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T2 relaxation time measurements in tibiotalar cartilage after barefoot running and its relationship to ankle biomechanics

Hyun Kyung Kim [a], Justin Fernandez [b,c], Christabel Logan [d], Gregory P. Tarr [d], Anthony Doyle [a,d], S. Ali Mirjalili [a,*]

[a] Faculty of Medical and Health Sciences, University of Auckland, Auckland, New Zealand
[b] Department of Engineering Science, Faculty of Engineering, University of Auckland, Auckland, New Zealand
[c] Auckland Bioengineering Institute, University of Auckland, Auckland, New Zealand
[d] Radiology Department, Auckland District Health Board, New Zealand

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ABSTRACT

The influence of ankle kinematics and plantar pressure from mid-range barefoot running on T2 relaxation times of tibiotalar cartilage is unknown. This study aimed to quantitatively evaluate the T2 relaxation time of tibiotalar cartilage and ankle biomechanics following 5 km barefoot running. Twenty healthy runners (who had no 5 km barefoot running experience) underwent 3.0-Tesla magnetic resonance (MR) scans and assessment of running gait before and after 5 km barefoot running. Participants were divided into two groups consisting of marathon-experienced (n = 10) and novice (n = 10) with equal number of males and females in each group. Three musculoskeletal radiologists measured T2 relaxation times in 18 regions of the ankle cartilage: anterior zone, central zone, and posterior zone, or lateral, middle, and medial sections in the sagittal plane. Three-dimensional ankle kinetics, kinematics, and plantar pressure were all also assessed during barefoot running. In the novice group, the T2 relaxation time in the posterior zone of tibial cartilage ($p = 0.001$) and lateral section in both tibial ($p = 0.02$) and talar ($p = 0.02$) cartilage were significantly increased after barefoot running. Ankle kinematics exhibited significant changes in females. Plantar loading was shifted from the medial to lateral aspect after running. This included a significant reduction in the loading under the toes and the 1st, 2nd and 3rd metatarsals, with a significant increase under the 4th and 5th metatarsals and lateral midfoot. The results suggest that plantar pressure may directly lead to local increases in cartilage T2 signal, which was not associated with changes in ankle kinematics.

1. Introduction

Barefoot running has been reported to be biomechanically beneficial for runners as it reduces impact force, impact rate, and stride length compared with traditional shod running (De Wit et al., 2000; Lieberman et al., 2010). However, it remains unclear whether the biomechanical effects of barefoot running on the ankle joint (tibiotalar cartilage) are exhibited in clinical imaging modalities, specifically Magnetic Resonance Imaging (MRI).

Magnetic Resonance Imaging (MRI) is a non-invasive imaging technique and has been proposed as a desired diagnostic tool for *in vivo* evaluation of degenerative or traumatic lesions in articular cartilage. Pathological and/or morphological changes, including bone marrow edema (BME) lesion, joint effusion, and cartilage deformation, have been reported after long-distance shod running (Hinterwimmer et al., 2014; Mosher et al., 2005; Schuetz et al., 2014; Stehling et al., 2011). However, previous MRI studies typically focused on the knee cartilage rather than ankle cartilage. A recent systematic review (Kim et al., 2017) also reported that little information is available on the ankle and foot structures in response to long-distance shod running, and reported subtle pathological and biochemical alteration in the ankle and foot after running.

Quantitative assessments of articular cartilage have been performed using MRI-derived T2 maps (Luke et al., 2010; Subburaj et al., 2012). T2 relaxation times are correlated with extracellular water content and collagen degradation in articular cartilage (Mosher and Dardzinski, 2004). When cartilage is compressed by

* Corresponding author at: FMHS, Building 502, Level 1, Room 185, 85 Park road, Grafton, Auckland 1023, New Zealand.
E-mail address: a.mirjalili@auckland.ac.nz (S.A. Mirjalili).

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applying an external force, water content and collagen fiber orientation of the extracellular matrix are altered, which is shown to be correlated with changes in T2 relaxation times (Liess et al., 2002). There is good evidence that changes in molecular organization and hydration of the extracellular matrix are associated with osteoarthritic cartilage (Heinegård and Saxne, 2011; Lorenz and Richter, 2006). Hence, T2 relaxation times can potentially indicate early cartilage degeneration, which appears as sites with increased T2 values (Dunn et al., 2004; Mosher and Dardzinski, 2004).

Significant T2 alteration in the knee cartilage has been reported even after 30 min of running in 20 young healthy runners (Subburaj et al., 2012). Thus, repetitive loading during mid to long distance shod running may place the articular cartilage at increased risk of damage. However, it has been reported that people generally lower their ground impact force when running barefoot compared with running shod (Lieberman et al., 2010). Although it is reasonable to expect that running barefoot may have a clinical benefit for ankle cartilage, quantitative evaluation of ankle cartilage using T2 mapping in response to barefoot running has not been presented together. Moreover, MRI findings including quantification of T2 values and qualitative analysis of ankle cartilage, and their relationship to running biomechanics in response to barefoot running are poorly understood. Hence, a study investigating the acute effects of barefoot running on ankle cartilage using T2 mapping will further advance our understanding of the benefits and/or limitations of barefoot running.

Therefore, the aims of this study are: (1) to quantitatively assess tibiotalar T2 cartilage relaxation time in response to 5 km barefoot running; (2) to investigate whether fitness level (novice and marathon-experienced) or gender, affects T2 values in the ankle cartilage in response to 5 km barefoot running; and (3) to evaluate whether plantar pressure, ankle kinematics, or both, are associated with T2 changes post 5 km barefoot running. It was hypothesized that: (1) T2 relaxation values are increased in the tibiotalar cartilage in response to 5 km barefoot running; (2) T2 relaxation values are increased with increased plantar pressure; and (3) T2 relaxation values are gender and fitness level specific.

2. Methods

Ethical approval was obtained from the University of Auckland Human Ethics Committee (ref: 016488) and informed participants signed their consent.

2.1. Study population

Ten marathon-experienced runners (ME) and ten age-matched novice runners (NOVICE) including males and females were recruited. To accurately determine their general activity levels, the Tegner scale (Stahl et al., 2008; Tegner and Lysholm, 1985) was employed and scored between 1 (sedentary behaviors) and 10 (highly competitive sports level). Inclusion criteria for the ME runners were: (1) they have regularly participated in half- or full marathon races in the last three years, and (2) the Tegner scale should be greater than 6. Inclusion criteria for the NOVICE runners were: (1) they may run recreationally, but have never been involved in any high-level sports and marathon races, and (2) the Tegner scale should be lower than 4. Common inclusion criteria for all participants were: (1) healthy Caucasian adults (18–50 years old), (2) no history of lower limb injuries and/or major pathologies, (3) run normally with shoes, and (4) have a heel strike running technique. The exclusion criteria were: (1) professionally or heavily participate in other sporting activities, (2) have a body mass index (BMI) outside the range of 18–30, and (3) contraindication to MRI.

