Combined gradient- and spin-echo EPI acquisition technique for high-resolution fMRI

H. Schmiedeskamp[1], S. J. Holdsworth[1], S. Skare[1], R. D. Newbould[2], G. H. Glover[1], and R. Bammer[1]

[1]Lucas Center, Department of Radiology, Stanford University, Stanford, CA, United States, [2]GlaxoSmithKline, London, United Kingdom

INTRODUCTION – Gradient-echo (GRE) based fMRI pulse sequences are most sensitive to larger vessels, including veins. The regions-of-interest for neuronal activity, however, are mainly within capillaries. Effective localization of brain activity would require that the BOLD signal is confined to the microvasculature. However, in GRE-based sequences BOLD signal changes tend to be located distant to the sites of increased brain activity [1], causing misregistration between BOLD signal localization and the sites of underlying neuronal activity. In contrast, the spin-echo (SE) based pulse sequence [2] is a promising alternative which gives higher sensitivity to the microvasculature, but lower overall BOLD-sensitivity. In order to increase resolution in BOLD-fMRI, increasing spatial resolution of the acquisition does help, but the addition of SE-based image acquisition will enhance the resolution even further. Incorporating GRE- and SE-readouts into one pulse sequence combines the advantages of higher overall BOLD-sensitivity of the GRE-signal with better specificity of the SE-signal. The extension of a multi-echo gradient-echo pulse sequence to acquire both GRE- and SE-signal has been shown useful for vessel size imaging [3] and DSC-PWI [4]. A similar approach [5] was used for low-resolution BOLD-fMRI to estimate vessel size by combining the acquisition of GRE- and SE-signals. In this study, we apply a combined GRE-/SE-EPI pulse sequence to acquire high-resolution BOLD-fMRI images. By increasing spatial resolution in BOLD-fMRI, image acquisition will increase as well – leading to prolonged readout times. Without parallel imaging (PI) acceleration, a two-fold increase in spatial resolution will increase acquisition time by a factor of approximately four. Assuming mono-exponential signal decay, GRE-based fMRI is most sensitive to BOLD signal changes at $TE \approx T_2^*$, and SE-based techniques are most sensitive at $TE \approx T_2$ [3,6]. At 3T, the T_2^* of brain tissue is around 35-40 ms, and T_2 equals 90-100 ms, adding timing-constraints to high-resolution acquisitions. In the present study, we used PI-acceleration to achieve shorter readout times, thus allowing the inclusion of a GRE-EPI readout between the 90° excitation pulse and the 180° SE-refocusing pulse.

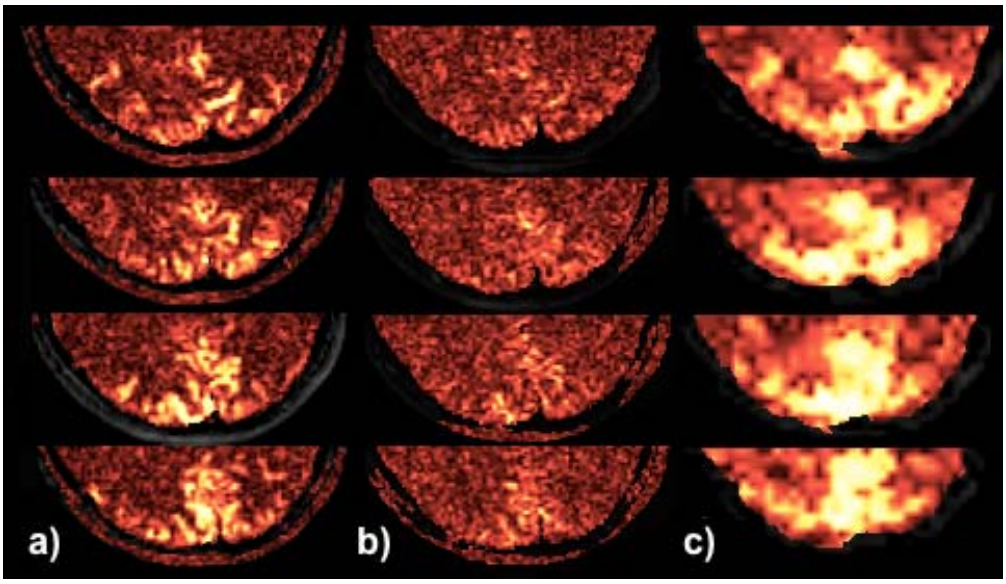
METHODS – BOLD-fMRI experiments were conducted at 3 Tesla (gradients = 40mT/m, 150mT/m/s), using an 8-channel phased array head receiver coil. Twelve slices covering the visual cortex were acquired within a TR = 2000 ms. Other imaging parameters were: a matrix size of 150×150 voxels, slice thickness = 2.5 mm (0.5 mm spacing), FOV = 24 cm, and a final image resolution of 1.6×1.6×2.5 mm. A combined GRE- and SE-pulse sequence [4] was used for image acquisition. Here, a fat-saturation pulse was followed by a 90° RF excitation pulse, a gradient-echo EPI readout train with TE_{GRE} = 25.5 ms, a 180° spin-echo refocusing pulse, and a spin-echo EPI readout train with TE_{SE} = 100 ms (Fig. 1d). The signal was measured with a PI reduction factor R = 3 to increase temporal resolution. PI reconstruction was performed using a 2D-GRAPPA kernel [7]. The first 3 temporal frames were acquired in an interleaved fashion for GRAPPA-calibration. Thereafter, only the first interleave was repeated throughout the experiment to avoid signal fluctuations from different interleaves. Block-design functional experiments were performed using a visual stimulus (checkerboard with alternating contrast, frequency = 8 Hz) with 9 off- and 8 on-cycles (18 s duration), resulting in an acquisition time of 5:06 min. The correlation of the BOLD-signal to a sinusoid function [8] was calculated for the correlation coefficient maps shown in Fig. 1a-c. For comparative purposes, a low-resolution single-shot EPI fMRI-experiment was conducted with in-plane resolution of 64×64 voxels, TE = 29.7 ms, and otherwise equal parameters.

