A Novel Approach to Positive Contrast using SPIOs in the Motional Averaging Regime

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Introduction - The promise of enhanced molecular imaging by means of superparamagnetic iron oxide nanoparticles (SPIOs) has largely been restricted due to the tendency of SPIOs to create negative contrast. As there are many sources of reduced signal in MRI, the characteristic signal voids of SPIOs create an undesirable ambiguity in the detection of these particles. As a result, there has been a steady interest in the development of signal-generating pulse sequences that result in an enhanced signal (positive contrast) at the site of the SPIOs. So far, the only published positive contrast sequences involve large SPIOs, generally within the static dephasing regime (SDR). Particles within the SDR are notorious for their minimal biodistribution and can usually only be administered through the external loading of cells. We propose a new approach involving a pre-T2 decay immediately followed by inversion-recovery as a means of generating positive contrast. This approach is optimized for novel classes of nanoparticles specifically designed to enhance both T1 and T2 within the motional averaging regime.

Theory and Methods — The characteristic T2-enhancement of SPIOs results in an accelerated decay of the transverse signal. If this pre-decayed magnetization is then inverted along the -z direction and allowed to grow back by T1 processes, it will have a 'head-start' back towards the equilibrium position. This 'head-start' results in a net signal surrounding the SPIOs as the rest of the magnetization passes through the null-point. Positive contrast can thus be obtained in a T1-process by means of a purely T2-weighted agent. Figure 1 shows an example pulse sequence that can be used to generate positive contrast from SPIOs within the motional averaging regime. The magnetization is initally flipped to the transverse plane and allowed to decay by T2-processes during the proceeding echo train. The magnetization is then inverted and allowed to regrow by T1 processes. The optimal inversion time is that which brings the non-SPIO surrounding magnetization through the null-point. The pulse sequence in Fig. 1, can be modified in other ways that might also change the T2-decay.

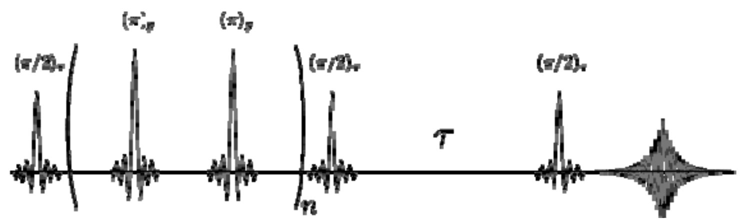

Fig. 1 - Pre-T2 weighted inversion-recovery sequence for R2/R1 enhanced

Results — As a proof of principle, a simple sample containing only SPIOs (known to have little T1 enhancement) is imaged with an ordinary inversion recovery sequence as well as a modified version of Fig. 1. Instead of the echo-train in Fig. 1, the results in Fig. 2 ultilized a spin-lock in place of the CPMG which would be expected to yield similiar T2-like decays. Figures 2B and 2E show the magnetization trajectories and corresponding optimal imaging contrast for an ordinary inversion recovery sequence using just SPIOs. Little T1 enhancement is observed as is to be expected. Figures 2C and 2F show the magnetization trajectories and corresponding optimal imaging contrast. Comparing Figs. 2E and 2F, it can be seen that by simply adding a T2-weighted sequence just prior to inversion recovery, a significantly improved T1-weighted positive contrast can be obtained from a T2-weighted agent. Figure 2D plots the contrast-to-noise ratio (CNR) for both sequences as a function of time by which it can be seen that a simple pre-T2 decay yields more than a 30-fold increase in CNR.

Discussion — It can be seen that the addition of a preliminary T2-decay prior to an inversion recovery sequence creates notable positive contrast from a purely T2-weighted agent. This contrast can be theoretically enhanced even further if the SPIO were synthesized in such a way as to enhance T1 as well. This would result in a quicker grow-back rate for SPIO signal and thus an even brighter positive contrast. Other groups have shown that through careful synthesis, the r2/r1 ratio of the particle can carefully be controlled. We have determined that this pre-T2 decay inversion recovery method is guaranteed to work so long as the r2/r1 ratio of the agent is greater than the local R2/R1 ratio. This condition is very readily met for ordinary SPIO as they are heavily T2 weighted. As a result, we expect an even larger improvement of CNR with even the slightest T1 enhancement of the particles. Very little T1 enhancement is required thus reducing toxicity concerns that are typical of most T1-weighted agents.

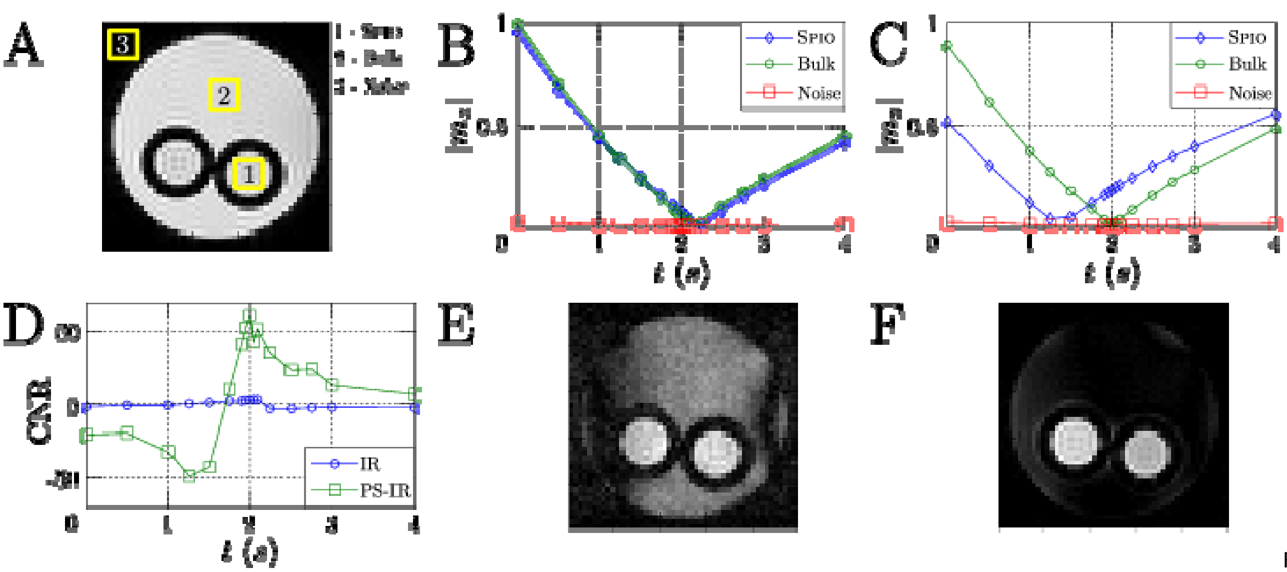

Fig. 2 — A) Spin-density image showing the 3 specific regions of interest: 1) SPIO, 2) water, and 3) noise. B) Magnetization trajectories for an ordinary inversion recovery sequence. C) Magnetization trajectories using a pre-T2 decayed inversion recovery sequence. D) Comparison of contrast-to-noise ratio between the two trajectories shown in B and C. E) Image taken at the null-point for the inversion recovery sequence. F) Image taken at the null-point fo the pre-T2 decayed inversion recovery sequence.