Comparison of T1rho relaxation times between ACL-reconstructed knees and contralateral uninjured knees

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Abstract

Purpose The goal of this study is to compare the cartilage of anterior cruciate ligament (ACL)-reconstructed and uninjured contralateral knees using $T_{1\rho}$ MRI 12–16 months after ACL reconstructions.

Methods Eighteen patients with ACL-reconstructed knees (10 women, 8 men, mean age = 38.3 ± 7.8 years) were studied using 3T MRI. Injured and contralateral knee MR studies were acquired 12–16 months post-operatively. Cartilage sub-compartment $T_{1\rho}$ values of each injured knee were compared with the contralateral knee's values. Sub-group analysis of sub-compartment $T_{1\rho}$ values in both knees was performed between patients with and without meniscal tears at the time of ACL reconstruction using a paired Student's t test.

Results In ACL-injured knees, the $T_{1\rho}$ values of the medial tibia (MT) and medial femoral condyle (MFC) were significantly elevated at 12–16 months follow-up compared to contralateral knees. Patients with a medial meniscal tear had higher MFC and MT $T_{1\rho}$ values compared to respective regions in contralateral knees. Patients with lateral meniscal tears had higher lateral femoral condyle and LT $T_{1\rho}$ values compared to respective regions in contralateral knees. There were no differences between the injured and contralateral knees of patients without meniscal tears.

Conclusions $T_{1\rho}$ MRI can detect significant changes in the medial compartments' cartilage matrix of ACL-reconstructed knees at 1 year post-operatively compared to contralateral knees. The presence of a meniscal tear at the time of ACL reconstruction is a risk factor for cartilage matrix degeneration in the femorotibial compartments on the same side as the meniscal tear.

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Introduction

The anterior cruciate ligament (ACL) is one of the most commonly injured ligaments in the knee. Patients with ACL-injured knees are at an increased risk of post-traumatic osteoarthritis [13, 20, 36]. Over 40 % of patients with ACL ruptures develop radiographic changes of osteoarthritis 10–20 years after the injury, primarily in the medial compartment of the injured knee [16, 22, 27, 30]. This increased rate of osteoarthritis was initially attributed to additional traumatic and progressive deterioration of the joint as a result of abnormal laxity and abnormal loading patterns in knees without ACL reconstructions [4, 23, 26]. However, recent studies have shown that 50–60 % of

patients with functionally stable ACL-reconstructed knees continue to develop degenerative changes in the knee, suggesting an alternative aetiology in the development of post-traumatic osteoarthritis [9, 14].

Advanced MRI techniques have been developed to detect macromolecular changes within cartilage matrix at the early stages of osteoarthritis. Among them, $T_{1\rho}$ imaging is an attractive candidate relative to standard MRI because it probes the interactions between water molecules and the cartilage extracellular matrix and can be sensitive to changes in proteoglycans [1, 11, 12, 21, 24, 28]. A change, specifically an increase, in $T_{1\rho}$ values represents damage to the extracellular matrix. While both $T_{1\rho}$ and T_2 values increase with the degree of osteoarthritis, studies suggest that $T_{1\rho}$ is more sensitive than T_2 for detecting early cartilage degeneration [18, 29].

$T_{1\rho}$ quantitative MRI is capable of detecting cartilage matrix changes in the cartilage overlying bone marrow edema-like lesions (BMEL) compared to healthy cartilage surrounding BMELs and detecting changes of the weight-bearing medial femorotibial cartilage matrix as early as 1 year after ACL reconstruction compared to age-matched, healthy control subjects [19, 33]. No study has used non-invasive quantitative MRI to compare the cartilage matrix properties of the ACL-injured knee to the contralateral healthy knee. A study comparing a patient's own ACL-injured knee's quantitative MRI cartilage values to their contralateral, uninjured knee is important, as it will help to provide an evaluation of the pathologic changes to a patient's injured knee, as the contralateral knee is the most appropriate internal control.

The objective of this study was to evaluate damage and potential early degeneration of cartilage in ACL-reconstructed knees by comparing cartilage $T_{1\rho}$ values of defined sub-compartments in ACL-reconstructed knees and the patient's own contralateral knee at 12 to 16 months after ACL reconstructions and to explore a potential effect of meniscal tears at the time of injury on cartilage $T_{1\rho}$ at 1 year after ACL reconstruction. The two hypotheses of this study are (1) the cartilage in the medial compartments of the injured knee will have significantly higher $T_{1\rho}$ signal changes compared to the respective compartments in the contralateral knee, and (2) patients with a meniscal tear will have higher $T_{1\rho}$ signal changes in the femoral and tibial compartments on the side of the meniscal tear compared to respective cartilage regions in contralateral knees.

Materials and methods

The study was approved by the Committee on Human Research at our institution. All patients with ACL injuries were referred by one orthopaedic surgeon (CBM) at our institution's Sports Medicine clinic. The inclusion criteria were clinically diagnosed acute complete ACL rupture using an increased anterior–posterior laxity scale (Lachman grade 2–3) [35] and confirmation by MRI, willingness to have an ACL reconstruction, and capability to undergo the standard pre- and post-injury/operative rehabilitation. The exclusion criteria include prior history of osteoarthritis, inflammatory arthritis, previous injury and surgery on either knee, and repeated injuries to either knee during the follow-up period. In addition, patients who required surgical intervention for ligamentous injuries, including collateral ligament and posterior cruciate ligament tears, were excluded from the study. All eligible patients provided written informed consent for their enrolment in the study.

