Characterization of spatial variation of BOLD-associated neuronal activity in fMRI

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Introduction: BOLD fMRI usually relies on the detection of contrast generated by BOLD-induced changes in local B0 field homogeneity [1, 2]. The work presented here introduces two new contrast mechanisms that arise from the spatial difference of BOLD-induced changes in local B0 field homogeneity and strength. These new contrast mechanisms are generated using a complex signal calculated from original fMRI signals. This signal, as it physically characterizes local B0 field variation in image space, is called "field variation signal" in this work. In a human fMRI experiment, it is demonstrated that a field variation signal can provide BOLD-related phase contrast that cannot be afforded by a conventional technique and the use of multiple field variation signals can specify the spatial difference of biophysical changes associated with BOLD effects between neighboring voxels in brain cortex. This novel approach to fMRI data analysis offers the potential to visualize the spatial variation of neuronal activity in BOLD fMRI.

Methods and Materials: A field variation signal S_{fv} is defined as:

$$S_{fv}(\vec{r},t,\Delta\vec{r}) = \frac{S_{fMRI}(\vec{r},t)}{S_{fMRI}(\vec{r}-\Delta\vec{r},t)} \quad (1),$$

where $S_{fMRI}(\vec{r}, t)$ represents an acquired fMRI signal in spatial-temporal domain, $\vec{r}$ is the spatial position vector, t is the time frame, and $\Delta\vec{r}$ represents a spatial shift. Since complex fMRI signals are used in Eq. 1 for data analysis, the generated signal S_{fv} has both magnitude and phase. It can be seen from Eq. 1 that a field variation signal has a magnitude equal to the ratio between the fMRI signal intensity at a position $\vec{r}$ and that at a position $\vec{r}-\Delta\vec{r}$, and a phase equal to the phase difference of the fMRI signals at the two positions. As neuronal activity may induce different changes of local B0 field homogeneity (MRI magnitude sensitive) and strength (MRI phase sensitive) at different spatial positions, the field variation signal characterizes the spatial difference of BOLD effects. As follows, we will use a human fMRI experiment as an example to show that field variation signals are sensitive to BOLD effects and they may provide BOLD-related phase contrast that cannot be afforded by a conventional technique. Also exemplified will be a novel approach to fMRI data analysis that can visualize the spatial variation of BOLD effects using multiple field variation signals to generate spatial pattern plots with the information about the difference of BOLD-induced changes in local B0 field homogeneity and strength between neighboring voxels in brain cortex.

A human fMRI experiment was performed using a finger tapping task as the stimulus with a period of 20s on and 20s off. Six subjects were scanned in a run of about 6 minutes on a 3T clinical MRI scanner. A total of 160 volume images were acquired using a single shot gradient echo EPI sequence (TR/TE 2000/30ms, Flip angle 70°, FOV 220mm, Matrix 128×128, Slice thickness 3mm, no gap, Number of slices 29). The analysis was based on a linear regression model with an order of 20. Two time model fittings were implemented with and without the linear regression model. *F*-statistics were calculated for each voxel based on the ratio of two residual sum of squares in the model fittings.

Results and Discussion: As an example, Fig. 1 illustrates how a field variation signal is calculated from the fMRI signals of two voxels in the motor cortex of a subject. It can be seen that the field variation signal gives BOLD contrast difference of the fMRI signals from two different locations, implying a field variation signal can visualize the spatial variation of BOLD effects associated with neuronal activity in image space. Attention should be paid to the phase time course which clearly shows BOLD contrast that can be hardly seen from the original fMRI signals. In this experiment, BOLD-related phase contrast clearly detectable as in Fig. 1 was observed from field variation signals in activated cortex regions without large blood vessels around. This gain should be attributed to the use of local phase difference that can effectively reduce destructive noise induced by global B0 field fluctuation of MRI or respiration. Fig. 2 shows a comparison between conventional fMRI data analysis using only the magnitude of fMRI signals and our new data analysis using the magnitude and phase of field variation signals. In the motor cortex, the correlation maps generated from all three signals give similarly high values indicating field variation signals indeed provide BOLD information. However, different patterns can be seen in correlation maps because original fMRI signals provide BOLD contrast, while field variation signals characterize the spatial difference of BOLD contrast. As a result, the magnitude and phase time course of field variation signals have two polarities with respect to the magnitude time course of original fMRI signals, i.e., they either increase (positive polarity) or decrease (negative polarity) as the magnitude of original fMRI signals increases. These different polarities can be seen from the examples of time course plots in Fig. 2. Since a field variation signal is generated by the division of the fMRI signals at two different voxels, the polarities provide information about how BOLD effects vary spatially from one voxel to the other: The magnitude polarity indicates whether the BOLD response level increases or decreases from one voxel to the other, and the phase polarity indicates whether BOLD effects induce a increase or decrease of local B0 field strength difference between the two voxels. Using the polarity information in multiple field variation signals calculated with one voxel spatial shift in different directions, we can generate spatial pattern plots to characterize the spatial difference of BOLD-induced changes in local B0 field homogeneity and strength between neighboring voxels in brain cortex. As demonstrated in Fig. 3, an arrow is used to indicate the polarity direction between every two neighboring voxels in a time course signal: Those arrows in the same direction as spatial shift indicate positive polarity, and otherwise negative. Two spatial pattern plots are generated respectively from the magnitude and phase of field variation signals. In either plot, one can easily find some "local extrema" voxels with higher (red dots that arrows direct to) or lower (blue dots that arrows direct from) BOLD-induced changes than all their neighbors. These are useful biophysical information that cannot be provided by a conventional fMRI analysis technique. We are currently investigating how to take advantage of the BOLD contrast and information in field variation signals to improve biophysical modeling and characterization of hemodynamic response in BOLD fMRI.

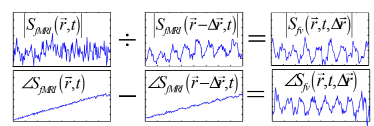

Fig. 1 Calculation of a field variation signal from fMRI signals. The plots are time course signals of magnitude (top row) and phase (bottom row).

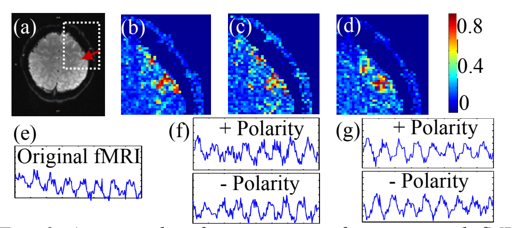

Fig. 2 An example of comparison of conventional fMRI analysis and new approach. Anatomical image (a) shows the motor cortex (rectangular box). Correlation maps are generated using magnitude of original fMRI signals (b), and magnitude (c) and phase (d) of field variation signals. The plots are examples of magnitude time course of original fMRI signals (e), and magnitude (f) and phase (g) time courses of field variation signals.

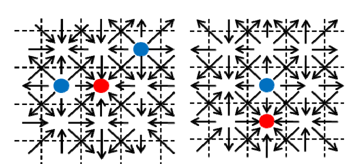

Fig. 3 Spatial pattern plots for characterizing the spatial difference of BOLD-induced changes of local B0 field homogeneity (left) and strength (right) in 9 neighboring voxels of the activated motor cortex (red arrow in Fig. 2).

Reference: [1]. Bandettini, P.A. et. al., MRM 1993, 30: 161-173. [2]. Ogawa, S. et. al., Proc. Natl. Acad. Sci. USA 1990, 87:9868-9872.