2.2. Experimental protocol

The experiment was conducted on two separate days. On the first day, the pre-run scan of the right foot and pre-run gait data during barefoot running were acquired. To minimize potential diurnal effect in the cartilage T2 values (Coleman et al., 2013), the pre-run scan was conducted in the morning. All participants were instructed not to participate in any training (24–48 h) before their pre-run scan day. On the second day, all participants ran for 5 km barefoot on a treadmill at a self-selected pace without incline. All participants used the same treadmill under laboratory conditions, hence, the temperature and humidity were always controlled. Immediately after running, post-run gait data was acquired, and 3.20 ± 0.97 h later (due to travel time), post-MR scans of the right foot were obtained with the same pre-scan methodology.

2.3. MR data acquisition

Scans of the right foot and ankle were acquired with a 3.0-Tesla MRI scanner (Siemens Skyra, Erlangen, Germany) using a 16-channel foot coil while the participant was lying supine with a neutral ankle position. To stabilize the ankle and foot within the coil, sponge cushions were used to minimize any inadvertent variation in the location of the ankle cartilage. The imaging parameters are summarized in Table 1.

2.4. MR image analysis

An experienced radiologist (30 years in musculoskeletal radiology) and a senior and junior radiology resident independently evaluated all MRI scans using Osirix Lite v.9.0.1 (Pixmeo, Geneva, Switzerland). Examiners were blinded to runners' information and to pre- and post-run scans.

2.4.1. Qualitative analysis

Pre- and post-run scans were reviewed separated by a two-week interval. The T1 weighted STIR and DESS images were evaluated for the presence of cartilage lesions in the ankle, bone marrow edema (BME) in the tibial cartilage (TBC) and talar cartilage (TLC), Os trigonum, and other pathologies: joint lesion/arthritis elsewhere in the foot, Achilles tendinopathy, ankle ligament tears, plantar fasciitis, and Haglund lesions.

2.4.2. Quantification of T2

The MR images were transferred to the Osirix Lite software for quantification of T2 relaxation times. To measure cartilage T2 values, three representative sagittal sections showing the tibiotalar cartilage were selected from the medial, middle, and lateral aspects of the tibiotalar joint from each image data set (Fig. 1). To minimize the effect of partial volume artefact, we excluded the medial and lateral malleolar regions of the ankle (including tibial, fibular, and talar) in the analysis. For the purposes of analysis, the joint cartilage was equally and manually divided into anterior zone (AZ), central zone (CZ), and posterior zone (PZ), with anterior and posterior cortices of the tibia and talus marking the anterior and posterior margins. Separate regions of interest were drawn around the TBC and TLC in these three zones on the T2 mapping images, cross referencing with the diagnostic MR for anatomical correlation. Hence, 18 regions were identified in the three sections of each ankle.

2.5. Gait test protocol

Barefoot running kinematics were collected using an 8-camera Vicon motion analysis system (Vicon Oxford Metrics, Oxford, UK)

Table 1
MRI parameters.

Pulse sequences	Flip angle (degrees)	Echo time (ms)	Repetition time (ms)	Slice thickness (mm)	Field of view (mm)	Bandwidth (Hz/Pixel)	Time of acquisition (minutes)
Sagittal T1 turbo spin echo	140	140	600	2.5	250	257	2.57
Sagittal T2 DESS gradient echo water excitation	28	5	12.9	0.6	250	310	4.51
Sagittal and coronal short tau turbo inversion recovery	150	50	4,000	2.5	250	248	4.18
Sagittal and coronal T2 mapping	180	13.8	1,600	3	140	230	4.16

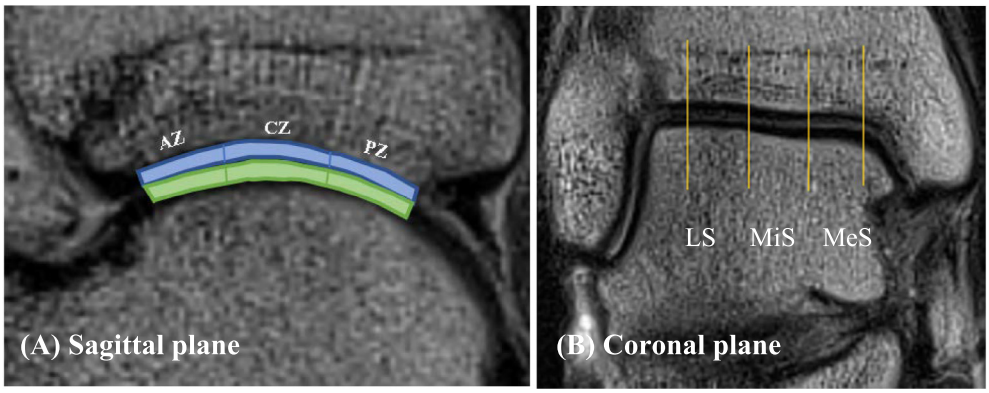

Fig. 1. T2 maps post-processing for quantification of T2 relaxation time in the ankle cartilage. (A): six zones of TBC and TLC in sagittal plane – anterior zone (AZ), central zone (CZ), and posterior zone (PZ). (B): three sections of ankle cartilage in coronal plane – lateral section (LS), middle section (MiS), and medial section (MeS).

with a sampling rate of 100 Hz. The ground reaction force was obtained simultaneously using three force plates (Bertec Corporation, Ohio, USA) with sampling rate of 1000 Hz. Based on the Cleveland marker set, 27 reflective markers were placed on the anterior superior iliac spines; the sacrum (midpoint); the lateral and medial femoral epicondyles of the knees; the medial and lateral malleoli of the ankles; the lateral side of the thighs and shanks (using a triad consisting of three markers); 2nd metatarsal heads; and the posterior aspect of the calcanei. All participants were asked to run barefoot across the force plates in the motion capture area. Participants ran the 5 km distance at their self-selected speed. They were then asked to repeat this run in the gait lab at that same self-regulated speed. Post-processing of the pre and post runs was used to assess if there were any differences in speed.

Plantar pressure of the right foot was measured with a Novel emed® pressure platform during running barefoot. The foot map was divided into 11 regions of interest (ROIs) for further analysis (Alfuth and Rosenbaum, 2011; Willems et al., 2012), including hallux (T1), toes 2–5 (T2-T5), all metatarsals (M1, M2, M3, M4, M5), medial and lateral midfoot (MM, LM), and medial and lateral heel (MH, LH).

