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Cartilage recovery in runners with and without knee osteoarthritis: A pilot study

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ABSTRACT

Objective: Running is an easy way of meeting physical activity recommendations for individuals with knee osteoarthritis (KOA); however, it remains unknown how their cartilage reacts to running. The objective of this pilot study was to compare the effects of 30 min of running on T2 and T1ρ relaxation times of tibiofemoral cartilage in female runners with and without KOA.

Methods: Ten female runners with symptomatic KOA (mean age 52.6 ± 7.6 years) and 10 without KOA (mean age 52.5 ± 7.8 years) ran for 30 min on a treadmill. Tibiofemoral cartilage T2 and T1ρ relaxation times were measured using magnetic resonance imaging prior to and immediately after the bout of running. Repeated-measures analyses of covariance (ANCOVA) were conducted to examine between-group differences across scanning times.

Results: No Group × Time interactions were found for T2 ($P \geq 0.076$) or T1ρ ($P \geq 0.288$) relaxation times. However, runners with KOA showed increased T2 values compared with pre-running in the medial and lateral femur 55 min post-running (5.4 to 5.5%, $P < 0.022$) and in all four tibiofemoral compartments 90 min post-running (6.9 to 11.1%, $P < 0.01$). A significant group effect was found for T1ρ in the medial femur, with greater values in those with KOA compared with controls.

Conclusion: While Group × Time interactions in T2 and T1ρ relaxation times remained statistically insignificant, the observed significant increases in T2 in runners with tibiofemoral osteoarthritis TFOA may suggest slower and continuing changes in the cartilage and thus a need for longer recovery after running. Future research should investigate the effects of repeated exposure to running.

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1. Introduction

Knee osteoarthritis (KOA) is globally considered to be one of the leading causes of disability, and its prevalence is projected to increase considerably over the next few decades [1]. Maintaining an active lifestyle that includes regular physical activity helps to relieve symptoms and optimize function of individuals with KOA [2]. Running represents an easy and accessible way of meeting physical activity recommendations; however, it remains unknown how cartilage of those with pre-existing KOA reacts to high-impact activities such as running.

Quantitative magnetic resonance imaging (MRI) techniques such as T2 and T1ρ relaxation mapping can be used to study cartilage properties and its immediate response to loading. T2 relaxation represents the time constant of the molecular motion of water in cartilage, which is influenced by the composition of collagen and specifically reflects changes to the extracellular matrix [3]. In contrast, T1ρ provides an indication of glycosaminoglycan concentration in cartilage [4]. Previous research has suggested that a single bout of running could measurably affect cartilage properties, as assessed using these MRI techniques [5]. For example, tibiofemoral T2 relaxation time decreased immediately following 15 to 45 min of running [6–9], while T1ρ relaxation time decreased after running for 30 min in young, healthy individuals. Together, these results suggest that water is expelled from cartilage secondary to high compression forces sustained during the stance phase of running, which can reach as much as 10.4 bodyweights [10].

Nevertheless, healthy cartilage is known to fully recover even after long periods of running. For instance, despite significant decreases in tibiofemoral cartilage volume observed immediately after 20 km of running, Kessler et al. reported a full return to pre-run values one-hour post-run. Similarly, talocrural cartilage has been shown to remain intact – and even partially regenerate – under extreme ultra-endurance loading conditions [11]. However, it must be noted that all of the aforementioned studies were conducted in individuals without radiological or clinical signs of osteoarthritis. Tibiofemoral cartilage in those with pre-existing KOA may not tolerate forces applied during running as well as healthy cartilage. Despite greater baseline T2 and T1ρ relaxation times in individuals with KOA compared with healthy controls [12], greater reductions in T1ρ in those with KOA under sustained simulated weightbearing conditions suggest a reduced capacity to retain water and dissipate loads. Thus, such deficits would hypothetically translate to decreased ability of osteoarthritic cartilage to normalize water content from loads applied during running. This could have important implications for sports medicine clinicians providing recommendations to runners with KOA.

The objective of this pilot study was to compare the effects of 30 min of running on T2 and T1ρ relaxation times of tibiofemoral cartilage in female runners with and without KOA. It was hypothesized that both T2 and T1ρ would significantly decrease in both groups immediately following running, but that a greater decrease would be observed in those with KOA. Additionally, it was hypothesized that values would return to baseline values in controls but remain depressed in runners with KOA up to 90 min after running.

2. Materials and methods

2.1. Participants

Ten female runners with symptomatic tibiofemoral osteoarthritis (TFOA group) and 10 healthy age-matched runners (controls) were recruited through advertisements in local sports medicine clinics, running stores, and online through social media

Table 1
Study participants.

