Visionaries 2015

Beyond Imaging

— Quantitative Techniques for Medical Modalities —

Creating a society in which everyone can live a healthy and worry-free life calls for the establishment of comprehensive healthcare as part of the infrastructure of society.
Meanwhile, the steadily rising cost of healthcare is becoming more severe, particularly in developed economies that are characterized by aging populations and the growing prevalence of lifestyle diseases.
The early diagnosis and treatment of illnesses are essential to simultaneously improving the quality and controlling the cost of healthcare.
In the field of medical modalities, Hitachi is developing techniques for obtaining biophysical information on the pathology of diseases in quantitative form.
Advances in diagnostic imaging that provide more accurate clinical information are set to open up new possibilities for healthcare in the future.

Color Imaging Made Possible by Technical Advances

Dealing with the societal healthcare problems of an aging society and the growing prevalence of lifestyle diseases have become urgent issues. The associated rise in healthcare costs has also become a serious concern for many developed economies.

The early diagnosis and treatment of illness based on accurate clinical information has an important role in controlling the cost of healthcare while improving its quality at the same time. This clearly requires improvements in the performance of the healthcare modalities* used in diagnosis, along with advances in the associated technologies.

Based around the Healthcare Company established in 2014, Hitachi supplies solutions that encompass every stage of the care cycle, covering everything from health promotion/disease prevention and examination to testing/diagnosis, treatment, and monitoring. The Central Research Laboratory of Hitachi, Ltd. undertakes leading-edge research and development in the healthcare field. Keiji Kobashi (Department Manager, Medical Systems Research Department, Central Research Laboratory, Hitachi, Ltd.), who researches the healthcare modality technologies that drive care cycle innovation, comments:

"The world of diagnostic imaging has been making dramatic progress. One analogy might be to photographs, which once could only be taken in black and white, but now can be taken in color."

In other words, in the same way that a color photograph provides much more information about the subject than a black and white one, functional progress in each modality provides medical practitioners with large amounts of information that was unobtainable in the past.

The advances made in diagnostic imaging over recent years in tandem with progress in technologies like computers and electronics has made it possible to use medical modalities to measure and quantify a variety of biophysical parameters. Within these new technologies lie important possibilities for things like the very early diagnosis of illness or the searching out of optimal treatments for individual patients. The Central Research Laboratory is working on the research and development of quantitative techniques for some important diseases, having already produced a variety of results.

Keiji Kobashi

* Classifications for the diagnostic equipment that is used in healthcare, such as magnetic resonance imaging (MRI) systems, X-ray computed tomography (CT) systems, and diagnostic ultrasound systems.

Imaging Iron in the Brain

In clinical settings, MRI systems basically provide diagnostic imaging through morphology, but they also have the ability to provide information on biological function without any associated exposure to radiation, unlike X-ray CTs.

The development of MRIs with high static magnetic field strengths in the 3-T range has seen the performance of these systems improve rapidly in recent years, including the ability to provide images with high contrast and high resolution. Also, the development of imaging techniques such as susceptibility weighted imaging, which utilizes phase differences due to spatial variations in magnetic susceptibility, has made possible the clear identification of things like microbleeds or veins.

Taking advantage of these developments, Hitachi is working with university hospitals on research into MRI techniques for the early diagnosis of neurodegenerative diseases such as Parkinson's and Alzheimer's. Hisaaki Ochi (Chief Researcher, Life Science Research Laboratory, Central Research Laboratory, Hitachi, Ltd.), who leads this research and development, explains as follows.

"Very small-scale degeneration appears during the early stages of neurodegenerative diseases. Specifically, deposits of iron occur in brain tissue and these cause an increase in magnetic susceptibility. Our aim is to achieve very early diagnosis of neurodegenerative disease by imaging the distribution of susceptibility to detect abnormalities in the iron turnover rate."

This susceptibility imaging technique can estimate a body's susceptibility distribution with high

Hisaaki Ochi

accuracy from phase information contained in the MRI signal. Its advantage over the previous susceptibility weighted imaging technique is that it can reveal iron deposition with greater clarity. It is also possible to estimate the iron concentration from pixel values for tissue in which iron deposition is occurring, and the oxygen extraction fraction from vein pixel values.

“It is no longer the case that MRI scans only provide morphology. It is our hope that the iron concentration, oxygen extraction fraction, and other physical quantities obtained by this technique will prove to have clinical significance in the future,” says Mr. Ochi.

The clinical value of the quantification of iron concentration extends beyond the very early diagnosis of neurodegenerative disease. There are also a number of other conditions similar to Parkinson’s that are difficult to distinguish from each other at an early stage. However, if iron deposition in brain tissue can be quantified, the early diagnosis and differentiation of these conditions should be possible based on links between these quantities and changes in pathology.

