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Development of Optical Topography for Noninvasive Measurement of Human Brain Activity

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Summary

We developed Optical Topography that measures noninvasively topographic images of human brain activity from the scalp using near-infrared light. Optical Topography detects concentration changes in oxy- and deoxy-hemoglobin caused by human brain activity, and has the advantages of portability, real-time measurement, and less sensitivity to movement by subjects compared with other functional imaging techniques. For the advantages, we expect that Optical Topography will be popular from large hospitals to clinics as a new medical instrument.

Key Words: Optical topography, Noninvasive, Brain activity, Hemoglobin

1. Introduction

The interest in brain function has greatly increased on a worldwide basis, and a great amount of national funding has been put towards development of scientific technologies related to brain function, in the U.S.A., Europe and Japan. Particularly in Japan, with a rapidly aging society coming in the near future, development of preventive diagnostic techniques for various cerebral diseases such as dementia is urgently required. For such medical care noninvasive measurement of brain activity, that is, cerebral function is one of the most important technical aspects.

Applications of cerebral function measurement can be expanded to various fields such as social welfare, human engineering, information engineering, etc. and the measurement of cerebral functions can be considered as the basis of many scientific technologies in the twenty-first century.

2. Concept of Optical Topography

Near-infrared spectroscopy, for noninvasive measurement of brain activities has come to attention recently 1)-4). Because the visible light is strongly scattered by tissue, it is very difficult to use it for measurement of brain through scalp. On the other hand, near-infrared light with longer wavelength has relatively higher transmissivity through skin and scalp, thereby the light can reach the cerebrum surface.

Such transmissivity can be experimentally observed by the phenomenon that reddish light with longer wavelength can be seen when sun light is observed through the finger or palm.

Thus, utilization of near-infrared light with more longer wavelength allows percutaneous measurement of cerebral cortex located just inside scalp through skin of scalp (Fig. 1).

In near-infrared spectroscopy, changes in concentration of oxy- and deoxy-hemoglobin as well as total hemoglobin, which corresponds to blood volume are measured. The optical absorption spectra of hemoglobin is shown in Fig. 2[5].

Brain activity is characterized by the firing of nerve cells. This neuro-activity results in active energy metabolism and causes secondary increases in blood volume and blood flow to supply glucose and oxygen to brain. Thus, the change in concentration of hemoglobin is also an important index to know brain activity.

Using the advantage of near-infrared spectroscopy, we have recently developed "Optical Topography" as a new concept to noninvasively image brain activity[6)-9)].

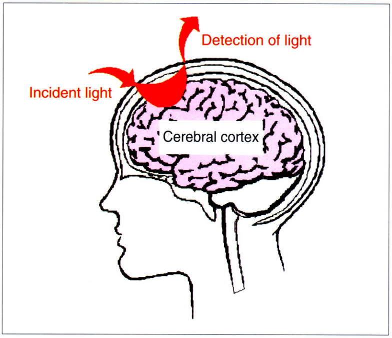

Fig. 1

Measurement of Cerebral Cortex by Near-infrared Light through Scalp

In this paper, the term Topography is used as 2-dimensional image measurement method. In this technique, cerebral cortex is the object to be measured and, by means of multi-channel optical measurement over skin of scalp (Fig. 3), activity of cerebral cortex is visualized.

The cerebral cortex is associated with high level functions such as motion, sensation, perception, language, etc., and nerve cells and blood vessels congregate densely on that surface. This means that the cerebral cortex is very suitable for noninvasive and effective measurement of changes in concentration of blood hemoglobin associated with brain activity.

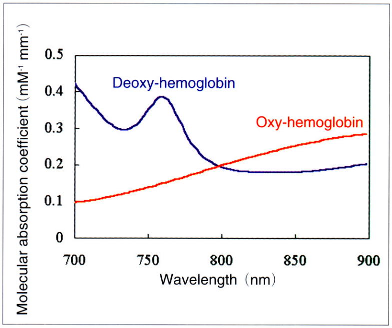

Fig. 2

Light Absorption Spectrum of Hemoglobin Optical fiber

Fig. 3

Measurement Probes for Optical Topography

Table 1 shows features of Optical Topography in comparison with other conventional cerebral functional imaging modalities such as PET, fMRI and magnetic encephalography.

The most favorable features of Optical Topography are the compact size, easy-operation and extremely low patient-restraint as compared with the conventional modalities.

