Fast positive contrast imaging using a spin-echo spiral sequence

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Introduction: There is an increasing interest in labeling cells using contrast agents including super-paramagnetic iron-oxide particles (SPIO) for visualization by MRI. The presence of these iron particles can be imaged either as a negative contrast or a positive contrast. Negative contrast imaging is limited by partial volume effects. It also has difficulty in differentiating iron particles from other voids in the images, which can come from motion or absence of tissue. Positive contrast imaging is reported to have improved specificity in iron detection [1]. In this abstract, we investigated positive contrast imaging of iron particles by a spectrally selective and also spatially selective spin-echo spiral sequence. We applied the sequence for both *in vitro* and *in vivo* studies.

Method: Iron particles cause a frequency shift in the surrounding water spins. Cunningham *et al.* [1] used a spectrally-selective 2DFT spin echo sequence to image labeled cells with a positive contrast method by only exciting these off-resonance spins. 2DFT spin echo sequences are inefficient and susceptible to motion artifacts, which makes them undesirable for *in vivo* studies when there is obvious respiratory or cardiac motion effect. Compared to 2DFT spin-echo, spiral spin-echo can increase the scan speed by a factor of 10. We developed a spiral spin-echo sequence with both spectral and spatial selectivity for positive contrast imaging of iron particles. We used a spectrally-selective excitation RF pulse to excite spins over specific resonant frequency range. The refocusing RF pulse is designed to be spatially-selective, so that undesired off-resonance signals from out of the slice are suppressed. A disadvantage of the spiral scan is that strong off-resonance can induce significant blurring. However, in positive contrast imaging, there is an inherent bulk off-resonance correction, since the center frequency is shifted to the off-resonance frequency. During our experiments, field map-based linear off-resonance correction [2] was used to further deblur the images. The iron particles may induce a local gradient perturbation, which can result in artifacts in either 2DFT or spiral imaging. However, this effect was not obvious in our experiments.

Results: We conducted both *in vitro* and *in vivo* studies on a Siemens Avanto 1.5T scanner (Siemens Medical Solutions). For *in vitro* studies, Ferumoxide solution (Feridex, Berlex Laboratories) was diluted to different concentrations and then put into agarose for imaging. Figure 1 shows one example of in vitro results. The iron solution is 55 microgram Fe/ml. The imaging volume of the iron solution was about 160 microliter. The sequence parameters were: slice thickness 5mm; TR/TE 4s/17ms; bandwidth of the excitation RF pulse 500 Hz. Figure 1a) shows the corresponding negative contrast image. Figure 1b) and 1c) are the positive contrast images acquired by shifting center frequency to 300 Hz and -300 Hz, respectively. Figure 1d) shows the field map we calculated for this phantom. The field map was set to zero where the image has no signal. The off-resonance pattern shown in the field map explains why shifting the center frequency in different directions causes the excitation of different regions around the iron particles. The scan efficiency has been greatly increased by using the spiral trajectory. We also implemented a 2DFT spin echo sequence for positive contrast imaging with same parameters. The 2DFT sequence required a scan time of 17.10 minutes, whereas only 56 seconds were required using the spiral method.

The *in vivo* experiment was conducted on a 2.5 year-old New Zealand White rabbit. A 4X clinical dose (2.2 mg/kg Fe) of Ferumoxide solution was injected IV. The scan started immediately after the injection. Figure 2a) shows a transverse negative contrast image of liver about 10 minutes after injection. The negative contrast image was acquired by same sequence with no center frequency shift of the spectrally selective RF pulse. Figure 2b) shows a positive contrast image acquired immediately after the negative contrast image. Parameters included: slice thickness 10mm; TR/TE 2seconds/16.6ms; center frequency shift 400 Hz; bandwidth of the excitation RF pulse 500 Hz. Notice the correlation between focal regions of enhanced signal in the positive contrast image with regions of signal loss in the negative contrast regions. There are several regions that show dark in the negative contrast image but are not visualized in the positive contrast image. The reason probably is that the SPIOs at these locations generated an off-resonance range which is not within the bandwidth of our spectrally selective RF pulse. One disadvantage of positive contrast imaging is that other off-resonance sources can also cause bright regions in the image. In Figure 2b), there are also bright regions (indicated by the white arrow) that are likely caused by the susceptibility variation at air-tissue interfaces. Figure 2c) shows the positive contrast image after we processed Figure 2b) by smoothing with a 2 by 2 averaging window, followed by thresholding. Figure 2d) shows the fusion of Figure 2c) and 2a). Notice the bright regions in Figure 2c) overlap well with the dark regions in Figure 2a). Also notice the bright regions we interpreted due to susceptibility variation induced off-resonance fall exactly in the region at air-tissue interface.

