Laminar analysis of high isotropic resolution BOLD activation with a resolution pattern stimulus in human V1 at 7T

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Introduction: With sufficient image encoding, the resolution of fine spatial-scale functional architecture of visual cortex with fMRI is limited by the biological point-spread function of the BOLD signal [1-3]. This spatial resolution is set by fundamental limits placed by both the local vascular density as well as by parameters in the measurement such as field strength, pulse sequence type, and weighting of the various hemodynamic properties that change during activation. For example, considerable effort has been expended by the community discussing the "brain vs. vein" sensitivity of various methods.

We propose that a high degree of immunity to spatial localization errors from larger veins can be achieved by simply performing high isotropic resolution EPI (1x1x1mm^3) registered to the cortical surface to within a fraction of a millimeter. In this case, the analysis can be limited to voxels which are confidently localized to the middle cortical lamina. These lamina are known to be free of the larger draining veins that abut the pial surface. To test the spatial resolution of the BOLD signal in primary visual cortex (V1), we designed a simple resolution stimulus that contains several easily identifiable features for measuring the spatial spread of the BOLD response across the cortical surface. We measured this spatial response pattern using a 1mm isotropic acquisition at 7T. Use of fast head gradients and a highly accelerated 32-channel coil limited image distortions to the point where a surface-based registration algorithm could align the EPI data to the undistorted T1 volumes used for surface reconstruction. The isotropic data could then be analyzed as a function of cortical lamina on the flattened cortex. Our measurements suggests that the majority of the BOLD spatial errors arise from near the pial surface and that avoiding these lamina can significantly improve the study of fine spatial scale activation in the visual cortex.

Methods: To produce a desired spatial pattern of activation on the V1 surface, the figure "M" was warped by the inverse of the known complex-logarithm transformation (see Fig.1) that describes the topographic mapping of the visual field onto the cortical surface [4] based on mapping parameter values measured (a=0.7°, γ_1=0.9) across a population of subjects [5]. The stimulus consisted of (i) a pre-warped figure (filled with a spatial noise pattern counterphase flickering at 8 Hz to strongly drive V1 neurons) surrounded by a gray background, and (ii) a negative image consisting of a gray figure superimposed on a flickering noise background. A fixation task was provided to aid in subject fixation performance. The stimulus followed a simple block design where each stimulus condition was presented alternately for 15 s separated by 10 s of a full screen of background gray.

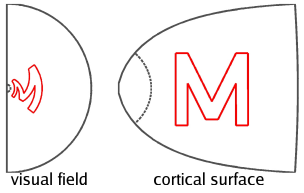

Figure 1: Pre-warping the "M" stimulus.

fMRI data was acquired on a 7T Siemens whole-body system (Siemens Healthcare, Erlangen, Germany) equipped with AC84 head gradients, and a custom-built 32-channel loop coil head array. For the BOLD acquisition we used a standard gradient echo multi-slice EPI protocol with 34 1-mm thick oblique-coronal slices positioned at the occipital cortex orthogonal to the calcarine sulcus. The protocol parameter values were TR=2500 ms, TE=24 ms, FOV = 192 mm, matrix=192x192, bandwidth = 2005 Hz/px, and 4-fold acceleration with standard online GRAPPA reconstruction. The time-series data were motion corrected then analyzed with FEAT (FSL, Oxford) to produce z-statistics for each voxel. The functional data was then automatically registered to a cortical surface reconstruction (computed with FreeSurfer) from 1x1x1mm^3 T1-weighted MPRAGE data by calculating a rigid transformation that aligned the surface to the gray-white boundary detected in the EPI data. Ten intermediate gray matter surfaces were generated between the white matter and pial surfaces, and the z-statistics within voxels intersecting each surface were projected onto the corresponding surface.

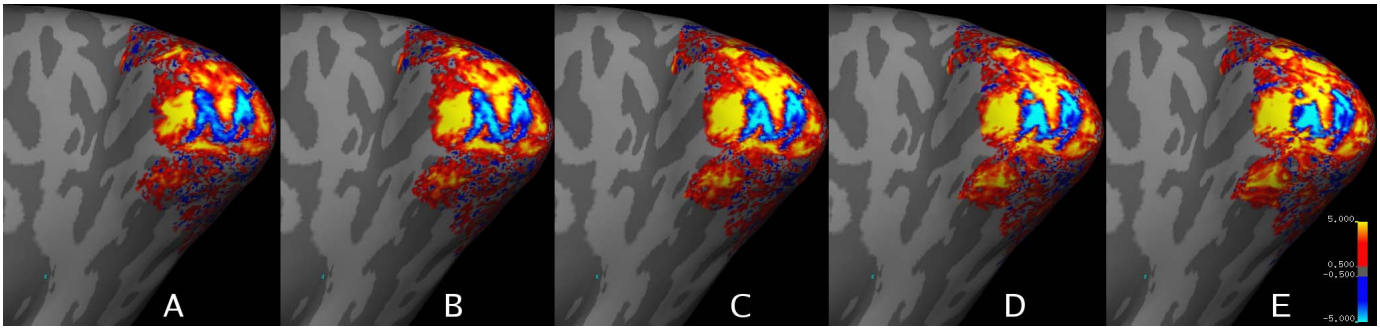

Figure 2: The differential activity pattern of the "M" stimulus displayed on the inflated cortical surface reconstruction of one subject. (A) Activity at lowest depth (near white matter). (B-D) Activity at intermediate depths. (E) Activity at shallow depth (near pial surface). Color scale for z-statistic values is provided on right.

Results: Fig. 2 demonstrates activity patterns from subject 2 across the cortical depths. The activity becomes stronger as the reconstruction moves from the white matter surface to the pial surface and deteriorates near the pial surface—consistent with a peak in the microvasuculature in layer 4 and a peak microvasculature at the pial surface.

Discussion: While techniques such as the "initial dip", flow-based functional contrast, and spin-echo EPI have all been suggested for improvement of the biological point-spread function of BOLD, our study suggests that gradient-echo EPI with small voxels limited to the center lamina of the cortex can also significantly improve spatial localization. Furthermore, this "vein avoidance" strategy of limiting the study to central lamina can be combined with the other sequence-based methods for point-spread function enhancement. Due to our knowledge of its topographic structure, the visuotopic mapping in V1 therefore can provide a valuable testing ground for measurements of spatial resolution in fMRI.

References: [1] Engel *et al.* (1997) *Cereb Cortex*, 7:181-92. [2] Shmuel *et al.* (2007) *Neuroimage,* 35:539-52. [3] Leite *et al.* (2004) Proc ISMRM, 1079. [4] Schwartz (1980) *Vis Research*, 20:645-69. [5] Polimeni *et al.* (2005) *Soc Neurosci.*

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