NeuroImage 135 (2016) 287–299

Contents lists available at ScienceDirect

NeuroImage

journal homepage: www.elsevier.com/locate/ynimg

Multi-subject and multi-task experimental validation of the hierarchical Bayesian diffuse optical tomography algorithm

Okito Yamashita [a,b,*], Takeaki Shimokawa [a], Ryota Aisu [a,c], Takashi Amita [d], Yoshihiro Inoue [d], Masa-aki Sato [a]

[a] Neural Information Analysis Laboratories, ATR, 2-2-2 Hikaridai, Keihanna Science City, Kyoto 619-0288, Japan
[b] Brain Functional Imaging Technologies Group, CiNet, 1-4 Yamadaoka, Suita City, Osaka 565-0871, Japan
[c] Nara Institute of Science and Technology, 8916-5 Takayama, Ikoma, Nara 630-0192, Japan
[d] Medical Systems Division Research and Development Department, Shimadzu Corporation, 1 Nishinokyo-Kuwabaracho, Nakagyo-ku, Kyoto 604-8511, Japan

ARTICLE INFO

Article history:
Received 28 December 2015
Revised 25 April 2016
Accepted 28 April 2016
Available online 03 May 2016

Keywords:
Diffuse optical tomography
Scalp blood flow
NIRS
Image reconstruction

ABSTRACT

Diffuse optical tomography (DOT) is an emerging technology for improving the spatial resolution and spatial specificity of conventional multi-channel near-infrared spectroscopy (NIRS) by the use of high-density measurements and an image reconstruction algorithm. We recently proposed a hierarchical Bayesian DOT algorithm that allows for accurate simultaneous reconstruction of scalp and cortical hemodynamic changes, and verified its performance with a phantom experiment, a computer simulation, and experimental data from one human subject. We extend our previous human case study to a multi-subject, multi-task study, to demonstrate the validity of the algorithm on a wider population and varied task conditions. We measured brain activity during three graded tasks (hand movement, index finger movement, and no-movement), in 12 subjects, using high-density NIRS and functional magnetic resonance imaging (fMRI), acquired in different sessions. The reconstruction performance of our algorithm, and the current gold-standard method for DOT image reconstruction, were evaluated using the blood-oxygenation-level-dependent (BOLD) signals of the fMRI as a reference. In comparison with the BOLD signals, our method achieved a median localization error of 6 and 8 mm, and a spatial-pattern similarity of 0.6 and 0.4 for the hand and finger tasks, respectively. It also did not reconstruct any activity in the no-movement task. Compared with the current gold-standard method, the new method showed fewer false positives, which resulted in improved spatial-pattern similarity, although the localization errors of the main activity clusters were comparable.

1. Introduction

Functional near-infrared spectroscopy (fNIRS) is a noninvasive optical imaging technique that measures the changes in oxygenated and deoxygenated hemoglobin concentrations (hemodynamic changes) in response to changes in neuronal activity. fNIRS is sensitive to hemodynamic responses analogous to the blood-oxygenation-level-dependent (BOLD) signals found in fMRI, yet offers the advantages of low cost, easy portability, and the possibility of extending brain measurements to include such subjects as babies, elderly people, and patients with an implanted electronic device. It also permits measurements to be made in ambient environments (for a historical review, see Ferrari and Quaresima, 2012).

The currently available fNIRS scalp topography methods have a couple of disadvantages that reduce the reliability of the results when used as a brain imaging method. First, the relative positions of the measurement channels to brain anatomy vary between subjects, and also between sessions within the same subjects. The activation foci consistently observed in the scalp topography do not necessarily indicate activation foci that consistently result from the same brain region. Second, fNIRS measurements are always affected by the hemodynamic changes in the scalp layer, and these changes may often dominate the contributions from cortical activity (Kirilina et al., 2012; Saager and Berger, 2005, 2007). Recently, one study showed that most of the oxyhemoglobin concentration changes measured from the forehead during a verbal fluency task were due to changes in scalp hemodynamics (Takahashi et al., 2011). Several signal processing methods for the removal of scalp artifacts have been proposed, these include the use of principle component analysis (PCA) (Zhang et al., 2005), independent component analysis (ICA) (Kohno et al., 2007), adaptive filters (Zhang

Abbreviations: fNIRS, functional near-infrared spectroscopy; DOT, diffuse optical tomography; HbR, deoxygenated hemoglobin; HbO, oxygenated hemoglobin; LE, localization error; AUC, area under the receiver-operating curve; SS, spatial-pattern similarity; FPA, false positive amount.

