MULTI-PARAMETRIC MRI CHARACTERIZATION OF ENZYMATICALLY DEGRADED ARTICULAR CARTILAGE

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INTRODUCTION

Various quantitative MRI techniques have been investigated for the assessment of articular cartilage degeneration. These include T_1, T_2, delayed gadolinium enhanced MRI of cartilage (dGEMRIC), magnetization transfer (MT) contrast and $T_{1\rho}$ imaging [1-4]. More recently, rotating-frame (RFR) techniques including adiabatic $T_{1\rho}$ and $T_{2\rho}$ mapping [5] and Relaxation Along a Fictitious Field (RAFF) [6] have been proposed for the assessment of slow molecular motion. These different methods, however, have not been systematically compared, and the sensitivity of different MR parameters obtained using these techniques to cartilage constituents remains unclear. The aim of this study was to compare an array of MR parameters acquired with the above mentioned approaches in collagen and glycosaminoglycan (GAG)-specific enzymatic degradation models. Finally, we characterized the association of MR parameters with biomechanical properties as measured by the equilibrium modulus.

METHODS

Sample preparation: Osteochondral cylinders (d = 25 mm, N = 6) were harvested from intact bovine patellae (N = 6) and cut to three sections. Subsequently, two of the sections were digested, one using 30 U/ml collagenase and the other using 0.1 U/ml chondroitinase ABC to induce specific collagen degradation or GAG depletion, respectively. The final section (control) was immersed in Dulbecco's Modified Eagle's Medium (DMEM). All sections were incubated at +37°C for 44 hours and subsequently frozen at -20°C. *Biomechanical testing*: Equilibrium moduli were determined using stepwise indentation stress-relaxation tests (each step 5% of uncompressed cartilage thickness) up to a strain of 20%. After the testing, a smaller osteochondral cylinder (d = 7.2 mm) was drilled from each section for MR measurements. *MRI:* MR experiments were carried out at 9.4 T (Oxford instruments Plc, Witney, UK) with a 19-mm quadrature RF transceiver (RAPID Biomedical GmbH, Rimpar, Germany) and Varian VnmrJ 3.1A console (Varian Inc. Palo Alto, CA, USA). Cartilage surface was oriented perpendicular to the main magnetic field. The MR experiments consisted of a preparation block followed by a fast spin echo (FSE) readout (ETL = 4, TR = 5 s, TE_{eff} = 5 ms, matrix = 256x128, slice thickness 1 mm, FOV = 16 x 16 mm^2). The preparation block was modified in order to measure 7 different parameters (Table 1). In order to characterize the MT effect, we measured the T_1 in presence of off-resonance saturation (T_{1sat}). Finally T_1 relaxation time was measured by varying the TR in the readout sequence in 7 steps from 80 to 5120 ms. Following the initial measurements, the samples were immersed in 1 mM Gd-DTPA for 24 hours followed by post-contrast T_1 measurement (T_{1Gd} or the dGEMRIC index) using similar fast spin echo sequence. *Data analysis*: Two ROIs were selected based on the T_2 appearance: superficial ROI consisting of the most superficial 25 % of the cartilage and full-thickness ROI covering the entire cartilage thickness. MTR was defined as $1\text{-}M_{sat}/M_0$. Correlation coefficients between the MR parameters and equilibrium moduli were calculated for the full-thickness ROI.

Table 1. Details of the preparation block elements. AHP = adiabatic half-passage pulse, AFP = adiabatic full-passage pulse, CW=continuous wave.

Param.	Preparation	Prep. parameter	Value of prep. parameter	Pulse power
T_2	Spin echo preparation	TE	4, 8, 16, 32, 64, 128 ms	-
CW $T_{1\rho}$	+AHP, CW SL pulse, -AHP [7]	SL pulse duration	0, 10, 20, 40, 80, 160 ms	γB_1 = 1 kHz
Adiab. $T_{1\rho}$	Train of AFPs [5]	# AFPs	[0, 4, 8, 12, 24] x 4.5 ms	$\gamma B_{1,max}$ = 2.5 kHz
Adiab. $T_{2\rho}$	+AHP, train of AFPs, -AHP [5]	# AFPs	[0, 4, 8, 12, 24] x 4.5 ms	$\gamma B_{1,max}$ = 2.5 kHz
T_{RAFF}	RAFF pulse train [8]	# RAFF pulses	[0, 2, 4, 6] x 9 ms	$\gamma B_{1,max}$ = 625 Hz
T_{1sat}	CW saturation at +10 kHz [9]	Saturation duration	0, 0.1, 0.2, 0.4, 0.8, 1.6, 3.5, 7 s	γB_1 = 250 Hz

