Characterization of Acoustically Induced Rotary Saturation (AIRS) Effect for Active Contrast Modulation in Molecular Imaging

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Introduction: Magnetic contrast agents can be imaged selectively by establishing a rotating frame resonance condition between the spin-locked water magnetization and the oscillating magnetic fields generated by mechanically or acoustically vibrated contrast agents. In the Rotary Saturation effect [1], the spin-locked signal is saturated by an externally applied audio-frequency field tuned to $\omega_{spin\_lock}=\gamma B_{1spin\_lock}$. Previous work showed that a vibrating magnetic particle or clump of particles can be used to create the magnetic field needed to saturate the spin-locked water signal. This Acoustically Induced Rotary Saturation (AIRS) method can be used to "activate" the contrast effect by applying the correct external vibration frequency or by turning the vibration source on and off. [2]. Because only regions effected by the oscillating fields of the contrast agent affect the water, we can selectively detect the location of these agents amongst the background tissue by performing a difference analysis of activated/on-resonance and non-activated/off-resonance conditions (Figure 1C). To better inform *in-vivo* applications using this method, we characterize how the contrast modulation changes with translational displacement, resonant frequency and duration of the spin-lock prep.

Methods: A glass capillary tube containing 2 mg of 25 nm Fe_3O_4 nanoparticles is lowered vertically into second tube immersed in a liquid water phantom (4 in. x 4 in. x 4 in.). The top of the glass tubes (extending out from the phantom opening) is glued to a piezoelectric bender actuator driven by a piezoelectric amplifier (T220-A4-203X model actuator and EPA-104-115 amplifier, Piezo Systems Inc, Woburn MA). Driven with an audio frequency function generator, the piezo induces vertical displacements of the nanoparticle-filled oscillating in time at a chosen frequency ω_{stim}. The "tube within a tube" configuration was chosen to limit motion of adjacent water during tube vibration.

Piezo displacements are calibrated and measured with laser doppler vibrometry. A spin-lock prepared single-shot HASTE pulse sequence (Figure 1A) is used in a 1.5T scanner (Siemens Avanto, Siemens Healthcare, Erlangen Germany) to capture $T_{1\rho}$ –weighted images with 256x256 matrix, 12-cm FOV, 5mm slice thickness, TE of 67 ms, and TR of 2.7 s. Average image intensity values in a 1 mm radius ROI centered at the contrast agent location are obtained in both on-resonance ($\omega_{stim}=\gamma B_{1spin\_lock}$) and off-resonance ($\omega_{stim}=\gamma B_{1spin\_lock}+\Delta\omega$) conditions, where $\Delta\omega$ was ~600Hz. The signal change $\Delta S/S$, was computed from the on-resonance to off-resonance signal difference. Relative signal change is observed while vibrational displacement of the sample is varied between 10 and 160 um, spin-lock resonant frequency γB_{1spin_lock} is swept from 50 to 250 Hz, and duration of spin-lock is varied from 10 to 100 ms.

Results: Contrast agent vibrations resonant with the spin-lock sequence generate image intensity changes that depend on vibration amplitude, spin-lock time, and spin-lock frequency. Figure 2A demonstrates a nearly linear relationship between $\Delta S/S$ and vibrational displacements in the range of ~10 to 160 µm; larger vibration amplitudes of magnetic agent cause spins to experience larger oscillating fields, increasing rotary saturation and thus $\Delta S/S$. Signal change monotonically increases in a nearly linearly fashion with increasing duration of spin-lock (Figure 2B), as rotary saturation is given more time to saturate the signal. Setting the spin-lock resonance to higher frequencies yielded higher signal changes (Figure 2C) presumably because the increased $T_{1\rho}$ relaxation time at higher rotating fields allows more effective saturation.

Discussion: The results demonstrate several considerations in advancing rotary saturation as a technique to image vibrating magnetic contrast agents. In stimulating contrast agent vibration, high displacements are preferable, although signal change can be detected with vibrations of tens of microns; such amplitudes can be achieved *in-vivo* through acoustic or piezoelectric drivers inducing shear waves in tissue, such as those used in performing MR elastography [4]. This is a stimulus mechanism we are actively evaluating with nanoparticle-insert agarose gel phantoms. On the detection end, long spin-lock times yield more signal change, but these have practical duration limits due to $T_{1\rho}$ and $T_{2\rho}$ signal decay as well as SAR considerations. Selecting higher spin-lock resonant frequencies is also advantageous, but SAR limits again become an issue as frequency increases. Despite these boundaries, significant and selective signal change for "activatable" contrast agent imaging has been shown to be attainable.

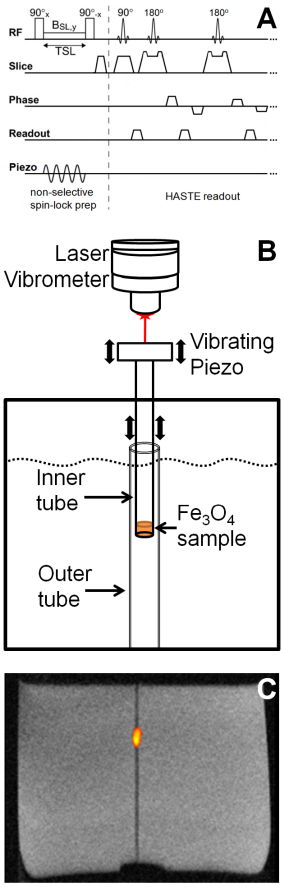

Figure 1:
(A) Pulse sequence diagram for spin-locked HASTE.
(B) Experimental setup for concentric tube Fe_3O_4 motion.
(C) Fe_3O_4 "activation:" image intensity change between on- & off-resonance $T1_\rho$ imaging.

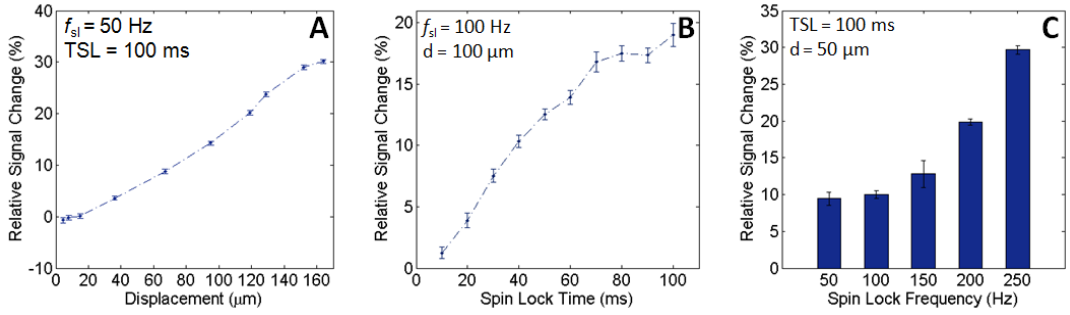

Figure 2: (A) Change in contrast agent image intensity (relative signal change) due to resonant $T_{1\rho}$ imaging is nearly linearly dependent upon contrast agent vibration displacement. (B) Relative signal change monotonically increases with increased spin-lock duration, and also with increased spin-lock frequency (C).

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Acknowledgements: This work was financially supported by P41RR14075.