	TFOA (n = 10)	Controls (n = 10)	*P*
Demographics			
Age (years)	52.6 ± 7.6	52.5 ± 7.8	1.00
Body mass index (kg/m^2)	23.0 ± 3.4	23.5 ± 2.5	0.684
Kellgren-Lawrence grade	Grade 2 (n = 8) Grade 3 (n = 2)	Grade 0 (n = 10)	–
Symptom duration (months)	78.1 ± 118.2	N/A	
KOOS score (0–100)	69.6 ± 14.4	95.4 ± 4.5	<**0.001**
Running experience (years)	11.1 ± 9.0	13.1 ± 8.7	0.481
Average running distance (km/week)	20.2 ± 9.9	25.3 ± 13.6	0.481
30-minute run			
Pain level during the run (0–10)	2.0 ± 2.3	0.2 ± 0.4	**0.030**
Treadmill speed (km/h)	7.5 ± 0.9	7.8 ± 1.2	0.353
Step rate (steps/min)	166.9 ± 6.7	158.6 ± 8.8	**0.015**
Running shoes Minimalist index (%)	21.2 ± 9.3	19.8 ± 5.8	0.631
Foot strike pattern (%)			0.587
Rearfoot	80	70	
Midfoot	20	20	
Forefoot	0	10	

Data presented as Mean ± SD
TFOA, tibiofemoral osteoarthritis group; KOOS, Knee Osteoarthritis Outcome Score

(Table 1). To be included, all participants had to: [1] be aged ≥40 years; [2] have run at least 10 km/week during the previous two years; and [3] be comfortable running on a treadmill for 30 min. Runners were included in the TFOA group if they showed radiographic signs of tibiofemoral osteoarthritis characterized by Grade ≥ 2 on the Kellgren-Lawrence scale as shown by weightbearing X-rays [13]. Additionally, they had to report regular knee pain of ≥3/10 on a numerical pain rating scale (0 = no pain; 10 = worst pain imaginable) during running, as well as during other activities of daily living such as going up or down stairs, kneeling or squatting. Runners were included in the control group if they showed no radiographic signs of tibiofemoral osteoarthritis (Grade 0 on the Kellgren–Lawrence scale) and were free of knee pain for the previous six months [13].

Potential participants were excluded from both groups if they reported: any history of traumatic knee injury or knee surgery, presence of a neurological or inflammatory arthritic condition, current lower limb pain during running (other than knee pain in the TFOA group), use of any oral or injected corticosteroids or viscosupplementation during the preceding six months, and presence of any contraindication for MRI (e.g. metal implants). This study was approved by the Institutional Clinical Research Ethics Board (H16-02059) and all participants signed a detailed informed written consent form.

2.2. Study design

The study consisted of a single session of data collection, during which quantitative knee MRI measurements were taken before and after 30 min of treadmill running (Figure 1).

Participants were instructed to avoid any running during the 24 h prior to data collection. Upon arrival, they were asked to rest in a seated position for 15 min while they completed questionnaires about demographics, running habits (experience, weekly running distance) and knee symptoms (Knee Osteoarthritis Outcome Score; KOOS) [14]. In total, participants unloaded their knee cartilage for approximately 30 min (filling-in questionnaires, preparation for MRI, survey scans) before collection of MRI data started, as per previous studies [6,9].

Thereafter, participants were scanned in a supine position with knees in 20° flexion. In the TFOA group, the most symptomatic knee was considered as the study knee if both knees were suitable for inclusion. A randomly chosen knee was selected for the control group.

Following baseline imaging, participants were transported to the laboratory by wheelchair so that knee cartilage loading was isolated to the bout of running. They were provided with one minute of walking to get accustomed to the treadmill before starting the 30-min run. In order to replicate habitual individual training conditions, participants self-selected their running speed and wore their usual running shoes. Step rate [15], foot strike pattern [16], and the level of minimalism of running shoes (rated using the Minimalist Index) [17] were documented to control for potential confounders between groups. Participants also rated their average level of knee pain during the 30-min run on a numerical pain rating scale (0 = no pain; 10 = worst pain imaginable).

Immediately after completing 30 min of running, participants sat on the wheelchair and were transported back to the MRI department and prepared for the post-run assessment, which consisted of the same scanning sequences as the pre-run MRI. Three additional T2 scanning sequences were conducted ($T2_{postA}$, $T2_{postB}$, $T2_{postC}$). Two additional T1ρ scanning sequences were run ($T1\rho_{postA}$, $T1\rho_{postB}$) in between T2 sequences (Figure 1). Participants remained supine in the MRI apparatus during the entire post-run imaging acquisition period.

