Depth sensitivity in multi-distance NIRS measurements in humans

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Abstract: We review different experiments using high-resolution diffuse optical tomography monitoring functional activation or brain perfusion in humans. We show the demand of an objective depth correction algorithm, especially when intrinsic contrast agents are used.

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1. Introduction

High-resolution diffuse optical tomography (HR-DOT) as a 3D modality of near infrared spectroscopy (NIRS) uses a dense grid of optical fibers, overlapping photon paths and image reconstruction procedure to achieve a time series of changes of interior optical properties in 3D volumes. There are different methods to solve the forward problem of light distribution in the investigated tissue, most notably, the finite-element-method solution of the diffusion equation and the Monte Carlo simulation of photon migration. The resulting weight- or sensitivity matrix (W) assigns the highest sensitivity to optical changes in the outermost (i.e., scalp) voxels and is charactereized by a strongly decreasing sensitivity toward deeper layers (i.e. brain tissue). When solving the inverse problem this leads to a distortion of the reconstructed results in a way that image features are pulled toward the surface. There are methods reported to account for this effect by manipulating W or by applying a spatial filter [1, 2]. The problem is to find objective criteria for manipulating W prior to the image reconstruction or to adjust the reconstructed images to the correct depth. Recently, our group reported different studies using HR-DOT to monitor cortical activation due to somatosensory stimulation [3] or to visualize brain perfusion using indocyanine green (ICG) as an exogenic contrast agent [4]. In this work we review and discuss the problem of sufficient depth localization, showing the need of objective criteria to compensate for the decreased sensitivity in the depth, especially when cortical activation is monitored.

2. Methods

All studies were performed using the DYNOT tomography imager (NIRx Medizintechnik GmbH, Berlin, Germany) which applies light of two wavelengths (λ=760 nm & λ= 830 nm) to the subject's head. 30 co-located optical fibers, serving as source and detector (inter-optode separation: 7.5 mm) were placed in a 5 x 6 optical fiber grid (see Fig 1a). With this dense fiber grid setup we obtained 900 overlapping optical data channels with a sampling frequency of 1.81 Hz.

We reconstructed time series of relative absorption changes using the normalized difference method [5]. In all experiments, the weight matrix was determined using BrainModeler (NIRx Medical Technologies, LLC, NY, USA), which provides a library of subvolumes from a finite element mesh (FE) with precalculated inverse parameters. This mesh is based on a single-subject brain atlas, obtained by an anatomical MR scan with 1 mm resolution. For each of these meshes there are approx. 400 boundary nodes on the head surface with a spatial resolution of 4 mm. These surface nodes are considered as potential source/detector positions. For each submesh the FEM discretized photon diffusion equation was solved using Type III boundary condition thus, providing the reference detector values and the weight function, respectively. The forward solution was computed based on the simplified assumption of homogenous interior optical properties (μ_a= 0.06 cm^{-1}, μ_s= 10 cm^{-1}). We selected the sub-mesh that best approximated the area of each measurement. No further depth correction schemes were applied.

The reconstruction procedure results in a 2D array containing reconstructed time courses for all nodes of the FE mesh. For visualization purpose, the results were later transformed into a volume using Matlab's standard routines. In the following we will discuss results from three experiments (E1-E3). For reasons of clarity, we summarize details about the methods in Table 1. E3 is a sub-experiment, using data and setup from E2.

Table 1 Details concerning the methods of the discussed experiments.

Experiment, Reference, # subjects	***Position of fiber grid***	***stimulus and data processing***
E1, [3], 8 subjects	C3	• vibrotactile stimulation of the 1st and 5th finger of right hand • induced by a piezoelectric transducer (vibration frequency 40 Hz) • 40 stimulations /finger, duration: 20 sec followed by 20sec rest, pseudo randomized order, additional fMRI • low-pass filter 0.4 Hz
E2, [4], 3 subjects	C4	• One subject received two boli of ICG (9 mg & 16 mg, 10 min delay) • two subjects received 12.5 mg ICG each • low-pass filter at 0.3Hz
E3, not published, 3 subjects	C4	• same as in E2, but only data from the pre-bolus baseline were used • time courses were band pass filtered (0.08-0.125Hz) • PSD (Welch method)

