

# Ultra-fast fMRI of human visual cortex using echo-shifted magnetic resonance inverse imaging

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## INTRODUCTION

Functional MRI (fMRI) with blood-oxygen level dependency (BOLD) contrast [1, 2] measures the hemodynamic response secondary to neural activity [3]. Typically fMRI uses the echo-planar imaging (EPI) [4] to acquire images covering the whole brain with a TR of a few seconds. Using the magnetic resonance inverse image (InI) technique, the scan time per brain volume can be reduced to 100 ms [5]. To detect the fine temporal property of hemodynamic response, we aim to increase the scanning rate to 40 Hz per volume. However, the optimal BOLD contrast is achieved at TE = 30 ms at 3T. Such an echo time limits the shortest TR using steady-state incoherent sequences. This challenge can be mitigated by echo-shifted pulse sequences, such as PRESTO [6]. Here we propose the echo-shifted InI (esInI) to achieve TR = 25 ms with whole-brain coverage with TE = 34 ms to achieve an unprecedented temporal resolution while maintaining the optimal functional contrast. We used an event-related design to probe the spatial and temporal properties of task-related hemodynamic responses in the human visual cortex. The accelerated esInI scans generated two dimensional projection images, which were subsequently reconstructed for volumetric images by the minimum-norm estimation (MNE) approach [7]. We found that esInI localized the visual cortex, and the time courses in functional areas were consistent with the waveforms measured by EPI.

## METHODS

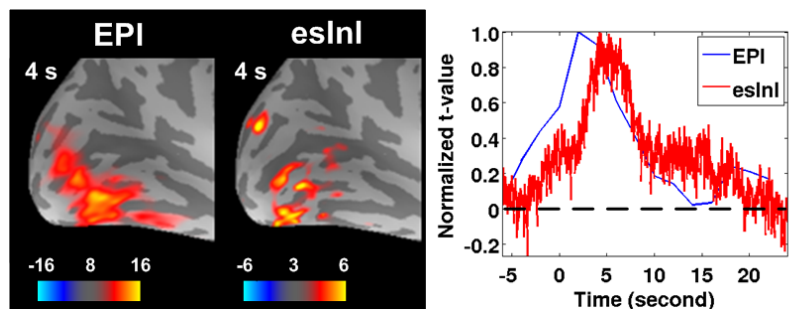
The esInI was collected using an echo-shifted single-shot echo-planar imaging (EPI) readout after exciting one thick sagittal slab covering the entire brain. The additional de-phasing gradients were applied on the phase gradient (GP) and readout gradient (GR) to avoid undesired interaction between echoes from consecutive excitations. Echo-shifting by 1TR was done by adding additional gradient moments to de-phase the magnetizations after the  $n^{\text{th}}$  RF excitation and to refocus the magnetizations excited by the previous  $(n-1)^{\text{th}}$  RF excitation ( $n \geq 1$ ). Specifically, additional de-phasing gradient moments of GP =  $0.75N_y/(\gamma FOV_y)$  and GR =  $0.75N_x/(\gamma FOV_x)$  were added before the ADC readout.  $N_y$  and  $FOV_y$  denote the number of voxels and the FOV along the GP direction respectively. Likewise,  $N_x$  and  $FOV_x$  denote the number of voxels and the FOV along the GR direction. After ADC readout, an additional rewinding gradient moment of GP =  $-1.5N_y/(\gamma FOV_y)$  and GR =  $-1.5N_x/(\gamma FOV_x)$  to help refocus the magnetization after the next RF pulse. To further shorten the TE and TR, we used 3/4 partial Fourier acquisition. Overall, we achieved TE=9 ms, TR=25 ms, and the effective TE was 34 ms. The reference scans of esInI were collected similar to accelerated scans but partition phase encoding was used to obtain the spatial information along the left-right axis.

The esInI signal  $\mathbf{y}$  generated from the unknown image  $\mathbf{x}$  in the presence of the noise  $\mathbf{e}$  can be formulated as  $\mathbf{y} = \mathbf{A}\mathbf{x} + \mathbf{e}$ , where  $\mathbf{y}$  and  $\mathbf{e}$  are vectors of length  $n$  and  $\mathbf{x}$  is vector of length  $m$  ( $m > n$  in general). The  $n$ -by- $m$  forward matrix  $\mathbf{A}$  consists of the RF coil sensitivity profiles and the projection operation, since only the central k-space line was acquired. To solve such an underdetermined inverse problem, we used the minimum-norm estimation (MNE) [7]:  $\mathbf{x}^2 = \mathbf{A}^H(\mathbf{A}\mathbf{A}^H + \lambda\mathbf{C})^{-1}\mathbf{y}$ , where  $\mathbf{C}$  is the noise covariance matrix of the  $\mathbf{y}$ .

We demonstrated esInI using an event-related fMRI experiment with an 8-Hz checkerboard visual stimulus shown on the participants' left or right hemifield. The paradigm consisted of 0.5 s checkerboard flashing with a 2 s of minimum inter-stimulus interval. Total 30 stimuli per run and 4 runs (2 minutes per run) were measured on a 3T scanner (Tim Trio, SIEMENS Medical Solutions, Erlangen, Germany) using a 32-channel head RF coil array. The spatial resolution in the left-right direction was calculated from esInI reconstruction. Parameters for the reference scan were FOV 256x256x256 mm<sup>3</sup>, image matrix 64x64x64, 64 partitions, TR=25 ms, effective TE =34 ms, 4mm thickness, 64 slices. Accelerated esInI acquisitions used the same imaging parameters in the reference scan except that the partition encoding steps were removed. Volumetric reconstruction was done time point by time point. Afterward, the esInI time series were analyzed by the General Linear Model using finite impulse response basis functions to estimate the hemodynamic responses to the visual stimuli with 30 seconds duration and 6 seconds baseline. To validate localization, EPI data were also collected using the following parameters: TR = 2s, TE = 30 ms, flip angle = 90° slice thickness = 4 mm. EPI data included 60 stimuli per run and 2 runs (4 minutes per run) in total.

## RESULTS

The figure at left shows the activated visual cortex identified by EPI and esInI at 4s after the onset of right hemifield visual stimulation. Two snapshots were the medial view of dynamic statistical parametric mapping (dSPM) of  $t$  statistics overlaid on the inflated left cerebral hemisphere. The time courses (right) show the EPI waveform (blue) and esInI waveform (red) within the visual cortex. Both esInI and EPI localized the visual cortex in the posterior occipital lobe. However, the significance level of functional activity revealed by esInI was found less than that of EPI. The esInI showed similar hemodynamic response waveform to that of EPI with time delay.



## DISCUSSION

We demonstrate the feasibility of ultra-fast imaging technique using InI combined with echo shifting. Validated by the EPI results, esInI has good spatial resolution with the unprecedented temporal resolution of 25 ms with the whole brain coverage. The SNR of esInI was found less than that of EPI, consistent with previous studies [8]. With such a high temporal resolution, we have chance to investigate the high-frequency properties of hemodynamic response up to 20 Hz without worrying aliasing. Although MNE is used for 3D reconstruction in this study, other InI localization techniques such as spatial filtering and k-space reconstruction can be used alternatively.

## REFERENCES

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