Eighteen patients (10 women and 8 men, mean age = 38.3 ± 7.8 years, age range = 28–53 years) with acute ACL injuries were studied. All patients underwent anatomic ACL reconstruction, which was performed by one orthopaedic surgeon (CBM). Anatomic reconstruction of the ACL was performed using standard surgical steps: sizing and preparation of the graft, arthroscopic takedown of the previously ruptured ACL, femoral tunnel drilling and measurement through an anteromedial portal, tibial drilling using a tibial guide, passage of the graft through the tunnels and subsequent graft fixation on the femur with an endo-button or a metal interference screw and on the tibia with a BioIntrafix screw. Post-operatively, patients were scanned between 12 and 16 months (12.8 ± 1.7 months) after their ACL reconstructions. Patients with meniscal tears were identified by chart review of each patient's post-operative dictation and note (arthroscopic diagnosis). Each patient's characteristics and graft type are summarized in Table 1. Information that was available regarding descriptive characteristics of each meniscal tear (i.e. location, size, type) is also presented in Table 1.

Magnetic resonance imaging

MR data were acquired with 3 Tesla GE MR scanners (Signa HDx, General Electric Healthcare, Milwaukee, WI, USA). The patients included in this study are sub-cohorts of two other ongoing studies in our group, and as a result, 7 patients were scanned using a transmit/receive quadrature knee coil (Clinical MR Solutions, Brookfield, WI, USA) on scanner #1 and 12 patients were scanned using an eight-channel phased array knee coil (Invivo, Orlando, FL, USA) on scanner #2. The imaging protocols for all subjects included sagittal 3D fat-suppressed high-resolution spoiled gradient-echo (SPGR) images, sagittal T_2-weighted fat-saturated fast spin-echo (FSE) images and sagittal 3D $T_{1\rho}$ quantification sequences. For scans with the 8-channel knee coil, parallel imaging was performed with an array spatial sensitivity technique (ASSET) using an acceleration

Table 1 Patient characteristics, injured knee, ACL reconstruction graft type and associated meniscal tear(s) and cartilage integrity at the time of ACL reconstruction

Patient	Age (sex)	Graft	Meniscal tear[a]	Meniscal treatment	Outerbridge (location)
1	31 (F)	Posterior tibialis allograft	Medial—complex; 50 % of mid & posterior horn	Partial medial meniscectomy	II (MFC)
			Lateral—not specified; healed		
2	52 (M)	Achilles tendon allograft	Lateral—not specified; healed	None	I (LT)
3	42 (M)	Semitendinosus allograft	Medial—not specified	Partial lateral meniscectomy	I (LT)
			Lateral—not specified; posterior horn		
4	34 (M)	Hamstring autogenous	Lateral—longitudinal tear; healed	None	I (LT)
5	35 (F)	Hamstring autogenous	Medial—bucket handle	Repair (all-inside)	I (patella, MFC)
6	53 (F)	Posterior tibialis allograft	Lateral—complex tear; posterior horn	Partial lateral meniscectomy	III (MFC)
					III (LT)
7	43 (M)	Posterior tibialis allograft	Medial—not specified; posterior horn	Partial medial & lateral meniscectomy	I (Patella, MFC, MT)
			Lateral—radial tear; near subtotal		
8	43 (F)	Posterior tibialis allograft	Medial—not specified	None	–
9	31 (M)	Hamstring autogenous	Medial—not specified; posterior horn	Partial lateral meniscectomy	I (patella)
			Lateral—root tear; posterior horn		II (LT)
10	29 (F)	Hamstring autogenous	Medial—flap; 50 % of mid and posterior horn	Partial medial meniscectomy; Lateral—root repair w/PDS suture & endobutton	I (patella)
			Lateral—root tear		I (LT)
11	47 (F)	Hamstring autogenous		–	I (LT)
12	35 (M)	Posterior tibialis allograft		–	–
13	42 (F)	Posterior tibialis augmentation		–	I (patella)
14	44 (M)	Posterior tibialis allograft		–	–
15	28 (F)	Posterior tibialis allograft		–	II (patella)
16	33 (F)	Hamstring autogenous		–	–
17	30 (F)	Posterior tibialis allograft		–	III (patella)
					I (LT)
18	38 (M)	Posterior tibialis allograft		–	–

F female, *M* male, *MFC* medial femoral condyle, *LT* lateral tibia

[a] All tears were located in the posterior horns of the medial and lateral menisci

factor of 2. The detailed parameters for each sequence are listed in Table 2.

