A Dixon Method for Positive Contrast Imaging of Very Small Superparamagnetic Iron Oxide Nanoparticles in MRI

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Purpose

Magnetic nanoparticles (MNP) have become popular MRI contrast agents because they are ideally suited for cellular imaging and cell labeling and can be detected by MRI[1] noninvasively. MNPs can be multifunctionalised to increase cell targeting and to allow local drug delivery. MNPs exhibit very large magnetic moments when brought into a magnetic field which cause susceptibility effects on T_2 and T_2^*-weighted MRI. However, identifying hypointense regions in MR images can be difficult which is why positive contrast techniques[2-4] have been developed. Here we sought to investigate the Dixon method as a positive contrast imaging method for the detection of very small superparamagnetic iron oxide particles (VSOPs) and compare it to established positive contrast imaging techniques.

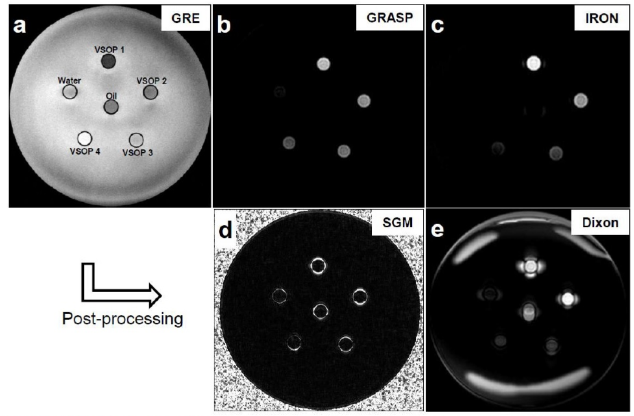

Figure 1: VSOP phantom imaged with a gradient echo sequence (a), GRASP (b), IRON (c), Dixon (e), and a postprocessed gradient echo image with the SGM software (d).

Methods

The Dixon sequence was changed so that the frequency shift between water and off-resonance images (usually fat image) could be changed manually to any value between 0 and 10 ppm. The phantom contained VSOP solution of 1.2 mM, 0.6 mM, 0.3 mM, and 0.15 mM as well as water and fat tubes. The optimal frequency shift was determined by maximising the signal in the VSOP vials and minimising signal intensities from all other areas in the field of view. As reference techniques we selected a T_2^*-weighted gradient-echo technique[2], GRadient-echo Acquisition for Superparamagnetic particles with Positive contrast (GRASP), where the refocusing gradient is manually changed to allow only those protons affected by the magnetic field of the MNPs to refocus. In addition, we also used an off-resonance technique[3], Inversion Recovery with ON-resonant water suppression (IRON), where a suppression pulse with a specific offset, bandwidth and angle is used to allow only the display of off-resonance protons. Finally, we also included a post-processing method[4], Susceptibility Gradient Mapping (SGM), that can be used on any T_2^*-weighted sequence to display hypointense regions as positive contrast images.

Results

Positive contrast images were achieved of a VSOP phantom with GRASP, IRON, SGM, and Dixon (fig 1). All four VSOP solutions can be seen on each of the four positive contrast images (fig 1 b-e). The optimal contrast for GRASP was achieved at a slice-select rephasing lobe strength of 58% of its original strength. IRON produced the best contrast at a frequency offset of the on-resonant water suppression pulse of 254 Hz with a bandwidth of 679 Hz. Both techniques display the VSOP solutions homogeneously within the phantom tubes. The SGM image (fig 1d) was calculated from a T_2^*-weighted gradient echo image (fig 1a) where the VSOP solutions are shown as hypointense. The optimal image with Dixon was achieved at a frequency shift of 1.9 ppm which corresponds to a frequency shift of 239.4 Hz. The positive contrast produced with all four techniques correlates linearly with the iron concentration (fig 2). The gradient of the linear fits is a measure of sensitivity of a particular method. Because the area of positive contrast and not only the signal intensity varied with the concentration of the VSOP solution for the SGM and Dixon method, only the enhanced area was considered for analysis (fig 2 c and d).

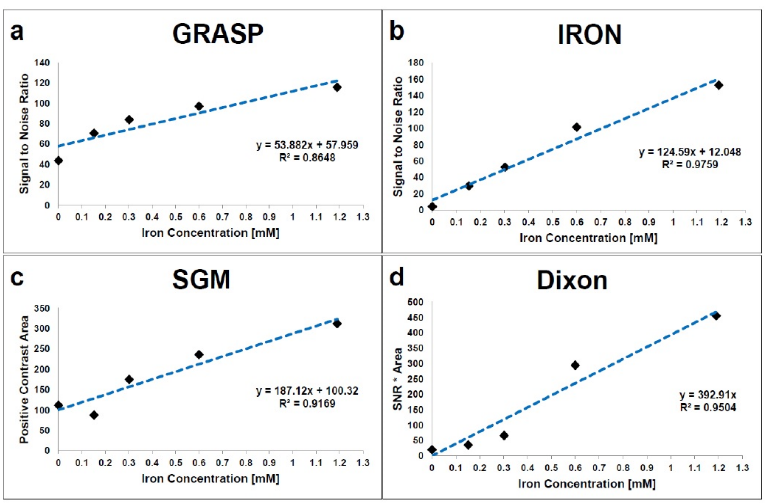

Figure 2: Linear fits of SNR versus iron concentration for GRASP (a) and IRON (b), positive contrast area versus iron concentration for SGM (c), and SNR multiplied with the positive contrast area over iron concentration for Dixon (d). The Gradient of the linear fit is a measure of sensitivity.

Discussion

With all four positive contrast methods investigated the signal intensity increases with increasing iron concentration. Good fat suppression for GRASP and IRON is achieved with the use of a frequency selective fat suppression prepulse. The SGM method only produces positive contrast at the rim of the tubes, however the amount (i.e. area) and intensity of positive contrast is concentration dependent. The graphs of figure 2 confirm the enhanced positive contrast of water for GRASP and SGM which is because of the changed magnetic field due to the tube material. An advantage of the Dixon method is the depiction of the MNP net dipole field. This dipole field is visible as lobes extending in all four major in-plane directions outside of the tube borders. The larger positive contrast area should aid in the detection of small amounts of MNP accumulation in vivo compared to the other three techniques. The gradient of the linear fit is greatest for the DIXON technique suggesting good sensitivity for the differentiation between small and high concentration of MNPs.

Conclusion

We have shown that Dixon can be used to achieve positive contrast images similar to those achieved by established techniques such as GRASP and IRON. The Dixon technique may be useful for the visualization of highly concentrated MNP contrast agents due to the depiction of the dipole field. Its main advantage lies in the ease of implementation and reliable measurement procedure.

References

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