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Brain Imaging
— Necessity for Reinforcement of Research and Development for Application of Non-Invasive Technology to Diagnosis and Treatment of Mental Disease —

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1.1 Introduction

The 1990s was regarded as "the decade of the brain" by the U.S. government, and brain research made rapid progress in those 10 years. Also in Japan, Brain Science Institute in RIKEN (the Institute of Physical and Chemical Research) and other similar organizations were established, with basic brain research was extensively advanced in the years. Brain researches have been conducted mainly on experimental animals such as mice and monkeys, while, in recent years, the research on humans is advanced with the development of brain imaging techniques, measurement of morphological brain structure and neurological activities by non-invasive methods. Particularly, technologies of functional magnetic resonance imaging (fMRI) and positron emission tomography (PET) have been remarkably progressed, making it possible to investigate changes in local neuronal activities and molecular movements in the brain. Using these techniques, brain science research on humans has been rapidly progressed, analysis of neuronal activities related to the higher brain functions, such as learning and memory, has advanced, and researches on the changes in neuronal activities associating with mental diseases, such as dementia and schizophrenia, came to be conducted.

In recent years, modern societies have taken more and more highly complicated structures according to the rapid development of science and technologies, and, as the result, the number of patients with mental diseases, including stress-induced depression and psychosomatic diseases, have increased and attracted considerable attention from the society. In addition, the increase of the elderly population has led to an increase of the number of patients with dementia, such as vascular dementia and Alzheimer's disease, and care of these patients has become an important social problem. Therefore, it should be an important theme in the future policy of science and technology in Japan to develop the technologies to diagnosis and treatment of these mental diseases and enrich the care of the patients. In this report, the author proposes establishment of an organization for collaborative research which can play the core role in tackling the above theme.

1.2 Major techniques for brain imaging

1.2.1 Methods for morphological measurement

Among the techniques for brain imaging, X-ray computerized tomography (CT-scan) and magnetic resonance imaging (MRI) are mainly used for observation of the brain shape and its detailed structure (Table 1). These methods of morphological measurement are used widely, and have become essential for diagnosis and treatment of neurological diseases, especially cerebrocardial infarction and brain tumors. In addition, diffusion tensor magnetic resonance imaging (DT-MRI) was recently developed, making it possible to observe the connection of nerve fibers in the brain[4, 5].

Table 1: Characteristics and comparison of typical morphological measuring methods

Measuring method	CT scan	MRI	DT-MRI
Principle of measurement	X-ray; tissue differences are distinguished by the difference in X-ray absorbency.	Nuclear magnetic resonance; tissues are distinguished based on the difference in the characteristics of resonance of hydrogen atoms in biological tissues.	Nuclear magnetic resonance; the diffusion of water molecules in tissues is examined to investigate the structure of fibrous tissues.
Subject for measurement	Bone, hematoma, and calcified tissues.	Difference in the structure of soft tissues and blood vessels.	Direction of fibers in tissues.
Advantages	Suitable for the measurement of skull fracture caused by head injury, and cerebral hemorrhage.	Suitable for the measurement of the minute brain structure, brain tumor, cerebral infarction, and cerebrovascular disease.	Provides observation of the shape of nerve fiber and the connection.
Disadvantages	Exposure to radiation.	Limitation due to an intensive magnetic field and long measurement time.	Same as those of MRI.

*For details of the respective methods, see Appendix [1].

