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Chondral Injury Associated With ACL Injury: Assessing Progressive Chondral Degeneration With Morphologic and Quantitative MRI Techniques

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Background: Anterior cruciate ligament (ACL) injuries are associated with a risk of post-traumatic osteoarthritis due to chondral damage. Magnetic resonance imaging (MRI) techniques provide excellent visualization and assessment of cartilage and can detect subtle and early chondral damage. This is often preceding clinical and radiographic post-traumatic osteoarthritis.

Hypothesis: Morphologic and quantitative MRI techniques can assess early and progressive degenerative chondral changes after acute ACL injury.

Study Design: Prospective longitudinal cohort.

Level of Evidence: Level 3.

Methods: Sixty-five participants with acute unilateral ACL injuries underwent bilateral knee MRI scans within 1 month of injury. Fifty-seven participants presented at 6 months, while 54 were evaluated at 12 months. MRI morphologic evaluation using a modified Noyes score assessed cartilage signal alteration, chondral damage, and subchondral bone status. Quantitative T1ρ and T2 mapping at standardized anatomic locations in both knees was assessed. Participant-reported outcomes at follow-up time points were recorded.

Results: Baseline Noyes scores of MRI detectable cartilage damage were highest in the injured knee lateral tibial plateau (mean 2.5, standard error (SE) 0.20, $P < 0.01$), followed by lateral femoral condyle (mean 2.1, SE 0.18, $P < 0.01$), which progressed after 1 year. Longitudinal prolongation at 12 months in the injured knees was significant for T1ρ affecting the medial and lateral femoral condyles ($P < 0.01$) and trochlea ($P < 0.01$), whereas T2 values were prolonged for medial and lateral femoral condyles ($P < 0.01$) and trochlea ($P < 0.01$). The contralateral noninjured knees also demonstrated T1ρ and T2 prolongation in the medial and lateral compartment chondral subdivisions. Progressive chondral damage occurred despite improved patient-reported outcomes.

Conclusion: After ACL injury, initial and sustained chondral damage predominantly affects the lateral tibiofemoral compartment, but longitudinal chondral degeneration also occurred in other compartments of the injured and contralateral knee.

Clinical Relevance: Early identification of chondral degeneration post-ACL injury using morphological and quantitative MRI techniques could enable interventions to be implemented early to prevent or delay PTOA.

Keywords: anterior cruciate ligament injury; post-traumatic chondral injury; post-traumatic osteoarthritis; quantitative and qualitative magnetic resonance imaging

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Anterior cruciate ligament (ACL) injuries are common, typically occurring in patients younger than 30 years of age, with an estimated yearly incidence up to 0.8 per 1000.[25,40] Management of ACL tears predominantly involves ACL reconstruction (ACLR), aiming to improve knee biomechanics and prevent further chondral and meniscal injuries.[23,25,34] One potential long-term consequence of ACL injury is an increased risk of post-traumatic osteoarthritis (PTOA), which has been shown to develop as early as 5 years after injury.[7,12,23,34] While ACLR has proved to be successful at restoring short-term functional stability of the injured knee and return to preinjury sports, it has not yet proved protective against PTOA.[7,17,23,25,34] Concomitant meniscal, cartilage, and ligamentous injuries sustained during initial ACL disruption also contribute to increased risk of PTOA; and meniscal injuries have been identified as an independent risk factor.[7,20,23] PTOA typically affects younger patients, resulting in a longer lifetime burden of disease compared with idiopathic osteoarthritis.[3,7,9]

Magnetic resonance imaging (MRI) is a noninvasive, multiplanar imaging modality that can accurately assess ACL and chondral injury.[20,34] Morphologic images using fast-spin echo (FSE) techniques are capable of detecting chondral lesions in the knee joint with high sensitivity (87%), specificity (94%), and accuracy (92%), as validated with direct arthroscopy.[35] One widely accepted grading system of articular cartilage is the modified Noyes score, in which the appearance and quantity of articular cartilage in the knee is scored using a semiquantitative scale.[26,29] This scale uses cartilage sequences that have high reproducibility, with a weighted kappa of 0.93.[35] Quantitative magnetic resonance imaging (qMRI) techniques such as T1ρ and T2 relaxation mapping correlate with the biochemical composition of the cartilage matrix, including proteoglycan content and the orientation of the collagen fibrils in the cartilage matrix, respectively.[18,21,42]

Prolongation of T1ρ and T2 values on MRI corresponds to changes in the extracellular cartilage matrix reflective of cartilage degeneration, which has been shown to be a reliable and validated marker of osteoarthritis.[4,24,28,30,31,48] qMRI techniques provide a noninvasive way of evaluating these early degenerative structural changes in the cartilage matrix, which often precede clinical or radiographic manifestations of established arthritis.[27,30,31,48,50]

Our earlier study reported the preliminary qMRI cartilage values post-ACL injury in a post-ACLR cohort for the first 6-month postoperative period. This demonstrated multiple regions of prolonged relaxation affecting the injured and contralateral knees.[2] This study aims to characterize the progressive degenerative changes after ACL injury using both morphologic MRI and qMRI techniques in the first 12 months after injury. We hypothesize that the initial cartilage injury at time of the ACL injury will correlate with progressive matrix depletion in the surrounding cartilage compartments, and this will be evident on morphologic MRI and qMRI techniques.

METHODS

Study Participants

This study is part of a multicenter, prospective longitudinal cohort study examining progressive cartilage degeneration in participants with acute unilateral ACL tears. Participants with unilateral ACL injuries were identified and recruited from 3 participating study locations, and underwent baseline MRI of their injured knee within 40 days of acute injury. A flow diagram of all patients recruited for this longitudinal cohort has been previously published by Amano et al,[2] and updated for this current study (Figure 1). The contralateral noninjured knee was imaged with MRI as a control. Participants were followed with bilateral knee MRI scans and clinical assessment at 6 months and 1 year time points after injury. Informed written consent was obtained from each participant before study commencement, with local institutional review board approval and Health Insurance Portability and Accountability Act (HIPPA) compliance at each site. Sixty-five participants were included for baseline imaging and clinical assessment, while 57 participants returned at 6 months, and 54 returned at 12 months (Figure 1).

Inclusion criteria were as follows: acute unilateral full-thickness ACL tear by MRI and clinical examination, <40 days between initial injury and MRI, and age between 13 and 70 years at the time of injury. Exclusion criteria were as follows: radiographic evidence of early osteoarthritis grade 1 or 2 (OARSI Atlas),[1] history of cartilage resurfacing procedure at the time of injury, varus or valgus instability requiring collateral ligament repair or reconstruction, other injuries requiring surgical intervention, inability to undergo pre- and postinjury rehabilitation, history of previous high-grade knee injury, prior surgery to either knee, and poor quality/motion degradation of MRI. Low-grade injury to the collateral ligaments not resulting in instability or surgery was not a criterion for exclusion. If an unanticipated significant articular cartilage injury was discovered during follow-up, the patient was withdrawn.

