$T_{1\rho}$ imaging: Techniques and Basis for Image Contrast

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Introduction

Nuclear spin relaxation plays a key role in imparting image contrast in magnetic resonance imaging (MRI). Traditionally, T_1 (spin-lattice relaxation) and T_2 (spin-spin relaxation) relaxation times and magnetization transfer (MT) contrast are exploited to better visualize a given tissue in a specific pathology. In recent years, $T_{1\rho}$ (spin-lattice relaxation in the rotating frame) is also utilized to study tissue specific properties. In this presentation, first we describe the $T_{1\rho}$ relaxation time and elicit its differences from the traditional relaxation times. Second, we discuss methods for $T_{1\rho}$ measurement, including types of imaging sequences used. Third, we present its role in studying collagen rich tissues such as cartilage and intervertebral disc. Last, we demonstrate some specific biomedical applications where $T_{1\rho}$ shows promise for characterizing tissue integrity. In what follows, a brief background on the aforementioned topics is presented.

T_1, T_2, MT and $T_{1\rho}$

In NMR, the spin dynamical information is contained in the spectral density functions associated with the spin-lattice relaxation in the laboratory or rotating frame (1-4). Depending upon the method used, the experiment may be simultaneously sensitive to more than one time scale. As is well known, T_1 relaxation is sensitive to the spin motional processes and hence spectral densities that are at or around the Larmor precession frequency. This means that by performing T_1 measurements at varying B_o field strengths, it is possible to study spin interaction/motional processes occurring at those frequencies (5,6). For high-resolution magnetic resonance, these frequencies are typically 10-500 MHz. Unfortunately, to measure very low frequency components (100 Hz to few KHz) measurements are performed at very low magnetic field strengths. This creates two problems: (1) at low fields the image signal to noise ratio (SNR) is poor and (2) these low field scanners are not readily available and hence this is not a viable alternative. This is where $T_{1\rho}$ plays a crucial role. On the other hand, $T_{1\rho}$ enables the measurement of low frequency processes while performing the imaging experiments at any currently available clinical MRI field strengths (7,8).

In a $T_{1\rho}$ experiment, the spin magnetization is first flipped into the transverse plane (in the rotating frame) by a 90^o pulse. Then a long, low powered (B_1) RF pulse, referred to as spin-lock (SL) pulse, is applied parallel to the magnetization. The magnetization nutates around the applied spin lock (B_1) field. The magnetization undergoes relaxation in the presence of the spin-lock field in the rotating frame, a situation similar to the rotation of longitudinal magnetization around the Bo field in the laboratory frame. This spin-locked magnetization will relax with a time constant $T_{1\rho}$, for the duration of the spin-locking pulse (TSL). In the rotating frame, the spin lock field B_1 plays the same role of Bo as in the laboratory frame. To measure T_1 dispersion one must perform measurements at different Bo fields, a time

intensive process. Whereas $T_{1\rho}$ dispersion can be measured simply by varying B_1 field amplitude at a constant Bo field using readily available hardware! The "$T_{1\rho}$ -dispersion" curve obtained in this case is governed by the spectral density components of the sample that in the neighborhood of ν_1 ($2\pi\nu_1=\gamma B_1=\omega_1$), typically in the range of few Hz to several KHz.

$T_{1\rho}$ phenomenon and associated relaxation theory was first introduced in the studies of solid-state materials (9,10)(9-10). Since then the technique has been utilized in solution state NMR to study protein dynamics and in biological tissues to investigate pathophysiology in different types of tissues (2,11).

T_2 relaxation processes produce dispersion or uncertainty in the energy gap between spin states. T_2 processes do not change the energy of the spin system, but they instead contribute to de-phasing of transverse magnetization.

$T_{1\rho}$ is related to T_1 and T_2 as follows: 1) as the frequency of the spin-locking pulse, ω_1, approaches zero, $T_{1\rho}$ approaches T_2; and 2) as ω_1 approaches the Larmor frequency, ω_o, $T_{1\rho}$ approaches T_1. For liquids that satisfy extreme narrowing conditions (i.e., $\omega_o\tau_c<<1$, where τ_c is the rotational correlation time), $T_{1\rho}$ is independent of ω_1 and, moreover, $T_1=T_2=T_{1\rho}$. For solids and many biological tissues one finds that $T_2>T_{1\rho}>T_1$ (4,5).