Source: Author's compilation based on reference material

Appendix [1] Major methods for morphological measurement

(a) CT-scan

X-ray radiography was the first technique introduced as a non-invasive method for measurement and diagnosis of human tissues including the brain. In a CT-scan, the X-ray beam is radiated through narrow slits, and data collected with a detector on the opposite side are processed on a computer to produce the sliced images of the tissues. With a CT-scan, the difference in the absorption and transparency efficiency of X-ray is measured to distinguish tissue structures, such as bone, tumor, hematoma and so on, similarly to X-ray pictures. Since its introduction in the early 1970s, CT-scan rapidly spread and became an essential device for the diagnosis and treatment of diseases. For neurological diseases, the device made it possible to diagnose brain tumors, cerebral hemorrhage, cerebral infarction, and chronic subdural hemorrhage that were difficult before, and the treatment of these diseases advanced revolutionarily. The spatial resolution of the CT-scan has been improved year after year, and the interval between sliced images was narrowed down to 0.5mm. This higher spatial resolution is one of the advantages of the CT-scan method. On the other hand, what may be given as disadvantages is the exposure to a relatively high dose of X-ray and the unavoidable low contrast in the brain images due to the surrounding skull. MRI was introduced to overcome these disadvantages of the CT-scan, and now both CT-scan and MRI are being used for diagnosis of neurological diseases. For hemorrhage, fracture and calcification, the CT-scan is still advantageous and it is the first choice for emergency treatment of head injury.

(b) MRI

MRI is a measurement technique based on the principle of nuclear magnetic resonance (NMR). The nucleus of each atom constituting substances is spinning with a specific character. If the spinning is arranged into one direction in a strong static magnetic field, each atomic nucleus absorbs electromagnetic waves at a particular frequency and resonances. The nuclear resonance depends on the state of each atom, and we can discriminate molecules in which each atom is incorporated and environment surrounding the molecule, such as tissues inside the body, with observation of the state of the resonance. Ordinary MRI is a device to measure the nuclear magnetic resonance of hydrogen atoms inside bodies as signals, and as the result, the device can discriminate the tissues containing the atoms, such as blood vessel, adipose tissue and cerebral cortex. The technique was advocated in the early 1970s, and put into practical use a few years later. MRI can provide observation of the detailed structure of tissues inside the body due to the functional character of the device, and it is particularly useful in observation of brain tumors and cerebral infarction because of its less influence from the skull surrounding the brain. It also provides observation of cerebrovascular structure (magnetic resonance angiography; MRA) without using a contrast medium, therefore, being used for diagnosis of cerebrovascular diseases. There are some limitations in the application of the device due to the strong static magnetic field and its relatively long time, at least 30min. to 1hr., for data acquisition from one patient.

(c) DT-MRI[4]

DT-MRI is a novel measurement method developed in the late 1990s based on the ordinal MRI technology. In this method, the fibrous structure of the tissues can be observed by following the movement of hydrogen atoms contained in water molecules. Water molecules usually show the Brownian movement and randomly diffuse in every direction, but the direction of the diffusion is limited internally in fibrous tissues such as muscles and neuronal axons. Therefore, we can determine the direction of fibrous structure in each tissue with measurement of the movement of water molecules inside the tissue. In the brain research, this method makes it possible to observe the state of axons inside the white matter of the brain, which was hardly observed by the ordinal MRI, and it reveals the extension of nerve fibers during development of infant brains, and the degeneration of nerve fibers with the disease, such as cerebral infarction[5].

1.2.2 Methods for nerve activity measurement

Major methods for measuring nerve activities are functional magnetic resonance imaging (fMRI, functional MRI) and positron emission tomography (PET), used for basic and clinical brain researches (Table2). Using fMRI and near-infrared spectroscopy (NIRS), change in the local blood flow is observed to monitor the local neuronal activities in the brain. Both MRI and fMRI are using basically the same data collection technology, however, they are using different method for data analysis to reveal morphology and nerve activities in the brain, respectively. Their performance is determined by the intensity of the static magnetic field used. For fMRI, more intensive magnetic field (1.5~7T) is used than that (1~1.5T) for ordinal MRI. Tesla (T) is a unit representing the intensity of a magnetic field, and 1T is corresponding to 10,000 gauss. Using PET and single photon emission computed tomography (SPECT), movement of specific type of molecules can be traced in association with nerve activities, to reveal the function of the molecules for nerve activities. On the other hand,

Table 2: Characteristics and comparison of typical measuring methods of nerve activities

