OPTICAL DIFFUSION TOMOGRAPHY

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ABSTRACT

Functional changes in living tissues are often associated with changes in their optical properties as well. The relatively low absorption of near-infrared light makes it possible to noninvasively study, e.g., the functions of the human cortex. Near-infrared imaging for tomographic investigations is, however, complicated due to the strong scattering of light. Nevertheless, optical diffusion tomography is developing into a new promising method with a number of applications both in basic research and in clinical work.

INTRODUCTION

The various modalities used for medical imaging are often classified into anatomical and functional imaging methods. The main methods for 3-D anatomical imaging are computed tomography (CT) and magnetic resonance imaging (MRI). Also ultrasound methods produce anatomical information.

In clinical use, there are several methods to obtain functional information of the human body. Bioelectromagnetic methods, such as electro/magnetocardiography or electro/magnetoencephalography provide functional information of the heart and the brain, respectively [1]. Nuclear medicine imaging modalities, e.g., single-photon or positron-emission tomography, are used for functional studies as well. As a research tool, functional magnetic resonance imaging is developing rapidly. Another recent method is optical diffusion tomography [2,3].

INTERACTION BETWEEN LIGHT AND TISSUE

Visible light penetrates only weakly into most human tissues. When near-infrared light is used instead, the penetration depth increases within the optical window at wavelengths approximately between 700 and 900 nm. Detection of the light is then possible even after transmission of several centimeters in the tissue. However, although the absorption of the infrared light is relatively low, the scattering is strong. In a simple collimated geometry, the attenuation of light intensity I as a function of path length d in the medium can be approximated by the Beer-Lambert law

$$I(d) = I_o e^{-(\mu_a+\mu_s)d}. \tag{1}$$

The absorption coefficient μ_a depends strongly on the concentrations of oxyhemoglobin (HbO_2) and deoxyhemoglobin (Hb) in the tissue, whereas the scattering coefficient μ_s is rather insensitive to their concentration changes. In pulse oximetry, relation (1) is applied to study the oxygen saturation in arterial blood. For imaging purposes, a more detailed model is needed to describe the migration of photons in the tissue (see Fig. 1).

In a chosen direction $\hat{s}$, the energy flow, as defined by the total radiance $L(\vec{r},\hat{s})$ in $[\mathrm{Wm^{-2}sr^{-1}}]$ leaving a reference surface, is obtained from

$$\frac{1}{c}\frac{dL(\vec{r},t,\hat{s})}{dt} + \frac{dL(\vec{r},t,\hat{s})}{ds} = -(\mu_a+\mu_s)L(\vec{r},t,\hat{s}) + \mu_s \int_{4\pi} p(\hat{s},\hat{s}')L(\vec{r},t,\hat{s}')d\Omega' + S(\vec{r},t,\hat{s}). \tag{2}$$

The first term on the right describes attenuation of radiance and the second term increase in radiance due to scattering. The function $p(\hat{s}, \hat{s}')$ is the scattering probability from the direction $\hat{s}'$ to $\hat{s}$. The term $S(\vec{r}, \hat{s})$ is a source at $\vec{r}$ in [$\mathrm{Wm^{-3}sr^{-1}}$]. Eq. (2) is of integrodifferential type and cannot, in general, be solved analytically. It should be noted that all the variables in the equation can be time dependent. In order to solve Eq. (2), the diffusion approximation, valid in the limit of strong scattering ($\mu_s >> \mu_a$), is often used. The governing differential equation in this approximation is obtained by truncating the spherical-harmonics expansion of Eq. (2). In the frequency domain with a modulation frequency of $\omega = 2\pi f$, this leads to an equation

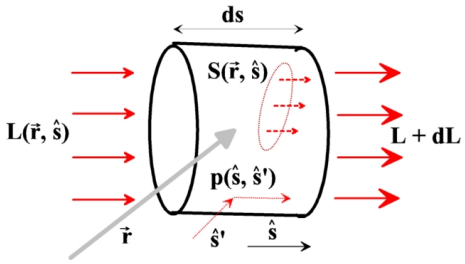

Fig. 1. A model for radiant energy flow in tissue.