* Corresponding author at: Neural Information Analysis Laboratories, ATR, 2-2-2 Hikaridai, Keihanna Science City, Kyoto 619-0288, Japan.
E-mail address: oyamashi@atr.jp (O. Yamashita).

http://dx.doi.org/10.1016/j.neuroimage.2016.04.068

et al., 2009, 2007), and short-channel regression (Gregg et al., 2010; Saager and Berger, 2005, 2007; Umeyama and Yamada, 2014; Zeff et al., 2007).

Diffuse optical tomography (DOT) is an emerging technology that may solve the above issues. It is a computer-assisted method for the three-dimensional reconstruction of images showing changes in cerebral hemodynamics. The technique uses a combination of high-density measurements, forward modeling, and an image reconstruction algorithm (Bluestone et al., 2001; Boas et al., 2004; Eggebrecht et al., 2014). High-density measurements with an inter-probe distance of around 10 mm allow multiple-distance channels and optical-path overlap between channels, which permits an increase in spatial specificity, in both the depth and surface directions. To exploit this increased spatial specificity, a forward model that quantitatively relates the activity inside the head tissue to the measured light intensity changes, is established by simulating a light migration process. An image reconstruction algorithm is then utilized to reconstruct a three-dimensional activity image from the observed light intensity changes. In principle, a reconstructed three-dimensional image allows for the separation and localization of scalp and cortical hemodynamic changes, improving the interpretation of results in terms of brain anatomy.

The quality of the reconstructed images depends on the image reconstruction algorithm, and a number of such algorithms have been proposed in previous studies. The image reconstruction problem is generally formulated as a linear inverse problem (Arridge, 1999; Boas et al., 2004), which is an underdetermined problem requiring a priori information to constrain possible solutions. One scheme for solving the inverse problem is the regularization approach, which uses a cost function consisting of the data fitting term and constraint terms representing a priori information (Boas et al., 2004; Cao et al., 2007; Culver et al., 2003; Lee et al., 2015). A DOT image is obtained by minimization of the cost function. Another approach is to use Bayesian modeling, which relies on a probabilistic model of observations and constraints called the likelihood function and prior distribution, respectively (Abdelnour et al., 2010; Guven et al., 2005; Shimokawa et al., 2012, 2013). A DOT image is obtained by computing the posterior distribution and utilizing the representative statistics of the posterior distribution (e.g., mean or mode). The probabilistic modeling and posterior computation developed in the Bayesian statistics (Gelman et al., 2014) provide a systematic way to compute meta-parameters (e.g., the regularization parameter) in the algorithm. This allows established knowledge to be incorporated into models in a more flexible manner.

Despite a variety of different image reconstruction algorithms, no research had proposed a DOT algorithm to accurately reconstruct both the scalp and cortical activity simultaneously, until we proposed the hierarchical Bayesian DOT algorithm (Shimokawa et al., 2013). Currently, a two-step approach is used for real experimental data, including visual, auditory, and resting paradigms (Eggebrecht et al., 2014; White et al., 2009; Zeff et al., 2007). In this two-step approach, scalp artifacts are removed by short-channel regression, which is then followed by cortical image reconstruction using the depth-compensation minimum norm method (Culver et al., 2003). As an alternative, our hierarchical Bayesian algorithm simultaneously reconstructs activity in the scalp and cortical layers using an individual head model. The key concept is a probabilistic model characterizing the distinct nature of the scalp and cortical hemodynamic changes. We assume a spatial smoothness prior for the scalp hemodynamics and a sparse-promoting prior for the cortical hemodynamics. This is made on the basis of the empirical observation that scalp hemodynamics change globally (Funane et al., 2014; Kohno et al., 2007; Zhang et al., 2005), but task-related cortical hemodynamics change rather locally. We have previously verified the performance of our algorithm using a two-layer phantom experiment and a computer simulation (Shimokawa et al., 2013). This was followed by experimental data from one human subject performing a right finger movement task (Yamashita et al., 2014).