Measurement technique	fMRI	PET and SPECT	SQUID	NIRS
Principle of measurement	Nuclear magnetic resonance; measures the difference in the influence of the oxidized condition of hemoglobin on the local magnetic field to determine the change in local blood flow.	Measurement of gamma rays; measures the metabolism of molecules containing radioisotope.	Flux density; the distribution of flux density on the head surface is measured to determine the intracerebral distribution of current.	Near-infrared light; the difference in absorption of near-infrared light due to the difference in oxidation of hemoglobin is measured to determine the change in local blood flow.
Subject for measurement	Change of local blood flow.	Movement of molecules such as neurotransmitters.	Movement of nerve current in the brain.	Changes of blood flow on the cortical surface.
Advantages	The space resolution is good (approx. 1 mm.).	The metabolism of specific molecules can be measured.	The time resolution is good (a few millisec.).	The degree of freedom during measurement is high, and it is advantageous for measurement of infants and patients.
Disadvantages	The time resolution is poor (a few dozens of sec.)	Use of radioisotope in the living body. Establishment of a radiation facility.	The space resolution becomes poor in some cases.	Due to the influence of absorption and diffusion from biological tissues, the deep brain is difficult to measure.

*For details on the respective methods, see Appendix [2].

Source: Author's compilation based on reference material

Appendix [2] Major methods for nerve activity measurement

(a) fMRI

The 1990s was regarded as the decade of the brain by the U.S. government, and the brain research made rapid progress in the 10 years. During this term, the technique of fMRI was highly developed, and it may be possible to say that it was a decade of fMRI [8]. fMRI uses the principle technique of nuclear magnetic resonance similarly to ordinal MRI, however, its purpose is to measure not the morphology of the brain but the status of activities in the brain. In this device, the technique, advocated by Dr. Seiji Ogawa (currently transferred to Ogawa Laboratories for Brain Function Research, Hamano Life Science Research Foundation, Japan) et al. in 1990, is generally used for measurement of the change of brain activities. With this technique, the change of blood flow in the brain is observed by blood oxygenation level dependent (BOLD) contrast method, and thereby the change of local brain activities is revealed [9]. Hemoglobin (oxyhemoglobin), which carries oxygen to tissues including the brain inside the body, transfers to deoxyhemoglobin after releasing oxygen in each tissue. Oxyhemoglobin and deoxyhemoglobin have different characters as a magnetic body. Oxyhemoglobin has no influence on the surrounding magnetic field, while deoxyhemoglobin is a paramagnetic body which causes a small distortion in the intensive magnetic field produced by MRI, resulting in a local decline of MRI signal (BOLD effect). The degree of the effect is proportionate to the concentration of deoxyhemoglobin, therefore changes in the local concentration of deoxyhemoglobin can be measured by the observation of the changes in the intensity of the BOLD effect on the MRI signal. In the brain, it is known that local vasodilation is caused by increasing of nerve activity, and thereby the blood flow is increased to meet the demand for oxygen at the site. The increment of the blood flow exceeds the actual oxygen consumption, and, as a result, it causes increase in the local amount of oxyhemoglobin and relative decrease in the concentration of deoxyhemoglobin, producing enhancement of the MRI signal at the site. Therefore, increase of nerve activity can be observed as more intensive MRI signal locally. In fMRI, these slight changes in the MRI signal from hydrogen atomic spinning is detected to reveal nerve activities in the brain. To strengthen the MRI signals, stronger static magnetic field (1.5-7T) is applied in fMRI than that (about 1-1.5T) in ordinal MRI used for usual morphological observation, and a device with further more intensive magnetic field (9.4T) was introduced. Increasing of the intensity of the static magnetic field can lead to strengthening of the signal, however, at the same time it also enhances the noise in the detection. Therefore, the technique of information technology for signal processing is important in the fMRI method, and close cooperation between brain researchers and engineers for information technologies is essential for development of the device.

The spatial resolution of fMRI is as high as less than 1mm, similarly to ordinal MRI used for morphological observation, whereas its time resolution is not so high, about a few dozens of a second, mainly attributed to the time for onset of the change in blood flow after increasing of the nerve activity and data acquisition from the faint signal.

