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Research article

Regional variation of ankle and hindfoot cartilage T2 mapping values at 3 T: A feasibility study

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ABSTRACT

Objective: To develop a method for T2 mapping of the entire tibiotalar/hindfoot articular surfaces and to examine regional T2 variation in asymptomatic volunteers, establishing necessary methods for future T2 mapping work in patients with ankle/hindfoot injury.

Materials and methods: Twenty-six asymptomatic volunteers (11 female/13 male, aged 23–64 years in final analysis) underwent sagittal T2 mapping. Tibiotalar and hindfoot cartilage surfaces were segmented by two raters. The tibiotalar joint cartilage was divided into subregions to assess T2 variation across the joint. The articular surface and subregion mean T2 values were compared using Tukey post hoc pairwise comparisons to test for statistical significance.

Results and conclusion: Mean ankle/hindfoot cartilage T2 ranged from 37 ± 3 to 47 ± 7 ms. Tibial plafond mean T2 was significantly different from the middle and posterior subtalar cartilage T2 (both articular surface comparisons resulted in $P < .05$). Talar dome mean T2 was significantly different from the posterior calcaneal-side and talar-side subtalar cartilage, and middle calcaneal-side subtalar cartilage ($P < .05$ for all comparisons). Tibial plafond middle versus lateral, anterior versus middle, middle versus posterior, and anterior versus posterior subregion T2 values were significantly different ($P < .05$ for all comparisons). Talar dome medial versus middle, middle versus lateral, anterior versus middle, and middle versus posterior subregion T2 values were significantly different ($P < .05$ for all comparisons). Ankle/hindfoot joint cartilage T2 mapping and segmentation was found to be feasible for all cartilage surfaces except the anterior subtalar joint facet. Mean T2 differed significantly between ankle/hindfoot joint and subregion cartilage in asymptomatic volunteers.

1. Introduction

Ankle and hindfoot joint cartilage injury is frequently associated with degenerative changes, even in the absence of symptoms [1]. Cartilage degeneration can be initiated by cartilage injury occurring with ankle sprain [2,3] or fracture [4,5], or abnormal loading due to chronic ankle instability [6–9] or anatomical variants [10].

Earlier treatment of cartilage damage with joint preservation operations include debridement, bone stimulation techniques such as microfracture, autologous chondrocyte implantation, realignment osteotomy, and osteochondral allograft or autograft transplantation [11–13] is clearly more successful. This makes early detection of cartilage degeneration desirable [11,14]. With the addition of newer ankle/hindfoot articular cartilage injury treatment procedures, such as the use of biologics, repair cartilage quality is an important outcome measure [13,15,16]. Objective, noninvasive tools for measuring early changes in cartilage health are needed to diagnose early damage, plan appropriate treatment, and judge treatment success.

T2 mapping magnetic resonance imaging (MRI) fulfills these requirements, providing objective quantitative information about cartilage collagen fiber network organization and water content [17]. Changes in talar dome cartilage T2 mapping values have been reported in subjects with ligament injury and chronic functional ankle instability [7,9,18,19]. In the hindfoot joints relationships between T2* and loading have been reported [10,20], with increased T2* values reported during acute load application [20] and during extended (> 1 month) periods of running-induced loading [20]. Quantitative mapping values have also been used to compare intact and repair cartilage to judge repair technique success [21–23]. T2 and T2* mapping provide similar information about collagen organization and water content and both

Abbreviations: MRI, magnetic resonance imaging; T2, transverse relaxation time; ICC, intra-class correlation coefficient; ROI, region of interest; MS, milliseconds

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have been applied in the ankle/hindfoot cartilage. T2 mapping was selected for this work because it is less susceptible to magnetic field inhomogeneity than T2* mapping and is well validated in cartilage [24].

Quantitative mapping may be valuable for predicting outcome and planning appropriate treatment but requires consistent application and region selection for clinical application. Absolute T2 values are not necessarily consistent between MR scanners or protocols and variation exists between individuals for what constitutes 'normal' cartilage values [22,25]. Internal comparisons between cartilage regions within a single subject address this problem [22], but care must be taken to ensure that the comparison regions are reliable and provide consistent relative cartilage T2 mapping values.

Cartilage T2 varies by joint [26], and by subregion in a single joint [27], but variation between the tibiotalar joint cartilage and cartilage of the hindfoot joints has not been examined. Our hypothesis is that significant differences in cartilage mean T2 will exist between ankle/hindfoot joints and subregions. The purpose of this study was to test the feasibility of applying T2 mapping to the entire articular surface in the ankle/hindfoot joints and to measure regional T2 variation between clinically relevant subregions in asymptomatic volunteers. The results of this study support the feasibility of applying these methods for future work using T2 mapping in patients with ankle/hindfoot injury.

2. Materials and methods

Twenty-six subjects aged 18–62 years were recruited for this Institutional Review Board approved prospective study between January to April 2014 at the Steadman Philippon Research Institute. Subjects provided written informed consent and were screened using a questionnaire for ankle/hindfoot symptoms/history and clinical examination by an orthopaedic foot and ankle surgeon for alignment, gait, visible or palpable abnormalities, range of motion, and ligament injury/laxity. Exclusion criteria included ankle surgery or ankle injury, inflammatory/crystalline joint disease, osteoarthritis, calcific tendonitis, and cartilage damage seen on subsequent MRI. This ankle cartilage T2 mapping subject group included 26 of 30 subjects from a prior paper reporting asymptomatic peroneal tendon T2* mapping values [29]. The subject age range was 23 to 62 years. Two of the 26 subjects were excluded for abnormalities on MRI, resulting in 24 subjects (12 left and 12 right ankles, 11 female/13 male), with 9 men/0 women in the youngest age group (18 to 32 years), 3 men/5 women in the middle age group (33 to 47 years), and 1 man/6 women in the oldest age group (48 to 62 years). Assuming two-tailed repeated measures testing with an overall $\alpha = 0.05$ adjusted with a Bonferroni correction to account for a maximum of 6 subregions being compared at once, based on clinically relevant regions and prior work in the tibiotalar and other joints [27,28], and requirement of 80% power, it was determined that the available sample of 24 subjects would be sufficient to detect an effect size of $d = 0.85$.