In this work, we extend our previous human case study to a multi-subject and multi-task experiment, to test the validity of our algorithm on a wider population and different task conditions. A human case study demonstrated remarkable consistency between reconstructed cortical images and fMRI images (Yamashita et al., 2014); however, with consideration of inter-subject variability in light transmission and head anatomy, it remains unclear whether the previous single subject study can be generalized to a group level study. It is also unclear how our hierarchical Bayesian method performs with cortical activity of different sizes and amplitudes. To address these questions, we measured brain activity with high-density NIRS and fMRI acquired in different sessions, using 12 subjects, who performed three graded tasks. The three tasks were right hand movement, right index finger movement, and no-movement. These were selected to experimentally modulate the size and amplitude of the activations in the left primary motor cortex. We validated the performance of our algorithm using fMRI as a reference. In addition, we compared it with the two-step approach, which is the current gold-standard method for DOT (Eggebrecht et al., 2014).

1.1. Hierarchical Bayesian image reconstruction model

We originally proposed a hierarchical Bayesian sparse image reconstruction algorithm (Shimokawa et al., 2012), and later extended it to human functional brain imaging (Shimokawa et al., 2013). Here we briefly describe our model, while the image reconstruction algorithm is described in the Appendix A.

We first reconstruct images of the absorption changes at multiple wavelengths, and then convert these to images of the hemodynamic changes (oxy- and deoxy-hemoglobin concentration) using spectral extinction coefficients (Shimokawa et al., 2013, Eq. 13). Let $\mathbf{x} = (x_1, x_2, \cdots, x_N)^t$ denote the absorption changes in the N voxels of the discretized head tissue and $\mathbf{y} = (y_1, y_2, \cdots, y_M)^t$ the log-ratio of the light intensity changes measured by the M pairs of the source and detector probes on the scalp. Under the condition that the absorption changes are small relative to the baseline condition, the Rytov approximation leads to a linear relationship between detected light intensity changes $\mathbf{y}$ and absorption changes $\mathbf{x}$ (Arridge, 1999; Durduran et al., 2010; Shimokawa et al., 2012):

$$\mathbf{y} = \mathbf{A}\mathbf{x} + \boldsymbol{\varepsilon}, \tag{1}$$

where A is the sensitivity matrix and $\boldsymbol{\varepsilon}$ represents the measurement noise. As absorption changes occur predominantly in the scalp and cortex where blood vessels exist, we assume measurements are affected by the absorption changes in these two layers. Thus Eq. (1) can be rewritten as

$$\mathbf{y} = \mathbf{A}^{\mathbf{c}}\mathbf{x}^{\mathbf{c}} + \mathbf{A}^{\mathbf{s}}\mathbf{x}^{\mathbf{s}} + \boldsymbol{\varepsilon}, \tag{2}$$

where $\mathbf{A}^{\mathbf{c}}, \mathbf{x}^{\mathbf{c}}$ and $\mathbf{A}^{\mathbf{s}}, \mathbf{x}^{\mathbf{s}}$ are the sensitivity and absorption changes in the cortical and scalp layers, respectively. Assuming measurement noise $\boldsymbol{\varepsilon}$ follows a Gaussian distribution $N(0, \sigma^{-1}\boldsymbol{\Sigma})$, the forward model (2) can be written as the following probabilistic model:

$$\mathbf{P}(\mathbf{y}, \mathbf{x}^{\mathbf{c}}, \mathbf{x}^{\mathbf{s}}, \boldsymbol{\sigma}) \sim \boldsymbol{N}(\mathbf{A}^{\mathbf{c}}\mathbf{x}^{\mathbf{c}} + \mathbf{A}^{\mathbf{s}}\mathbf{x}^{\mathbf{s}}, \sigma^{-1}\boldsymbol{\Sigma}), \tag{3}$$

where $\boldsymbol{\Sigma}$ is a scale-normalized noise covariance matrix computed from the data during the baseline period, and σ is the precision (inverse variance).

We assume the spatial smoothness and sparseness priors for the scalp and cortical absorption changes, respectively. For the scalp absorption changes, we implemented the spatial smoothness prior by assigning high probabilities to the small values of the spatial derivative of absorption changes $\mathbf{z}^{\mathbf{s}}$ as follows:

$$\mathbf{z}^{\mathbf{s}} = \mathbf{L}\mathbf{x}^{\mathbf{s}}, \tag{4}$$