2.6. Gait data processing and analysis

Motion capture data was exported to the 'Nexus' software (Oxford Metrics, Oxford, UK) and were filtered using an 8 Hz low-pass, fourth-order, zero-lag Butterworth filter (Stefanyshyn and Nigg, 1997; Winter, 1983). Trials were valid if the participant stepped onto the force plate so that ground reaction force measurements were available during one stride with all markers visible. The three best of these valid trials were used for gait analysis. Three-dimensional angle, torque, and power at the lower limb joints were calculated using Polygon (Oxford Metrics, Oxford, UK). Power ($W.kg^{-1}$) and torque ($Nm.kg^{-1}$) were normalized by body weight, and the maxima and minima were obtained from the stance phase for statistical analysis. The angle (degree) at the initial foot contact, maxima, and minima were also acquired from the full gait cycle for statistical analysis. Peak plantar pressure (kPa) was obtained from each ROI.

2.7. Reproducibility measurements

An intra-class correlation coefficient (ICC) was performed to determine the reproducibility of T2 measurements in the ankle cartilage regions. Inter and intra-reliability on the T2 measurements were estimated between investigators.

2.8. Statistical analysis

SPSS Version 20 (IBM Corporation, Armonk, NY, USA) was used for statistical analysis. The 20 participants were divided into four groups based on their fitness level (ME and NOVICE) and gender (FEMALE and MALE). The normality test was initially performed using the Kolmogorov–Smirnov and Shapiro–Wilk tests. The Wilcoxon signed rank test was used to compare qualitative MRI parameters between pre- and post-run scans. For testing the difference of T2 relaxation time between pre- and post-run, a paired (two-tailed) *t*-test was conducted for each TBC and TLC region. The effect size (Cohen's *d* coefficient) was also calculated and the scores were interpreted as follows: $0.15 \leq d < 0.4$ small difference; $0.4 \leq d < 0.75$ moderate difference; $0.75 \leq d < 1.1$ large difference; $d > 1.1$ very large difference. To investigate the differences in T2 relaxation time within ankle cartilage regions and within the groups, a one-way analysis of variance (ANOVA) was employed with the Tukey's honest significant difference *post hoc* test. Additionally, a two-way analysis of covariance (ANCOVA) was conducted to evaluate whether fitness level or gender affects the T2 values in response to 5 km barefoot running whilst controlling for pre-run values as a covariate. The significance level was set at $p \leq 0.05$.

3. Results

All 20 participants completed the 5 km barefoot run over 31.66 ± 6.84 min. The mean speed between pre- and post-run gait tests were not significantly different (Table 2). The ICC for reproducibility of T2 measurements on the TBC and TLC showed good agreement for both intra- (TBC, range: 0.71–0.85; TLC, range: 0.73–0.87) and inter-reliability (TBC, range: 0.92–0.97; TLC, range: 0.7–0.9).

3.1. Study population

Demographic information on 20 healthy volunteers is presented in Table 3. Age and height revealed no statistical difference between the four groups. Weight and BMI were significantly higher in the MALE group compared to the FEMALE group, while the ME and NOVICE groups showed no statistical difference. Regarding training status, the Tegner scale, running distance per week, running days per week and training years were significantly greater in the ME group when compared with the NOVICE group. The training status showed no statistical difference between the FEMALE and MALE groups.

3.2. Qualitative analysis of ankle MR before and after exercise

The qualitative results of MRI-identified pathology are presented in Table 4. There were no major structural abnormalities in any imaged ankles between pre- and post-run scans. No participant presented with cartilage lesions, plantar fasciitis, or Haglund lesions. Two out of 10 ME females showed minor ankle ligament tears, not observed in other groups. Two out of 10 ME (one male and one female) revealed asymptomatic Achilles tendinopathy, whereas others showed no tendinopathy. The BME in TBC was observed in only 2 people (female novice and experienced male). The NOVICE group showed no BME in TLC before the 5 km running, but one of them (male) revealed BME after running. One out of 10 ME females showed BME in TLC in both pre- and post-run scans.

3.3. Quantification of T2 cartilage maps before and after exercise

Tibiotalar cartilage T2 changes before and after 5 km barefoot running are presented in Figs. 2, 3 and Table 5. Comparing pre- and post-run scans, the NOVICE group was significantly affected by running barefoot. Specifically, the NOVICE group demonstrated that T2 values measured in the PZ of the TBC ($p = 0.001$) increased

Table 2
Mean values of gait speed (km/h) during gait tests for each group. A paired *t*-test was conducted to compare between pre- and post-run for each group. Presented as mean ± standard deviation.

	NOVICE (n = 10)		ME (n = 10)		MALE (n = 10)		FEMALE (n = 10)	
	Pre	Post	Pre	Post	Pre	Post	Pre	Post
Gait speed (km/h)	11.08 ± 1.39	10.77 ± 1.43	11.07 ± 1.59	10.21 ± 1.35	11.53 ± 1.51	11.12 ± 1.44	10.74 ± 1.51	9.96 ± 1.32
P value	0.07		0.42		0.16		0.27	

Table 3
Demographic information for each group. One-way ANOVA was conducted to compare demographic information between groups. When warranted, the Tukey's honest *post hoc* test was performed to determine which groups differed. Presented as mean ± standard deviation.

Parameters	NOVICE (n = 10)	ME (n = 10)	FEMALE (n = 10)	MALE (n = 10)	*P value*
Gender (F:M)	5:5	5:5	–	–	
Age (yr)	29 ± 6.8	31.2 ± 9.9	27.1 ± 6.5	33.1 ± 9.1	0.4
Height (m)	1.69 ± 0.1	1.73 ± 0.1	1.68 ± 0.1	1.75 ± 0.1	0.2
Weight (kg)	65.6 ± 9.8	65.4 ± 9.9	59.5 ± 4.8	71.5 ± 9.5	0.02[€]
BMI (kg/m^2)	22.7 ± 2	21.7 ± 1.5	21.1 ± 1.2	23.3 ± 1.6	0.02[€]
Training status					
Tegner scale	2.9 ± 1.8	6.5 ± 0.7	5 ± 1.8	4.4 ± 2.7	0.001[¥]
Distance/week (km)	5.4 ± 6.9	31.4 ± 26.1	13.6 ± 14.3	23.2 ± 29.1	0.04[¥]
Days/week	1.1 ± 1.2	3.5 ± 1.5	2.2 ± 1.6	2.4 ± 2	0.01[¥]
Years training	2.4 ± 2.9	9.4 ± 5.6	4.9 ± 5.2	6.9 ± 6.2	0.02[¥]

[€] Indicates a significant difference between the FEMALE group and the MALE group according to the Tukey's honest *post hoc* test.
[¥] Indicates a significant difference between the NOVICE group and the ME group according to the Tukey's honest *post hoc* test.

