Accuracy and Precision in Quantitative Rotating Frame Relaxometry at High and Ultra-High Magnetic Fields

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Purpose: This work is based on the review of novel MRI methods for generating the longitudinal relaxation contrast, $T_{1\rho}$, and the transverse relaxation contrast, $T_{2\rho}$ in the rotating reference frame regime at high and ultra-high magnetic fields. Clinical application of the $T_{1\rho}$ and $T_{2\rho}$ contrasts using the on- or off-resonance spin-lock (SL) radiofrequency (RF) irradiation has been a challenging task. Long acquisition time and high RF energy deposition into the tissue (specific absorption rate i.e., SAR) in the SL based methods are the major problems. SL RF pulse cluster and adiabatic RF pulses based MRI acquisition schemes for accurate and precise quantitative estimation of $T_{1\rho}$ and $T_{2\rho}$ have been reviewed in detail in this work.

Outline of Content: $T_{1\rho}$ and $T_{2\rho}$ are the sensitive biomarkers of changes at the cellular level and in the amount of iron in the Parkinson's and Alzheimer's diseases, respectively [1], [2]. $T_{1\rho}$ can be used as a sensitive marker for the gene therapy monitoring [3] and it has potential to characterize the neoplastic tissue [4]. In Parkinson's disease, adiabatic $T_{2\rho}$ is more sensitive than T_2 to pathological changes in the brain, which reflects the iron accumulation in the substantia nigra area [1]. The rotating frame relaxations are sensitive to the dynamic molecular processes which occur close to the effective frequency ($\omega_{eff}=\gamma B_{eff}$) in the order of kilohertz. Therefore, $T_{1\rho}$ and $T_{2\rho}$ are sensitive to the slow molecular motion as compared to the T_1 and T_2 relaxation rates. $T_{1\rho}$ relaxation originates from the spin-lattice energy exchange mechanism. In the tradition spin-locking (SL) scheme, the low-frequency components of the lattice, that are equivalent to the RF amplitude, cause the $T_{1\rho}$ relaxation. The low-frequency components manifest physio-chemical processes, such as, slow exchange mechanism (proton water exchange with hydroxyl and amide functional groups), slow rotation, and static dipolar or quadruple interactions. The low-frequency interactions between the macromolecular protons and the bulk water protons can be detected if the correlation times, τ_c, fulfill the condition $\tau_c=1/\gamma B_1$, where the nutation frequency is γB_1. Theoretical formalism to characterize the relaxation due to dipolar interactions in the case of two identical spins and anisochronous exchange is well described in literature. Adiabatic on-resonance RF irradiation (where the flip angle and the effective field are time dependent) is another technique employed for the rotating frame relaxation measurement. Adiabatic half passage (AHP) adiabatic pulses have been used for measuring $T_{1\rho}$. During the on-resonance adiabatic full passage (AFP) adiabatic irradiation, $T_{1\rho}$ is affected by the dipolar interactions in the fast motional regime ($T_{1\rho\text{-}dd}$) and existence of anisochronous exchange between spins having different chemical shifts in the fast exchange regime ($T_{1\rho\text{-}ee}$). Consequently, the $T_{1\rho}$ relaxation can be expressed as an average of the instantaneous time-dependent contributions due to the aforementioned relaxation channels ($T_{1\rho\text{-}dd}$ and $T_{1\rho\text{-}ee}$) [5]. The expressions of $T_{2\rho\text{-}dd}$ and $T_{2\rho\text{-}ee}$ transverse relaxations have been given in [5]. Assuming that the major source of the $T_{2\rho}$ contrast comes from the dipolar contributions and the RF pulse amplitude is much less than the Larmor frequency, $1/T_{2\rho}$ is approximately equals the average of the sum of $1/T_1$ and $1/T_2$. Moreover, different models for estimating the rotating frame relaxation rates, based on the mono-exponential decay, solution of the Bloch equations in the rotating frame, and the steady-state signal equation have been proposed in literature. Generally, the $T_{1\rho}$ and $T_{2\rho}$ MRI sequences are composed of two modules i.e., magnetization preparation module which is used to sensitize the signal to the relaxation phenomenon, and the magnetization acquisition module. After the magnetization preparation module (traditional SL pulse cluster or adiabatic irradiation pulse cluster), the resulting magnetization can be acquired by using gradient echo, spin echo, EPI or segmented-EPI. The sequences that employ delay periods to wait for equilibrium restoration of the longitudinal magnetization are inherently time inefficient. Therefore, it is desirable to acquire the $T_{1\rho}$-weighted signal under the rapid steady-state magnetization conditions with high signal-to-noise ratio (SNR) and contrast. There are a few $T_{1\rho}$ steady-state MRI sequences that employ short delay times with the magnetization preparation-3D acquisition scheme allows recovery of longitudinal magnetization. $T_{1\rho}$ imaging has been performed within SAR guidelines in human brain using the AHP adiabatic pulses with the segmented EPI readout. On the other hand, the 2D multislice pulse sequences for measuring $T_{1\rho}$ have a combination of $T_{1\rho}$ and saturation weighting. In a 2D multislice technique that uses non-selective SL, the saturated longitudinal magnetization is modeled and measured independently as $T_{2\rho}$ decay and then corrections for $T_{1\rho}$ measurements can be preformed subsequently. According to another approach, elimination of the intrinsic $T_{2\rho}$ weighting from the multislice $T_{1\rho}$ measurements by using a separate single multiecho scan can be accomplished. Quantification of $T_{2\rho}$ relaxation due to chemical exchange during the AFP pulses can be performed using the CP spin-echo sequence. Sensitivity to the chemical exchange and the rotational correlation times has been manifested by two adiabatic pulses, HS1 and HS4, using different modulation functions for the adiabatic pulses. Recently, a SL steady-state free-precession (slSSFP) pulse sequence is used to measure $T_{1\rho}$ and compares the slSSFP signal with the well-known balanced steady-state free-precession (bSSFP) signal.

