Patient-reported Outcomes are associated with Cartilage T1ρ and T2 Quantification and Whole-Organ Magnetic Resonance Imaging Score (WORMS) after acute ACL injuries

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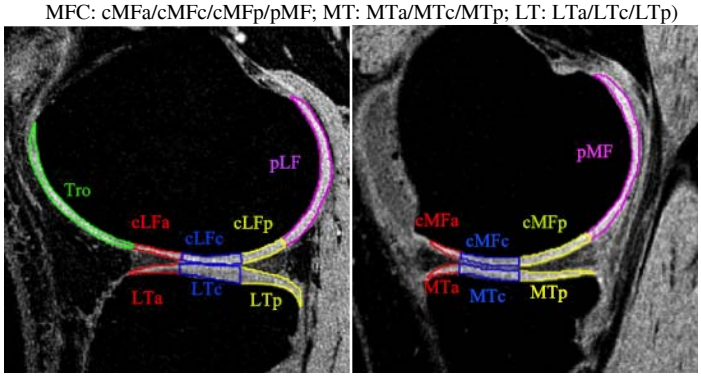
INTRODUCTION: Anterior cruciate ligament (ACL) injury has been suggested as a high risk factor for accelerating joint degeneration and eventually leading to post-traumatic osteoarthritis (OA) development in a high proportion of patients (1). Advanced quantitative magnetic resonance imaging (MRI) techniques, such as T1ρ and T2, have been shown to detect early cartilage changes in OA knees (2-5). Whole-Organ Magnetic Resonance Imaging Score (WORMS), a semi-quantitative morphological scoring method for multi-feature evaluation of OA, can grade knee abnormalities using conventional MR images (6). Knee injury and Osteoarthritis Outcome Score (KOOS) is a validated patient self-administered questionnaire that is widely used for measuring post-traumatic knee injuries (7). However, to the best of our knowledge, no studies have yet documented the association of patient-reported outcomes with T1ρ and T2 quantitative cartilage MRI and WORMS, respectively. The goal of this study is to evaluate the relationship between cartilage MRI quantification, WORMS and patient-reported outcomes after acute ACL injuries.

METHOD: A total of forty-two subjects with ACL acute ruptured (23 male, 19 female, age = 28.9 ± 8.7 years, body mass index (BMI) = 23.9 ± 2.9 kg/m^2) were recruited for this study and scanned at baseline (after injury and prior to ACL reconstruction, time to injury (days from injury to MR scan at baseline) = 67.4 ± 66.9 days) using a 3 Tesla GE MR scanner and an 8-channel phased array knee coil. The imaging protocol included sagittal T2-weighted 3D fast spin-echo (FSE) images (CUBE) and sagittal 3D T1ρ and T2 quantification using a combined MAPSS sequences (8) (T1ρ: time of spin-lock = 0/10/40/80 ms, spin lock frequency = 500Hz; T2: preparation TE = 0/13.7/27.3/54.7ms; Matrix = 256x128, 4 mm slice thickness). Cartilage was segmented semi-automatically using in-house developed software in CUBE images into six compartments: lateral/medial femoral condyle (LFC/MFC), lateral/medial tibia (LT/MT), patella (PAT) and trochlea (TRO) and subcompartments of femoral-tibial cartilage were defined as shown in Figure 1. The regions of interest (ROI) were overlaid to reconstructed T1ρ and T2 maps after registration, and the mean T1ρ and T2 values were calculated in each compartment. All patients filled in the Knee Injury and Osteoarthritis Outcome Score (KOOS) questionnaire during the MR visit. A questionnaire of KOOS, consisting of 5 subscales: pain, other symptoms, activities in daily living (ADLs), function in sport and recreation (Sport/Rec), and knee-related quality of life (QoL) (100 indicating no symptoms and 0 indicating extreme symptoms), is filled out by each patient. The knee structural abnormalities, such as cartilage lesions (assessed six compartments: MFC/LFC, MT/LT and Tro/Pat), meniscal abnormalities (Medial/Lateral meniscus lesion total scores), bone marrow edema pattern (in six locations: MFC/LFC, MT/LT and TRO/PAT) and joint effusion were graded using the Whole-Organ MRI Score. After adjusted BMI and time to injury, spearman correlation coefficients between each subscales of KOOS and T1ρ and T2 values in each compartment were calculated. A multivariate linear regression model was used to determine the association of independent subscales of KOOS with WORMS, age, BMI, and time to injury.

