High Resolution Positive Contrast via Post-Processing from Conventional 3D Imaging

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Introduction The detection of contrast agents based on iron oxides (e.g. super paramagnetic iron oxide SPIO particles) is hampered by the fact that they induce negative image contrast. SPIOs are usually imaged via T2 or T2* weighted sequences, which show signal losses at the site of contrast agent accumulation, due to field disturbances induced by the susceptibility of the SPIOs. Several MR sequences have been proposed to convert this dark signal into a positive contrast [1-3]. The different approaches show bright positive contrast images, but prior knowledge about the strength of the field disturbance is required in order to optimize positive image contrast. This is avoided by means of several post-processing methods that have been proposed to calculate the positive contrast from a gradient echo image [4-6]. The advantage of saving scan time leads to the disadvantage of lower resolution in the positive contrast image compared to the gradient echo image for all post-processing methods. We show that positive contrast images can be calculated from gradient echo images at the same resolution by applying a method that was recently introduced for the distortion correction in gradient-echo EPI [7]. We show that our implementation of the methods leads to high resolution positive contrast images of iron-oxide labeled cells in a rat tumor model, and enables e.g. imaging of vessels in human brain at 7T.

Theory An object with a magnetic susceptibility that deviates from its surrounding locally creates an inhomogeneous magnetic field. During the acquisition of a gradient echo based image, these susceptibility gradients locally alter the imaging gradients that are applied. In addition to the well-known geometric distortion, this leads to a shift of the affected echo in k-space [4]. Determination of this shift for every imaging voxel leads to a map of the susceptibility induced gradients. In order to find the position of the shifted echo, k-space lines are subsequently truncated and zero filled. Truncation starts at the lowest k-space line e.g. for k_x-lines. After zero filling of this line, an image is reconstructed. This is subsequently continued, i.e. more and more lines are zero filled and images are reconstructed. This generates *n* images, where *n* is the x-resolution. An example of the intensity of two voxels vs. the number of truncated k-space lines is plotted in Fig. 1. If truncation reaches the k-space center, a sudden change in intensity will be observed. For a voxel that experienced an echo shift towards positive x-direction, this change in intensity will occur at a later kx-line (see Fig. 1). For a 3D dataset subsequent zero filling can be performed in all dimensions respectively. By detecting the k-space line at which the intensity change occurs for every voxel, the shift in k-space for each voxel can be determined. In order to robustly determine the echo shift, k-space truncation was performed separately for both halves of k-space: from $+k_{max}$ to k_0 and from the other direction $-k_{max}$ to k_0. If the echo is e.g. shifted towards positive k values, the intensity will drop while truncating from $+k_{max}$ to k_0. Subtracting the area under both intensity curves and normalizing to the voxel intensity leads to the shift of the echo for each voxel. Performing this procedure in all spatial dimensions allows for the generation of a susceptibility gradient map.

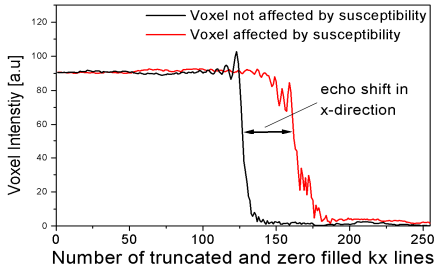

Fig. 1: Intensity variation of two voxels vs. number of zero filled k_x-lines. If echo top has been shifted, intensity change occurs not at k-space center.

Materials and Methods In vivo experiments were performed on nude rats on a 3T whole-body scanner (Philips Intera) using a dedicated 7cm rat solenoid RF-coil. C6 glioma cells were labeled with Ferumoxides-protamine sulfate (FEPro) complexes using procedures previously described [8]. The rats were implanted subcutaneously with 1×10^6 FEPro labeled C6 glioma cells and on the other flank with the same amount of unlabeled C6 glioma cells. The tumors were imaged 14 days after implantation by means of 3D gradient echo imaging, which was performed with: TR=15ms, TE=4.6ms, flip angle: 20°, Matrix: 256x256x32, FOV: 60x60x28.8 mm. Neuro imaging was performed on a 7T whole-body scanner (Philips Achieva) using a T/R head coil at: TR=18.8ms, TE=10.9ms, flip angle: 15°, FOV: 230×230×49, Matrix: 384×384×70, NEX=1.