Ankle/hindfoot MRI was performed with a Siemens Magnetom Verio 3 T scanner (Siemens Medical Solutions, Erlangen, Germany) with a gradient strength of 40 m T/m, using an 8-channel foot-ankle array receive coil (Invivo, Gainesville, FL, USA). Subjects were allowed to participate in their typical daily and athletic activities prior to their scans. Volunteers were positioned supine with the ankle in neutral. The protocol included a sagittal plane fat-suppressed proton-density turbo-spin-echo Sampling Perfection with Application-optimized Contrasts using different flip angle Evolutions (SPACE) sequence and multi-echo spin-echo T2 mapping sequence. Table 1 lists the sequence parameters. T2 mapping was performed 20 min after participants entered the scanner to minimize loading-related effects [7,10]. T2 values were calculated using a pixel-wise, mono-exponential, non-negative least square decay curve fit including all echoes (Siemens MapIt, Siemens Medical Solutions, Erlangen, Germany).

The tibiotalar, subtalar, calcaneocuboid, and talonavicular cartilage surfaces were independently segmented using a stylus and touchscreen (WACOM Cintiq, Wacom Technology Corporation, Portland, OR) in Mimics (Materialise, Plymouth, MI) on each slice of the second echo of the T2 mapping sequence by a musculoskeletal radiology fellow with 15 years of experience [Rater 1] and a third-year medical student [Rater 2]. The anterior talocalcaneal joint cartilage was excluded due to inconsistent visualization.

Table 1
Acquisition parameters for T2 mapping and SPACE sequences.

Sequence	T2 map (sagittal)	SPACE (sagittal)
Repetition time [ms]	1810	1200
Echo time [ms]	10.7,21.4,32.1,42.8,53.5	45
Field of view [mm]	120	150
Matrix	256 × 256	256 × 256
Voxel size [mm]	0.47 × 0.47 × 2.00	0.59 × 0.59 × 0.70
Slice thickness [mm]	2.00	0.70
Slice spacing [mm]	2.00	–
Distance factor [%]	100	–
Number of slices	30	144
Examination time [min:sec]	6:56	7:16

Initial training segmentation was performed by both raters with feedback by a senior musculoskeletal radiologist (C.P.H.), followed by the first round of segmentation for T2 mapping analysis. The corresponding fat-suppressed SPACE images were referred to for accurate exclusion of synovial fluid and chemical shift artifact. The raters were instructed to include only clearly visualized cartilage, excluding edge regions with partial volume averaging. Fig. 1 shows examples of the appearance of the second echo T2 mapping and SPACE images for corresponding sagittal slices in one subject. Due to time constraints Rater 1 did not segment the talonavicular and calcaneocuboid cartilage. A third rater (Rater 3, an imaging researcher with 3 years of experience in cartilage segmentation) completed the talonavicular and calcaneocuboid segmentations. Rater 2 segmented all cartilage surfaces. Rater 2 performed a second segmentation round of all subjects to assess intrarater reliability, following four weeks between rounds to avoid bias.

The cartilage segmentations were overlaid on the T2 map images in a custom MATLAB program (MATLAB Release 2013a, The MathWorks, Inc., Natick, Massachusetts, United States) to define the regions of interest (ROI). Subregions of the tibial plafond and talar dome cartilage were defined automatically in MATLAB (Fig. 2). The most anterior and posterior pixels of the tibial plafond and talar dome cartilage masks were identified automatically and the anterior-to-posterior distance was divided into equal anterior, middle, and posterior subregions (Fig. 2a and c). The most medial and lateral pixels at the anterior-to-posterior midpoint of each anterior-to-posterior third were identified automatically and the cartilage was divided into equal medial, middle, and lateral subregions (Fig. 2b and d) aligned to the medial and lateral cartilage edges.

The subject median T2 values for each ROI were calculated. The means and standard deviations of the joint and subregion median T2 values were calculated for all subjects. Statistical analyses were performed in R (R version 3.2.3, R Development Core Team, Vienna, Austria) [30] using a repeated measures analysis via random-intercepts mixed-effects models (nlme: Linear and Nonlinear Mixed Effects Models, R Development Core Team) with assumed exponential spatial correlation structure and no assumption of equal variance. Statistical significance was assessed using Tukey post hoc pairwise comparisons ($P < .05$).

The regions compared included:

1) Tibial, talar, and middle, posterior subtalar joint surfaces (6 regions)
2) Talonavicular, calcaneocuboid joint surfaces (4 regions)
3) Medial, middle, lateral tibial plafond subregions (3 regions)
4) Anterior, middle, posterior tibial plafond subregions (3 regions)

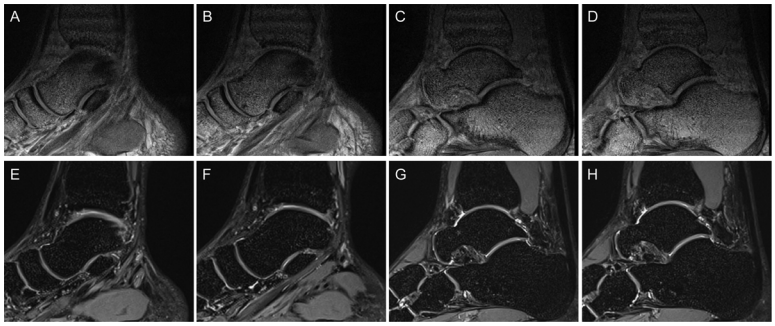

Fig. 1. Example sagittal images from one subject showing corresponding T2 mapping (a-d) and SPACE (e-h) sequence images.

5) Medial, middle, lateral talar dome subregions (3 regions)
6) Anterior, middle, posterior talar dome subregions (3 regions)

We tested for potential sex-related differences in T2 for each cartilage region using Welch's *t*-test with statistical significance defined at the level of $P < 0.05$. Median T2 intrarater and interrater measurement reliability was assessed using a two-way random effects model to calculate the single measures, absolute agreement version of the intraclass correlation coefficient (ICC), interpreted as: ICC < .40 = poor agreement; .40 ≤ ICC ≤ .75 = fair to good agreement; ICC > .75 = excellent agreement [31].