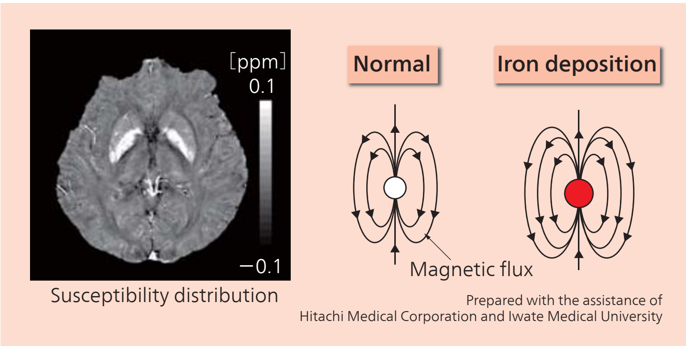
Meanwhile, stroke may turn out to be one of the applications for oxygen extraction fraction imaging. Strokes are the result of blockages in the blood vessels that supply the brain. When abnormalities in these blood vessels cause inadequate blood flow, it is known that the oxygen extraction fraction of brain cells increases in order to obtain as much oxygen as possible from a small amount of blood, making the ability to look at things like blood flow, oxygen extraction fraction, and metabolism important for diagnosis. While patients are typically scanned using positron emission tomography (PET), MRI imposes less of a burden because it is non-invasive. Although susceptibility imaging using MRI is very new, it is likely to enter practical use in the future following clinical testing based on further data collection.

Determining Heart Blood Flow Dynamics

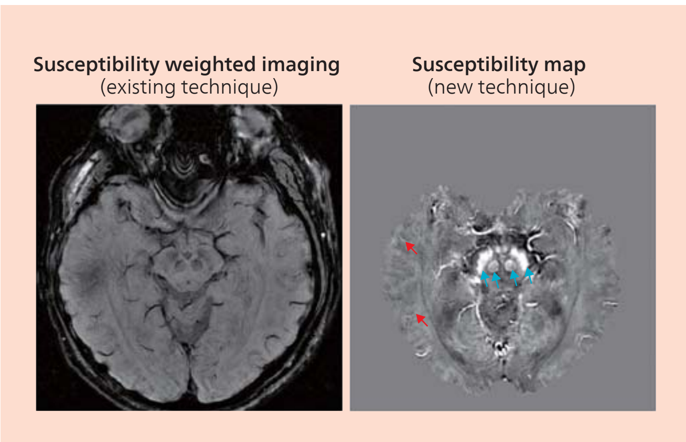
Because of their excellent realtime characteristics, ultrasound systems are frequently used for examination and diagnosis of circulatory organs such as the rapidly beating heart. This movement of the heart can be imaged by detecting the ultrasound waves that are reflected off of heart muscles or valves. It is also possible to measure the speed of blood flow from the information contained in ultrasound waves reflected off of blood cells. The speed and direction of blood flow can be displayed in a color-coded format using a color Doppler method developed in the 1980s.

While the cardiac ultrasound system is indis-


3-T superconducting MRI system (Hitachi Medical Corporation)



Example of susceptibility distribution imaging. With the aim of enabling early detection, Hitachi is developing a technique for the identification of very small-scale degeneration in the early stages of neurodegenerative disease.



Comparison of images for magnetic susceptibility in the brain obtained using the existing and new (susceptibility imaging) techniques. The new technique clearly identifies iron deposition. Also, the iron concentration can be estimated from the pixel values for tissues in which iron deposits are present (indicated by the blue arrows), and oxygen extraction fraction can be estimated from the pixel values for veins (red arrows).

pensable as an essential piece of equipment for examination and diagnosis of cardiovascular disease, Hitachi has also developed vector flow mapping (VFM), an advanced technique for obtaining detailed information about blood flow in the heart. Hiroki Tanaka (Senior Researcher, Medical Systems Research Department, Central Research Laboratory, Hitachi, Ltd.), who took part in the development, explains it as follows.

"VFM is a blood flow imaging technique that combines ultrasound measurement with a fluid dynamics model. Our aim is to help assess heart and other cardiovascular conditions by enabling information to be acquired on detailed blood flow phenomena that posed a problem in the past, such as vortices inside the ventricle."

The principle behind VFM is to display the velocity vector distribution, using the speed in the vertical direction obtained by the color Doppler method and the heart wall speed obtained by speckle tracking as boundary conditions, and using the conservation of mass to calculate the speed in the horizontal direction.

