Longitudinal Changes in the Heterogeneity of Cartilage T_2 in Osteoarthritis Subjects

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Introduction

Quantitative T_2 relaxation time has been used as a non-invasive marker of cartilage degeneration, as it is sensitive to tissue hydration and biochemical composition. In early cartilage degeneration, changes in the extracellular matrix (e.g. disorganization and breakdown of the collagen network) increase the mobility of water, thus increasing T_2 relaxation time. Previous studies have demonstrated elevated T_2 relaxation time in osteoarthritis (OA) subjects as compared to healthy subjects (1), and have found spatial variations in T_2 values from the radial zone to the articular cartilage surface (2). Dray et al. (3) found no difference between mean T_2 values in OA cartilage; however, they showed visual differences in the spatial distribution of the T_2 values. These results demonstrate the necessity to characterize and quantify the spatial distribution of cartilage T_2 values.

Texture analysis, a method developed by Haralick et al. (4), can be used to examine the spatial distribution of pixel values in an image. This method has been used to analyze trabecular bone structure (5) and Alzheimer's disease (6). Texture analysis supplements standard measures of cartilage T_2 (such as mean and standard deviation), by providing information on the variation between neighboring pixels. This method involves calculating a co-occurrence matrix, which determines the frequency that neighboring grey-level values occur in an image. Analysis can be performed at a defined orientation (e.g. 0°, 90°) and a defined spacing (e.g. spacing = 1 for nearest-neighbor pixels). Texture parameters such as angular second moment (ASM) and entropy are calculated from the co-occurrence matrix. ASM is a measure of homogeneity of an image, and entropy is a measure of disorder in an image. The purpose of this study is to examine the changes in spatial heterogeneity of cartilage T_2 in OA patients and healthy subjects using second order texture measures over 9 months.

Methods

Magnetic resonance (MR) imaging was performed at 3 T on 8 female OA patients (Kellgren Lawrence grade 2-3, BMI > 30) and 8 age-matched female controls (Kellgren Lawrence grade 0, BMI < 30) at two time points separated by 9 months. High-resolution, fat-suppressed, 3D SPGR sagittal MR images (TE = 7.5 ms, TR = 20 ms, resolution = .29 x .29 x 1.5 mm^3, FOV = 15 cm) were acquired for assessing cartilage morphology, and 2D dual echo FSE sagittal images (TE_1/TE_2 = 8.5/34.1 ms, TR = 3600 ms, resolution = .62 x .62 x 3 mm^3, FOV = 16 cm) were acquired for measuring cartilage T_2 relaxation time. Articular cartilage was segmented from the SPGR images using a spline-based, semi-automatic technique and was defined in five regions: medial and lateral tibia, and medial and lateral femur, and trochlea. The segmented regions of interest were superimposed on the T_2 maps. A grey level co-occurrence matrix was defined for each cartilage region and used for texture analysis. Second order texture measures including entropy and angular second moment (ASM), were calculated at 0° (corresponding to the anterior-posterior axis) and at 90° (corresponding to the superior-inferior axis), with pixel offsets ranging from 1-3 pixels. At baseline, differences in texture measures between the OA patients and controls were assessed by unpaired *t* tests. Differences in texture measures from baseline to 9 months were assessed using paired *t* tests.

Results

At baseline, the ASM (0° and 90°, 1-3 pixel offsets) of cartilage T_2 was greater in control subjects than in OA patients in all compartments ($p < 0.05$ in ASM (0°, 1 pixel)). The entropy (0° and 90°, 1-3 pixel offsets) of cartilage T_2 was lower in control subjects than in OA patients in all compartments ($p < 0.05$ in entropy (0°, 1-3 pixel offsets). The longitudinal data shows increases in the ASM of cartilage T_2 in OA patients (Figure 1), and decreases in the entropy of cartilage T_2 in OA patients in all cartilage compartments (Table 1). A trend was shown ($p < 0.10$) for ASM (0° and 90°, 1 pixel offset) and entropy (90°, 1 pixel offset), and significance ($p < 0.05$) was reached for entropy (0°, 1 pixel offset). There was no significant difference from 0 to 9 months in entropy or ASM in control subjects. The entropy was greater in the OA patients compared to control subjects at both time points.

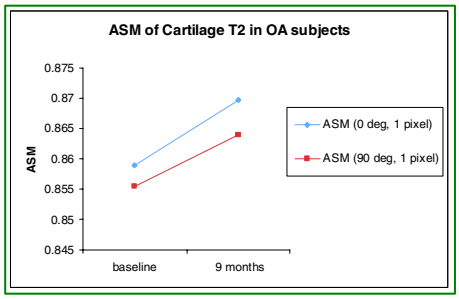

Figure 1: Increased ($p < 0.10$) cartilage T_2 ASM was evident in OA patients from 0 to 9 months.

	Baseline Entropy (0°, 1 pix)	9 Months Entropy (0°, 1 pix)	P value
OA	0.222	0.206	0.05
Control	0.188	0.194	0.44

Table 1: Differences in cartilage T_2 entropy from 0 to 9 months were evident in OA patients and controls. A significant decrease in entropy was evident in OA subjects, but not in controls.

Discussion

Overall, at baseline, cartilage T_2 entropy was elevated, and ASM was decreased in OA patients compared to controls. Longitudinally, the entropy of cartilage T_2 decreased, and the ASM of cartilage T_2 increased in OA patients. These results demonstrate that cartilage T_2 values are more heterogeneous in OA patients than in controls at baseline. Over 9 months, the heterogeneity of cartilage T_2 decreased in OA subjects, and did not change significantly in control subjects. These longitudinal changes may be affected by disease progression and changes in cartilage hydration. The evolution of cartilage T_2 heterogeneity may be affected by disease severity, as well as the time-period investigated. The limitations of this pilot study include a limited number of subjects and the use of two echo times in the T_2 mapping sequence. Additional echo times may increase the accuracy of cartilage T_2 quantification and texture analysis. Overall, this study demonstrates that textures measures of cartilage T_2 are different in OA subjects and controls, and may reflect the evolution of OA. The T_2 quantification sequence selected, the number of echoes, the fitting routine, and the impact of noise are all factors that may affect the calculation of texture parameters. Further long-term studies on the changes in cartilage T_2 heterogeneity at different angular orientations, time points, and disease stages are warranted.

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