3. Results

The mean cartilage T2 values for the ankle and hindfoot articular surfaces ranged from 37 to 47 ms with between-subject standard deviations of 3 to 9 ms, as shown in Fig. 3. The specific values for each articular surface, as well as the inter- and intrarater absolute agreement ICC values are listed in Table 2. Fig. 4 illustrates intrarater and interrater T2 variation in the two largest cartilage regions, showing the tibial plafond intrarater (Fig.4a) and interrater (Fig. 4b) and talar dome intrarater (Fig. 4c) and interrater (Fig. 4d) T2 differences in the form of Bland-Altman plots.

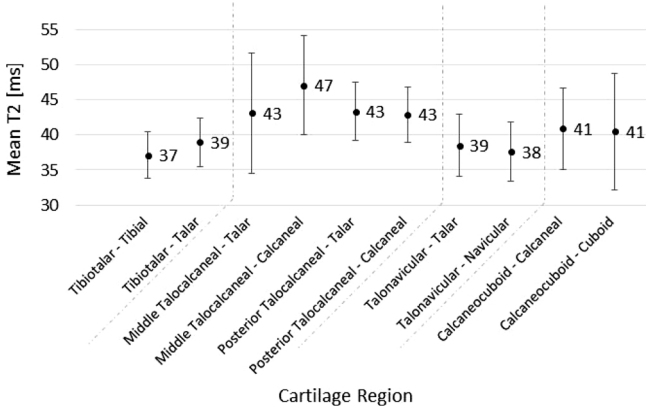

Fig. 3. Mean cartilage T2 value for each articular surface with error bars showing between-subject standard deviation.

Fig. 5 shows a boxplot of the region median T2 values for the

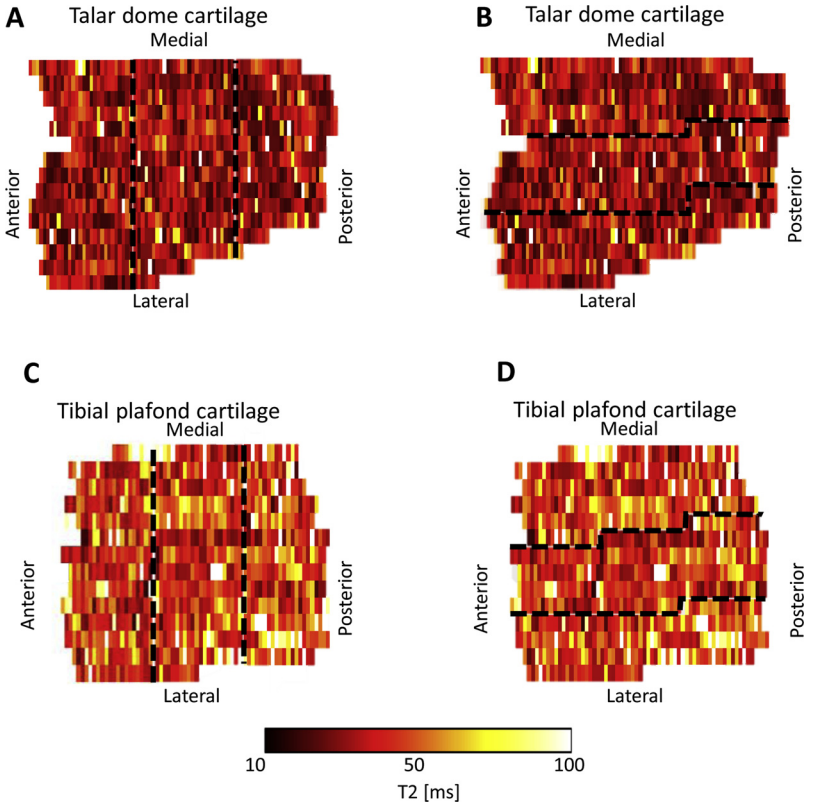

Fig. 2. Anterior, middle, and posterior subregions of tibial plafond (a); medial, middle, and lateral subregions of tibial plafond (b); anterior, middle, and posterior subregions of talar dome (c); and medial, middle, and lateral subregions of talar dome (d) illustrated with dashed lines on the superior-inferior view of the cartilage segmentation with T2 map color-scale.

Table 2
Mean T2 ± standard deviation for each region/subregion and interrater and intrarater absolute agreement ICC values.

