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Longitudinal changes in MR T1ρ/T2 signal of meniscus and its association with cartilage T1ρ/T2 in ACL-injured patients

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SUMMARY

Objective: To evaluate the longitudinal changes in meniscal T1ρ/T2 signal post-reconstruction in patients with acute anterior cruciate ligament (ACL) injury and to investigate the association with T1ρ/T2 signal in articular knee cartilage.

Method: In this prospective study, knees of 37 patients with ACL-injury and reconstruction in addition to 13 healthy controls were scanned using magnetic resonance imaging (MRI) T1ρ/T2 mapping. Quantitative analysis of the meniscus was performed in the anterior/posterior horns of lateral/medial meniscus fourteen sub-compartments of cartilage spanning the medial/lateral area of the tibia and femoral condyles. Meniscus T1ρ/T2 signals were compared between injured, contralateral and control knees at baseline, 6-months, 1-year and 2-years using *t*-tests for cross-sectional comparisons and a mixed model for longitudinal comparisons. Pearson-partial correlations between meniscal and cartilage T1ρ/T2 were evaluated.

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Conflicts of interest

All authors have no conflicting interests to disclose.

Supplementary data

Supplementary data related to this article can be found at https://doi.org/10.1016/j.joca.2018.02.001.

Results: There was a significant decrease of T1ρ/T2 signal in the posterior horn of lateral meniscus (PHLAT) of injured knees during a 2-year period. In the posterior horn of medial meniscus (PHMED), T1ρ/T2 signal of injured knees was significantly elevated at all time points post-reconstruction compared to contralateral and control knees. Within injured knees, PHMED T1ρ/T2 signal showed significant positive correlations with medial tibia (MT) cartilage T1ρ/T2 signal at all time points.

Conclusion: A significant decrease in PHLAT T1ρ/T2 signal by 2-years suggests potential tissue recovery after ACL-injury. Elevated T1ρ/T2 signal in the PHMED of injured knees at 2-years correlating with knee cartilage T1ρ/T2 signal elevations suggests involvement of the PHMED in subacute cartilage degeneration after ACL-injury and reconstruction.

Keywords

Meniscus; T1ρ; T2; Quantitative magnetic resonance imaging; Anterior cruciate ligament injury; Osteoarthritis

Introduction

Patients with acute anterior cruciate ligament (ACL) injury are at high risk for the development of post-traumatic osteoarthritis despite the functional stability provided by surgical reconstruction[1,2]. The menisci are important structures that provide protection for articular cartilage and stabilization of the joint[3]. Acute meniscal tears often occur alongside traumatic ACL tears, especially in the lateral meniscus[4]. In addition, osteoarthritis and chronic ACL-injured patients present with higher rates of tears in the medial meniscus[5]. The specific associations and longitudinal relationships between meniscal injury and osteoarthritis in patients with ACL-injury are still under active investigation.

Quantitative magnetic resonance imaging (qMRI) provides information on early tissue matrix degeneration significantly earlier than standard morphological assessment of clinical magnetic resonance imaging (MRI) studies[6]. While many studies have demonstrated elevated T1ρ and T2 values in the articular knee cartilage of patients with osteoarthritis or ACL injuries compared to controls, studies quantifying changes in the meniscus matrix associated with osteoarthritis or joint injury are very limited[7–12]. T1ρ and T2 imaging allows for evaluation of meniscal fibrocartilage which consists of 98% type I collagen, 1% proteoglycans and 1% water[13,14]. Meniscal injury is characterized by biochemical changes in this collagen-proteoglycan matrix, which are in turn strongly associated with osteoarthritic cartilage[15,16]. Previous studies have used T1ρ and T2 imaging successfully to quantify tissue composition allowing for differentiation between the menisci of healthy controls and those of patients with early osteoarthritis[5,10]. Prior studies show that mean meniscal T1ρ and T2 relaxation times in the lateral meniscus are significantly higher in ACL-injured knees compared to control and contralateral knees after acute, traumatic injury[17]. However, no studies have yet reported longitudinal changes of meniscus matrix after acute ACL-injury. While longitudinal changes in T1ρ/T2 relaxation times in knee cartilage following ACL-injury are widely documented, it is unclear whether longitudinal change occurs in the meniscus and whether these possible changes vary by the location[11,18,19]. In addition, while studies have demonstrated the relationship between gross

morphologic changes of the meniscus and T1ρ/T2 relaxation times of articular cartilage, it is unclear whether a relationship exists between T1ρ/T2 relaxation times of the meniscus and those of articular cartilage[20,21].

