Off-Resonance Saturation, an MRI Sequence for Positive Contrast with Superparamagnetic Nanoparticles

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Introduction

Superparamagnetic iron oxide nanoparticles (SPM particles) are MRI contrast agents used to track tumors or infections. They generate negative contrast on conventional T_2-weighetd MR images [1]. Unfortunately, the negative contrast can be caused by other sources, which makes difficult the SPM particle detection in an MR image (Fig. 1).

To overcome this problem, new MRI sequences able to produce positive contrast near SPM particles have been developed. The Off-Resonance Saturation (ORS) sequence [2] is studied in this work.

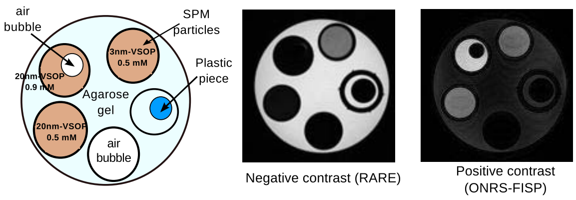


Fig. 1: Specificity of the positive contrast to SPM particles. The negative contrast image shows black spots where the artefacts and the particles are situated. The positive contrast image is specific to the particles.

Methods

The ORS sequence principle is to subtract an image obtained with the application of a pre-saturation pulse, tuned to spoil the protons near the SPM particles, from one obtained without it (Fig. 2). In this study, the acquisition sequence was a FISP [3].

Numerical simulations [4] and experiments with a 11,7 T scanner on agarose gel phantoms containing SPM particles are performed to study this sequence.

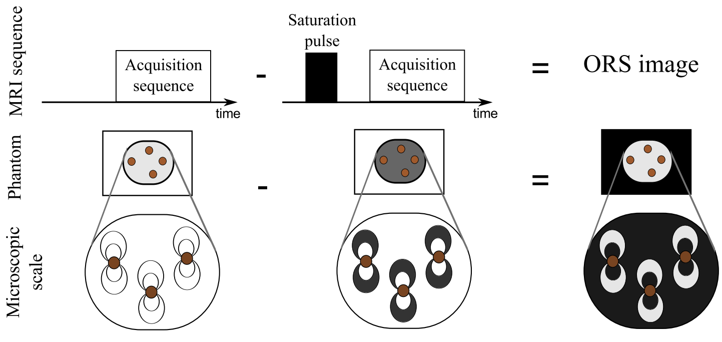


Fig. 2: ORS-FISP sequence principle. The SPM particles create a dipolar magnetic field inducing a Larmor frequency shift of the protons. The saturation pulse is tuned to only spoil the protons near the SPM particles. The positive (ORS) contrast is achieved by subtracting the two images.

Theory

A theoretical expression of the contrast is given by:

$$C = \Phi(Cc, M_s, \omega_0, \Delta\omega) \sin\alpha M_z^0 \, e^{-Cc\, TE\, r_2^*} \quad (1)$$

Cc is the iron concentration of particles, r_2^* and M_s are the SPM particles' transverse relaxivity and magnetization, ω_0 and $\Delta\omega$ are the saturation pulse shift and bandwith and Φ is the fraction of protons spoiled by the saturation pulse (Fig. 3).

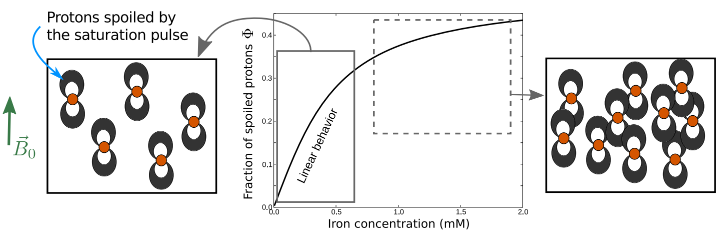
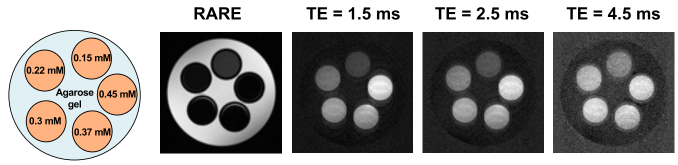


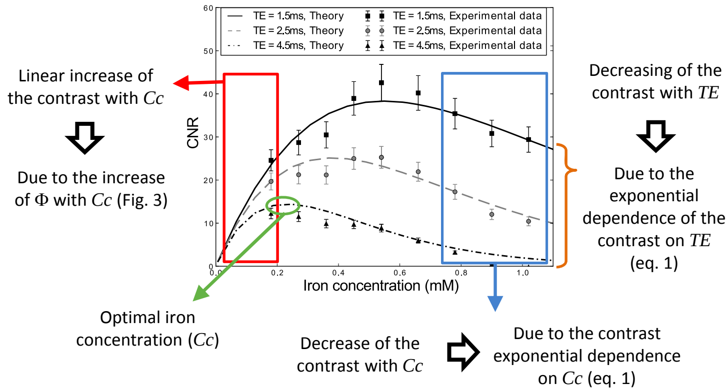
Fig. 3: Fraction of protons spoiled by the saturation pulse.

Results

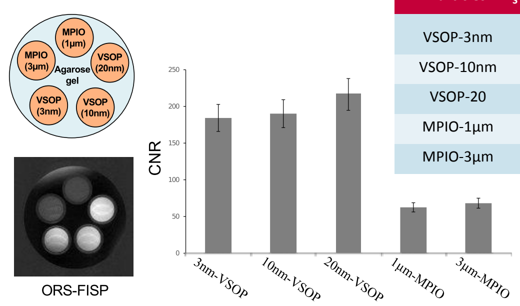
- Experimental results:
  - The contrast increases with the iron concentration
  - Good contrast is achieved with small iron concentrations (~ 0,3 mM [Fe])



- Comparison of the experiments to theory:
  - MR images show a contrast increase followed by a decrease when the iron concentration further increases
  - Theory (eq. 1) is congruent with experimental data



- Influence of the SPM particle parameters:
  - Particles presenting the lower r_2^* produce the best contrast



Particles	M_s (Am²/kg[Fe])	r_2^* (mM⁻¹s⁻¹)
VSOP-3nm	81,1	90
VSOP-10nm	76,5	170
VSOP-20	83,3	240
MPIO-1µm	105,7	600
MPIO-3µm	99,9	600

Conclusions

- The ORS-FISP sequence was shown to produce positive contrast with SPM particles
- A theoretical model able to predict the MRI contrast was developed
  - ➔ It can be used to optimize the sequence and the SPM particle parameters
- Experimental results, coupled with theory, predict a maximum contrast for an optimum iron concentration. Small echo times and particles presenting a low r_2^* should be used.
- Future studies will be devoted to the contrast generated by SPM particles in targeted cells and in-vivo.

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[3] Zhi-Pei Liang and al. "Principles of magnetic resonance imaging : a signal processing perspective". IEEE Press, New York, 2000.

[4] Q. L. Vuong et al., *"New simulation approach using classical formalism to water nuclear magnetic relaxation dispersions in presence of superparamagnetic particles used as MRI contrast agents"*, J. Chem. Phys. 137 (2012)