Summary: Merits and demerits of different MRI acquisition schemes to establish the accurate and precise $T_{1\rho}$ and $T_{2\rho}$ measurements have been presented. Analysis of clinical applicability of the MRI sequences, with respect to different experimental parameters, such as, SAR, SNR, magnetization response, etc, have been given. It is concluded that new mechanisms of adiabatic irradiation at high and ultra-high field MRI are required to achieve the lower levels of SAR with significant SNR in the clinically acceptable time for the accurate and precise $T_{1\rho}$ and $T_{2\rho}$ measurements.

References: [1] Michaeli S, Oz G, Sorce D, Garwood M, Ugurbil K, Majestic S, Tuite P. Assessment of Brain Iron and Neuronal Integrity in Patients with Parkinson's Disease Using Novel MRI Contrasts. Movement Disorders 2007; 22:334-340. [2] Borthakur A, Sochor M, Davatzikos C, Trojanowski J, Clark C. $T_{1\rho}$ MRI of Alzheimer's disease. NeuroImage 2008; 41:1199–1205. [3] Hakumäki J, Gröhn O, Tyynelä K, Valonen P, Ylä-Herttuala S, Kauppinen R. Early gene therapy–induced apoptotic response in BT4C gliomas by magnetic resonance relaxation contrast T_1 in the rotating frame. Cancer Gene Therapy 2002; 9:338–345. [4] Pitkanen A, Nissinen J, Nairismagi J, Lukasiuk K, Gröhn O, Miettinen R. Progression of neuronal damage after status epilepticus and during spontaneous seizures in a rat model of temporal lobe epilepsy. Prog Brain Res 2002; 135:67–83. [5] Mangia S, Liimatainen T, Garwood M, Michaeli S. Rotating frame relaxation during adiabatic pulses vs. conventional spin lock: simulations and experimental results at 4 T. Magn Reson Imag 2009; 27:1074–1087.