Functional Quantitative Susceptibility Mapping in Comparison with BOLD and PET

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Target Audience: Researchers who are interested MRI, PET, fMRI, QSM, and EPI-phase processing.

Purpose: In functional MRI, information complementary to signal-magnitude variations, such as time-course phase and quantitative susceptibility data are increasingly taken into account[1,2,3,4] . The purpose of this work was to directly compare traditional magnitude BOLD-based fMRI and PET data with corresponding quantitative susceptibility data for activations triggered by visual stimuli.

Materials and Methods: **MRI**: Gradient-echo-EPI (FA=90, TR=3s, TE=35ms, voxel dimensions =1.8, 1.8, 4mm) images of two consenting volunteers were acquired on a 3T MR system (Ingenia, Philips Healthcare, Best, The Netherlands). **Paradigm:** A visual stimulation paradigm in a blocked (15s/block=5 dynamics) on-off experimental design was used, with 8 blocks of rest condition (grey screen with focus crosshair) alternated with 8 blocks of visual stimulation (black/white polar checkerboard on grey background, 8 Hz). Dicom images representing manufacturer-provided reconstructions of real and imaginary data were obtained from the scanner. **PET:** The regional cerebral blood-flow (CBF) response to the above-described stimulus was also measured for the same volunteers with $H_2{}^{15}O$ tracer kinetics. Two 180 s scans were performed, during 5 min baseline/stimulation. Stimulation was started 1 min before tracer injection. Tracer uptake in the first 60 s was averaged and Gaussian filtered (6mm kernel). Image algebra was used to subtract baseline CBF from CBF during stimulation and the resulting activation map was overlaid on the T1 MR anatomical reference. **QSM:** Dicom real and imaginary data from the scanner were used to calculate phase images, which were unwrapped and subject to background-field removal by the Laplacian-based SHARP (threshold parameter = 0.2) method[5] . Background noise and convolution artifacts were reduced by element-wise multiplication with the eroded binary whole-brain mask (FSL-BET[6], threshold=0.1). Quantitative susceptibility, ΔX, maps were obtained from the SHARP images by an inversion, using the relation $\Delta X = FT^{-1}(\frac{FT(-SHARP/(\gamma B_0 \Delta TE))}{g})$, $g = \frac{1}{3} - \frac{k_z^2}{k^2}$, $k^2 = k_x^2 + k_y^2 + k_z^2$, where FT = Fourier Transform, γ = gyromagnetic ratio, B_0 = field strength, ΔTE = echo-time increment. The threshold for division in k-space was 0.25, and the inverse was scaled by multiplying with the square of "g / 0.25" to smooth thresholding-induced discontinuities[5,7] . Calculated susceptibility maps and EPI-Magnitude "BOLD" images were Gaussian filtered (std =1 pixel) (**Fig.1**). Pearson coefficients for the correlation between Negative-QSM (inverted sign for visualization purposes) and BOLD time-course data with the ON/OFF visual stimulation paradigm time curve (**Fig.3e**) were calculated for each voxel, and summarized in correlation-coefficient maps (**Fig.2a-b**). For a selected ROI, shown in **Figure 2**, the time course of phase, SHARP, Negative-QSM and BOLD data are shown in **Figure 3**. Phase, SHARP and BOLD results were normalized to the absolute values of the corresponding first dynamic scan.

Results & Discussion

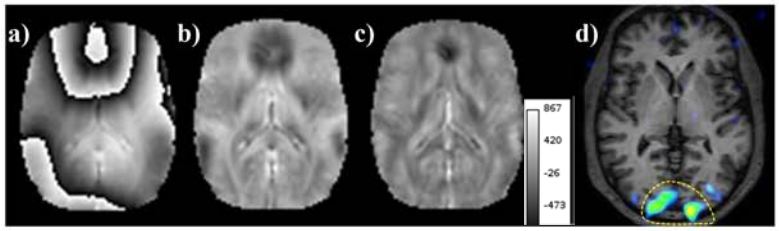

Fig.1: Post-processing image pipeline, a) phase (TE=35ms), b) Laplacian-based SHARP c) QSM (values in ppb) d) activation pattern from PET overlaid on an anatomical MRI reference

Figure 1 shows the QSM post-processing steps of the EPI data (a-c), and the PET-derived areas of neuronal activation (d) of one volunteer. The PET image showed the expected areas of visual stimulation, which are marked with a yellow ROI. **Figure 2** shows Pearson correlation-coefficient maps of Negative-QSM and BOLD with the visual paradigm. BOLD- or signal-magnitude based Pearson correlation maps (**Fig.2b**) agreed well with PET. Similar activation regions also showed up in Negative-QSM based Pearson correlation maps (**Fig.2a**); however there are a substantial number of other regions that correlated with the stimulation paradigm. In particular we can identify frontal areas located above the frontal cavities and orbita, and other areas that we tentatively associate with large cerebral veins.