2.3. Magnetic resonance data acquisition

All data were collected on a 3T MRI scanner (Philips Achieva) equipped with an eight-channel SENSE knee coil. T2 relaxation time was measured using a multi-slice, multi-echo, spin echo scan with seven echoes (TE_1 = 13 ms, echo spacing = 13 ms, TR = 4477 ms, acquired voxel size = 0.4 × 0.4 × 3 mm^3, reconstructed voxel size = 0.31 × 0.31 × 3 mm^3). Sagittal images were acquired using SENSE in two directions (anterior–posterior factor 2, foot-head factor 1.3). T1ρ mapping was performed using a three-dimensional (3D) spoiled gradient echo sequence with sagittal readout and five spin lock durations (TSL = 1/10/20/30/40 ms). The spin lock frequency was 500 Hz, as determined by the duration and angle of the spin lock pulses (TE 1.37 ms, TR 4.3 ms, acquired voxel size 0.6 × 0.8 × 3.0 mm^3, reconstructed voxel size 0.48 × 0.48 × 1.5 mm^3). A fat suppression (SPIR) and inversion pre-pulse (delay 1700 ms) were applied to avoid signal shifts due to the presence of fat and free fluid. A total of 26 slices was acquired for T2 and 66 slices for T1ρ. A 3D sagittal water selective fluid scan (WATSf) was acquired for segmentation

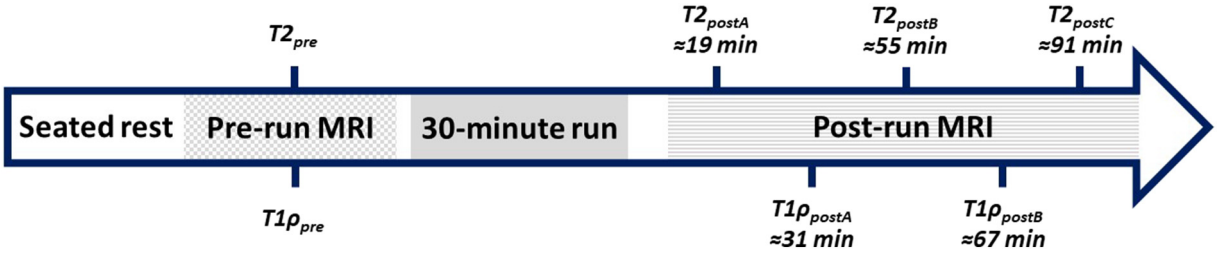

Figure 1. Timeline for the data collection session. Post-run times represent the time elapsed between the end of the run and the different sequences.

purposes. This scan employed a fat suppression pulse (ProSet 1331) and was acquired at $0.6 \times 0.6 \times 1.5$ mm^3, reconstructed to $0.29 \times 0.29 \times 1.5$ mm^3 with TE = 4.6 ms, TR = 20 ms. Parallel imaging was used in the anterior-posterior direction, with a SENSE factor of 2.

2.4. Data processing

After data collection, image files were anonymized and assigned a random number. Data analysis for T2 and T1ρ relaxation times was performed by a member of the research team (MJ, physicist experienced in MRI analyses) who was blinded to group and scanning time. Four regions of interest (ROI) were considered in the analyses: lateral femur, lateral tibia, medial femur and medial tibia. The segmentation of these ROIs was manually performed slice-by-slice on the WATSf scans in the sagittal plane. On each slice, the weightbearing cartilage was bounded in the posterior–anterior plane by the margins of the meniscus. In the medial-lateral plane, ROIs were bounded by the point of separation of the tibial and femoral cartilage, and the intercondylar fossa. A threshold value of 200 ms was used to exclude voxels containing tissues other than cartilage.

T2 relaxation maps were obtained directly from the scanner and based on voxel-wise, mono-exponential fitting of the decay curves. Similarly, T1ρ maps that were computed offline employed a mono-exponential, voxel-wise fitting procedure. Image processing was performed in Python using the Nipy suite of analysis tools along with custom code [18].

T2 maps were aligned to the WATSf image space using SPM 12's coreg function with default parameters in Matlab (The MathWorks Inc., Natick, MA) [19]. T1ρ maps were aligned using ANTs, a non-linear transformation tool [20], also with default parameters. Registrations were visually checked for accuracy and manual corrections to the cartilage segmentations were made as necessary.

2.5. Outcome measures

The primary outcomes of this study were tibiofemoral cartilage T2 and T1ρ relaxation times, which were averaged over the full thickness. T2 relaxation is a recommended imaging outcome for clinical trials in individuals with KOA, as determined by the Osteoarthritis Research Society International (OARSI) [21]. Such measurements have been shown to be valid and reliable assessments of tibiofemoral cartilage integrity [22,23]. Shorter T2 relaxation times indicate less water in cartilage [12]. Though less established than T2, T1ρ relaxation time is also advocated by OARSI guidelines [21], and has shown low inter-session coefficients of variation (5.3%) with no diurnal variation between morning and afternoon scans [23]. Shorter T1ρ relaxation times after activity-related compression correspond to areas of increased glycosaminoglycan and collagen concentration [4,24].

