## Multi-echo Parallel Imaging Accelerated fMRI with Susceptibility-induced Off-resonance Compensation

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**Introduction** fMRI requires fast imaging sequences such as EPI or spiral imaging. These sequences can suffer from severe image distortions and dropouts, precluding fMRI in areas of field inhomogeneities. In-plane distortions can be reduced by parallel imaging, but through-plane intra-voxel dephasing remains. Through-plane distortions are mainly caused by susceptibility differences at air-tissue interfaces such as above the nasal cavities and ear canals. Several techniques have been presented to overcome these dropouts. The most prominent is the z-shim technique (initially proposed in [1]), which introduces multiple refocusing gradients in z-direction to rephase spins at a certain off-resonance frequency. Several ways of how to use this technique have been proposed (e.g. [2], [3], [4], [5]), however no single solution suitable for all applications in fMRI has been presented yet. The biggest issue is the additional scan time necessary to acquire at least 2 images with different z-shim gradients to eliminate susceptibility-induced off-resonances. The issues with [2] and [3] are higher in-plane image distortions compared to regular EPI; [4] and [5] lead to prolonged image acquisitions. In this study, we propose using a multi-echo EPI approach together with parallel imaging to acquire multiple echo trains following a single signal excitation. Different z-shim gradients are applied before each readout to compensate for susceptibility-induced signal loss.

**Methods** Using our recently developed PERMEATE multi-echo pulse sequence with parallel imaging acceleration [6], several echoes can be acquired within one single signal excitation (Fig.1). Every R-fold undersampled echo image can be reconstructed to a full k-space data set using GRAPPA-weights derived from the first R interleaves of each measurement. Using PERMEATE with R=2 and a matrix size of 96x96 voxels, three echoes fit into the same acquisition time required for a single echo measurement with a near-optimal TE of 50 ms at 1.5T. The area of the rephasing gradient in the slice-select direction was reduced to induce a z-shim gradient before the first echo train (Fig.1), resulting in high was then completed prior to the second echo train to be most sensitive to the main resonance frequency (Fig.2b/c). For overall brain coverage, the root-sum-of-squares of the three images was created (Fig.2d).



Fig.1: PERMEATE pulse sequence [6] with additional z-shim gradients (highlighted in red) on the slice-select gradient axis. The first z-shim gradient is incorporated into the slice-select rephasing gradient.



Fig.2: 3-echo acquisition using z-shim susceptibility compensation: a) first image at TE1=23 ms, z-shim gradient was induced to acquire signal from offresonant locations; b) second echo image at 48.9 ms, on-resonance; c) third echo image at 74.8 ms, on resonance; d) combination of the three images.

A 1.5T GE Signa 12X Excite unit with an 8-channel phased array head receiver coil (Invivo Cooperation) was used for all measurements. TE's were set to 23ms, 48.9ms, and 74.8ms. A flip angle of  $70^{\circ}$  and a TR of 1500ms were applied. The slice-select rephasing gradient was set to 30% of its original area. A second refocusing gradient in z-direction was applied following the first echo train to fully rephase the spins in regions without off-resonance effects. 15 5mm-slices were acquired. A breath-holding experiment was performed by the volunteer to stimulate functional activation in all areas of the brain. A baseline period of 16.5s was followed by a 3s-long breath-in period and a 16.5s long breath-holding period. The on-/off-cycle was repeated eight times, followed by a 18s long off-period, and resulting in a total scan time of 5:06 min. The correlation of the stimulus response with a sinusoid function [7] was calculated for the first echo image and the average of the second and third echo images separately, resulting in two separate correlation maps. The correlation coefficient of the first echo image was considered for all voxels in which the signal magnitude of the first echo image. For all other voxels, the values derived from echo two and three were used to create the final activation map. Finally, a correlation threshold of r=0.3 was applied, above which a particular voxel was considered activated by the stimulus.

**<u>Results</u>** Fig.2 shows slice images from one time point in the fMRI experiment. In the non-compensated echo images (Fig.2b/c), dropout regions are clearly visible, while the signal from these regions was recovered in the susceptibility-compensated first echo image (Fig.2a). Signal dropouts were almost eliminated in the combined root-sum-of-squares images (Fig.2d). Fig.3 shows the resulting fMRI activation maps from a) the susceptibility-compensated method and b) a separate 3-echo fMRI experiment using a regular rephasing gradient (no z-shimming). The fMRI signal could be successfully restored in the aforementioned dropout regions (encircled in green in the non-compensated experiment).

**Discussion** The results clearly show restored signal in typical dropout regions usually "invisible" to the scanner. In terms of the fMRI experiment, activation could be restored in these regions. In more uniform regions, the fMRI signal was not compromised by the lack of signal from the first echo image. Therefore, our susceptibility-compensated multi-echo fMRI acquisition technique can be used to acquire fMRI data with whole-brain coverage without significant reduction in sensitivity. The averaging of two echo images (echoes two and three) restores most of the sensitivity that was lost by parallel imaging. Furthermore, this technique does not prolong scan time compared to standard acquisition techniques, making it a valuable alternative for whole-brain fMRI measurements where dropout regions are a concern.

**<u>References</u>** [1] Frahm *et al*, MRM 6:474-480, 1988; [2] Song *et al*, MRM 46:407-411, 2001; [3] Gu *et al*, NeuroImage 17:1358-1364, 2002; [4] Posse *et al*, NeuroImage 18:390-400, 2003; [5] Yang *et al*, MRM 52:1418-1423, 2004; [6] Newbould *et al*, MRM 58:70-81, 2007; [7] Lee *et al*, MRM 33:745-754, 1995

<u>Acknowledgements</u> NIH (2R01EB002711, 1R21EB006860), Center of Advanced MR Technology at Stanford (P41RR09784), Lucas Foundation, and Oak Foundation.



Fig.3: Activation maps with susceptibility compensation (a) and in a non-compensated experiment (b). Dropout regions in the non-compensated experiment are encircled