RESULTS – Fig. 1 shows correlation coefficient maps for two experiments with the same volunteer. As expected, the low-resolution experiment was much more sensitive to the stimulus, resulting in functional activity all over the posterior head (Fig. 1c). However, functional activity in this experiment appears blurry and it was impossible to resolve finer structures or a more distinct profile of functional activity. In contrast, functional maps resulting from our pulse sequence showed greater detail in the gradient-echo images (Fig. 1a) acquired with comparable echo time to the low-resolution images. Fig. 1a resolved large areas of functional activity into much more detail than Fig. 1c, showing activated areas side-by-side with inactivated areas, whereas the low-resolution scans resulted in large uniform areas of high correlation to the stimulus (best seen in the center of the second slice from the top). In contrast, the correlation coefficients in the spin-echo images were very small, caused by the low sensitivity of spin-echo fMRI compared to gradient-echo fMRI. Although the lack of sensitivity, it was possible to resolve some more detailed structures not seen in the gradient-echo images (third slice from the top in Fig. 1b).

DISCUSSION – Our results from fMRI experiments with stimulation of the visual cortex revealed great detail about the location of functional activity within the human brain. With our combined GRE-/SE-EPI acquisition, it was possible to resolve much more detailed profiles of functional activity with comparable temporal resolution to standard fMRI experiments. Despite lower signal-to-noise ratio, the gradient-echo EPI images resolved a substantial amount of functional activity, showing much more detail compared to a low-resolution, high-sensitivity scan. It was possible to increase spatial resolution further by the acquisition of additional spin-echo EPI images showing even more distinct areas of functional activity due to larger sensitivity to the microvasculature. With this combined high-resolution GRE-/SE-pulse sequence, we hope to deliver a valuable tool for clinical applications of fMRI, where exact spatial localization of neuronal activity is highly relevant.

References: [1] Turner, NeuroImage 2002;16:1062-67, [2] Kiselev *et al*, MRM 2005;53:553-63, [3] Bandettini *et al*, NMR Biomed 1994;7:12-20, [4] Newbould *et al*, Proc. ISMRM 2007;p1451, [5] Jochimsen *et al*, NeuroImage 2008;40:228-36, [6] Menon *et al*, MRM 1993;30:380-86, [7] Qu *et al*, JMR 2005;174:60-67, [8] Lee *et al*, MRM 1995;33:745-54

Acknowledgements: NIH (2R01EB002711, 1R01EB008706, 1R21EB006860, P41RR09784), Lucas Foundation, Oak Foundation.



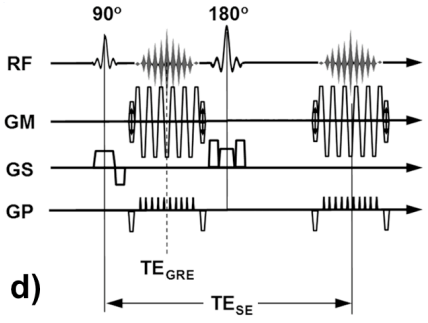


*Fig.1: fMRI correlation maps in response to a functional stimulus in the visual cortex. Comparison of **(a,b)** combined gradient- and spin-echo acquisition with a matrix size of 150x150 and **(c)** gradient-echo acquisition with a matrix size of 64x64. **(d)** Pulse sequence design with a combined gradient- and spin-echo EPI readout train (fat saturation pulse not shown).*