Delta relaxivity enhanced MR (dreMR): Theory of T1-slope weighted contrast

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Introduction: Delta relaxivity enhanced MR (dreMR) is a novel MR method, introduced here, for producing image contrasts related to the magnetic field dependence of tissue relaxation rates. Applications include cellular/molecular MRI, where dreMR may significantly increase the detection sensitivity/specificity to in-vivo target molecules. Realization of the dreMR concept requires the use of a variable field-strength (field-cycled) [1] main magnet as well as "activatable" contrast agents, or MR probes, that demonstrate steep relaxivity slope changes upon recognition of the target molecule. The relaxivity of a contrast agent indicates its efficiency at increasing the relaxation rate (R1 = 1 / T1) of surrounding tissues and thereby enhancing signal in MR images. The relaxation rate slope (R1´ = ΔR1 / ΔB0) is a measure of the rate of change in relaxation rate with respect to magnetic field strength. The novelty of the dreMR concept lies in its ability to generate image contrast that is dependent on R1´, not on R1.

Exploitation of the benefits of dreMR in clinical, static-field MR is achievable through the addition of an actively shielded B0 insert coil. With carefully timed magnetic field shifts during evolution of longitudinal magnetization it is possible to produce images in which all tissue signal is suppressed except that due to the activated contrast agent (probe). One such class of contrast agent is the protein-binding gadolinium chelates, which are designed for large increases in relaxivity upon activation by protein binding. The relaxivity, or r1, of a contrast agent indicates the agent's ability to increase the relaxation rate of surrounding tissues. Figure 1 shows a typical relaxivity curve of a generic protein-binding gadolinium chelate in the presence and absence of the target protein. A key feature of this relaxivity curve is the striking increase in relaxivity slope, upon activation, particularly in the range 0.5T – 1.5T. The dreMR concept exploits this large slope increase to generate selective images of the activated agent.

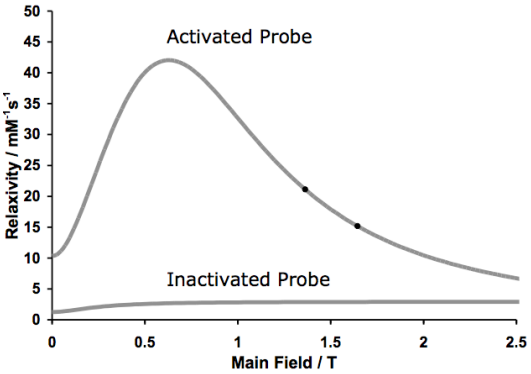

Figure 1 compares the relaxivity curves for MR probe in the activated and inactivated state. Points on the relaxivity curve corresponding to 1.5 ± 0.15T are indicated.

Methods: There are several pulse-sequence implementations of dreMR; here we describe just one: a double inversion recovery (DIR) preparation method with variable length bipolar field shifts of equal but opposite amplitudes ± ΔB. The DIR sequence has three periods of magnetic evolution as shown in Figure 2. The upper time series, labeled B0, illustrates the main field during each period. The imaging sample is exposed to the static field strength for a period P0. For the durations of P1 and P2 the field is first increased and then decreased by ΔB. The second time series of Figure 2 details the RF pulses that are applied around these main field perturbations. All RF pulses are applied at a time when the magnetic field is at the static field strength B0, implying that no modifications to the RF hardware of the clinical scanner are required. The initial 90° RF pulse resets longitudinal magnetization, while the following 180° pulses and associated field pulses and evolution periods serve to null the longitudinal magnetization of all non-activated tissues (R1´ ≈ 0) while maximizing magnetization of activated tissues (R1´≠ 0) by the beginning of the acquisition period. The lower time series of Figure 2 represents the temporal evolution of longitudinal magnetizations for tissues demonstrating non-zero R1´ (solid line) and those with zero R1´ (dashed line). At the completion of the DIR sequence, the magnetization is proportional to R1´ but not to R1.

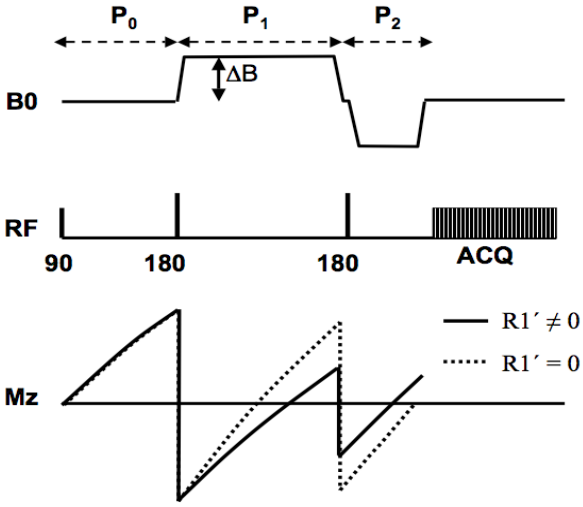

Figure 2. The total magnetic field, applied RF pulses, and longitudinal magnetizations are shown during a single DIR dreMR pulse sequence.

To facilitate comparison of the dreMR DIR sequence against standard T1-weighted sequences, a computer simulation was written to solve the Bloch equations to predict magnetization for any arbitrary pulse sequence [2]. For the simulation, T1 values were modeled using Bottomley's tissue model [3], while contrast agent relaxivities were simulated based on published models [4]. The relative magnetizations of blood + 0.15mM of blood-protein activated MR probe, fat, muscle, white-matter (WM), and grey-matter (GM) were calculated for a T1-weighted sequence (TR = 300ms) and a DIR dreMR sequence (B0 = 1.5T, ΔB = 0.15 T). The relaxivity vs. B0 curve from Figure 1 was used to model the activatable agent; black dots on the curve representing the boundary (1.5 ± 0.15 T) of the relaxivity range used in the simulation.

Results: Figures 3a and 3b show the relative magnetizations generated by a standard T1-weigthed sequence and a DIR dreMR sequence, respectively. The T1-weighted sequence is insufficient to separate the enhanced blood from typical biological tissues. Conversely, in Figure 3b the DIR dreMR sequence generates magnetization for the activated probe while effectively suppressing magnetization in the unenhanced biological tissues or the non-activated agent (not shown).

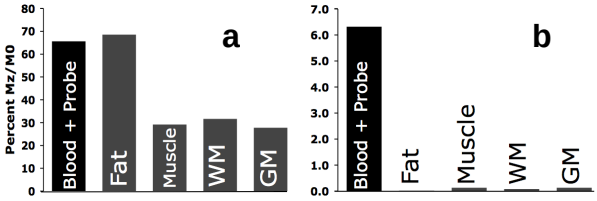

Figure 3a shows the relative magnetization produced from a T1-weighted sequence (TR = 300ms). Figure 3b shows dreMR contrast for the same tissues and contrast agent concentrations.

Discussion: dreMR is a unique, new MR method capable of selectively imaging activatable contrast agents. In the given example, a blood-protein activated MR probe was shown to produce R1′ enhancement, which was transformed into selective contrast via the dreMR DIR sequence. With the recent completion of an actively shielded B0 insert coil, which will allow dreMR to be performed on a clinical MR scanner, our group is advancing dreMR from theory into practice.

References:

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