Spatial Characteristics of VASO fMRI at Ultra-high Resolution

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INTRODUCTION: Vascular-Space-Occupancy (VASO) dependent fMRI is a new approach to detect changes in cerebral blood volume (CBV) during functional stimulation as well as other physiological challenges (1). Although it has been tested extensively using different stimulus paradigms and different field strengths, its signal change mechanism is still not entirely clear. In particular, since the VASO signal change has a direct relationship with the changes in CBV (1), the amplitude of the signal as a function of resolution may provide important information regarding the mechanism. We previously found a signal change of 2-3% at both 1.5T and 3T at a resolution of 2x2x5 mm^3. Here we performed VASO fMRI at very high spatial resolution (0.78x0.78x3mm^3) and studied the distribution of the signal changes in the activated voxels.

METHODS Experiment: Experiments were performed on a 3.0T MR system (Philips Medical Systems). Informed written consent was obtained. Visual stimulation of flashing checkerboard (visual angle 25°) was used with 30 seconds ON and 30 seconds OFF. Each fMRI run was 7 minutes long and was repeated 4 times. Segmented-EPI (2 shots) was used with the following parameters: TR=3000ms, TI=889ms (1, 2), FOV 112x112mm^2, imaging matrix 144x144, reconstruction matrix 256x256, single slice encompassing calcarine fissure, slice thickness 3mm, SENSE factor 1.5.

Data processing: Data were processed using MATLAB. After 2D motion correction, the data from the four runs were averaged. Activation detection was performed by correlating the signal time-courses with a boxcar function that represents the stimulus paradigm. Activation criteria were: cc >0.20, minimal cluster size 15, p<0.005. A minimal SNR of 6 was used as an additional requirement for a voxel to be defined as "activated". This is because of the unique contrast of the VASO images in which regions containing large vessels have low signal intensities due to blood nulling. The fractional signal changes were calculated for each voxel.

RESULTS and DISCUSSION: Fig. 1a shows the VASO images, which are characterized by a thin layer of gray matter, surrounded by dark regions of blood vessels and bright white matter (due to short T_1). When overlaying the activation map on the VASO image, the activated voxels appear to be mainly localized in the gray matter layer (Fig. 1b). Fig. 2a plots the averaged time-course of the activated voxels, showing a robust negative signal change of ~4%. Fig. 2b shows the histogram of the signal changes. Fig. 3 shows a scatter plot (blue symbols, 604 voxels) of fractional signal changes versus signal intensities in the VASO image, i.e. Fig. 1a, illustrating the effect of the SNR threshold (voxels in the yellow box have low SNR even though their cc values were above the cc threshold). Since the product of the MR signal (y-axis) and fractional signal change (x-axis) is proportional to CNR, one can plot a series of iso-CNR curves (curves in Fig. 3). Interestingly, even though the fractional signal change and functional signal intensity vary dramatically among activated voxels, most of them have a CNR of within 4 fold of difference. Considering the expected variance in neuronal activity, this range is small, suggesting that the VASO technique has a rather homogeneous sensitivity.

In terms of the amplitude of signal changes, our results show that the VASO signal decreases by 3.98% during activation. According to equations in Lu et al (1), this would correspond to a CBV increase of 83% when assuming a baseline CBV of 4.7ml of blood/100 ml of brain (3). This is significantly higher than any values in the literature (4). We propose the following 4 possible explanations for such discrepancy: **1**. In Lu et al (1), only blood and extravascular tissue were considered. However, the MRI voxel may also contain some CSF. By including CSF (15%) in the model, the quantification reduces to 68% of CBV increase. **2**. The baseline CBV value was assumed to be 4.7, taken from Leenders et al (3). However, partial volume with some blood vessels may result in larger baseline CBV, which would correspond to a smaller CBV change for the same VASO signal. **3.** The measured changes in hemodynamic parameters are known to be dependent on spatial resolution (5). Belliveau et al observed a CBV increase of 32% at 3x3x10mm^3. Our experiments were performed at resolution of 0.78x0.78x3mm^3, and therefore may indeed result in a larger value due to highly localized voxel selection. This is supported by the evidence in the literature that the diameters of microvessels can increase by 30% (6), corresponding a 69% of CBV increase. **4**. It is, in principle, possible that mechanisms other than CBV changes may contribute to the observed signal changes. For instance, one can show that a tissue T_1 increase of merely 13ms can also result in a 4% of signal decrease, in the absence of CBV changes. However, there is no known mechanism by which the extravascular tissue T_1 can increase during activation. Note that increase in oxygenation will cause a slight increase in blood T_1 (2). However, such increase is small in amplitude (<50ms) and our simulation shows that it does not contribute significantly to the VASO signal.

In summary, our results show that high-resolution VASO fMRI is feasible and provides excellent localization to gray matter. The VASO signal mechanism may require more complete modeling of various components. Caution should be used in quantification and interpretation of VASO results.

REFERENCES: 1) Lu MRM 50: 263 (2003); 2) Lu MRM 52: 679 (2004); 3) Leenders Brain 113: 27 (1990); 4) Belliveau Science 254: 716 (1991); 5) Pfeuffer MRM 47: 903 (2002); 6) Lee MRM 45: 791 (2001). **Acknowledgements**: NIBIB EB004130

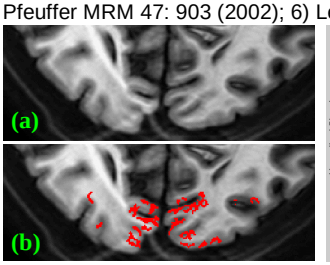

Fig. 1: (a) VASO image and (b) visual activation map at 0.78x0.78x3 mm^3 resolution

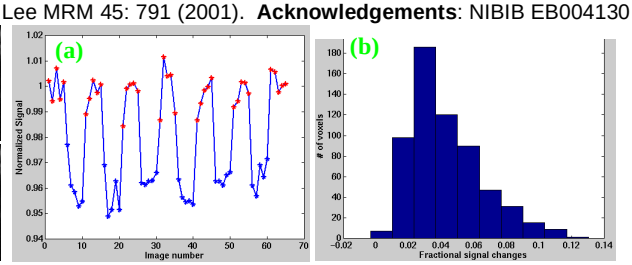

Fig. 2: (a) time-course of activated voxels. Blue dots indicate activation period. (b) histogram of fractional signal changes (604 voxels in total).

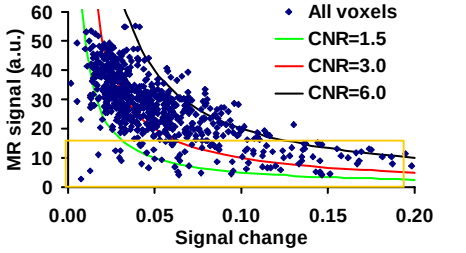

Fig. 3: Scatter plot of fractional signal changes (magnitude) versus baseline MR signal. The symbols in the yellow box have low SNR and were not consider in Figs. 1 and 2. The lines are iso-CNR curves.