Parametric relaxation measurements in bovine patellar cartilage

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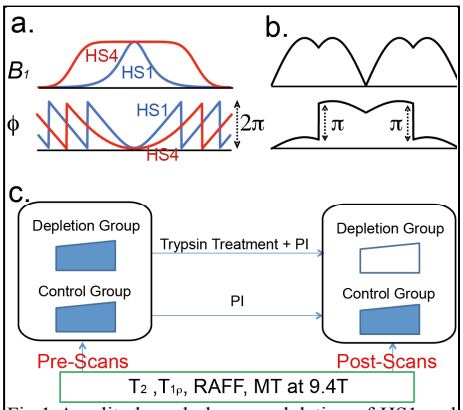

Fig.1 Amplitude and phase modulation of HS1 and HS4 pulses used in $T_{1\rho}$ preparation (a), and SC pulses in RAFF preparation (b); (c) Experimental design: In the depletion group cartilage plugs (n=4) underwent MRI scanning before and after trypsin treatment. The control group (n=4) was scanned at the same time points. Protease inhibitors (PI) was applied.

Introduction & Theory: Articular cartilage alterations of the macromolecular architecture, including loss of proteoglycans (PG) at very early stage, are the hallmark of Osteoarthritis (OA). Continuous-wave $T_{1\rho}$ ($T_{1\rho\text{-CW}}$) has been established to be a biomarker for cartilage integrity [1]. Alternatively, $T_{1\rho}$ contrast can be created using frequency-modulated (FM) pulses, which for some types of experiments offer advantages over the classical $T_{1\rho\text{-CW}}$ experiment (e.g. greater tolerance to B_1-inhomogeneity and resonance offsets). The latter method typically uses adiabatic pulses based on the hyperbolic secant family, HS1 and HS4 (Fig. 1a, $T_{1\rho\text{-HS1}}$ and $T_{1\rho\text{-HS4}}$, respectively) [2,3]. $T_{1\rho\text{-HS1}}$ and $T_{1\rho\text{-HS4}}$ exhibit great sensitivity to dynamic processes such as exchange and dipolar interactions, from fast to intermediate motional regime[3]. Recently, a new FM method entitled RAFF (Relaxation Along a Fictitious Field) has also been introduced. RAFF creates rotating frame relaxation contrast using *sine* and *cosine* modulation functions (SC pulses, Figure 1b) pulses operating in a sub-adiabatic condition and thus the RF power can be reduced, which is important for in vivo application [2, 4]. When sweeping the pulse frequency sub-adiabatically, the vector sum of $d\alpha/dt$ and ω_{eff} leads to the so-called fictitious filed, E. Locking the magnetization along E field produces RAFF contrast[4]. In the present work, systematic studies have been performed on bovine patella cartilage plugs to compare the efficiency of $T_{1\rho\text{-HS1}}$, $T_{1\rho\text{-HS4}}$, RAFF, our modified version of magnetization transfer (MT, details listed below), along with the established T_2 method.

Materials & Methods: Bovine patellar plugs were used to compare the proposed MRI methods between a depletion and a control (n=4 in each group) group, respectively. Following the initial scanning (pre- scan), the patellae in the depletion group were treated with trypsin (0.8mg/mL PBS, 24 hrs, 20°C, Aldrich), stored in protease inhibitor (PI, Aldrich) solution before undergoing post-treatment scans (post-scan). The experimental design was identical for the control group with the exception of trypsin treatment(Fig. 1c). MRI measurements were performed on a 31cm bore 9.4T scaner (Oxford Magnet/VanmrJ Consol) using a volume coil. T_2 maps were obtained using multi-echo multi-slice sequence (MEMS). Fast spin echo multi-slice technique was used as readout in $T_{1\rho}$, RAFF and MT. Other imaging parameters were: matrix size 512x256, slice thickness 2 mm, TR 5s. ω_1^{max}= 625Hz for RAFF, 200 Hz for MT, and 2000 Hz for $T_{1\rho\text{-HS1}}$ and $T_{1\rho\text{-HS4}}$. Intensities of T_2 and $T_{1\rho}$ were fitted into a mono-exponential decay. In RAFF and MT, two measurements, with and without water inversion prior to the preparation train, were conducted. The fittings to data were performed using models $S_{\pm Z}=S_{0,\pm Z}\exp(-t/T)-S_{SS}$ $(1-\exp(-t/T_{SS}))$ for decaying and rising signal intensities. Here $S_{\pm Z}$ are measured signals without and with the prior water inversion, S_0 is the signal intensity without weighting and S_{SS} the level of steady state with corresponding relaxation time constants T and T_{SS}, respectively. The K_f maps were then extracted from MT according to $(1-S_{ss}/S_0)/T$ [5].

