Exchange Rate Selective Imaging Using $T_{1\rho}$ Dispersion

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Target Audience: Investigators interested in novel image contrasts reflecting chemical exchange mechanisms.

Purpose: A novel type of MR image contrast and method for quantitative tissue characterization has been developed based on the behavior of rates of spin-lattice relaxation in the rotating frame, $R_{1\rho}$ (= $1/T_{1\rho}$). At high fields, $R_{1\rho}$ (and R_2) may be dominated by the effects of chemical exchange between water and labile protons of different chemical shift(s), but their magnitude also depends on the amplitude of the RF field used for spin-locking experiments [1]. An appropriate analysis of the behavior of $R_{1\rho}$ with different locking fields ($R_{1\rho}$ dispersion) may thus be used to characterize exchange effects. Whereas other exchange-sensitive methods (such as CEST) identify protons of specific chemical shifts, the approach proposed here can theoretically separate species by identifying a specific rate of exchange for the species of interest.

Methods: Chopra et al. derived an expression for exchange effects on $R_{1\rho}$ that can be simplified to $R_{1\rho} = R_{2A} + p_B\left[R_{2B} + \frac{r_B\Delta\omega_B^2}{r_B^2+\Delta\omega_B^2+\omega_1^2}\right]$, where R_{2A} and R_{2B} are the transverse relaxation rates of the A (water) and B (exchanging) pools respectively, p_B, r_B, $\Delta\omega_B$ denote the exchanging pool fractional population, exchange rate and chemical shift respectively, and ω_1 is the spin-locking field amplitude [2]. This is valid when $r_B >> R_{2B} > R_{1B}$ as is always the case in practice. If we consider three measurements of $R_{1\rho}$ taken at three different values of ω_1 (low (≈ 0), high ($\approx \infty$) and a selected value ω_1), we can define an Exchange Rate Contrast (ERC) that may only take on values between 0 and 1: $ERC(\omega_1) = 4\frac{\left(R_{1\rho}(\omega_1=0)-R_{1\rho}(\omega_1)\right)\left(R_{1\rho}(\omega_1)-R_{1\rho}(\omega_1=\infty)\right)}{\left(R_{1\rho}(\omega_1=0)-R_{1\rho}(\omega_1=\infty)\right)^2}$. Note that $R_{1\rho}(\omega_1= 0) \approx R_2$, while $R_{1\rho}$ ($\omega_1=\infty$) $\approx R_1$. Using the first two equations we obtain $ERC(\omega_1) = 4\frac{\alpha^2}{(1+\alpha^2)^2}$ where $\alpha^2 = \frac{\omega_1^2}{3\omega_e^2}$ and $3\omega_e^2 = r_B^2 + \Delta\omega_B^2$; the locking frequency ω_e corresponds to the field at which the dispersion of $R_{1\rho}$ with ω_1 shows an inflection. The ERC has a maximum value (=1) when α=1, i.e. when the selected locking field $\omega_1 = \sqrt{\frac{r_B^2+\Delta\omega_B^2}{3}}$. The ERC, simulated in figure 1, may be fit to experimental data to calculate ω_1 and subsequently r_B. Three samples were prepared to demonstrate the effects described above, 0.2 M glucose (Sigma-Aldrich Co. St. Louis, MO), 0.2 M creatine (Sigma-Aldrich Co. St. Louis, MO), and a 50% by volume mixture of the two, all in D.I. water. $R_{1\rho}$ dispersion measurements were performed with a standard spectroscopic spin-locking sequence and the samples were subsequently imaged at 7T (Varian Inc. Palo Alto, CA, USA) utilizing a standard spin-locking Fast Spin Echo sequence and varying the spin-lock amplitudes from ~0 - 7,000 Hz with a 64 x 64 data matrix size and a 25mm x 25mm FOV. The images were combined according to the above ERC equation for every intermediate spin-lock amplitude, and the pixel intensities were averaged for each to measure the ERC as a function of spin-lock amplitude. In the mixture of species, a comparison of the rates at different locking fields can in principle be used to deconvolve the separate contributions by $\omega_1^2\left[R_{1\rho}(\omega_1) - R_{1\rho}(\omega_1=\infty)\right] = \sum_i \frac{A_i}{1+\alpha_i^2}$ where $A_i = p_i r_{bi}\Delta\omega_{bi}^2$ and $\alpha_i = \sqrt{\frac{3\omega_{ei}^2}{\omega_1^2}} = \sqrt{\frac{r_{bi}^2+\Delta\omega_{bi}^2}{\omega_1^2}}$. Fitting $\omega_1^2\left[R_{1\rho}(\omega_1) - R_{1\rho}(\omega_1=\infty)\right]$ to an expression of the form $\sum_i \frac{A_i}{1+\alpha_i^2}$ will yield A_i and α_i and comparisons of $R_{1\rho}$ at different locking field strengths will weight the relative contributions very differently. Assuming the chemical shifts are known, exchange rates may be explicitly derived.

