Longitudinal clinical evaluation of cartilage and meniscus UTE-T2* following ACL reconstruction

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Introduction: ACL-injury is a well-known risk factor for meniscus degeneration, cartilage loss, and development of knee osteoarthritis^{1,2}. In ACL-injured knees, the strain due to weight-bearing, particularly at 30° of flexion, is concentrated in the posterior horn of the medial meniscus³. Ultrashort TE-enhanced T2* mapping (UTE-T2*) is sensitive to short T2* signals (T2 <10ms) that are found in meniscus and deep articular cartilage and has the potential to provide prognostic indication of otherwise clinically occult osteoarthritis (OA)^{4,5}. Previous cross-sectional UTE-T2* mapping studies of ACL-injured subjects without clinical evidence of subsurface cartilage or meniscus abnormality found significant elevations of UTE-T2* values in both meniscus and articular cartilage^{5,6}. The purpose of the current work is to use clinical UTE-T2* mapping to examine longitudinal change in 1) the posterior horns of intact menisci in ACL-injured knees, and 2) cartilage of the posterior femoral condyles, the region contacting the posterior horns of the menisci at 30° of knee flexion.

Methods: Twenty-six subjects participated in these studies: 10 asymptomatic subjects (5 female, 27±5 yrs; BMI 24±3) with no known or suspected knee pathology and 16 subjects with ACL injury (ACLT) requiring ACL reconstruction surgery (8 female, 29±10 yrs; BMI 27±6). All subjects provided informed consent for these IRB-approved studies. The injured knees of all ACLT subjects were scanned twice: prior to (pre-SX) and 12-months after ACL reconstruction surgery. The left knees of asymptomatics were scanned once. 3-D AWSOS (acquisition-weighted stack of spirals)⁷ images were acquired on all subjects using a 3T Siemens MAGNETOM Trio scanner and an 8-channel knee coil (In vivo Inc.). Eleven echo images, TE ranging 0.6-40ms were collected with 140mm FOV and 256 matrixes for 547µm resolution in-plane and 2mm section thickness. Other acquisition parameters were: 60 slices, 24 in-plane spirals, 11.52ms spiral readout time, 5µs data sampling interval, and FA/TR 30/80ms. Scan time was 1.92 min per TE-image. TE images were interpolated to a 512 matrix prior to T2-curve fitting. UTE-T2* maps were generated with a mono-exponential pixel-by-pixel T2-fit routine using MRIMapper software (© Beth Israel Deaconess and MIT 2006). Regions of interest (ROIs) were manually segmented from one section from the center of each condyle (1 medial, 1 lateral) to separately evaluate the superficial and deep portions of the articular cartilage in the posterior medial and lateral femoral condyle cartilage (pMFC, pLFC) and posterior medial and lateral horns of the menisci. Non-parametric statistical analyses, including Wilcosin Signed Rank Tests (WSRT), Mann-Whitney U Tests (MWUT), and paired Spearman's rho tests, were performed with IBM SPSS.

