Experimental investigation of the relation between gradient echo BOLD fMRI contrast and underlying susceptibility changes at 7T

Dávid Z Balla[1], Rosa M Sanchez Panchuelo[2], Samuel J Wharton[2], Gisela E Hagberg[1,3], Klaus Scheffler[1,3], Susan T Francis[2], and Richard W Bowtell[2]
[1]*High-field MR Centre, Max Planck Institute for Biological Cybernetics, Tübingen, Germany,* [2]*Sir Peter Mansfield Magnetic Resonance Centre, University of Nottingham, Nottingham, United Kingdom,* [3]*Department for Biomedical Magnetic Resonance Imaging, University of Tübingen, Tübingen, Germany*

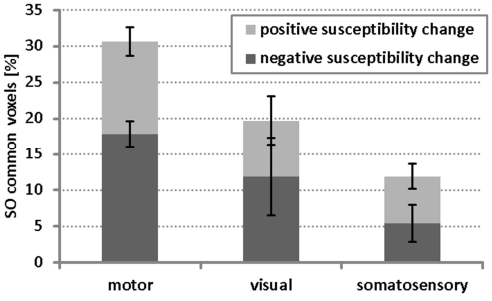
Introduction: Functional MRI (fMRI) based on gradient echo (GE) acquisition at coarse sampling resolutions and conventional field strengths (e.g. 1.5T) yields a local contrast, which can be linearly proportional to the activation related susceptibility changes averaged over a single voxel. Early numerical simulations showed that such a linear relation is expected only in large veins [1], corroborating the conclusion of experiments at 1.5T that the main source of the functional blood oxygenation dependent (BOLD) contrast is pial veins on the cortical surface [2]. Since then the dependence of BOLD-contrast on several physiological and MR-related parameters has been studied, and it is widely acknowledged that there is not generally a linear relation between contrast and susceptibility changes. Recent numerical simulations investigated the effect of surrounding vasculature on intra-voxel BOLD-contrast and found an external contribution of up to 10% even in a distribution of randomly oriented capillaries [3]. In order to experimentally assess the relation between local susceptibility changes and fMRI contrast in different cortical regions, we applied an optimized version of the recently proposed functional susceptibility mapping (fQSM) technique [4] to high resolution GE time-series, and compared the results with the outcome of a conventional fMRI analysis applied to the magnitude data.

Materials and Methods: Multiple orientation (MO, n=4) and single orientation (SO, n=3) experiments were performed on 4 experienced volunteers using a 7T Philips Achieva system equipped with a 32-channel receive coil. The MO experiments implied 4 repetitions with the subject's head rotated differently relative to B_0 around the RL and SI-axes (~±15°). fMRI was performed with stimulation block-paradigms, involving a motor-task in the case of the MO experiments and visual, somatosensory and motor paradigms in the SO experiments. Time-series were acquired using zoomed, multi-slice GE-EPI with TR/TE = 3000/25 ms at 1mm isotropic resolution. Reference susceptibility maps ($\Delta\chi$) were reconstructed from 3D-FLASH datasets with TR/TE = 30/15 ms and (0.7mm)³ resolution. Data processing was optimized in several ways relative to the originally proposed fQSM pipeline [4] based on explicit quantitative comparison of the outcomes of 11 spatio-temporal filtering alternatives and other similar analyses. BOLD signal and susceptibility change maps ($\Delta I_B/\bar{I}$ and $\Delta\chi_B$) were threshold at a statistical t-score of 2.3 (p<0.1, uncorrected). We focused on voxels with significant magnitude and susceptibility changes ("common" voxels). This approach constrained the $\Delta\chi_B$ maps to voxels with coincident intensity changes in fMRI maps ($\Delta\chi_B^{com}$).

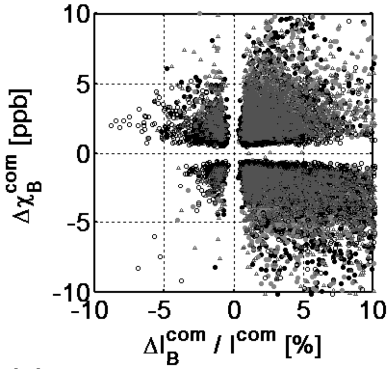
Results: In order to select the most efficient spatio-temporal filter for the fQSM pipeline, power spectral density maps, phase-specific noise ($tSD_{\square}/tSNR^{-1}$) maps, fQSM ($\Delta\chi_B^{com}$) to fMRI ($\Delta I_B/\bar{I}$) hit and fail rates, cross correlation ratios and linear fit parameters at common voxel positions were compared. As a result, the combination of bias-compensated DORK [5,6] with SHARP [7] was selected as the optimal approach in the fQSM pipeline, while robust homodyne filtering [5] was kept in reserve. Fig.1 shows masked $\Delta\chi_B^{com}$ and $\Delta I_B/\bar{I}$ activation maps for representative SO visual (V - transverse), SO somatosensory (S - sagittal) and MO motor (M - transverse) datasets overlaid onto the reference $\Delta\chi$ maps. The substantial negative BOLD activation in the conventional fMRI maps for the visual and somatosensory experiments is an effect of the stimulation paradigms. Our expectation was that fMRI contrast and underlying fQSM values have opposite signs (e.g. positive $\Delta I_B/\bar{I}$ → diamagnetic shift → negative $\Delta\chi_B$). The bar plot in Fig. 2 presents the ratios of common voxels in SO-fQSM relative to the total number of voxels in fMRI (100%) for the three stimulation paradigms used, suggesting a regional tissue specificity of GE-fMRI depending also on cortical structure, vein density and paradigm efficiency. The covariance scatter diagram in Fig. 3 highlights the interesting observation that for all subjects fQSM and fMRI contrast had the same sign in a significant number of voxels, indicating a strong non-local component of the conventional method in respective voxels. Maps in Fig. 1 focusing on the motor area (M) demonstrate that the expected negative $\Delta\chi_B$ changes only appear close to the cortical surface, whereas in deeper layers the activation induced positive $\Delta\chi_B$ and $\Delta I_B/\bar{I}$ values. Cross correlation coefficients (CC) of the absolute contrasts improve with increasing number of dynamics in time-series and for MO relative to SO-fQSM reconstructions from CC = 0.65 for 80 dynamics (SO motor) to CC = 0.81 for 640 fMRI and 160 fQSM dynamics (MO motor, same subject). The average CC of 0.81±0.01 for the MO results (which have the highest contrast to noise ratio) suggests that the conventional GE-fMRI contrast in an active voxel depends not only on susceptibility changes in that voxel.

Conclusion: Activation induced local susceptibility change and GE intensity contrast was compared using an optimized fQSM pipeline and conventional fMRI analysis. It is shown experimentally that the GE-BOLD contrast is a function of the local and surrounding susceptibility changes, which are specific for different activation areas in the brain. The unexpected but robust observation of positive $\Delta\chi_B$ values in the motor cortex calls for further investigation.

References: [1] Ogawa et al. (1993) Biophysical J 64:803; [2] Lai et al. (1993) MRM 30:387; [3] Chen et al. (2010) Med Phys 37:1778; [4] Balla et al. (2011) ISMRM #325; [5] Hagberg et al. (2012) Neuroimage 59:3748; [6] Pfeuffer et al. (2002) MRM 47:344; [7] Schweser et al. (2011) Neuroimage 54:2789



(2) The ratio of + and - common voxels relative to the total number of activated voxels in magnitude maps for different stimulation paradigms.



(3) Susceptibility change and BOLD contrast in common voxels for the 4 MO motor experiments (different markers).