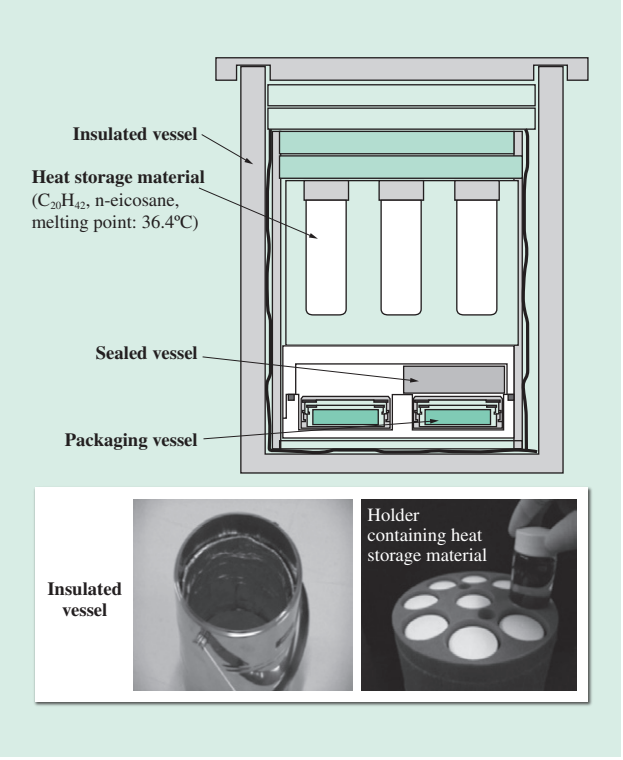

Fig. 2—Cell Transportation Vessels.
By utilizing the latent heat of a heat storage material to avoid the need for a power supply, these vessels enable safe transportation by air.

process. It is also important that transportation does not compromise the cleanliness achieved at the CPF.

Hitachi has developed cell transportation vessels suitable for use with cell sheets produced using regenerative medicine[10), (11)]. To enable air freighting, the vessels are designed to maintain temperature by using the latent heat from a heat storage material that does not require a power supply. To ensure that the cells are held in a suitable environment during transportation, the vessels are designed to control the pressure as well as the temperature, and to maintain the same level of cleanliness as the clean room used for culturing (see Fig. 2). The vessels are currently used mainly for clinical research that spans multiple facilities, primarily Osaka University – The University of Tokyo and Osaka University.

WIDER ADOPTION OF REGENERATIVE MEDICINE DRIVEN BY OPEN INNOVATION

In the future, Hitachi aims to deepen open innovation, adopt the correct approach to the challenges of cell production for regenerative medicine, and achieve mass culture production at CPFs through the development and automation of cell processing technology. This involves establishing a smart cell value chain by integrating with related businesses, which include CPFs, bacteriological analyzers, process management systems, analyzers for biochemical and immunological testing, diagnostic imaging systems, and information technology (IT) management. In this way, it aims to create total solutions for regenerative medicine that can supply patients around the world with safe and effective cells (see Fig. 3). Through a combination of its technologies and business activities, Hitachi is working toward the wider adoption of regenerative medicine.

CONCLUSIONS

This article has described the progress of development by Hitachi of automated cell culture equipment that facilitates the wider adoption of regenerative medicine by playing a core role in cell production, and transportation technology for supplying cells to patients around the world. Hitachi intends to supply total solutions and contribute to the wider adoption of regenerative medicine by establishing a smart cell

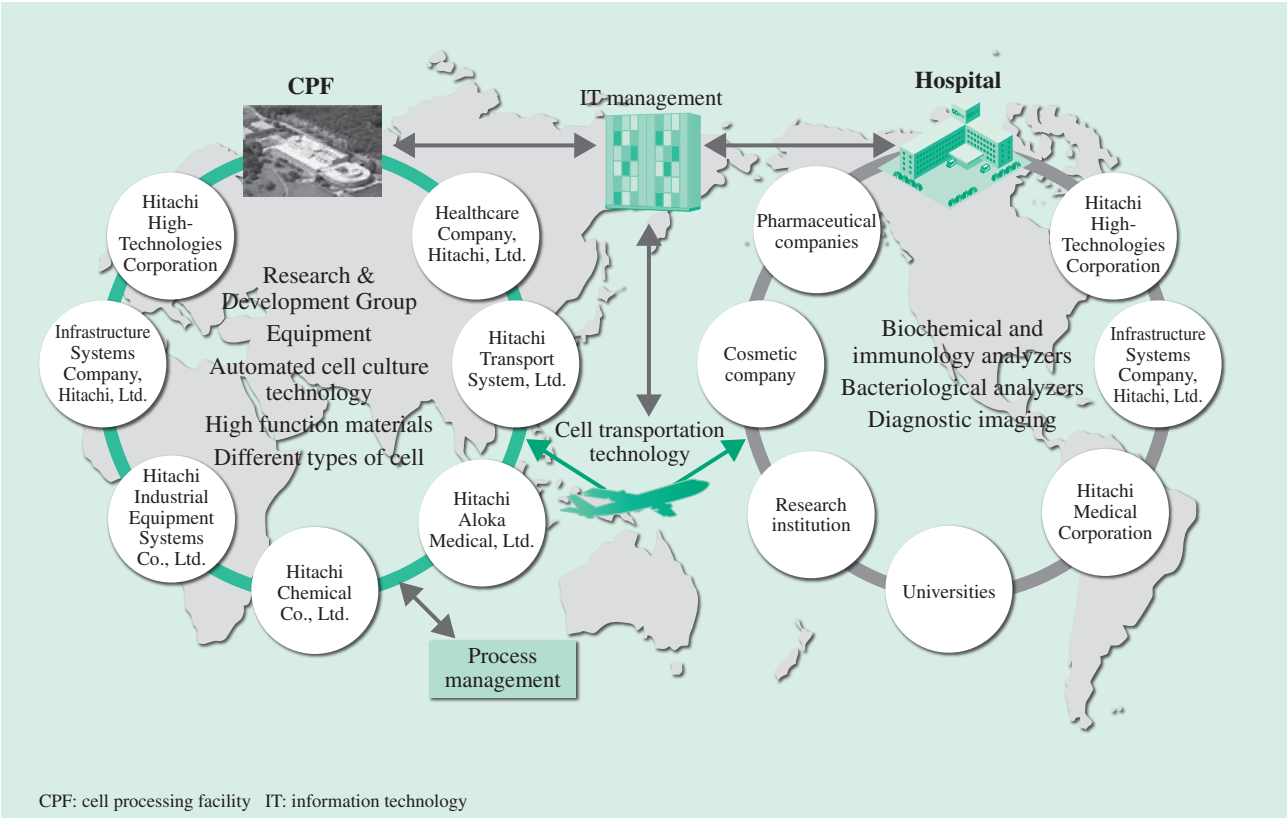

Fig. 3—Future Form of Total Solutions for Regenerative Medicine Provided by Hitachi.
By combining technologies from affiliated companies, Hitachi is establishing a smart cell value chain to satisfy customer needs.

value chain based on IT management systems through the integration of this research and development with its existing CPF and other healthcare businesses.

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