There is an excellent agreement in quantification of cartilage morphology and relaxation times between measurement with ASSET (acceleration factor = 2) and without ASSET [38]. In this study, cross-validation experiments in three healthy controls were performed. The controls were scanned twice within a week using the quadrature and 8-channel knee coil on the two scanners, respectively, with the protocol listed in Table 2. $T_{1\rho}$ relaxation times were quantified in five compartments of the knee, the lateral and medial femoral condyles (LFC/MFC), the lateral and medial tibias (LT/MT), and the patella (Fig. 1a), resulting in 15 compartments with 2 repeated measures in each compartment. From these compartments, the root-mean-square coefficients of variation (%), defined as 100 times

the standard deviation divided by the mean, were calculated for the $T_{1\rho}$ values.

Furthermore, during analysis of this study (as detailed in the section of statistical analysis), $T_{1\rho}$ values in the injured knees were compared to the uninjured contralateral knee, which was used as an internal control for each patient. Such analysis will minimize any potential bias to the results introduced by potential difference in $T_{1\rho}$ quantification between the two scanners.

Cartilage processing

Cartilage segmentation

Semi-automatic cartilage segmentation was performed on the sagittal SPGR images using proprietary software

developed with Matlab (Mathworks, Natick, MA, USA) based on Bezier splines and edge detection [6]. The medial and lateral femoral condyles and tibias were also divided into sub-compartments with regard to the meniscus (Fig. 1b). The medial and lateral femoral condyles were divided into 5 regions. MFC/LFC-1 and MFC/LFC-5 were cartilage regions anterior and posterior to the anterior and posterior horns of the meniscus, respectively (Fig. 1b). MFC/LFC-2 and MFC/LFC-4 were the cartilage regions overlying the anterior and posterior horns of the meniscus, respectively (Fig. 1b). MFC-3 was the cartilage region between the anterior and posterior horns of the meniscus (Fig. 1b). The tibia was divided into three sub-compartments. MFC/LFC-1 and MFC/LFC-3 were the cartilage regions overlying the anterior and posterior horns of the meniscus, respectively (Fig. 1b). MT-2 was the cartilage

region between the anterior and posterior horns of the meniscus (Fig. 1b). The segmentation was corrected manually to avoid synovial fluid or other surrounding tissue. The mean cartilage thickness of all segmented cartilage compartments and sub-compartments was calculated using an in-house developed software [6]. The root-mean-square CV for intra-observer reproducibility of cartilage thickness quantification using this algorithm was between 2.4 and 3.7 %, as reported previously [5].

Cartilage $T_{1\rho}$ relaxation quantification

$T_{1\rho}$ maps were reconstructed using a proprietary developed fitting algorithm. $T_{1\rho}$-weighted image intensities obtained for different time of spin-lock were fitted pixel by pixel to the following equation:

Table 2 Imaging protocols used in this study

| Sequences	Quadrature coil on scanner 1	8-channel knee coil on scanner 2 (ASSET acceleration factor = 2)
Sagittal fat-saturated T_2-weighted fast spin-echo (FSE) images	TR/TE = 4300/51 ms, FOV = 14 cm matrix size = 512 × 256, NEX = 2, slice thickness = 2.5 mm, gap = 0.5 mm	TR/TE = 4300/51 ms, FOV = 14 cm matrix size = 512 × 256, NEX = 2, slice thickness = 2.5 mm, gap = 0.5 mm
Sagittal 3D fat-suppressed spoiled gradient-echo (SPGR) images	TR/TE = 15.0/6.7 ms, FOV = 14 cm flip angle = 12°, NEX = 0.75, matrix = 512 × 512, slice thickness = 1 mm	TR/TE = 18.2/3.5 ms, FOV = 14 cm flip angle = 12°, NEX = 1, matrix = 512 × 512, slice thickness = 1 mm
Sagittal 3D $T_{1\rho}$ quantification using MAPSS [23]	TR/TE = 9.3/3.7 ms, FOV = 14 cm matrix size = 256 × 128, slice thickness = 4 mm, view per segment = 64, time of recovery = 1.5 s, time of spin-lock = 0, 10, 40, 80 ms, frequency of spin-lock = 500 Hz	TR/TE = 7.4/2.7 ms, FOV = 14 cm matrix size = 256 × 192, slice thickness = 4 mm, view per segment = 64, time of recovery = 1.5 s, time of spin-lock = 0, 10, 40, 80 ms, frequency of spin-lock = 500 Hz
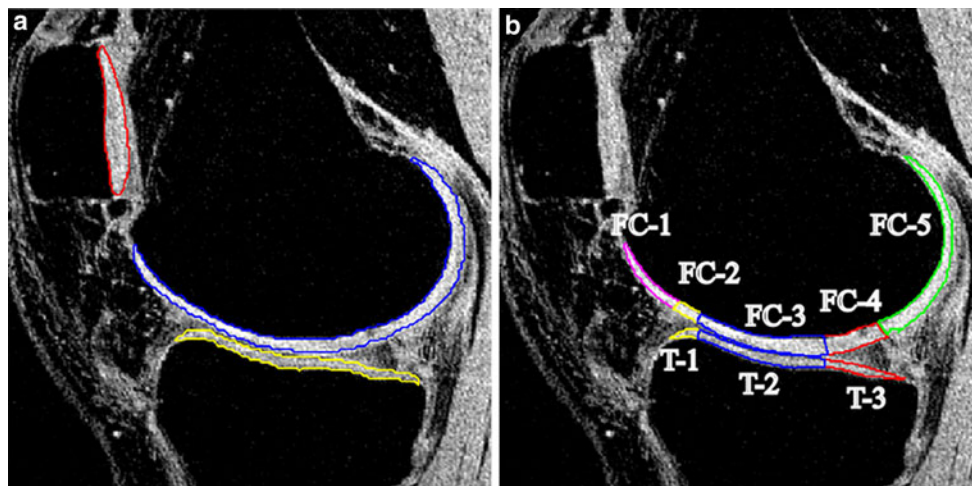
Fig. 1 Representative sagittal 3D water excitation high-resolution spoiled gradient-echo images with segmented cartilage of ACL-reconstructed knees. **a** To evaluate global compartmental $T_{1\rho}$ values, the patella (*red spline*), femoral condyles (*blue spline*) and tibias (*yellow spline*) are segmented. **b** For regional analysis, the cartilage of the femur and tibia is subdivided with respect to the meniscal horns. The femoral condyles are divided into 5 sub-compartments (FC-1,2,3,4,5), and the tibia is divided into three sub-compartments (T-1,2,3)

