A QUANTITATIVE SPATIAL COMPARISON OF HIGH-DENSITY DIFFUSE OPTICAL TOMOGRAPHY AND FMRI MAPPING OF VISUAL CORTEX

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Objective:
Functional neuroimaging commands a dominant role in current neuroscience research. However its use in neuro-scientific or bedside clinical studies has been limited because the current tools lack the combination of being non-invasive, non-ionizing and portable while maintaining moderate resolution and localization accuracy. Optical neuroimaging satisfies many of these requirements, but, until recent advancements in high-density diffuse optical tomography (HD-DOT), has been hampered by limited resolution. While early results of HD-DOT have been promising, a quantitative voxel-wise comparison and validation of HD-DOT against the gold standard of functional magnetic resonance imaging (fMRI) has been lacking. Herein, we provide a quantitative voxel-wise comparison and validation of HD-DOT against the gold standard of functional magnetic resonance imaging (fMRI) using matched visual stimulation protocols in a single group of subjects (n=5) during separate HD-DOT and fMRI scanning sessions. To attain the needed voxel-to-voxel correspondence between modalities, we developed subject-specific head modeling for HD-DOT, incorporating MRI anatomy, detailed segmentation, and alignment of source and detector positions.

Methods:
Our high-density DOT (HD-DOT) imaging system is a continuous wave system using two near-infrared wavelengths (750 and 850 nm) at each source position (Zeff et al., 2007) (Fig. 1). We developed procedures that segment anatomical MRIs for each subject, locate and co-register HD-DOT cap placement on the subject's head, and solve the forward light model within the subject-specific space providing for the co-localized data set of fMRI and HD-DOT necessary for a full image-space comparison. Functional MRI images are collected using a series of asymmetric gradient spin-echo echo-planar (EPI) sequences (TR = 2000 ms, 4 x 4 x 4 mm voxels) to measure the blood-oxygenation-level-dependent (BOLD) contrast. The fMRI activation is smoothed to match the DOT point-spread function of 13 mm. Visual cortex was mapped using standard visual stimuli (Engel et al.,1994, White et al., 2010) consisting of phase encoded retinotopic stimuli. We quantified the localization error within four visual quadrants using two different methods. The center-of-mass of an activation within a quadrant is calculated for each of the hemoglobin species concentrations as well as the BOLD data for a frame within the center of each of the quadrants of the visual cortex. The center-of-mass error is defined as the three-dimensional Euclidean distance separating the recorded activations from each modality. To quantify the localization error at every voxel within the field-of-view (FOV), we calculated each voxel's phase error as the difference between the phase measured with HD-DOT to that measured via fMRI. The phase error is converted to a distance error by dividing the phase of each voxel by the norm of the gradient of the phase map for every voxel (Sereno et al., 1995).

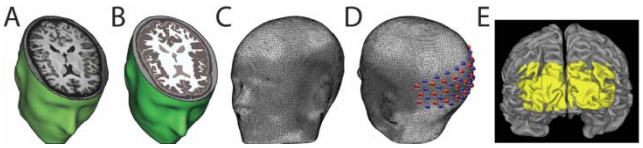

Figure 1: Subject-specific head modeling. (A) T1-weighted MRI volume. (B) Segmented head volume displaying scalp, skull, CSF, gray matter and white matter. (C) High-density tetrahedral mesh to use in finite element forward light model. (D) Optode positions localized on mesh. The high-density optode grid is composed of 24 sources (red) and 28 detectors (blue). (E) Surface rendering of cortex. Yellow coloring denotes FOV of HD-DOT imaging pad.

Results:
We find quantitative correspondence of quadrant locations between the two modalities, with an average center-of-mass error of 5.0 +/- 1 mm. Using phase maps to calculate localization error in every voxel across the field of view provides an average localization error in the HD-DOT of 4.4 +/- 1 mm. Along the cortical ridges we find excellent agreement between the modalities.

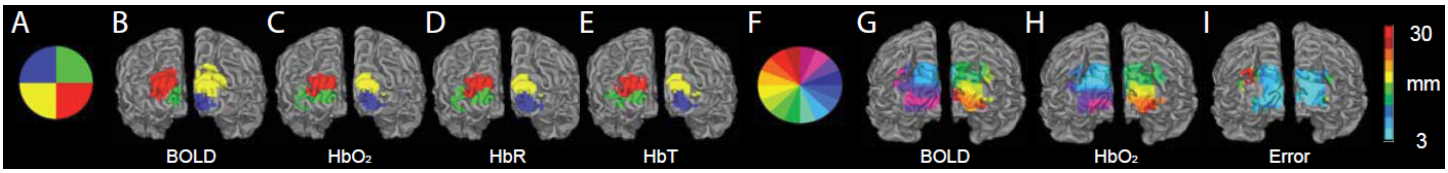

Figure 2:**Error analysis in Subject 1**. (A) Key for stimuli in each of four visual quadrants. (B) fMRI recorded activation. (C-E) HD-DOT recorded activation for each hemoglobin concentration species. Note the qualitative agreement between the BOLD activation and each of the hemoglobin concentrations both in activation location and spatial extent. (F) Key for stimuli phase. Phase of fMRI (G) and HD-DOT (H) for wedge stimuli. The error (I) is calculated by converting the phase error to a distance error. Note that the error is around the size of a voxel throughout the majority of the FOV.

Conclusions:
These results show that HD-DOT maps brain function with good (< 5 mm localization error) voxel-to-voxel correspondence with fMRI. This study directly addresses issues limiting previous HD-DOT studies (Custo et al., 2010; Zeff et al., 2007), namely accurate head modeling with proper optode placement, co-registration of the data set to not only the specific subject anatomy but also to an additional modality of investigation, and contiguous mapping of an extend region of the cortex. The comparison reveals that the localization errors in functional maps of visual cortex are on average within the size of a gyral ridge. Thus, the future of HD-DOT functional imaging holds exciting possibilities with freely behaving, interacting, bed-constrained subjects, and others who are not ideal candidates for traditional functional neuroimaging modalities.

References:
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