Therefore, the objectives of this study were (1) to follow longitudinal changes in T1ρ and T2 values in the meniscus after acute ACL injury and reconstruction, and (2) to investigate the relationship between meniscus damage and cartilage matrix health evaluated by T1ρ and T2 imaging.

Methods

Patients

This longitudinal prospective study included two groups of patients: 37 patients with unilateral ACL injuries (16 females) with an average age of 29.6 (+/− 8.0 years) and an average BMI of 23.8 (+/− 2.5 kg/m^2); and 13 controls (5 females) with an average age of 31.3 (+/− 4.8 years) and an average BMI of 23.5 (+/−1.9 kg/m^2). There was no significant difference in age, gender or BMI between ACL-injured patients and controls. ACL-injured patients were scanned at baseline (BL) prior to surgery (the average time to injury was 47 days) and then again post-reconstruction at 6 months (6mo), 1 year (1yr) and 2 years (2yr). Controls without a prior history of knee injury, surgery or clinical symptoms of osteoarthritis were scanned at BL and then again at 2yr following initial scan. Additionally, four healthy volunteers were scanned two times during the same MRI session to assess the reproducibility of our data collection and processing method. All the images were first segmented manually and the scan/rescan coefficients of variation (CVs) were computed, these results were then compared with CVs obtained when just the first scans were segmented manually and the second ones were computed automatically, by applying the registration technique described above. This study obtained IRB approval and informed consent was obtained from all enrolled patients.

Surgery

All ACL-injured patients had single-bundle ACL reconstruction done by one of four experienced sports fellowship-trained orthopaedic surgeons from a single institution. Anteromedial portal drilling was used to drill the femoral tunnels. Soft tissue grafts were used for reconstruction: either hamstrings (autograft of allograft) or posterior tibialis allograft. Some patients received partial meniscectomies at the time of ACL reconstruction: two patients with medial partial meniscectomies, four patients with lateral partial meniscectomies and one patient with both medial and lateral partial meniscectomies. In addition, two other patients received lateral meniscus repair and three other patients received chondroplasty (one in the lateral tibia (LT) and two in the patella). All patients underwent similar postoperative rehabilitation programs at the same institution’s sports medicine clinic.

MRI protocol

Knees were scanned using a 3 T MRI scanner (General Electric, Milwaukee, WI, USA) with an 8-channel phased array knee coil (Invivo, Orlando, FL, USA) for all times points. In ACL-injured patients, the injured knee was scanned before the contralateral, uninjured knee.

In control patients, the knee that was scanned first was randomized. Imaging protocols included (1) sagittal T2-weighted 3D fast spin-echo (CUBE) images [repetition time (TR)/ echo time (TE) = 1500/25 ms, field of view (FOV) = 16 cm, matrix = 384 × 384, slice thickness = 1 mm, echo train length 50, bandwidth = 50 kHz, number of excitations 0.5] and (2) sagittal 3D T1ρ and T2 quantification sequences [TR/TE = 9 ms/min full, FOV = 14 cm, matrix = 256 × 128, slice thickness = 4 mm, Views per, segment = 64, time of recovery = 1.2 s, spin-lock frequency = 500 Hz, ARC phase AF = 2, time of spin lock (TSL) = 0/10/40/80 ms for T1ρ, and preparation TE = 0/13.7/27.3/54.7 ms for T2][22]. The combined time for acquisition of the T1ρ and T2 sequences was 9 min and 37 s with the total time for one knee scan, including setup, being less than 1 h. CUBE images were used for segmentation and clinical morphological scoring of the meniscus and articular cartilage of the knee. The above protocol was used to measure T1ρ and T2 in both meniscus and articular cartilage but for meniscus analysis, the last echo time (80 ms for T1ρ, 54.7 ms for T2) was omitted because the last image had a very low signal-to-noise ratio (SNR) in the meniscus.

Clinical morphological analysis

CUBE images were used to perform semi-quantitative clinical grading of the meniscus and cartilage by two experienced musculoskeletal radiologists. Both radiologists were blinded to both patient information and T1ρ/T2 values. Meniscus and cartilage abnormalities were graded using a modified whole-organ magnetic imaging scoring (WORMS) method[23]. WORMS scores in the meniscus were defined as follows: 0 = normal meniscus, 1 = signal abnormality, 2 = non-displaced tear, 3 = displaced or complex tear without deformity, 4 = complete maceration of the meniscus.

