Specialty Area: Quantitative Imaging and Modeling

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Highlights:

- Quantitative longitudinal relaxographic imaging (T_1 mapping) techniques are information rich and high-quality ^1H_2O T_1 maps can now be obtained in very reasonable acquisition times.
- Intrinsic ^1H_2O T_1 values are strongly correlated with tissue macromolecular content, but iron content can also be important.
- Contrast agent applications provide a mechanism to perturb ^1H_2O T_1 in select tissue spaces and with pharmacokinetic modeling extract quantitative information on contrast agent extravasation kinetics, distribution volumes, and also trans-compartmental equilibrium water exchange.

Title: Modeling Tissue Structure, Function, and Chemistry with Quantitative Relaxation Techniques

Target Audience: Magnetic resonance scientists, engineers, and physicists

Learning Objectives: To more completely appreciate the primary determinants of tissue ^1H_2O longitudinal relaxation time constant (T_1), gain insight into ways to measure and extract quantitative T_1 values with high spatial and/or temporal resolution, understand applications and limits of various modeling techniques.

Discussion: The longitudinal relaxation time constant, T_1 (= $1/R_1$), is a fundamental NMR signal property (1) that offers excellent sensitivity to local tissue chemistry. It is the MRI contrast mechanism of choice when high definition anatomical detail is required. Quantitative ^1H_2O T_1 mapping techniques find a wide range of applications in biological magnetic resonance, including tissue segmentation, lesion classification, and dynamic contrast enhanced perfusion studies. Although quite powerful, conventional T_1 mapping techniques suffer a serious drawback – they require substantial acquisition time. This is because for many desired *in vivo* applications sampling requirements are high, not only must the T_1 recovery be well sampled, but high spatial resolution and coverage also are demanded. To handle these demands a large number of innovative approaches has been developed (2-5), and now high-quality T_1 maps featuring highly sampled recovery from inversion ($N_{TI} > 32$), good spatial resolution (2 mm)^3 and whole brain coverage can be acquired in less than 6 minutes (6). The class of technique is flexible in that spatial resolution and/or coverage can be compromised to improve temporal resolution, with some highly sampled inversion recovery acquisitions being collected with 2 s temporal resolution. Most accelerated acquisitions typically are achieved at the expense of non-linear distortions in T_1 values. However, accurate T_1 values can be obtained by appropriate models that account for the relevant timings and effective flip angles of applied radiofrequency pulses and other details of the pulse sequence.

There are several applications that illustrate the strength of quantitative ^1H_2O T_1 mapping techniques. ^1H_2O T_1 mapping offers a precise way to characterize brain tissue *in vivo* and has

potential for objective evaluation of both extensive and intensive properties. ^1H_2O T_1 values differ between gray matter, white matter and cerebrospinal fluid water and, at sufficiently high magnetic field, these differences give T_1 histograms definable structure, which can be used to generate volumetric images of the different tissue types in an unsupervised way with excellent tolerance to radiofrequency bias. Local voxel-wise T_1 values provide insight into macromolecular volume fraction and intrinsic paramagnetic metal (mostly iron) content (7).

Contrast agents find widespread use in MRI, most notably to characterize lesions of the central nervous system and elsewhere in the body (8, 9-10). Unlike nuclear medicine tracers, MRI contrast agents are detected indirectly through the extent to which the ^1H_2O signal is perturbed; in dynamic contrast enhanced studies this typically is accomplished by measuring signal intensity changes during contrast agent passage through tissue using a T_1-weighted acquisition series. The indirect nature of MRI contrast agent detection provides an opportunity to measure tissue intercompartmental water exchange kinetics (10-11); a class of equilibrium exchange measurements that is a well-recognized and unique strength of NMR techniques. The experiment described by Fabry and Eisenstadt (12) measuring equilibrium water exchange across red blood cell membranes represents an early and elegant example of the approach. Using the appropriate pharmacokinetic models, changes in tissue ^1H_2O longitudinal relaxation time constants following injection of an MRI contrast agent can be used to probe the agent distribution volume, gain insight into vascular permeability, and also investigate water exchange dynamics (10,11,13). Such techniques have been used to estimate the permeability of tumor vasculature to low and high molecular weight contrast agents, the permeability of the normal blood-brain barrier to low molecular weight contrast agents, and intravascular water residence times in normal and pathological regions of human and non-human primate brain.

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