Table 4
Qualitative MRI analysis before and after 5 km barefoot running in each group. The Wilcoxon signed-rank test was conducted to compare between pre- and post-run for each group. Presented data are number of patients.

	NOVICE (n = 10)			ME (n = 10)			FEMALE (n = 10)			MALE (n = 10)		
	Pre	Post	*P* value	Pre	Post	*P* value	Pre	Post	*P* value	Pre	Post	*P* value
Ankle cartilage lesions	0	0	–	0	0	–	0	0	–	0	0	–
Tibia cartilage BME	1	1	–	1	1	–	1	1	–	1	1	–
Talus cartilage BME	0	1	0.32	1	1	–	1	1	–	0	1	0.32
Os trigonum	1	1	–	1	1	–	2	2	–	1	1	–
Achilles tendinopathy	0	0	–	2	2	–	1	1	–	1	1	–
Ankle ligament tears	0	0	–	2	2	–	2	2	–	0	0	–
Plantar fasciitis	0	0	–	0	0	–	0	0	–	0	0	–
Haglund deformity	0	0	–	0	0	–	0	0	–	0	0	–

Abbreviation: BME – bone marrow edema

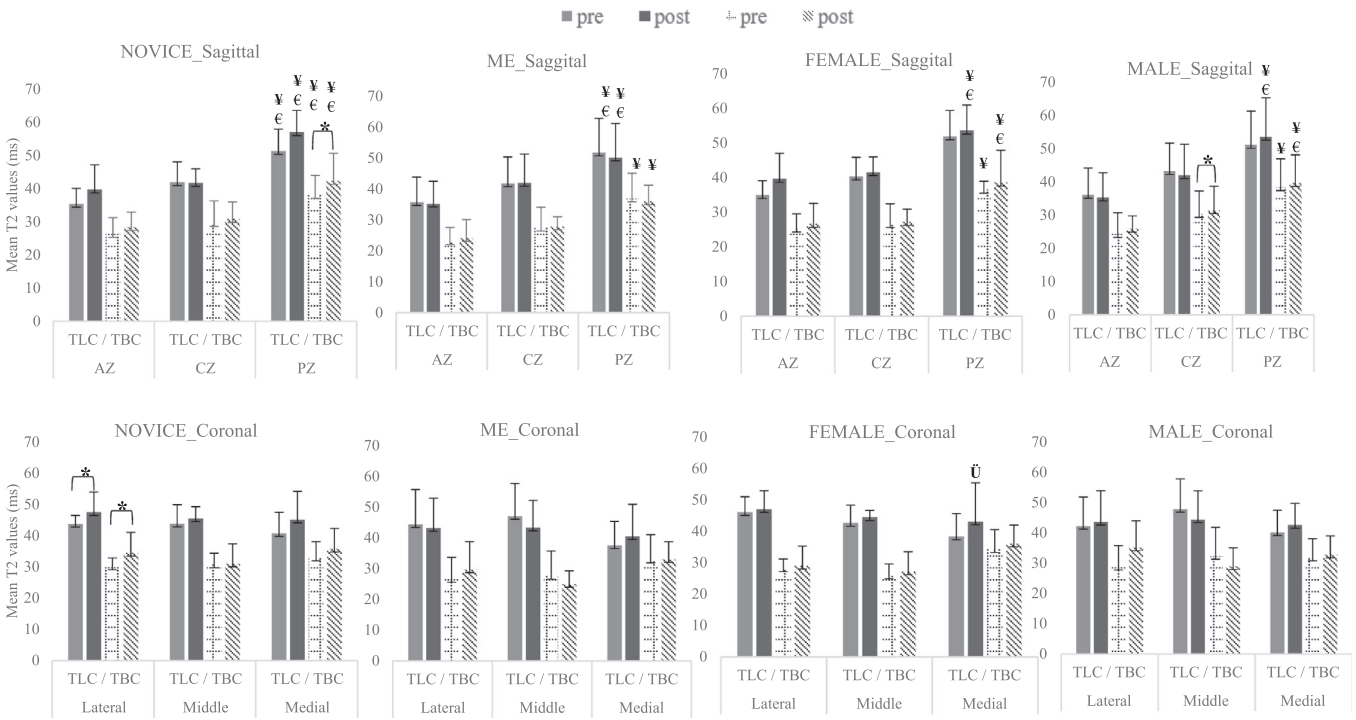

Fig. 2. T2 relaxation times in the pre- and post-barefoot run for three zones/sections of TLC and TBC for each group. A paired *t*-test was conducted to compare between pre- and post-run for each group. One-way ANOVA was conducted to investigate the zonal difference. When warranted the Tukey's honest *post hoc* test was performed to determine which zones differed. * indicates a significant different ($p \leq 0.05$) between pre and post according to a paired *t*-test. ¥ indicates a significant zonal different ($p \leq 0.05$) between AZ and PZ according to the Tukey's honest *post hoc* test. € indicates a significant zonal different ($p \leq 0.05$) between CZ and PZ according to the Tukey's honest *post hoc* test. Ü indicates a significant zonal different ($p \leq 0.05$) between lateral and medial sections according to the Tukey's honest *post hoc* test.