Quantitative MRI analysis

All the image post processing was performed with a MATLAB (Mathworks, Natick, MA, USA) program developed in-house[24]. CUBE images were rigidly registered onto the first T1ρ weighted image (TSL = 0) and subsequently used for cartilage and meniscus segmentation at the baseline time point. Segmentations were done at baseline and T1ρ and T2 maps were calculated using methods previously demonstrated[10,25]. Articular cartilage and menisci were analyzed in separate yet parallel processes.

Menisci were segmented by a single trained user (AW) on registered baseline CUBE images into four compartments: anterior/posterior horn of lateral meniscus (AHLAT/PHLAT) and anterior/posterior horn of medial menisci (AHMED/PHMED). Three consecutive segmentations were used in each compartment. For all the later time points, a longitudinal non-rigid registration was adopted to align the follow up image on the baseline scan. The registration technique was an intensity based multi resolution pyramidal approach[26,27] previously adopted and extensively evaluated for articular cartilage automatic segmentations in the knee and in the hip[28,29]. Sample longitudinal segmentations with T1ρ and T2 maps are shown in Fig. 1. After registration, all the images were quality checked by a single user (JK) and errors in the automatic process were corrected with autosegmentation correctly defining 91.4% of all ROIs. The registration deformation field was computed in the T1ρ-weighted image with TSL = 0 characterized by higher SNR and then applied on all the later

echoes. T1ρ and T2 maps were then computed voxel-by-voxel by fitting the mono-exponential decay:

$$\mathrm{S(TSL)}\alpha \exp\left(-\frac{TSL}{T1\rho}\right)$$

$$\mathrm{S(TE)}\alpha \exp\left(-\frac{TE}{T2}\right)$$

For articular cartilage, six cartilage compartments were identified using a semiautomatic strategy: medial femoral condyle (MF), medial tibia (MT), lateral femoral condyle (LF), LT, patella (P) and trochlea (TrF). These were then further subdivided into 14 total compartments defined by the edges of the menisci as previously described[11]. Cartilage longitudinal registration was performed applying the same technique described for the meniscus. The T1ρ and T2 values of each compartment of articular cartilage and meniscus were computed as the mean value of all pixels in each ROI.

Statistical analysis

Mean and standard deviations of T1ρ and T2 relaxation times for menisci sub-compartments were calculated at all time points for injured, contralateral, and control knees. For longitudinal comparisons, statistical analysis was performed using STATA version 14 software (StataCorp LP, College Station, TX). Mixed models (accounting for changes over time, multiple knees *per* control and adjusted for age, gender and BMI) were used to assess the differences in sub-compartments of the meniscus from baseline to 2-year follow-ups between injured, contralateral and control groups. All other statistical analyses were performed using SPSS Statistics version 23.0 (IBM, Armonk, NY). For cross-sectional analyses, paired *t*-tests were performed when comparing injured knees vs. contralateral knees of the same patient and unpaired student's *t*-tests were performed when comparing injured or contralateral knees to control patients' knees. Pearson-partial correlation coefficients were calculated for meniscal T1ρ/T2 values vs. meniscal WORMS score, cartilage WORMS score and cartilage T1ρ/T2 values after adjustment for age, gender and BMI. Significance was defined as a *P*-value <0.05 for *t*-tests, mixed models and regression analysis.

Results

Reproducibility

Across the four volunteers that were scanned two times, scan/rescan reproducibility showed an average CV of 3.07% of average T1ρ/T2 values when the scan was manually segmented and the rescan was automatically segmented using the scan segmentation as reference. The scan/rescan CV was 4.33% of average T1ρ/T2 values when both scan and rescan were manually segmented.

Longitudinal MR T1ρ and T2 values of menisci

Fig. 2 shows the mean T1ρ and T2 values with standard deviations of the posterior horn of medial meniscus (PHMED) and PHLAT. See Supplementary Table 1 for raw numerical values of all four compartments at each time point. At all-time points in all compartments, injured knees demonstrated greater average T1ρ and T2 values compared to contralateral and control knees, regardless of significance.