Cartilage region	Mean ± standard deviation [ms]			Interrater (Rater 1* round 1 vs. Rater 2 round 2) *Rater 3 for talonavicular, calcaneocuboid			Intrarater (Rater 2 round 1 vs. Rater 2 round 2)		
Joint Regions	Rater 1, round 1	Rater 2, round 1	Rater 2, round 2	Agreement ICC	95% CI LB	95% CI UB	Agreement ICC	95% CI LB	95% CI UB
Tibial plafond	36 ± 4	38 ± 4	37 ± 3	0.71	0.01	0.95	0.67	0.38	0.83
Talar dome	44 ± 4	43 ± 4	39 ± 3	0.32	−0.03	0.65	0.54	0.33	0.71
Subtalar, posterior facet, calcaneal side	41 ± 3	43 ± 4	43 ± 4	0.33	−0.08	0.75	0.87	0.73	0.95
Subtalar, posterior facet, talar side	42 ± 3	43 ± 5	43 ± 4	0.71	0.33	0.88	0.87	0.67	0.95
Subtalar, middle facet, calcaneal side	43 ± 5	48 ± 9	47 ± 7	0.60	0.33	0.78	0.57	−0.00	0.84
Subtalar, middle facet, talar side	43 ± 6	42 ± 6	43 ± 9	0.66	0.49	0.87	0.83	0.61	0.97
Talonavicular, navicular side	38 ± 3	40 ± 4	38 ± 4	0.84	0.37	0.96	0.68	0.30	0.88
Talonavicular, talar side	37 ± 4	40 ± 5	39 ± 4	0.65	0.31	0.92	0.77	0.53	0.89
Calcaneocuboid, cuboid side	39 ± 5	44 ± 8	41 ± 8	0.90	0.74	0.97	0.84	0.48	0.97
Calcaneocuboid, calcaneal side	40 ± 4	43 ± 7	41 ± 6	0.66	0.38	0.84	0.78	0.48	0.95
Tibiotalar Subregions									
Tibial plafond, anterior	38 ± 5	38 ± 5	37 ± 4	0.60	−0.51	0.96	0.62	0.18	0.90
Tibial plafond, middle	33 ± 3	35 ± 4	35 ± 3	0.62	0.08	0.86	0.75	0.55	0.89
Tibial plafond, posterior	39 ± 5	44 ± 6	41 ± 5	0.54	−0.01	0.84	0.57	0.32	0.82
Tibial plafond, medial	37 ± 6	38 ± 5	37 ± 3	0.40	−0.13	0.85	0.66	0.40	0.85
Tibial plafond, middle	34 ± 4	36 ± 4	36 ± 4	0.81	0.59	0.89	0.75	0.43	0.92
Tibial plafond, lateral	37 ± 3	41 ± 6	39 ± 5	0.40	−0.11	0.73	0.66	0.42	0.83
Talar dome, anterior	42 ± 5	44 ± 5	40 ± 4	0.62	0.21	0.87	0.44	0.31	0.65
Talar dome, middle	44 ± 5	40 ± 6	38 ± 4	0.45	−0.01	0.80	0.81	0.63	0.89
Talar dome, posterior	49 ± 5	46 ± 5	40 ± 4	0.04	−0.10	0.23	0.35	0.09	0.64
Talar dome, medial	48 ± 5	45 ± 5	40 ± 5	0.13	−0.06	0.40	0.53	0.32	0.71
Talar dome, middle	43 ± 5	41 ± 4	38 ± 3	0.41	−0.01	0.73	0.55	0.30	0.74
Talar dome, lateral	42 ± 4	42 ± 6	39 ± 4	0.59	0.08	0.95	0.67	0.41	0.83

ms = milliseconds.
ICC = intra-class correlation coefficient.
CI = confidence interval.
LB = lower bound.
UB = upper bound.

tibiotalar and subtalar cartilage regions. The tibial plafond cartilage mean T2 (37 ± 3 ms) was found to be significantly different from the mean T2 of all four subtalar joint cartilage regions (middle subtalar joint, talar side: 43 ± 9 ms, $P = .0157$; middle subtalar joint, calcaneal side: 47 ± 7 ms, $P < .001$; posterior subtalar joint, talar side: 43 ± 4 ms, $P < .001$; posterior subtalar joint, calcaneal side: 43 ± 4 ms, $P < .001$). The talar dome cartilage mean T2 (39 ± 3 ms) was found to be significantly different from the mean T2 of both posterior subtalar joint cartilage regions (calcaneal side $P = .0018$, talar side $P < .001$) and the middle subtalar joint, calcaneal side cartilage region ($P < .001$).

Fig. 6 shows a boxplot of the region median T2 values for the talonavicular and calcaneocuboid cartilage regions. With the number of subjects available, no significant differences were detected between those four regions.

Fig. 7 shows a boxplot of the region median T2 values for the tibial plafond cartilage regions. The middle and lateral subregion mean T2 values were found to be significantly different (36 ± 4 versus 39 ± 5 ms, $P < .001$), as were the T2 values for the anterior versus middle (37 ± 4 versus 35 ± 3 ms, $P = .0495$), middle versus posterior (35 ± 3 versus 41 ± 5 ms, $P < .001$), and anterior versus posterior subregions ($P = .0017$).

Fig. 8 shows a boxplot of the region median T2 values for the talar dome cartilage regions. The medial versus middle (40 ± 5 versus 38 ± 3 ms, $P < .001$), and middle versus lateral (38 ± 3 versus 39 ± 4, $P = .0098$) subregion mean T2 values were found to be significantly different, as were the T2 values for the anterior versus middle (40 ± 4 versus 38 ± 4, $P = .0133$) and middle versus posterior subregions (38 ± 4 versus 40 ± 4, $P = .0156$).

Significant differences in mean T2 were found between the male and female groups for the anterior tibial (35 ms female average T2 versus 38 ms male average T2, t(17.48) = -2.33, $P = .0315$) and posterior talar (42 ms average female T2 versus 38 ms average male T2, t(20.78) = 2.31, $P = 0.0314$) cartilage regions.

4. Discussion

This study establishes a T2 mapping and clinically relevant subregion division method and tests feasibility for T2 mapping and subregion definition in asymptomatic volunteers. These methods can be applied in the future to the evaluation of injured or degenerated ankle/hindfoot cartilage. The results of this study demonstrate that significant differences in cartilage mean T2 exist between several articular surfaces and subregions of the ankle and hindfoot. These results support the importance of considering regional variation when utilizing T2 mapping for evaluation of ankle and hindfoot cartilage health following ankle injury or other biomechanical alterations and after treatment of cartilage injury with conventional or newer biologically-augmented techniques.

This study is one of the few, in addition to those by Lim et al. [27] and Cha et al. [32], to compare ankle cartilage mean T2 between articular surfaces or subregions. In contrast, most previous studies have compared mean subregion T2 between control and injury groups but have not compared subregions against one another. This study is also unique because it includes T2 mapping values over the entire articular surfaces of the hindfoot in contrast to prior quantitative mapping studies of the hindfoot joint cartilage which were limited to measuring T2 over a single subtalar facet [10] or a single slice within each articular surface [20]. T2 mapping of all the articular surfaces in the hindfoot rather than a single slice or facet provides comprehensive T2 mapping information about the hindfoot joint cartilage health and may allow detection of small localized changes not captured in more limited T2