(b) PET and SPECT

PET and SPECT measure gamma rays emitted from radioisotope with a short half-life, administered into the body to observe the state of intracerebral metabolism of molecules containing the isotope. In PET, positrons (one type of gamma rays) are emitted from the isotope and bind to surrounding electrons in the tissues to release two 511 keV gamma rays (annihilation) to the opposite direction on a straight line. The position and timing of the binding between the positrons and electrons can be specified precisely by simultaneous detection of these two gamma rays with one pair of gamma ray detectors located at opposite sides of the body. Using of these two detectors results in the high definition of the measurement by PET. In SPECT, gamma rays are directly emitted from the isotopes and detected with one gamma ray detector. This method can be conducted using a relatively simple device as compared to PET, whereas spatial resolution and ability of quantitative analysis of the detection is lower than that of PET. With selection of the molecules containing radioisotope, these method have the advantages for obtaining information about the metabolism of specific type of molecules, such as blood flow, glucose consumption, binding of neurotransmitters to the receptors, and so on, associated with nerve activities. In PET, 11C, 13N, 15O and 18F are used as positron emitting nuclides, and their half-life is about 10-100 min. Therefore, a radiation facility such as cyclotron must be installed to produce the isotopes at the institution where the devices, PET and SPECT, are used. On the other hand, regardless of this limitation, observation of the molecular metabolism using the PET and SPECT is getting more and more important to elucidate the functions of the molecules, that are discovered and identified in the brain with the recent progress of molecular biological research, such as the completion of the human genome analysis, inside the living body for the diagnosis and treatment of neurological diseases.

(c) SQUID (EEG/MEG)

Nerve activity is principally based on the electric activity caused by movement of ions. Therefore, the most direct approach for measurement of the brain activity is to observe changes in the electric potentials and the magnetic field. Electroencephalogram (EEG) is a measurement method for the difference in the electrical potential between two points on the head surface, while magnetoencephalogram (MEG) is a method for observation of the density distribution of magnetic flux on the head surface, generated by the electric activity inside the brain. Using the superconductivity technology, superconducting quantum interference device (SQUID) made it possible to measure faint magnetic flux on the head surface. Recently, the device with a large number of channels (e.g., 256 channels) for detecting points was developed to improve the spatial resolution, and it became possible to determine intracerebral electric current distribution from the observed distribution of magnetic flux on the head surface.

The advantage of SQUID for observation of nerve activity is its direct measurement of the electric activity in the brain, whereas the other methods measure indirect indexes, such as blood flow and metabolism of bio-molecules, as a result of nerve activity. SQUID has very high time resolution to measure the nerve activity in the order of millisecond. The device also shows good spatial resolution for detection of the intensive signals such as the spike current in epilepsy to specify its focal point. However, changes in the magnetic flux associated with normal nerve activity are too slight to be detected with good spatial resolution by SQUID. With all the non-invasive methods including SQUID, it is necessary to determine the status of nerve activity within the brain from information obtained outside of the head. Among the devices, SQUID detects magnetic flux on the head surface with poorer positional information in comparison with the other methods which detect signals from inside the brain, i.e. electromagnetic waves including radiation and near-infrared light. Therefore, it is more difficult to determine the precise position as a mathematical single-meaning solution with SQUID. It would be necessary to improve the device to raise the detection ability, and, at the same time, to raise the spatial resolution by the development of analytical technique for reverse problems with mathematical engineering.

(d) NIRS

NIRS is a method to detect changes in intracerebral blood flow using near-infrared light around the wavelength of 800 nm. The near-infrared light shows a low absorbency in biological tissues as compared with other visible lights, and its tomography through the brain or its topography on the surface layer of the brain can be detected although the signal intensity is very weak. Between oxy- and deoxy-hemoglobin, the absorption spectrum is reversed and the difference in absorption is enlarged for the light around 800nm wavelength. The changes of local blood flow can be measured through monitoring of the changes in concentration of oxy- and deoxy-hemoglobin in the tissue. Similar to fMRI, the blood flow changes according to the nerve activity, therefore, the local nerve activity can be revealed by observation of the changes in the local blood flow. The data collection device of NIRS is small and the subject can move freely during the measurement, making it effective for observation of infants and patients who have difficulty in staying in one position for long time. On the other hand, comparing with X-rays and gamma rays, near-infrared light cannot avoid being absorbed and scattered by biological tissues, therefore, it is difficult to obtain information of the deep inside of brain, in addition to its poor spatial resolution. In the future, the usefulness of NIRS may increase for monitoring of the brain activity, because of the raising ability of the device for measurement through technological development including the use of a laser diode as a light source and a multi-channel detector (64-channel) [10].

using superconducting quantum interference device (SQUID), the density distribution of magnetic flux is observed on the surface of the head, to determine the current distribution within the brain.