Table I shows the *P*-values for comparisons between injured, contralateral and control knees. There was no significant difference between contralateral and control knees at any time point. In PHLAT, both T1ρ and T2 were significantly higher in the injured knees than the contralateral knees at BL (T1ρ: $P < 0.0005$, T2: $P = 0.008$), 6mo (T1ρ: $P = 0.009$, T2: $P = 0.037$) and 1yr (T1ρ: $P = 0.005$, T2: $P = 0.013$) and significantly higher in T1ρ than control knees at BL ($P = 0.003$), while this significance disappeared at 2yr. In PHMED, T1ρ and T2 were significantly higher in the injured knees than the contralateral knees and control knees at all time points except for BL T1ρ. No significance was observed for anterior horns except for AHLAT T2 at BL ($P = 0.005$) and T1ρ at 6mo ($P = 0.004$) which were significantly higher in injured knees than contralateral knees.

For the longitudinal analysis of changes in T1ρ and T2 values between baseline and 2 years, a mixed model was generated as described above. Only the PHLAT showed significant changes from baseline to 2 years demonstrating a significantly negative rate of change in T1ρ signal during this time period ($P < 0.001$). No other compartment demonstrated significant longitudinal changes in T1ρ or T2 values. In addition, only the PHLAT showed a significant difference between the rates of change of T1ρ values of injured knees compared to contralateral knees ($P = 0.029$). No other compartments demonstrated significant differences in the rate of change of T1ρ or T2 values between any groups. See supplementary Tables 2 and 3 for complete results in all compartments.

Within the ACL-injured group, there was no significant difference in T1ρ and T2 values between those with partial meniscectomies and those without in any compartment at any time point. In addition, there was no significant difference in the longitudinal rates of change between these two groups.

Meniscus WORMS and correlations with T1p/T2

WORMS scores for PHLAT and PHMED of ACL-injured knees at each time point are shown in Table II. The WORM scores were all 0 for the AHMED and predominantly 0 (>95%) in the AHLAT. There was no significant difference in average WORMS score of injured knees between any time point in any compartment. ACL-injured knees had significantly higher average WORMS scores compared to contralateral and control knees in each compartment (contralateral and control knees are not shown). Table III shows adjusted Pearson-partial correlation coefficients and *P*-values between WORMS and T1ρ and T2 values at each corresponding time point in the PHMED. Significant positive correlations between Meniscus WORMS scores and T1ρ/T2 relaxation times were seen in the PHMED at all time points. As expected, strong baseline correlations persisted up through 2 years between WORMS and T1p/T2 relaxation times. In the PHLAT, only one significant positive

correlation was seen at 6 months between T2 and WORMS (P= 0.041). Also, as expected, there were no significant correlations between meniscus WORMS and T1ρ/T2 values in the AHLAT and AHMED.

Meniscus T1ρ/T2 correlations with cartilage T1ρ/T2

Significant positive correlations were found between meniscus T1ρ/T2 values in the PHMED and cartilage T1ρ/T2 relaxation times. Notable significant correlations are shown in Table IV. Baseline T1ρ values in the PHMED showed positive correlations with T1P values in MT cartilage at all time points post-reconstruction, especially in the posterior MT. Baseline T2 values in the PHMED showed significant correlation with baseline posterior MT cartilage and both global and posterior MT cartilage at 6 months and 2 years. A positive but nonsignificant correlation between T2 values in the PHMED and global and posterior MT cartilage was seen at 1 year. No other compartments of the knee (AHLAT, AHMED, PHLAT) had any significant correlations with any sub-compartments of cartilage in the tibia, femur or patella.

Discussion

This longitudinal study used qMRI to track changes in T1ρ/T2 relaxation times in the menisci of patients with ACL-injury and to determine their association with T1ρ/T2 relaxation times of articular cartilage. Notably, we found a significant decrease in PHLAT T1ρ signal and a persistent elevation in PHMED T1ρ/T2 signal in injured knees compared to contralateral and control knees from baseline to 2 years. In addition, we demonstrated a significantly positive correlation with baseline PHMED T1ρ/T2 signal and longitudinal T1ρ/T2 signal in overlying articular cartilage up to 2 years. This is the first study to demonstrate longitudinal changes in T1ρ and T2 relaxation times in menisci, and their interrelationship with cartilage matrix health after ACL-injury and reconstruction.

Longitudinal T1ρ and T2 values

This study demonstrates an initial elevation in meniscal T1ρ and T2 relaxation times in acute ACL-injured knees compared to uninjured knees. We, again, demonstrated the baseline elevations in T1ρ and T2 in the PHLAT of ACL-injured patients as seen in a previous baseline study of patients with ACL-injury and subsequent reconstruction, despite a smaller sample size (52 vs. 37 ACL-injured patients)[25].