ACLR was not an inclusion or exclusion criterion in this study; however, the majority of patients did undergo surgery (n = 61, 94%). Fifty-four participants from this cohort who underwent ACLR have previously been reported, which examined the initial baseline and 6-month postoperative clinical and quantitative MRI findings.[2] Surgery occurred at 3 institutions in the United States, performed by 11 sports fellowship-trained orthopaedic surgeons. Days to surgery across the 3 institutions from initial injury was mean 48 days.[2]

Patient-reported outcome measures (PROMs) were recorded at baseline and on subsequent follow-up visits. Participants completed the validated Knee Injury and Osteoarthritis Outcome Score (KOOS) and the Western Ontario and McMaster Universities Osteoarthritis Index (WOMAC).[5,39]

Magnetic Resonance Image Acquisition

Participants underwent bilateral MRI knee scans at each study visit: baseline, 6 months, and 1 year postinjury. MRI evaluations were all performed utilizing identical 3 Tesla MRI units (GE

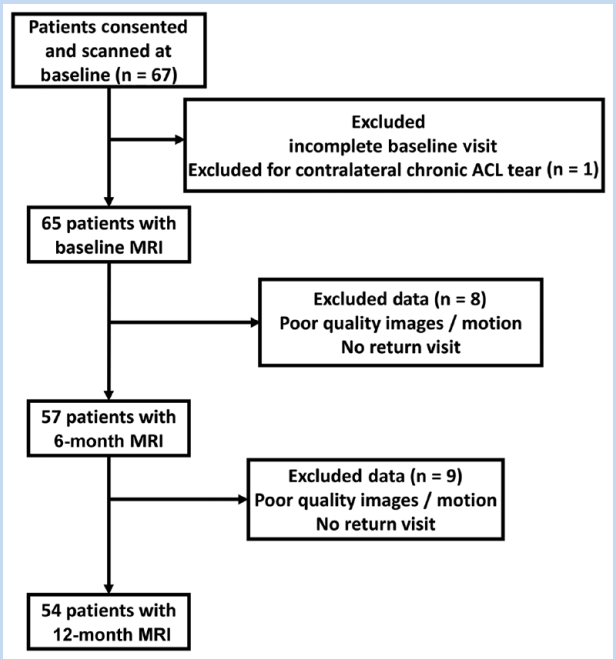

Figure 1. Flowchart for patient inclusion, and follow-up time points. ACL, anterior cruciate ligament; MRI, magnetic resonance imaging.

Healthcare) at each site, with 8-channel phased array knee coils (Invivo). The MRI protocol included the following: 2-dimensional (2D) FSE techniques in axial, sagittal, and coronal planes: repetition time/echo time [TR/TE] 5100/33.2 ms, voxel size 0.31 × 0.33 × 3.5 mm^3, echo train length 13, number of excitations 1 to 2, matrix 512 × (416-480), slice thickness 3.5 mm^3, field of view 14 to 16 cm, scan time 15 min; 3-dimensional (3D) FSE TR/TE 1500/26.7 ms, voxel size 0.41 × 0.41 × 0.5 mm^3, echo train length 32, frequency selective fat saturation, scan time 6 min; quantitative combined T1ρ/T2 mapping, TEs = 0/12.87/25.69/51.39 ms, spin-lock time (TSL) = 0/10/40/80 ms, spin-lock frequency 500 Hz, voxel size = 0.55 × 1 × 4 mm^3, scan time 10 min.

Longitudinal Cross-Site Scanner Calibration

Cross-calibration of the MRI scanners at each participating site was achieved by monthly scanning of phantoms of differing concentrations of agarose, created from a single-source solution for quality control and longitudinal T1ρ and T2 quantification reproducibility.[35] Additional calibration was obtained by scanning 2 volunteers at all 3 sites at the beginning of patient enrollment and at 1 year.[22] Excellent longitudinal reproducibility was demonstrated with no significant difference in T1ρ and T2 values using root mean square coefficient of variation with values <3% over a 13 to 29 month period.[22]

Magnetic Resonance Morphologic Evaluation

Morphologic evaluation of cartilage on MRI was performed using a modified Noyes scoring system, based off the original Noyes system which used direct arthroscopic confirmation of cartilage status (Table 1).[26,29] Factors assessed included cartilage signal alteration (mild or extensive hyperintensity), surface chondral damage (< or >50%), and status of the subchondral bone (intact or eroded). Lesions ≥15 mm were assigned twice the points as lesions measuring 10 to 14 mm due to the greater area of surface damage.[29] Similar to the original Noyes system, lesions <10 mm were not assigned points as they have not been found to be clinically significant.[29] Cartilage was assessed at the lateral tibial plateau (LTP), lateral femoral condyle (LFC), medial femoral condyle (MFC), medial tibial plateau (MTP), trochlea, and patella.

The bone marrow edema (BME) pattern was assessed at the femoral condyles and tibial plateaus, quantified as absent, mild (<10 mm^2), or severe (≥10 mm^2).[34] The presence of medial and/or lateral meniscal tears was evaluated using the morphologic images and scored (modified WORMS)[33] as intact (0) or torn (1, horizontal cleavage or peripheral longitudinal tear; or 2, bucket handle, radial, or displaced flap). Posterior cruciate and collateral ligaments were assessed, but not included in this analysis. All MRI studies were evaluated by a senior, board-certified musculoskeletal radiologist with over 20 years' experience in MRI interpretation. Assessment of MRI cartilage grading reproducibility and interexaminer repeatability for this radiologist has been previously published.[35] The radiologist was blinded to the follow-up time point but was aware that it was a follow-up examination in certain patients as ACL reconstructive surgery was evident on the imaging.

Magnetic Resonance Quantitative Evaluation

After image acquisition, semiautomatic segmentation of 3D FSE images was performed to define standardized anatomic location regions of interest (ROIs) obtained for quantitative T1ρ and T2 mapping, which included the LTP, LFC, MFC, MTP, trochlea, and patella. Tibial plateau and femoral condyle ROIs were subdivided into anterior, central and posterior regions for more precise regional mapping. Care was taken to not include the subchondral plate or synovial fluid, and to avoid sampling at the magic angle. Quantitative T1ρ and T2 values were calculated by taking the natural logarithm of the signal decay curve in a selected ROI, using data sets analyzed on a pixel-by-pixel basis with a 2-parameter weighted least squares fit, assuming a monoexponential decay.[31] An average T1ρ or T2 value was generated for each compartment.

Statistical Analysis

Statistical analysis was performed using generalized linear models to assess differences of all ordinal morphologic grades and continuous quantitative MRI datasets over time between the injured and contralateral limbs. Full factorial models were used to test longitudinal and between-group differences of the injured and contralateral knees. Bonferroni corrections were used for post hoc multiple correlation evaluations. Spearman correlations were evaluated between BME and morphologic (Noyes scores) and quantitative outcome measures (T1ρ and T2). Statistical significance was set at $P < 0.05$.

Table 1. Modified Noyes MRI scoring system

MRI Feature	Lesion (points)		
	10-14 mm	≥15 mm	
Cartilage Signal			
Mild hyperintensity	0	0	
Extensive hyperintensity	1	2	
Surface Damage			
≤50% Thickness	2	4	
>50% Thickness	3	6	
Subchondral Bone			
Intact	5	10	
Eroded	5	10	
Bone Marrow Edema Pattern	Absent	Mild (<10 mm^2)	Severe (>10 mm^2)
Meniscal Tears[a]	0	1	2

MRI, magnetic resonance imaging.
Modified Noyes scoring uses MRI features derived from the Noyes arthroscopy scoring system. The lesions were scored at the lateral tibial plateau, lateral femoral condyle, medial femoral condyle, medial tibial plateau, trochlea, and patella.
[a]Medial and lateral meniscus scoring: 0, intact meniscus; 1, horizontal cleavage tear or peripheral longitudinal tear; 2, bucket handle tear, radial tear, or displaced flap.

