Regional Variations in Tibiofemoral Cartilage Thickness 10+ Years After ACL Reconstruction

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INTRODUCTION: Anterior cruciate ligament (ACL) injury and subsequent reconstruction surgery (ACLR) are known risk factors for posttraumatic osteoarthritis (PTOA).[1] While cartilage loss is a hallmark feature of PTOA progression, cartilage swelling precedes the more advanced stages of the disease and is an early indicator of PTOA pathogenesis.[2] We therefore performed a sub-regional analysis of cartilage thickness in ACLR patients with the hypothesis that regional cartilage thickening and thinning would be present at 10-15 years after ACLR.

METHODS: Data from 36 ACLR patients (17M/19F; 36.8 ± 9.2 years; 39% isolated ACL tears) and 24 healthy control participants with no history of knee injury (13M/11F; 39.2 ± 8.4 years) who had participated in a longitudinal clinical trial (NCT00434837)[3] were included in this IRB-approved study. Cartilage thickness models were generated from a deep-learning-based auto-segmentation pipeline from magnetic resonance images (DESS sequence; 0.364mm in-plane resolution, 0.7mm slice thickness).[4,5] Six knee cartilage surfaces were evaluated: medial and lateral femoral condyles (MFC; LFC), medial and lateral tibia plateaus (MTP; LTP), patellofemoral groove (PG) and the patellar cartilage (PC). Seven participants had MRI artifacts that partially occluded certain cartilage surfaces; therefore, only the unaffected surfaces were included for analysis. Proportionally distributed sub-regions were generated based on the width and curvature of each cartilage surface such that the sub-regions were standardized across all subjects.[5] Cartilage thickness was quantified as a percentage difference from the corresponding sub-region of the contralateral limb. Mixed models were used to compare regional cartilage thickness between ACLR and healthy controls. Pairwise comparisons were conducted via orthogonal contrasts, and the Holm test was used to adjust for multiple comparisons.

RESULTS: Overall, ACLR patients had thicker medial compartment cartilage (MFC 4.3% thicker [$p=0.001$] and MTP 5.0% thicker [$p=0.002$]) compared to control subjects when data from all sub-regions were pooled. There was a moderation effect of sub-regions ($p<0.01$) for all surfaces except for the PG cartilage. In the medial compartment, 42% of the sub-regions (19/45) were significantly thicker in ACLR patients compared to the same regions in control subjects. On the MFC, these significant sub-regions were on average 6.9% ± 1.1% ($p<0.04$) thicker relative to controls and were located along the medial aspect of the condyle (Figure 1). On the MTP, the significant sub-regions were on average 9.3% ± 3.3% ($p<0.05$) thicker than controls and were located centrally (Figure 2). Conversely, the significant sub-regions on the LTP were on average 7.5% ± 0.5% ($p<0.02$) thinner than controls, located along the central-posterior aspect of the plateau (Figure 2). Although our analyses revealed that tibial and patellofemoral cartilage thickness varied by sex, there was no consistent pattern in thickening or thinning. In cases with a meniscus injury that occurred after initial enrollment and required a separate surgery (n=3 ACLR; n=2 Controls), the cartilage was 22.7% ± 3.9% ($p<0.04$) thicker along the posterolateral aspect of the MFC, and 15.2% ± 7.1% ($p<0.03$) thinner cartilage on the lateral-posterior aspect of the LTP relative to controls. In this same cohort, the MTP surface presented with scattered thickening in the central region of the plateau and thinning closer to the edges.

DISCUSSION: Our sub-regional analysis suggests that PTOA pathogenesis is likely underway in the ACLR patients enrolled in the present study, with regional variation in cartilage thickening and thinning. Medial compartment cartilage thickening within the first 5 years post-ACLR has been previously reported[1,6-8] and the present findings suggest that this is maintained 10+ years after ACLR. Thinning of LTP cartilage has also been previously associated with early radiographic osteoarthritis;[2] our results suggest these patients may be on this trajectory as we have previously proposed.[3] Although our sample size was small, subjects that required a separate meniscal surgery had more dramatic cartilage variation which fits with the known elevation in PTOA risk following meniscus injury.[9] Inclusion of both contralateral data and control group enhanced our sensitivity to detect small changes in cartilage thickness, which can be appreciated in our exploratory analysis of the effects of sex that were heterogeneous in this small cohort.

SIGNIFICANCE/CLINICAL RELEVANCE: The analysis presented here highlights cartilage areas of interest that may be susceptible to PTOA progression. With future steps to increase the pipeline's autonomy, this approach could potentially monitor changes earlier in the disease trajectory when interventions may be more effective.

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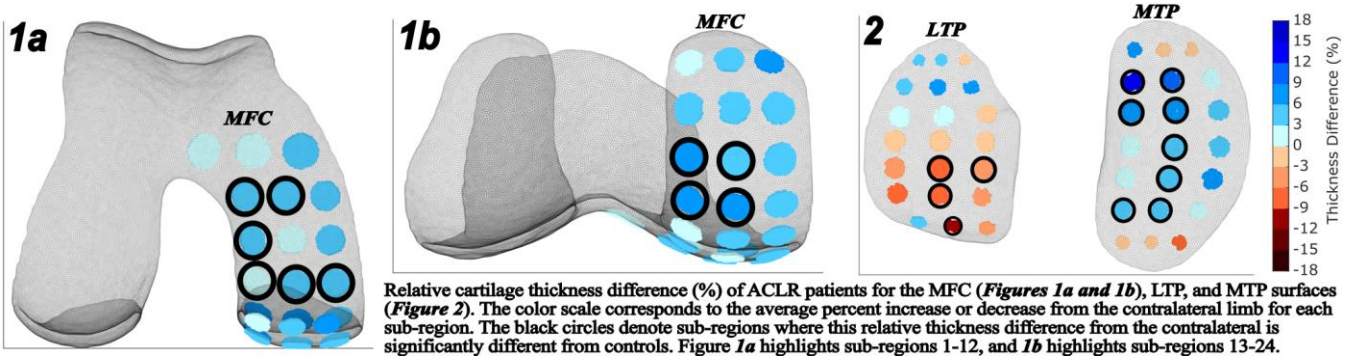
IMAGES AND TABLES:



Relative cartilage thickness difference (%) of ACLR patients for the MFC (*Figures 1a and 1b*), LTP, and MTP surfaces (*Figure 2*). The color scale corresponds to the average percent increase or decrease from the contralateral limb for each sub-region. The black circles denote sub-regions where this relative thickness difference from the contralateral is significantly different from controls. Figure *1a* highlights sub-regions 1-12, and *1b* highlights sub-regions 13-24.