Significant differences were more often located in the posterior horns of the meniscus throughout the study. This agrees with previous studies that have demonstrated higher T1ρ values in the posterior horn of menisci compared to the anterior horn and more tears in the posterior horn than anterior horn in ACL-injured patients[30,31]. This observation makes sense mechanically, as when the ACL is disrupted there is anterior subluxation of the tibia relative to the femur causing the femoral condyle to slide over the posterior margin of the tibia and apply significant contact stress on the posterior menisci[32,33].

At baseline, while multiple compartments had significantly elevated baseline qMRI values (AHLAT, PHLAT, PHMED), not all compartments were consistent in T1ρ/T2 elevations. The PHLAT not only had the highest baseline elevation in T1ρ/T2 values compared to

contralateral and control knees, but it was also the only compartment with significant elevation in both T1ρ/T2 values. These results further the conclusions of previous qMRI and structural studies that suggest involvement of the lateral meniscus in acute ACL-injury[16,34–36]. This study demonstrates that the PHLAT of injured knees was the only compartment that showed a significantly negative rate of change in T1ρ relaxation time over a 2-year period. This finding aligns with a previous study that tracked the development of structural changes in the lateral meniscus and observed a decrease in lateral meniscus tears in a chronic ACL-injured group compared to the acutely ACL-injured, postulating potential healing in this compartment in a chronic time course[4]. While our study was quantitative and not structural, our results align with the theory that the acute damage sustained by the lateral meniscus may be reversed over time.

In the PHMED, the elevation of T1ρ and T2 relaxation times in ACL-injured knees compared to control groups may represent prolonged degeneration which agrees with structural studies linking chronic ACL-injury with medial meniscus pathology[34,36]. While there was not a significant increase in T1ρ or T2 values over this time period in the PHMED, it was the only compartment that stayed consistently elevated at each cross-sectional time point over a 2-year period, demonstrating a potential inability for this compartment to recover from initial damage. This is the first qMRI study to demonstrate chronic medial meniscal pathology in ACL-injured patients but several studies have linked osteoarthritis to medial meniscal pathology[16,37–39]. The mechanism behind these changes remains unknown. While ACL-reconstructed knees have closer kinematics to uninjured knees compared to ACL-deficient knees, biomechanical abnormalities persist in the reconstructed group[40–42]. It could be that these kinematic change in knees with ACL-injury and subsequent reconstruction lead to greater reliance on the medial meniscus as a secondary stabilizer of the knee, subsequently causing greater force transmission through the PHMED and degeneration[43,44]. Whatever the cause may be, the significant number of ACL-injured patients who develop osteoarthritis implicate the PHMED as a potential contributor.

Relationship to meniscus WORMS

In this study, we found a strong positive correlation with WORMS in the PHMED at baseline. In addition, longitudinally we found that the correlation between WORMS and T1ρ/T2 relaxation times persists at all time points in the PHMED. This finding further supports the notion of chronic injury to the meniscus being localized to PHMED. Previous studies have found positive correlation between T1ρ and T2 relaxation times and WORMS scores in the menisci of patients with osteoarthritis, especially in the medial meniscus[5,16]. Interestingly, in the PHLAT we saw no significant changes in WORMS scoring when comparing 2 years to baseline scores while there were significant longitudinal changes in T1ρ and T2 values in this compartment. These findings show the potential of T1ρ/T2 imaging as a more powerful tool to evaluate subacute, subclinical changes in meniscus structure and composition in comparison to gross structural studies[5,16].

Relationship of meniscus T1ρ/T2 to cartilage T1ρ/T2

Prior studies have demonstrated an association with structural lesions of the PHMED and tibial cartilage T1ρ/T2 values in ACL-injured patients but none have looked at the direct