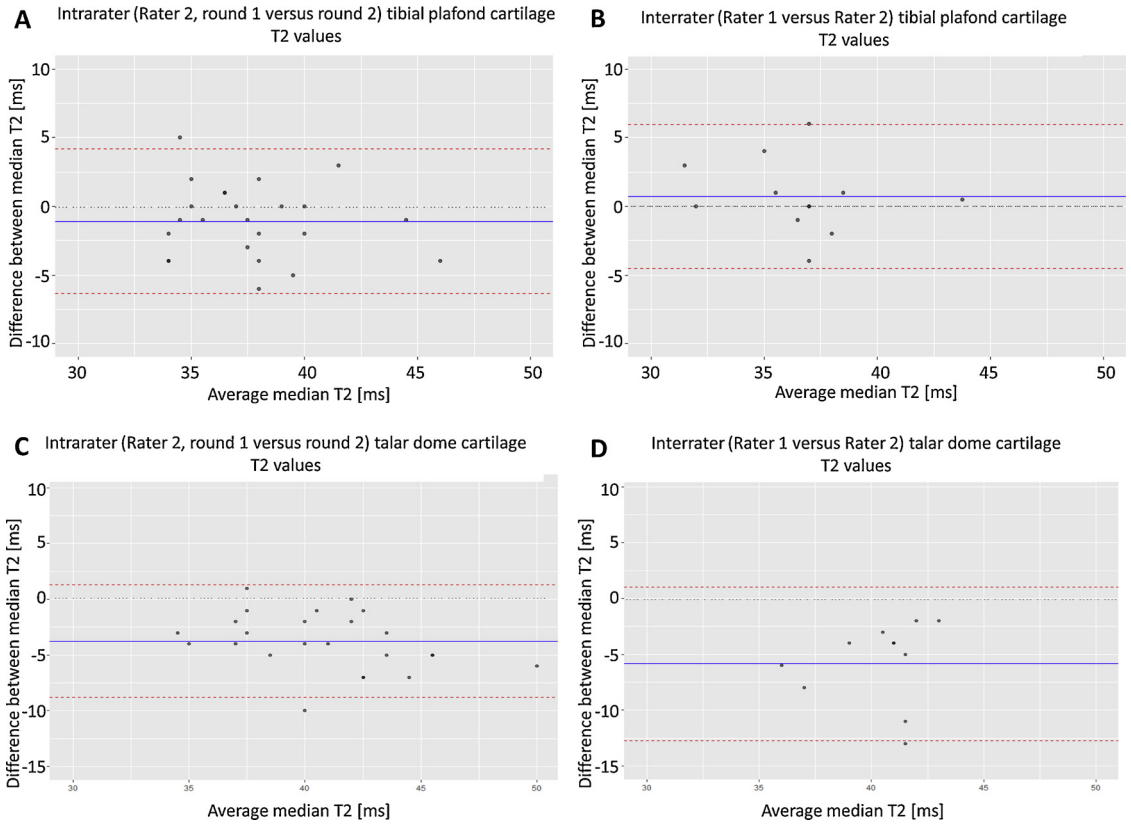

Fig. 4. Bland-Altman plots for the tibial plafond intrarater (a) and interrater (b) comparisons, as well as for the talar dome intrarater (c) and interrater (d) comparisons.

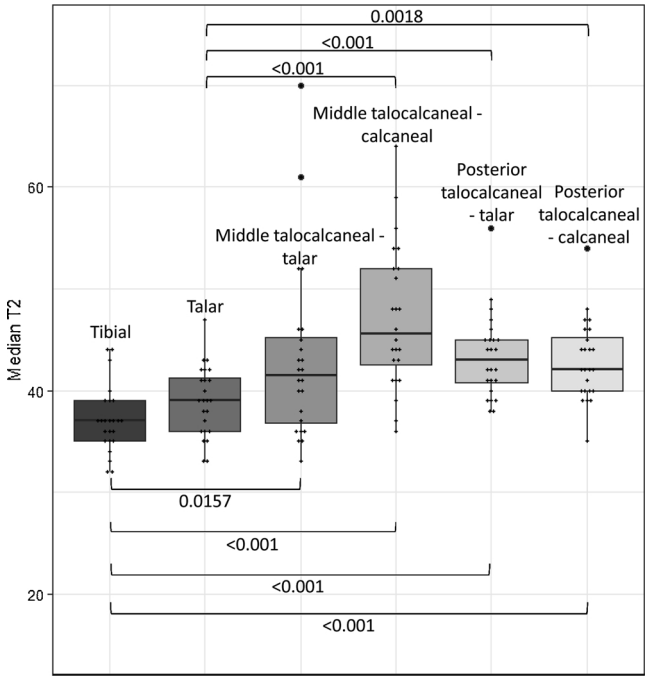

Fig. 5. Boxplots for tibiotalar and subtalar joint articular surface cartilage region T2 values. Significant differences between regions are indicated with brackets labeled with associated *P*-values.

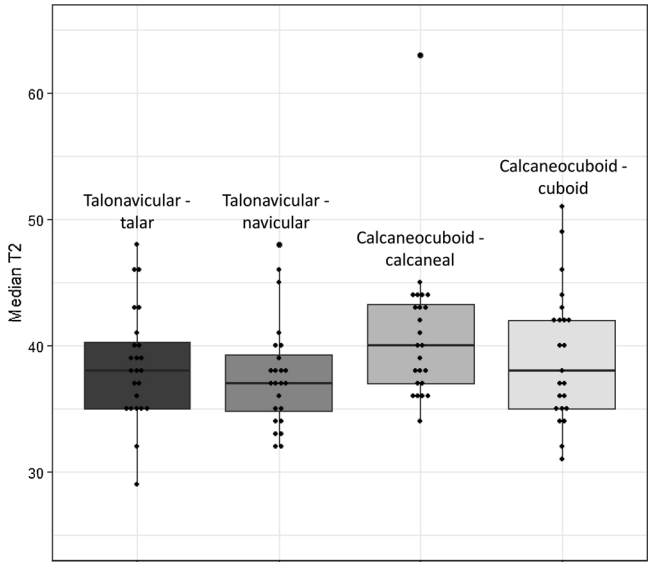

Fig. 6. Boxplots for talonavicular and calcaneocuboid joint articular surface T2 values.

mapping regions of interest.

