ENHANCED CONTRAST OF SUPERPARAMAGNETIC IRON OXIDE CONTRAST AGENTS BY SPIN-LOCK MR

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Target audience. (Pre)clinical scientists interested in novel contrast mechanisms for molecular imaging applications.

Introduction. Spin-lock MR has been explored for its endogenous $T_{1\rho}$ contrast and $T_{1\rho}$ dispersion in a variety of (pre)clinical applications. Recently, some studies have focused on $T_{1\rho}$ changes in the presence of contrast agents, such as exchange-mediated contrast agents[1], latex beads[2] and albumin-binding gadolinium-based contrast agents[3]. In this study we investigate the effects of superparamagnetic iron oxides (SPIO) and ultra-small SPIO (USPIO) on $T_{1\rho}$ dispersion at 1.41T.

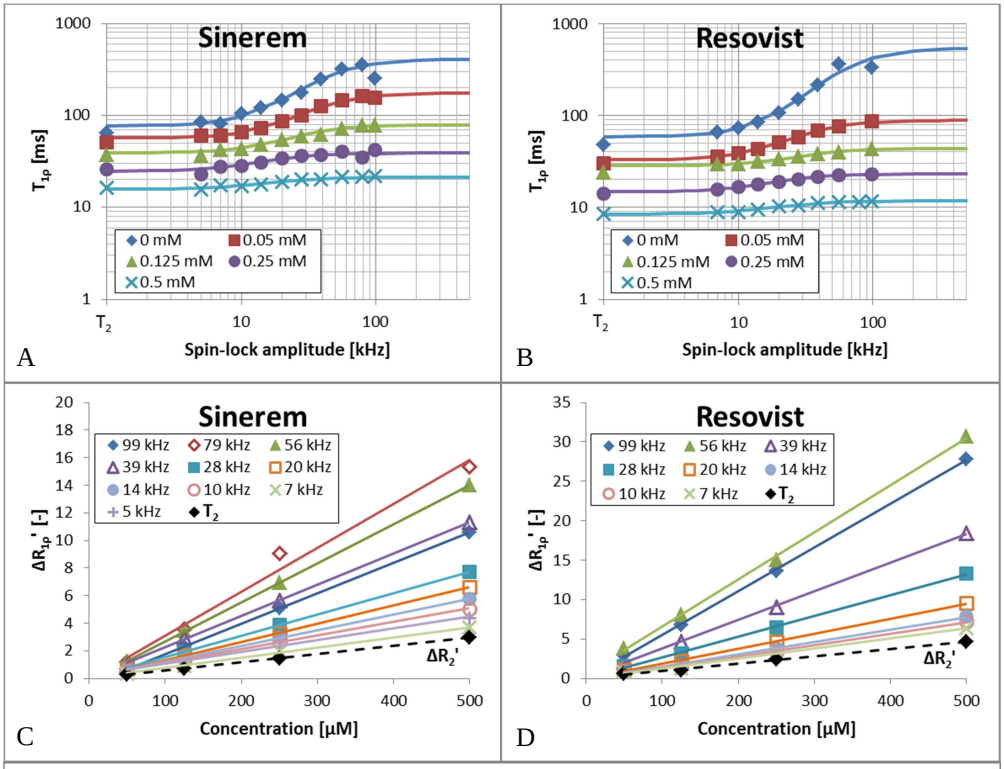

Figure 1 (A&B) $T_{1\rho}$ values decreased and dispersion flattened with increasing concentrations of contrast agent. Lines are fits to the data; data points on vertical axis are T_2. (C&D) Normalized ΔR_2' and $\Delta R_{1\rho}$' vs. concentration. Note the high contrast generated by $T_{1\rho}$ in comparison to T_2.

Materials & methods. All experiments were performed with a 60MHz (1.41T) NMR spectrometer (Minispec60, Bruker, Germany) at 293K. Agar gels (2%) containing increasing concentrations (0, 50, 125, 250 & 500µM) of Resovist (SPIO, ferucarbotran, Schering AG, Germany) or Sinerem (USPIO, ferumoxtran, Guerbet, France) were put in 5mm glass tubes. The spin-lock sequence consisted of a 90° excitation pulse directly followed by a continuous wave spin-lock pulse and FID read-out. $T_{1\rho}$ dispersion was measured over a range of spin-lock amplitudes (γB_1) between 5 and 99kHz. $T_{1\rho}$ was determined by exponential fitting of signal intensities from 10 different spin-lock durations, logarithmically distributed between 1ms and 10 to 50ms, with the maximum depending on γB_1 and hardware restrictions. Dispersion was fitted using a two-pool exchange model, assuming on-resonance spin-lock[4]:
$R_{1\rho} = R_2^0 + A\frac{\tau_{ex}}{1+\omega_1^2\tau_{ex}^2}$, with R_2^0 the transverse relaxation without exchange, $A = p_f p_b \Delta\omega^2$ the fractions of free and bound water multiplied by the square of their frequency difference, τ_{ex} the exchange rate and ω_1 the spin-lock frequency. $R_{1\rho}(\omega_1=0)$ was compared to R_2 measured by the CPMG sequence. Normalized relative change in $R_{1\rho}$, $\Delta R_{1\rho}' = \frac{R_{1\rho CA}-R_{1\rho 0}}{R_{1\rho 0}}$, was used as a sensitivity parameter to assess the efficacy of the contrast agent to induce changes in $T_{1\rho}$. Analogue to this $\Delta R_2' = \frac{R_{2CA}-R_{2,0}}{R_{2,0}}$ was used to compare to R_2 sensitivity.

Results and discussion. With increasing concentrations of both contrast agents $T_{1\rho}$ values decreased and $T_{1\rho}$ dispersion flattened (Fig. 1A,B). T_2 as measured by CPMG matched T_2 calculated from $T_{1\rho}$ dispersion model fits reasonably well, except for the lowest contrast agent concentrations for which T_2 by CPMG was somewhat lower. This is probably due to additional signal attenuation by diffusion during the CMPG sequence, which becomes less prominent at higher contrast agent concentrations. $\Delta R_{1\rho}$' was linear with contrast agent concentration (R^2>0.98) for all spin-lock amplitudes, as was ΔR_2 (Fig 1C,D). Importantly, with increasing γB_1 contrast increased. Furthermore $\Delta R_{1\rho}$' contrast was consistently higher than ΔR_2'. Highest $\Delta R_{1\rho}$' was obtained at a spin-lock amplitude of 56kHz, for which $\Delta R_{1\rho}$' was 4.8-fold (Sinerem) and 6.6-fold (Resovist) higher as compared to ΔR_2'. For even higher γB_1 (>56kHz) both $T_{1\rho}$ and $\Delta R_{1\rho}$ decreased again, which was probably caused by power loss near hardware limits. The mechanism behind the increased contrast is found in the flattening of the $T_{1\rho}$ dispersion, which we attribute to the loss of spin-lock in the presence of high local field gradients that surround the superparamagnetic contrast agent.

Conclusion. $T_{1\rho}$ provides enhanced sensitivity for the detection of SPIO and USPIO contrast agents in comparison to T_2.

References. 1. Cobb 2012, Magn Reson Med 67:1427-33 **2.** Cobb 2012, Magn Reson Med **3.** Richardson 2012, Magn Reson Med 68: 1234-38
4. Cobb 2011 Magn Reson Med 66: 1563-71
This research was supported by the Center for Translational Molecular Medicine and the Dutch Heart Foundation (PARISk).