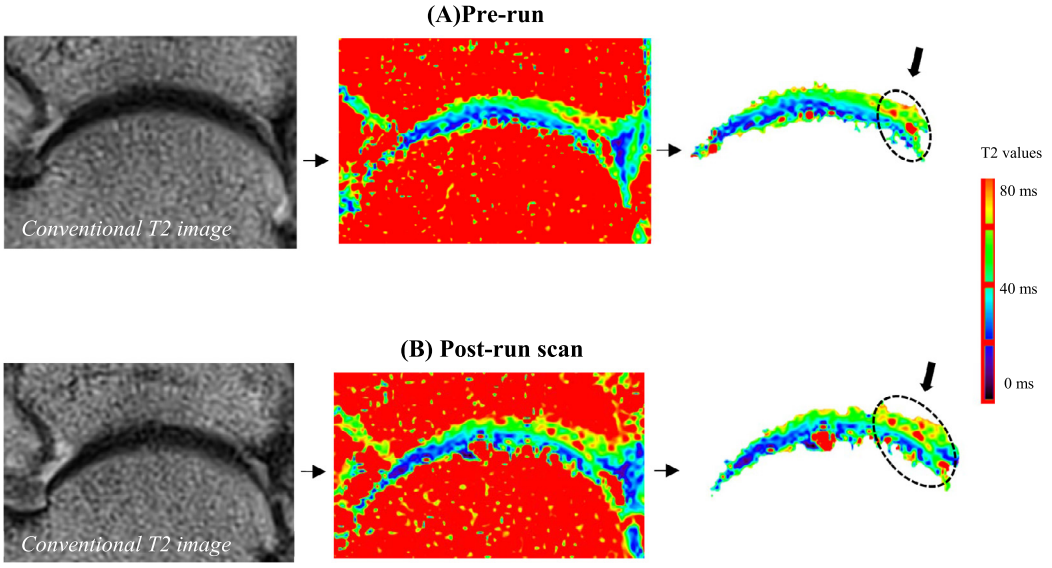

Fig. 3. Example of T2 changes in pre- (A) and post-run (B) scans of the tibiotalar cartilage in the lateral section sagittal plane. 34-year-old male novice runner showed high T2 values (ms), indicated by red pixels, in the PZ after running. High T2 values were also generally observed in the border of the cartilage. (For interpretation of the references to colour in this figure legend, the reader is referred to the web version of this article.)

after running. Moreover, when the T2 values were analyzed in the coronal plane, only the NOVICE group showed a significant elevation in the lateral section (TLC, $p = 0.02$; TBC, $p = 0.02$) after running barefoot. The MALE group also showed a significant T2 elevation in the CZ of the TBC ($p = 0.02$), but the effect size was small. There was no gender effect on the T2 values according to the two-way ANCOVA. However, there was a significant effect of fitness level on T2 in the PZ (TBC, $p = 0.03$) and in the lateral section (TBC, $p = 0.05$). There was no interaction effect on T2 values between fitness level and gender. Regarding the zonal differences in the sagittal plane, T2 values measured in the PZ exhibited the highest values, while the AZ showed the lowest values in the four groups for both pre- and post-run scans. There was no significant difference between AZ and CZ across groups.

Table 5
Mean values of T2 (ms) for each group. A paired *t*-test was conducted to compare between pre- and post-run for each group. Two-way ANCOVA was conducted to investigate whether fitness level or gender affects T2 values. It showed main- and interaction-effects of the fitness level and gender on T2 values. Presented as mean ± standard deviation.

		TBC (ms)			TLC (ms)			TBC (ms)			TLC (ms)		
		AZ	CZ	PZ	AZ	CZ	PZ	Lateral	Middle	Medial	Lateral	Middle	Medial
Pre	NOVICE	35.38 ± 4.7	41.83 ± 6.2	51.27 ± 6.6	26.31 ± 4.9	29.55 ± 6.7	38.02 ± 5.9	43.81 ± 2.8	43.85 ± 6.1	40.81 ± 6.7	30.12 ± 2.8	30.76 ± 5.1	33 ± 6.6
	ME	35.64 ± 8.2	41.72 ± 8.6	51.66 ± 11.1	23.01 ± 5.6	27.36 ± 6.5	27.36 ± 6.5	44.38 ± 11.4	47.08 ± 10.6	37.55 ± 7.8	26.61 ± 7.1	27.65 ± 8.1	32.94 ± 8.1
	FEMALE	34.9 ± 4.2	40.3 ± 5.5	51.86 ± 7.5	25.27 ± 4.2	26.56 ± 5.8	36.47 ± 2.4	50.08 ± 15.6	49.81 ± 23.3	41.45 ± 12.4	32.33 ± 13.6	30.21 ± 14	35.66 ± 7.4
	MALE	36.05 ± 8.1	43.11 ± 8.5	51.08 ± 10.2	24.28 ± 6.4	30.26 ± 6.9	38.34 ± 8.5	42.27 ± 9.7	47.86 ± 10	40.13 ± 7.4	30.89 ± 7.1	32.32 ± 9.6	31.81 ± 6.8
Post	NOVICE	39.67 ± 7.5	41.62 ± 4.3	56.98 ± 6.6	28.35 ± 4.5	30.72 ± 5.2	42.3 ± 8.2	47.64 ± 6.4	45.55 ± 3.8	45.18 ± 9	34.48 ± 6.6	31.07 ± 6.4	35.82 ± 6.5
	ME	35.16 ± 7.3	41.84 ± 9.4	50.84 ± 11.1	24.09 ± 4.5	27.79 ± 6.7	35.88 ± 8.2	43.18 ± 9.8	43.35 ± 8.9	40.5 ± 10.5	29.66 ± 9.1	25.04 ± 4.3	33.06 ± 5.7
	FEMALE	39.61 ± 7.3	41.53 ± 4.4	53.5 ± 4.4	26.61 ± 6	27.1 ± 3.8	38.58 ± 9.2	47.06 ± 5.9	44.47 ± 2.2	43.11 ± 12.3	28.99 ± 6.3	27.22 ± 6.3	36.07 ± 5.9
	MALE	35.21 ± 7.5	41.93 ± 9.4	53.51 ± 11.7	25.83 ± 3.9	31.42 ± 7.2	39.59 ± 8.5	43.76 ± 10.3	44.43 ± 9.5	42.57 ± 7.2	35.08 ± 5.1	28.89 ± 6.2	32.81 ± 6.2
Paired t-test for comparing between pre and post for each group													
NOVICE		0.09	0.92	0.87 [ü]	0.18	0.51	0.06	0.02*, 0.86 [ü]	0.41	0.13	0.02*, 0.78 [ü]	0.87	0.1
ME		0.92	0.7	0.84	0.44	0.92	0.88	0.3	0.55	0.99	0.72	0.24	0.3
FEMALE		0.84	0.53	0.76	0.69	0.49	0.79	0.54	0.48	0.82	0.56	0.57	0.88
MALE		0.58	0.31	0.58	0.18	0.02*, 0.2 [ü]	0.54	0.2	0.1	0.14	0.07	0.09	0.75
Two-way ANCOVA for the effect of participants' fitness level and gender on T2 values													
Fitness level (F)		0.25	0.4	0.03¥, 0.3 [ü]	0.21	0.26	0.15	0.05¥, 0.2 [ü]	0.9	0.83	0.79	0.07	0.41
Gender (G)		0.19	0.72	0.89	0.61	0.12	0.71	0.92	0.22	0.41	0.1	0.7	0.33
F × G		0.92	0.52	0.27	0.12	0.53	0.51	0.36	0.84	0.83	0.47	0.65	0.48

* indicates a significant different ($p \leq 0.05$) between pre and post according to a paired *t*-test.
[ü] indicates an effect size. It was reported when only the p-value was significant.
¥ indicates a significant ($p \leq 0.05$) fitness level effect on T2 values according to the two-way ANCOVA.