$$S(\text{time of spin - lock}) \alpha \exp\left(- \text{time of spin - lock}/T_{1\rho} \right)$$
$$(1)$$

$T_{1\rho}$ maps were registered to SPGR images, and cartilage contours generated from SPGR images after segmentation were overlaid to the registered $T_{1\rho}$ maps. The average $T_{1\rho}$ values of the full-thickness of each cartilage compartment and its sub-compartments were quantified for the injured and contralateral knees. The $T_{1\rho}$ values of the weight-bearing and non-weight-bearing regions of the femoral condyles were determined by averaging the average $T_{1\rho}$ values of the sub-compartments overlying and between the anterior and posterior horns of the meniscus (LFC/MFC-2,3,4). To reduce artefacts caused by partial volume effects with synovial fluid, regions with relaxation time >150 ms in $T_{1\rho}$ maps were manually removed from the data used for quantification. The scan–rescan coefficients of variation (CV) of cartilage $T_{1\rho}$ quantification using the same technique have been reported to range between 1.7 and 8.7 % [17, 18], indicating excellent in vivo reproducibility of the MR $T_{1\rho}$ technique.

Statistical analysis

Overall statistical analysis included the two major statistical comparisons. The average $T_{1\rho}$ values of the five knee compartments (LFC, LT, MFC, MT and patella; Fig. 1a) were compared between injured and uninjured knees using a paired, one-tailed Student's t test. The average $T_{1\rho}$ values of the defined sub-compartments (LFC/MFC-1,2,3,4,5; LT/MT-1,2,3, Fig. 1b) were compared between injured and uninjured knees using a paired, one-tailed Student's t test. A sub-analysis of patients with and without meniscal tears included three statistical comparisons. The average $T_{1\rho}$ values of the MFC and MT and defined sub-compartments (MFC-1,2,3,4,5; MT-1,2,3) of patients with *medial meniscal tears* were compared between injured and uninjured knees using a paired, one-tailed Student's t test. The average $T_{1\rho}$ values of the LFC and LT and defined sub-compartments (LFC-1,2,3,4,5; LT-1,2,3) of patients with *lateral meniscal tears* were compared between injured and uninjured knees using a paired, one-tailed Student's t test. The average $T_{1\rho}$ values of the five knee compartments (LFC, LT, MFC, MT and patella) and of the defined sub-compartments (LFC/MFC-1,2,3,4,5; LT/MT-1,2,3) in patients *without* meniscal tears were compared between injured and uninjured knees using a paired, one-tailed Student's t test. Identical analysis was used for cartilage thickness in knee compartments and respective sub-compartments between injured and uninjured knees. All statistical analyses were calculated using Microsoft Excel. A p value <0.05 was considered statistically significant for all comparisons.

Results

Cross-validation analysis of the two knee coils used to scan patients in this study showed a 4.6 % root-mean-square coefficients of variation of the $T_{1\rho}$ values of cartilage in knees. This value is within the in vivo reproducibility of the $T_{1\rho}$ quantification using the 3D MAPSS sequence as previously reported [17].

The medial tibia and medial femoral condyle in ACL-injured knees 12–16 months post-reconstruction had $T_{1\rho}$ values that were significantly elevated compared to respective regions in contralateral knees (Fig. 2a); the cartilage thickness in the medial compartments was not different between injured and uninjured knees (Table 3). While no differences were found between the injured and uninjured knees with respect to global $T_{1\rho}$ values of the LFC, LT and patella (Fig. 2a), the cartilage thicknesses of the LFC and LT were significantly less in the injured knee compared to the uninjured knee (Table 3).