association between the T1ρ/T2 values of the meniscus and those of tibial cartilage[20,21]. In accordance with previous studies in patients who have already developed osteoarthritis, we show a significant positive correlation with baseline T1ρ/T2 relaxation times in the PHMED and 2-year T1ρ/T2 relaxation times in the MT[15,16]. As expected the strongest associations were seen between the PHMED and the cartilage of the posterior MT as this compartment of the meniscus directly overlies this sub-compartment of knee cartilage. This result suggests that baseline PHMED damage may predict subsequent degeneration of the underlying tibial cartilage. Lesser but still significant associations were seen between the PHMED and central MT and global MT compartments, suggesting potential global degeneration of the MT due to PHMED damage. Interestingly, the PHLAT showed no significant positive associations with any cartilage compartment despite having the largest baseline elevation in T1ρ/T2 relaxation times of any compartment of the meniscus, further supporting the previously discussed notion that the PHLAT is more associated with acute, traumatic knee injury rather than chronic knee degeneration. Studies in patients with OA have demonstrated variable patterns of T1ρ/T2 relaxation times elevation in specific knee cartilage compartments but most studies agree on a significant elevation of articular cartilage T1ρ/T2 relaxation times in patients with OA[7,39,45]. Studies in patients with acute ACL-injury and reconstruction also show varying patterns of T1ρ/T2 relaxation times elevation in knee cartilage compartments, but all agreed on a significant elevation in the MF cartilage in the range of 1–5 years post-injury[18,46,47]. Interestingly, two of these previously mentioned studies demonstrated increased T1ρ/T2 relaxation times in the weight bearing regions of the tibiofemoral condyle in patients with PHMED injury in agreeance with our results.

Many studies have focused on initial meniscus and cartilage T1ρ/T2 values in patients with ACL-injury or later values in patients with osteoarthritis. The exactly interplay between meniscus damage, cartilage damage and the development of osteoarthritis remains elusive. This is the first study to study the longitudinal development of meniscus T1ρ/T2 relaxation times and correlate them to cartilage T1ρ/T2 relaxation times. These findings demonstrate the utility of quantitative MR imaging as a more sensitive detector of compositional differences within the meniscus compared to a morphological grading system.

Limitations

Despite the promising results, there were limitations to this study. First, our cohort was only followed for 2 years limiting our study to the subacute time period, well before clinical or radiographic signs of osteoarthritis can be observed. This short time period also influenced our ability to distinguish true osteoarthritic knee degeneration from subacute changes due to traumatic injury. In addition, no concurrent knee pathology that may have contributed to cartilage degeneration, for example synovitis, was assessed either clinically or by synovial fluid analysis. The impact of this error is likely limited by our relatively young and healthy patient population but as we did not truly assess any other potential pathology, the possibility of a confounding factor cannot be excluded. Also, due to the nature of longitudinal studies, loss to follow up presented a limitation to the power of this study giving us a modest cohort size. Finally, our study was limited to quantitative MR data with no inclusion of clinical data. Therefore, while our findings may be statistically significant and compelling, the clinical relevance will need to be determined.

Conclusion

The sensitivity of quantitative MRI can be valuable in elucidating the mechanisms of subtle degenerative changes in the cartilage of patients with traumatic knee injuries compared to a morphological grading system. In addition, the changes in quantitative MRI signal demonstrated in this study suggest a greater role for the meniscus in the development of knee cartilage degeneration after acute, traumatic knee injury. In the future, quantitative MR may be a method by which we can predict and track future cartilage degeneration. With more sensitive quantitative measurements, we can better determine patients' responses to medical treatment including preventative treatment of osteoarthritis.

Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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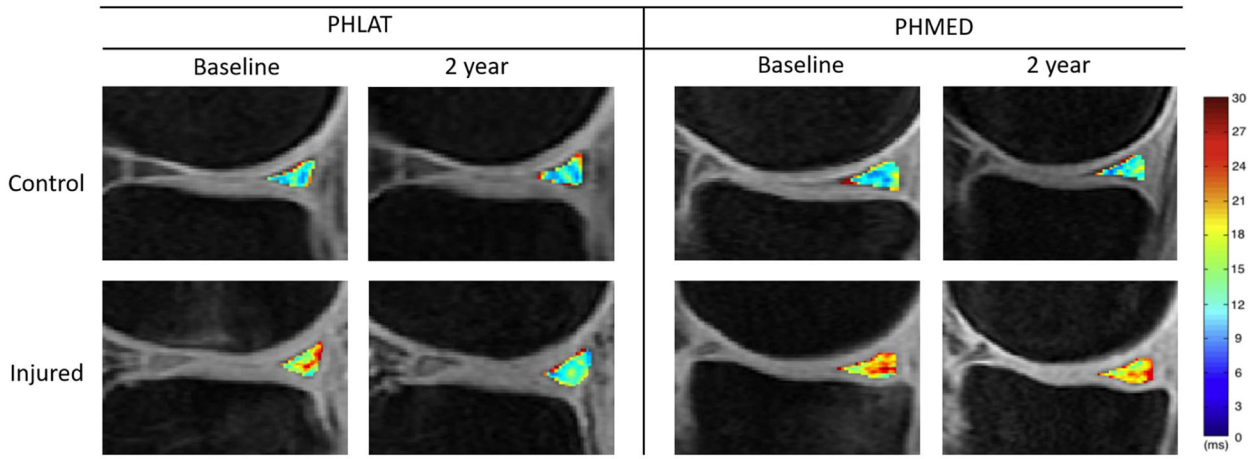