In Optical Topography, semiconductor laser and photodiode technologies have realized a compact, easy-to-operate measuring system and the highly flexible optical fiber requires no immobilization of patient head. These features allow the patient to undergo real-time examination of cerebral functions for a long time at any place and environment.

Currently, spatial resolution of Optical Topography is about 20mm, which is inferior to those of the other technologies and its improvement is under technical development. Since the fraction of light irradiated through the scalp and reaching deep inside the brain is very little, the measurable zone is limited to cerebral cortex in adults and the measurement is not suitable for the deep inside of the brain. In fMRI, contrast is determined by the change in concentration of deoxy-hemoglobin, however, in Optical Topography changes in concentration of deoxy-hemoglobin and oxy-hemoglobin as well as total hemoglobin can be simultaneously obtained, thus changes in blood flow dynamics associated with brain activity can be evaluated from diversified angles.

Table 1 Comparison with Conventional Modalities

	PET	fMRI	Magnetic encephalography	Optical topography
Measurement with low patient-restraint · In any environment · Lengthy measurement	×	×	×	◎
Spatial resolution	△ (~15mm)	○ (~2mm)	(○) (5~15mm)	△ (~20mm)
Deep brain measurement	○	○	△	×
Measurable object	Blood Metabolic materials	Blood Deoxy-hemoglobin	Neuro-current	Blood Oxy-hemoglobin Deoxy-hemoglobin

3. Optical Topography System

3.1 System configuration

The Optical Topography system configuration is shown in Fig.4. In this system, the intensity of light emitted from 8 pairs of semiconductor lasers with wavelength of 780nm and 830nm is modulated with sine waves of different frequencies (in a range from 1kHz to 10kHz). The light beams with 2 different wavelengths are guided through 8 optical fibers onto different regions of the patient. That is, each semiconductor laser is coded with different modulation frequency for each wavelength and irradiation region.

The intensity of this radiation light is 1mW/mm^2 that is less than the maximum allowable light exposure value (2mW/mm^2) specified by JIS (Japan Industrial Standards C6802) for laser radiation to skin.

Reflected light from the patient is detected with 8 photodiode detectors (PD) via 8 detector optical fibers. The signal output from the PDs are distributed and input to the multi-channel lock-in amplifiers. The lock-in amplifier is a filter circuit with high selectivity for modulated signal, and reflected light intensity is separated for each of wavelength and irradiation region and simultaneously measured. The signal from the lock-in amplifier is A/D-converted and the data are acquired in 0.5sec intervals by computer.

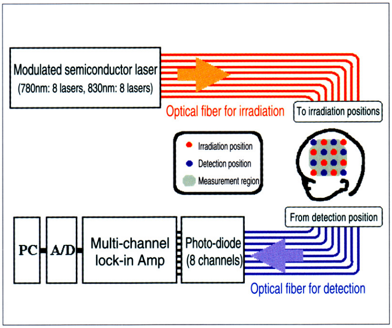

Fig. 4

Optical Topography System Configuration

3.2 Layout of measurement regions

To acquire information on cerebral cortex percutaneously, an interval between irradiation and detection positions must be about 30mm [10]. Therefore, 8 irradiation fiber probes and 8 detector fibers are alternately arrayed on square grid pattern in 30mm intervals. An array example of the irradiation and detection positions is shown in Fig. 5. Since light mainly penetrates the cerebral cortex at the mid point between each irradiation and detection position, the mid point between each adjacent irradiation position and detection position is set as measurement region (measurement channel).

According to this measurement array, 24 measurement channels can be set.

3.3 Measured signal process

Amount of the detected light $R(\lambda)$ with the wavelength λ at each measurement position is expressed by the following equation.

$$-\ln\left[\frac{R(\lambda)}{R_0(\lambda)}\right]=\varepsilon_{\mathrm{oxy}}(\lambda)C_{\mathrm{oxy}}d+\varepsilon_{\mathrm{deoxy}}(\lambda)C_{\mathrm{deoxy}}d+a(\lambda)+s(\lambda)\cdots\cdots(1)$$

where,

$R_0(\lambda)$: Amount of irradiation light.

$\varepsilon_{\mathrm{oxy}}(\lambda)$ and $\varepsilon_{\mathrm{deoxy}}(\lambda)$: Molecular absorption efficiency of oxy- and deoxy-hemoglobin at wavelength λ.

C_{oxy} and C_{deoxy} : Concentration of oxy- and deoxy-hemoglobin.

d : Effective length of optical path in active region of cerebral cortex.

