T1RHO DISPERSION IN CONSTITUENT-SPECIFIC DEGRADATION MODELS OF ARTICULAR CARTILAGE WITH CORRELATION TO BIOMECHANICAL PROPERTIES

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INTRODUCTION

Spin-lattice relaxation in the rotating frame, $T_{1\rho}$, has been proposed as a marker for articular cartilage degeneration [1,2]. $T_{1\rho}$ is primarily associated with the proteoglycan (PG) content of articular cartilage [1-3], although association with the structure of the collagen network has also been reported [4]. As $T_{1\rho}$ relaxation time constant depends on the spin-lock field (γB_1) we hypothesize that spatial distribution of $T_{1\rho}$ will be significantly affected also by the choice of γB_1. Therefore in this study, $T_{1\rho}$ dispersion was characterized in constituent-specific cartilage degeneration models with clinically relevant locking fields ($\gamma B_1 \leq 1$ kHz). Biomechanical (equilibrium moduli) and biochemical (uronic acid content) properties of cartilage were also determined and correlated with measured $R_{1\rho}$ ($=1/T_{1\rho}$) values.

METHODS

Osteochondral cylinders (d = 25 mm, N = 6) were drilled from intact bovine patellae (N = 6) and subsequently cut to three sections. To induce specific collagen degradation or PG depletion, one of the sections was digested in 30 U/ml collagenase and the other in 0.1 U/ml chondroitinase ABC, respectively. The final section was used as intact control. All sections were incubated at +37°C for 44 hours and subsequently frozen. For MR experiments and biomechanical testing, the sections were thoroughly thawed and cartilage thickness was measured. Equilibrium moduli were determined using stepwise stress-relaxation tests up to a strain of 20%. After the biomechanical testing, a smaller osteochondral cylinder (d = 7.2 mm) was drilled from the center of each section for MR measurements. Uronic acid (UA) content, corresponding to bulk tissue PG content, was determined from the adjacent tissue spectrophotometrically [5]. MR experiments were carried out at 9.4 T (Oxford instruments Plc, Witney, UK) interfaced to a Varian VnmrJ 3.1A console (Varian Inc. Palo Alto, CA, USA) with a 19-mm quadrature RF transceiver (RAPID Biomedical GmbH, Rimpar, Germany). The cartilage surface was oriented carefully perpendicular to the main magnetic field. $T_{1\rho}$ was measured using a global preparation block consisting of a continuous-wave spin-lock pulse with spin-lock durations of 0-160 ms in six steps embedded between two adiabatic half-passage pulses [6]. Experiment was repeated using γB_1 = 125, 250, 500 and 1000 Hz. The preparation block was followed by a single slice fast spin echo readout (ETL = 4, TR = 5 s, TE_{eff} = 5 ms, imaging matrix = 256x128, slice thickness 1 mm, FOV = 16 x 16 mm^2). Two ROIs were determined: a ROI covering the most superficial 25 % of cartilage (degraded area) and a bulk full-thickness ROI to compare with reference measurements. Additionally, depth-wise $R_{1\rho}$ profiles were averaged over a 1 mm wide region at the centre of each sample. Linear correlation coefficients were determined between $R_{1\rho}$ and equilibrium modulus and uronic acid content.

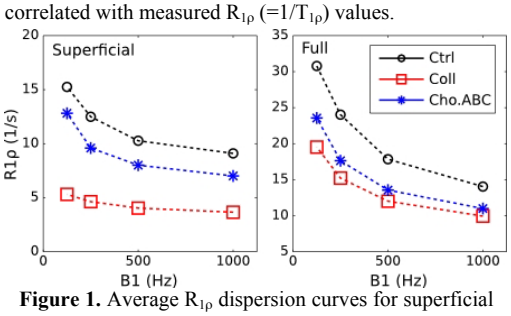

Figure 1. Average $R_{1\rho}$ dispersion curves for superficial and full-thickness ROIs.

Table 1. Correlation coefficients (r) for $R_{1\rho}$ with equilibrium modulus (E_{eq}) and uronic acid content (UA). (*/** $p<0.05$ / $p<0.01$, respectively).

