Tissue (Brain) Water Longitudinal Relaxation is Biexponential

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Introduction: An accurate assessment of longitudinal relaxation is critical for numerous MR methods. Longitudinal relaxation of water ^{1}H magnetization in mammalian brain *in vivo* is typically analyzed on a per voxel basis using a monoexponential magnetization-recovery model, thereby assigning a single relaxation rate constant to all ^{1}H magnetization within a given voxel. Reported herein are highly accurate, pure inversion recovery experiments at 4.7T and 11.74T revealing that longitudinal relaxation is biexponential in mammalian (rat) brain. The source of this biexponential behavior is shown to be magnetization transfer between mobile water and the solid-like macromolecular matrix. This effect is present in other tissues (e.g., muscle) and should be recognized in quantitative assessment of experiments that leverage longitudinal relaxation to influence tissue contrast.

Materials and Methods: Male Sprague-Dawley rats were anesthetized with urethane (1.8g/kg administered intraperitoneally) and placed in a MR-compliant head holder. A slice for subsequent EPI data collection was identified using multi-slice gradient-echo images, and manual shimming was performed on the slice using a LASER pulse sequence. Highly time-resolved inversion recovery EPI data using 64 or 128 TI values exponentially spaced from 4 ms to 6 s (TR = 5 × T_1) were collected using a nonselective square inversion pulse followed by a spin-echo (34 ms TE) EPI readout over a 4 × 4 × 0.2 cm^3 field of view. A 1 ms crusher gradient was applied immediately following the inversion pulse to suppress any residual transverse magnetization arising from pulse imperfections. Bayesian probability theory was used to calculate absorption-mode images and for exponential model selection and parameter estimation on a per voxel basis using a family of discrete exponential models (2,3). The posterior probability for each model was determined and the most probable model selected (Figure 1).

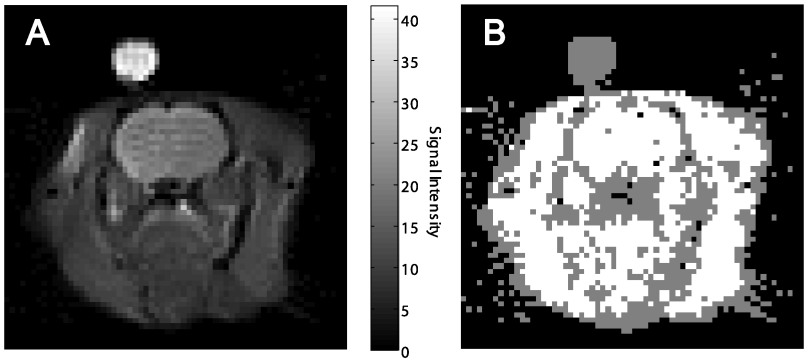

Figure 1: 4.7 T SE-EPI data. A) Anatomic reference image showing the rat and a 0.1 mM Omniscan™ phantom. B) Bayesian model selection map. The *in vivo* rat data are best modeled with a biexponential function (white voxels) and the aqueous Omniscan™ phantom data are best modeled with a monoexponential function (gray voxels).

Results and Discussion: IR-EPI data from rat brain are biexponential at 4.7 T (R^+ = 44 ± 12 s^{-1}, R^- = 0.66 ± 0.04 s^{-1}, R^+ amplitude fraction = 3.4 ± 0.7 %) and at 11.7 T (R^+ = 19 ± 5 s^{-1}, R^- = 0.48 ± 0.02 s^{-1}, R^+ amplitude fraction = 6.9 ± 0.9 %). A parametric map of the R^+ amplitude fraction clearly displays white-matter structures (Figure 2). Aside from pulse sequence and scanner induced artifacts, four putative mechanisms were carefully examined to explain this non-monoexponential IR relaxation behavior: blood flow, radiation damping, multiple non-exchanging compartments, and a special case of multiple compartments - magnetization transfer (MT). Magnetization transfer between bulk water and macromolecular-associated water was determined to be the source of biexponential longitudinal relaxation.

In vivo MRI voxel resolution is coarse on the scale of tissue microstructure. It follows that water exists in a variety of magnetic environments ("compartments") within a single voxel. Each such compartment potentially provides a unique water-relaxation environment. Consistent with this concept, a variety of tissues display multiexponential T_2 relaxation, and multiple T_1 components have been described for peripheral nerve or white matter, though not for brain gray matter (1). Herein we show biexponential longitudinal relaxation to be a general phenomenon in mammalian tissue *in vivo* and find the genesis of the rapidly relaxing component to be magnetization transfer. Quantification of longitudinal relaxation is fundamental to a variety of MR methods, including dynamic contrast enhanced techniques. Such methods may benefit from taking the biexponential nature of tissue water longitudinal relaxation explicitly into account.

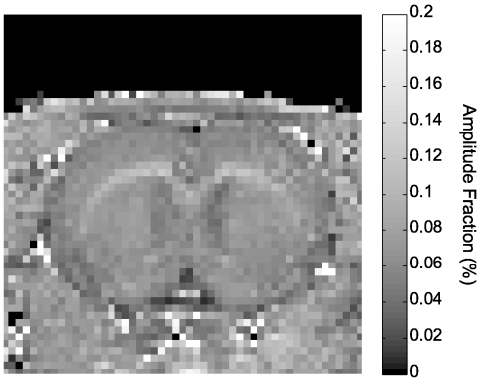

Figure 2: Parametric map of the amplitude fraction for the fast relaxing component obtained at 11.7 T. The map is an enlarged region from an image collected with a data matrix of 128 × 128. Anatomic structures are visible and white matter (corpus callosum and external capsule) has a larger amplitude fraction of fast relaxing water than gray matter.

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References: 1) Does MD, Gore JC. Magn. Reson. Med. 2002;47(2):274-283. 2) Bretthorst GL, Hutton WC, Garbow JR, Ackerman JJH. Concepts Magn. Reson. 2005;27A(2):64-72. 3) Bretthorst GL, Hutton WC, Garbow JR, Ackerman JJH. Concepts Magn. Reson. 2005;27A(2):55-63.