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Cartilage morphology and $T_{1\rho}$ and T_2 quantification in ACL-reconstructed knees: a 2-year follow-up

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SUMMARY

Objective: To describe cartilage matrix and morphology changes, assessed using quantitative magnetic resonance imaging (MRI), after acute anterior cruciate ligament (ACL) injury relative to controls and longitudinally during 2 years following reconstruction.

Method: Fifteen patients with acute ACL injuries and 16 healthy volunteers with a similar demographic profile but no history of osteoarthritis or knee injury were studied. The injured knee of each participant was imaged with a 3.0 T MR scanner at baseline (prior to ACL reconstruction); patients' knees were re-imaged 1 and 2 years after ACL reconstruction. Cartilage $T_{1\rho}$ and T_2 values in full thickness, superficial layers, and deep layers, and cartilage thickness of the full layer were quantified within subcompartments of the knee joint.

Results: In the posterolateral tibial cartilage, $T_{1\rho}$ values were significantly higher in ACL-injured knees than control knees at baseline and were not fully recovered 2 after ACL reconstruction. $T_{1\rho}$ 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. T_2 values in cartilage of the central aspect of the medial femoral condyle at the 2-year follow-up were significantly elevated compared with control knees. Cartilage in the posterior regions of the lateral tibia was significantly thinner, while cartilage in the central aspect of the medial femur was significantly thicker than that of controls. Patients with lesions in the posterior horn of the medial meniscus exhibited significantly higher $T_{1\rho}$ values in weight-bearing regions of the tibiofemoral cartilage than that of control subjects over the 2-year period, whereas patients without medial meniscal tears did not.

Conclusion: Quantitative MRI provides powerful *in vivo* tools to quantitatively evaluate early changes of cartilage matrix and morphology after acute ACL injury and reconstruction, which may possibly relate to the development of post-traumatic osteoarthritis in such joints.

Introduction

Anterior cruciate ligament (ACL) rupture is a common and serious knee injury. 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 5–15 years after surgery, radiographic studies document that approximately 50% of patients who have undergone ACL reconstruction are susceptible to post-traumatic osteoarthritis (OA)[2–6]. In many young individuals, this injury leads to the development of OA with knee-related symptoms that severely affects their quality of life[7,8].

Standard magnetic resonance imaging (MRI) techniques, which include fat-saturated T_2-weighted, proton density-weighted fast spin echo (FSE) and T_1-weighted spoiled gradient echo (SPGR) sequences, have been found to be useful in detecting morphological changes associated with cartilage breakdown noninvasively[9]. These sequences, however, are limited from detecting early degenerative changes of the cartilage matrix[10,11]. Recent developments in MRI techniques, such as $T_{1\rho}$, T_2, and delayed gadolinium-enhanced MRI

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of cartilage (dGEMRIC), can be used to quantify the biochemical changes in cartilage matrix and detect early cartilage degeneration[12–19]. A few previous studies applied $T_{1\rho}$, T_2, and dGEMRIC imaging to detect cartilage matrix composition changes after ACL injury and reconstruction[20–24].

Our group previously reported that $T_{1\rho}$ quantification was able to detect persistent damage in the lateral tibial cartilage and early degeneration in the medial tibiofemoral cartilage of ACL-injured knees 1 year after reconstruction[21]. Consistent with previous clinical studies, our study also reported that patients with medial meniscal injury had a higher $T_{1\rho}$ increase than those without, which suggests that meniscal injury is a potential risk factor for post-traumatic OA development[3–5].

Despite promising results, the 1-year study warranted a longer follow-up to better understand the changes that were observed. Thus, the objectives of the present study are to (1) quantify longitudinal changes in cartilage morphology and matrix in ACL-injured knees 2 years after ACL reconstruction using quantitative MRI (thickness, $T_{1\rho}$, and T_2 quantification); and (2) identify baseline MR measures that predict cartilage morphology and matrix $T_{1\rho}$ and T_2 progression at 2 years. We hypothesize that (1) early degeneration of the lateral and medial tibiofemoral cartilage of ACL-injured knees will persist 2 years after reconstruction and that (2) baseline meniscal injury and bone marrow edema-like lesions (BMELs) may predict cartilage degeneration progression 2 years after reconstruction.

