24-month longitudinal assessment of cartilage status in subjects at risk of developing OA: T_2 mapping following ACL tear & reconstruction surgery

Ashley Williams[1], and Constance R Chu[1]
[1]*Cartilage Restoration Center, University of Pittsburgh, Pittsburgh, PA, United States*

Introduction Anterior cruciate ligament tear (ACLT) is a known risk factor for osteoarthritis (OA) development[1,2]. Impact injury to deep cartilage sustained at the time of joint injury and secondary insults to superficial cartilage in response to inflammation and instability of the joint following ACLT are likely contributors to later development of OA[3,4]. T2 mapping can be used to non-invasively monitor longitudinal changes to the hydration and structural integrity of the articular cartilage collagen matrix following ACL injury[5,6]. This clinical study examines longitudinal T2 values of superficial and deep knee cartilage over 2 years following ACL injury.

Methods Twenty-six human subjects were included in these studies. Sixteen subjects (undergoing arthroscopy to treat ACLT 8 female, mean age = 33 ± 11 yrs; mean BMI = 26 ± 6) and 10 asymptomatic subjects with no known or suspected knee injury (5 female, mean age = 29 ± 4 yrs; mean BMI = 26 ± 5) provided informed consent and participated these IRB-approved protocols. ACLT subjects underwent longitudinal 3T multislice fast spin echo T2-weighted MR imaging using the NIH-sponsored Osteoarthritis Initiative (OAI) sequences and scanner at 4 time points: pre-, 6, 12, and 24 months post-surgery. Asymptomatic subjects were scanned by the OAI T2 mapping protocol at one time point. T2 maps were generated with a mono-exponential pixel-by-pixel fitting routine, excluding the first echo, using MRIMapper software (© Beth Israel Deaconess and MIT 2006). T2 values were assessed in the superficial and deep halves of tissue on the central weight-bearing zone of both medial and lateral femoral condyles (cMFC, cLFC). At surgery, cMFC cartilage of ACLT subjects was evaluated using a modified Outerbridge scale. Repeated measures ANOVA compared matched regions of interest (ROIs) across time-points for ACLT subjects. Post-hoc comparison with Bonferroni adjustment assessed pairwise differences between time-points. Non-parametric Kruskal-Wallis tests assessed differences between pre-surgery cMFC T2 values of ACLT subjects with arthroscopically firm (grade 0) and intact (grade 1) cartilage and asypmptomatic subjects. Mann-Whitney U tests assessed pairwise cMFC T2 differences between ACLT subjects and asymptomatics. Statistical analyses were performed with IMB SPSS and Microsoft Excel.

Results Among ACLT subjects, deep cartilage T2 values to both cMFC and cLFC varied significantly over the 24 months following ACL reconstruction surgery (repeated measures ANOVA, F = 15.6, 8.8, P<0.0005, 0.001, respectively, Figure 1). Pairwise comparisons indicate that deep cartilage T2 values were stable over the first 12 months following surgery and then dropped significantly between 12 and 24 months post-surgery (medial mean difference = ¯7.0ms, 95% CI(¯10.3 - ¯3.7), P<0.0005; lateral mean difference = ¯5.6ms, 95% CI(¯10.5 - ¯0.7), P=0.02). Superficial cartilage T2 values did not vary significantly over 24 months post- surgery (repeated measures ANOVA, F = 0.6, 0.6, P=0.63, 0.60; for medial and lateral, respectively). Arthroscopic evaluation of cMFC cartilage at the time of ACLT reconstruction surgery determined that 7 subjects had intact and 'firm' cartilage (grade 0), 8 subjects had intact and 'softened' cartilage (grade 1), and 1 subject demonstrated fine surface fibrillations (grade 2). Pre-surgery deep T2 values of ACLT subjects varied significantly with degree of joint pathology (Kruskal-Wallis, P=0.02, Figure 2). Pre-surgery deep cMFC T2 values of ACLT subjects with softened cartilage (grade 1, n=8) were 28% higher than deep cMFC T2 values of asymptomatics (n=10; Mann-Whitney U, P=0.01). Pre-surgery deep cMFC cartilage of ACLT subjects *without* arthroscopic evidence of injury (grade 0, n=7) also demonstrated elevated T2 values (21% higher) compared to asymptomatics, but the difference was not significant (n=10; Mann-Whitney U, P=0.06). Longitudinal T2 changes dichotimized by arthroscopic grade were significant in deep cMFC cartilage graded 'firm' (n=7, grade 0, repeated measures ANOVA F=4.8, P=0.03) and also 'softened' (n=8, grade 1, repeated measures ANOVA F=19.5, P<0.0005). The largest pairwise change was detected in deep softened (grade 1) cMFC cartilage between 12 and 24 months post-surgery (n=8, mean difference = ¯8.4ms (95% CI(¯13.8 - ¯2.7), P=0.006). Pre-surgery superficial cMFC T2 values did not vary with joint pathology (Kruskal-Wallis, P=0.10), and longitudinal superficial cMFC T2 changes dichotomized by scope grade were not significant (P=0.1, 0.5, grades 0,1).

