Title: Bilateral assessment of cartilage with UTE-T2* quantitative MRI and associations with knee center of rotation following anterior cruciate ligament reconstruction

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Keywords: Anterior cruciate ligament, UTE T2*, Gait, Biomechanics, Knee center of rotation

Purpose:
Anterior cruciate ligament (ACL) tear greatly increases the risk of knee osteoarthritis (OA), even when patients undergo ACL reconstruction surgery (ACLR). Changes to walking kinematics following ACLR have been suggested to play a role in this degenerative path to post-traumatic OA by shifting the location of repetitive joint contact loads that occur during walking to regions of cartilage not conditioned for altered loads. Recent work has shown that changes to the average knee center of rotation during walking (KCOR) between 2 and 4 years after ACLR are associated with long term changes in patient reported outcomes at 8 years. Changes to KCOR result in changes to contact patterns between the femur and the tibial plateau. However, it is unknown if changes to this kinematic measure are reflected by changes to cartilage as early as 2 years after surgery. Ultrashort TE-enhanced T2* (UTE-T2*) mapping has been shown to be sensitive to subsurface changes occurring in deep articular cartilage early after ACL injury and over 2 years after ACLR that were not detectable by standard morphological MRI. Thus, the purpose of this study was to test the hypothesis that side to side differences in KCOR correlate with side to side differences in UTE-T2* quantitative MRI (qMRI) in the central weight bearing regions of the medial and lateral tibial plateaus at 2 years following ACLR.

Methods:
Thirty-five human participants (18F, Age: 33.8±10.5 yrs, BMI: 24.1±3.3) with a history of unilateral ACL reconstruction (2.19±0.22 yrs post-surgery) and no other history of serious lower limb injury received bilateral examinations on a 3T MRI scanner. UTE-T2* maps were calculated via mono-exponential fitting on a series of T2*-weighted MR images acquired at eight TEs (32μs -16 ms, non-uniform echo spacing) using a radial out 3D cones acquisition. All subjects completed bilateral gait analysis. Medial-lateral (ML) and anterior-posterior (AP) coordinates of average KCOR during stance of walking were calculated for both knees. Side to side differences in KCOR were tested for correlations with side to side differences in mean full thickness UTE-T2* quantitative values in the central weight bearing regions of the medial and lateral tibial plateau using Pearson correlation coefficients.

Results:
There was a distribution in UTE-T2* values, with some subjects having higher UTE-T2* and some lower in the ACLR knee relative to the contralateral knee. A significant correlation ($R=0.407$, $p=0.015$, Figure 1A) was observed between UTE-T2* and the ML KCOR with a more lateral KCOR corresponding to higher values of UTE-T2* for the medial tibia. Similarly, for the lateral tibia, a lower UTE-T2* was correlated with a more posterior KCOR ($R=0.363$, $p=0.032$, Figure 1B). Significant correlations were not observed for UTE-T2* in the lateral tibia with the ML position of KCOR or for UTE-T2* in the medial tibia with the AP position of KCOR.

Conclusions:
The results of this study support the hypothesis that side to side differences in mean full thickness UTE-T2* qMRI correlate with side to side differences in knee kinematics at 2 years after ACLR. The finding that a more lateral KCOR in the ACLR knee correlates with UTE T2* values in the medial tibia that were higher than the contralateral side suggests that this kinematic change, which has been previously shown to result in more relative motion between the femur and tibia in the medial compartment, could be affecting subsurface matrix integrity, inducing changes detectable by UTE-T2* mapping. Additionally, the finding that a more posterior KCOR in the ACLR knee correlated with UTE-T2* values in the lateral tibia that

were lower than the contralateral knee further suggests that the UTE-T2* metric may reflect early changes in cartilage health. When interpreted within the context of prior work showing that a posterior shift in KCOR from 2 to 4 years post-surgery correlated with improved clinical outcomes at 8 years, the observed lower UTE-T2* with a more posterior KCOR, which is reflective of improved quadriceps recruitment, suggests positive cartilage matrix properties. In spite of the limitations of this cross-sectional and exploratory study, and the difficulty accounting for changes in the contralateral knee, these results support future studies of the relationship between UTE-T2* and KCOR to provide new insight into predicting the risk for OA after ACLR.