Sub-compartment analysis of the medial tibia revealed the weight-bearing contact region (MT-2) in the injured knee had greater $T_{1\rho}$ values and less thick cartilage compared to the MT-2 of the uninjured knee (Fig. 2b; Table 3). It was also found that the MFC's most anterior cartilage compartment (MFC-1) and weight-bearing regions (MFC-2,3,4) had greater $T_{1\rho}$ values compared to the respective sub-compartments in the uninjured knee (Fig. 2b). The cartilage thickness of MFC-3 in injured knees was significantly thinner than the respective compartment in uninjured knees (Table 3). On the lateral side of the knee, the cartilage thicknesses of LT-1 and LT-3 in injured knees were significantly thinner than the respective compartments in uninjured knees (Table 3). LFC-2 and LFC-5 were also found to have significantly greater $T_{1\rho}$ values compared to the respective regions in the uninjured, contralateral knee (Fig. 2b). No significant difference was noted in the individual sub-compartments of the LFC with respect to cartilage thickness (Table 3).

To analyse the effect of a meniscal tear in the ACL-injured knee, a sub-analysis between injured and uninjured knees in patients with meniscal tears and a separate sub-analysis of injured and uninjured knees in patients without meniscal tears were performed. Ten patients had meniscal tears, of which 5 patients had lateral and medial meniscal tears, 3 patients each had an isolated lateral meniscal tear and 2 patients each had an isolated medial meniscal tear (Table 1). All meniscal tears were located in the posterior horn of the medial and lateral menisci. There were a variety of tears, including 1 root tear, 1 longitudinal tear, 1 radial tear and 2 complex tears (Table 1), and treatment of each was tailored based on the tear's location, size and type.

Patients without meniscal tears were found to have no significant differences in global $T_{1\rho}$ values in all five

Fig. 2 a Average global articular cartilage $T_{1\rho}$ values of the lateral femoral condyle (LFC), lateral tibia (LT), medial femoral condyle (MFC), medial tibia (MT) and patella in ACL-injured knees and uninjured, contralateral knees. Note that the $T_{1\rho}$ values in the MFC and MT of injured knees are significantly elevated compared to the values of respective regions in uninjured knees. The $T_{1\rho}$ values of the LFC, LT and MFC of injured knees are also elevated relative to the respective sub-compartments' values of uninjured knees. **b** Average articular cartilage $T_{1\rho}$ values in sub-compartments of the LFC, MFC, LT, MFC and MT in ACL-injured and contralateral, uninjured knees. Note that the injured knees have significantly higher $T_{1\rho}$ values in LFC-2,5, MFC-1,2,3,4 and MT-2
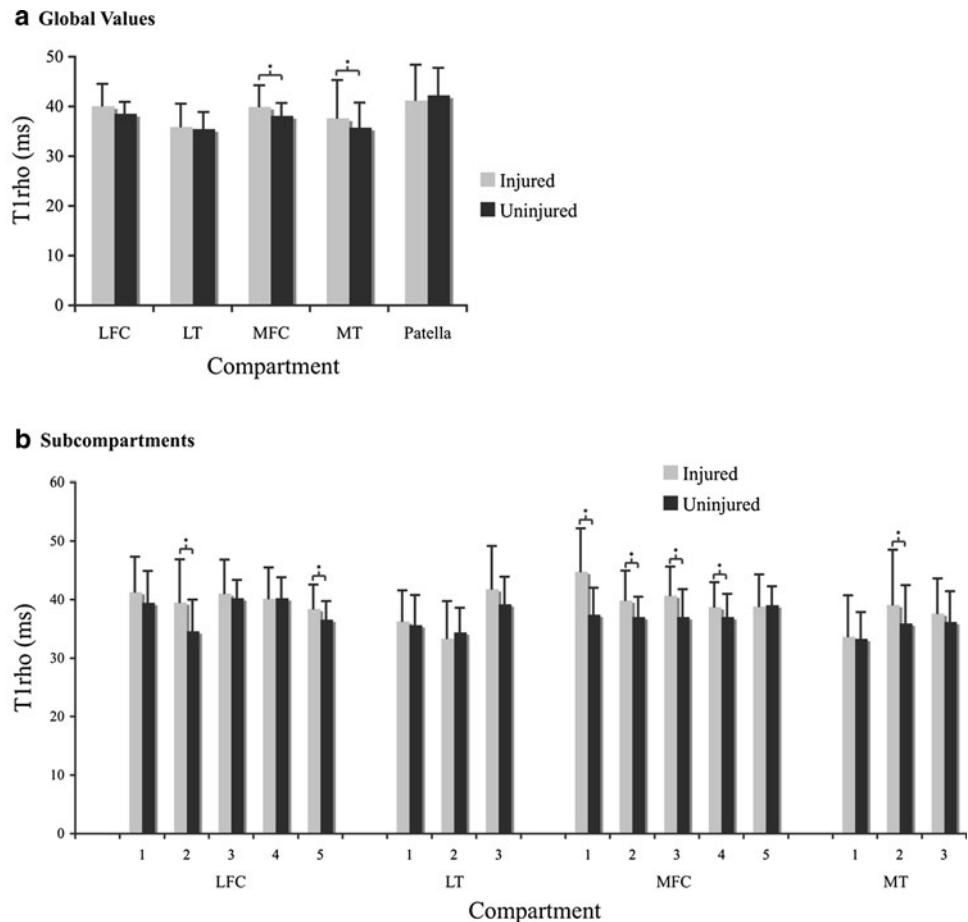
cartilage compartments (Fig. 3a). The 7 patients with medial meniscal tears were found to have significantly higher global $T_{1\rho}$ values in the MFC and MT compared to respective regions in contralateral knees (Fig. 3b). The 8 patients with lateral meniscal tears were found to have elevated global $T_{1\rho}$ values in the LFC and LT compared to respective regions in contralateral knees (Fig. 3c; $p = 0.06$).