The performances of these measuring methods, i.e. sensitivity, time- and spatial- resolution, are not yet sufficient, and further technological development of the devices is still necessary for progress of the brain research. Particularly, engineering technologies, such as electronics and information processing, are important for data analysis which is one of core parts of these measuring methods. In some few cases researchers and engineers are collaborating together for the technological development of the device in Japan, however, in most cases these methods are based on the technologies from U.S.A. and Europe. For example, fMRI of 3T or more and PET are imported from U.S.A. and European countries, such as England and Germany. In Japan, further cooperation between the fields of medicine and engineering should be attempted to develop further these measuring techniques in the future and to bring forward basic and clinical researches for human brains based on these technologies.

Table 3: Number of introduced CT and MRI in major countries (No. of units per population of 1 million)

Country	CT	MRI
Japan	84.4	23.2
Korea	22.9	4.3
Italy	19.6	6.7
Germany	17.1	6.2
U.S.	13.2	7.6
France	9.7	2.5
England	6.1	4.5

Source: Author's compilation based on the OECD statistic material [6]

1.3 Recent status of the introduction of the measuring technologies in Japan (in comparison with other major countries)

According to the newest OECD report (1999 edition)[6], the number of CT and MRI (per population) introduced in Japan is the highest in the world, outstandingly high even among advanced countries (Table 3). These devices are commonly used for morphological observation of the brain in Japan for the diagnosis of nerve diseases, such as cerebral infarction and brain tumor, although they are applied for other tissues.

On the other hand, techniques to measure brain activities are being used for basic researches of the human brain, and devices of advanced technology with higher performances in resolution and sensitivity are being introduced. For example, about 10 units of 3~4 tesla (T) fMRI were introduced to universities and other research institutes in Japan (Table 4). fMRI of 7~9.4 T are being used on humans in the United

Table 4: Major institutions that introduced fMRI in Japan (devices of 3T or more for use on humans)

Institution name	Intensity of static magnetic field	Year of introduction
Iwate Medical University (Iwate)	3T	Fiscal 2000
National Institute for Physiological Science, Okazaki National Research Institutes (Aichi)	3T	Fiscal 2000
Ogawa Laboratories For Brain Function Research (Tokyo)	3T	Fiscal 2001
Kyoto University Hospital (Kyoto)	3T	Fiscal 2002
Institute of Biomedical Research and Innovation (Hyogo)	3T	Fiscal 2002
Neuroscience Research Institute, National Institute of Advanced Industrial Science and Technology (Ibaraki)	3T	Fiscal 1997
Brain Research Institute, Niigata University (Niigata)	3T (vertical type and horizontal type)	Fiscal 1995
BF Research Institute (Osaka)	3T	Fiscal 1998
Fukui Medical University (Fukui)	3T	Fiscal 1997
Brain Science Institute, RIKEN (Saitama)	4T	Fiscal 1996

Source: Author's compilation based on published materials

States, and the device of 7T will be operated at the Niigata university this year in Japan.

For PET device, a radiation facility is required to be accompanied with the device to produce short half-life radioisotopes; therefore, the number of the devices is not large in Japan, about 50 units having been introduced in the whole country, mainly in university hospitals. In some facilities, PET is the main device applied for diagnosis of cancer or other diseases, and the number of devices will gradually increase in Japan.

For SQUID method, the large equipment is required for ultra-low temperature cooling, and the machines only provided a small number of detective points and the corrected information was not so much, and, therefore, the number of devices is small, about 20 units introduced in the whole country of Japan.