Fig. 1.

Representative MR images showing the posterior horn of lateral and medial meniscus in injured patients and controls at both baseline and 2-year illustrating the relative longitudinal changes in these compartments in each patient group.

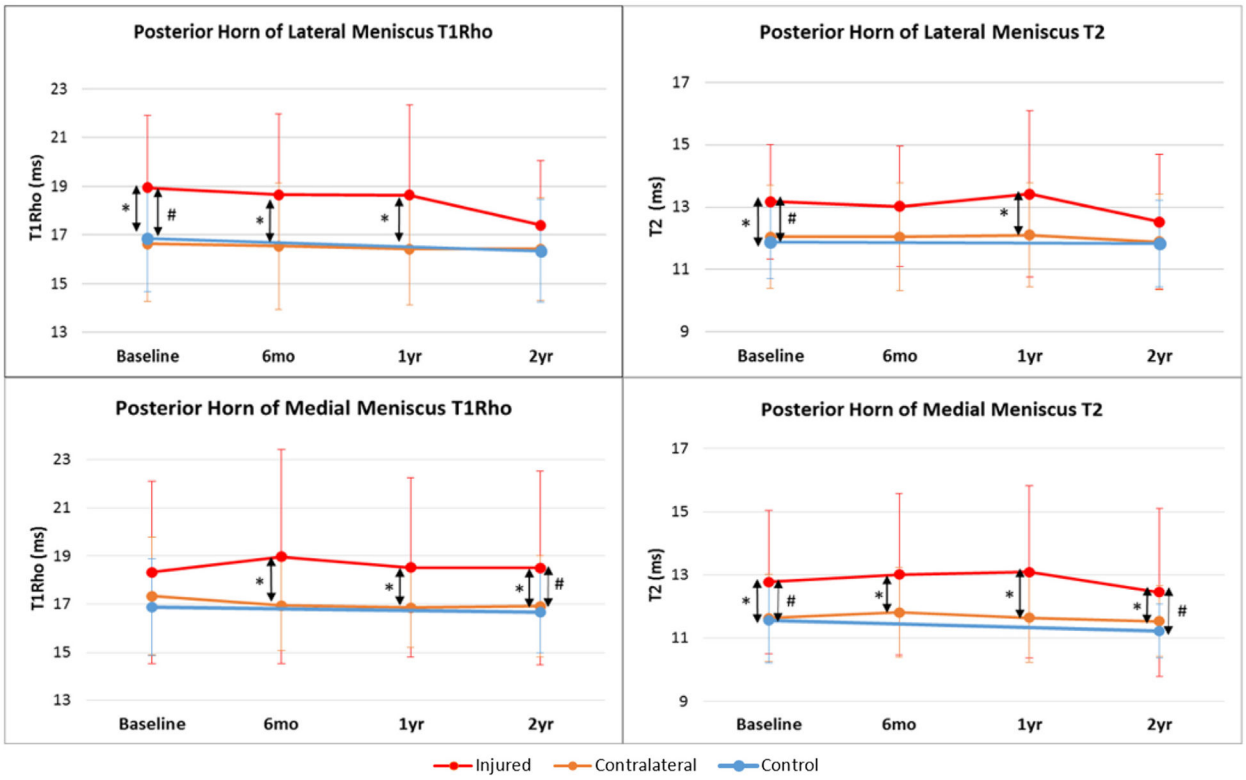

Fig. 2.

Longitudinal T1ρ and T2 values in the posterior horn of lateral and medial meniscus with standard deviations and significant comparisons highlighted. A * indicates a significant cross-sectional difference between injured and contralateral knees of injured patients. A # indicates a significant cross-sectional difference between injured knees and control knees.