With regard to cartilage sub-compartments, patients without meniscal tears were found to have no significant difference in $T_{1\rho}$ values in all sub-compartments between injured and contralateral knees (Fig. 4a). Patients' injured knees with associated medial meniscal tears were found to have significantly greater $T_{1\rho}$ values in the MFC-1,3,4 and MT-3 compared to respective regions in the contralateral knees (Fig. 4b). The $T_{1\rho}$ values in MFC-2,5 and MT-2 of patients with medial meniscal tears were greater than the values in contralateral knees (Fig. 4b; $p = 0.07–0.08$). Patients with associated lateral meniscal tears were found to have significantly greater $T_{1\rho}$ values in the LFC-1 and LFC-2 compared to respective regions in the contralateral knees (Fig. 4c). The $T_{1\rho}$ values in LFC-5 and LT-3 of patients with lateral meniscal tears were greater than the values in contralateral knees (Fig. 4c; $p = 0.07–0.08$).

Discussion

The most important finding of this study is that medial femorotibial compartments in ACL-injured knees 12–16 months after surgical reconstruction had significantly greater $T_{1\rho}$ values compared to the medial compartments in the contralateral, uninjured knee. In particular, the contact region between the medial femur and tibia (not protected by meniscus; MT-2) and the weight-bearing regions of the MFC in the injured knee showed significantly elevated $T_{1\rho}$ values compared to the uninjured, contralateral knee. As $T_{1\rho}$ is sensitive to proteoglycan loss, and that loss of proteoglycan is suggested as an initiating event of osteoarthritis [10], the observed $T_{1\rho}$ elevations in the medial compartments suggest early cartilage matrix degeneration and thus ultimately may represent "hot spots" in the cartilage at which post-traumatic osteoarthritis develops after ACL injury. This is consistent with a previous study that found significantly elevated $T_{1\rho}$ values in the weight-bearing sub-compartments of medial femorotibial cartilage in ACL-injured knees at 1-year postoperative follow-up compared with values in knees of a healthy control cohort [19]. They also suggested that the degeneration in the medial compartments starts from the

superficial layer of the cartilage, as they observed significantly greater $T_{1\rho}$ values in superficial layers of the medial compartment's contact region at 1-year follow-up in

Table 3 Cartilage thickness in knee compartments and respective sub-compartments in patients after ACL reconstruction

	Knee	
	Injured	Uninjured
LFC (whole)	1.4 ± 0.5	1.5 ± 0.5*
LFC		
1	1.4 ± 0.5	1.4 ± 0.5
2	0.8 ± 0.3	1.0 ± 0.3
3	1.1 ± 0.4	1.2 ± 0.4
4	1.5 ± 0.6	1.5 ± 0.6
5	1.3 ± 0.5	1.5 ± 0.5
LT (whole)	1.9 ± 0.9	2.0 ± 1.0*
LT		
1	1.1 ± 0.6	1.2 ± 0.5*
2	2.0 ± 0.8	2.1 ± 0.7
3	1.5 ± 0.8	1.7 ± 0.9*
MFC (whole)	1.4 ± 0.5	1.5 ± 0.5
MFC		
1	0.6 ± 0.4	0.7 ± 0.4
2	0.8 ± 0.4	0.9 ± 0.4
3	1.2 ± 0.5	1.4 ± 0.5*
4	1.3 ± 0.5	1.4 ± 0.4
5	1.4 ± 0.5	1.4 ± 0.5
MT (whole)	1.2 ± 0.5	1.2 ± 0.5
MT		
1	0.7 ± 0.4	0.8 ± 0.4*
2	1.1 ± 0.4	1.3 ± 0.5*
3	0.9 ± 0.4	1.0 ± 0.4

All thickness measurements in millimetres

* Denotes statistical significance, $p < 0.05$

ACL-injured knees compared with values in control knees [19]. No significant differences were observed in the deep layers [19]. Interestingly, while there were no significant differences noted in cartilage thickness between the whole medial compartments of injured and uninjured knees, the cartilage of areas not protected by menisci, MFC-3 and MT-2, was significantly thinner in injured knees. While minor, these changes in thickness may represent early cartilage loss.

The changes presented herein of the knees' medial compartments are consistent with previous studies by Carpenter et al. [7] and Seon et al. [31] who suggested that ACL reconstruction does not fully restore normal knee kinematics, particularly in the compartments of the medial knee. Specifically, Carpenter et al. [28] found that normal motion on the lateral side of the knee but not on the medial side was restored after ACL reconstruction, which resulted in increased internal tibial rotation when moving from full extension to 40° of flexion. In addition to reconstructing the ACL, addressing other injuries about the knee, including posterolateral corner tears, is critically important to improving knee kinematics. Griffith et al. [15] found that only medial compartment cartilage matrix injury, as determined by increased $T_{1\rho}$ relaxation times, was detectable when Grade III posterolateral knee injuries were created in a canine knee model and tested under different biomechanical loads. This change in biomechanics due to missed injuries or after ACL reconstruction subsequently may cause joint loads to be shifted to infrequently loaded areas of the cartilage and lead to early cartilage degeneration [8].

