Assessing the detection sensitivity of iron loaded cells in spoiled gradient echo imaging

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Introduction: Compartimentalized superparamagnetic iron oxide particles (SPIO) are used in high-resolution MRI experiments as a contrast agent to localize single iron-loaded cells of subvoxel dimension [1]. The induced susceptibility inhomogeneities alter the high spatial frequencies of the phase and magnitude images of spoiled gradient echo (sSSFP) experiments [2-4]. The goal of this work is to compare the iron detection sensitivities of sSSFP phase and magnitude images and to evaluate the possible gain in iron detection sensitivity when combining phase and magnitude information.

Methods: *Numerical simulations:* Susceptibility inhomogeneities are simulated by calculating the frequency shifts created by the dipolar field of one single point particle as defined in [1]. The sSSFP signal is calculated at various echo times (TE=1, 2, 10, 30, 40ms) under the assumption of static dephasing regime. The iron detection sensitivity of magnitude, phase, commutator [2] and complex bivariate [5] (defined as $s_c = (s_{real}^{iron} - s_{real}^{ref})^2 + (s_{imag}^{iron} - s_{imag}^{ref})^2$) filtered images is assessed based on a statistical analysis by comparison with a iron-free reference dataset. Statistical maps of p-values (p-maps) for magnitude and phase images are further combined using Fisher combining function [6] and the corresponding p-map computed. Activation thresholds are defined using a corrected Bonferroni or False Discovery Rate procedure [7]. *Cellular imaging*: human mesenchymal stem cells (line hTERT) were loaded with iron oxide particles (Resovist) via electroporation in initial solutions with iron concentrations of 0, 50, 100 and 200pgFe/cell. Cells were dispersed in 4 collagen Type I hydrogels (5000 cell/ml) and imaged using a vertical 11.7T Avance Bruker spectrometer. 3D sSSFP images were recorded with TE=1.5, 5, 10, 15 and 20ms. Bandwidth=25kHz and 100kHz. Resolution: 100x100x100µm^3. Matrix size 200x200x200. Highpass filtered phase and magnitude images, as well as commutator and homodyne bivariate filtered images are computed and the sensitivity to iron is assessed by visual inspection.

Results: Figure 1a shows typical p-maps of filtered simulations. It illustrates the results of the statistical analysis summarized in fig. 1b and 1c: magnitude contrast appears always more sensitive than phase contrast. P-maps of complex bivariate filtered and magnitude-phase Fisher combined filtered images are very similar: they successfully combine high iron sensitivity with a large number of activated voxels typical of phase images. Finally commutator filtered images show very good positive contrast at the price of reduced spatial resolution. Experimental measurements on stem cells have shown the same contrast behavior between phase, magnitude and complex bivariate filtered images.

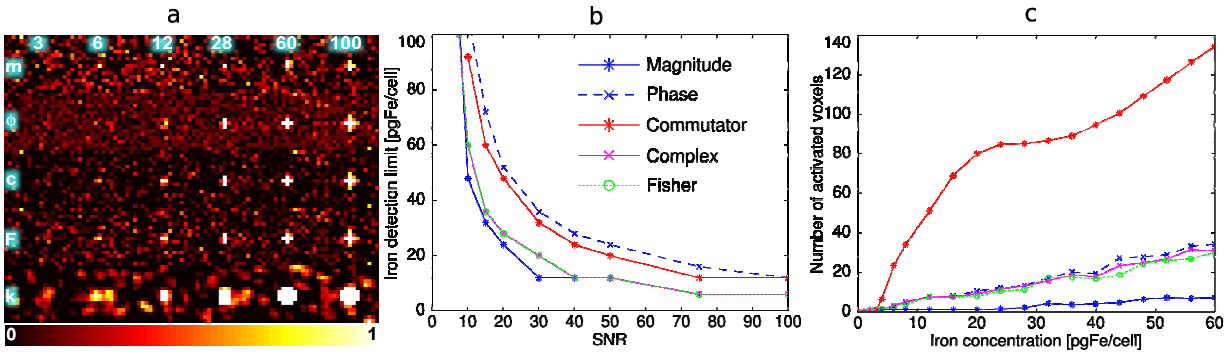

Figure 1a: From top to bottom: 16x16 p-maps of simulated sSSFP coronal images filtered using magnitude (m), phase (ϕ), complex bivariate (c), Fisher (F) and commutator (k) filters. Matrix size of original 3D dataset: 16x16x16. From left to right: 16x16 p-maps as a function of iron concentration in pgFe/cell. Absolute scale for all p-maps goes from 0 to 1 times the Bonferrroni threshold condition with α=0.05: activated voxels are white colored. T1/T2/T2' [ms] =1000/300/15. Voxel size: 100µmx100µmx100µm. Subvoxel size: 4µmx4µmx4µm. TE=1ms. SNR=50. **Figure 1b**: same as fig. 1.a. Averaged lowest iron concentration needed to activate at least one voxel with a probability of 95% as a function of SNR. TE=1ms. **Figure 1c**: number of activated voxels as a function of iron concentration. TE=3.75ms. SNR=50.

Discussion and Conclusion: Susceptibility weighted imaging (SWI) [8] is successful at increasing CNR of magnitude images between tissues of different susceptibilities when susceptibility effects can be reduced to a unique frequency shift. As shown here, in the presence of strong local gradients, simulations and experimental measurements demonstrate that the iron induced phase contrast of sSSFP images in a homogeneous environment has lower detection sensitivity than pure magnitude contrast images and that combining phase and magnitude information does not decrease the limit of sensitivity to iron detection of isolated iron-loaded cells in sSSFP experiments. Nevertheless efficiently combining phase and magnitude information might increase the number of activated voxels and yield useful positive iron contrast.

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