Multi-parametric MRI assessment of articular cartilage degeneration

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INTRODUCTION

Various MRI biomarkers have been proposed for the quantitative assessment of articular cartilage, among them T_2 relaxation time (sensitive to the properties of the collagen network) [1] and delayed contrast-enhanced MRI of cartilage (dGEMRIC-technique, related to the GAG content) [2]. Furthermore, $T_{1\rho}$ [3] and magnetization transfer (MT) techniques [4] have been applied in the characterization of cartilage tissue. However, the sensitivity and specificity of these MR parameters for different cartilage constituents have not been systematically evaluated. This study aims at a comprehensive multi-parametric characterization of articular cartilage in two constituent-specific enzymatic degradation models as well as using human cartilage with varying degrees of degeneration. To that end, we utilized a range of established MR techniques (T_2, dGEMRIC and continuous-wave (CW) spin-lock $T_{1\rho}$ relaxation mapping and the measurement of magnetization transfer ratio (MTR)) as well as an array of novel rotating-frame techniques (adiabatic $T_{1\rho}$ and $T_{2\rho}$ [5] and Relaxation Along a Fictitious Field (RAFF) [6]) to study the degenerative changes in articular cartilage.

METHODS

For the first part of the experiment, cartilage-bone blocks (~ 4 x 4 mm^2 surface, N = 4) were harvested from visually intact bovine patellae (N = 2). Subsequently, two of the samples were digested for 44 h, one using collagenase and the other using chondroitinase ABC to induce specific collagen or GAG depletion, respectively. For the second part, cartilage-bone plugs (d = 6 mm, N = 2) were harvested from tibial plateaus of patients undergoing joint replacement surgery with permission from the local authority. According to histological evaluation (data not shown), one human specimen was degenerated, while the other appeared intact. 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 DirectDrive console (Varian Inc. Palo Alto, CA, USA). 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, imaging matrix = 256x128, slice thickness 1 mm, FOV = 19.2 x 19.2 mm^2). The preparation block consisted of: **a)** 7 s irradiation pulse at γB_1 = 100 Hz, +6 kHz (M_{sat}) and -100 kHz offset (M_0) from water frequency (MTR); **b)** a continuous-wave spin-lock pulse with γB_1 of 425 Hz and 4 durations between 10-100 ms (CW- $T_{1\rho}$); **c)** a train (number of pulses 0, 4, 8, 12, 24) of 4.5 ms adiabatic full-passage (AFP) pulses with $\gamma B_{1,max}$ of 2.5 kHz ($adiabatic\ T_{1\rho}$); **d)** a train (number of pulses 0, 4, 8, 12, 24) of AFP pulses embedded between adiabatic half-passage (AHP) pulses ($adiabatic\ T_{2\rho}$); **e)** a spin echo preparation with 6 TEs from 3.2-100 ms (T_2); and **f)** an optimized RAFF preparation block described in [7]. Finally T_1 relaxation time was measured using saturation recovery FSE sequence with 7 TR steps from 80 to 5120 ms. After the first measurements, the samples were immersed in 1 mM Gd-DTPA^{2-} for 24 hours followed by post-contrast T_1 measurement (T_{1Gd} or the dGEMRIC index) using the same FSE sequence. For further analysis, a ROI from superficial cartilage was selected based on the T_2 appearance. MTR was defined as M_{sat}/M_0. To assess the effect of degeneration, ratios of the relaxation times between degraded and intact tissue were determined in the selected ROI.