RESULTS

Sixty-five participants with acute ACL tears were included in the study, with patient demographics and clinical details summarized in Table 2. Sixty-one patients underwent ACL reconstructive surgery with the type of reconstruction varying depending on the surgeon preference. The majority of patients had bone patella tendon bone autografts (44%), followed by hamstring tendon autografts (34%). Arthroscopic examination included description of chondral lesions and meniscal tears, and were recorded for each patient who had surgical management.

Morphologic MRI Changes

At initial injury, MRI-detectable cartilage injury was greatest in the lateral compartment of the injured knee with baseline Noyes scores (Figure 2) highest in the LTP (mean 2.5, standard error (SE) 0.20, $P < 0.01$), followed by the LFC (mean 2.1, SE 0.18, $P < 0.01$). At 6 months and 1 year postinjury, the Noyes scores remained elevated in the LTP and LFC, progressively worsening over time ($P < 0.01$, Figures 2 and 3). The remaining compartments of the injured knee and contralateral knee demonstrated low Noyes score at baseline, without appreciable change in cartilage morphology over time (Figure 2). Figure 3 demonstrates an example of progressive chondral injury on MRI predominantly affecting the LTP.

Quantitative MRI Changes

T1ρ values in the injured knee (Table 3) displayed significant longitudinal prolongation between baseline and 1-year time points for MFC globally ($P < 0.01$) and all its subdivisions; LFC globally ($P < 0.01$), and its central-anterior and posterior subdivisions ($P < 0.01$); as well as the trochlea ($P < 0.01$). Prolongation at 6 months was also present in the MFC globally ($P < 0.01$) and its central subdivisions, the LFC anterior central subdivision ($P < 0.01$), and the trochlea ($P < 0.01$). No significant prolongation of T1ρ values was seen in any other subdivision or global ROI values.

T2 values in the injured knee (Table 3) also demonstrated significant longitudinal prolongation after 1 year compared with baseline affecting the MFC globally ($P < 0.01$) and its central-anterior and central subdivisions ($P < 0.01$); LFC central-anterior and posterior subdivisions ($P < 0.01$); LTP posterior subdivision ($P < 0.01$); and the trochlea ($P < 0.01$). At 6 months, prolongation was already evident at the MFC central-anterior and central subdivisions ($P < 0.01$, $P = 0.02$), LFC central-anterior subdivision ($P = 0.02$), and trochlea ($P < 0.01$). Global T2 values for the LFC and LTP of the injured knee were not significantly prolonged at either 6 months or 1 year. Representative relaxation maps of T1ρ and T2 of the lateral femorotibial joint in an injured knee

Table 2. Participant demographics

Parameter	Value
Number of participants, n	65
Age, y	29 (range, 13-56; SD, 13)
Men, n	37
BMI, kg/m^2	24.5 (range, 17.8-32.3; SD, 3)
ACLR, n	61
BPTB, %	44
Hamstring tendon autograft, %	34
Allografts, %	21.5

ACLR, anterior cruciate ligament reconstruction; BMI, body mass index; BPTB, bone patella tendon bone autograft.

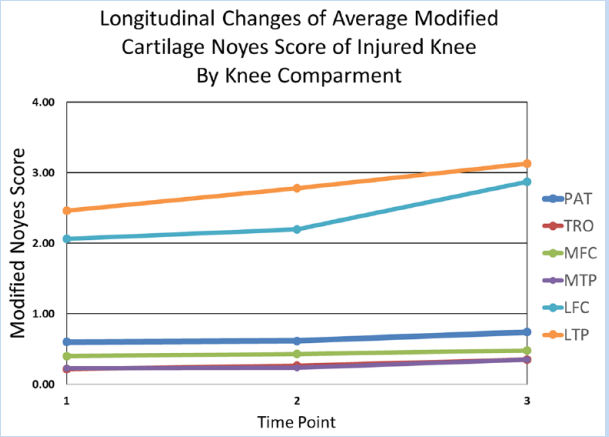

Figure 2. Progression of average modified Noyes scores in the injured and contralateral knee over time in each compartment. Modified Noyes scores assessed on MRI scans performed at baseline, 6 months, and 1 year. Compartments: PAT, patella; TRO, trochlea; MFC, medial femoral condyle; MTP, medial tibial plateau; LFC, lateral femoral condyle; LTP, lateral tibial plateau. MRI, magnetic resonance imaging.

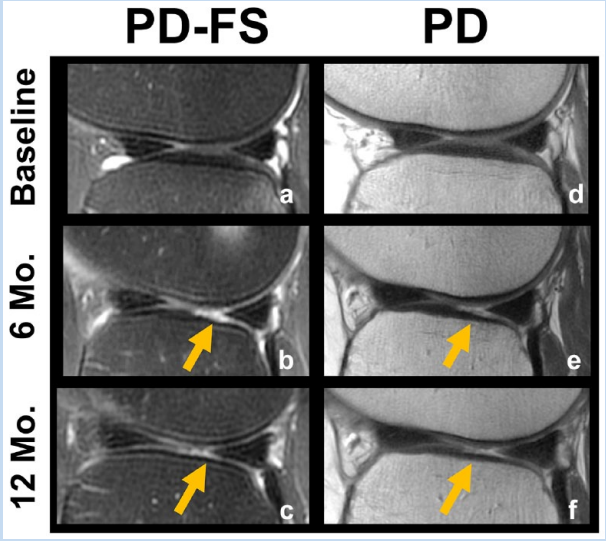

Figure 3. Sagittal fat-suppressed fast-spin echo (a-c) and sagittal fast-spin echo (d-f) MRI sequences of the lateral compartment on a 56-year-old female patient with injured left knee at baseline (a, d), 6 months (b, e), and 1 year (c, f). Images demonstrate progression of articular cartilage injury over the lateral tibial plateau (arrows). PD-FS, proton density-fat saturated.

are shown in Figure 4 with areas of prolongation indicated by arrows.

In the contralateral noninjured knee (Table 3), T1ρ prolongation was seen to affect the LFC central-anterior and LTP posterior subdivisions after 1 year ($P < 0.01$, $P < 0.01$), whereas T2 prolongation was present after 1 year affecting the MFC central-anterior ($P = 0.04$), LFC central-anterior and posterior subdivisions ($P < 0.01$, $P < 0.03$), and the LTP anterior subdivision ($P < 0.04$). None of the global T1ρ or T2 values in the contralateral limb demonstrated statistically significant prolongation.

Significant positive correlations were found between the morphological Noyes grade and T1ρ or T2 values in the LTP and patella of the injured knee, as well as the LTP, MFC, and patella of the contralateral knee (Table 4).

