

# Dynamic Magnetic Resonance Inverse Imaging of Human Brain Function

F.-H. Lin<sup>1</sup>, L. L. Wald<sup>1</sup>, K. K. Kwong<sup>1</sup>, S. P. Ahlfors<sup>1</sup>, M. S. Hamalainen<sup>1</sup>, J. W. Belliveau<sup>1</sup>

<sup>1</sup>Martinos Center for Biomedical Imaging, Massachusetts General Hospital, Charlestown, MA, United States

## INTRODUCTION

Due to its high spatial resolution, non-invasiveness, and the flexibility of contrast preparation, MRI has also been considered for its potential to detect fast dynamic functional changes in human. However, efforts have been hampered by the lack of temporal resolution that would allow un-ambiguous identification of dynamic changes on the millisecond time scale. In this study, we propose MR Inverse Imaging (InI) to achieve an order-of-magnitude speed-up in the MRI acquisition rate. MR Inverse Imaging was inspired by the source localization methods in electroencephalography (EEG) and magnetoencephalography (MEG) [1]. InI is a generalization of MR imaging methodology that uses information from multiple channels in an RF coil array to solve for the dynamic spin density distribution. Inverse Imaging covers both traditional over-determined parallel MRI [2], as well as under-determined ultra-fast single-echo acquisition [3]. In InI, both spatially resolved estimates of dynamic changes and the associated statistical inference can be obtained in millisecond scale using a linear estimation approach. We present a theoretical framework of InI and demonstrate it with classical BOLD fMRI with 20-ms temporal resolution.

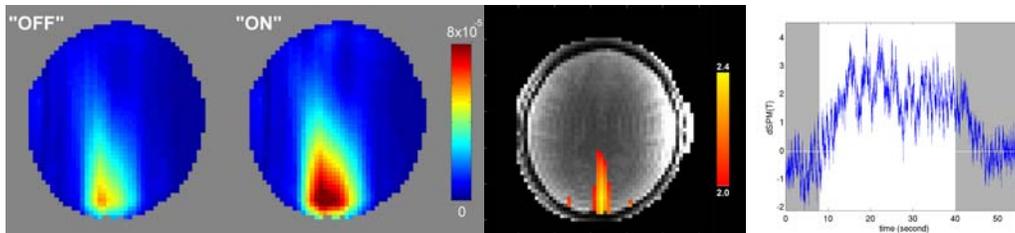
## METHODS

MR Inverse Imaging solves the time resolved spin density distribution by minimizing the cost function:  $\| \mathbf{C}^{-1/2} \mathbf{y}'(t) - \mathbf{C}^{-1/2} \mathbf{A} \mathbf{x}'(t) \|^2 + \lambda^2 \| \mathbf{x}'(t) \|^2$ , where  $\mathbf{A}$  is the "forward operator" consisting of the sensitivity profiles of the channels in the array, and  $\mathbf{C}$  is the noise covariance matrix of the channels.  $\mathbf{y}'(t)$  contains the stacks of instantaneous changes over a defined baseline on the channels.  $\mathbf{x}'(t)$  indicates the dynamic change of the spin density at time  $t$ . Note that this cost function requires no *a priori* image to resolve the dynamic changes. Statistical inference can be obtained by normalizing  $\mathbf{x}'(t)$  over the baseline noise estimate. Note that  $\mathbf{y}'(t)$  represents the dynamic changes measured in a single central k-space line (point) acquisition for 1D (2D) InI. Solving for  $\mathbf{x}'(t)$  is an inverse problem analogous to MEG/EEG source localization based on the spatial information encoded in the forward model  $\mathbf{A}$ . The inverse solution based on only fractional sampling of the k-space makes an ultra-fast temporal resolution possible.

We demonstrated 1D InI (using a single readout gradient to encode the second spatial direction) in a visual fMRI experiment with blocked design 8-Hz flickering checkerboard stimulus. The experimental paradigm consisted of 56 seconds, including 8-s "OFF", followed by 32-s "ON", and finally 16-s "OFF" with total 20 repetitions. We used PRESTO sequence [4] to collect ultra-fast MR InI acquisitions with TR=20ms, Flip angle=20 deg. and TE=43 ms on a 1.5T scanner (Avanto, SIEMENS Medical Solution, Erlangen, Germany) using our 90-channel head RF coil array. After InI reconstruction, fMRI time courses from all channels were first linearly de-trended and subsequently averaged across experiments to improve the SNR. Reconstructed data were also spatially smoothed by 6-mm FWHM isotropic Gaussian kernel. We defined the "baseline" as the 24-s interval in "OFF" condition and calculated the dynamic  $t$ -statistics maps in 20-ms temporal resolution. We also analyzed the point spread function of the reconstruction using simulated data.

## RESULTS

As a proof of concept, we acquired BOLD fMRI experiment at 20-ms temporal resolution. Using Inverse Imaging reconstructions, we generated 2800 dynamic statistical parametric maps. The temporal average images of InI reconstructions during "ON" and "OFF" conditions before statistical inference calculation were shown in Figure 1. Note that both images showed occipital lobe activity since the baseline for comparison included post-stimulus delayed response, while "ON" condition in averaged had stronger activity. The  $t$ -statistic comparison between conditions is shown in Fig. 2. The averaged time-resolved  $t$ -statistics over an occipital lobe ROI are shown in Figure 3. We observed a clear elevated statistical significance level during visual stimulation. We also clearly resolved non-aliased oscillations that follow the cardiac and respiratory cycles.



**Fig.1** (left) The temporally averaged InI reconstructed images during "ON" and "OFF" conditions. The images were shown in arbitrary unit.

**Fig.2** (Middle) The temporally averaged InI  $t$ -statistics maps during "ON" conditions. Note that localized activation was found around the occipital lobe.

**Fig.3** (Right) The averaged BOLD fMRI time course of 20-ms temporal resolution within occipital lobe ROI. The gray-shaded period indicates the "OFF" condition, while the white period indicates the "ON" condition. Elevated statistical significance values were observed during the "ON" condition.

## DISCUSSIONS

In this research, we present MR Inverse Imaging (InI) methodology to improve the temporal resolution of dynamic MR measurement into the millisecond scale. The experimental design of InI is similar to evoked response experiments in MEG/EEG. Not only is ultra-fast MR imaging (on the scale of 100 frames per second) mandatory as a tool for testing any novel direct neuronal contrast mechanisms, it may not be possible to discern a contrast change which occurs and then disappears on a 10 ms scale without an imaging technique with similar temporal resolution. Although the spatial localization was degraded compared to gradient encoded methods, it was found to improve with image SNR. We expect that higher field acquisition as well as dedicated, optimized RF coil arrays with disparate spatial information can further improve localization ability. The proposed Inverse Imaging is expected to extend the temporal resolution of MRI time-series and provide increased flexibility in the trade-off between spatial and temporal resolution for further elucidation of dynamic activation patterns in the human brain.

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