In-Vivo Assessment of Multi-Component Relaxation of Articular Cartilage using mcRISE at 3.0T

Fang Liu[1], Alexey Samsonov[1], Pouria Mossahebi[2], Rajeev Chaudhary[2], Wally Block[1,2], and Richard Kijowski[3]

[1]*Department of Medical Physics, University of Wisconsin-Madison, Madison, Wisconsin, United States,* [2]*Department of Biomedical Engineering, University of Wisconsin-Madison, Madison, Wisconsin, United States,* [3]*Department of Radiology, University of Wisconsin-Madison, Wisconsin, United States*

Introduction: Nuclear magnetic resonance (NMR) studies have identified multiple water components within cartilage (1-2). Our previous study using multi-component Driven Equilibrium Single Pulse Observation (mcDESPOT) has shown the feasibility of multi-component T2 analysis for assessing a rapidly relaxing water component tightly bound to proteoglycan (W_{PG}) and a slowly relaxing bulk water component (W_{BW}) of the entire knee joint at 3.0T (3). However, one limitation of mcDESPOT is the lack of consideration of magnetization transfer (MT) exchange between the water compartments and macromolecular protons which was shown to bias estimation of fundamental MR relaxation rates for those steady-state sequences (4-5). In this study, we propose a new method named **m**ulti-component **R**elaxation **I**maging using **S**teady-state signal **E**volution (**mcRISE**) to correct the multi-component T2 estimation. Our technique introduces a macromolecular proton pool in exchange with mcDESPOT water pools and uses a combined model aimed for providing more robust and unbiased multi-component T2 values along with additional quantitative MT parameters, which may provide a new set of biomarkers for assessing the cartilage extracellular matrix in-vivo.

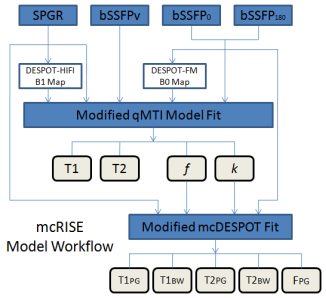

Figure 1: The incremental fitting approach for mcRISE model. Four sets of steady-state images are needed including SPGR, bSSFP with phase cycling on ($bSSFP_{180}$) and off ($bSSFP_0$), and bSSFP with varying RF pulse width (bSSFPv).

Methods: Simultaneous fitting for all parameters of the extended model is not feasible due to the size of the search space. Hence, we attempted an incremental fitting approach. Namely, we first derive measures describing macromolecular proton pools such as bound pool fraction *f* and exchange rate *k* using balanced steady-state free precession (bSSFP) based estimation of the MT parameters (6), where varying excitation RF pulse width (bSSFPv) was applied for exploring on-resonance MT effect. Then, we use these values as fixed parameters in the full model fit, which involves the mutually exchanging slow and rapid relaxing water compartments and the bound proton pool. The details implementing mcRISE model are shown in Figure 1. The B1 and B0 map are first obtained from DESPOT-HIFI (7) and DESPOT-FM (8), respectively. A modified quantitative MT imaging (qMTI) model (6) takes into account both B1 and B0 map, then simultaneously fits for both varying flip angle SPGR and bSSFP signals for resolving unbiased and MT corrected single component T1, T2, *f* and *k*. The modified mcDESPOT model involving MT exchange is then fitted using both SPGR and bSSFP signals along with the obtained *f* and *k* maps, resulting in MT corrected multi-component T2 maps for both W_{PG} component ($T2_{PG}$) and W_{BW} component ($T2_{BW}$), and a corrected water fraction map for W_{PG} component (F_{PG}). To test the feasibility of mcRISE in-vivo, an MRI scan of the knee was performed on a healthy adult volunteer using a 3.0T scanner (Discovery MR750, GE Healthcare; Waukesha, WI) and 8-channel knee coil (InVivo, Orlando, FL). The mcRISE parameters included: 1) Spoiled gradient echo (SPGR) scans with TR/TE=4.6/2.2ms over a range of flip angles (α=3, 4, 5, 6, 7, 9, 13, 18°); 2) Two bSSFP scans with RF phase cycling on ($bSSFP_{180}$) and off ($bSSFP_0$), with TR/TE=5.0/2.4ms over a range of flip angles (α=2, 5, 10, 15, 20, 30, 40, 50°); 3) One bSSFPv scans over a range of RF pulse width (T_{RF}) at T_{RF}/TR=0.2/5.6ms, 0.3/5.6ms, 0.4/5.6ms, 0.6/5.6ms, 0.8/5.7ms, 1.2/5.8ms, 1.6/6.1ms, 2/6.5ms and α=35°. 4) Inversion recovery SPGR scan with TR/TE=4.6/2.2ms, TI=450ms, and α=5°. All scans were performed in the sagittal plane covering the entire knee with a 16cm field of view, 256×256 matrix, 3mm thickness. Total scan time was 24 minutes. An ROI was drawn on the lateral tibia plateau from where the average T2, $T2_{PG}$, $T2_{BW}$, F_{PG} from both mcDESPOT and mcRISE were obtained for comparison. *f* and *k* from mcRISE were also obtained for comparing with literature values.