2.6. Statistical analyses

Statistical analyses were conducted by a member of the research team (JFE) who was not involved in data processing. Mann–Whitney U (continuous variables) and Chi-square (foot strike pattern) tests were used to compare both groups' demographics and running habits. Time separating the end of the run and T2 and T1ρ sequences were compared between groups using independent sample *t*-tests. The effects of running on tibiofemoral cartilage were assessed using repeated-measures ANCOVA (General Linear Model). Given the known influence of speed on knee joint forces during running [25], treadmill speed was included as a covariate in T2 and T1ρ relaxation time analyses. Step rate was also added as a covariate, since it was significantly different between TFOA and controls, and because it has been shown to influence tibiofemoral contact forces [15]. Alpha level was set at 0.05, and Bonferroni corrections were applied to adjust for multiple comparisons. All statistical analyses were conducted using the Statistical Package for Social Sciences (SPSS) version 22 (IBM Corporation, Armonk, NY, USA).

3. Results

All participants completed the study without adverse effects. The TFOA group reported a significantly greater level of knee pain than the control group during the bout of running ($P = 0.03$; Table 1). Time elapsed between the end of the run and the post-run MRI data acquisition was not significantly different between groups ($P \geq 0.08$; Table 2).

Table 2
Time (in minutes) elapsed between the end of the run and MRI sequences.

	TFOA (n = 10)	Controls (n = 10)
$T2_{postA}$	20.9 ± 6.3	16.9 ± 3.6
$T1\rho_{postA}$	33.6 ± 6.3	29.3 ± 3.7
$T2_{postB}$	56.4 ± 6.6	52.8 ± 3.7
$T1\rho_{postB}$	68.9 ± 6.5	64.7 ± 3.6
$T2_{postC}$	92.6 ± 6.9	88.6 ± 3.7

Data presented as Mean ± SD.
MRI, magnetic resonance imaging; TFOA, tibiofemoral osteoarthritis group

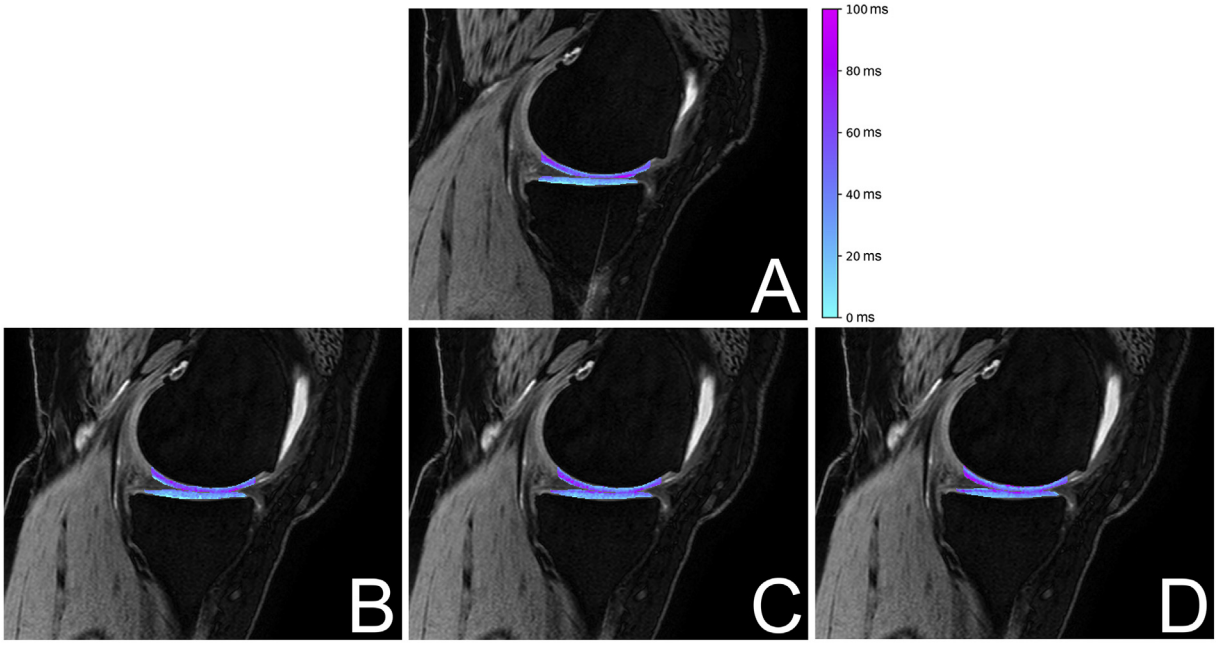

Figure 2. Example of T2 relaxation time (A) T2pre; (B) T2postA; (C) T2postB; (D) T2postC

A visual representation of pre-run and post-run T2 relaxation time in a runner from the TFOA group is presented in Figure 2. No main effects for group or time were found for T2 relaxation time in any ROI (Table 3 and Figure 3). Non-statistically significant trends were found for group × time interaction effects ($P = 0.076$–0.089; Table 3). However, TFOA showed significantly higher T2 relaxation times at $T2_{postB}$, than at $T2_{pre}$ for lateral (+5.4%, $P = 0.003$) and medial femur (+5.5%, $P = 0.022$). At $T2_{postC}$, TFOA values were higher than at baseline for all four ROIs (lateral femur, +7.0%, $P = 0.003$; lateral tibia, +9.1%, $P = 0.01$; medial femur, +6.9%, $P = 0.005$; medial tibia, +11.1%, $P = 0.01$; Table 3). In the control group, none of the post-run T2 values were significantly different from pre-run ($P \geq 0.06$).

