Absorber's Effect Projected Directly Above Improves Spatial Resolution in Near Infrared Backscattered Imaging

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Abstract: The spatial resolution of near infrared spectroscopic imaging in brain function mapping studies needs to be improved. Most near infrared spectroscopic imaging systems use optical fibers that are arranged like a lattice. The light source and the detector have one-on-one correspondence at intervals of about 3 cm. In this study, we apply several detectors against one source to improve spatial resolution. We assume that a local absorber within a strong scattering medium is a model for local cerebral activation. When we calculate absorbance, which is used to spectroscopically calculate hemoglobin concentration, the peak position shifts away from above the position where an absorber is located. As far

as absorbance is calculated, we cannot obtain spatial information about the absorber even if many detectors are used against one source. When we calculate the difference between detected light intensities, however, we demonstrate that an absorber projected onto the measuring surface has an influence directly above it. We predict this property from a light diffusion equation and also prove it experimentally through measurements of a uniform resinous phantom with an absorber. This is one of the basic principles supporting the achievement of higher spatial resolutions with near infrared spectroscopic imaging. [The Japanese Journal of Physiology 54: 79–86, 2004]

Key words: near infrared light, backscattered imaging, spatial resolution, polyacetal phantom, brain science.

Near infrared spectroscopic imaging has become one of the most powerful tools in the study of human brain functions. It can detect human brain activations noninvasively because near infrared light transmits living tissue well [1]. Transmitted and scattered light can be detected at points several centimeters away from the injection point after near infrared light has been directed onto the scalp. Part of the detected light passes through the brain cortex [2]. We can calculate changes in oxygenated hemoglobin concentrations and deoxygenated hemoglobin concentrations that are caused by brain activity because hemoglobin has characteristic

absorption spectra. Human brain functions measured by near infrared light obtained by use of a pair of light source and detector probes were reported in 1993 by Chance *et al.*, Villringer *et al.*, Hoshi and Tamura, and Kato *et al.* [3–6]. Subsequently, researchers using multiple probes reported diffuse tomographic imaging [7–10].

Present human brain function studies use a near infrared spectroscopic imaging system that visualizes hemodynamic changes in the cortex as a topographic image. This system makes topographic images from data sets measured through spatially set multiple

Received on December 16, 2003; accepted on February 6, 2004

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probe pairs [11–13]. Many basic studies on brain functions have been done with the near infrared spectroscopic imaging system. For example, this system detected detailed hemodynamic changes in the primary cortex [14, 15] and could be used for simultaneous recording with magnetic resonance imaging (MRI) [16–18]. Moreover, research that could only have been carried out with a near infrared spectroscopic imaging system has been reported. For example, the system has been used to detect brain activation during gait [19], to measure the brain activation of infants [20–22], and to simultaneously record with transcranial magnetic stimulation (TMS) [23]. When the system is used, the light source and the detector are placed apart at intervals of about 3 cm. It is believed that the ratio of light passing through the brain cortex is low when the interval is less than 3 cm [24, 25]. The spatial resolution of near infrared spectroscopic imaging has been fixed by this probe interval distance.

In brain function mapping studies, however, improved spatial resolution is needed. Studies that have aimed at improving the spatial resolution of near infrared spectroscopic imaging have been reported. Yamamoto *et al.* multiplied the density of probe pairs and improved the accuracy of spatial information [26]. However, the practice of one data item being represented by one probe pair at an interval of about 3 cm has remained unchanged.

In this study, our aim was to detect the absorber's position independent of probe interval distances. We introduced an approach with multiple detectors against one source and not the conventional probe pair, which consisted of a single detector against one source. We assumed that changes in local absorption occurred within a strong scattering medium in a model of human brain activation at the cerebral cortex. We discuss this theoretically from the viewpoint of a light diffusion equation and also experimentally from the measurement of a resinous phantom with an absorber.

Light diffusion equation. During optical measurement, light is injected from a point source to a medium, and changes in light signal at a detector are measured. Light propagation in tissue with strong scattering can be described through a light diffusion equation [27]. The contribution of internal optical properties to the signal, in other words, the photon-measurement density function (PMDF), has been investigated [25, 28, 29]. This corresponded to the change in signal that is caused by moving the absorber's position in the medium when the source and the detector are fixed. In our study, we fixed the posi-

tions of the source and absorber first and considered how the absorber influenced signals at the measuring surface. This corresponded to the contribution of signals detected by multiple detectors against one source. This is another model that is different from PMDF.

