Relaxivity of Gd-DTPA in Solution with Different Macromolecular Content at Different Field Strengths from 0.7 to 8.0 Tesla

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Synopsis

Relaxivity for paramagnetic MR contrast agents has to be known for quantitative studies of contrast agent uptake in tissue. Relaxivity changes with field strength and in the presence of macromolecules. We measured relaxivity for Gd-DTPA in water, bovine serum albumin (BSA), and skim milk. T1 relaxivity increases with solid concentration by weight and decreases with field strength, thus making Gd-DTPA a less efficient agent for ultra-high field MRI. T2 times are unchanged or slightly increase with increasing Gd-DTPA concentration in BSA and milk.

Introduction

Several MRI methods make use of T1 relaxation time changes to quantify tissue concentration of paramagnetic contrast agents. For example Gd-DTPA is used for quantitative assessment of tissue vascularity and perfusion [1], cartilage degradation in osteoarthritis [2], or spinal cord injury [3]. In order to determine contrast agent concentration from measured T1 changes, one has to know the relaxivity R1 of the paramagnetic agent, which is defined as

$$\frac{1}{T1} = \frac{1}{T1_0} + R1 \cdot [c]$$

where $T1_o$ is the T1 of the solvent and [c] the concentration of the agent. An analogous equation defines the T2 relaxivity R2. The relaxivities R1 and R2 change with field strength, temperature, and pH. For many agents, R1 relaxivity is known in aqueous solution at 1.5T, however it was shown [2,4,5] that R1 for Gd-DTPA increases in solutions containing macromolecules. Other authors have observed increase or decrease of the Gd-DPTA T1 relaxivity in tissue or cell cultures [6-10]. In this paper, we present measurements of Gd-DTPA relaxivity R1 and R2 at 0.7, 1.5, and 8T in water and solutions of BSA and skim milk. The long-term goal of this work is to study cell cultures and tissue for assessment of novel contrast agents and their utility at different field strengths.

Methods

Samples with 0-2.0mM Gd-DTPA (Magnevist) in water, 1.5, 3.0, and 4.5% bovine serum albumin (BSA, 68kDa, Boehringer, Mannheim), and 5%, 10%, and 20% skim milk (Kroger) were prepared in 0.5mL Eppendorf tubes. Tubes were placed in a holder and immersed in a solution of 0.5mM Gd-DTPA and 0.125M NaCl to minimize susceptibility effects and for appropriate RF coil loading. Images were acquired using wrist phased array coils at 0.7 and 1.5T (GE, Medical), and with single or dual strut TEM coils (8T/80cm Magnex, Bruker). At 0.7 and 1.5T, T1 measurements used IR-FSE with TR/TE=8000/12, ETL=8, and TI ranging from 50 to 4000ms; T2 measurements were obtained using single echo Hahn spin echo sequences with TR=2500ms and TE 11,50,100,250,500ms. At 8T, T1 measurements used IR-SE with TR/TE=4000/12.7ms, and nine TI ranging from 25-3500ms. T2 measurements were obtained with both single echo Hahn and 16-echo CP sequences (TR=2000, TE=12.7-400ms). In all cases, one coronal slice with 3mm thickness and $0.43 \times 0.85 mm^2$ in-plane resolution was acquired. To minimize detrimental effects from RF inhomogeneity at 8T only 16 samples placed in a $7 \times 7 cm^2$ area were scanned at once. In addition, B1 field maps were acquired to assess the spatial flip angle variability. Identical samples were used at all field strengths. Data at 0.7T and 8T were acquired on the same day. All data were analyzed by mono-exponential fitting, and relaxivity was determined by linear regression.

Results

T1 relaxivities for Gd-DTPA in water were 4.66±0.07, 4.32±0.07, and 4.12±0.07 $(mM\ s)^{-1}$ for 0.7, 1.5, and 8T respectively. Hahn echo T2 relativities in water were 4.57±0.09, 4.57±0.11, and 5.02±0.13$(mM\ s)^{-1}$ for the three field strengths. These results are in agreement with previously published results [2,4,5,10]. T1 and T2 relaxivities for Gd-DTPA with different macromolecular content and field strengths are shown as a function of the solid content by weight in Figs. 1 and 2. T1 relaxivity increased approximately linearly with macromolecular content (0.41±0.04, 0.27±0.01, and 0.19±0.01 $(mM\ s)^{-1}$ per % solid for 0.7, 1.5, and 8T respectively). While this trend was observed in prior studies [2,4], we measured larger slopes with macromolecular content compared to prior studies (0.096 $(mM\ s)^{-1}$ per % solid at 1.5T [4]; 0.026 $(mM\ s)^{-1}$ per % solid at 9.4T [2]). Surprisingly, T2 values remained the same or *slightly increased* with increasing Gd-DTPA in BSA and milk. Nevertheless linear regression was applied to evaluate the behavior of the data, leading to *negative "T2 relaxivities"* for 10% and 20% milk at all field strengths albeit with significant standard deviations. For 0.7T and 1.5T, T2 stayed essentially constant in BSA solutions independent of Gd-DTPA concentration. At 8T, T2 relaxivity in BSA was higher. The origin of this difference is not known, the only difference between low field and high field studies may have been a small difference in temperature (room temperature 20°C at low field and 12°C at 8T due to water cooled gradients).

Conclusions

In accordance with prior studies, T1 relaxivity increases with macromolecular content, but to a much lesser extend at higher field strength. Thus Gd-DTPA is a less effective T1 agent for ultra-high field imaging. While a number of studies have evaluated T1 relaxivity for Gd-DTPA, much less information is available for T2 relaxivity [10]. Further measurements are needed to evaluate the unexpected behavior of the T2s.

References

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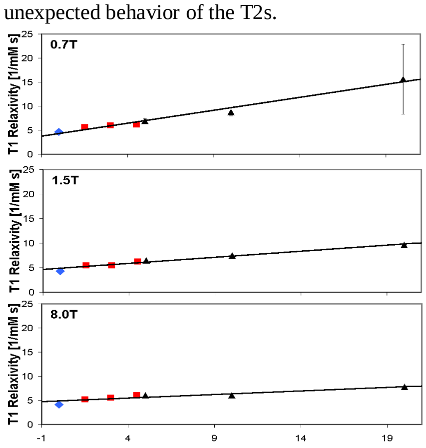

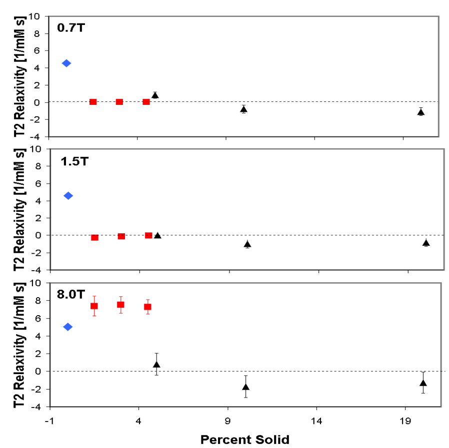

Fig 1 (left): T1 relaxivity with solid concentration and linear regression fits.
Fig 2 (right): Slope of T2 versus Gd-DTPA concentration termed "T2 relaxivity" plotted versus solid content (blue=water, red=BSA, black=milk).