1.4 Establishment of a core collaborative research organization and reinforcement of the research for brain imaging

1.4.1 The present status and problem of research on neurological diseases

Based on recent development in brain imaging technology, basic researches on neurological diseases have been widely conducted in the world including Japan, achieving various results. For example, it has been observed using fMRI and PET that decreases in the rate of blood flow and saccharometabolism occur in the brain of patients with Alzheimer's disease, prior to morphological changes such as cerebral degeneration and atrophy. For other neurological diseases such as depression, it became known that the release and movement of neurotransmitters changed in the brain of the patients. Advancing of the researches might reveal the cause and mechanism of the neurological diseases.

On the other hand, based on these results of basic researches, it is necessary to develop application techniques for clinical diagnosis and therapies of neurological diseases including depression and dementia among general citizens, returning the profits of the results of basic researches to the society. At this time, it is possible to delay progression of Alzheimer's disease thorough taking medication, although it is difficult to cure the disease. Medication method has also been developed for the therapy of other neurological diseases such as depression. It is important to make early and exact diagnosis of the diseases for application of these therapeutic treatments, in order to improve the quality of life of patients and their families and to reduce various social burdens caused by the care of the patients.

In fact, considering the technological progress of fMRI and PET and the results of basic researches on neurological diseases using them, it will be possible to make the early and exact diagnosis of the neurological diseases by the brain imaging methods. To promote utilities of the brain imaging technologies, it might be necessary to spread the most advanced devices across the whole country for the daily diagnostic and therapeutic use of them. However, it may be economically difficult and take time to spread them all over the country, because of the expensive price (more than 1,000 million yen) of the 3T fMRI device. Instead of it, it may be more realistic to attempt utilization of MRI devices already introduced in hospitals, more than 3,000 units, across the whole country for morphological observation, as stated in the previous chapter. For this purpose, it is necessary to develop application technologies for general diagnosis utilizing MRI with low intensity of the magnetic field, based on the results of basic researches obtained using fMRI with higher intensity of the magnetic field. PET requires a radiation facility next to the device, and, therefore, the number of units spread out in Japan is small as compared with MRI, about 50 units in the whole country. On the other hand, using PET, we can investigate not only the changes of blood flow rate but also the metabolism of important substances (e.g., saccharometabolism), realizing a detailed analysis of brain activity. It would be necessary to develop a diagnostic technique combining MRI and PET for medical care of neurological diseases among general citizens.

1.4.2 Establishment of a core collaborative research organization

In Japan to date, as stated in the above paragraph, brain imaging devices were dispersedly introduced in universities and research organizations across the whole country. In each institution, results of basic researches relating to neurological diseases have been achieved by experienced researchers and their colleagues. These basic researches are important to clarify the fundamental mechanism of the brain function and to elucidate the cause of neurological diseases, and it will be necessary to promote them continuously in future. On the other hand, at these small-scale, dispersed institutions, researchers are busy with doing their own basic researches, and, therefore, it is difficult to develop simultaneously application techniques, such as a general diagnostic method, for neurological diseases in addition to the basic researches.

In this situation, for establishment of general diagnostic methods based on the results of basic researches, it may be necessary to establish a core organization for collaborative researches to conduct development of application techniques systematically. The purpose of the organization is to establish application techniques for general diagnosis and therapies of neurological diseases. For this purpose, newest devices should be introduced to reinforce its research system and the technological development of brain imaging methods should be conducted in the organization.

There are several possible structural forms for the organization: (1) An organization constructed of the assembly of several small-scale institutions selected from already existing research sites in the country. (2) An organization centered with a newly constructed institution. Whatever form it may take, the organization must create close relationships with existing related research institutions to form a collaborative research system, efficiently promoting research of neurological diseases and development of technologies for cure of them. For example, after construction of a network connecting research institutions distributed across the whole country and a database collecting and organizing their results of basic researches, it may become possible to utilize their results mutually and effectively for efficient researches on neurological diseases in Japan.

1.4.3 System required for a collaborative research organization

There are several important points for the system to establish therapeutic techniques for neurological diseases, in addition to the above.