ROI	γB_1 (Hz)	r ($R_{1\rho}$ vs E_{eq})	r ($R_{1\rho}$ vs UA)
Sup.	1000	0.504*	-
	500	0.493*	-
	250	0.490*	-
	125	0.408	-
Full	1000	0.649**	0.293
	500	0.533*	0.311
	250	0.459	0.285
	125	0.392	0.188

RESULTS

Significant dispersion was observed in all groups for full ROI (Fig. 1). In the superficial ROI, however, collagen degradation clearly reduced dispersion. Collagen degradation resulted in significantly lower $R_{1\rho}$ values at all B_1 amplitudes in superficial cartilage, and at the γB_1s of 250 to 1000 Hz in full-thickness cartilage, as compared to control group ($p<0.05$, Wilcoxon signed ranks test). Although a trend towards decreased $R_{1\rho}$ in PG-depleted tissue was seen, the difference was not statistically significant. Depth-wise $R_{1\rho}$ profiles (Fig. 2) show significant variation in $R_{1\rho}$ over the tissue depth and locking field; particularly in the region from ~40 to ~90 % from the cartilage surface significant dispersion was detected. Correlation of the equilibrium modulus with $R_{1\rho}$ increased with increasing locking field strength, reaching statistically significant positive correlations in the full-thickness ROI for γB_1=500 and 1000 Hz. The correlation for superficial cartilage was also significant but moderate for higher locking fields (Table 1). No significant relationships were observed between full-thickness $R_{1\rho}$ and uronic acid content (Table 1).

DISCUSSION

$T_{1\rho}$ contrast and $T_{1\rho}$ dispersion in cartilage have been previously linked with PG through chemical exchange [1,9] and with collagen through dipolar interactions [4,7]. The present results suggest that dipolar interactions may significantly influence the $T_{1\rho}$ relaxation spatial distribution in cartilage at clinically relevant locking field strengths, as $R_{1\rho}$ dispersion exhibited significant depth-wise variation particularly in collagenase-treated tissue. The effect of tissue organization is relatively evident at lower locking fields (Fig 2): both control and PG-depleted tissue show superficial $R_{1\rho}$ changes characteristic to the laminar structure of cartilage [8]. In the collagenase-treated tissue, the laminar features are lost and the dispersion vanishes in surface which is the most affected by the enzyme, resulting in organizationally randomized, degraded tissue. Furthermore, no significant correlations were found between uronic acid content and full-thickness $R_{1\rho}$ values, supporting the hypothesis that dipolar interaction may dominate $T_{1\rho}$ dispersion. The PG depletion had a smaller effect on $R_{1\rho}$ than collagen degradation; however, at higher spin locking field, the relative change approached that of collagen degradation, indicating increased sensitivity to PG content. This is supported by previous studies reporting increase in the contribution of exchange with the increase of γB_1 [4,7]. Statistically significant correlations were found between $R_{1\rho}$ and equilibrium modulus of cartilage, suggesting a possible relationship between MR parameters and the functional properties of the tissue.

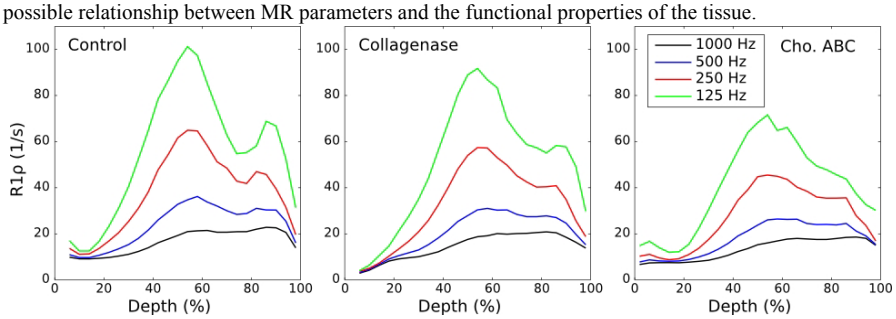

Figure 2. Average depth-wise $R_{1\rho}$ profiles for different spin-lock fields and treatments.

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