T2 texture change to articular cartilage over 6 months is associated with change to knee health and cartilage thickness over 2 years following ACL injury and reconstruction

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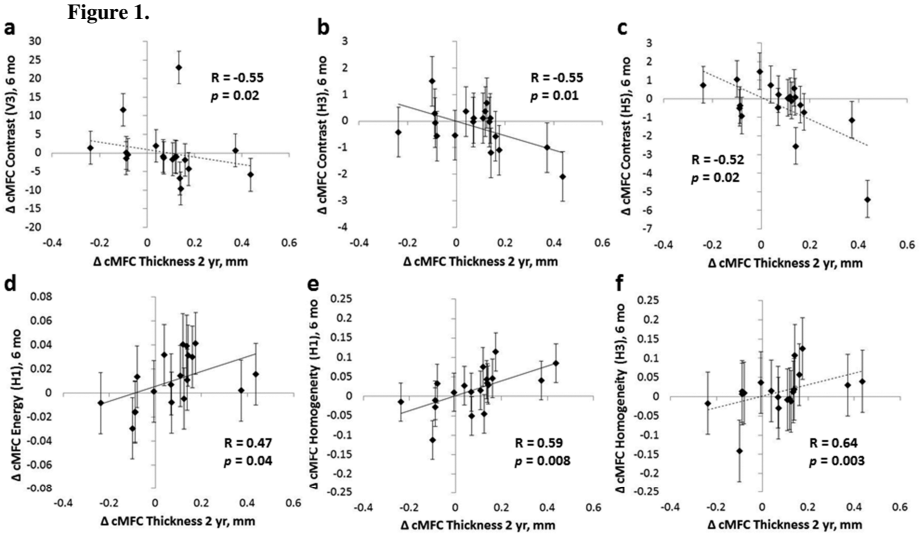
Introduction: Patients who suffer anterior cruciate ligament (ACL) tear and reconstruction experience a 19-fold increase in risk for cartilage loss to the medial femoral condyle 7-11 years following ligament reconstruction surgery[1] and are at heightened risk of developing osteoarthritis (OA). Clinically occult indications of future degeneration, including biochemical and histopathic characteristics of OA, may be present in cartilage as early as the time of ligament reconstruction[2,3]. Non-invasive clinical tools to detect early warning signs are essential for the timely introduction of targeted interventions after ACL reconstruction. Texture analysis of T2 maps permits assessment of the organizational and structural integrity of the cartilage collagen matrix and may detect changes to matrix architecture that can occur in OA[4,5]. Previous studies have established that T2 texture analysis can both discriminate patients with mild OA from controls[6] and predict which subjects at risk of OA will show symptomatic progression of the disease 3 years later[7]. This clinical study tests the hypotheses that textural changes to cartilage T2 maps measured over the first 6 months following ACL-reconstruction predict (1) changes to cartilage thickness, and (2) changes to knee health assessed from morphologic MRI measured over the first 2 years following ligament reconstruction.