(1) Interdisciplinary research system

All the imaging techniques as stated above (Table 2) are still in the halfway of development for optimal measurement of neuronal activities, and, therefore, it is necessary to promote research and development of the technologies in each research institute for advancing them. Particularly, development of information technologies for signal processing is important to determine the range of monitoring subject and the precision of measurement, and specialists for engineering of electronics and information technologies have significant roles for the development of brain imaging methods.

Owing to the recent development of molecular biology, functions of molecules inside the brain are being revealed, and collaborative researches between molecular biologists and physiologists using the brain imaging technologies are necessary to combine their results together for the integrated viewing of the brain activities and functions. As stated above, in this organization, it is necessary to form research groups including researchers of different fields, such as medicine, basic science and engineering, creating an interdisciplinary research system, irrespectively of the ordinal academic fields, to develop efficiently the brain imaging technologies and to advance effectively the researches using them.

(2) Training system of researchers and engineers

The number of members of the society for neuroscience in Japan is 2,000~3,000, 1/10 as compared with that of the United States, and those who are engaged in brain imaging research are only part of them. Considering that basic researches of higher functions in the brain (e.g., thinking, learning and memory) and diagnosis and therapy of neurological diseases, such as dementia and depression, will become more and more important in the future, the number of researchers relating to the brain imaging is considerably small and insufficient in Japan. To realize general medical care of neurological diseases on the whole country, it is necessary to train a large number of medical engineers who operate the machines to conduct the measurements. Therefore, at present, the important problem is training of researchers and engineers for the brain imaging, in order to promote the research on neurological diseases and realize medical care of them for general citizens. Brain imaging methods are fusion technologies of different fields, such as medicine, basic science and engineering, and, therefore, training of researchers and engineers in the brain imaging research needs special education, combining these fields together. However, curriculum is divided into the ordinal research fields in the present educational system of universities, so it is difficult to effectively conduct education of the fused region from different categories of technology. Education of brain imaging techniques is only being conducted at each of the research institutions on a small scale. Therefore, it is necessary to create an interdisciplinary training system in the newly constructed research organization, giving professional education of brain imaging using machines with advanced technologies to students, researchers and engineers of different fields from universities and research institutions across the whole country.

(3) System for effective usage of human resources and long-term research and development

In some cases, the present dispersed research system may lead to lacking of the mutual cooperation between individual laboratories and institutions, and even inflexible sectionalism of them. This may be one of the causes of inhibited mobility of human resources. On the other hand, this dispersed system may also cause problems in accumulation of the research results and continuation of the research and development in the long-term research field, such as brain imaging. In the new research organization, research themes will be selected among candidates applied from the whole country, and access to the research facilities with advanced technologies and the budget for research expenses will be provided for the adopted theme. This system will give an opportunity for using non-invasive measuring devices to researchers, who could not use them before, and, at the same time, it may be necessary to promote mobility of human resources, researchers and engineers for brain imaging, all over the country centering on the organization. The organization should have not only constancy to carry through the researches and accumulate their results, but also flexibly to change its research themes in corresponding with the changes in the social demand, if it is necessary, with periodical review of the performance of the organization.

1.5 Conclusion

As stated above, it is necessary to establish a collaborative research organization which can play the core role for promoting more research and development of brain imaging techniques, in order to develop and spread the techniques for medical care of neurological diseases, such as dementia.

In the United States, the National Institute of Biomedical Imaging and Bioengineering (NIBIB) was established within the National Institutes of Health (NIH) in 2000, and plays a major role in the development of imaging techniques for not only the brain but also the whole body, conducting researches in collaboration with other institutes. The mission of the NIBIB is to "improve health by promoting fundamental discoveries, design and development, and translation and assessment of technological capabilities. The Institute coordinates with biomedical imaging and bioengineering programs of other agencies and NIH institutes to support imaging and engineering research with potential medical applications and facilitates the transfer of such technologies to medical applications. [7]"

The theme of the core research organization of the brain imaging in Japan proposed in this article is the same as the NIBIB, returning the results of scientific research to the society. The organization should have a purpose "to promote fundamental and clinical researches in neurological diseases, and, based on the results, to develop diagnostic and therapeutic techniques for these diseases in order to improve the national health."

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