3.4. Ankle biomechanics

After 5 km barefoot running (Fig. 4, A and Table 6), the FEMALE group exhibited a significant reduction of peak plantarflexion ($p = 0.005$) and peak internal rotation ($p = 0.006$), and a significant elevation of peak inversion ($p < 0.0001$) and peak external rotation ($p = 0.004$). The ME group only showed a significant increase in peak plantarflexion after running ($p = 0.02$). No overall ankle kinematic and kinetic changes occurred in the NOVICE and MALE groups. Following 5 km barefoot running, kinetic alteration was only observed in the FEMALE group, decreasing the ankle plantarflexion torque ($p = 0.02$).

Regarding the peak plantar pressure (Fig. 4, B, Table 6), loading under the toes and medial forefoot was decreased after running, while loading under the lateral forefoot and lateral midfoot showed elevation. Specifically, significant pressure reduction under T1 in the FEMALE ($p = 0.005$) and NOVICE ($p = 0.03$) groups, and T2-T5 in the NOVICE ($p = 0.03$) group were observed. All groups showed a significant decrease under M1, but only the MALE and ME groups showed a significant reduction under M2 and M3. In contrast, a significant elevation under M4 ($p = 0.03$) and M5 ($p = 0.007$) in the FEMALE group and M5 in the NOVICE group ($p = 0.04$) was found. Peak pressure under LM also showed a significant increase in the ME ($p = 0.05$), FEMALE ($p = 0.004$), and NOVICE ($p = 0.01$) groups.

4. Discussion

This study investigated the effects of 5 km barefoot running on T2 relaxation times of the tibiotalar cartilage and its relationship to ankle biomechanics in young, healthy, first time barefoot runners. The results of this study support the following conclusions. First, 5 km barefoot running was found to increase T2 relaxation time values in the tibiotalar cartilage in NOVICE runners, while ME runners showed no change. It also appears that runners' fitness level affects T2 values in the PZ and lateral sections of the tibiotalar cartilage, while there was no gender effect. Given this evidence, 5 km barefoot running may have a considerable biochemical effect on tibiotalar cartilage in NOVICE runners, while barefoot running may only be suitable for experienced runners. High T2 values in the PZ and lateral aspect of tibiotalar cartilage in the NOVICE group may indicate early cartilage degeneration or high functional demand during barefoot running. Second, T2 increases observed in the NOVICE group on the lateral section of the tibiotalar cartilage were associated with increased plantar pressure on the 5th metatarsal and lateral midfoot. This suggests plantar pressure may play a role in tibiotalar cartilage fluid development. Third, following qualitative analysis, it was observed that no significant structural abnormalities were detected in any of the imaged ankles between pre- and post-run scans. Asymptomatic pathologies were observed in the pre-run scans but remained in the post-run scans. This suggests a single 5 km barefoot run is a suitable mid-range distance to evaluate the effects on T2 values from repetitive loading without introducing further pathology that may confound the findings of this study.

Our results agree with previous studies that running had an acute effect on the lower limb articular cartilage through observation of a significant alteration in T2 relaxation values (Mosher et al., 2005; Stehling et al., 2011). After a marathon race, 13 non-professional runners showed a significant T2 elevation in all meniscus compartments, but those T2 values reduced after 3-month follow-up (Stehling et al., 2011). Another study also reported a small but significant T2* elevation in knee cartilage after a marathon race in 10 non-professional runners (Hesper et al., 2015). However, four weeks later this value was reduced to baseline levels. To the best of our knowledge, only one study