Our results for the relative T2 values of the tibial and talar cartilage are similar to those reported by Lim et al., with the mean T2 of the talar dome cartilage being higher than that of the tibial plafond cartilage [27]. Our finding of significantly higher mean T2 in the posterior subregion of the tibial plafond than in the anterior and middle subregions of the tibial plafond, and in the posterior subregion of the talar dome than in the middle subregion of the talar dome, is consistent with the results of Lim et al. and Cha et al., who reported significantly higher T2 in the posterior tibiotalar subregions versus the corresponding anterior and middle subregions [27,32]. Potential contributors to this variation in T2 between tibiotalar cartilage subregions include magic angle artifact due to differences in cartilage orientation relative to the

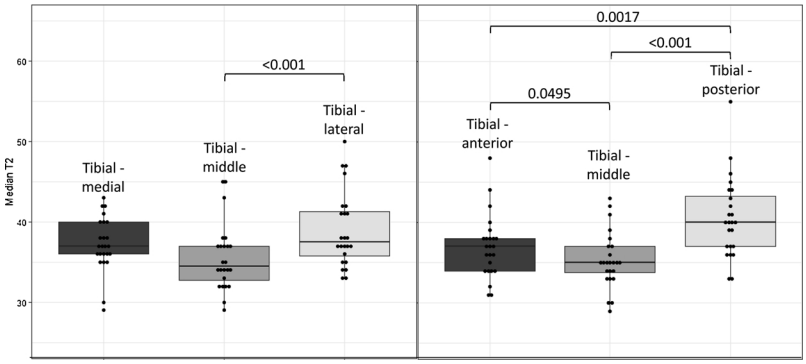

Fig. 7. Boxplots for tibial plafond subregion T2 values. Significant differences between regions are indicated with brackets labeled with associated *P*-values.

main magnetic field and differences in cartilage loading between the subregions [27].

The significant differences in mean T2 between the male and female subject groups for the anterior tibial and posterior talar cartilage regions have some similarity to the results from Lim et al., which showed significantly greater T2 for male versus female subjects in the overall tibial cartilage and anterior and middle tibial and talar cartilage regions [27]. However, their results showed consistently higher T2 for males, while we found that males only showed significantly higher T2 than females in one subregion, and that females had higher T2 in at least one subregion. These differences in results could be due to the wider subject age range and smaller number of subjects per group in our study compared to the larger and more narrowly age matched groups studied by Lim et al. (25 male, 25 female subjects aged 20 to 27 years in the study by Lim et al. versus 13 male, 11 female subjects aged 23 to 64 years in this present study).

This study has several limitations. First, limited T2 mapping resolution prevented us from separating the deep and superficial cartilage layers, which have been shown to have different T2 mapping values [7,23]. With in-plane resolution limited to 0.47 mm/pixel the thickness of the talar dome cartilage, which has been shown to be approximately 1.1 to 1.4 mm on average [33], consisted of only 2 to 3 pixels, making segmentation precision challenging. The resolution and slice thickness limitations also cause partial volume averaging between the cartilage and the subchondral bone and synovial fluid, as visualized in Fig. 1. Post-acquisition interpolation has been used to increase T2 map image resolution in the ankle [7] and may reduce partial volume averaging effects, but needs to be validated against high acquisition resolution T2 mapping values.

In addition, the interrater reliability was poor for the talar dome and calcaneal-side posterior subtalar facet, and medial and posterior talar dome subregions. The intrarater reliability was also poor for the posterior talar dome subregion. The poor segmentation reliability in these areas could be due to the disparate rater experience levels, the thin cartilage and previously mentioned partial volume averaging at the cartilage-bone and cartilage-synovial fluid interfaces, and challenge in defining the peripheral cartilage margins due to partial volume averaging. The challenge of reliable manual segmentation highlights the need for automated segmentation methods, which remove subjectivity and reduce segmentation time, both of which will be necessary for wide-spread clinical implementation of T2 mapping in the ankle/hindfoot joint cartilage.

We did not analyze several subject-specific characteristics that may affect cartilage T2 mapping values. Subtalar joint configuration has been shown to be correlated with the T2* value of the posterior subtalar joint facet cartilage but was not analyzed in this study [10]. Also, we did not exclude subjects with contralateral ankle/foot injury or symptoms, which could cause gait changes and altered load on the asymptomatic, imaged ankle/hindfoot.

Lastly, we did not perform subgroup analysis by age due to the relatively small number of subjects per group, uneven distribution of male and female subjects in the youngest versus oldest age groups, and lack of precise age data for all subjects due to some subjects having had only the age group recorded rather than precise age in years. Age-related changes in cartilage T2 have been demonstrated in the knee and likely exist in the ankle/hindfoot joints [34,35]. While this study was limited by relatively low subject numbers, the methods and initial results of this work can be applied to future work in a larger number of subjects for more robust analysis of potential age and sex-related T2 differences in the ankle and hindfoot cartilage over clinically-relevant subregions.

Other limitations include a short unloading period, which could create variation as the ankle cartilage T2 has been shown to change with unloading over a 30-minute scan [7], and the use of standard clinical positioning rather than a more precise positioning technique, potentially creating variation in the effects of magic angle. These and additional factors (e.g. diurnal and activity-induced cartilage water content variation) could influence scan-rescan repeatability, which was not assessed in this study. Longitudinal repeatability of ankle T2

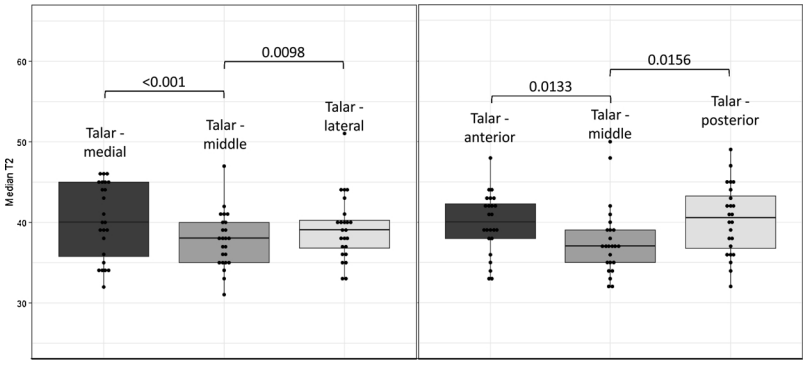

Fig. 8. Boxplots for talar dome subregion T2 values. Significant differences between regions are indicated with brackets labeled with associated *P*-values.

measurements remains to be tested.