In biological tissues, the MT mechanism involves exchange modulated dipolar interaction mediated cross relaxation between bound/restricted pool of water with that of free/mobile pool of water. In cartilage, it has been shown that the magnetization transfer effect is predominantly due to the collagen component and there is only a very small contribution from PG (12). The bound water residence time on the collagen is in the order of microseconds leading to a line width of several hundred KHz. In fact, the bound pool of water in cartilage has a T_2 of ~10 μs and results in ~100 KHz line width. Upon off-resonance saturation these spins exchange with bulk water, which results in the reduction in the amplitude of free water signal.

Measurement of $T_{1\rho}$

In a typical $T_{1\rho}$ MRI experiment, TSL is incremented while the amplitude of SL pulse (ν_1=0.1 to few KHz) is fixed. Magnetization measured as function of TSL duration is fitted to an exponentially decaying function to compute $T_{1\rho}$ at the ω_1 of interest. In imaging applications, it is often more convenient to spin-lock prepare the magnetization and then store it along the longitudinal axis with a -90^o RF pulse and recall it by a suitable imaging readout sequence. A crusher gradient is then applied to dephase any residual transverse magnetization (7,8).

Mechanisms that contribute to $T_{1\rho}$ relaxation

In biological tissues, several types of motional processes/interactions contribute to $T_{1\rho}$ relaxation (4). Depending on the tissue, more than one relaxation mechanism may be operative simultaneously, but with different relative contributions. In general, predominant contributions in tissues are chemical exchange, dipole-dipole interactions, spin-spin coupling, diffusion and slow rotational motions of spins on large macromolecules (4-6,13).

$T_{1\rho}$ MRI of collagen rich tissues

In collagen rich tissues such as cartilage, the primary mechanisms that contribute to $T_{1\rho}$ are from chemical exchange and dipole-dipole interactions, which in turn contribute to image, contrast and give a handle to compute changes in the matrix macromolecular content and structure.

In cartilage, the dipolar interaction of water protons on highly oriented collagen significantly broadens the water proton line. Due to spatial variations in collagen orientation, the dipolar interaction causes the so-called tri-laminar appearance in cartilage (14-17). Because of this property, T_2 weighted images are prone to the "magic angle effect" and this enables the detection of structural or compositional changes in collagen. The low frequency exchange of –OH and –NH protons on the Glycosaminoglycans (GAG) chains of aggrecan with bulk water protons alter both T_2 and $T_{1\rho}$ relaxation times. However, the dominant dipolar interaction masks smaller changes in T_2 relaxation time caused by the exchange mechanism. However, the spin locking in the $T_{1\rho}$ experiment refocuses or attenuates/minimizes the dipolar interaction and makes the $T_{1\rho}$ relaxation sensitive to other relaxation mechanisms such as low frequency proton exchange. This leads to an enhanced dynamic range of $T_{1\rho}$ compared to T_2 (14,15). For the same reason, in $T_{1\rho}$ weighted images the magic angle effect is minimized. This enables the detection of changes in other macromolecular (e.g. aggrecan) composition in cartilage with high degree of accuracy. Besides this, $T_{1\rho}$ MRI has other advantages such as minimizing susceptibility effects, refocusing chemical shifts and attenuating effects due to diffusion through inhomogeneous fields (7,18-21).

$T_{1\rho}$ MRI has been performed on bovine cartilage subjected to enzymatic degradation (22-24), human osteoarthritic cartilage specimens (25), animal models of osteoarthritis (OA) (26) and healthy as well OA subjects and demonstrated its potential in characterizing early OA and hence cartilage integrity (27-36). Recently, $T_{1\rho}$ MRI of intervertebral disc has been performed and its potential of detecting disc degeneration is demonstrated (37,38).

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