Bone Marrow Edema

In the LTP of the injured limb, the extent of the BME at baseline was significantly associated with prolonged T2 values ($P = 0.01$); however, no association was found over time at 6 months or at 1 year. No correlations were found between BME, Noyes

Table 3. Quantitative MRI (T1p and T2 values) in injured and contralateral knees at variable time points

Location	Time Point Comparison	T1ρ Values				T2 Values			
		Injured Knee		Contralateral Knee		Injured Knee		Contralateral Knee	
		Mean Diff.	*P* Value	Mean Diff.	*P* Value	Mean Diff.	*P* Value	Mean Diff.	*P* Value
MFC (global)	BL vs 6M	–1.9324b	<**0.01**	–0.545	1.00	–0.842	0.14	–0.609	0.85
	BL vs 1Y	–3.4705b	**0.00**	0.117	1.00	–1.9492b	<**0.01**	–0.218	>0.99
	6M vs 1Y	–1.5382b	**0.03**	0.662	1.00	–1.107	0.13	0.390	>0.99
MFC (central-anterior)	BL vs 6M	–3.4802b	**0.00**	0.010	0.99	–2.7500b	<**0.01**	0.243	0.75
	BL vs 1Y	–6.3429b	**0.00**	–1.089	0.65	–4.6542b	**0.00**	–1.7527b	**0.04**
	6M vs 1Y	–2.8627b	<**0.01**	–1.099	0.65	–1.9042b	**0.02**	–1.9957b	**0.03**
MFC (central-central)	BL vs 6M	–3.2647b	<**0.01**	0.043	0.97	–2.2145b	**0.02**	–0.130	0.88
	BL vs 1Y	–5.5263b	**0.00**	1.064	0.88	–3.2561b	**0.00**	0.934	0.68
	6M vs 1Y	–2.2616b	**0.03**	1.021	0.88	–1.042	0.24	1.064	0.68
MFC (central-posterior)	BL vs 6M	–2.1014b	**0.02**	–0.391	0.93	–0.457	>0.99	–0.709	0.66
	BL vs 1Y	–3.0638b	**0.00**	0.594	0.93	–0.899	0.67	0.665	0.66
	6M vs 1Y	–0.962	0.25	0.985	0.72	–0.441	>0.99	1.374	0.21
MFC (posterior)	BL vs 6M	–1.277	0.17	–0.844	0.86	–0.301	0.64	–0.860	0.54
	BL vs 1Y	–2.6993b	<**0.01**	–0.181	0.86	–1.250	0.16	–0.263	0.75
	6M vs 1Y	–1.423	0.17	0.663	0.86	–0.950	0.31	0.597	0.75
LFC (global)	BL vs 6M	–1.173	0.12	–0.966	0.35	–0.478	0.58	–0.671	0.52
	BL vs 1Y	–2.0264b	<**0.01**	–0.447	0.84	–1.024	0.12	–0.632	0.52
	6M vs 1Y	–0.854	0.19	0.520	0.84	–0.546	0.58	0.038	0.94
LFC (central-anterior)	BL vs 6M	–3.1422b	<**0.01**	–0.428	0.62	–1.6958b	**0.02**	–0.277	0.70
	BL vs 1Y	–4.5305b	**0.00**	–3.0695b	**0.01**	–4.2525b	**0.00**	–4.1611b	**0.00**
	6M vs 1Y	–1.388	0.12	–2.6412b	**0.01**	–2.5568b	<**0.01**	–3.8843b	**0.00**

(continued)

Table 3. (continued)

Location	Time Point Comparison	T1ρ Values				T2 Values			
		Injured Knee		Contralateral Knee		Injured Knee		Contralateral Knee	
		Mean Diff.	*P* Value	Mean Diff.	*P* Value	Mean Diff.	*P* Value	Mean Diff.	*P* Value
LFC (central-central)	BL vs 6M	–1.994	0.06	–0.645	0.48	–1.296	0.35	–0.369	0.66
	BL vs 1Y	–1.451	0.20	1.031	0.48	–0.048	0.96	1.11	0.38
	6M vs 1Y	0.542	0.55	1.677	0.19	1.249	0.35	1.48	0.27
LFC (central-posterior)	BL vs 6M	–1.130	0.34	–1.095	0.38	–0.226	0.75	–1.05	0.29
	BL vs 1Y	–0.369	0.62	–0.119	0.87	1.516	0.08	0.227	0.76
	6M vs 1Y	0.761	0.62	0.976	0.39	1.742	0.06	1.278	0.27
LFC (posterior)	BL vs 6M	–0.486	0.53	–1.153	0.28	–0.069	0.916	–0.768	0.39
	BL vs 1Y	–3.0072b	**0.00**	–1.497	0.18	–1.8366b	<**0.01**	–1.5443b	**0.03**
	6M vs 1Y	–2.5217b	<**0.01**	–0.344	0.67	–1.7671b	<**0.01**	–0.776	0.39
MTP (global)	BL vs 6M	0.780	>0.99	–0.246	0.88	0.515	>0.99	0.307	>0.99
	BL vs 1Y	0.592	>0.99	0.686	0.88	0.044	>0.99	–0.313	>0.99
	6M vs 1Y	–0.187	>0.99	0.932	0.88	–0.471	>0.99	–0.620	>0.99
MTP (anterior)	BL vs 6M	–0.704	>0.99	–0.616	0.83	–0.204	>0.99	–0.024	0.97
	BL vs 1Y	–0.122	>0.99	0.728	0.83	–0.663	>0.99	–0.827	0.81
	6M vs 1Y	0.582	>0.99	1.343	0.43	–0.459	>0.99	–0.803	0.81
MTP (central)	BL vs 6M	1.083	0.83	–0.269	>0.99	0.549	>0.99	0.269	>0.99
	BL vs 1Y	0.478	>0.99	0.616	>0.99	–0.251	>0.99	–0.465	>0.99
	6M vs 1Y	–0.605	>0.99	0.885	>0.99	–0.800	>0.99	–0.734	>0.99
MTP (posterior)	BL vs 6M	0.893	0.64	0.000	>0.99	0.530	0.81	0.521	0.91
	BL vs 1Y	1.812	0.14	1.740	0.17	1.137	0.32	0.902	0.60
	6M vs 1Y	0.919	0.64	1.740	0.17	0.607	0.81	0.381	0.91

(continued)

Table 3. (continued)

Location	Time Point Comparison	T1ρ Values				T2 Values			
		Injured Knee		Contralateral Knee		Injured Knee		Contralateral Knee	
		Mean Diff.	*P* Value	Mean Diff.	*P* Value	Mean Diff.	*P* Value	Mean Diff.	*P* Value
LTP (global)	BL vs 6M	–0.765	0.83	0.005	>0.99	–0.024	>0.99	–0.423	0.63
	BL vs 1Y	0.133	0.87	–0.441	>0.99	0.243	>0.99	–1.202	0.33
	6M vs 1Y	0.898	0.83	–0.445	>0.99	0.267	>0.99	–0.779	0.63
LTP (anterior)	BL vs 6M	–1.090	0.69	0.608	0.94	0.100	>0.99	–0.177	0.82
	BL vs 1Y	–0.539	>0.99	–0.661	0.94	–0.520	>0.99	–2.0240b	**0.04**
	6M vs 1Y	0.552	>0.99	–1.269	0.54	–0.620	>0.99	–1.847	0.05
LTP (central)	BL vs 6M	–0.448	>0.99	0.164	0.85	–0.239	>0.99	–0.426	0.60
	BL vs 1Y	0.032	>0.99	–0.815	0.82	0.079	>0.99	–1.539	0.18
	6M vs 1Y	0.480	>0.99	–0.979	0.82	0.317	>0.99	–1.113	0.38
LTP (posterior)	BL vs 6M	–1.279	0.17	–0.353	0.70	0.054	0.95	–0.549	0.54
	BL vs 1Y	4.3704b	**0.00**	2.7426b	**0.01**	4.1729b	**0.00**	1.974	0.06
	6M vs 1Y	5.6497b	**0.00**	3.0958b	**0.01**	4.1192b	**0.00**	2.5233b	**0.02**
Patella (global)	BL vs 6M	–0.335	>0.99	–0.360	>0.99	0.184	>0.99	–1.290	0.07
	BL vs 1Y	–0.341	>0.99	0.423	>0.99	0.208	>0.99	–1.030	0.15
	6M vs 1Y	–0.006	>0.99	0.784	0.94	0.024	>0.99	0.260	0.66
Trochlea (global)	BL vs 6M	–2.8717b	**0.00**	–0.347	>0.99	–2.2295b	**0.00**	–0.306	>0.99
	BL vs 1Y	–3.6348b	**0.00**	–0.224	>0.99	–2.2370b	**0.00**	0.303	>0.99
	6M vs 1Y	–0.763	0.28	0.122	>0.99	–0.008	0.99	0.609	0.95