Farrell *et al.* derived an analytical solution of light diffusion equation to the semi-infinite condition [27]. The geometry of the model is illustrated in Fig. 1, and the origin of the coordinates is defined as the source position on the medium. The ρ axis is taken as a line parallel to the measuring surface, and the z axis is taken as a line directed directly below the source. We applied an extrapolated boundary condition, which satisfied the condition that the summation of a positive real source and a negative image source was zero. Fluence rate ϕ at point (ρ, z) in the medium is described by Eqs. 1–8 [27].

$$\phi(\rho, z) = \frac{1}{4\pi D} \cdot \left(\frac{\exp(-\mu_{\text{eff}} \cdot r_p)}{r_p} - \frac{\exp(-\mu_{\text{eff}} \cdot r_n)}{r_n} \right) \quad (1)$$

where r_p is the distance between the positive source and point (ρ, z) , and r_n is the distance between the negative source and point (ρ, z) .

$$r_p = \sqrt{(z - z_0)^2 + \rho^2} \quad (2)$$

and

$$r_n = \sqrt{(z + z_0 + 2z_b)^2 + \rho^2} \quad (3)$$

Fig. 1. Concept of light propagation in strong scattering medium in semi-infinite model. Fluence rate in the medium is calculated by extrapolated boundary. The extrapolated boundary is a zero boundary, which is the sum of a positive and negative source. The position of an extrapolated boundary that has a zero value is z_b . The distance between a positive source and a point (ρ, z) is r_p , and the distance between a negative source and a point (ρ, z) is r_n .

$$\mu_{\text{eff}} = \sqrt{3\mu_a \cdot \mu_s'} \quad (4)$$

$$z_0 = \frac{1}{\mu_s'} \quad (5)$$

$$z_b = 2AD \quad (6)$$

$$A = (1 + r_d)/(1 - r_d) \quad (7)$$

and

$$r_d = -1.440n_{\text{rel}}^{-2} + 0.710n_{\text{rel}}^{-1} + 0.668 + 0.0636n_{\text{rel}} \quad (8)$$

where μ_{eff} is the effective attenuation coefficient, μ_a is the absorption coefficient, μ_s' is the reduced scattering coefficient, z_b is the distance of extrapolated boundary from the origin, and n_{rel} is the relative refractive index of the medium-air interface.

$$D = \frac{1}{3\mu_s'} \quad (9)$$

where D is the diffusion constant, which contains only μ_s' [30]. In reflectance measurement, the signal intensity, which is proportional to the fluence rate at the surface, can be measured experimentally.

We considered an inhomogeneous case, which has an absorber in high scattering media, as the model for local cerebral activations. Figure 2 has an illustration of the model. In this paper, we made two assumptions. The first was decreased fluence rate because of the absorber at position $(\rho_{\text{absorber}}, z_{\text{absorber}})$, which was defined as “Dark fluence rate,” and described by Eq. 10.

$$\text{Dark fluence rate} = \text{dark_fr}(\rho, 0) \Big|_{\text{Absorber}(\rho_{\text{absorber}}, z_{\text{absorber}})} \quad (10)$$

Fig. 2. An absorber $(\rho_{\text{absorber}}, z_{\text{absorber}})$ produces a dark fluence rate. The origin of the ρ - z plane is set as the source position. Dark fluence rate is calculated as a multiplication fluence rate at the absorber position and the transfer function from an absorber to the measuring surface. The circular dotted curves indicate $f_{\text{absorber-surface}}$, which is the transfer function from an absorber to the measuring surface.

The second was measurable fluence rate $\Phi(\rho)$ at the measuring surface under the case with the absorber equaled the sum of the fluence rate $\phi(\rho, 0)$ under the case without an absorber and “Dark fluence rate,” $\text{dark_fr}(\rho, 0)$. This assumption was derived from first-order born approximation to the light diffusion equation. Our assumptions are described in Eq. 11.

$$\Phi(\rho) = \phi(\rho, 0) + \text{dark_fr}(\rho, 0) \Big|_{\text{Absorber}(\rho_{\text{absorber}}, z_{\text{absorber}})} \quad (11)$$

The light diffusion equation was basically applied only to the homogeneous medium. In this study, however, we assumed that the light diffusion equation would be able to be applied to calculate the influence of local absorbance change within the medium had on signals at the measuring surface.