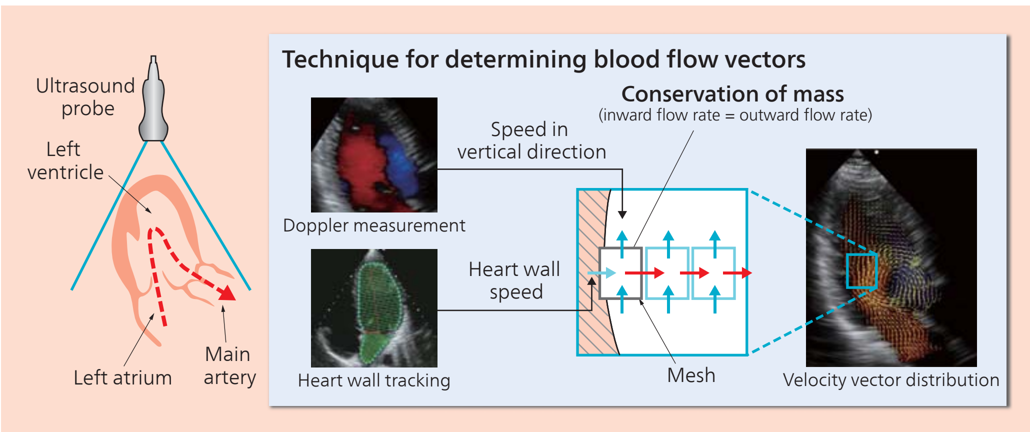
Advances in clinical cardiovascular testing have found that vortex flow patterns are changed by specific conditions such as heart failure. That is, a detailed picture of blood flow in the heart can be used to determine the seriousness of a condition and its pathology. Because VFM can image in detail the flow of blood from the left atrium through the left ventricle to the aorta, it provides more reliable assessments.

As to what benefits to cardiovascular diagnosis will result from the detailed understanding of blood flow in the heart and other blood vessels provided by VFM, this will depend to a large extent on the outcome of future clinical research.

Mr. Tanaka says, "First of all, I believe the ability to quantify is important. VFM has provided us with a way of determining the energy loss in blood flow as a physical quantity. The use of physical quantities that relate directly to heart disease, rather than the heart functions shown by previous diagnostic imaging, has the potential in the future to provide things like predictions of deterioration in heart function or a metric for assessing the benefits of improved treatments."

In research and development work, it has been demonstrated that, in contrast to blood flow information obtained by methods that use a laser, VFM is accurate to within a few percent. In the future, metrics obtained using VFM should bring a new perspective to cardiovascular medicine.

Diagnostic ultrasound system and DAS-RS1 + VFM software for personal computers (PCs) (Hitachi Aloka Medical, Ltd.)



Ultrasound VFM can obtain a detailed picture of blood flow in the heart. Its use in cardiovascular medicine has found that vortex flow patterns are changed by specific diseases.

Hiroki Tanaka

Atsushi Maki

An Objective View of Mental Health

Optical topography is a brain activity imaging technique that uses near-infrared light to identify localized changes in blood flow in the brain. The first in the world to develop the technology, Hitachi is working on healthcare applications such as clinical uses for psychiatric disorders as well as its use in brain function research. Looking back at the progress to date, Atsushi Maki (Chief Researcher, Life Science Research Laboratory, Central Research Laboratory, Hitachi, Ltd.), who has been engaged in the research and development of optical topography for many years, makes the following comment.

"For healthcare, our research has included work that leads toward the differential diagnosis of depression by imaging blood flow distribution to assess brain activities specific to particular disorders. Depression is characterized by weaker activity than other disorders, and we have succeeded in differentiating conditions such as schizophrenia and bipolar disorder (manic depression), which has proven difficult in the past. A healthy person, on the other hand, demonstrates strong activity across their frontal lobes."

A psychiatric disorder with a diverse range of symptoms, depression is difficult to diagnose, as is differentiating it from other conditions such as bipolar disorder and schizophrenia. However, because each condition requires different medication, a mistaken differential diagnosis can delay treatment. Optical topography, on the other hand, provides an objective basis for differential diagnosis.