$a(\lambda)$: Attenuation due to light absorption by pigments (such as cytochrome aa_3) other than hemoglobin.

$s(\lambda)$: Attenuation due to light scattering through Tissues.

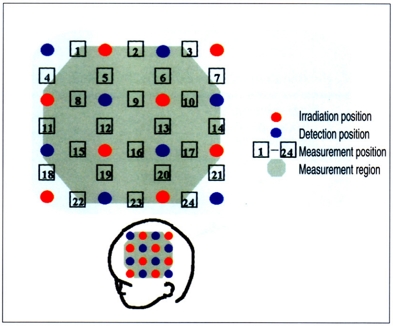

Fig. 5

Array of Measurement Positions

When stimulation is given to brain, the concentration and oxygenation of hemoglobin changes, and amount of detected light changes accordingly as follows.

$$-\ln\left[\frac{R^{\mathrm{sti}}(\lambda)}{R_0(\lambda)}\right]=\varepsilon_{\mathrm{oxy}}(\lambda)C^{\mathrm{sti}}_{\mathrm{oxy}}d+\varepsilon_{\mathrm{deoxy}}(\lambda)C^{\mathrm{sti}}_{\mathrm{deoxy}}d+a^{\mathrm{sti}}(\lambda)+s(\lambda)\cdots\cdots(2)$$

where, the character superscript "sti" represents a value of each variable under stimulation.

Because the total light absorption by hemoglobin in live body in the near-infrared region is about 10 times greater than that of cytochrome aa_3 that is the major term of $a(\lambda)$, neglecting change in $a(\lambda)$ caused by stimulation, an assumption of $a(\lambda)=a^{\mathrm{sti}}(\lambda)$ is given. Furthermore, by subtracting the equation (1) from the equation (2), the following equation can be obtained.

$$-\ln\left[\frac{R^{\mathrm{sti}}(\lambda)}{R(\lambda)}\right]=\varepsilon_{\mathrm{oxy}}(\lambda)\Delta C_{\mathrm{oxy}}+\varepsilon_{\mathrm{deoxy}}(\lambda)\Delta C_{\mathrm{deoxy}}\cdots\cdots\cdots(3)$$

where, $\Delta C_{\mathrm{oxy}}=(C^{\mathrm{sti}}_{\mathrm{oxy}}-C_{\mathrm{oxy}})d$ and $\Delta C_{\mathrm{deoxy}}=(C^{\mathrm{sti}}_{\mathrm{deoxy}}-C_{\mathrm{deoxy}})d$ is defined.

Since it is actually difficult to obtain the effective length d of the optical path in the active region of cerebral cortex, relative changes in concentration, ΔC_{oxy} and $\Delta C_{\mathrm{deoxy}}$, of hemoglobin associated with brain activity are obtained in mM·mm unit.

The measurement with dual wavelengths at each measurement position allows the solution of simultaneous equations (3) for ΔC_{oxy} and $\Delta C_{\mathrm{deoxy}}$. By applying cubic spline interpolation to the acquired concentration values of these hemoglobins at each measurement position, the topographic image can be obtained.

4. Measurement of Cerebral Functions

Using the Optical Topography method, brain activity associated with finger motion was measured first.

As the brain activity associated with finger motion has been clarified by the conventional technologies such as PET and fMRI, this measurement was made to verify the effectiveness of Optical Topography for cerebral function measurement. Volunteers were 5 right-handed healthy persons of 29 to 53 years old. The measurement area of head was set at the region from forehead to vertex of left head. The volunteers closed their eyes and lay in rest supine position. As stimulation to brain, random tapping motion of fingers (touching thumb to other finger randomly) was repeated for 30sec. each for right hand and left hand and 10 times alternately. The data from these measurements made 10 times were added up in signal processing.

From the measurements of light detected at each wavelength in the rest period and stimulation period, changes in concentrations of oxy- and deoxy-hemoglobins and total hemoglobin were obtained, and displayed as topographic images. A typical result is shown in Fig. 6. With regard to kinetic function, the left cerebral hemisphere governs the right part of the body, and it was demonstrated that during motion of right fingers the concentrations of oxy-hemoglobin and total hemoglobin remarkably increased regionally and the concentration of deoxy-hemoglobin decreased regionally. On the other hand, there was little change during stimulation by left fingers which has little association with the left cerebral hemisphere.