“Dark fluence rate” in the medium can be calculated as follows. First, we should calculate the fluence rate that reaches the absorber and how much is absorbed by it. Next, let us consider by using the light diffusion equation how the absorber’s influence propagates to the measuring surface. We define the fluence rate at the absorber’s position as $\phi(\rho_{\text{absorber}}, z_{\text{absorber}})$ and the transfer function from the absorber to the measuring surface as $f_{\text{absorber-surface}}$. “Dark fluence rate,” at the detector position is given by Eq. 12.

$$\begin{aligned} \text{dark_fr}(\rho, 0) \Big|_{\text{Absorber}(\rho_{\text{absorber}}, z_{\text{absorber}})} \\ = -\phi(\rho_{\text{absorber}}, z_{\text{absorber}}) \cdot f_{\text{absorber-surface}} \cdot k \end{aligned} \quad (12)$$

where k is a constant, including the absorbance coefficient of the absorber and optical path length in the absorber. Equation 13 is derived according to Eqs. 11 and 12.

$$\begin{aligned} \Phi(\rho) &= \phi(\rho, 0) + \text{dark_fr}(\rho, 0) \Big|_{\text{Absorber}(\rho_{\text{absorber}}, z_{\text{absorber}})} \\ &= \phi(\rho, 0) - \phi(\rho_{\text{absorber}}, z_{\text{absorber}}) \cdot f_{\text{absorber-surface}} \cdot k \end{aligned} \quad (13)$$

We calculated Abs, which is a logarithmic calculation, and Diff, which is subtraction as the absorber’s effect. Abs was calculated by the use of Eq. 14.

$$\begin{aligned} \text{Abs} &= -\log_{10} \left(\frac{\Phi(\rho)}{\phi(\rho, 0)} \right) \\ &= -\log_{10} \left(\frac{-\phi(\rho_{\text{absorber}}, z_{\text{absorber}}) \cdot f_{\text{absorber-surface}} \cdot k}{\phi(\rho, 0)} + 1 \right) \end{aligned} \quad (14)$$

Diff was calculated by the use of Eq. 15.

$$\begin{aligned} \text{Diff} &= \Phi(\rho) - \phi(\rho, 0) \\ &= -\phi(\rho_{\text{absorber}}, z_{\text{absorber}}) \cdot f_{\text{absorber-surface}} \cdot k \quad (15) \end{aligned}$$

$\phi(\rho, 0)$ has spatially spreading values, which are exponentially decaying from the light source position. The solution to Eq. 14 includes $\phi(\rho, 0)$, but that of Eq. 15 does not include $\phi(\rho, 0)$. This does not affect the spatial information of either Abs or Diff when the positions of the source and the detector are fixed for PMDF. However, this has a bad influence on the spatial information of Abs when the positions of the detector are not fixed. We expected that spatial information on the absorber would be concealed in the Abs calculation because of $\phi(\rho, 0)$ [31]. On the contrary, Diff is calculated, the absorber's effect propagates to the measuring surface directly above it in manner of diffusion. Because diffusion is a function of distance, attenuation is small when the distance is short. The position on the measuring surface, which has the shortest distance between the absorber and measuring surface, is directly above the absorber. Consequently, we expected that the absorber would affect projection to the measuring surface directly above the absorber when the difference between the detected light intensities was calculated.

METHODS

We used the near infrared optical imaging system (OPTIM_A) developed by our group [13, 16]. This system has 12 optical source probes bundling three laser diodes (780, 805, and 830 nm) and 12 detector probes leading to the photo multiplier tubes. The diameter of both probes is 2 mm. We generally placed these probes in latticed positions to acquire topographic images. The system could acquire topographic functional images of relative changes in oxygenated, deoxygenated, and total hemoglobin concentrations. We could use it not only in clinical use, but also in basic optical-measurement studies by using a subset of its function. In this study, we used only one probe pair from this system, and we used a 780 nm wavelength light-source and a constant gained photo-multiplier.