Figure 1: Definition of the knee cartilage subcompartments (LFC:cLFa/cLFc/cLFp/pLF; MFC: cMFa/cMFc/cMFp/pMF; MT: MTa/MTc/MTp; LT: LTa/LTc/LTp)



RESULTS:KOOS decreased significantly with increased age (R = -0.316, P = 0.041 for QoL) and increased time to injury (R = 0.313, P = 0.047 for ADL). No significant correlation with BMI and no significant difference was found between male and female patients. Significant correlations were observed between MRI T1ρ and T2 (especially in LTa, MTc, cLTc and cLFa in T1rho; LTa in T2) and KOOS (especially with the subscale of Qol and Sport/Rec) after adjusted for age, gender and time to injury (Table 1). In the multivariate linear regression model, CartLesLFC (Cartilage lesion on LFC) showed the significant association with all subscales of KOOS except Pain (P = 0.005 for Symptoms, P = 0.002 for ADL, P = 0.002 for Sports/Rec and P = 0.006 for QoL). Age, gender, BMI, time to jury, Meniscus lesion and joint effusion did not cause a significant effect. Lateral tibial bone marrow edema has significant effect on Pain (P = 0.018) ADL (P = 0.006), and QoL (P = 0.001) in our regression model. Additionally, another significant association was found between trochlear cartilage lesion and ADL (P = 0.018).

DISCUSSSION AND CONSLUSION: This study reported for the first time the relationship between quantitative MRI and patient-reported outcomes after acute ACL injuries. Quantitative MRI, such as T1ρ and T2, are sensitive for detecting early degeneration in the cartilage matrix. Significant correlations were observed between KOOS and cartilage T1ρ and T2 after adjusted for age, BMI and time to injury, indicating an independent relationship between cartilage damage and patient outcomes after acute injuries. Interestingly, in this study, the correlations between KOOS and WORMS and T1ρ and T2 measures are located not only in the lateral side (LFC/LT and lateral meniscus, the primary injury side after ACL tear), but also in MT, suggesting a global disturbance of cartilage homeostasis within the whole joint after the injury. Higher WORMS scores on cartilage lesion and bone marrow edema, especially on lateral side of knee joint, are obviously related with worse patient's outcome. It revealed that the recovery of lateral focal lesion potentially greatly affected the patient's daily living quality. We currently are continuing to recruit more patients to confirm these findings and will follow these patients after ACL reconstruction to further explore the relationship between patient outcomes and cartilage T1ρ and T2 as well as joint morphological abnormalities.

Table 1. All significant correlation results (Correlation coefficients, R (P-Value) between KOOS

	T1ρ						T2
	cMFa	MT	MTc	cLFa	cLFc	LTa	LTa
Pain	NS	-0.323 (0.037)	-0.0358 (0.02)	NS	NS	-0.462 (0.002)	NS
Symptoms	NS	NS	-0.317 (0.041)	NS	-0.384 (0.012)	-0.428 (0.005)	NS
ADL	NS	NS	NS	NS	NS	-0.399 (0.009)	NS
Sports/Rec	NS	-0.308 (0.047)	-0.365 (0.018)	-0.307 (0.048)	NS	-0.486 (0.001)	-0.35 (0.023)
QoL	-0.322 (0.038)	-0.375 (0.014)	-0.416 (0.006)	-0.492 (0.001)	NS	-0.569 (0)	-0.306 (0.049)

Table 2. All significant correlation results (Correlation coefficients, R (*P-Value*) between KOOS and WORMS with *P-Values* (≤ 0.05) in the multivariate linear regression model. (CartLesT: trochlea cartilage lesion; CartLesLFC: lateral femoral condyle cartilage lesion; BmeLT: lateral tibial bone marrow edema)

	CartLesT	CartLesLFC	BmeLT
Pain	NS	NS	-0.48 (0.018)
Symptoms	NS	-0.421 (0.005)	NS
ADL	-0.209 (0.018)	-0.385 (0.002)	0.405 (0.006)
Sports/Rec	NS	-0.76 (0.002)	NS
QOL	NS	-0.30 (0.006)	-0.436 (0.001)