To clarify the active region anatomically, the morphologic brain of the same person was scanned by MRI and the central sulcus as one of sulci was projected on the skin of scalp. The region associated with kinetic function (motor area) of fingers is located near the central sulcus and it is shown that the region is located at the same position as the active region obtained by Optical Topography.

As a result of the above analysis, it was verified that the cerebral function was accurately measured by Optical Topography.

5. Measurement of Epilepsy Focus Position

Optical Topography was applied to measure epilepsy focus position, and its clinical effectiveness was evaluated. In case of refractory epilepsy difficult to cure even by medication, surgical removal at the epilepsy focus has been adopted, and for that purpose it is necessary to locate the epilepsy focus to be removed.

However, there are many cases in which it is difficult to determine which cerebral hemisphere the focus is located. Conventional examinations include encephalography for which several electrodes are put on the surface of brain or inserted deep into the brain or SPECT for which a radioactive isotope is injected into blood as tracer. In either case, the examination is difficult for the patient.

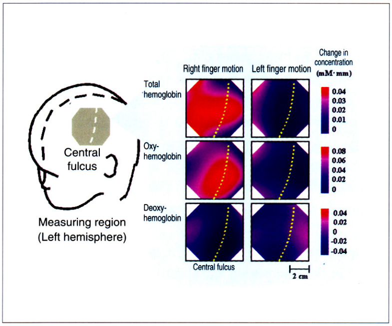

Fig. 6

Measurement of Cerebral Function for Finger Motion

Simultaneously during SPECT examination, noninvasive Optical Topography was also applied to measure activities in both right and left cerebral hemispheres at the time of epileptic attack. In this case the irradiation and detection regions were distributed to the right and left cerebral hemispheres.

A case of this measurement results is shown in Fig. 7. In the case that increase in blood flow volume in the right hemisphere was noticed at the time of epileptic attack by SPECT examination, the Optical Topography also demonstrated increase in concentration of total hemoglobin in the right hemisphere and the same result as that of SPECT examination was obtained.

The summary of the clinical results for the 7 cases according to the final diagnosis, SPECT examination and Optical Topography for positions of epilepsy focuses in right and left cerebral hemispheres are shown in Table 2. From this table, it is verified that the results by Optical Topography agree with those of the final diagnosis in all cases and the new diagnostic modality of Optical Topography is effective in measurement of position of epilepsy focus.

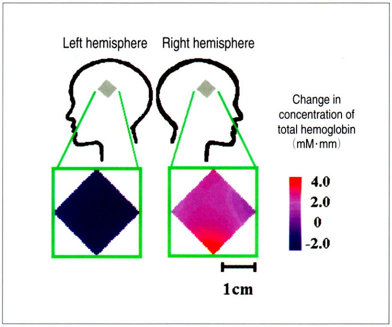

Fig. 7

Application to Measurement of Epilepsy Focus Position

Table 2 Examination Results on Epilepsy Focus Position

	Final diagnosis of Focus position (Right & left cerebral hemisphere)	SPECT	Optical Topography
Case 1	Right	Right	Right
Case 2	Left	Not clear	Left
Case 3	Left	Left	Left
Case 4	Right	Right	Right
Case 5	Left	Left (small difference)	Left
Case 6	Left	Left	Left
Case 7	Right	Right	Right

6. Conclusion

Optical Topography, which can be applied to image cerebral functions by using light noninvasively, has been developed. It is verified that the system can be effectively used for imaging brain activities associated with finger motion and for clinical measurement of epilepsy focus position.

There are still technical challenges to be solved for improvement of performance of the system such as expansion of measurable region, time and spatial resolution, etc., however, application of the Optical Topography can be considered hopeful in wide clinical fields in the future because of the noninvasive examination and low patient-restraint.

We have just developed a new optical topography system with higher performance, which can be expected to widen its application further (Fig. 8).

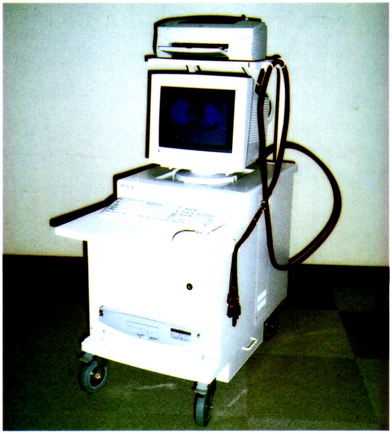

Fig. 8

Optical Topography System

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