Discussion: The main advantage of our positive contrast sequence is that it can be applied to rapid imaging. When applying 2DFT positive contrast imaging sequence to our *in vivo* experiment, we observed obvious respiratory motion artifacts. While the current version is a single slice technique, a spectral-spatial pulse combined with spiral spin-echo sequence should be able to achieve multi-slice rapid positive contrast imaging. Future sequence improvements should also address suppression of non-iron induced frequency shift and detection of lower concentrations of iron oxide particles. A field map measurement may be helpful to solve these difficulties since an accurate field map does not only provide the off-resonance value but also the off-resonance patterns. The iron particles may present a specific off-resonance pattern which can be distinguished in the field map.

Conclusion: We proposed a rapid spin-echo spiral sequence for positive contrast imaging. We achieved positive contrast imaging *in vivo* by using this sequence. The developed technique is less sensitive to respiratory motion than 2DFT positive contrast imaging sequences.

Reference: [1] Cunningham CH *et al.*, MRM 53, p. 999 (2005) [2] Irarrazabal *et al.*, MRM 35, 278-282 (1996)

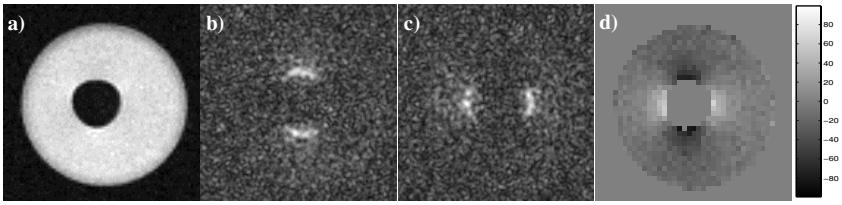

Figure 1: a), b), c), and d) show the negative contrast image, the positive contrast image acquired by spiral spin echo sequence with 300 Hz and -300 Hz center frequency shift, and the corresponding field map respectively. The iron concentration is 55 microgram Fe/ml. The imaging volume of iron solution is 160 microliter.

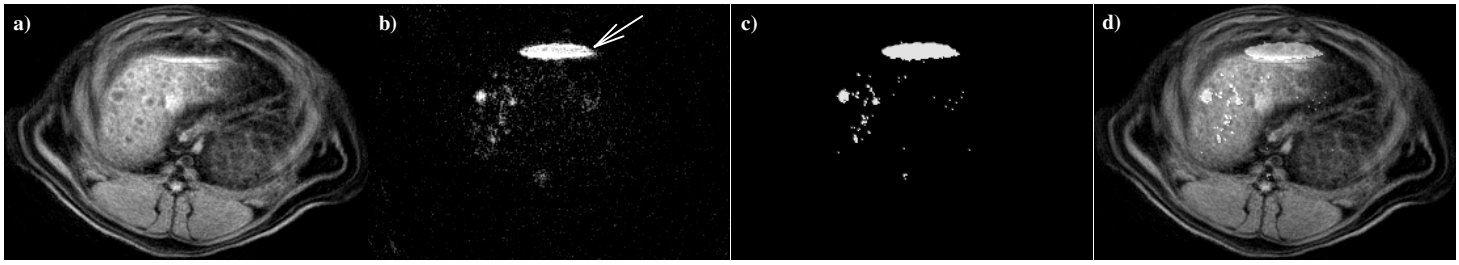

Figure 2: *In vivo* results on a rabbit. a) Negative contrast image acquired about 10 minutes after 4X clinical dose (2.2 mg/kg Fe) of Ferumoxide solution was injected IV. b) Positive contrast image acquired with our spiral spin-echo sequence. The data was acquired immediately after we acquired image a). The arrow indicates positive contrast likely caused by susceptibility variations at air-tissue interfaces. c) Positive contrast image after smoothing and thresholding image b). d) Overlay of image c) and a). Note that the positive contrast image shows a strong correlation with negative contrast image in the regions with iron presence. Also note that the region indicated by the arrow in plot b) corresponds to air-tissue interfaces.