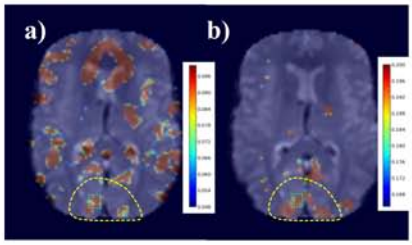

Fig.2: Pearson coefficient maps for a) Negative QSM, b) BOLD, with selected ROI (green box) overlaid on the magnitude EPI image.

The square ROI in the visual cortex exhibits high correlation coefficients for both maps (**Fig.2**), i.e. decreased apparent susceptibility and increased signal magnitude during visual stimulation. Mean phase, SHARP, QSM and magnitude results within the square ROI vs. time are plotted in **Figure 3**. **Figures 3a)** and **b)** show that the SHARP processing intrinsically eliminates substantial fractions of the observed long-term phase shift in **Fig. 3a)**. The Pearson correlation between the BOLD and Negative-QSM time-curves that are averaged within the square ROI and shown as red and blue trends in **Figure 3d)**, was 0.5, with a significant p-value below 0.0001. While the Negative-QSM time-course in the visual cortex ROI correlates well with the BOLD based time course and the stimulation paradigm, there are several areas in the brain that do not light up in either PET or BOLD based activation maps. Most prominent are the frontal areas, which in this study based on dynamic EPI data, would have been eliminated by standard BET-program masking but were included in the current evaluation by a lower threshold value (0.1, default: 0.5). Tentative explanations for the highlighting of these areas in the Negative-QSM based correlation maps may be eye movement or changed breathing patterns during the visual stimulation only. Highlighted veins in Negative-QSM based activation maps would a priori only be expected in areas associated with neuronal activations, as opposed to other areas that we found.

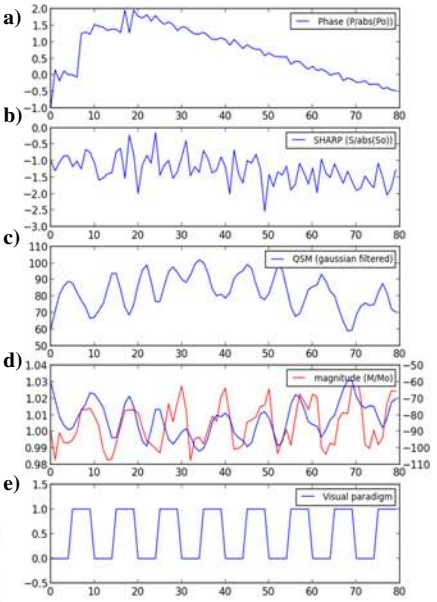

Fig.3: Time-evolution of ROI shown in Fig.2 (b). a) Signal phase b) sharp c) Gaussian Filtered QSM d) Negative Gaussian Filtered QSM (blue, sign-inverted scale in ppb on the right) and BOLD (red, left scale, normalized) (Pearson coefficient between Negative-QSM and BOLD = 0.5, $p < 0.0001$) e) Visual stimulation paradigm

Conclusion: Whereas Negative-QSM based Pearson correlation maps highlight additional areas, there is a good correlation between Negative-QSM and BOLD-magnitude signal time courses within regions of PET- and BOLD-identified neuronal activation. SHARP-related phase-processing methods may play an important role in eliminating long-term phase drifts in functional phase and QSM imaging with gradient-echo EPI sequences.

References: [1] Balla et al. (2012) ISMRM #325; [2] Balla et al. (2013) ISMRM #300; [3] Balla et al., Int.Workshop on MRI Phase Contrast & QSM, p19, 2013 [4] Biancardi et al., Hum Brain Mapp. 2013 doi: 10.1002/hbm.22320 [5] Schweser et al., Magnetic Resonance in Medicine 69:1582–1594 2013 [6] Smith et al., 17(3):143-155 2002 [7] Haacke et al., J Magn Reson Imaging 32(3):663-76 2010