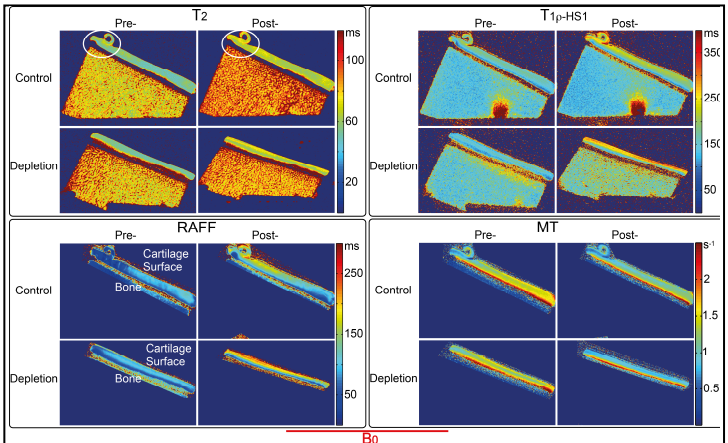

Fig.2 Representative map of T_2, $T_{1\rho\text{-HS1}}$, RAFF, and exchange rate maps K_f ($T_{1\rho\text{-HS4}}$ not shown). The largest change was identified within the superficial and tangential layer on T1rho and RAFF maps following the trypsin treatment.. Note that part of the cartilage in control group has some mechanical damage (the white circle), which is excluded in ROI for calculation. The red bar indicates the B_0 direction.

Results & Discussion: Fig. 2 shows representative maps obtained with T_2, $T_{1\rho\text{-HS1}}$, RAFF, K_f map in partially depleted bovine patellar cartilage plugs. $T_{1\rho\text{-HS1}}$ and RAFF map exhibit enhanced contrast between depletion and control in post-scans. Since trypsin only has minor effect on collagen matrix, T_2 and MT do not expect to change much between control and depletion group [6,7,1]. However, there exists contrast between pre- and post-scans longitudinally on both samples, which suggests that natural degradation occurs in collagen matrix even with PI existing. Figure 3 depicts the quantitative values measured in the region of interest in both groups. The relaxation measurements using $T_{1\rho\text{-HS1}}$ demonstrated the highest values in all specimens. In addition, RAFF and $T_{1\rho\text{-HS1}}$ have the largest change in contrast. Two reasons may contribute to the less deviation of $T_{1\rho\text{-HS1}}$: i) HS pulses highly tolerate to off-resonance effect and B_1-inhomogeneities[2]; ii) $T_{1\rho}$ can attenuate residual dipolar interaction, hence enhances the dynamic range of exchange-based contrast[1]. Histological confirmation was performed (data not shown). While both T_2 and MT are sensitive to collagen matrix, our MT had larger contrast_to_noise ratio compared to T_2 (11.2% vs 6%)[7, 6]. It is noteworthy that the $T_{1\rho\text{-HS1}}$ value reported here is larger than that of $T_{1\rho\text{-CW}}$ reported in the similar experimental condition[7], which is also consistent with the theoretical prediction[4]. Conclusion: Our results here demonstrate adiabatic $T_{1\rho}$ is also a robust and sensitive method for cartilage integrity related to trypsin induced PG loss. *Acknowledgement: This research was funded by ISMRM Seed Grant 2009, NIH P41 RR008079, and the WM KECK Foundation.*

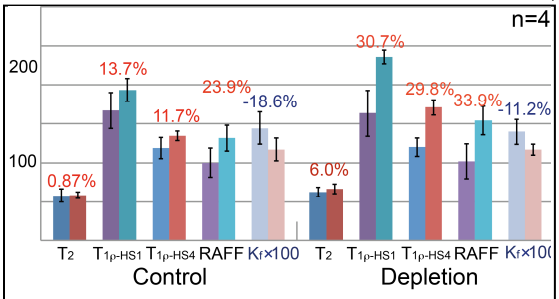

Fig.3 The statistics of T_2, $T_{1\rho\text{-HS1}}$, $T_{1\rho\text{-HS4}}$, RAFF and MT on control group (n=4) and depletion group (n=4). The percentage changes are shown on the top of the chart. The rate constant K_f in unit of s^{-1}; relaxation time constants are in unit of ms. To facilitate visualization, the value of K_f displays as K_fx100.

References: [1] Reddy R, ISMRM 2010 weekend course. [2] Garwood M et al, JMR 2001;153:155. [3] Michaeli S et al. Curr Anal Chem 2008;4:8. [4] Liimatainen T et al, MRM 2010; 64:983. [5] Mangia S et al. Proceedings of 51st ENC 2009. [6] Shinar H et al, proceesings of ISMRM 2007 :385. [7] Nieminen et al, MRM2001, 43 :676 ;[8] Akella et al, MRM 2001;46:419.