## Longitudinal Texture Analysis of the Infrapatellar Fat Pad in ACL-Injured Knees

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**Introduction:** Anterior cruciate ligament (ACL) injury is frequently associated with the subsequent development of posttraumatic osteoarthritis (PTOA), with incidence as high as 87% <sup>1-3</sup>. The different mechanisms behind cartilage degeneration and subsequent OA development following ACL injury are multifactorial, involve multiple compartments within the knee, and are not fully understood. The infrapatellar fat pad (IPFP) has been implicated as a potential source of OA development and progression due to its inflammatory phenotype and high innervation of substance-P containing fibers<sup>4</sup>. Texture analysis is a quantitative image analysis technique that characterizes the spatial variations in pixel intensity and distributions within imaged tissues. Previous work has demonstrated that MRI-based IPFP texture features show greater discrimination for knee osteoarthritis than clinical scores<sup>5</sup>. Further, ACL injury and surgery has been linked to IPFP abnormalities, including inflammatory markers and fibrosis<sup>67</sup>. However, it is not clear how MRI-based IPFP texture features may change over time post ACL-injury and post ACL reconstruction (ACLR). Therefore, the objectives of this study were to: 1) Quantify texture features of the IPFP in patients with acute, isolated ACL injury preand post-ACLR, and 2) Compare texture features between injured and contralateral knees.

Methods: This study had IRB approval, with informed consent obtained from all participants. Bilateral MRI images were acquired at baseline (TP0), 6 months post-ACLR (TP1), and 1-year post-ACLR (TP2) from patients with acute, unilateral ACL tears. This cohort was previously evaluated for morphologic and quantitative changes to the articular cartilage<sup>8</sup>. Patients were treated with 1 of 4 graft types: hamstring tendon, tibialis posterior, bone–patellar tendon–bone (BTB), or Achilles tendon. The full volume of the IPFP in the injured and contralateral knees was segmented to define ROIs using semantic segmentation software (Mathworks, Natick, MA) and manually edited in ITK-Snap. Pixel intensity data within the ROIs was processed to calculate the gray level co-occurrence matrix (GLCM) to quantify the distribution and spatial organization of voxel intensity values. The texture features derived from the GLCM included: entropy (local image disorder), inverse difference moment (local

image homogeneity), correlation (gray level linear dependence between neighboring pixels), contrast (local image variability), and angular second moment (local image homogeneity). Paired t-tests were performed to compare differences in texture features between injured and contralateral knees at each timepoint, and texture features within each knee between timepoints. T-tests were performed to compare texture features between those who received bone–patellar tendon–bone (BTB) grafts vs. soft tissue grafts at each timepoint. A Bonferroni correction was applied to correct for multiple comparisons. **Results:** 48 patients were included in the study (18 female, 30 male; Age: 28.2 ± 11.7 yrs; BMI: 24.5 ± 2.4). Graft tissues included 18 hamstring tendon autografts, 20 BTB grafts, 6 posterior tibialis tendon allografts, and 4 Achilles tendon allografts. *ACLR vs Contralateral Knees*: At baseline, GLCM texture features did not differ between injured and contralateral knees. At 6 months post-ACLR, the injured knees had higher entropy (+12%, p<0.0001), lower inverse difference moment (-42%, p<0.0001), and lower contrast (-18%, p=0.003). At 1-year post-ACLR, injured knees had higher entropy (+15%, p < 0.0001), lower inverse difference moment (-53%, p<0.0001), lower contrast (-13%, p=0.005), and lower angular second moment (-76%, p<0.001). *Within ACLR Knees*: At 6 months post-ACLR, contrast was lower (-23%, p=0.005) but entropy was higher (+7%, p=0.001) as compared to baseline.

Between 6 months post-ACLR and 1-year post-ACLR, texture features did not differ within ACLR knees. At 1-year post-ACLR, entropy remained higher (+6%, p=0.002) and correlation was higher (+15%, p = 0.01) as compared to baseline. Texture features did not differ between graft types at any timepoint. *Within Contralateral Knees*: Texture features did not differ between baseline and 6-months or between 6-months to 1-year but angular second moment was increased (+34%, p=0.001), inverse difference moment was increased (+20%, p=0.003), and entropy was decreased (-6%, p=0.005) 1-year post-ACLR compared to baseline (Figure 1).

**Discussion**: The IPFP of ACL-injured knees was found to have greater texture variability as compared to healthy contralateral knees up to 1-year post-ACLR (Figure 2). These results agree with previous findings that heterogeneous signal alterations of the IPFP indicate pathologic changes<sup>5,9</sup>. Within injured knees, heterogeneity of the IPFP increases 6 months post-ACLR but appears to stabilize by 1-year post-ACLR. However, even at 1-year post-ACLR the IPFP is still more heterogeneous than at baseline, indicating long-term changes in the IPFP. Within healthy contralateral knees, homogeneity appears to increase in the IPFP with time; however, these differences were not apparent until 1-year later. Unexpectedly, the finding of decreased contrast in injured knees is inconsistent with the other texture findings and may require further examination. Our results suggest that IPFP heterogeneity is increased in injured knees post-ACLR and texture analysis can differentiate between injured and contralateral knees. **Conclusion**: Texture heterogeneity of the IPFP of ACL-injured knees were higher up to 1-year

Non-Injured Knee Injured Knee

Figure 2. Entropy texture distribution of the IPFP for a 38 yr old female with a hamstring tendon graft. Entropy increases in the injured knee 1-year post-ACLR and is higher compared to the contralateral knee.

post-ACLR compared to healthy contralateral knees. MRI texture analysis can be used to differentiate between injured and contralateral knees. **Acknowledgements:** The authors would like to acknowledge funding from the Arthritis Foundation and the Arthritis Foundation ACL Consortium who contributed data to this study and the support of Drs. Scott Rodeo, Kimberly Amrami, Aaron Krych, and Benjamin Ma for their clinical contributions to this study. **References:** <sup>1</sup>Shelbourne et al, Sport. Traumatol. Arthrosc 1997; <sup>2</sup>Nakata et al, J. Arthrosc. Relat. Surg. 2008; <sup>3</sup>Friel et al, Clin Sports Med 2013; <sup>4</sup>Dragoo et al, Sport. Med 2012; <sup>5</sup>Li et al, Radiology 2022; <sup>6</sup>Heilmeier et al, Osteoarthr. Cartil. 2020; <sup>7</sup>Murakami et al, Am. J. Sports Med. 1997; <sup>8</sup>Davidson et al., 2023, Sports Health (Accepted), <sup>9</sup>Han et al, Annals Rheumatic Diseases 2016.

Figure 1. Boxplot displaying differences in Entropy between injured and contralateral knees and within knees over time.