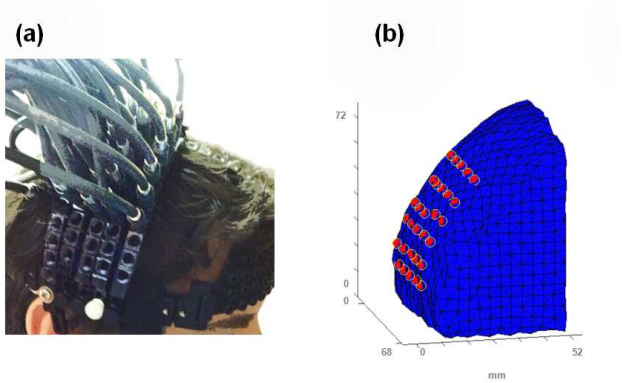

Fig. 1 (a) Imaging setup. Absorption changes were measured with a HR-DOT imaging system (DYNOT, NIRx Medizintechnik GmbH, Berlin, Germany). A 5x6 fiber grid with 30 co-located sources and detectors was placed pericentrally over the right (E3, E4) or the left (E1) hemisphere. (b) One example for a finite element sub-mesh that was used for image reconstruction of relative absorption changes. Red dots indicate the positions of the optical fibers in the forward geometry.

3. Results

Fig. 2 shows results from the three experiments. Fig. 2a) depicts one example from the somatosensory stimulation experiment. We found activated voxels (defined as a significant decrease in deoxygenated hemoglobin (HbR)) in the region and orientation where they were expected. Nevertheless, both activation patterns were placed outside the brain. We see both activations located in different depths, indicating that there is relative depth discrimination, but the absolute position is ~15 mm outside the cortex. In Fig. 2b) we see results from the experiment using ICG as an exogenic, highly absorbing contrast agent. When depicting the volume with the voxels color-coded by the arrival time of ICG (in s after bolus injection) we see an early increase in absorption at a depth of ~10-12 mm. This is in good agreement with the better perfusion of brain tissue compared to skin. Although it was not confirmed by other imaging modalities, the depth position is in good agreement with the location of the cortical surface, about 12-14 mm below the scalp for the model brain at this position. Fig 2 c) and d) show results from a spectral analysis of the pre-bolus baseline. We find low frequency oscillations (LFO) in the 0.1Hz band in both compartments, skin and brain, and in both Hb species. Because of the optical measurements' greater sensitivity to surface-near signals, the skin voxels show a much greater absolute power in the LFO band, for either Hb state. Within each compartment, the LFO power in the HbO time courses exceeds that of the Hb signals. This is in agreement with the assumed origin of the LFO signal from the arterial compartment and confirms reports of many research groups dealing with functional NIRS. An objective depth positioning of the signals is needed to correctly determine the contributions of the different layers of the volume to the reconstructed time courses. Although at this point no further quantitative analyses have been applied, this demonstrates the potential of hemodynamic power spectral analysis to serve as an

intrinsic depth-sensitive metric, which may proof useful in the evaluation and development of objective depth-correction schemes.