Table I

P-values of MR T1ρ and T2 *t*-test comparisons

Injured vs. Contra (Paired *t*-test)								
	T1ρ				**T2**			
	BL	**6mo**	**1yr**	**2yr**	**BL**	**6mo**	**lyr**	**2yr**
AHLAT	0.168	**0.004**	0.690	0.362	**0.005**	0.091	0.741	0.125
PHLAT	**<0.0005**	**0.009**	**0.005**	0.149	**0.008**	**0.037**	**0.013**	0.140
AHMED	0.758	0.677	0.653	0.701	0.255	0.302	0.017	0.413
PHMED	0.096	**0.005**	**0.015**	**0.049**	**0.005**	**0.008**	**0.003**	**0.033**

Injured vs. Control (Unpaired *t*-test)					**Contra vs. Control (Unpaired *t*-test)**				
	T1ρ		**T2**			**T1ρ**		**T2**	
	BL	**2yr**	**BL**	**2yr**		**BL**	**2yr**	**BL**	**2yr**
AHLAT	0.371	0.268	0.136	0.137	AHLAT	0.994	0.653	0.505	0.818
PHLAT	**0.003**	0.097	**0.004**	0.163	PHLAT	0.711	0.892	0.600	0.891
AHMED	0.985	0.774	0.545	0.243	AHMED	0.823	0.995	0.685	0.544
PHMED	0.081	**0.045**	**0.017**	**0.026**	PHMED	0.436	0.641	0.815	0.233

Bold = significant comparison (*P* value < 0.05).

Table II

WORMS Grades for each compartment of anterior cruciate ligament (ACL)-injured knees at each time point

	Baseline	6 months	1 year	2 years
PHLAT				
Grade 0	18	19	18	17
Grade 1	7	5	6	6
Grade 2	10	11	11	12
Grade 3	2	2	2	2
Grade 4	-	-	-	-
PHMED				
Grade 0	22	22	22	22
Grade 1	5	3	3	3
Grade 2	7	9	9	9
Grade 3	2	2	2	2
Grade 4	1	1	1	1

Table III

Meniscus T1ρ and T2 Correlation with Meniscus WORMS in posterior horn of medial meniscus (PHMED) and posterior horn of lateral meniscus (PHLAT) at each time point

		T1ρ				T2			
		BL	6mo	1yr	2yr	BL	6mo	lyr	2yr
PHMED	r	**0.720**	**0.604**	**0.564**	**0.513**	**0.658**	**0.667**	**0.467**	**0.583**
WORMS	P	**<0.0005**	**<0.0005**	**<0.0005**	**0.001**	**<0.0005**	**<0.0005**	**0.004**	**<0.0005**
PHLAT	r	0.207	0.329	0.235	0.272	0.014	**0.353**	0.121	0.141
WORMS	P	0.240	0.057	0.182	0.120	0.935	**0.041**	0.497	0.428

Legend: *r* = pearson–correlation coefficient, *P* = *P*-value.

Significant correlations in **Bold**.

Table IV

T1ρ/T2 in PHMED Correlated with Cartilage T1ρ/T2 in medial tibia (MT)

T1ρ									
		BL Cartilage		**6mo Cartilage**		**1yr Cartilage**		**2yr Cartilage**	
		Glbl. MT	**Post. MT**	**Glbl. MT**	**Post. MT**	**Glbl. MT**	**Post. MT**	**Glbl. MT**	**Post. MT**
Baseline	r	0.242	0.249	**0.499**	**0.584**	**0.517**	**0.596**	**0.420**	**0.478**
Meniscus	P	0.174	0.163	**0.003**	**<0.0005**	**0.002**	**<0.0005**	**0.015**	**0.005**
T2									
		BL Cartilage		**6mo Cartilage**		**lyr Cartilage**		**2yr Cartilage**	
		Glbl. MT	**Post. MT**	**Glbl. MT**	**Post. MT**	**Glbl. MT**	**Post. MT**	**Glbl. MT**	**Post. MT**
Baseline	r	0.315	**0359**	**0.478**	**0.540**	0.293	0.268	**0.414**	**0.447**
Meniscus	P	0.07	**0.037**	**0.004**	**0.001**	0.098	0.132	**0.015**	**0.008**

Legend: *r* = pearson–correlation coefficient, *P* = *P*-value, MT = Medial Tibia, Glbl. = Global, Post. = Posterior.

Significant correlations in **Bold**.