We prepared a phantom as the measuring object (Fig. 3). It was made of white resin (polyacetal, absorption coefficient: 0.001 mm^{-1} ; reduced scattering coefficient: 1 mm^{-1}) that had a scattering characteristic comparable to living tissue. It consisted of a fixed body and a slidable slab. The slider was 10 mm thick and slid horizontally at a depth 10 mm from the measuring surface. It had a tablet pocket, which was a hole 10 mm in diameter. We made white and black

Fig. 3. Diagram of phantom for measuring object. The phantom consists of a body and a slider. The slider is 10 mm thick. It has a tablet pocket 10 mm in diameter. The body, slider, and white tablet have the same optical properties. The black tablet is an absorber. The tablets are 10 mm in diameter and 5 mm thick.

Fig. 4. Experimental scheme to measure phantom. The detector positions are 10, 15, 20, 25, 30, 35, 40, and 45 mm on the ρ_1 axis, and the tablet positions are 20, 25, 30, and 35 mm on the ρ_2 axis, which is 12.5 mm beneath the ρ_1 axis.

tablets, which were cylinders 10 mm in diameter and 5 mm in thickness. The white tablet was made of the same resin as the body, and the black tablet was the absorber. Thus we could place the tablet at the position being aimed at.

Figure 4 shows the experimental scheme. The ρ_1 axis is taken as the line where the detector is placed, and the origin of this axis is defined as the source position. The ρ_2 axis is also taken as a line parallel to the ρ_1 axis that passes through the center of the tablet, and the origin of the ρ_2 axis is defined as being directly below the source. The experiment was done as follows. First we placed the white tablet into the tablet pocket in the slider. We placed the detector on the phantom 10 mm away from the source and detected light intensity. The detector was placed at 5 mm steps away from the source, and the light intensity was measured at 8 points (10, 15, 20, 25, 30, 35, 40, and 45 mm on ρ_1 axis). The detected light intensities were defined as white tablet data for reference. Next we placed the black tablet into the tablet pocket. The cen-

ter of the black tablet was placed at a depth of 12.5 mm from the measuring surface. We repeated the sequence of measurements under four black tablet conditions (20, 25, 30, and 35 mm on ρ_2 axis). We then obtained the data sets under all conditions as black tablet data.

RESULTS

We plotted the detected light intensity at each detector position when the tablet was positioned 25 mm on the ρ_2 axis. Figure 5(a) shows this in logarithmic scale, and Fig. 5(b) shows it in linear scale. The plot indicates the reference data when the white tablet was used. As the source-detector distance is wider, detected light intensity decreased exponentially. The detected light intensity with the black tablet is smaller than that of the white tablet.

We detected light intensity at each detector position and at each tablet position. We calculated “Abs” and “Diff” as the absorber’s effect from the data sets for the white and black tablets.

We calculated the Abs with Eq. 16.

Fig. 5. Light intensity with white or black tablets. The black tablet is 25 mm on ρ_2 axis as an absorber. (a) Light intensity is indicated by a logarithmic scale. (b) Light intensity is indicated by a linear scale.

$$\text{Abs} = -\log_{10} \left(\frac{\text{black tablet data}}{\text{white tablet data}} \right) \quad (16)$$

This calculation corresponds to the differences between the two curves in Fig. 5(a). Figure 6(a) shows that the peak for the absorber’s effect in Abs shifts away from above the black tablet. We also calculated Diff with Eq. 17.

$$\text{Diff} = \text{black tablet data} - \text{white tablet data} \quad (17)$$

This calculation corresponds to the differences between the two curves in Fig. 5(b). Figure 6(b) shows that the peak for the absorber’s effect in Diff appears directly above the black tablet.

Figure 7 plots Diff data sets under each tablet position (20, 25, 30, 35 mm on ρ_2 axis). The peak intensity decreases as the distance between the source and tablet increases.

DISCUSSION

When we produce images from spatially multiple measured data sets to establish where the absorber is, the peak for the data should indicate the absorber’s position. Figure 6(a) shows that the peak position for

Fig. 6. Differences with and without absorber. (a) Abs indicates change in absorbance. (b) Diff indicates change in light intensity.

