Cartilage T1ρ and T2 Quantification in ACL-reconstructed Knees: A 2-year Follow-up

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Introduction: ACL-injured knees are currently treated by reconstructing the ligament with biological tissue grafts, and this surgical procedure has been shown to improve the stability and function of the knee in most patients [1]. However at 5 to 15 years after surgery, studies have demonstrated that patients who had undergone ACL reconstruction were susceptible to post-traumatic osteoarthritis (OA) [2]. Recent developments in MRI techniques, such as $T_{1\rho}$ and T_2 relaxation time can be used to quantify the biochemical changes in cartilage matrix and detect early cartilage degeneration [3,4]. Thus, the objective of the present study is to 1) quantify longitudinal changes in cartilage morphology and matrix using quantitative MRI (thickness and $T_{1\rho}$ and T_2 quantification) in ACL-injured knees at baseline, 1-year and 2-years after ACL reconstruction; 2) identify baseline MR measures that predict cartilage morphology and matrix $T_{1\rho}$ and T_2 progression at 2-year.

Methods: *Subjects* Fifteen patients with acute ACL injuries (8 female, mean age = 35.1 ± 6.7 years, range = 23 - 49 years, BMI = 23.3 ± 2.1 kg/m^2) and sixteen healthy volunteers (8 female, mean age = 32.8 ± 10.0 years, range = 23 - 57, BMI = 24.4 ± 3.3 kg/m^2) were recruited for this study. The mean time from injury to baseline MRI was 46.1 days and from injury to ACL reconstruction was 83.1 days. *Imaging Protocol* All MR examinations were acquired using a 3 T GE Signa MR scanner and images were taken at baseline (after injury and before ACL reconstruction) and at 1 and 2 years after surgery. The control subjects were imaged at baseline only. The imaging protocol included sagittal 2D T_2-weighted fat-saturated FSE images (TR/TE = 4300/51 ms, FOV = 14 cm, matrix size = 512 × 256, slice thickness = 2.5 mm, intersection gap = 0.5 mm), and sagittal 3D fat-suppressed high-resolution spoiled gradient-echo (SPGR) imaging (TR/TE = 15/6.7 ms, flip angle = 12°, FOV = 14 cm, matrix size = 512 × 512, slice thickness = 1 cm). Sagittal 3D $T_{1\rho}$ and T_2 quantification were acquired based on spin lock techniques and 3D SPGR acquisition (TR/TE = 9.3/3.7 ms, FOV = 14 cm, matrix size = 256 × 192, slice thickness = 4 mm, View Per Segment = 64, for $T_{1\rho}$: Time of Spin Lock = 0, 10, 40, 80 ms, Spin Lock Frequency = 500 Hz; for T2: magnetization preparation echo time of 2.9, 13.6, 24.3, and 45.6 ms). *Image Analysis* Clinical MR images were graded using the modified Whole-Organ MRI Score (WORMS) system [5]. Cartilage of the patella, medial/lateral femoral condyle (MFC/LFC), and the medial/lateral tibia (MT, LT) were segmented semi-automatically in SPGR images using a program developed in-house. The LFC, MFC, LT, and MT were further divided into subcompartments (Figure 1A) and two equally spaced layers, superficial and deep. The $T_{1\rho}$ and T_2 maps were reconstructed by fitting the $T_{1\rho}$- and T_2-weighted images pixel by pixel and were subsequently aligned to SPGR images. $T_{1\rho}$, T_2, and thickness values were obtained for each subcompartment and layer. Bone marrow edema-like lesions (BMEL) were on T_2-weighted fat-saturated FSE images and were segmented semi-automatically [6]. *Statistical Analysis* A restricted maximum- likelihood mixed-effects regression model was used to estimate $T_{1\rho}$, T_2, and mean cartilage thickness as a function of side (lateral/medial), bone (femur/tibia), group (patients/controls), and year (baseline, 1-year, or 2-years), adjusted for subcompartment. $T_{1\rho}$ was also modeled as a function of demographic characteristics (age, sex, BMI), graft type used during reconstruction, presence of meniscal injury at baseline, and baseline BMEL volume.