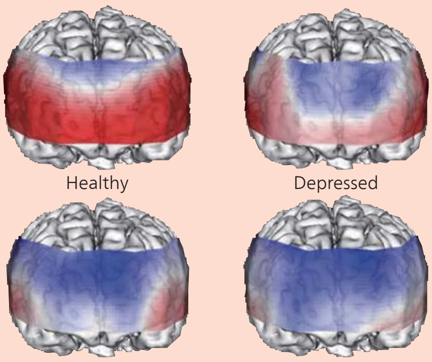
With this accumulation of findings, the insurance-funded clinical use of optical topography has commenced following the acceptance of the "use of optical topography examinations to aid differential diagnosis of depressive symptoms" for insurance coverage in Japan in FY2014. Whereas psychiatric care has primarily involved patient consultations in the past, it is anticipated that optical topography will be able to lead to accurate and early diagnosis, treatment, and medication at an early stage by providing an objective means of assessment.

The scope of potential healthcare applications for optical topography is growing, with work also progressing on basic research and clinical applications for other mental disorders such as attention deficit hyperactivity disorder (ADHD) and post-traumatic stress disorder (PTSD). This includes the development by Hitachi of a technique for quantifying depressed moods with a view to preventing the onset of depression.

As Mr. Maki says, "We have demonstrated a correlation between brain activity metrics obtained using optical topography and scores for depressed mood obtained from questionnaires. That is, it is possible to visualize what is happening before the disorder manifests and use this to help prevent the onset of depression."

A topic of interest during the development of this technology was prefrontal area 46, which is the seat of working memory function and associated with mood. In an experiment, optical topography was used to obtain a value for brain activity by measuring changes in blood flow in the prefrontal areas of subjects when they were given a problem to solve, and to obtain a score for depressed mood by using a questionnaire to provide a benchmark mood assessment. This experiment found a strong correlation between the two values. The experiment also demonstrated the ability to track changes in depressed mood over time. That is, it found that metrics obtained using optical topography

ETG-4000P optical topography system (Hitachi Medical Corporation)



Blood flow distribution in brain obtained using optical topography. Since this technique can assess brain activity distinctive of particular mental conditions or other illnesses, it has the potential for use in the prevention and treatment of depression.

Quantitative Diagnostic Imaging Techniques with Clinical Benefits

Eiju Watanabe (Professor and Chairman, Department Neurosurgery, Jichi Medical University Hospital) has been providing medical advice and direction to Hitachi's research and development since the joint development of optical topography with the Central Research Laboratory of Hitachi, Ltd. in 1994.

"Neurosurgery can be thought of as the discipline with the greatest need for imaging in the diagnosis of illness. While there have been some remarkable developments in technology over recent years, to use the current situation with focal cortical dysplasia (a cortical malformation linked to epilepsy) as an example, the two lowest of the four grades used to classify these malformations are often not visible in an MRI scan. In this sense, I believe imaging technology will continue to grow in importance in the future.

While functional MRI (fMRI) is useful for obtaining fundamental and detailed data, optical topography is able to capture information about brain activity while the subject goes through the motions of his or her normal daily life. In medical practice, I believe that combining these different modalities in accordance with their respective advantages will be important.

In putting medical modalities to use, attention is currently focused on the ability to obtain quantitative clinical information. One example is an initiative being launched to use optical topography to quantify the efficacy of medication for children with ADHD. In addition to determining the efficacies of different medications, this elucidates the mechanism of how each medication works, and therefore should help reduce the number of patients trying out medications with a low level of efficacy. Fundamental findings have also been obtained that can be used as a basis for personalized treatments tailored to each patient's individual symptoms. Furthermore, since recovery from aphasia or other cognitive impairment involves the brain healing itself, work is proceeding on the use of optical topography to obtain information on this plasticity. The data obtained from this study may well provide metrics that can be used in the future for rehabilitation.

These metrics and other quantitative data will become important factors when considering treatments. I look forward to Hitachi's support for medical practice through the establishment of quantitative techniques with clinical benefits."


Professor Eiju Watanabe

provided an effective self-checking mechanism for day-to-day changes in mood.

Mr. Maki says, "Given the increasing number of people developing depression in recent times, there is a need to prevent its onset and to provide early detection, treatment, and rehabilitation. While the early identification of downturns in mood is important for prevention, the quantification of depressed mood has the potential to go beyond this to become a solution that can help empower the mental health of the general public."

Achieving Care Cycle Innovation

Mr. Kobashi says, "It seems likely that applications that quantify biophysical information will grow in importance in the future along with advances in diagnostic imaging systems. My hope is that, in time, the utilization of this technology in areas such as the very early detection of disease or more accurate diagnosis will lead to innovation throughout the care cycle."

As the amount of quantitative data with medical significance grows, its deployment can be anticipated in healthcare information technology (IT) applications that collect this information and put it to use. Advances in diagnostic imaging systems have a significance that transcends merely providing information about diseases. Hitachi intends to continue working on research and development that aims to enable very early detection, control healthcare costs, and to create a society in which people can live long and healthy lives.