Abs shifts away from above the absorber because of the spatial distribution in the reference data. This means that as far as Abs is calculated, we cannot know where the absorber is. It is widely known that light pathways between the light source and the detector within a medium have a banana shape. When the positions of the source and detector are fixed, the midpoint between them has the best sensitivity with or without an absorber. This is a different model from this study's in that the optimal detection point is sought after the position of the source and the absorber is fixed. When we fix source and absorber positions and calculate Abs, we can only say that the optimal detector position shifts from above the absorber. In reflectance imaging, estimating the absorber's position by calculating Abs is very difficult.

We demonstrated that the Diff absorber's effect appears directly above the absorber from theoretical and experimental results in Fig. 6(b). This means that the peak for measured data indicates that the absorber's position is in contrast to Abs. In an estimation of the absorber's position, Diff has an advantage over Abs, which is conventionally calculated for hemoglobin concentration changes. Improved spatial resolution is expected when we use multiple detectors against one source and calculate Diff.

As we can see in Fig. 7, the absorber's effect appears directly above the absorber in calculating Diff regardless of source-detector distances. We divided the curve for Diff in Fig. 7 by the value measured when the detector is placed above the absorber. After this standardization, we overlapped the four curves in Fig. 8 as the relative positions between the absorber and the detector positions were the same. The shapes of the four curves in Fig. 8 acquired from different source-detector distances are approximately consistent. Diff is calculated as $-\phi(r_{\text{absorber}}, z_{\text{absorber}}) \cdot f_{\text{absorber-source}} \cdot k$ in the light diffusion equation. We can interpret that this equation has a light source whose fluence rate is $-\phi(r_{\text{absorber}}, z_{\text{absorber}}) \cdot k$ and the diffusion from the source is represented as $f_{\text{absorber-source}}$. According to this interpretation, $-\phi(r_{\text{absorber}}, z_{\text{absorber}}) \cdot k$ is proportional to the peak for the curve in Fig. 7, and $f_{\text{absorber-source}}$ corresponds to how much the curve in Fig. 8 is blurred. Constant curve blur independent of the source-detector distance is expected from the light diffusion equation when the depth of absorber z_{absorber} is constant. Figure 8 indicates that the experimental data are consistent with this theoretical expectation.

The curves in Fig. 8 are more expanded than the actual size of the absorber. The image of the absorber has blurred because light is scattered. From the experimental data in Fig. 8, we defined the full width at

Fig. 7. Difference in light intensity under four absorber positions. An absorber is at 20, 25, 30, or 35 mm on the p_2 axis.

Fig. 8. Standardization of difference in light intensity under four absorber positions. Four curves for relative distance between absorber and detector positions are plotted as absorber positions are centered. The FWHM of four curves are approximately the same.

half-maximum (FWHM) of the curve as the degree of blurring. Under these experimental conditions, we observed an absorber with an actual diameter of 10 mm as being about 23 mm at FWHM. Here we defined the spatial resolution as 13 mm, which was derived by subtracting 10 mm from 23 mm. We demonstrated that we could effectively obtain spatial information different from the conventional measurement method that had only one data item per about 30 mm. Functional MRI (fMRI) has the highest spatial resolution of all current noninvasive brain function measuring equipment. MRI certainly acquires functional images in the mm-order scale. However, in many cases, the images need to be smoothed in preprocessing analysis. The effective spatial resolution of fMRI data depends on the Gaussian kernel size used for smoothing. Worsley and Friston discussed it and used kernel sizes of 4, 8, and 16 mm; they recommended that smoothness should be at least twice the voxel size [32]. It can be said that an effective spatial resolution of fMRI data

for analysis is effectively about 1 cm. Compared to fMRI, our results indicate that near infrared spectroscopic measurements satisfied the values required by noninvasive human brain function studies.

Present human brain function studies, in other words human brain function mapping studies, have tended to attach importance to obtaining the position of activation instead of determining the quantity of activation. We need studies like this one that are oriented toward obtaining detailed positions for activation to obtain clearer findings on human brain function studies. When we use multiple detectors against one source and calculate Diff, we can directly obtain the position of the absorber. This property is one of the basic principles in improving the spatial resolution of near infrared spectroscopic imaging in studies on human brain functions.

We would like to thank Dr. I. Sase, Dr. T. Murata, and the other brain information group members for their critical discussions. This work was supported in part by a Research Fellowship Grant (JSPS-H13-DC1-01120) from the Japan Society for the Promotion of Science for Young Scientists.

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