BL, baseline; LFC, lateral femoral condyle; LTP, lateral tibial plateau; MFC, medial femoral condyle; MRI, magnetic resonance imaging; MTP, medial tibial plateau; PAT, patella; TRO, trochlea; 6M, 6 months; 1Y, 1 year.
Quantitative MRI values in the injured and contralateral noninjured knees measured at baseline, 6 months and 1 year time points.
Global cartilage values were assessed as well as subdivisions of the medial and lateral tibiofemoral compartment cartilage.
Significant *P* values are set in bold type.

Table 4. Spearman correlations between Noyes scores and T1ρ and T2 values

Region	Injured knee		Contralateral knee	
	T1ρ	T2	T1ρ	T2
Lateral femoral condyle	–0.11	0.04	–0.04	–0.04
Lateral tibial plateau	**0.29***	0.23	**0.36***	**0.35***
Medial femoral condyle	0.18	0.25	**0.48***	**0.41***
Medial tibial plateau	0.13	0.14	0.13	0.16
Patella	**0.32***	**0.26***	**0.38***	**0.33***
Trochlea	–0.14	–0.17	–0.08	–0.12

*Statistically significant correlations ($P < 0.05$) are set in bold type.

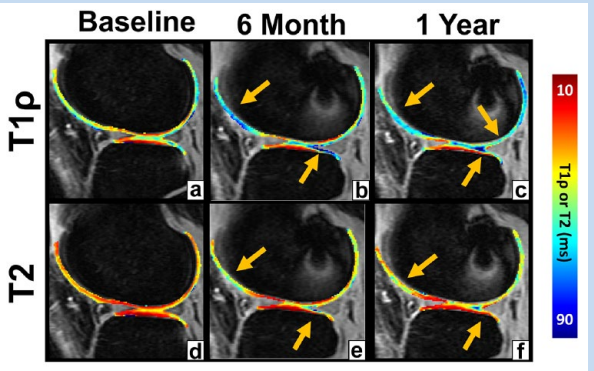

Figure 4. Longitudinal sagittal quantitative T1ρ (a-c) and T2 (d-e) relaxation time maps of the lateral femorotibial joint cartilage in the same 56-year-old female patient, from baseline (a, d), 6 months (b, e), and 1 year (c, f) time points, show progressive prolongation of both T1ρ and T2 relaxation times. Orange arrows indicate specific areas of prolongation. Relaxation time maps are color coded to reflect T1ρ and T2 values ranging from 10 milliseconds (orange) to 90 milliseconds (blue).

scores, T1ρ or T2 values at baseline or the follow-up time points for the remainder of the imaged compartments.

Meniscal Injury

At baseline, 46 participants were found to have sustained a meniscal tear in the injured knee on MRI, without predominance to either medial or lateral meniscus (32 and 31, respectively), and 17 sustained injury to both. Nine of the participants had evidence of meniscal tear in the contralateral knee at baseline MRI. In the participants who underwent surgery to the injured knee, 20 tears in the medial meniscus and 29 tears in the lateral meniscus were confirmed intraoperatively. The majority of all tears were either repaired (49%) or excised (34%), while the remainder underwent no treatment, with a few showing signs of healing response. At 1 year, only 1 new meniscal tear in the injured knee was evident on MRI, while in the contralateral knee, a further 3 new tears were evident. The presence of any meniscal tear (medial or lateral) was not found to have any statistically significant correlation in cartilage morphology or qualitative cartilage analysis over time. T1ρ values of the LTP tracked similarly between subjects with an intact or torn meniscus (Figure 5).

Patient-Reported Outcome Measures

The KOOS and WOMAC scores (Figure 6) showed significant improvement in all measured outcomes at 6 months and 1 year follow-up compared with baseline. The scores remained elevated between 6 months and 1 year.

DISCUSSION

After acute ACL injury, morphological and quantitative MRI cartilage damage in the injured knee was found predominantly to affect the lateral tibiofemoral compartment with progressive degeneration at 6 months and 1 year.

This corresponds to the findings by Potter et al,[34] in which 7 to 11 years after ACL injury, morphological MRI chondral damage most severely affected the lateral tibiofemoral compartment, attributed to the transcondylar impaction.[34]

Meanwhile, positive correlations were also found to affect the injured knee patella, with similar findings demonstrated in the studies by Potter et al[34] and Van Meer et al.[48] When evaluating only quantitative MRI values, more chondral compartments of the injured knee were affected than was appreciated on the morphological MRI assessment. The T1ρ values showed significant prolongation in the femoral condyles and trochlea, while T2 values were prolonged in the femoral condyles, lateral tibia, and trochlea. Longitudinal prolongation of T1ρ in multiple compartments of the injured knee after ACL injury has been

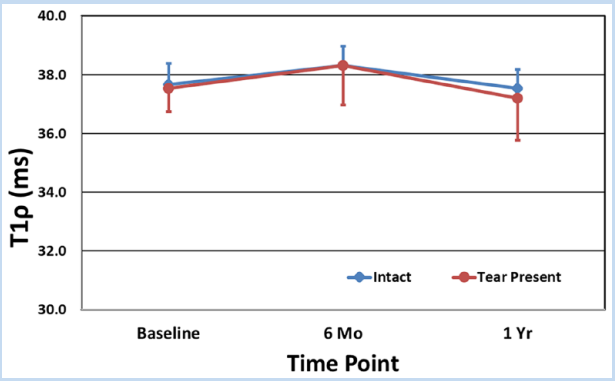

Figure 5. Longitudinal changes in T1ρ values of the lateral tibial plateau in subjects with a torn lateral meniscus as compared with subjects with an intact lateral meniscus. Graph displays the mean ± standard deviation T1ρ value at each of the evaluated time points.

demonstrated in other studies; however, there is disagreement as to which compartments are the most affected.[42,44,48] In a 10-year longitudinal follow-up study of post-ACLR knees, the greatest chondral matrix prolongation occurred in the medial compartment and trochlea, but when compared with a healthy control knee, all subcompartments showed higher matrix values.[50]

