Optimal Positive Contrast of Labeled Cells via Conventional 3D Imaging

H. Dahnke[1], W. Liu[2], J. Frank[3], T. Schaeffter[1]

[1]Philips Research Laboratories, Hamburg, Germany, [2]Philips Research Laboratories, Briarcliff, New York, United States, [3]National Institutes of Health, Bethesda, Maryland, United States

Introduction The detection of contrast agents based on iron-oxides (e.g. super paramagnetic iron oxide SPIO particles) is an important prerequisite for visualizing labeled cells. 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 concepts of converting this dark signal into a positive contrast have been proposed [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. It was shown that images of different susceptibility gradient strengths can be reconstructed from a 3D gradient echo dataset [4]. Based on this, we developed a technique for obtaining an optimized positive contrast image. The proposed technique does not require any prior adaptation and can be performed without the use of special sequences, i.e. via a conventional single gradient echo 3D examination.

Theory An object with a magnetic susceptibility that deviates from the surrounding creates a local inhomogeneous magnetic field. For instance, SPIO labeled cells introduce local susceptibility gradients in their vicinity. These local susceptibility gradients act additionally to the imaging gradients and lead to shifts of the echo-top in k-space for the part of the signal that stems form the affected voxel [4]. The local susceptibility gradient strength G_{suscep} is proportional to the shift in k-space M and the echo time TE: $G_i^{suscep} \approx - M_i \cdot G_i^{imaging} \cdot \tau_i \cdot TE^{-1}$, with i=x,y,z, whereas τ represents the gradient duration. By measuring this shift in all three dimensions, a map of the susceptibility gradients can be created that allows the depiction of the optimal positive contrast for every voxel.

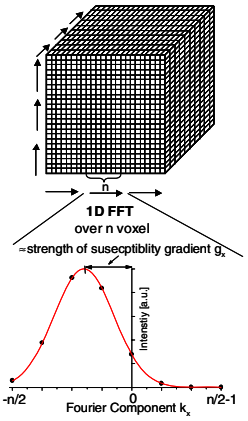

Fig.1:Exemplary illustration for the determination of the susceptibility gradient induced echo shift in one spatial dimension.

Method The following technique allows the calculation of a susceptibility gradient map: A 1D Fourier transformation is performed separately in all three dimensions over a subset of n neighboring voxels, creating a 3D dataset at an n-fold lower resolution in one dimension. The resulting Fourier components (–n/2 to n/2-1) are shown in Fig.1 exemplary for the x-direction. The maximum of these Fourier components is shifted proportionally to the local field gradient acting in the direction of the 1D FFT. From the discrete Fourier components the position of the maximum is found at a sub Fourier component level by means of a least squares quadratic fit. Individually determined maxima for all three spatial dimensions allows for the composition of a vector that contains the relative strength and direction of the susceptibility gradient for every voxel. The magnitude of this vector can be visualized in a susceptibility gradient parameter map. By linear interpolation to the initial spatial resolution and by assigning grey values to the susceptibility gradient values, an optimal positive contrast image can be generated from a complex 3D dataset. It can be adapted to weak and high susceptibility gradients via a standard image level and window operation.

Materials and Experiments Phantom experiments have been performed on a 1.5 T whole-body scanner (Philips Achieva). A cylindrical gelatin phantom was used, containing four holes filled with different substances to avoid susceptibility influences of glass or plastic tubes. 10% Agarose gel was filled in holes (a) and (c) shown in Fig. 2. Different concentrations of Resovist (SPIO, Schering AG) were filled in holes (b) (0.5 µmol Fe/ml) and (d) (0.25 µmol Fe/ml). 3D gradient echo imaging was performed with: TR=98ms, TE=11ms, flip angle: 30°, Matrix. 256x256x12. A susceptibility gradient parameter map was calculated from the acquired data with a size of n=4 of the 1D FFT subset in all spatial direction.

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 [5]. The rats were implanted subcutaneously with 1×10^6 FEPro labeled C6 glioma cells. 3D gradient echo imaging was performed with: TR=15ms, TE=3.1ms, flip angle: 30°, Matrix: 256x256x32. The positive contrast image was also reconstructed with n=4 in all spatial directions.

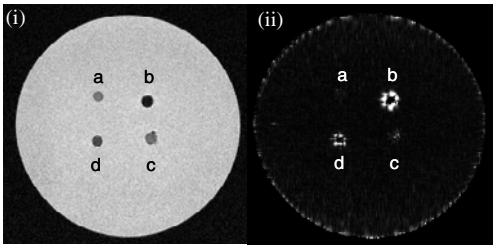

Fig. 2 Gelatin Phantom containing 10% Agarose (a,c) and different SPIO concentrations (b,d). Positive contrast allows discriminating between Agarose and SPIOs that induce susceptibility gradients.

Results Fig. 2 shows one slice of the gradient echo images (i) as well as the susceptibility gradient parameter map (ii), depicting the positive contrast induced by the susceptibility of the SPIO. In the gradient echo image the SPIO and the Agarose gel cannot be distinguished, since both show a short T2* decay. The calculated positive contrast image from the same dataset allows a differentiation of the different fillings due to the highlighted susceptibility gradients. The difference in SPIO concentration between (b) and (d) is reflected in the positive contrast image. Of note, a small air bubble at the top of hole (c) induces a positive contrast.

Fig. 3 shows an exemplary in-vivo result. Due to tumor growth, the labeled cells are not uniformly distributed over the tumor but concentrated in an area indicated in Fig. 3. Due to the positive contrast analysis (ii), a clear assignment of the SPIO labeled cells to the dark spot in the gradient echo image (i) becomes possible. Other regions that are influenced by susceptibility e.g. due to air/tissue interfaces also appear bright in the positive contrast.

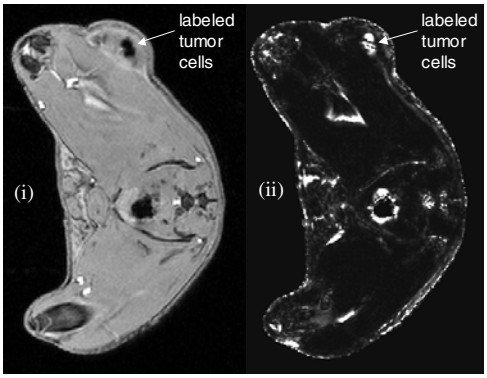

Fig. 3. SPIO labeled tumor cells implanted into rats that induced tumor growth. The SPIO distribution can be seen in the positive contrast image (ii).

Conclusion We demonstrated that a positive contrast image can be produced from a 3D anatomical dataset by calculating the susceptibility gradient map. This technique allows an optimal positive contrast imaging without the use of dedicated sequences. If only the susceptibility gradients in the x-y plane are of interest the method can also be performed on 2D images. Since the susceptibility gradient vector is calculated also the direction of the susceptibility gradient and the distribution of anisotropy can be analyzed. Further studies will be performed to evaluate the possibility of quantification of the SPIO concentration via this method.

References [1] S. Posse et al, MRM 1992;25:12–29. [2] JH Seppenwoolde et al, MRM 2003;50:784–790. [3]CH Cunningham et al, MRM 2005;53:999–1005. [4] JR Reichenbach et al, JMRI 1997;7:266-279. [5]A Arbab at al, Blood 2004;104:1217-1223.