Methods: Thirty human subjects, 19 undergoing surgery to reconstruct a torn ACL (ACLR) and 11 uninjured controls, participated in this IRB approved study. ACLR subjects underwent study protocol MR exam on a 3T scanner (MAGNETOM Trio, Siemens, Erlangen, Germany) at 3 time-points: within 24 days prior to, and 6-months and 2-years after ACL reconstruction. Controls were imaged once. T2 images were acquired using a 2-D multi-slice, multi-echo spin-echo (MSME-SE) sequence with 6 echo images, TEs ranging 20-88ms and TR= 2700ms. Effective resolution was 416x416µm in-plane, 3mm slice thickness. 3-D DESS (double-echo steady-state) images[8] were acquired at the preoperative and 2-year time-points on ACLR subjects. Test-retest MSME-SE sequences, collected as part of pilot OAI studies, were obtained for each of 5 control knees[9]. T2 maps were generated using MRIMapper software (© Beth Israel Deaconess and MIT 2006). Regions of interest (ROIs) were manually segmented from a single section to evaluate full-thickness cartilage in the central medial femoral condyle and central medial tibial plateau (cMFC, cMTP). Grey-level co-occurrence matrix (GLCM) image analysis was used to examine the spatial distribution of T2 values via second-order texture statistics[4-6,10]. Image texture analysis with GLCM statistics was performed on the calculated T2 maps using in-house developed software based on MATLAB's 'graycomatrix' and 'graycoprops' functions (The MathWorks, Natick, MA) as previously described[11]. Texture features were measured parallel (H) and perpendicular (V) to the bone-cartilage interface, at 1,3 and 5 pixel offsets. Root mean square (RMS) error was calculated from test-retest image sets as a measure of T2 texture repeatability. Morphologic study MRIs as well as preoperative, non-protocol clinical knee MRIs, when available (16/19), were independently interpreted by one expert musculoskeletal radiologist blinded to the T2 map data for the presence, location and size and/or severity of cartilage lesions, bone marrow edema-like lesions and joint effusion. Preoperative and 2-year follow-up DESS images were evaluated for thickness changes in the medial femoral condyle and tibial plateau cartilage plates (Chondrometrics GmbH, Ainring, Germany).

Results: Six of 20 T2 texture features assessed in femoral cartilage demonstrated changes over 6 months that correlated to cartilage thickness change over 2 years in the same region, Figure 1. Change to the T2 texture feature 'contrast' over 6 months in cMFC cartilage negatively correlated while changes to 'energy' and 'homogeneity' positively correlated to 2-yr thickness change. No correlations were found between mean T2 change over 6 months and thickness change over 2 years in cMFC cartilage (p=0.48), nor between any 6-mo tibial cartilage T2 texture feature or T2 mean change with cMTP thickness 2-yr change (p>0.31). RMS reproducibility errors for T2 texture analyses of 5 test-retest scan pairs of knees are displayed as error bars on the graphs in Figure 1.

Figure 1.



Six-month changes to T2 texture, but not T2 mean, were found to vary with change in knee health over 2 years. Improvement or worsening of "knee health" was determined by change in morphologic MRI-assessed knee structures: 8/19 ACLR subjects 'worsened', 6/19 improved, 5/19 were unchanged. Six-month changes to the 'energy' features in cMFC cartilage varied significantly with change to knee health, showing progressive increases with improving knee health over 2 years (ANOVA p=.002, .008, .05, .02; for V1,V3 and H1,H3, respectively). Six-month changes to cMFC mean T2 did not vary with 2-yr change to knee health (p=.68).

The number and magnitudes of textural differences between ALCR subjects and controls diminished over time (p<.03). At the pre-operative and 6-mo time-points, 10 T2 texture features differed between uninjured controls and ACLR subjects (p<.05, .05). At 2-yrs post-reconstruction, only 1 texture feature differed (p<.05). Mean T2 was elevated (10%) in medial femoral cartilage of ACLR subjects compared to controls at the pre-surgery time-point but dropped to levels not different from controls by 2 years after surgery (p>.14). In ACLR subjects, six-month changes T2 mean also correlated to 2-yr change in T2 mean (R=.58, p=.009).

Conclusions: In this observational study of 19 ACL-injured subjects over 2 years following ligament reconstruction, 6-mo change to T2 texture, but not T2 mean, was associated with 2-yr change to clinical MRI metrics of knee health including cartilage thickness and morphologic joint status. Textural and mean T2 differences observed between ACLR and control subjects at the time of ligament reconstruction resolved over the following 2 years. Although increases to cartilage thickness, elevations of T2 mean, and changes to T2 texture features, have previously been associated with OA[1,6,12] interpretation of these changes in the current cohort remains elusive. Since there was limited evidence of disease progression at 2 yrs post-reconstruction, with 11/19 (58%) subjects showing no change or improvement of knee health, it is possible that we are observing repair of cartilage matrix damage in some subjects.

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