Cartilage damage affecting the injured knee is multifactorial and has been attributed to the initial cartilage and subchondral injury, altered cartilage matrix homeostasis and inflammatory synovial cytokine cascade, and from surgery if ACLR and meniscal repair/meniscectomy is performed.[34,41,45] Cartilage degeneration after ACL injury also includes a complex interplay of altered gait change leading to shifts in the load applied to cartilage, altered compressive and tensile forces, and the metabolic sensitivity of chondrocytes to the mechanical environment.[8] Bone shape changes of the femoral sphericity, tibial slope and notch width have been demonstrated to occur after ACL injury and ACLR, correlated with changes in cartilage matrix prolongation.[51] In the short term, the primary aim of ACLR is to restore anterior and rotational laxity of the joint, and return patients to activity, but so far, unfortunately, it has not been proved to reduce the long-term risk of developing PTOA.[13,20,23,25,34] Aberrant gait biomechanics have been linked to the development of PTOA in the post-ACL injured knee, correlated with prolonged T1p and T2 values.[6,14,46] Greater total motion of the medial compartment, and prominent vertical forces during the stance phase of gait, have been demonstrated in the post-ACLR population.[6,19,46,49]

In this current study, cartilage matrix prolongation also occurred in the contralateral knee, mainly affecting the femoral condyles and LTP; with positive correlations with the cartilage morphology involving the femoral condyles and patella. This was despite low scoring on Noyes morphology alone. Positive correlations between Noyes and quantitative changes may be attributable to subtle signal alterations in cartilage morphology, associated with a low Noyes score. Quantitative techniques are sensitive to small changes in the extracellular matrix, often preceding morphologically apparent focal defects and diffuse chondral changes.[24]

Contralateral knee cartilage matrix prolongation after ACL injury and surgery has also been demonstrated in other studies. In the study by Pedoia et al,[32] cartilage prolongation also occurred in the contralateral knee in the first year, whereas Xie et al[50] demonstrated significantly prolonged values up to 10 years postinjury mainly affecting the lateral tibiofemoral and patellofemoral compartments.[32,50] Interestingly, Xie et al[50] found all subcompartments of the contralateral knee demonstrated higher T1p and T2 values compared with the control group. Prolonged cartilage relaxation times have also been demonstrated to affect the contralateral knee in a post-ACLR individual up to 2 years postinjury in studies assessing gait biomechanics and tibial motion analysis.[19,49] The changes have been demonstrated to be independent of normal aging, with control knees showing no significant changes to rotation and translation kinematics.[8,19,49,50] The cause of early cartilage matrix changes in the uninjured contralateral knee in this study is probably due to adapted biomechanical unloading patterns after ACL and ACLR, which has also been postulated by a number of other studies.[8,32,49,50]

Meniscal tear in either the injured or contralateral knee was not found to correlate with degenerated cartilage morphology or chondral matrix signal alteration at 1 year in this study. This is suspected to be due to the relatively short interval follow-up period. Meniscal injury has already been demonstrated to be an important risk factor in the development of symptomatic knee osteoarthritis in patients who have undergone ACLR, with changes apparent 10 years postinjury.[16,22,42-44,48] The recent study by Jones et al[16] found that concomitant meniscal injury requiring repair or partial meniscectomy correlated with worse whole joint chondral degeneration in the ACLR knee as early as 2 to 3 years.[16] An interesting finding of that study was that high grade articular cartilage lesions at the time of pivot-shift injury did not correlate with MRI cartilage degeneration at 2 to 3 years in the medial and lateral compartment, supporting other factors such as meniscal tear as important contributors to progressive chondral degeneration.[16] With ongoing surveillance of the patients in this current study, progressive chondral degeneration is felt likely to correlate with meniscal tear.

In this study, progressive chondral degeneration and PROMs were not found to be correlated in the first year after ACL injury. However, as demonstrated by other studies, cartilage loss eventually reaches a point where it becomes clinically apparent, occurring as early as 5 years postinjury.[34,37] Symptomatic PROMs typically indicate established osteoarthritis which is difficult to reverse.[36] Strategies to delay and prevent PTOA include early rehabilitation focusing on improving biomechanics and muscle strengthening, limiting contact/sheer stresses, as well as addressing excessive body weight.[23] Early identification of progressive chondral damage post-ACL injury such as with the

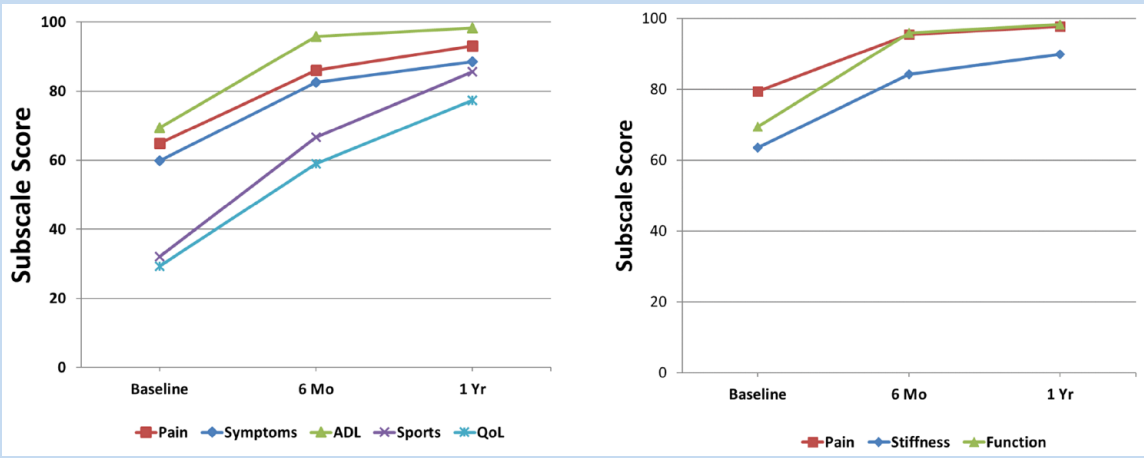

Figure 6. Longitudinal change in KOOS scores (left) and WOMAC scores (right). ADL, activities of daily living; KOOS, Knee Injury and Osteoarthritis Outcome Score; WOMAC, Western Ontario and McMaster Universities Osteoarthritis Index; QoL, Quality of Life.

use of morphological and quantitative MRI could enable these preventive strategies to be implemented before PTOA becomes established.[10] A future study analyzing correlations between PROMS with quantitative and qualitative MRI techniques could be performed.

Associations between established BME, osteoarthritis, and clinical symptoms are often reported.[11,15,38] In this study, BME in the LTP of the injured knee had prolonged T2 relaxation initially, without association at 1 year. No correlation between BME and Noyes scores in any compartment was found, and progressive cartilage changes also occurred in compartments not directly affected by the acute bone contusion. These findings are consistent with Potter et al[34] in which transcondylar impaction accounted for the early BME pattern and cartilage shear injury, without an association over time found. More widespread cartilage injury beyond the site of direct impaction supports the concept that after acute ACL injury global cartilage homeostasis is affected.[34,45]

This study was initially designed to include the contralateral noninjured knee MRI of the subjects as a control, as supported by the literature.[47] However, the cartilage in the contralateral knee of a patient who has sustained an ACL injury is also affected, as seen in our study, and recently by Xie et al[50] and Pedoia et al,[32] and therefore a limitation to this current study is the lack of a control group. The modified Noyes scoring system is a validated measure of cartilage status based on the original Noyes scoring systems for direct arthroscopic cartilage assessment.[26,29] However, it should be noted that the total chondral surface area is not calculated in these scoring systems, nor is patient size. The follow-up period examined in this study was relatively short to assess the early morphological chondral changes and matrix signal prolongation after ACL injury. A longer period of observation (1-5 years) would help characterize these early changes over time and correlate them with the development of symptomatic PTOA. A limited number of participants was evaluated at follow-up with a dropout rate of approximately 17% at 1 year. Age analysis was not performed for this current study but has been previously reported for this longitudinal cohort.[2] Another limitation to the study was that preinjury imaging was not performed, and therefore some of the baseline chondral changes detected on MRI could have been from preexisting degeneration. However, as patients were recruited to the study after ACL injury, obtaining preinjury films is difficult to standardize and is challenging clinically. ACLR was not an inclusion or exclusion criterion in this study; however, as patients were recruited from 3 study locations, the clinical management differed slightly, including surgery versus no surgery, type of graft used, and time to surgery from injury. The details of 4 patients deciding not to undergo surgery was not available to the researchers of this study. This study, however, was successful in completing a multi-institutional longitudinal evaluation of participants with ACL injury, while maintaining high rigor of scanner reproducibility in the quantitative metrics.[22] The modified Noyes system has previously been shown to have high reproducibility and consistency[3,35]; therefore, the authors were satisfied that the results would be reproducible.