Materials and methods

Subjects

The study was approved by the Committee for Human Research at our institution and all subjects gave informed consent. Sixteen healthy controls and 15 patients with clinically diagnosed acute ACL rupture were studied. The exclusion criteria included knee radiograph Kellgren–Lawrence (KL) score >0 for controls and KL score >2 for patients, prior diagnosed inflammatory arthritis, or previous injury on either knee. Patients who required surgical intervention for other injuries, including collateral ligament and posterior cruciate ligament tears, were excluded from the study. All patients underwent ACL reconstruction [all but one were performed by (CBM), an experienced orthopedic surgeon]. One patient underwent concomitant lateral meniscal repair, two patients underwent medial meniscectomy, and one underwent debridement of the posterior lateral horn.

Imaging protocols

Knee radiography was performed after injury but prior to ACL reconstruction (baseline). The standard knee radiographic protocol included bilateral semiflexed weight-bearing view, 30° flexion lateral view, and bilateral patellofemoral sunrise view. All MR examinations were acquired using a 3 T GE Signa MR scanner (HDx, General Electric Healthcare, Milwaukee, WI) with a transmit/receive quadrature knee coil (Clinical MR Solutions, Brookfield, WI). MR images were taken at baseline ($n = 15$) and at 1 ($n = 15$) and 2 ($n = 12$) years after surgery. Controls were imaged at baseline only. Table I summarizes the clinical, $T_{1\rho}$, and T_2 quantification sequences previously developed by our lab[21].

Conventional radiographic and clinical diagnostic MR assessment

All radiographs and clinical MR images were reviewed by two experienced musculoskeletal radiologists (LN and TML). The radiographic findings were scored according to the KL scale[25]. The MR images were analyzed for meniscal lesion, effusion, and cartilage lesion by using modified subscores of the Whole-Organ MRI Score system, Table II[26].

Quantification of BMELs

In all subjects, BMELs were defined as focal subchondral high signal intensity lesions on T_2-weighted fat-saturated FSE images. BMELs were segmented semi-automatically using a threshold developed previously by our lab[27]. The final regions based on the threshold were verified by a radiologist (LN).

Cartilage thickness and MR relaxation time quantification

Cartilage was segmented semi-automatically on sagittal SPGR images by using an in-house program[28]. The lateral femoral condyle (LFC), medial femoral condyle (MFC), lateral tibia (LT), and medial tibia (MT) were further divided into subcompartments with regard to the meniscus as shown in our 1-year report[21]. An iterative minimization process was used to calculate the thickness of each subcompartment.

The $T_{1\rho}$ and T_2 maps were reconstructed by fitting the images pixel by pixel to the following equations: $S(TSL) \propto S_0\exp(-TSL/T_{1\rho})$ for $T_{1\rho}$ and $S(TE) \propto S_0\exp(-TE/T_2)$ for T_2, where TSL is the time of spin lock, TE is the echo time, and S is the signal intensity. The signal-to-noise ratio for each subcompartment in images with TSL = 80 ms or TE = 45.6 ms ranged from 6.8 to 14.8, which is sufficient for robust $T_{1\rho}$ and T_2 quantification.

$T_{1\rho}$ and T_2 maps were registered to SPGR images, and cartilage contours generated from the SPGR images were overlaid onto the registered $T_{1\rho}$ and T_2 maps. To reduce artifacts caused by partial volume effects with synovial fluid, relaxation times greater than 150 ms on $T_{1\rho}$ and relaxation times greater than 100 ms on T_2 were automatically removed from quantification. In addition, $T_{1\rho}$ and T_2 values were quantified for two equally spaced layers, the deep and the superficial, by using an in-house program[29].

Statistical analysis

Restricted maximum-likelihood mixed-effects regression models were used to analyze outcomes that were measured at multiple times and/or locations within individuals. Subjects are

Table I
Sagittal imaging protocol at 3.0 T

Sequence	Imaging parameters						
	TR/TE* (ms)	FOV (cm)	Matrix size	Slice thickness	Flip angle	VPS	Other parameters
T_2-weighted fat-saturated FSE	4300/51	14	512 × 256	2.5 mm	–	–	–
3D fat-suppressed high-resolution SPGR	15/6.7	14	512 × 512	1 cm	12°	–	–
3D $T_{1\rho}$	9.3/3.7	14	256 × 192	4 mm	–	64	TSL (ms): 0, 10, 40 80 FSL (Hz): 500
3D T_2	9.3/3.7	14	256 × 192	4 mm	–	64	Preparation TE (ms): 2.9, 13.6, 24.3, 45.6

* TR/TE: repetition time/echo time; FOV: field of view; VPS: view per segment; TSL: time of spin lock; FSL: frequency of spin lock.