

# The Relationship Between the Spatial Distribution of Cartilage MR $T_2$ and Longitudinal Changes in Pain: Data from the Osteoarthritis Initiative

G. Blumenkrantz<sup>1</sup>, J. Carballido-Gamio<sup>1</sup>, C. E. McCulloch<sup>2</sup>, J. A. Lynch<sup>2</sup>, T. M. Link<sup>1</sup>, and S. Majumdar<sup>1</sup>

<sup>1</sup>Department of Radiology and Biomedical Imaging, University of California, San Francisco, San Francisco, CA, United States, <sup>2</sup>Department of Epidemiology and Biostatistics, University of California, San Francisco, San Francisco, CA, United States

## Introduction

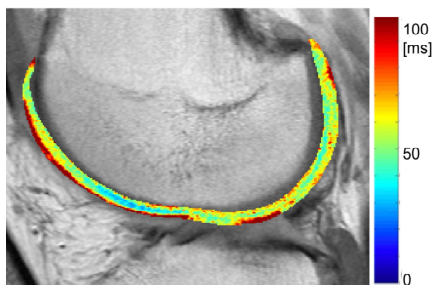
The Osteoarthritis Initiative (OAI) is a multi-center, longitudinal study aimed at assessing biomarkers in osteoarthritis (OA) including those derived from magnetic resonance (MR) imaging. The MR images from the OAI can be used to quantify cartilage parameters such as thickness and  $T_2$  relaxation time. Cartilage  $T_2$  relaxation time is sensitive to biochemical composition, collagen damage, and tissue hydration, and may therefore be an important marker for cartilage degeneration. The purpose of this study is to [1] examine changes in MR knee cartilage parameters including thickness,  $T_2$ , and spatial distribution of cartilage  $T_2$  and [2] examine whether these baseline MR parameters predict change in knee pain.

## Methods

Thirteen subjects from the OAI with radiographic OA at baseline (mean age =  $55.7 \pm 10.6$  years, BMI =  $30.1 \pm 3.7$ , Kellgren-Lawrence grade = 2-3, right knee, progression cohort) were evaluated. Western Ontario and McMaster Universities (WOMAC) pain score was assessed in each patient at baseline, year 1, and year 2. MR images of the knee joint including sagittal 3D DESSwe (TR = 16.3 ms, TE = 4.7 ms, interpolated in-plane resolution =  $0.365 \times 0.365$  mm, slice thickness = 0.7 mm) and sagittal 2D MSME (TR = 2700 ms, TE<sub>1</sub>-TE<sub>7</sub> = 10-70 ms) images were analyzed. Articular cartilage was segmented from the DESSwe images in six regions: medial and lateral tibia, medial and lateral femur, trochlea, and patella, using a spline-based, semi-automatic technique. 3D cartilage thickness was calculated from the DESSwe segmentations. The 2D MSME images were used to generate  $T_2$  maps assuming mono-exponential signal decay (Figure 1). Using the MSME first echo and DESSwe to compute a rigid-body transformation,  $T_2$  maps were registered to the DESSwe images, and the segmented regions of interest were superimposed on the registered  $T_2$  maps. Median cartilage  $T_2$  was calculated in each region. Texture analysis, a method developed by Haralick et al. (1), was used to examine the spatial distribution of  $T_2$  relaxation times in an image. Texture analysis supplements standard measures of cartilage  $T_2$  (such as mean and standard deviation), by providing information on the spatial association of  $T_2$  values. Using this method, a grey level co-occurrence matrix (GLCM), which tabulates the frequency of co-occurrence of pairs of grey-level values of adjacent pixels in an image, was defined. Texture parameters including angular second moment (ASM), entropy, homogeneity, and contrast were calculated from the GLCM. Analysis was performed using a symmetric GLCM at different orientations ( $0^\circ$  - corresponding to the anterior-posterior axis,  $45^\circ$ ,  $90^\circ$  - corresponding to the superior-inferior axis,  $135^\circ$ ). GLCM-ASM and GLCM-entropy are measures of orderliness, while GLCM-homogeneity and GLCM-contrast are measures of contrast in an image. Statistical analysis was performed using JMP 7.0 software (SAS Institute, Cary, NC, USA). Cartilage parameters were averaged in all compartments except the lateral tibia based on their positive correlation, in order to reduce multiple testing issues. Mixed random effects approaches (treating the subject as a random effect) were used to model the annual rate-of-change in cartilage parameters and to test for an association of baseline cartilage parameters with change in WOMAC pain score over the two years of follow-up.

## Results

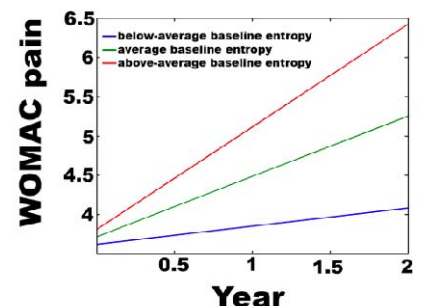
Longitudinal decreases in mean cartilage thickness were evident in all cartilage compartments over two years. The annual rate of cartilage loss was significant ( $p < 0.05$ , Table 1) in the lateral femur (-2.66% per year), lateral tibia (-1.41% per year), and medial tibia (-3.63% per year). The mean cartilage  $T_2$  showed little change over time, with exception of the lateral tibia, which decreased -4.00% annually ( $p < 0.05$ ). Texture analysis of cartilage  $T_2$  using GLCM showed longitudinal increases in mean contrast and entropy, and decreases in mean ASM and homogeneity. Entropy of cartilage  $T_2$  at baseline (all compartments combined except the lateral tibia) was associated with an increase in WOMAC pain score over 2 years ( $p < 0.05$ ). Figure 2 shows the fitted model of the effect of baseline entropy on WOMAC pain score over 2 years in three cases: average baseline entropy, above-average baseline entropy, and below-average baseline entropy. The model illustrates that patients with high entropy at baseline have a greater longitudinal rate-of-change in WOMAC pain score.



**Figure 1:** A representative  $T_2$  map overlaid on the first echo (TE = 10 ms) of the MSME sequence.

Compartment	Cartilage thickness	
	Annual % change	P value
Lateral femur	-2.66	0.007
Medial femur	-1.28	0.440
Lateral tibia	-1.41	0.049
Medial tibia	-3.63	0.009
Patella	-4.00	0.097
Trochlea	-1.71	0.442

**Table 1:** Annual percentage changes in cartilage thickness, calculated using data from baseline, 1-year and 2-year follow-up.



**Figure 2:** A model illustrating the effect of baseline entropy of cartilage  $T_2$  on changes in WOMAC pain over time.

## Discussion

In this study, OA patients from the progression cohort of the OAI exhibited a significant decrease in cartilage thickness over two years, demonstrating morphologic OA progression over time. Of all MR parameters evaluated (including cartilage thickness and mean  $T_2$ ), only the baseline entropy of cartilage  $T_2$  was significantly associated with longitudinal rate-of-change in pain. The results of this pilot study suggest that the cascade of events leading to pain in OA may encompass changes in the internal structure and organization of cartilage, as measured by the entropy of cartilage  $T_2$ . Further long-term studies investigating the relationship between spatial distribution of cartilage  $T_2$  and the onset of OA in the incidence cohort, are underway.

## Acknowledgements

This study was funded by NIH U01 AR055079.

We would like to acknowledge Dr. Ying Lu for his assistance with the statistical analysis.

## References

1. Haralick RM, Shanmugam K, Dinstein I. Textural Features for Image Classification. IEEE Transactions on Systems, Man, and Cybernetics 1973;SMC-3(6):610-618.