Assessment of Human Articular Cartilage Using Novel Quantitative MRI Relaxation Parameters with Correlation to Histology and Biomechanical Properties

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TARGET AUDIENCE

Osteoarthritis (OA) researchers focusing on articular cartilage.

PURPOSE

The study was performed to evaluate the sensitivity of quantitative MRI techniques (T1, T1Gd, T2, continous wave (CW) T1ρ, adiabatic T1ρ, adiabatic T2ρ, relaxation along a fictious field (RAFF) and magnetization transfer (MT)) for assessment of human tibial articular cartilage with varying degrees of degeneration. For reference, biomechanical measurements and quantitative histology methods were used.

METHODS

Osteochondral samples (n = 28) of 6 mm in diameter from tibial plateau were obtained from total knee replacement patients. The experiments were approved by the local ethics committee. MRI was performed at 9.4 T (Oxford instruments Plc, Witney, UK) with a 19-mm quadrature RF volume transceiver (RAPID Biomedical GmbH, Rimpar, Germany) and Varian DirectDrive console (Varian Inc. Palo Alto, CA, USA). Prior to imaging, the specimens were thawed, placed inside a Teflon test tube and immersed in perfluoropolyether with the cartilage surfaces perpendicular to the main magnetic field B_0. A magnetization preparation (MP) block was modified for measurement of adiabatic T1ρ (γB_{1max} = 2.5 kHz), adiabatic T2ρ (γB_{1max} = 2.5 kHz), CW-T1ρ dispersion with spin-lock powers γB_1 = 125, 250, 500 and 1000 Hz, RAFF and T1 during saturation (T1sat) at +10 kHz off-resonance (MT experiment). The MP block was followed by a fast spin echo (FSE) readout (TR = 5 s, ETL = 4, TE_{eff} = 5 ms, 256x128 matrix size, slice thickness 1 mm, FOV of 16 x 16 mm^2, 62.5 µm depth-wise resolution). T2 was measured with both spin echo and adiabatic double echo (DE) techniques. T1 mapping was performed before and after 24 hours immersion in 1 mM Gd-DTPA^{2-} (T1Gd) with saturation recovery FSE sequence.

Biomechanical properties of the cartilage were measured using indentation testing[1] with a plane-ended intender (1 mm diameter). Equilibrium modulus was measured using a step-wise stress-relaxation test (4x5 % of cartilage thickness step), and the dynamic modulus was determined from 1 Hz sinusoidal loading test. Finally, the samples were evaluated histologically. The histological sections were stained with Safranin-O (proteoglycans, PG) and graded by three observers according to the Osteoarthritis Research Society International (OARSI) grading system[2] (scale 0-6, with 0 = healthy cartilage). PG content and collagen fibril anisotropy were quantified with digital densitometry and polarized light microscopy from Safranin-O and unstained sections, respectively. Furthermore, the water content of the cartilage was determined from the samples as the ratio of dry and wet weights.

Due to partial or full-thickness loss of cartilage, only 14 samples with complete datasets with all of the measurements were done and included in the analysis. In MRI relaxation time maps, cartilage was divided to three layers (ROIs): tangential (5 % depth), transitional (20%) and radial (75%) for calculation of mean and standard deviation (STD) of values. A full-thickness cartilage ROI was also included in the analysis. The specimens were divided into two groups based on OARSI grade; early OA (grade <1.5, n = 5) and advanced OA group (grade > 1.5, n = 9).[3] Pearson correlation analysis between full-thickness values of MRI parameters and reference methods was performed. Statistical differences in the MRI parameters were investigated with the Mann-Whitney U test.

RESULTS

The OARSI grades of the samples varied from 0.9 to 4.1 (average values). All MRI parameters, except T1Gd, showed a statistically significant difference between early and advanced OA groups in tangential and full-thickness ROI (CW-T1ρ, γB_1 = 1 kHz only in tangential) (Fig 1). In transitional ROI, the differences in adiabatic T1ρ, T2ρ, CW-T1ρ (500 Hz), T1 and T1sat were statistically significant. T1Gd did not show a significant difference between the groups. CW-T1ρ showed significant dispersion in all ROIs. OARSI grade showed the highest correlation with adiabatic T1ρ, T2ρ, T1sat and RAFF (Table 1). PG content correlated moderately with adiabatic T1ρ, T2ρ and T1sat, while collagen anisotropy correlated significantly with DE-T2 and CW-T1ρ at lowest spin-lock field. At higher spin-lock fields, except 1 kHz, CW-T1ρ correlated significantly with PG content. Furthermore, a moderate correlation was found between water content and adiabatic T1ρ, CW-T1ρ and T1sat parameters. Correlations with biomechanical parameters were high or moderate for most MR parameters, while T1Gd did not show a significant correlation.