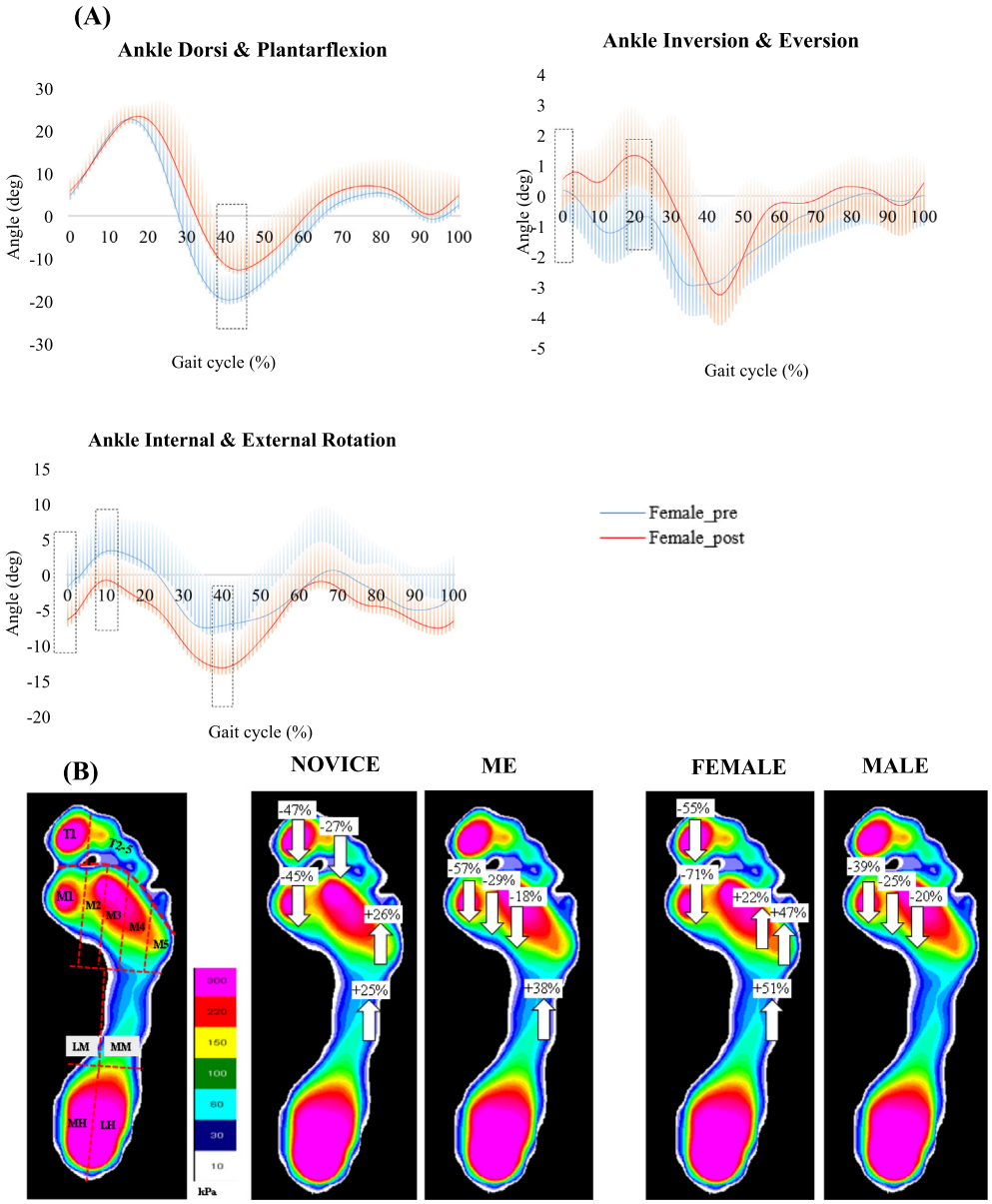

Fig. 4. (A) Ankle kinematic changes in the FEMALE group before and after the 5 km run. Dotted squares indicate significant different between pre- and post-run at the peak and/or initial foot contact. Positive values indicate dorsiflexion, inversion, and internal rotation. (B) Plantar pressure map – 11 regions of interests. Arrows indicate significant changes of plantar pressure after the 5 km run for each group.

(Schuetz et al., 2014) quantitatively (using T2* maps) evaluated ankle cartilage over ultra-marathon shod running. That study found T2* values were significantly increased during the initial 2,000–2,500 km, but T2* values decreased for distances beyond 2,500 km. This suggested that the human ankle may have a capacity to repair over time. Alteration in T2 values has been associated with cartilage damage such as osteoarthritic cartilage (Dunn et al., 2004; Koff et al., 2007), and high physical activity is also likely to modify T2 values (Stehling et al., 2010). The current study has no further monitoring of T2 values after barefoot running beyond the immediate post-run assessment. It is highly possible that elevation of T2 values in tibiotalar cartilage may return to baseline levels after a rest period. Further time points would be required to determine if the return of T2 relaxation time was the same in healthy and osteoarthritic cartilage.

There are few MRI studies investigating the effect of barefoot running on the ankle and foot complex. A previous study (Ridge et al., 2013) evaluated BME in runners' feet after a 10-week transition from traditional running shoes to bare-simulated shoes, compared with controls. That study reported that more people running bare-simulated increased in BME in the 2nd and 3rd metatarsals, talus, calcaneus, and navicular after the 10-week period when compared with controls, but both groups showed no soft-tissue changes. One case study (Giuliani et al., 2011) found 2nd metatarsal stress fractures in two experienced runners after 3 to 6 weeks of training with bare-simulated shoes. However, it was unclear what the acute effect of a single barefoot run on the ankle cartilage and biomechanics may be. In the current study, only one NOVICE male runner revealed BME in TLC after 5 km barefoot running. A previous study also reported BME changes in sedentary individuals who ran shod for 30 min a day for 7 days in a row (Trappeniers et al., 2003). Repetitive loading during running may add stress to the ankle cartilage and this could result in BME. However, as this BME change was not statistically significant between pre- and post-run, a single 5 km barefoot run is less likely to induce pathologies in the ankle.

Table 6
Mean values of three-dimensional kinematic and kinetic data at the ankle joint and peak plantar pressure for each group. A *t*-test was conducted to compare between pre- and post-run for each group. This table includes only parameters that showed significant changes. Presented as mean ± standard deviation.

Ankle	NOVICE (N = 10)				ME (N = 10)				MALE (N = 10)				FEMALE (N = 10)			
	Pre	Post	*P value*	Effect size	Pre	Post	*P value*	Effect size	Pre	Post	*P value*	Effect size	Pre	Post	*P value*	Effect size
Plantar-dorsiflexion																
Peak plantarflexion (°)	−18.9 ± 6.3	−14.7 ± 8.3	0.07	0.6	−22.6 ± 5.3	−17.2 ± 6.4	**0.02***	**0.92**	−19.5±5	−17.1 ± 6.9	0.16	0.4	−22 ± 6.9	−14.8 ± 8	**0.005***	**0.96**
Peak plantarflexion moment ($Nm.kg^{-1}$)	2.7±0.5	2.5±0.6	0.07	0.4	2.8 ± 0.8	2.3 ± 0.9	0.12	0.59	2.4 ± 0.5	2.1 ± 1.1	0.26	0.35	3.1 ± 0.5	2.5 ± 0.7	**0.02***	**0.99**
Inversion-eversion																
Angle at IFC (°)	0.7 ± 1.4	0.3 ± 0.3	0.85	0.4	0.6 ± 0.5	0.5 ± 0.7	0.89	0.16	1 ± 1.1	0.3 ± 0.8	0.21	0.72	0.1 ± 0.6	0.5 ± 0.3	**0.05***	**0.93**
Peak inversion (°)	1.9 ± 1.65	1.86 ± 1.3	0.95	0.03	1.3 ± 0.6	1.8 ± 1.2	0.18	0.53	1.9 ± 1.6	1.1 ± 0.9	0.06	0.61	1.1 ± 0.7	2.5 ± 1.1	**<0.0001***	**1.51**
Internal-external rotation																
Angle at IFC (°)	−4.8 ± 7.9	−5 ± 5.7	0.27	0.03	−4.53 ± 5.1	−4.46 ± 3.8	0.98	0.02	−6.9 ± 5.5	−3.5 ± 5.3	0.27	0.63	−1.8 ± 5	−6.3 ± 3.4	**0.01***	**1.05**
Peak internal rotation (°)	7.6 ± 5	5.16 ± 3.1	0.34	0.6	6.9 ± 3.7	2.9 ± 2.8	0.08	1.2	4.7 ± 3.5	3.1 ± 3	0.56	0.49	9.9 ± 3.2	5 ± 3	**0.006***	**1.57**
Peak external rotation (°)	−12.8 ± 7.4	−14.1 ± 6.6	0.61	0.2	−11.4 ± 5.9	−14.4 ± 3.3	0.19	0.63	−13.6 ± 6.8	−11.6 ± 5.8	0.39	0.32	−10.6±6.3	−16.9 ± 2.4	**0.004***	**1.32**
Peak pressure (kPa)																
T1	480.7 ± 217.9	296.4 ± 127.3	**0.03***	**0.93**	426.9 ± 162.2	309.5 ± 196	0.11	0.65	438.9 ± 204.5	340.6 ± 166.7	0.26	0.53	468.7 ± 181.9	265.3 ± 154.3	**0.005***	**1.21**
T2-5	230.2 ± 89.1	174.9 ± 87.2	**0.03***	**0.63**	239.9 ± 81.9	219.7 ± 77.6	0.42	0.25	246.7 ± 95.7	207.5 ± 90.6	0.16	0.42	223.4 ± 72.5	187.1 ± 79.3	0.15	0.48
M1	510.6 ± 175.8	313.7 ± 139.1	**0.008***	**1.25**	571.2 ± 249.8	316.5 ± 250.4	**0.008***	**1.02**	576.7 ± 267.1	389.8 ± 241.3	**0.02***	**0.74**	505.1 ± 145.4	240.4 ± 106.7	**0.003***	**2.09**
M2	413.2 ± 165.6	351.4 ± 79.5	0.31	0.5	472.9 ± 173.6	354 ± 58.7	**0.04***	**0.9**	458.5 ± 155.9	356.1 ± 76.3	0.09	0.84	427.5 ± 186.2	349.3 ± 62.6	0.18	0.56
M3	406.2 ± 114.6	369.9 ± 68.1	0.37	0.4	434.7 ± 76.7	364.9 ± 32.3	**0.02***	**1.2**	446.6 ± 105.3	365 ± 68.1	**0.04***	**0.92**	394.3 ± 82.9	369.8 ± 32.3	0.38	0.4
M4	353.8 ± 124.7	351.6 ± 117.6	0.93	0.02	343.9 ± 85.9	360.7 ± 103.8	0.69	0.18	396.3 ± 106.2	336 ± 93.8	**0.01***	**0.6**	301.4 ± 81.9	376.3 ± 122.3	**0.03***	**0.72**
M5	302.8 ± 145.9	394.1 ± 219.2	**0.04***	**0.5**	263.1 ± 141.8	332 ± 193.4	0.26	0.41	307.2 ± 130.4	310.9 ± 188.1	0.92	0.02	258.6 ± 154.8	415.2 ± 214.9	**0.007***	**0.84**
MM	92.6 ± 58.6	86.5 ± 61.8	0.68	0.11	107.6 ± 51.9	113.2 ± 58.8	0.72	0.11	115.8 ± 46.6	129.6 ± 46.6	0.24	0.3	84.4 ± 59.5	70.2 ± 59.4	0.41	0.24
LM	200.4 ± 72.3	257.4 ± 96.5	**0.01***	**0.67**	149.1 ± 32.7	219.7 ± 93.7	**0.05***	**1.01**	197 ± 69.1	218.7 ± 95.2	0.12	0.25	152.5 ± 43.4	258.4 ± 94.5	**0.004***	**1.45**
MH	315.6 ± 120.5	296.6 ± 137.9	0.63	0.15	367.5 ± 104.8	376.7 ± 120.4	0.83	0.08	339.9 ± 121.2	382.4 ± 103.8	0.14	0.38	343.1 ± 111.1	290.8 ± 147.1	0.27	0.41
LH	313.2 ± 124.3	301.4 ± 148.6	0.77	0.09	353.3 ± 93.9	362.6 ± 105.9	0.82	0.09	336.6 ± 123.9	386.6 ± 108.4	0.08	0.43	329.9 ± 98.9	277.4 ± 130.4	0.26	0.45