Results: Metal artifact from surgical hardware obscured the medial condylar cartilage in one ACLT subject's 12-month follow-up images. Among the other 15 ACLT subjects, UTE-T2* values from deep pMFC cartilage decreased by an average of 36% between pre-SX and follow-up imaging (mean±SD, 17.7±7.4 v.s. 11.3±4.4 ms, n=15, WSRT P=0.003, Figure 1). Although pre-SX deep UTE-T2* values in ACLT subjects were significantly elevated compared to asymptomatics (n=10, 11.8±2.5 ms; MWUT P=0.04), no difference in deep pMFC UTE-T2* values between ACLT and asymptomatic subjects remained at follow-up (MWUT P=0.39). Superficially, mean pMFC UTE-T2* values of ACLT subjects did not significantly change over 12-months (n=15, 33.7±5.1 v.s. 32.7±4.3 ms, WSRT P=0.65) and were not found to differ from comparable asymptomatics values (n=10, 32.3±3.1 ms) at either time-point (MWUT P=0.44, 0.89 for pre-SX, follow-up). When dichotomized by meniscus tear status, deep pMFC UTE-T2* values from subjects with concomitant medial meniscus tear (n=7) decreased 40% over the first year of recovery (18.9±8.7 v.s. 11.3±5.0 ms, WSRT P=0.03), while deep pMFC UTE-T2* values from subjects with intact menisci (n=8) did not change significantly (16.6±6.5 v.s. 11.4±4.1 ms, WSRT P=0.06). Sample pre-SX and follow-up MFC UTE-T2* maps are shown in Figure 2. Laterally, neither superficial nor deep UTE-T2* values in the pLFC region were found to differ between pre-SX and 12-month scans (n=16, P>0.5), nor were they found to differ from comparable UTE-T2* measures in asymptomatics at either time-point (MWUT P>0.69). Dichotomizing superficial and deep pLFC UTE-T2* values by lateral meniscus tear status also did not reveal any significant changes over time (WSRT P>0.5; P>0.4, respectively). The mean meniscus UTE-T2* value across all ACLT subjects with intact menisci (8 medial, 11 lateral) was elevated with respect to the mean asymptomatic (n=10) meniscus UTE-T2* value at both pre-SX and 12-month time-points (MWUT: pre-SX, P=0.01, 0.01; 12-month, P=0.02, 0.02, for medial, lateral). Considerable variation of meniscus UTE-T2* change was observed between ACLT subjects within each group. Among ACLT subjects with intact medial menisci at surgery, posteromedial meniscus UTE-T2* values increased in 3/8 subjects, decreased in 3/8, and 2/8 did not change. Among ACLT subjects with intact lateral menisci, the posterolateral meniscus UTE-T2* values increased in 4/11 subjects, decreased in 6/11, and 1/11 did not change. In ACLT subjects with intact medial menisci (n=8), changes in posteromedial meniscus UTE-T2* over 12 months significantly correlated to changes in the adjacent superficial pMFC articular cartilage UTE-T2* values (Spearman's rho = -0.713, 2-tailed P=0.05). Changes in posteromedial meniscus UTE-T2* were not found to correlate to changes in deep pMFC cartilage (P=0.38), nor were changes in posterolateral meniscus UTE-T2* correlated with changes to superficial or deep pLFC cartilage UTE-T2*.



Figure 1. (left) Longitudinal UTE-T2* evaluation of 15 ACLT subjects suggests that damage to deep posterior medial femoral condyle cartilage (pMFC) heals during the first 12 months following ACL reconstruction surgery. Deep articular cartilage UTE-T2* values fell 36% (P=0.003) over 12 months, bars are ± SEM.





down to levels observed in asymptomatic controls. Error bars are \pm SEM. **Figure 2. (above)** Sample UTE-T2* maps of an ACL-injured subject (a) pre-SX, and (b) 12 months after ACL reconstruction surgery. UTE-T2* values of deep pMFC articular cartilage decreased (white arrows) resulting in a laminar pattern similar to the pattern observed in asymptomatics.

Conclusions: Initial elevations followed by significant decreases of UTE-T2* values in deep pMFC articular cartilage of ACLT subjects (down to asymptomatic levels) suggest healing of the deep articular cartilage matrix over 12 months following ACL reconstruction surgery. By contrast, half of the subjects demonstrating elevated UTE-T2* values in intact menisci following ACL injury continued to show elevated or further increased meniscus UTE-T2* values at follow-up, demonstrating evidence of persistent subsurface meniscus degeneration a year after operative stabilization of the ACL-injured knee. UTE-T2* values in cartilage adjacent to intact menisci were not found to change significantly during the follow-up period, likely indicating that cartilage in knees with intact menisci were relatively spared from damaging impact at or after ACL-injury. Together these findings suggest that UTE-T2* provides a useful non-invasive tool to monitor cartilage and meniscal status in knees at risk of developing OA.

<u>References:</u> [1] Lohmander, AJSM, 2007; 35(10):1756. [2] Potter, AJSM, 2012;40:276. [3] Jiang, Indian J Orthop, 2012;46:514. [4] Du, MRI, 2011;29:470. [5] Williams, OAC, 2012;20(6):486. [6] Williams, ISMRM, #49, 2012. [7] Qian, MRM, 2008;60(1):135. <u>Acknowledgments:</u> NIH funded, RO1 AR052784 (CR Chu).