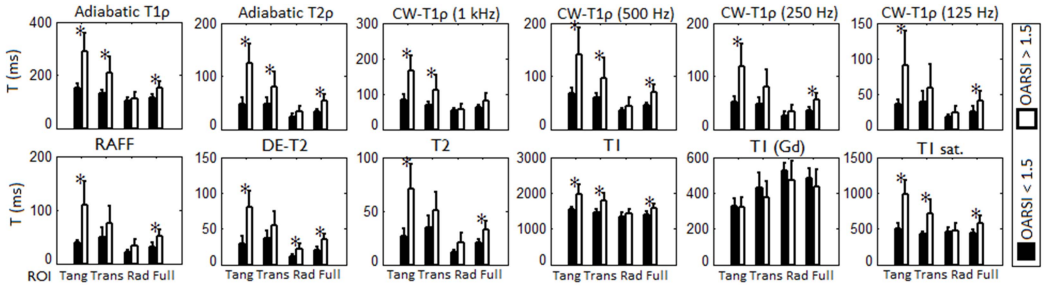

Figure 2. Mean±STD values of MRI parameters in tangential, transitional, radial and full-thickness ROIs (bars left to right) of cartilage for early OA (OARSI < 1.5) and advanced OA (OARSI > 1.5) groups. *p<0.05 between the groups

Table 1. *Pearson correlation coefficients between the MRI parameters (full-thickness ROI) and equilibrium moduli (E(eq), dynamic moduli (E(dyn), water content, optical density (OD, measure of PG content), collagen anisotropy and OARSI grade.*p<0.05 **p<0.01*

Parameter (n = 14)	E(eq)	E(dyn)	Water content (%)	OD	Collagen anisotropy	OARSI
Adiabatic T1ρ	-0.800**	-0.778**	0.615*	-0.585*	-0.241	0.806**
Adiabatic T2ρ	-0.816**	-0.707**	0.515	-0.608*	-0.378	0.852**
CW-T1ρ, γB_1 = 1.0 kHz	-0.642*	-0.675**	0.659*	-0.320	-0.295	0.630*
CW-T1ρ, γB_1 = 500 Hz	-0.807**	-0.763**	0.602*	-0.602*	-0.281	0.777**
CW-T1ρ, γB_1 = 250 Hz	-0.801**	-0.719**	0.593*	-0.593*	-0.322	0.802**
CW-T1ρ, γB_1 = 125 Hz	-0.672**	-0.621*	0.477	-0.344	-0.540*	0.683**
RAFF	-0.740**	-0.592*	0.402	-0.495	-0.394	0.735**
DE-T2	-0.727**	-0.568*	0.472	-0.324	-0.542*	0.692**
T2	-0.648*	-0.493	0.308	-0.241	-0.523	0.588*
T1	-0.710**	-0.684**	0.445	-0.339	-0.274	0.641*
T1Gd	0.477	0.518	-0.462	0.448	-0.087	-0.399
T1sat	-0.757**	-0.806**	0.573*	-0.532*	-0.316	0.802**

DISCUSSION

According to the present results most MRI parameters were able to differentiate between early and advanced OA. Furthermore, rotating frame methods adiabatic T1ρ, adiabatic T2ρ, CW-T1ρ and RAFF and MT experiment (T1sat) correlated highly with biomechanical parameters and the OARSI grade, suggesting increased sensitivity of the methods for cartilage degeneration. CW-T1ρ dispersion was observed and the technique showed features of laminar structure of cartilage at lowest field (125 Hz), which correlated significantly with collagen anisotropy. Since these ex vivo results are very promising for the rotating frame methods, an in vivo validation is warranted in the future.

CONCLUSION

The degree of degeneration in human articular cartilage, as determined by OARSI grading was sensitively detected with advanced MRI techniques, especially with rotating frame relaxation parameters.

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