Multi-parametric MRI assessment of degeneration of human articular cartilage – association to histopathological grade

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TARGET AUDIENCE

Scientists and clinicians aiming to apply quantitative MRI techniques for assessing cartilage.

PURPOSE

The purpose of this study was to evaluate the sensitivity of both established (T_1, T_{1Gd}, T_2, magnetization transfer ratio MTR and continuous-wave (CW) $T_{1\rho}$) and novel (adiabatic $T_{1\rho}$ and $T_{2\rho}$, T_{RAFF} and T_1 in the presence of saturation (T_{1sat})) MR parameters to cartilage degeneration in human articular cartilage during osteoarthritis (OA). The degree of degeneration was assessed histopathologically using the Osteoarthritis Research Society International (OARSI) grading system[1].

METHODS

Osteochondral samples (d = 6 mm, N = 19) were harvested from the tibial plateaus of patients undergoing total knee arthroplasty with permission from the local ethical committee. The MR experiments were performed at 9.4 T with a 19-mm quadrature RF transceiver and Varian DirectDrive console. The experiments consisted of a global magnetization preparation block coupled to a fast spin echo (FSE) readout (ETL = 4, TR = 5 s, TE_{eff} = 5 ms, slice thickness 1 mm, resolution along cartilage depth 62.5 µm). The preparation block was modified to measure T_2, CW $T_{1\rho}$ (with locking field γB_1 = 1 kHz), adiabatic $T_{1\rho}$ and $T_{2\rho}$, T_{RAFF}, T_{1sat} and MTR (at +10 kHz off-resonance)[2]. T_1 was measured by varying the TR of the readout sequence in 7 steps. T_1 measurements were conducted initially and after 24 hour immersion in 1 mM Gd-$DTPA^{2-}$ (T_{1Gd}). After the MR experiments, the samples were processed for histology. Three Safranin-O stained slices per sample were graded by three individual observers according to the OARSI grading system with sub-grades [1], and the mean of these evaluations was taken as the final OARSI grade of the sample. *Data analysis:* The samples were divided into two groups based on the OARSI grade: normal/mild OA (OARSI grade ≤ 1.5, N = 5) and advanced OA (OARSI grade > 1.5, N = 14)[3]. Two ROIs were selected from MRI data: a superficial ROI covering the most superficial 25 % of the tissue and a full-thickness ROI covering the entire cartilage. To compare the ability of various MR parameters to differentiate the two groups, receiver operating characteristics (ROC) analysis was performed and areas under ROC curves (AUC) were determined. Spearman's rank correlation coefficients were determined between MR parameters and OARSI grade in the full-thickness ROI.

Table 1. ROC AUCs for MR parameters and Spearman's rank correlation coefficients (ρ) between OARSI grade and MR parameters for superficial and full-thickness ROIs. All AUC values were significantly ($p < 0.05$) greater than 0.5, except for MTR in both ROIs.

Param. / ROI	AUC		ρ (w/OARSI grade)
	Sup.	Full	Full
T_1	0.857	0.829	0.498 (p = 0.030)
T_{1Gd}	0.943	0.871	-0.680 (p = 0.001)
T_2	0.829	0.829	0.443 (p = 0.057)
CW $T_{1\rho}$	0.786	0.743	0.419 (p = 0.074)
Adiab. $T_{1\rho}$	0.871	0.871	0.569 (p = 0.011)
Adiab. $T_{2\rho}$	0.871	0.871	0.556 (p = 0.013)
T_{RAFF}	1.000	1.000	0.653 (p = 0.002)
T_{1sat}	0.857	0.829	0.572 (p = 0.010)
MTR	0.543	0.521	-0.158 (p = 0.519)

RESULTS

All MR parameters except for CW $T_{1\rho}$ and MTR exhibited statistically significant differences between the two sample groups in both superficial and full-thickness ROI (Fig. 1). ROC analysis showed that apart from MTR, all parameters sensitively detected the different degrees of degeneration, with T_{RAFF} and T_{1Gd} being the most sensitive (Table 1). The mean OARSI grades were 1.34±0.26 in normal/mild OA and 3.78±1.50 in advanced OA groups (statistically significant difference with $p < 0.001$, Mann-Whitney U test). Moderate but significant correlation to OARSI grade was observed with T_1, T_{1Gd}, adiabatic $T_{1\rho}$ and $T_{2\rho}$, T_{RAFF} and T_{1sat} (Table 1).

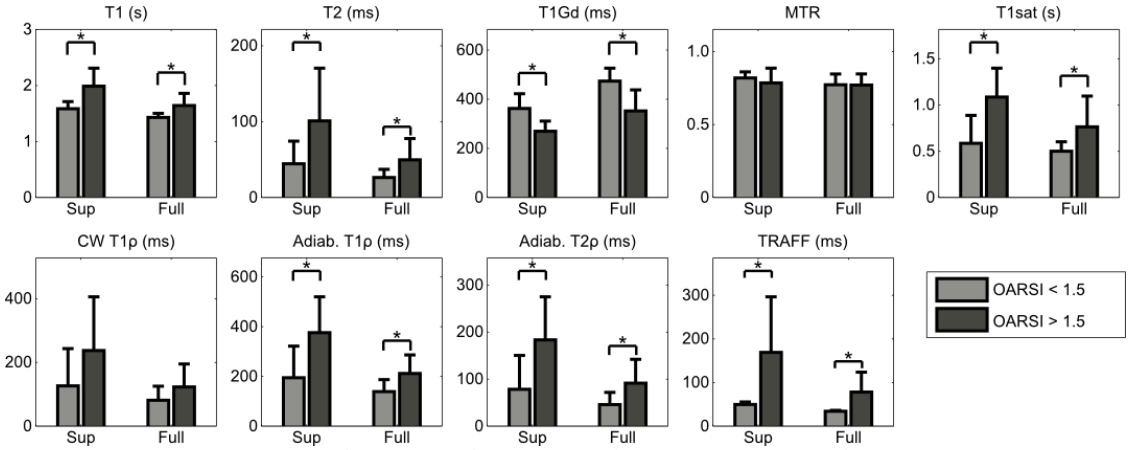

Fig. 1. Average MR parameter values from the superficial (Sup) and full-thickness (Full) ROIs for the normal/mild OA (OARSI grade ≤ 1.5) and advanced OA (OARSI grade > 1.5) groups (*p<0.05, Mann-Whitney U test).

DISCUSSION

Most MR parameters investigated were able to sensitively detect the differences between the normal/mild OA group and advanced OA. Particularly the endogenous contrasts, T_1, T_{1sat}, T_{RAFF} and adiabatic $T_{1\rho}$ and $T_{2\rho}$, seemed to be sensitive to OA changes. This is also evident in the relationships between OARSI grade and MR parameters where statistically significant correlations were observed. The sensitivity of these parameters to the changes in tissue structure and composition during OA are possibly due to the increased sensitivity to slow molecular motion. Of the more established MR techniques, T_2 performed nearly as well as the aforementioned MR parameters, whereas CW $T_{1\rho}$ did not show any significant changes between the two sample groups. However, there was a trend toward increased CW $T_{1\rho}$ in the advanced OA group, consistently with the other techniques. The dGEMRIC index, T_{1Gd}, is extremely sensitive to cartilage degeneration and correlates well with the OARSI grade. However, it must be noted that the presently used protocol of 24 h immersion in contrast agent is limited to experimental settings.

CONCLUSIONS

Novel MR parameters can sensitively detect different degrees of degeneration in human cartilage. Further studies are warranted to investigate the sensitivity of these MR parameters to tissue structure and constituents.

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