Conclusion Longitudinal T2 mapping of knee cartilage following ACL tear and reconstruction surgery suggests that time and tissue depth may influence cartilage degeneration and recovery following reconstruction surgery. T2 decreases observed in deep cartilage between 12 and 24 months after ACL surgery may reflect changes in the articular matrix due to healing or coinciding with patients' return to more full-activity that typically occurs a year after surgery. Differences between T2 values measured in ACLT patients prior to reconstruction surgery and asymptomatic subjects suggests that T2 mapping may be sensitive to early , subclinical alteration of the subsurface cartilage matrix that is not detected by arthroscopy. The clinical relevance of these T2 changes remains to be determined by comparison to clinical measures of disease progression. T2 mapping's ability to non-invasively quantify and monitor cartilage status has the potential to be an important tool in identifying disease states amenable to treatment and to assess the efficacy of therapeutic interventions.

Figure 1

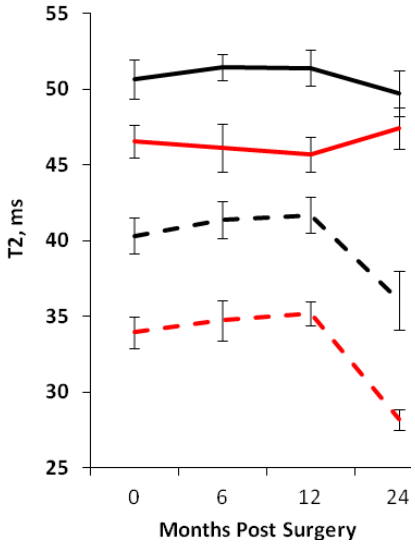
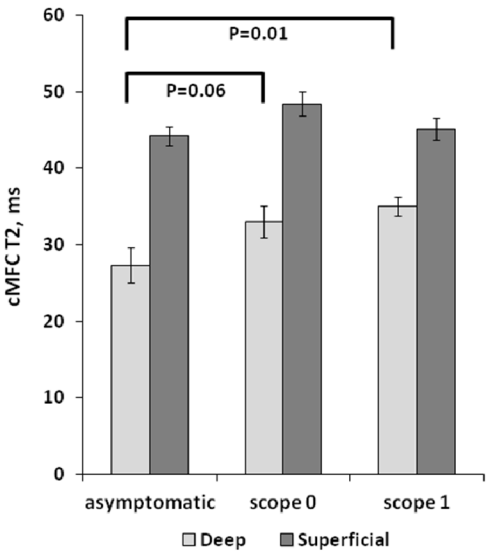


Figure 1 (Left) – Substantial decreases in deep cartilage T2 values were observed between 12 and 24 months following ACL surgery perhaps indicating cartilage healing from impact trauma sustained during ACL injury. Deep T2 values in cMFC (dashed red line) and cLFC (dashed black line) cartilage were relatively stable over the first 12 months of recovery and then dropped significantly between 12 and 24 months (cMFC 20% decrease, P<0.0005; cLFC 13% decrease, P=0.02). Superficial T2 values (solid lines) did not differ over 24 months of recovery. Error bars are ± SEM.

Figure 2 (Right) - Prior to reconstruction surgery, deep T2 values of ACLT subjects with intact but softened cMFC cartilage (grade 1) were 28% higher than deep T2 values of asymptomatics (P=0.01), consistent with deep tissue damage due to impact injury. ACLT subjects who did not show clinical evidence of cartilage injury at the time of surgery (grade 0) also showed a trend for elevated T2 values in deep cartilage suggesting that T2 may be sensitive to sub-clinical changes in the cartilage matrix acutely after ACL injury. Error bars are ± SEM.

Figure 2



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