$$-i\frac{\omega}{c}\phi_\omega(\vec{r}) - \nabla \cdot \kappa(\vec{r})\nabla\phi_\omega(\vec{r}) + \mu_a(\vec{r})\phi_\omega(\vec{r}) = s_\omega(\vec{r}), \tag{3}$$

where $\kappa(\vec{r}) = [3(\mu_a(\vec{r}) + \mu_s'(\vec{r}))]^{-1}$ is the diffusion coefficient and (') indicates that the coefficient has been corrected for forward bias. The source term s is in [$\mathrm{Wm^{-3}}$] and the quantity ϕ is the flux density in [$\mathrm{Wm^{-2}}$]. It can be considered as the total radiant flux (power) in [W] received per unit area:

$$\phi(\vec{r}) = \int_{4\pi} L(\vec{r}, \hat{s}) d\Omega.$$

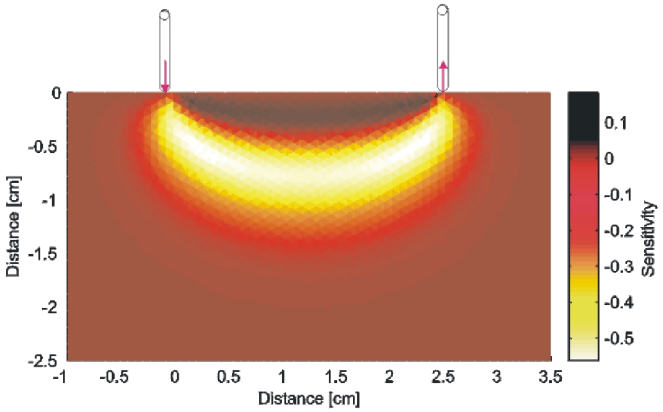

Fig. 2. Sensitivity of a frequency-domain measurement of phase with respect to the absorption coefficient in a homogeneous medium in a semi-infinite geometry. The medium is characterized by the effective scattering coefficient $\mu_s' = (1-g)\mu_s$ having a value of $\mu_s' = 20$ cm^{-1} and an absorption coefficient of $\mu_a = 0.25$ cm^{-1}, which simulate optical properties of human-brain tissue. A light source of unit strength was assumed, collimated to a depth of 0.5 mm at origin. The Robin boundary condition (RBC) was utilized. [4]

Fig. 2 shows a spatial sensitivity profile of measured signal phase with respect to changes in the absorption coefficient. The parameters are chosen to simulate strongly scattering brain tissue, although the medium was considered homogeneous. We have used the Finite Element (FE) method in these kinds of 2-D sensitivity analyses.

OPTICAL IMAGING

For optical infrared imaging, several different measurement geometries can be used. Transmission studies are feasible only for objects whose thickness is of the order of a few centimeters or less. Typically, light sources and detectors are placed on the same side of the object as is the case in Fig 2.

In near-infrared spectroscopy (NIRS), several wavelengths are used. In its simplest form, NIRS can be carried out using continuous-wave light sources and a detector, placed a few centimeters apart from each other to measure the backscattered radiation. The choice of the wavelengths is made not only on the basis of sufficient penetration, but they have to be suitable for determining, e.g., the relative quantities of HbO_2 and Hb in the

tissue. By investigating the temporal properties of the measured signal, it is possible to obtain quantitative information of the path lengths of light in tissue. In time-domain studies, such information is obtained by using short light pulses and by measuring the time-of-flight distribution of the detected photons. In the frequency domain, similar information is gained by intensity modulating the light source at a radio frequency and by measuring the amplitude and the relative phase of the detected light signal.

OPTICAL TOMOGRAPHY

In tomographic imaging, either a single light source is moved on the object surface or several optodes (optical fiber heads, attached on the object surface) are used. In principle, optical measurements can reveal a 3-dimensional image of the object [3]. However, the inverse problem is complicated, considerably more difficult than, e.g., in CT or MR imaging and thus mainly topographical (2-D) solutions have been reported in practice.

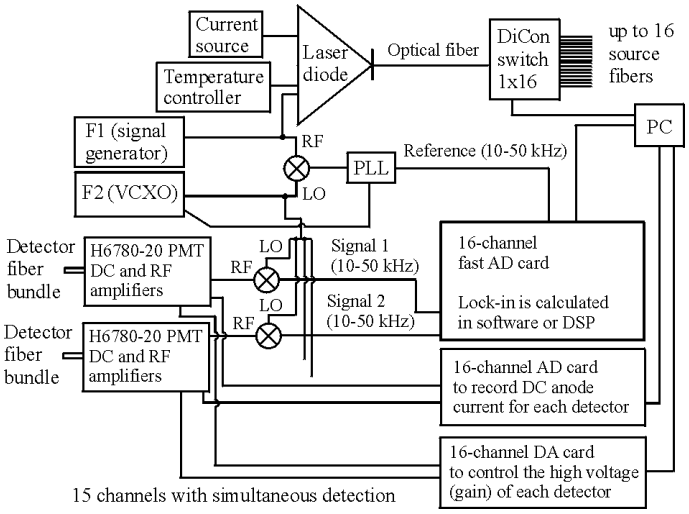

Fig. 3. Imaging system suitable for diffuse optical tomography. In this instrument, up to 16 optical fibers are used to deliver the infrared light into tissue. Light is collected via optical fiber bundles. Presently, the instrument has 4 parallel detection channels. The amplitude and phase of the signal are measured using lock-in techniques. VCXO = voltage-controlled crystal oscillator, PLL = phase-lock loop.