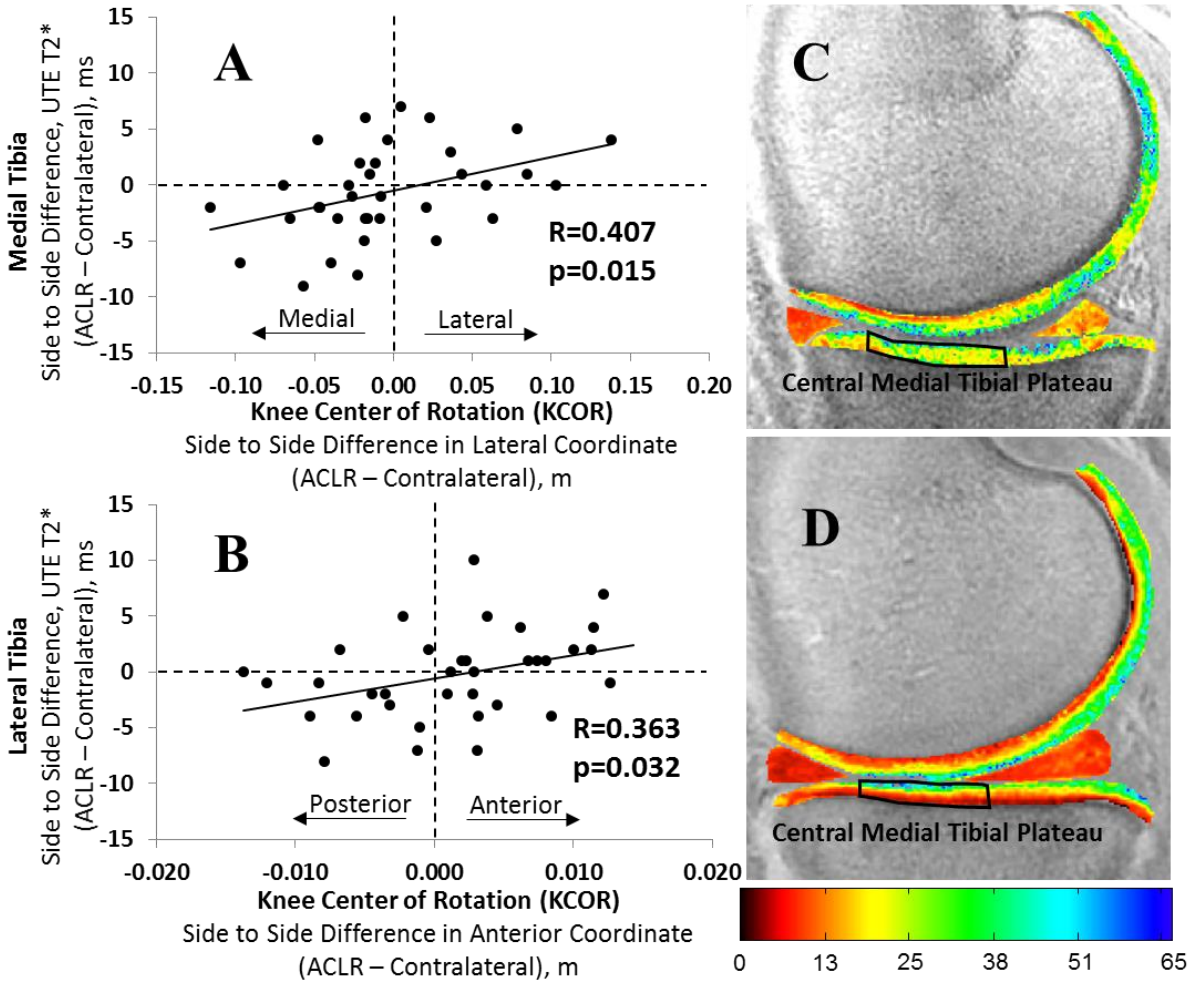

Figure 1. (A & B) Significant correlations between side to side differences in UTE T2* and KCOR. On the right, UTE T2* maps of the medial compartment of the tibiofemoral joint characteristic of a subject with (C) high mean UTE T2* and (D) low mean UTE T2* in the central weight bearing region of the medial tibial plateau.