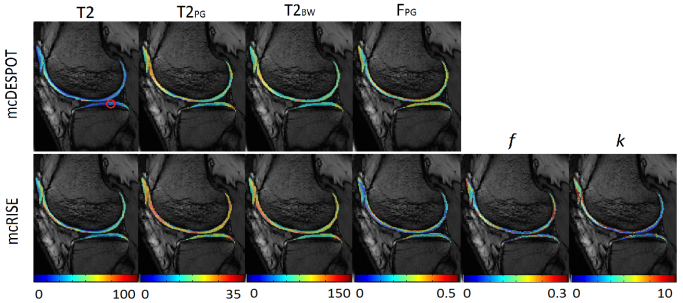

Figure 2: Parameter maps obtained from mcDESPOT and mcRISE, ROI is shown as red circle on tibia plateau. mcRISE provides higher T2, $T2_{PG}$, $T2_{BW}$ and lower F_{PG} values compared to mcDESPOT. The *f* and *k* map from mcRISE provides additional MT related information.

	T2 [ms]	$T2_{PG}$ [ms]	$T2_{BW}$ [ms]	F_{PG} [frac.]	*f* [frac.]	*k* [s^{-1}]
mcDESPOT	26	19.3	78.7	0.28		
mcRISE	39	22.0	84.1	0.22	0.18	2.1
Literature	37[a]	25.2[b]	96.3[b]	0.15[b]	0.25[c]	2[c]

Table 1: Parameter comparison for mcDESPOT and mcRISE. [a] from ref. 11, [b] from ref. 1, [c] from ref. 12

Results/Discussion: mcRISE was able to create T2 and water fraction maps for the rapid and slowly relaxing water components (W_{PG} and W_{BW} respectively) and *f* and *k* maps of the entire knee joint at 3.0T in a clinically feasible scan time (Figure 2). The spatial variation of the T2 relaxation time and water fraction values for the W_{PG} and W_{BW} components within the knee joint is consistent with our previous report (3). However, mcRISE provides higher single component T2, $T2_{PG}$, $T2_{BW}$ and lower F_{PG} values compared to values obtained from original mcDESPOT (Table 1), which agrees with our numerical simulation results (not shown). It is postulated that the estimation of mcDESPOT is affected by the MT exchange that has a strong influence on the multi-component spin exchange model which represents cartilage matrix microstructure. Similar reports have been found for myelin water fraction estimation in brain imaging using mcDESPOT (9). The mcRISE model decouples the multi-component T2 estimation from the MT effect, and thus may provide better approximation of the complex cartilage matrix proton environment. Additional information of macromolecule bound proton fraction *f* and water proton exchange rate *k* from the mcRISE model provides a new set of potential biomarkers which may provide information regarding collagen fiber content and structure as reported from our previous studies (10). However, further validation of these new parameters regarding their sensitivity and specificity to collagen within cartilage is needed. Additional studies with larger number of subjects are also needed to determine the potential applications of mcRISE for evaluating articular cartilage in clinical practice and osteoarthritis research studies.

References: (1) Reiter D. MRM, 2010. (2) Reiter D. NMR Biomed, 2011. (3) Liu F, JMRI, 2013. (4) Bieri O. MRM, 2006. (5) Mossahebi P, MRM, 2013. (6) Gloor M. MRM, 2008. (7) Deoni S. JMRI 2007. (8) Deoni S. JMRI, 2009. (9) Zhang J. ISMRM, 2013. (10) Mossahebi P, ISMRM, 2013. (11) Gold GE. AJN, 2004. (12) Stikov N. MRM, 2011.