As altered biomechanics and joint loads in the ACL-injured knee play important proposed roles in the development of post-traumatic injury, this study addressed whether an additional mechanical injury, such as a meniscal tear, further increases one's risk for cartilage matrix
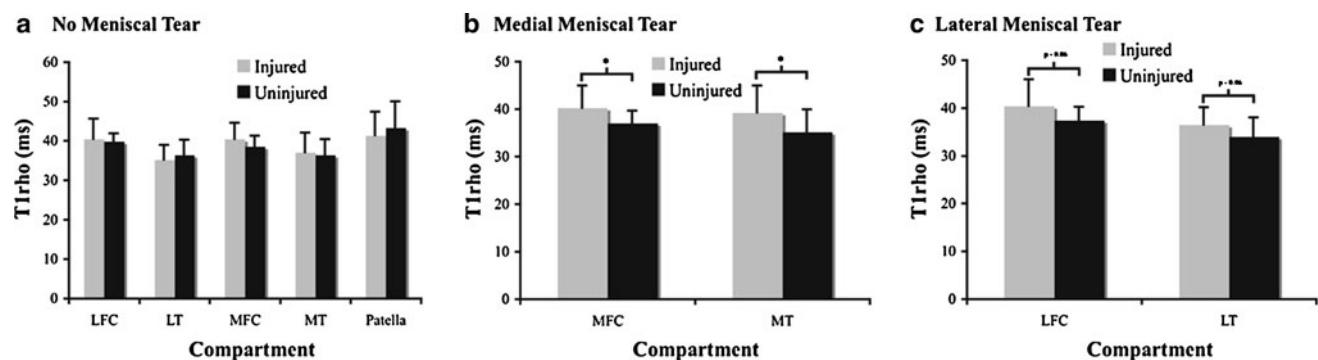

Fig. 3 Analysis of global articular $T_{1\rho}$ values in LFC, LT, MFC and MT in patients with and without medial and/or lateral meniscal tears. **a** Note that there are no differences in $T_{1\rho}$ values in all cartilage compartments between injured and uninjured knees in patients without meniscal tears. **b** In patients with a medial meniscal tear, the MFC and MT have significantly higher global $T_{1\rho}$ values compared to the respective regions in uninjured, contralateral knees. **c** Patients with lateral meniscal tears have elevated global $T_{1\rho}$ values in the LFC and LT compared to respective regions in uninjured, contralateral knees, with the difference approaching significance
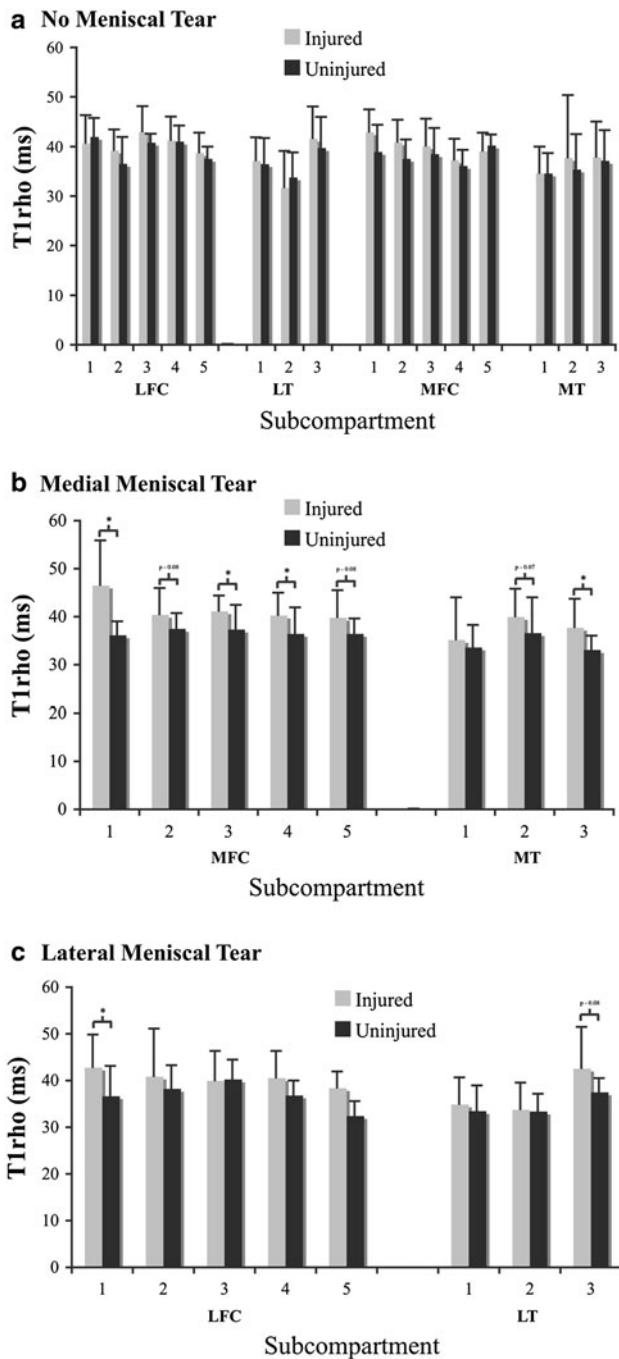
Fig. 4 Analysis of articular $T_{1\rho}$ values in sub-compartments of the LFC, LT, MFC and MT in patients with and without medial and/or lateral meniscal tears. **a** Note that there are no differences in $T_{1\rho}$ values in all cartilage sub-compartments between injured and uninjured knees in patients without meniscal tears. **b** In patients with a medial meniscal tear, the entire MFC and the femorotibial contact region and posterior cartilage region in the MT (MT-2,3) have higher global $T_{1\rho}$ values compared to the respective regions in uninjured, contralateral knees. **c** Patients with lateral meniscal tears have elevated $T_{1\rho}$ values in the anterior and posterior cartilage regions of the LFC (LFC-1,2,5) and the posterior LT (LT-3) compared to respective regions in uninjured, contralateral knees