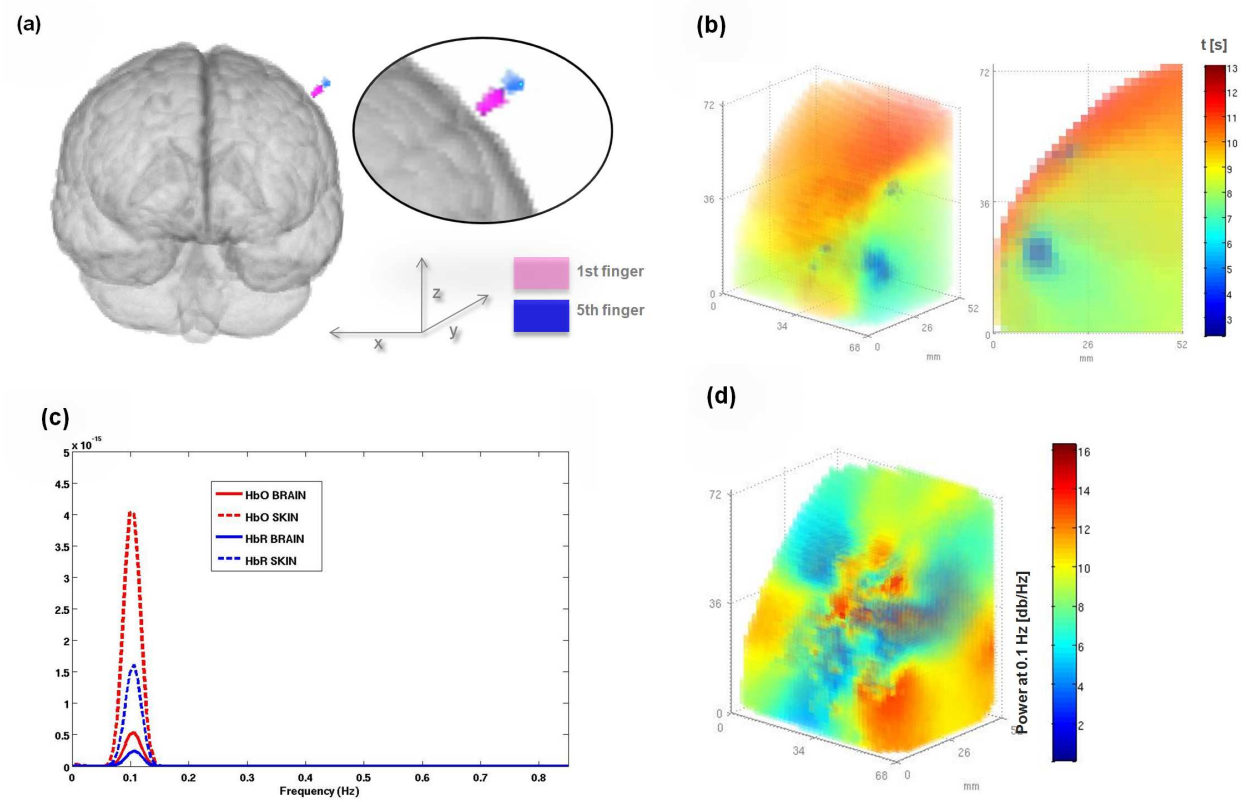

Fig. 2 Results of different HR-DOT experiments. (a) Results of the vibrotactile stimulation experiment. Frontal view on the individual's brain with co-registered activation clusters. Significant activation for the first and the fifth finger (based on a t-test of HbR time courses) are displayed in pink and blue. (b) Reconstruction volume with results from the ICG experiment of brain perfusion. Voxels are color-coded in s by the arrival time of the absorber after ICG injection. The early arriving bolus is located in deeper layers. (c) Results from spectral analysis of LFO show these hemodynamic features in the skin and in the brain. (d) Reconstructed volume with each voxel color-coded with the normalized power of LFO. An individual pattern of isolated local amplitude maxima is revealed in both superficial and deeper regions.

4. Conclusions

In this work we present a review of results from functional and physiological experiments using HR-DOT. In all experiments we found significant activation (in terms of decreased HbR concentration) or absorption changes due to the arriving ICG bolus. Relatively weak signals, such as activation.related HbR concentration changes can be resolved stemming from different depths but still are grossly misplaced and projected outside the brain. When using exogenic, highly absorbing contrast agents instead of intrinsic chromophores the depth positioning problem seems to be eased because the high increase of absorption compensates for the decreased sensitivity in the depth. Nevertheless, in most studies, especially in functional NIRS, changes of intrinsic chromophores are measured. Even for perfusion monitoring, in the long run it is more desirable to be able to rely on changes in the pattern of hemodynamic features rather than injecting a contrast agent. The spectral study of intrinsic hemodynamics may afford yet another way of benchmarking correct depth localization in HR-DOT.

5. References

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