Imaging macromolecular dipolar interactions by combining DQF NMR and UTE MRI

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Introduction: All commonly used clinical MRI methods employ water magnetization to obtain anatomical and functional information based on diffusion coefficients and relaxation times. However, due to short dephasing times of protons within macromolecules (MM), common in extracellular matrix (ECM), and connective tissues like cartilage, ligaments and tendons, and within the water molecules associated with them, these methods provide only limited information about the MM. One way to overcome this limitation is to select the subpopulation of MM-associated protons using double quantum filtering combined with magnetization transfer (DQF-MT MRI) (1,2) and Ultra-Short TE (UTE) MRI to obtain images with contrast that distinguishes among tissue compartments on the basis of differences in their MM content.

Materials and Methods: We conjoin a double quantum filter and magnetization transfer filters (DQF-MT) following by a UTE MRI sequence: 90°-τ-90°-t_{DQ}-90°-τ-90°-t_{LM}-UTE, where τ is the evolution period, and t_{DQ} and t_{LM} are the double quantum coherence and longitudinal magnetization evolution time intervals, respectively. This approach enables one to select the protons to be excited on the basis of the strength of their dipolar interactions, ω_D, and thus is more sensitive to the properties of the MM and enabling one to obtain contrast from MM-associated protons. MRIs were obtained using a 14T Bruker BioSpin μMRI system with an Avance III console. Discs and vertebrae were obtained from rat-tail of previously sacrificed animals and soaked in saline, so as not to disturb the macromolecular structure extracellular matrix proteins.

Results: In Figs. 1 and 2 we show images of axial slices of discs and vertebrae in rat tail as function of τ. On a time scale of 30μs the intensities of the tendons, muscles, and annulus fibrosus decline by 1.3:2:1.9 respectively in disc. For the slice through the vertebrae the tendons, muscle, and vertebrae decay by 1.3:2.5:1.5 respectively. The very short time scale of the decay is a clear indication of dephasing due to dipolar interaction within the MM while differences in the decay rates reflect differences in the MM composition of the various compartments.

Discussion: Since water molecules are far more mobile than the MM their intramolecular dipolar interactions are significantly averaged out (i.e., ω_D, the residual value is less than 1kHz). This property can be used to suppress the water signal and retain only that of the MM-associated protons whose motion is highly restricted, and whose dipolar interactions are not entirely averaged out. Previous NMR spectroscopic studies of MM such as collagen yielded a spectral width of tens of kHz, which cannot be detected by MRI even with methods using UTE. In previous studies of neuronal tissue this problem was overcome by using the DQF-MT NMR where the MM transverse magnetization was converted to the longitudinal axis and subsequently, by proton exchange, to water, whose magnetization could be used for conventional MRI (2). Though the method provides detailed information about MM in neuronal systems, its application to connective tissues was still limited due to the short water transverse relaxation time (T_2), preventing the use of gradient and spin-echo MRI, and requiring large slice thicknesses and low voxel resolution to increase SNR. These properties of MM have made the study of their content and composition difficult. In recent years methods with UTE enabled imaging of tissues with short T_2 like tendons (3), and its combination here with DQF-MT is novel. The differences in the decay of the MM magnetization in the various compartments mentioned in the results section are consistent with the presence of different types of collagen (type I and II). In the tendon and the annulus fibrosus

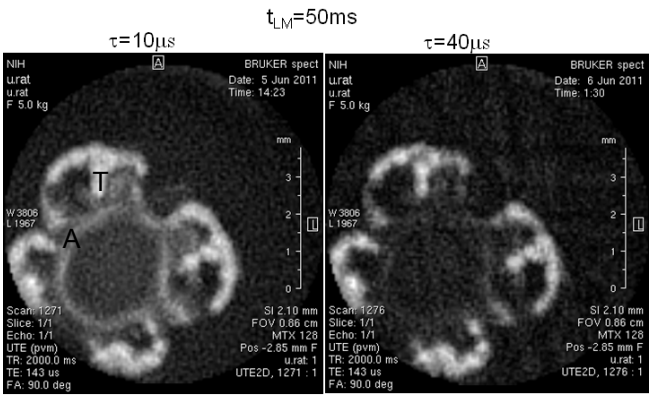

Fig. 1: An axial slice of rat-tail disc obtained by combining DQF-MT and UTE MRI. Slice thickness=2 mm, TE=143 μs.

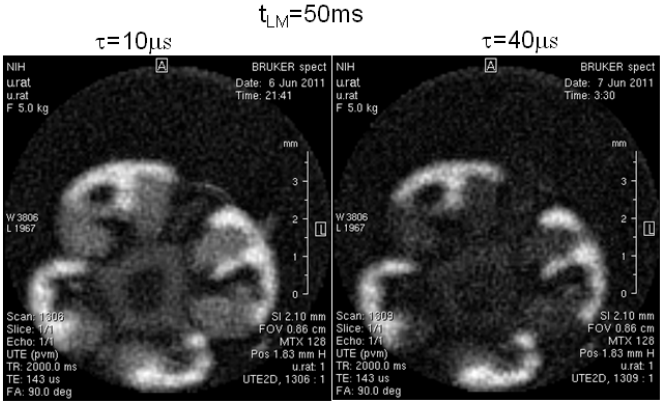

Fig. 2: An axial slice of rat-tail vertebrae obtained by combining DQF-MT and UTE MRI. Slice thickness=2 mm, TE=143 μs.

References:

(1) Eliav & Navon, JACS, 124 (2002) 3125 (2) Neufeld et al., MRM 50 (2003) 229 (3) Gatehouse & Bydder, Clin Radiol 58 (2003) 1.