The findings of this study add to the growing body of evidence that early cartilage matrix changes are associated with early morphological cartilage damage and, as demonstrated by other studies, have been found eventually to lead to clinically evident PTOA.[3,20,28,35]

CONCLUSION

After acute ACL injury, the dominant location for articular cartilage damage occurs in the lateral tibiofemoral compartment using morphological and quantitative MRI techniques. Chondral matrix prolongation also occurred in the surrounding compartments of the injured knee, and throughout the

contralateral knee. Early identification of chondral degeneration post-ACL injury using morphological and quantitative MRI techniques could enable interventions to be implemented early to prevent or delay PTOA.

KEY RESULTS

1. After ACL injury, acute chondral damage on MRI predominantly affected the injured knee lateral tibiofemoral compartment with progression at 1 year postinjury. Quantitative MRI techniques demonstrated more widespread cartilage degeneration affecting both the injured and contralateral knees.
2. Patient-reported outcomes improved over time despite progressive chondral degeneration on MRI. Identification of early chondral degeneration post-ACL injury with MRI could enable interventions to be implemented, before clinical progression and PTOA is established.

CLINICAL RECOMMENDATIONS

After acute ACL injury, progressive chondral degeneration occurs most in the injured knee at the lateral compartment at the sites of transcondylar impaction. The more widespread chondral changes affecting the injured and contralateral knees are likely to be multifactorial in etiology. Morphologic and quantitative MRI techniques could be used to identify early progressive chondral degeneration, enabling early interventions to be implemented. (SORT A, level 1. Prospective cohort study.)

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REFERENCES

1. Altman RD, Gold GE. Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthr Cartilage*. 2007;15:A1-A56.
2. Amano K, Li AK, Pedoia V, et al. Effects of surgical factors on cartilage can be detected using quantitative magnetic resonance imaging after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2017;45:1075-1084.
3. Andersson C, Odensten M, Gillquist J. Knee function after surgical or nonsurgical treatment of acute rupture of the anterior cruciate ligament: a randomized study with a long-term follow-up period. *Clin Orthop Relat Res*. 1991;264:255-263.
4. Atkinson HF, Birmingham TB, Moyer RF, et al. MRI T2 and T1ρ relaxation in patients at risk for knee osteoarthritis: a systematic review and meta-analysis. *BMC Musculoskelet Dis*. 2019;20:182.
5. Bellamy N, Buchanan WW, Goldsmith CH, Campbell J, Stitt LW. Validation study of WOMAC: a health status instrument for measuring clinically important patient relevant outcomes to antirheumatic drug therapy in patients with osteoarthritis of the hip or knee. *J Rheumatol*. 1988;15:1833-1840.
6. Bjornsen E, Schwartz TA, Lisee C, et al. Loading during midstance of gait is associated with magnetic resonance imaging of cartilage composition following anterior cruciate ligament reconstruction. *Cartilage*. 2022;13:19476035211072220.
7. Bodkin SG, Werner BC, Slater LV, Hart JM. Post-traumatic osteoarthritis diagnosed within 5 years following ACL reconstruction. *Knee Surg Sports Traumatol Arthr*. 2020;28:790-796.
8. Chaudhari AMW, Briant PI, Bevill Sl, Koo S, Andriacchi TP. Knee kinematics, cartilage morphology, and osteoarthritis after ACL injury. *Med Sci Sports Exerc*. 2008;40:215-222.
9. Cohen M, Amaro JT, Ejnisman B, et al. Anterior cruciate ligament reconstruction after 10 to 15 years: association between meniscectomy and osteoarthrosis. *Arthrosc J Arthrosc Relat Surg*. 2007;23:629-634.
10. Eagle S, Potter HG, Koff MF. Morphologic and quantitative magnetic resonance imaging of knee articular cartilage for the assessment of post-traumatic osteoarthritis. *J Orthopaed Res*. 2017;35:412-423.
11. Felson DT, Niu J, Guermazi A, et al. Correlation of the development of knee pain with enlarging bone marrow lesions on magnetic resonance imaging. *Arthr Rheum*. 2007;56:2986-2992.
12. Gillquist J, Messner K. Anterior cruciate ligament reconstruction and the long term incidence of gonarthrosis. *Sports Med*. 1999;27:143-156.
13. Everhart JS, Jones MH, et al.; The MOON Group. The clinical radiographic incidence of posttraumatic osteoarthritis 10 years after anterior cruciate ligament reconstruction: data from the MOON nested cohort. *Am J Sports Med*. 2020;49:1251-1261.
14. Haughom B, Schairer W, Souza RB, Carpenter D, Ma CB, Li X. Abnormal tibiofemoral kinematics following ACL reconstruction are associated with early cartilage matrix degeneration measured by MRI T1rho. *Knee*. 2012;19:482-487.
15. Hunter DJ, Zhang Y, Niu J, et al. Increase in bone marrow lesions associated with cartilage loss: a longitudinal magnetic resonance imaging study of knee osteoarthritis. *Arthr Rheum*. 2006;54:1529-1535.
16. Jones MH, Altahawi F, Reinke E, Spindler KP. Is meniscus treatment a predictor of worse articular cartilage damage on MRI 2 years after ACL reconstruction? The MOON Nested Cohort. *Osteoarthr Cartilage*. 2021;29:S279-S280.
17. Jones MH, Spindler KP. Risk factors for radiographic joint space narrowing and patient reported outcomes of post-traumatic osteoarthritis after ACL reconstruction: data from the MOON cohort. *J Orthopaed Res*. 2017;35:1366-1374.
18. Kelly BT, Potter HG, Deng X-H, et al. Meniscal allograft transplantation in the sheep knee: evaluation of chondroprotective effects. *Am J Sports Med*. 2006;34:1464-1477.
19. Li AK, Ochoa JK, Pedoia V, et al. Altered tibiofemoral position following ACL reconstruction is associated with cartilage matrix changes: a voxel-based relaxometry analysis. *J Orthop Res*. 2020;38:2454-2463.
20. Li H, Chen S, Tao H, Chen S. Quantitative MRI T2 relaxation time evaluation of knee cartilage: comparison of meniscus-intact and -injured knees after anterior cruciate ligament reconstruction. *Am J Sports Med*. 2015;43:865-872.
21. Li X, Ma CB, Link TM, et al. In vivo T1ρ and T2 mapping of articular cartilage in osteoarthritis of the knee using 3T MRI. *Osteoarthr Cartilage*. 2007;15:789-797.
22. Li X, Pedoia V, Kumar D, et al. Cartilage T1ρ and T2 relaxation times: longitudinal reproducibility and variations using different coils, MR systems and sites. *Osteoarthr Cartil OARSs Osteoarthr Res Soc*. 2015;23:2214-2223.
23. Lohmander LS, Englund PM, Dahl LL, Roos EM. The long-term consequence of anterior cruciate ligament and meniscus injuries: osteoarthritis. *Am J Sports Med*. 2007;35:1756-1769.
24. MacKay JW, Low SBL, Smith TO, Toms AP, McCaskie AW, Gilbert FJ. Systematic review and meta-analysis of the reliability and discriminative validity of cartilage compositional MRI in knee osteoarthritis. *Osteoarthr Cartilage*. 2018;26:1140-1152.
25. Majewski M, Susanne H, Klaus S. Epidemiology of athletic knee injuries: a 10-year study. *Knee*. 2006;13:184-188.
26. McGibbon CA, Trahan CA. Measurement accuracy of focal cartilage defects from MRI and correlation of MRI graded lesions with histology: a preliminary study. *Osteoarthr Cartilage*. 2003;11:483-493.
27. Nieminen MT, Töyräs J, Rieppo J, et al. Quantitative MR microscopy of enzymatically degraded articular cartilage. *Magnet Reson Med*. 2000;43:676-681.
28. Noyes FR, Barber SD, Simon R. High tibial osteotomy and ligament reconstruction in varus angulated, anterior cruciate ligament-deficient knees: a two- to seven-year follow-up study. *Am J Sports Med*. 1993;21:2-12.
29. Noyes FR, Stabler CL. A system for grading articular cartilage lesions at arthroscopy. *Am J Sports Med*. 1989;17:505-513.
30. Pedersen D, Martin Thedens D, Klocke Roberts N, Goetz J. Imaging biopsy composition at ACL reconstruction. *Orthop Res Rev*. 2013;5:35.
31. Pedoia V, Li X, Su F, Calixto N, Majumdar S. Fully automatic analysis of the knee articular cartilage T1ρ relaxation time using voxel-based relaxometry. *J Magn Reson Imaging*. 2016;43:970-980.