damage. This question was addressed by performing a sub-analysis comparing the injured and uninjured knees of patients with an ACL injury and an associated meniscal tear. The injured knees of patients with medial meniscal tears had significantly elevated $T_{1\rho}$ values throughout the MFC and in the MT, particularly in the contact region of the medial tibia (MT-2) and the cartilage underlying the posterior meniscal horn (MT-3). Additionally, the injured knees of patients with lateral meniscal tears had significantly elevated $T_{1\rho}$ values in the cartilage underlying the posterior meniscal horn (LT-3) and in the most anterior and posterior cartilage sub-compartments of the LFC (LFC-1,2,5). Importantly, no differences were found between sub-compartments of the injured knee and uninjured, contralateral knee in patients without meniscal tears (data not shown). The data presented herein suggest that the presence of meniscal damage at the time of ACL injury is a risk factor for cartilage degeneration in the femorotibial compartments on the side of the injured meniscus. These results are consistent with reports from long-term observational cohort studies [20, 32, 34, 37]. For example, von Porat et al. [32] found that 59 % of subjects with a meniscus tear at the time of ACL tear had radiographic changes equivalent to Kellgren and Lawrence grade 2 or worse compared to 1 % of patients without a meniscal tear. Wu et al. [33] also found that patients who had undergone any degree of meniscal resection had worse subjective and objective functional outcomes 10.4 years after ACL reconstruction compared to those without a meniscal tear.

This study has limitations, which include its cross-sectional design, the relatively few number of patients evaluated, the absence of correlation between MRI findings and post-operative clinical laxity, histologic cartilage samples, arthroscopic evaluations or functional outcome scores, that is, KOOS, IKDC and no comparison to a control cohort with two "normal" knees. Additionally, the heterogeneity of each meniscal tear (i.e. location, size, type) is an important limitation of the study, as different types of tears in different locations and subsequent treatments are known to result in significantly different effects on tibiofemoral contact forces and overall knee biomechanics [2, 3, 25]. As the study evaluates patients at only the 12–16-month post-operative time point, conclusions cannot be drawn as to whether the observed $T_{1\rho}$ values represent lower, stable or higher values relative to the time of injury and early post-operative follow-up time points. However, the observed increased $T_{1\rho}$ values in the medial compartment of the knee likely represent a change from earlier post-operative time points, as previous studies have found that the medial compartment's cartilage $T_{1\rho}$ values are not elevated initially after the injury and subsequently increase overtime [33]. A significant question that should be addressed is

whether the observed $T_{1\rho}$ values remain elevated at later time points following ACL injury and whether the observed radiographic properties correlate with histologic cartilage samples and/or whether they can predict current or future functional status. Answers to these questions are critical, as they may elucidate whether these regions represent cartilage "hot spots" for post-traumatic osteoarthritis following ACL injury in reconstructed knees. In order to address all these pressing questions, future studies ideally should be prospective in nature, include longer follow-up time points and correlate radiographic findings to histologic samples, arthroscopic findings and/or functional outcome scores.

Conclusion

Quantitative $T_{1\rho}$ MRI is capable of detecting cartilage matrix changes in the medial compartments of ACL-injured knees compared to uninjured, contralateral knees as early as 12 months post-ACL reconstruction. The presence of a meniscal tear may be a significant risk factor for cartilage matrix injury in the femorotibial compartments on the side of the meniscal tear. Thus, $T_{1\rho}$ MRI holds great potential as a modality for detection of early, asymptomatic cartilage damage in ACL-reconstructed knees. Such capability of non-invasive and early detection of cartilage matrix changes will be helpful clinically in stratifying patients, monitoring early joint degeneration and allowing potential early pharmacologic and/or rehabilitation interventions to ultimately improve patient management after acute injuries.

Conflict of interest The authors declare that they have no conflict of interest.

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