T2 mapping MRI has the potential to provide objective quantitative information about cartilage health for early detection of cartilage degeneration, treatment planning, and measurement of post-treatment cartilage quality. Significant differences in mean T2 in the tibiotalar and subtalar joint cartilage between articular surfaces and across the subregions of the tibial plafond and talar dome cartilage found in this study emphasize the necessity of considering regional variation when utilizing T2 mapping values. This is essential for comparison between control and ankle/hindfoot-injury groups or when selecting comparison regions for longitudinal measurement of ankle cartilage T2 values following injury or cartilage repair.

Competing interests

The authors declare that they have no conflict of interest.

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Conflict of interest

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References

[1] S.T. Canale, R.H. Belding, Osteochondral lesions of the talus, J. Bone Joint Surg. Am. 62 (1980) 97–102.
[2] M. Takao, F. Komatsu, K. Naito, Y. Uchio, M. Ochi, Reconstruction of lateral ligament with arthroscopic drilling for treatment of early-stage osteoarthritis in unstable ankles, Arthroscopy 22 (2006) 1119–1125, https://doi.org/10.1016/j.arthro.2006.06.012.
[3] I. Taga, K. Shino, M. Inoue, K. Nakata, A. Maeda, Articular cartilage lesions in ankles with lateral ligament injury: an arthroscopic study, Am. J. Sports Med. 21 (1993) 120–127, https://doi.org/10.1177/036354659302100120.
[4] B. Hintermann, P. Regazzoni, C. Lampert, G. Stutz, A. Gächter, Arthroscopic findings in acute fractures of the ankle, J. Bone Joint Surg. Br. 82 (2000) 345–351.
[5] N. Leontaritis, L. Hinojosa, V.K. Panchbhavi, Arthroscopically detected intra-articular lesions associated with acute ankle fractures, J. Bone Jt. Surg.-Am. Vol. 91 (2009) 333–339, https://doi.org/10.2106/JBJS.H.00584.
[6] J.E. Bischof, C.E. Spritzer, A.M. Caputo, M.E. Easley, J.K. DeOrio, J.A. Nunley, L.E. DeFrate, In vivo cartilage contact strains in patients with lateral ankle instability, J. Biomech. 43 (2010) 2561–2566, https://doi.org/10.1016/j.jbiomech.2010.05.013.
[7] T. Golditz, S. Steib, K. Pfeifer, M. Uder, K. Gelse, R. Janka, F.F. Hennig, G.H. Welsch, Functional ankle instability as a risk factor for osteoarthritis: using T2-mapping to analyze early cartilage degeneration in the ankle joint of young athletes, Osteoarthr. Cartil. 22 (2014) 1377–1385, https://doi.org/10.1016/j.joca.2014.04.029.
[8] F. Bonnel, E. Toullec, C. Mabit, Y. Tourné, Chronic ankle instability: biomechanics and pathomechanics of ligaments injury and associated lesions, Orthop. Traumatol. Surg. Res. 96 (2010) 424–432, https://doi.org/10.1016/j.otsr.2010.04.003.
[9] S. Lee, Y.C. Yoon, J.H. Kim, T2 mapping of the articular cartilage in the ankle: correlation to the status of anterior talofibular ligament, Clin. Radiol. 68 (2013) e355–e361, https://doi.org/10.1016/j.crad.2013.01.023.
[10] A. Van Ginckel, S. De Mits, K.L. Bennell, A.L. Bryant, E.E. Witvrouw, T2* mapping of subtalar cartilage: precision and association between anatomical variants and cartilage composition, J. Orthop. Res. 34 (2016) 1969–1976, https://doi.org/10.1002/jor.23214.
[11] S.A. Labib, S.M. Raikin, J.T. Lau, J.G. Anderson, N.F. SooHoo, S. Carette, S.J. Pinney, Joint preservation procedures for ankle arthritis, Foot Ankle Int. 34 (2013) 1040–1047, https://doi.org/10.1177/1071100713496385.
[12] C. Nüesch, C. Huber, J. Paul, H.B. Henninger, G. Pagenstert, V. Valderrabano, A. Barg, Mid- to long-term clinical outcome and gait biomechanics after realignment surgery in asymmetric ankle osteoarthritis, Foot Ankle Int. 36 (2015) 908–918, https://doi.org/10.1177/1071100715577371.
[13] T.O. Clanton, N.S. Johnson, L.M. Matheny, Use of cartilage extracellular matrix and bone marrow aspirate concentrate in treatment of osteochondral lesions of the talus, Tech. Foot Ankle Surg. 13 (2014) 212–220, https://doi.org/10.1097/BTF.0000000000000054.
[14] B. Bittersohl, H.S. Hosalkar, F.R. Miese, J. Schibensky, D.P. Konig, M. Herten, G. Antoch, R. Krauspe, C. Zilkens, Zonal T2* and T1Gd assessment of knee joint cartilage in various histological grades of cartilage degeneration: an observational in vitro study, BMJ Open 5 (2015), https://doi.org/10.1136/bmjopen-2014-006895 e006895–e006895.
[15] A.H. Carter, N. Guttierez, T.K. Subhawong, H.T. Temple, B.P. Lesniak, M.G. Baraga, J. Jose, MR imaging of BioCartilage augmented microfracture surgery utilizing 2D MOCART and KOOS scores, J. Clin. Orthop. Trauma (2017), https://doi.org/10.1016/j.jcot.2017.08.017.
[16] L.A. Fortier, H.S. Chapman, S.L. Pownder, B.L. Roller, J.A. Cross, J.L. Cook, B.J. Cole, BioCartilage improves cartilage repair compared with microfracture alone in an equine model of full-thickness cartilage loss, Am. J. Sports Med. 44 (2016) 2366–2374, https://doi.org/10.1177/0363546516648644.
[17] T.J. Mosher, B.J. Dardzinski, Cartilage MRI T2 relaxation time mapping: overview and applications, Semin. Musculoskelet. Radiol. 08 (2004) 355–368, https://doi.org/10.1055/s-2004-861764.
[18] S.Y. Park, Y.C. Yoon, J.G. Cha, K.S. Sung, T2 relaxation values of the talar trochlear articular cartilage: comparison between patients with lateral instability of the ankle joint and healthy volunteers, Am. J. Roentgenol. 206 (2016) 136–143, https://doi.org/10.2214/AJR.15.14364.
[19] H. Tao, Y. Hu, Y. Qiao, K. Ma, X. Yan, Y. Hua, S. Chen, T2-mapping evaluation of early cartilage alteration of talus for chronic lateral ankle instability with isolated anterior talofibular ligament tear or combined with calcaneofibular ligament tear, J. Magn. Reson. Imaging 47 (2018) 69–77, https://doi.org/10.1002/jmri.25745.
[20] U. Schütz, C. Billich, D. Schoss, M. Beer, J. Ellermann, MRI cartilage assessment of the subtalar and midtarsal joints during a transcontinental ultramarathon – new insights into human locomotion, Int. J. Sports Med. 39 (2018) 37–49, https://doi.org/10.1055/s-0043-118008.
[21] S. Nehrer, S.E. Domayer, C. Hirschfeld, D. Stelzeneder, S. Trattnig, R. Dorotka, Matrix-associated and autologous chondrocyte transplantation in the ankle: clinical and MRI follow-up after 2 to 11 years, Cartilage 2 (2011) 81–91, https://doi.org/10.1177/1947603510381095.
[22] S.E. Domayer, G.H. Welsch, D. Stelzeneder, C. Hirschfeld, S. Quirbach, S. Nehrer, R. Dorotka, T.C. Mamisch, S. Trattnig, Microfracture in the ankle: clinical results and MRI with T2-mapping at 3.0 T after 1 to 8 years, Cartilage 2 (2011) 73–80, https://doi.org/10.1177/1947603510380901.
[23] S.E. Domayer, S. Apprich, D. Stelzeneder, C. Hirschfeld, M. Sokolowski, C. Kronnerwetter, C. Chiari, R. Windhager, S. Trattnig, Cartilage repair of the ankle: first results of T2 mapping at 7.0 T after microfracture and matrix associated autologous cartilage transplantation, Osteoarthr. Cartil. 20 (2012) 829–836, https://doi.org/10.1016/j.joca.2012.04.015.
[24] E.C. Argentieri, D.B. Sneag, O.K. Nwawka, H.G. Potter, Updates in musculoskeletal imaging, sports health multidiscip, Approach 10 (2018) 296–302, https://doi.org/10.1177/1941738118780230.
[25] S.E. Domayer, F. Kutscha-Lissberg, G. Welsch, R. Dorotka, S. Nehrer, C. Gäbler, T.C. Mamisch, S. Trattnig, T2 mapping in the knee after microfracture at 3.0T: correlation of global T2 values and clinical outcome – preliminary results, Osteoarthr. Cartil. 16 (2008) 903–908, https://doi.org/10.1016/j.joca.2007.11.014.
[26] V. Juras, Š. Zbýň, V. Mlynarik, P. Szomolanyi, B. Hager, P. Baer, I. Frollo, S. Trattnig, The compositional difference between ankle and knee cartilage demonstrated by T2 mapping at 7 Tesla MR, Eur. J. Radiol. 85 (2016) 771–777, https://doi.org/10.1016/j.ejrad.2016.01.021.
[27] Y. Lim, J.G. Cha, J. Yi, S.J. Kang, Y.K. Lee, S.J. Lee, H.-J. Kim, B.R. Lee, Topographical and sex variations in the T2 relaxation times of articular cartilage in the ankle joints of healthy young adults using 3.0T MRI, J. Magn. Reson. Imaging 43 (2016) 455–462, https://doi.org/10.1002/jmri.25004.
[28] R.K. Surowiec, E.P. Lucas, E.K. Fitzcharles, B.M. Petre, G.J. Dornan, J.E. Giphart, R.F. LaPrade, C.P. Ho, T2 values of articular cartilage in clinically relevant subregions of the asymptomatic knee, Knee Surg. Knee Surg. Sports Traumatol.