Results: At baseline, 10 patients showed meniscal injury, 13 patients showed cartilage lesions and all patients showed BMEL. No significant changes in meniscal and cartilage lesions during follow up while BMEL decreased significantly. The estimated mean cartilage $T_{1\rho}$ ($P = 0.04$) and T_2 ($P = 0.01$) values were significantly elevated in patients compared to controls. No significant changes during the two-year follow-up period were identified by T_2 ($P = 0.49$); however, $T_{1\rho}$ measurements showed significant interaction between side and year ($P = 0.0037$), with $T_{1\rho}$ increasing in the medial side and decreasing in the lateral side during follow-up. Neither $T_{1\rho}$ nor T_2 mean values varied significantly between sides but both varied significantly between bones, among subcompartments, and between superficial and deep layers (all $P < 0.001$). Post hoc analysis showed that in the posterolateral tibial cartilage, $T_{1\rho}$ values were significantly higher in ACL-reconstructed knees than control knees at baseline and were not fully recovered at the 2-year follow-up (Figure 1B). $T_{1\rho}$ values of medial tibiofemoral cartilage in ACL-injured knees increased over the 2-year study and were significantly elevated compared to that of the control knees (Figure 1B). The estimated mean cartilage thickness did not differ significantly between patients and controls ($P = 0.31$) but showed an increasing trend during follow-up ($P = 0.095$). After adjustment for baseline $T_{1\rho}$, the estimated mean cartilage thickness increased significantly during follow-up in patients ($P = 0.027$). No significant effect of meniscal injury ($P = 0.28$) or BMEL volume ($P = 0.42$) at baseline on $T_{1\rho}$ or T_2 progression was observed. Post-hoc analysis showed that patients with meniscal lesions at baseline had significantly higher $T_{1\rho}$ and T_2 values in medial tibial-femoral cartilage at 2-year follow-up compared to healthy control knees ($P < 0.05$), while no significant difference in $T_{1\rho}$ and T_2 values was observed between patients without meniscal lesions and healthy control knees.

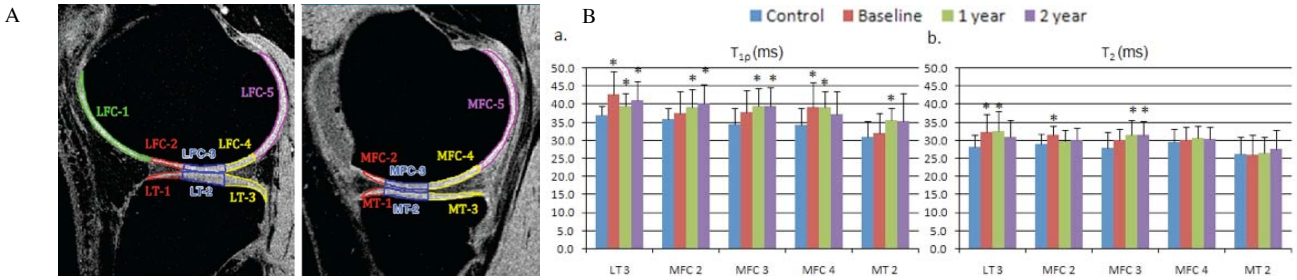

Figure 1 (A) Subcompartment definition of the lateral (left) and medial (right) side. (B) $T_{1\rho}$ (left) or T_2 (right) values of controls and patients with ACL injuries.

Discussion and Conclusion: This study used 3 T MRI to characterize the cartilage matrix ($T_{1\rho}$ and T_2) and morphology (clinical grading and thickness) of ACL-injured knees two years after surgical reconstruction. Elevated $T_{1\rho}$ values and thicker medial compartments in ACL-injured patients over the two-years suggested that abnormal tibiofemoral joint kinematics may cause early degeneration in these regions with increase of water content, decrease of proteoglycans, and cartilage swelling. A high prevalence of BMEL and elevated $T_{1\rho}$ and T_2 values in the posterior lateral tibia at baseline suggest that this region experienced the most severe damage during acute ACL injury. However, decreased $T_{1\rho}$ and T_2 values and cartilage thinning in the posterior lateral tibia during follow up indicated decreased cartilage swelling and partial recovery of cartilage in this region. These results suggest quantitative MRI can be a powerful tool for stratifying injury, monitoring and potentially predicting post-traumatic OA development in ACL-injured joints. Future investigations with larger cohorts and longer follow up are warranted to confirm findings from this study.

References: 1. Fu et al. Am J Sports Med 2000; 28: 124-130; 2. Lohmander et al. Am J Sports Med 2007; 35: 1756-1769; 3. Li et al, Radiology; 258: 505-514; 4; 4. Potter et al, Am J Sports Med 2012; 40: 276-285; 5. Peterfy et al. Osteoarthritis Cartilage 2004; 12: 177-190; 6. Li et al. J Magn Reson Imaging 2008; 28: 453-461.

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