RESULTS AND DISCUSSION

Both collagenase and chondroitinase ABC treatments resulted in significantly decreased equilibrium moduli ($p<0.05$, Wilcoxon signed ranks test, Fig. 1), demonstrating the effect of specific collagen and GAG depletion. The MRI relaxation time constants exhibited different responses to the enzymatic treatments (Fig. 2): both native and contrast-enhanced T_1 exhibited significant differences between control and GAG-depleted tissue in full-thickness ROI, however, T_2, T_{1sat} and all RFR time constants showed significant changes only after collagenase treatment. While T_2 has been shown to be related to the structural properties of the collagen network, CW $T_{1\rho}$ has been mainly associated with the tissue GAG content due to its sensitivity to exchange. The present results suggest that the structure of the collagen network has a significant effect on $T_{1\rho}$. Moreover, the other RFR-parameters were also sensitive to collagen depletion. Magnetization transfer contrast in cartilage has been suggested to originate from the overall macromolecular content of the tissue, dominated by collagen [4]. This was reflected by increased T_{1sat} in collagenase-treated tissue. Significant ($p<0.05$) correlations were observed between equilibrium moduli and MR parameters in collagenase-treated tissue, T_2, T_{1sat} and all RFR-parameters had significant correlation to equilibrium modulus (r = -0.740– -0.589), whereas in chondroitinase ABC – treated tissue the correlation coefficients between relaxation time constants and the equilibrium modulus were higher (r = -0.800– -0.605). While the collagenase treatment induced significant changes in almost all relaxation time constants, the largest relative differences between control and PG depleted samples were in $T_{2\rho}$ and CW $T_{1\rho}$, i.e., 39 % and 34 %, respectively. These results suggest that MR parameters may be sensitive to detect mechanical alterations in articular cartilage.

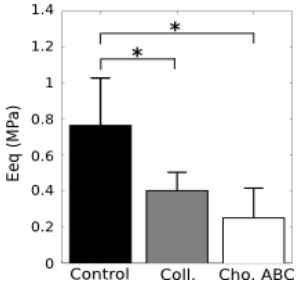

Figure 1 (Right). Average equilibrium moduli of the sample groups. (* $p<0.05$, Wilcoxon signed ranks test).

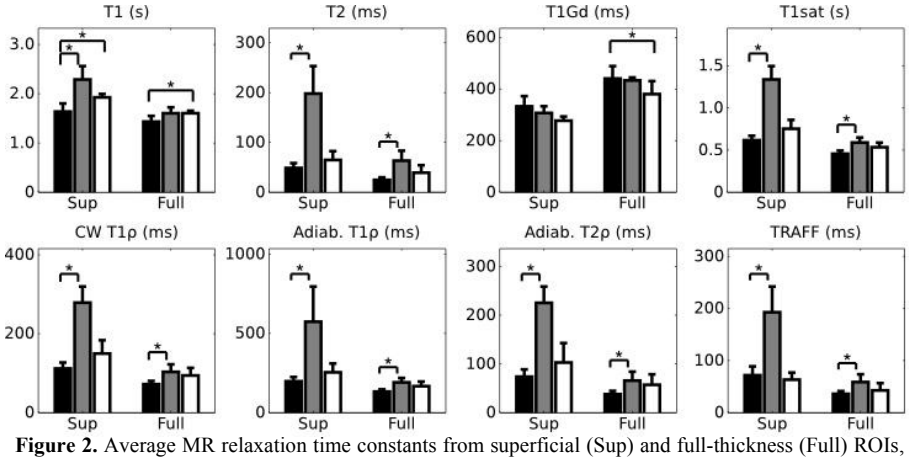

Figure 2. Average MR relaxation time constants from superficial (Sup) and full-thickness (Full) ROIs, for the control (black), collagenase (gray) and chondroitinase ABC (white) treated groups. (* $p<0.05$, Wilcoxon signed ranks test).

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