Quantitative MRI of parallel changes of articular cartilage and trabecular bone

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INTRODUCTION

Quantitative MRI methods have been introduced to evaluate the status of articular cartilage and trabecular bone. T_2 and dGEMRIC are able to predict the mechanical properties of cartilage [1], while T_2* relaxation time and MRI derived structural parameters are related to bone mineral density (BMD) and strength [2]. Typically, bone and cartilage are investigated separately but the interrelations of the MRI variables of bone and cartilage are rarely studied. The objective of the present study was to determine the relationship between quantitative MRI variables of bone and cartilage obtained at 1.5T in reference to histological and mechanical properties and pQCT measurements of BMD in normal and degenerated human patellae.

METHODS

Intact patellae of human cadavers (N=14, age 55±18 years) were equilibrated overnight in 0.5mM Gd-DTPA$^{(2-)}$ solution. It has previously been shown that low contrast agent concentration has a minimal effect on T2 relaxation time of cartilage [3]. Six locations were defined to cover the entire articular surface of each patella. For MRI measurements, a clinical 1.5T scanner and a 3" receiving coil were used (GE Healthcare, Milwaukee, WI). The articular surface was oriented parallel to B_0 field to emulate clinical patient positioning. T_2 maps of cartilage were calculated from multi-slice multi-echo spin echo experiments (GE prototype sequence with improved slice profile, TR=1000ms, TE=10.3-82.4ms, ETL=8, 3-mm slice thickness, 0.313mm pixel size, room temperature). dGEMRIC maps were obtained from single-slice inversion recovery fast spin echo experiments (TR=1700ms, TE=11ms, TI=50-1600ms, ETL=6). dGEMRIC and T2 values from the most superficial 1 mm of each region (width 3 mm) were averaged to characterize the superficial tissue. T_2* maps of trabecular bone were calculated from multi-slice gradient echo experiments (TR=100ms, TE=4.7-28ms, flip angle=30°), and bulk T_2* values of a 7x7mm region of interest (ROI), localized into the trabecular bone beneath the sites of cartilage MRI, were calculated.

Full-thickness cartilage disks (dia.= 4 mm) without subchondral bone were prepared and equilibrated in phosphate buffered saline solution to wash out the contrast agent. Stress-relaxation tests in unconfined geometry were conducted to determine the Young's modulus (E_s) from the equilibrium response [4]. Blind-coded safranin-O –stained histological sections of cartilage were graded for degeneration using a modified Mankin score system [5] independently by three of the authors. To test the influence of cartilage degeneration on the interrelationships between cartilage and bone parameters, samples were divided into two groups according to their Mankin score (normal/minimal degeneration (MS<4), advanced degeneration (MS≥4)).

Bone mineral density (BMD) was measured by using a clinical peripheral quantitative computed tomography scanner (pQCT, 58kV, 0.175mA, in-plane resolution 0.200mm, 0.5-mm slice thickness; XCT2000, Stratec, Birkenfeld, Germany). For mechanical testing of trabecular bone, cylindrical samples (dia.=7mm, thickness = 7mm) were isolated from the sites of MRI and pQCT analyses, and tested destructively (Instron FastTrack 8874, Instron, Norwood, MA, USA). Yield stress (σ_y) and maximum compressive stress (ultimate strength, σ_u) were calculated from the stress-strain curve [6]. Bone volume fraction (BV/TV_{REF}) was calculated from unstained microscopic sections for samples too short for mechanical testing (N=24).

RESULTS

Significant differences were observed in T_2, E_s, BMD, σ_u and σ_y between the groups with normal/minimal degeneration and advanced degeneration ($p < 0.05$, Kruskal-Wallis test). The linear correlation coefficients were calculated for the group with Mankin score < 4 and for all samples (Table 1). dGEMRIC correlated significantly with several bone parameters when the samples with Mankin score < 4 were evaluated. T_2 of cartilage did not correlate significantly with bone variables, and the linear correlation with E_s was higher when all samples were included. Most of the correlation coefficients were higher when the sample group of normal/minimal degeneration was considered separately. The difference of the correlation coefficients was significant ($p < 0.05$) between dGEMRIC and BMD, E_s and T_2*, E_s and BMD and between T_2* and BV/TV ($p < 0.05$, standard Fisher Z-score test).

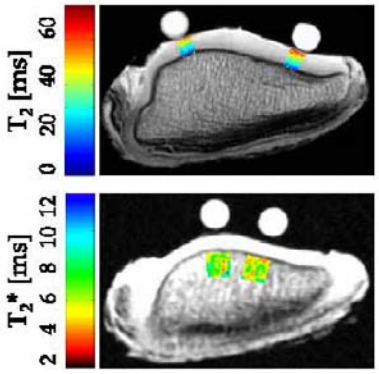

Figure 1. The localization of regions of interest for representative bone and cartilage samples. Only the most superficial 1 mm of cartilage was analyzed.

DISCUSSION

The present results demonstrate significant relationships between the properties of articular cartilage and trabecular bone. Significant changes in these relationships are induced in the course of tissue degeneration, suggesting that the degenerative processes of bone and cartilage components advance at different rates. Previously significant, degeneration dependent variation has been independently established for MRI, structural and mechanical parameters of cartilage [7] and structural parameters of trabecular bone [8]. The present results suggest a more significant relationship between cartilage and bone changes at early stages of OA. Further, different techniques may be required to reveal parallel changes at different stages of tissue degeneration. The degeneration of joint tissue is a complex process where several components are involved and interacting. The exact timeline of degenerative processes in joints remains open, and quantitative MRI techniques may provide powerful tools to address this process non-invasively.

Table 1. The linear correlation coefficients calculated for the samples with Mankin score < 4 and for all samples and p-values of the statistical differences in correlation coefficients between these two groups. Only the comparisons with significant correlations are shown.

	MS < 4	all samples	p-value
dGEMRIC vs. T_2*	0.48**	0.32**	0.38
dGEMRIC vs. BMD	-0.66**	-0.32**	0.04
dGEMRIC vs. σ_u	-0.47*	-0.23	0.34
dGEMRIC vs. σ_y	-0.46*	-0.23	0.36
dGEMRIC vs. BV/TV	-0.82*	-0.14	0.10
E_s vs. T_2*	0.70**	0.39**	0.04
E_s vs. BMD	-0.47*	-0.02	0.03
dGEMRIC vs. E_s	0.38*	0.30**	0.68
T_2 vs. E_s	-0.24	-0.54**	0.11
T_2* vs. BMD	-0.56**	-0.31**	0.15
T_2* vs. BV/TV	-0.86*	0.09	0.05
BMD vs. BV/TV	0.91*	0.58**	0.16

statistical significance for correlation coefficients:
** $p < 0.01$; * $p < 0.05$

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