Table 3
T2 relaxation values at the different time points, and mean difference with pre-running values.

	T2 relaxation time values (ms)				Mean difference with $T2_{pre}$ (ms)			
	$T2_{pre}$	$T2_{postA}$	$T2_{postB}$	$T2_{postC}$	$T2_{postA}$	$T2_{postB}$	$T2_{postC}$	
Lateral femur								
TFOA	50.4	50.3	53.1	53.9	−0.2	**2.8**	**3.5**	Group: 0.402
	[47.6, 53.2]	[46.6, 53.9]	[49.7, 56.6]	[50.5, 57.4]	[−2.5, 2.1]	**[0.6, 4.8]**	**[1.1, 6.0]**	Time: 0.120
Controls	49.6	48.7	49.6	52.0	−0.9	0.0	2.4	Interaction: 0.076
	[46.8, 52.4]	[45.0, 52.3]	[46.1, 53.0]	[48.5, 55.4]	[−3.2, 1.4]	[−2.1, 2.1]	[−0.1, 4.8]	
Lateral tibia								
TFOA	31.6	31.3	33.6	34.5	−0.4	2.0	**2.9**	Group: 0.515
	[28.5, 34.7]	[28.6, 33.9]	[30.6, 36.6]	[31.7, 37.3]	[−2.4, 1.7]	[−0.4, 4.4]	**[0.6, 5.2]**	Time: 0.190
Controls	33.8	33.6	33.7	35.2	−0.2	−0.1	1.4	Interaction: 0.088
	[30.7, 36.9]	[30.9, 36.3]	[30.7, 36.7]	[32.4, 38.0]	[−2.2, 1.9]	[−2.5, 2.3]	[−0.8, 3.7]	
Medial femur								
TFOA	51.1	51.3	53.8	54.6	0.2	**2.8**	**3.5**	Group: 0.051
	[48.1, 54.1]	[48.2, 54.3]	[51.2, 56.6]	[51.7, 57.5]	[−2.4, 2.7]	**[0.3, 5.3]**	**[0.9, 6.1]**	Time: 0.345
Controls	48.5	47.1	48.6	50.0	−1.5	0.0	1.5	Interaction: 0.078
	[45.5, 51.5]	[44.0, 50.1]	[45.9, 51.2]	[47.2, 52.9]	[−4.0, 1.1]	[−2.4, 2.5]	[−1.1, 4.1]	
Medial tibia								
TFOA	34.8	34.6	38.0	38.6	−0.2	3.2	**3.8**	Group: 0.226
	[31.5, 38.1]	[30.9, 38.3]	[34.3, 41.7]	[34.9, 42.3]	[−3.6, 3.2]	[−1.2, 7.5]	**[0.8, 6.9]**	Time: 0.638
Controls	34.1	31.5	32.6	35.8	−2.5	−1.4	1.7	Interaction: 0.089
	[30.8, 37.4]	[27.8, 35.2]	[28.9, 36.3]	[32.1, 39.5]	[−5.9, 0.8]	[−5.8, 2.9]	[−1.3, 4.8]	

Results presented as mean [95% CI] after controlling for treadmill speed and step rate.
TFOA, tibiofemoral osteoarthritis group; $T2_{pre}$, T2 relaxation time before the run; $T2_{postA}$, T2 relaxation time at first post-run scan; $T2_{postB}$, T2 relaxation time at second post-run scan; $T2_{postC}$, T2 relaxation time at third post-run scan.
Bold values indicate significant within-group changes based on 95% CI limits.