32. Pedoia V, Su F, Amano K, et al. Analysis of the articular cartilage T1ρ and T2 relaxation times changes after ACL reconstruction in injured and contralateral knees and relationships with bone shape. *J Orthopaed Res*. 2017;35:707-717.
33. Peterfy CG, Guermazi A, Zaim S, et al. Whole-Organ Magnetic Resonance Imaging Score (WORMS) of the knee in osteoarthritis. *Osteoarthr Cartilage*. 2004;12:177-190.
34. Potter HG, Jain SK, Ma Y, Black BR, Fung S, Lyman S. Cartilage injury after acute, isolated anterior cruciate ligament tear. *Am J Sports Med*. 2012;40:276-285.
35. Potter HG, Linklater JM, Allen AA, Hannafin JA, Haas SB. Magnetic resonance imaging of articular cartilage in the knee. an evaluation with use of fast-spin-echo imaging*. *J Bone Joint Surg*. 1998;80:1276-1284.
36. Riordan EA, Little C, Hunter D. Pathogenesis of post-traumatic OA with a view to intervention. *Best Pract Res Clin Rheumatol*. 2014;28:17-30.
37. Risberg MA, Oiestad BE, Gunderson R, et al. Changes in knee osteoarthritis, symptoms, and function after anterior cruciate ligament reconstruction: a 20-year prospective follow-up study. *Am J Sports Med*. 2016;44:1215-1224.
38. Roemer FW, Guermazi A, Javaid MK, et al. Change in MRI-detected subchondral bone marrow lesions is associated with cartilage loss: the MOST Study. A longitudinal multicentre study of knee osteoarthritis. *Ann Rheum Dis*. 2009;68:1461.
39. Roos EM, Lohmander LS. The Knee injury and Osteoarthritis Outcome Score (KOOS): from joint injury to osteoarthritis. *Health Qual Life Out*. 2003;1:64.
40. Selmi TAS, Fithian D, Neyret P. The evolution of osteoarthritis in 103 patients with ACL reconstruction at 17 years follow-up. *Knee*. 2006;13:353-358.
41. Struglics A, Larsson S, Pramhed A, Frobell R, Swärd P. Changes in synovial fluid and serum concentrations of cartilage oligomeric matrix protein over 5 years after anterior cruciate ligament rupture: an exploratory analysis in the KANON trial. *Osteoarthr Cartilage*. 2018;26:1351-1358.
42. Su F, Hilton JF, Nardo L, et al. Cartilage morphology and T1ρ and T2 quantification in ACL-reconstructed knees: a 2-year follow-up. *Osteoarthr Cartilage*. 2013;21:1058-1067.
43. Suter LG, Smith SR, Katz JN, et al. Projecting lifetime risk of symptomatic knee osteoarthritis and total knee replacement in individuals sustaining a complete anterior cruciate ligament tear in early adulthood. *Arthr Care Res*. 2017;69:201-208.
44. Theologis AA, Haughom B, Liang F, et al. Comparison of T1rho relaxation times between ACL-reconstructed knees and contralateral uninjured knees. *Knee Surg Sports Traumatol Arthrosc*. 2014;22:298-307.
45. Tiderius CJ, Olsson LE, Nyquist F, Dahlberg L. Cartilage glycosaminoglycan loss in the acute phase after an anterior cruciate ligament injury: delayed gadolinium-enhanced magnetic resonance imaging of cartilage and synovial fluid analysis. *Arthr Rheum*. 2005;52:120-127.
46. Titchenal MR, Chu CR, Erhart-Hledik JC, Andriacchi TP. Early changes in knee center of rotation during walking after anterior cruciate ligament reconstruction correlate with later changes in patient-reported outcomes. *Am J Sports Med*. 2017;45:915-921.
47. Tourville TW, Johnson RJ, Slauterbeck JR, Naud S, Beynnon BD. Assessment of early tibiofemoral joint space width changes after anterior cruciate ligament injury and reconstruction: a matched case-control study. *Am J Sports Medicine*. 2013;41:769-778.
48. Van Meer BL, Oei EHG, Meuffels DE, et al. Degenerative changes in the knee 2 years after anterior cruciate ligament rupture and related risk factors: a prospective observational follow-up study. *Am J Sports Med*. 2016;44:1524-1533.
49. Williams JR, Neal K, Alfayyadh A, et al. Knee cartilage T2 relaxation times 3 months after ACL reconstruction are associated with knee gait variables linked to knee osteoarthritis. *J Orthop Res*. 2022;40:252-259.
50. Xie D, Murray J, Lartey R, et al. Multi-vendor multi-site quantitative MRI analysis of cartilage degeneration 10 years after anterior cruciate ligament reconstruction: MOON-MRI protocol and preliminary results. *Osteoarthr Cartilage*. 2022;30:1647-1657.
51. Zhong Q, Pedoia V, Tanaka M, et al. 3D bone-shape changes and their correlations with cartilage T1ρ and T2 relaxation times and patient-reported outcomes over 3-years after ACL reconstruction. *Osteoarthr Cartilage*. 2019;27:915-921.