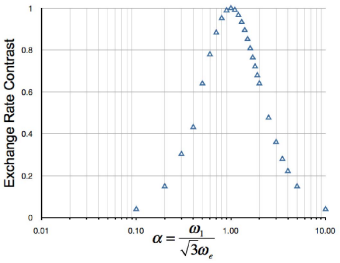

Figure 1: Variation of Exchange Rate Contrast with Locking Field.

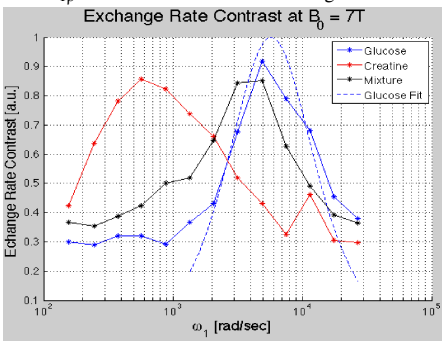

Figure 2: Exchange Rate Contrast curves calculated from mean pixel intensities at 13 intermediate spin-lock amplitudes. The dotted line represents the ERC fit for the glucose curve.

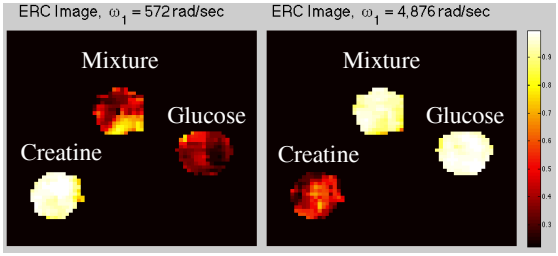

Figure 3: ERC Images at ω_1= 572 rad/sec and ω_1= 4,876 rad/sec, the corresponding frequencies of the peaks in the ERC curves in figure 2 for creatine and glucose.

Results: Glucose and creatine exhibited ERC peaks at different spin-lock amplitudes due to different chemical exchange rates shown in figure 2. Judiciously choosing the intermediate spin-lock amplitude to be the peak of either the glucose or creatine ERC curve, we maximize the image intensity for that sample and ensure lower intensity of the other sample shown in figure 3. The ERC data were fit using a least squares method to calculate ω_e = 5,750 Hz for glucose and ω_e = 499 Hz for creatine, reasonably close to literature values [3,4].

Discussion: The ERC imaging method produced images that emphasized different chemical exchange rates and was also analyzed to explicitly calculate exchange rates of each species in model systems. The technique can theoretically be extended to compute exchange rates of pools in mixtures, as well as pool fractions. This new method shows potential for deriving exchange rate dependent images and quantifying metabolite concentrations in vivo.

Conclusion: A new approach has been developed using $R_{1\rho}$ imaging sequences to selectively emphasize contrast based on differences in exchange rates, rather than simply chemical shifts, in a regime that is well suited for practical imaging. Assuming the chemical shifts are known, exchange rates of separate pools and their pool sizes in mixture systems may be calculated.

References: [1] Cobb et al, Magn Reson Med 67:1427-1433, 2012. [2] Chopra S. et al, J Magn Reson 59:361-372, 1984. [3] Wu et al, Contrast Media Mol Imaging 7:384-389, 2012. [4] Ren et al, Magn Reson Med 60:1047-1055, 2008.