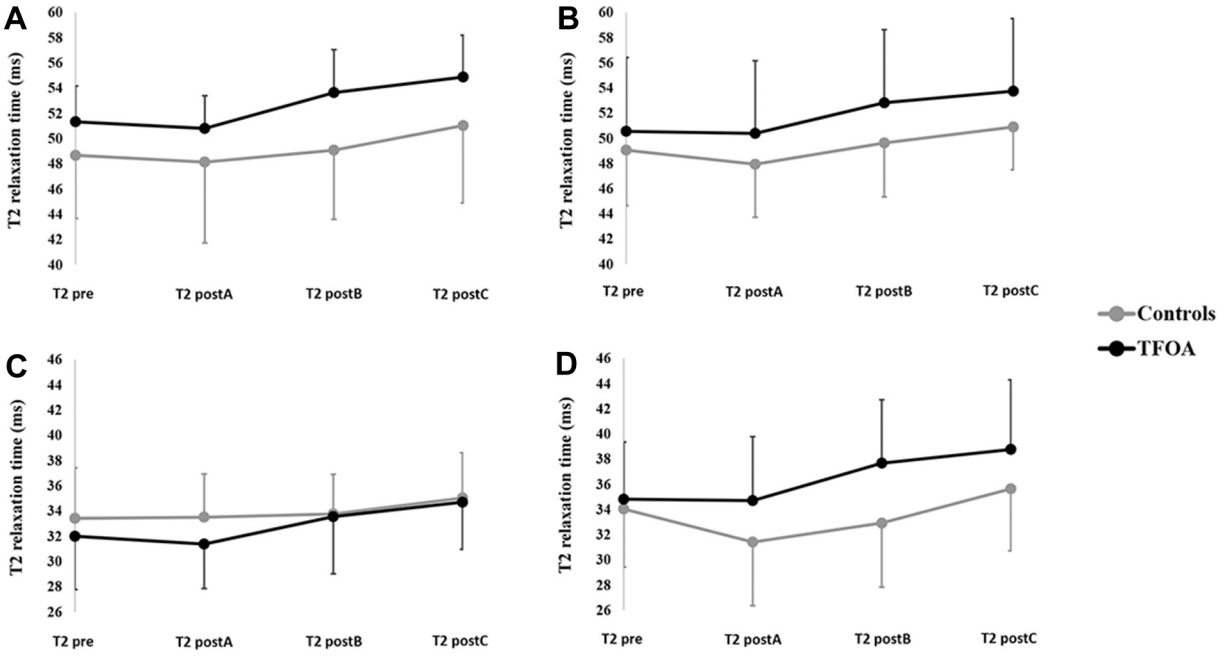

Figure 3. Mean T2 relaxation time (ms) before and after running for (A) lateral femur; (B) medial femur; (C) lateral tibia; (D) medial tibia. Error bars represent SD. TFOA, tibiofemoral osteoarthritis group; $T2_{pre}$, T2 relaxation time before the run; $T2_{postA}$, T2 relaxation time at first post-run scan; $T2_{postB}$, T2 relaxation time at second post-run scan; $T2_{postC}$, T2 relaxation time at third post-run scan.

As for T1ρ, a significant group effect was found in the medial femur ($P = 0.016$), indicating greater values in TFOA than in controls (Table 4 and Figure 4). A trend for a group effect was also found for the lateral femur ($P = 0.099$). T1ρ after running was significantly different from baseline in controls: $T1\rho_{postA}$ was 4.7% lower in the lateral femur ($P = 0.015$) and 4.5% lower in the medial femur ($P = 0.029$). No main effect of time or group × time interaction effects were found for T1ρ in any ROI (Table 4).

4. Discussion

This is the first study to compare the effects of running on T2 and T1ρ relaxation times in the tibiofemoral cartilage of runners with and without KOA. The relatively long post-run scanning time used in this pilot study is novel and allowed detection of

Table 4
T1ρ relaxation values at the different time points, and mean difference with pre-running values.

	T1ρ relaxation time values (ms)			Mean difference with $T1\rho_{pre}$ (ms)		
	$T1\rho_{pre}$	$T1\rho_{postA}$	$T1\rho_{postB}$	$T1\rho_{postA}$	$T1\rho_{postB}$	
Lateral femur						
TFOA	52.5 [49.7, 55.4]	51.4 [49.1, 53.7]	52.5 [49.9, 55.1]	−1.1 [−3.1, 0.8]	0.0 [−2.1, 2.1]	Group: 0.099
Controls	50.4 [47.6, 53.3]	48.0 [45.7, 50.3]	48.8 [46.2, 51.4]	**−2.4 [−4.3, −0.4]**	−1.6 [−3.7, 0.5]	Time: 0.192
						Interaction: 0.288
Lateral tibia						
TFOA	33.8 [31.0, 36.6]	32.8 [30.7, 34.9]	33.3 [31.1, 35.6]	−1.0 [−2.9, 0.9]	−0.5 [−2.8, 1.9]	Group: 0.326
Controls	35.8 [33.0, 38.7]	34.3 [32.3, 36.4]	34.6 [32.4, 36.9]	−1.5 [−3.4, 0.4]	−1.2 [−3.6, 1.1]	Time: 0.234
						Interaction: 0.693
Medial femur						
TFOA	53.4 [50.6, 56.2]	51.7 [49.1, 54.3]	53.6 [51.4, 55.8]	−1.7 [−3.7, 0.3]	0.2 [−1.9, 2.2]	**Group: 0.016**
Controls	49.1 [46.4, 51.9]	46.9 [44.4, 49.5]	49.0 [46.8, 51.2]	**−2.2 [−4.2, −0.2]**	−0.1 [−2.2, 1.9]	Time: 0.675
						Interaction: 0.882
Medial tibia						
TFOA	30.9 [28.0, 33.9]	31.0 [28.4, 33.6]	30.7 [28.2, 33.3]	0.0 [−3.5, 3.5]	−0.2 [−4.1, 3.7]	Group: 0.681
Controls	32.1 [29.1, 35.1]	31.7 [29.1, 34.3]	30.9 [28.3, 33.4]	−0.4 [−3.9, 3.1]	−1.2 [−5.1, 2.7]	Time: 0.901
						Interaction: 0.863