Abbreviations, IFC-initial foot contact; T1-hallux; T2-T5- toes 2–5; M1, M2, M3, M4, M5-all metatarsals; MM-medial midfoot; LM- lateral midfoot; MH- medial heel; LH-lateral heel (MH, LH).
* Indicates a significant different ($p \leq 0.05$) between pre and post according to a paired *t*-test.

In the current study, we noted a significant T2 elevation in the PZ and the lateral section of the ankle cartilage after 5 km barefoot running in the NOVICE group. The plantar pressure data also showed consistent patterns, shifting the loading from the medial to lateral aspect of the foot after 5 km barefoot running. In contrast to our findings, however, long-distance shod running revealed a significant T2* elevation in the medial ankle cartilage (Schuetz et al., 2014) and a significant reduction of foot loading under the lateral toes (Willems et al., 2012) and the lateral midfoot (Alfuth and Rosenbaum, 2011). Therefore, our considerably high T2 values in the PZ and lateral section as well as the increased plantar loading under the lateral aspect of the foot may indicate barefoot running is functionally demanding in these zones as weight-bearing areas. The PZ and lateral section of cartilage may also be at high risk of damage during barefoot running.

Ankle kinematics were significantly altered after 5 km barefoot running in the FEMALE group. The decrease in peak plantarflexion and peak internal rotation, and increase in peak inversion and peak external rotation is associated with supination of the foot. It has been reported that over-supination may induce running-related injuries due to inefficient shock absorption (Burns et al., 2005). However, this ankle kinematic difference observed in the FEMALE group was not associated with T2 value changes. Furthermore, T2 values changed significantly in the NOVICE group with no associated ankle kinematic changes, suggesting kinematic changes may not be associated with T2 relaxation values. However, the plantar pressure was transferred from the medial to lateral side and the T2 increase was only pronounced in NOVICE runners on the lateral tibiotalar joint. This suggests that plantar pressure is more likely associated with T2 relaxation times.

The current study has limitations that should be acknowledged. Firstly, five people showed asymptomatic ankle ligament tears, Achilles tendinopathy, and BME in their ankle cartilage. However, these conditions were considered to be very minor by our radiology team, and there were no observed changes in the images pre- and post-run. We also conducted one-sample *t*-test to investigate whether T2 values in these individuals were significantly different from the other subjects. This analysis showed that their T2 values were not significantly different from the other subjects. Furthermore, medical general practitioners considered that this would not affect the results of this study and so we included the data from these subjects. Secondly, whilst the sample size was limited we were able to detect a significant effect of fitness level on T2 relaxation values. We included the effect size statistic to give readers an appreciation for the sample size on our findings. Thirdly, it should be noted that pre-run scans were always performed in the morning (to minimize potential diurnal effect in the T2 values), while post-run scans were always performed in the afternoon following 5 km running on the same day. However, it was consistent and we believe this would not affect our study conclusions. Although there was a time-delay for acquiring the post-run scans, a previous study reported T2 elevation after 48–72 h following a marathon (Stehling et al., 2011) and this did not affect that study's conclusions. Fourth, the fitness level of the participants was self-reported, although the Tegner scale was employed for objectively assessing the activity level. Fifth, all participants reported that they are right footed, but one person was ambidextrous although they showed no significant differences in gait. Finally, this study recruited Caucasian participants only due to reported differences in foot morphology between ethnicities (Hawes et al., 1994).

This study has highlighted some useful insights for barefoot running in people who normally run shod. Novice runners appear to develop elevated fluid levels in their ankle cartilage. In contrast to marathon experienced, novice runners appear to have an elevated lateral plantar pressure following 5 km running and this is associated with elevated T2 values. Hence fitness levels should be accommodated when considering barefoot running performance in people who normally run shod.

Declaration of Competing Interest

The authors declare no conflicts of interest.

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