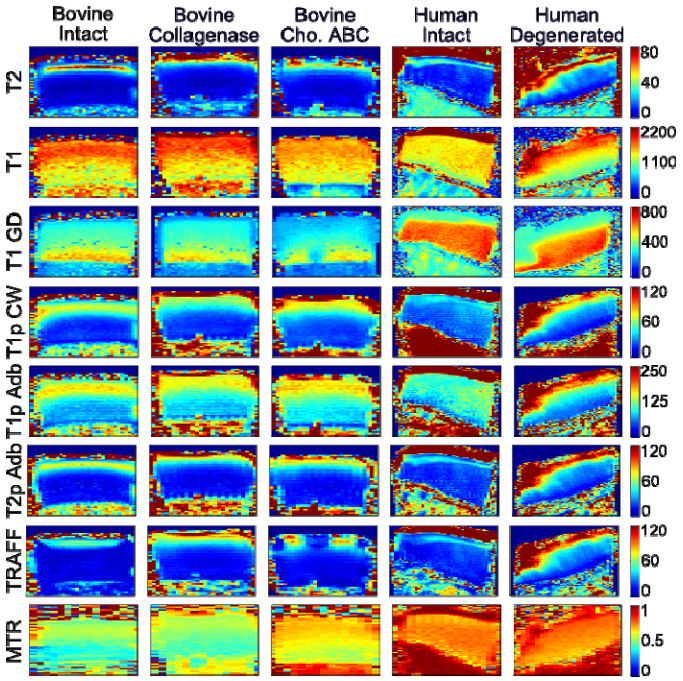

Fig. 1. Representative relaxation time (ms) maps of a pair of intact and collagenase-treated samples, a chondroitinase ABC-treated sample and intact and degenerated human samples.

RESULTS AND DISCUSSION

In intact samples (both bovine and human), a laminar appearance was observed in T_2, $T_{2\rho}$ and RAFF relaxation time (T_{RAFF}) maps (Fig. 1), suggesting sensitivity of these parameters to the properties of the collagen network. In degraded and degenerated tissue, irrespective of the treatment, superficial T_2, $T_{2\rho}$ and T_{RAFF} were elevated. Other parameters exhibited less complex depth-wise appearance; however, T_1, CW-$T_{1\rho}$ and adiabatic $T_{1\rho}$ were higher in superficial cartilage of all specimen types, possibly due to the lower macromolecular content and higher water content in this part of the tissue. In collagenase-digested bovine and degraded human cartilage T_2 was markedly elevated in the superficial ROI (Fig. 2), supporting the hypothesis on sensitivity for changes in the collagen network. In addition to T_2, also T_{RAFF} and CW-$T_{1\rho}$ were elevated in collagenase-digested tissue as well as in degenerated human tissue (Fig. 2). CW-$T_{1\rho}$ was the most sensitive contrast to GAG depletion (108 %). The dGEMRIC index appeared lowered in the chondroitinase ABC-treated tissue, but the change remained small (24 %) compared to the change noted in CW-$T_{1\rho}$ (108 %) and T_2 (67 %). Change in MTR in the superficial cartilage remained low. Although the human cartilage samples from different patients may not be directly comparable, the observed difference between visually intact and degenerated samples illustrates the range of the relaxation parameters. In conclusion, these preliminary results show that there are marked differences in the sensitivity of the various MRI parameters to specific tissue constituents. Novel rotating-frame techniques may sensitively detect changes in the status of cartilage.

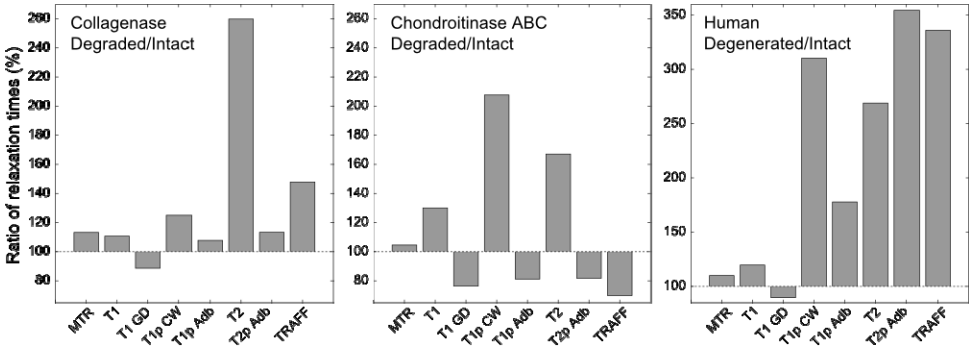

Fig. 2. Relaxation time ratios between degraded and intact tissue in superficial zone.

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