Results presented as mean [95% CI] after controlling for treadmill speed and step rate.
TFOA, tibiofemoral osteoarthritis group; $T1\rho_{pre}$, T1ρ relaxation time before the run; $T1\rho_{postA}$, T1ρ relaxation time at first post-run scan; $T1\rho_{postB}$, T1ρ relaxation time at second post-run scan.
Bold values indicate significant within-group changes based on 95% CI limits.

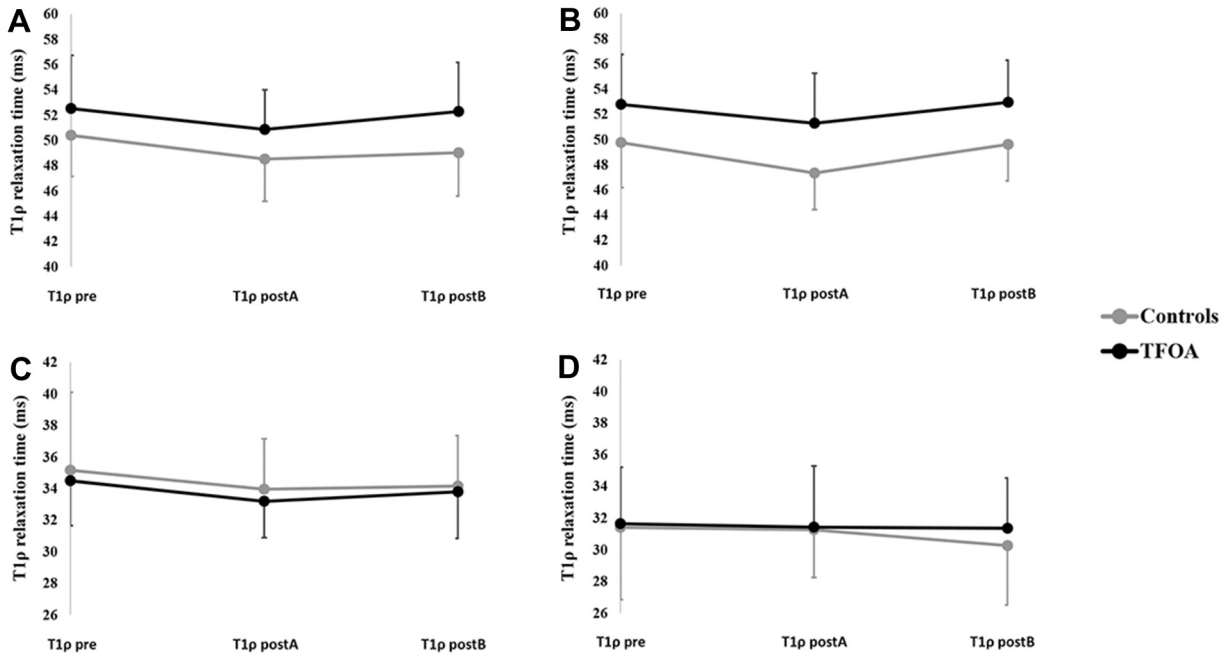

Figure 4. Mean T1ρ relaxation time (ms) before and after running for (A) lateral femur; (B) medial femur; (C) lateral tibia; (D) medial tibia. Error bars represent SD. TFOA, tibiofemoral osteoarthritis group; $T1\rho_{pre}$, T1ρ relaxation time before the run; $T1\rho_{postA}$, T1ρ relaxation time at first post-run scan; $T1\rho_{postB}$, T1ρ relaxation time at second post-run scan.

potential differences in cartilage recovery in runners with KOA, which will help inform future research. Based on previous studies in healthy runners, it was hypothesized that the TFOA group would experience a greater immediate decrease along with delayed normalization of relaxation times after running.

Unlike previous studies, no statistically significant changes were observed in T2 relaxation time in either group immediately following 30 min of running (i.e. $T2_{postA}$). Behzadi et al. reported reductions of 12.3–13.2% immediately after a 45-minute run [7], while Subburaj et al. noted decreased T2 relaxation times after 30 min of running, albeit only in the medial tibiofemoral compartment (5.4%) [6]. Gatti et al. also found that 15 min of running was sufficient to reduce tibial T2 values by 6.1% [9]. Interestingly, these previous studies were all conducted in healthy young individuals (mean age < 30 years). While age has not been found to significantly influence T2 response to running in previous studies [8,26], perhaps a combination of age and running experience could have influenced the current findings. Indeed, the cohort comprised experienced recreational runners (average 12.1 years of experience, running 22.7 km/week). It has been previously suggested that greater baseline levels of physical activity could lead to smaller changes in tibiofemoral T2 values after loading [6,9]. Cartilage adaptation to loading could potentially lead to less T2 variations after a bout of running, and perhaps a longer run would have been necessary to observe reductions in T2 values in this cohort of experienced runners.