Arthrosc. 22 (2014) 1404–1414, https://doi.org/10.1007/s00167-013-2779-2.
[29] K.J. Wilson, R.K. Surowiec, N.S. Johnson, C.A. Lockard, T.O. Clanton, C.P. Ho, T2* mapping of peroneal tendons using clinically relevant subregions in an asymptomatic population, Foot Ankle Int. 38 (2017) 677–683, https://doi.org/10.1177/1071100717693208.
[30] R Core Team. R: A language and environment for statistical computing., (n.d.). https://www.r-project.org/ (accessed April 4, 2018).
[31] J.L. Fleiss, The Design and Analysis of Clinical Experiments, John Wiley & Sons, Inc., New York, NY, 1986.
[32] J.G. Cha, J.S. Yi, J.K. Han, Y.K. Lee, Comparison of quantitative cartilage T2 measurements and qualitative MR imaging between professional ballet dancers and healthy volunteers, Radiology 276 (2015) 199–206, https://doi.org/10.1148/radiol.15142021.
[33] K. Sugimoto, Y. Takakura, Y. Tohno, T. Kumai, K. Kawate, K. Kadono, Cartilage thickness of the talar dome, Arthrosc. J. Arthrosc. Relat. Surg. Off. Publ. Arthrosc. Assoc. N. Am. Int. Arthrosc. Assoc. 21 (2005) 401–404, https://doi.org/10.1016/j.arthro.2004.12.005.
[34] T.J. Mosher, B.J. Dardzinski, M.B. Smith, Human articular cartilage: influence of aging and early symptomatic degeneration on the spatial variation of T2—preliminary findings at 3 T, Radiology 214 (2000) 259–266, https://doi.org/10.1148/radiology.214.1.r00ja15259.
[35] T.J. Mosher, Y. Liu, Q.X. Yang, J. Yao, R. Smith, B.J. Dardzinski, M.B. Smith, Age dependency of cartilage magnetic resonance imaging T2 relaxation times in asymptomatic women, Arthritis Rheum. 50 (2004) 2820–2828, https://doi.org/10.1002/art.20473.