Fig. 3 shows the block diagram of a frequency-domain imaging system capable for both topographic and tomographic studies. The system has four parallel measurement channels and 16 time-multiplexed source fibers. A fiber-optic switch (Dicon Fiberoptics, VX500) is used for the time multiplexing. A temperature-stabilized 5-mW laser diode is modulated at either 100 MHz or 450 MHz and photomultiplier tubes (Hamamatsu H6780-20) are used for light detection. The rf-signal frequency is mixed into an intermediate frequency (10-50 kHz) before the amplitude and phase shift of the signal are measured with a four-channel digital lock-in amplifier. The whole instrument is carefully rf shielded.

APPLICATIONS

Optical tomography has potential for several types of applications. For mammographic imaging, the differences in the optical absorption and scattering coefficients between normal and abnormal breast tissue can be utilized. The changes in the tissue parameters can also be used to identify, e.g., tumors [5] and hematomas [6]. The contrast between a suspected abnormal and the background tissue can be enhanced by injecting contrast agents into blood vessels or tissue [5].

Optical imaging of human brain functions is an area with several potential applications. It is possible both to study the neurovascular coupling and to localize brain activation [2]. Measurements of the oxygenation state of muscles [7,8] and brain are feasible. Simultaneous studies using both the optical modality and transcranial magnetic stimulation [9] or nuclear magnetic resonance [5] etc. are also possible.

As an example, a study of motory-evoked signals in human brain is presented in Fig. 4. The applied instrument is the one presented in Fig. 3. Fig. 4a shows the placement of the optodes on the right side of the subject's head. Five source fibers (x) and 4 receiving bundles (o) were used, covering an area of 6 cm x 6 cm. The stimulus was a tapping of the left-hand index finger in an undefined rate. The paradigm consisted of alternating rest and

tapping periods. The amplitude data from the 12 closest-neighbour source-detector pairs were utilized. The data corresponding to the stimulation and the rest periods were collected into separate groups for each source-detector pair. A map is formed from the relative difference values and the corresponding spatial positions, which in this case were the points in the middle between the source and detector. The maps were further interpolated using a triangle-based cubic algorithm.

Fig. 4b presents the 2-D activation map of the motor cortex, measured at 808 nm, where the specific extinction coefficients of HbO_2 and Hb are approximately equal. The yellow colour indicates a decrease in the optical signal and thus an amount of total hemoglobin increase in the underlying cortical region. Correspondingly, the blue colour represents a decrease in the amount of hemoglobin. The numerical values indicate the relative changes in the magnitude of the amplitude signal (stimulation vs. rest). Fig. 4b therefore indicates a hemoglobin maximum close to the primary motor cortex.

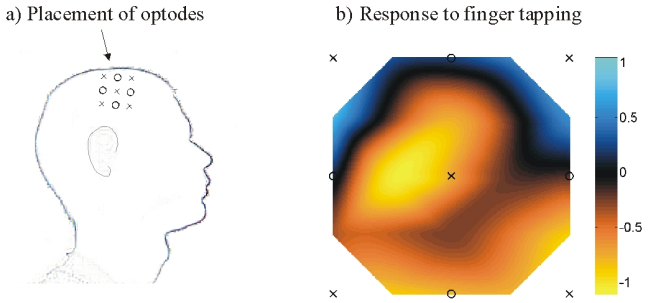

Fig. 4. Motory-evoked activation map during a finger-tapping experiment. The spacing of the grid formed by the source fibers (x) and receiving fiber bundles (o) is 3 cm.

SUMMARY

Optical tomography offers several advantages. The imaging system is safe, of low cost, relatively simple and, in most cases, even transportable. Optical imaging is non-invasive and provides both spatial and temporal information. Its spatial resolution is better than in electromagnetic studies, but not comparable to CT or MRI. On the other hand, the temporal resolution of optical imaging may exceed that of CT and MRI, but is not as fast as the electromagnetic methods. Diffuse optical tomography is still at a rapidly developing stage, but many useful applications have already been demonstrated. A big challenge for optical imaging is to further develop the theoretical models and image reconstruction methods. Several research groups are actively working on these problems. In addition, advances in the measurement techniques and data processing are also constantly reported. As a result, both spatial and temporal resolutions as well as the image quality in general will improve in the future.

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