Another potential explanation for the absence of immediate effects of running on T2 is the time elapsed between the end of the run and the post-run scans. While every effort was made to commence MRI as soon as possible, $T2_{postA}$ started nearly 20 min after the run. In comparison, studies that reported significant decreases in T2 commenced data collection <4 min after running [7,9]. The longer period in the current study could have allowed water to migrate back into the cartilage before measurements took place. Although decreased T2 values were still observed in young active males 30 min after running for 30 min [27], cartilage of young healthy runners recovered in as little as 60 min even after 20 km of running [28]. Therefore, it cannot be excluded that this prevented detection of true immediate changes immediately after running.

In the current study, decreased T1ρ relaxation time was observed solely in the controls' femoral cartilage immediately following the run, thereby only partially confirming the first hypothesis. Using similar 30-minute treadmill running protocols, previous studies have reported significant T1ρ reductions in both the medial and lateral tibiofemoral compartments [6,29]. The absence of changes in TFOA and in the controls' tibias could be due to the lower running speed in the current study (average 7.7 km/h) compared to previous studies (average 10.4–10.7 km/h). However, altered cartilage behaviour as a consequence of KOA may provide a better explanation for the current findings. Between-group differences in femoral T1ρ values (significant group effect for medial femur, trend for lateral femur) could be indicative of alterations in proteoglycan structure or content in TFOA [4]. Since T1ρ is also thought to be influenced by both collagen composition and cartilage hydration [30], the absence of changes in TFOA after loading may reflect reduced capacity for fluid movements, which are necessary for maintaining homeostasis [31].

The current findings also did not confirm the second hypothesis, which stated that values in the TFOA group would remain lower after running in comparison with controls. Instead, statistical analyses indicated trending group × time interaction effects for increased post-run T2 values in all four ROIs only in TFOA. Interestingly, increased $T2_{postB}$ (femur, tibia) and $T2_{postC}$ values

compared with baseline values are indicative of greater water content in TFOA [4]. Given that participants from the TFOA group were all symptomatic during habitual running, it is possible that the treadmill run triggered an acute overload response in the knee joint, thereby increasing cartilage fluid. However, the amount of time needed for T2 values to recover to baseline is unknown. Impaired ability of the knee joint to recover from running has previously been reported in individuals with post-anterior cruciate ligament repair. In addition to greater pre-run T2 values in the medial femur compared with controls, which may be indicative of increased cartilage fluid, Van Ginckel et al. showed that cartilage volume had still not recovered fully 45 min after running [32]. A trend towards increased bone marrow edema as much as 48 h following a marathon has also been reported in eight runners with a previous anterior cruciate ligament reconstruction, in comparison with their healthy knee [33]. Therefore, future studies in runners with KOA should consider a sequential series of scans to better understand the time-course of cartilage recovery. This could provide more information on the readiness of cartilage to sustain subsequent impact, which would help provide specific training frequency and volume recommendations to those with symptomatic KOA. Even if impact exercise or maintaining a running program has not been found to be deleterious for KOA progression [34–36], little is known about optimal running parameters in that population.

This study has limitations. First, the relatively small sample size of this pilot study may not have been sufficient to detect between-group differences in cartilage recovery. Second, only female runners were included. Thus, results may not be generalizable to male runners with similar characteristics. Recruiting only one sex allowed the influence of potential systemic and hormonal confounders to be minimized, and is an approach common in previous studies investigating the effects of running on knee cartilage [7,9,26–28,37]. Third, analyzing mean values for the different ROIs irrespective of cartilage depth may have limited interpretation of results. It is possible that superficial and deep layers recovered differently after running [8]; however, the resolution of the current images did not allow depth-specific analyses. Fourth, the interpretation of results was limited by the absence of detailed data on running biomechanics. It is believed that only Kersting et al. paired biomechanical data with cartilage analysis in healthy runners [38]. Given that they reported significant associations between joint contact force and reductions in cartilage volume following a bout of running, future studies should consider including a detailed biomechanical analysis to supplement cartilage behaviour data in those with KOA. In addition to clarifying how running mechanics affect cartilage, this would provide a mechanistic basis for potential biomechanical interventions in this population.

5. Conclusion

Despite the absence of statistically significant differences in cartilage recovery following 30 min of running between female runners with and without symptomatic KOA, a delayed increase in T2 relaxation times in those with KOA suggests that cartilage may need more time to recover in that population. Further research should investigate the effects of repeated exposure and running mechanics to aid in formulating evidence-based clinical recommendations to older runners with KOA.

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Declaration of Competing Interest

The authors report no conflict of interest relevant to this work.

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