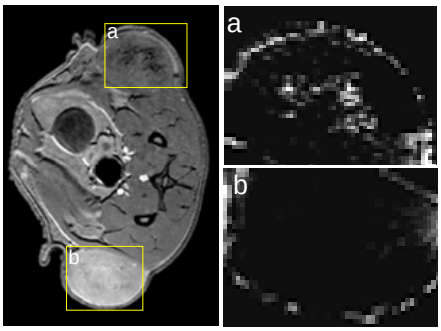

Fig. 2: Rat tumor model, 2 weeks old tumor a) implanted with SPIO labeled cells, b) tumor implanted with non-labeled cells. Positive contrast cutouts depict labeled cells selectively.

Results Fig. 2 shows the selective imaging of labeled cells in tumor tissue. The dark spots in the gradient echo image can be identified as positive contrast at the same resolution. Measuring the contrast to noise ratio by calculating the mean signal over the bright voxels in the center of the tumor, leads to CNR=11.5 for the positive contrast image and CNR=6.9 for the gradient echo image. Fig. 3 shows that the susceptibility gradient induced by blood vessels at 7T is large enough to be imaged by this method. This can also be seen in Fig. 4, which shows a cutout of the measured dataset, in which the positive contrast inducing vessels were volume rendered.

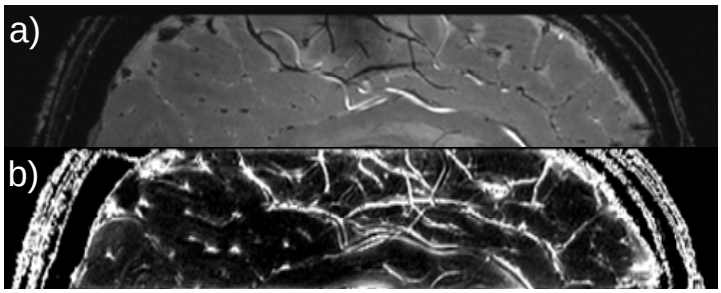

Fig. 3: Sagittal brain slice at 7T. a) gradient echo, b) positive contrast image.

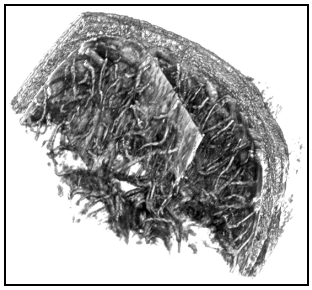

Fig. 4: Volume rendering of Fig. 2

Discussion and Conclusion The cell imaging results show that the method selectively depicts iron oxide induced susceptibility gradients. At the air tissue interface of both tumors, also the influence of susceptibility gradients can be observed. Inside the tumor, the influence of the cells strongly dominates. Also the CNR was higher for the positive contrast image in this example, but comparing a post processing method to images is difficult and needs further investigation. The susceptibility of blood vessels can be imaged selectively, the signal to noise in the positive contrast image is high enough to produce a volume rendering of the vessels. Due to the higher susceptibility gradients induced in veins, it should be possible to discriminate veins from arteries, since absolute values of the susceptibility gradient can be calculated. This will be further investigated. Overall, we show a method that combines the high resolution, up to now only achieved by means of dedicated positive contrast sequences, with the advantages of a post-processing method that requires no extra measurement time and less a-priori knowledge about the induced susceptibility.

References [1] JH Seppenwoolde et al, MRM 2003;50:784–790. [2]CH Cunningham et al, MRM 2005;53:999–1005. [3] M Stuber e al. ISMRM 2005, #2608. [4] S. Posse et al, MRM 1992;25:12–29. 361 [5] CJ Bakker MRM 2006; 55:92-97. [6] H Dahnke et al. ISMRM 2006, #361. [7] N. Chen, Neurimage, 2006;31:609-622 [8] A Arbab at al, Blood 2004;104:1217-1223