



Original Article

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Feasibility of Ultrashort Echo Time T2* Mapping in Comparison With T2 Mapping for Quantitative Evaluation of Meniscal Degeneration

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Purpose: This study aimed to assess the feasibility of ultrashort echo time (UTE)-T2* mapping in comparison with T2 mapping for quantitative evaluation of meniscal degeneration.

Materials and Methods: This study included 208 menisci of 99 patients (59 women and 40 men, median age 52 years old [16–80 years]) who underwent knee MRI with both standard T2 mapping and UTE-T2* mapping sequences. A radiologist reviewed the images and graded meniscal degeneration according to the morphologic criteria on T2-weighted and proton density-weighted sequences. Manually drawn regions of interest were placed along the outline and hyperintensity subregion within the meniscus, and in the same location on midsagittal images of each T2 and UTE-T2* sequence. Meniscal T2 and T2* values (T2m and T2*m) as well as T2 and T2* values of hyperintensity subregions (T2h, T2*h) were calculated.

Results: There was a strong correlation between T2m, T2*m, T2h, and T2*h, and morphological grades (correlation coefficient 0.793–0.943, 95% CI). On morphologic analysis, 50, 52, 50, and 56 menisci were graded as 0, 1, 2, and 3, respectively. T2m, T2*m, T2h, and T2*h were found to be significantly different in all the grades and tended to be higher in the more degraded meniscus ($p < 0.001$ for both). Mean T2m was 10.78 ± 2.91 ms, 15.81 ± 2.99 ms, 20.26 ± 3.19 ms, and 30.80 ± 7.38 ms and mean T2*m was 7.10 ± 1.12 ms, 9.64 ± 1.27 ms, 12.01 ± 1.58 ms, and 18.98 ± 4.67 ms for grades 0, 1, 2, and 3, respectively. Mean T2h was 20.05 ± 3.67 ms, 24.39 ± 4.73 ms, and 38.92 ± 9.49 ms and mean T2*h was 10.94 ± 1.65 ms, 13.67 ± 2.41 ms, and 22.36 ± 5.20 ms for grades 1, 2, and 3, respectively.

Conclusion: UTE-T2* mapping was feasible for quantitative evaluation of meniscal degeneration in patients. With a few improvements UTE-T2* mapping is a potential substitute for the standard T2 mapping, with improved efficacy.

Keywords: Magnetic resonance imaging; Diagnostic Imaging; Analysis, computer-assisted Image; Knee; Cartilage, articular; Meniscus

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INTRODUCTION

The meniscus protects and stabilizes the knee joint via shock absorption and load distribution [1]. While asymptomatic meniscal tears are commonly found on knee MRI [2], a diagnosis should be carefully evaluated as these tears can lead to knee osteoarthritis (OA); degenerative-type meniscal tear is strongly associated with both radiographic OA and symptomatic radiographic OA [3,4].

However, little is known about meniscal degenerative processes and early OA pathogenesis [3-5]. During meniscal degeneration, some components in the meniscal tissue such as proteoglycans, water, and collagen can change, affecting the molecular environment of the degenerating tissue. Such changes in the molecular environment would affect the T1, T1 rho, T2, and T2* relaxation times of degenerating tissue on quantitative MRI [5,6].

The normal meniscus has very short intrinsic T2 relaxation times due to abundant type I collagen and highly ordered collagen structure [5,7]. The ultrashort echo time (UTE) sequence uses very short echo time (TE) for imaging, so it can capture rapidly decaying signals from short T2 tissues such as the meniscus [5]. With UTE sequences, the internal structure of the meniscus can be assessed using mapping techniques, and the quantification of T2 and T2* values is also possible [7]. Quantitative MRI using T2 mapping or UTE-T2* mapping can demonstrate the integrity of the collagen matrix, enabling assessment of the meniscal tissue composition using quantitative values that correlate well with the degree of meniscal degeneration [8-10].

Recent studies have suggested that T2 mapping and comparison with histological grades of degeneration as a reference standard is the most robust method for the characterization of meniscal tissue in early OA [11]. However, compared to T2*, T2 mapping is more time-consuming and T2* mapping has a better signal-to-noise ratio [12]. Nonetheless, T2* mapping has a few technical limitations; the meniscus shows considerable changes in T2* values based on orientation [13] and T2* decay reflecting the anisotropic properties of the meniscal collagen fibers is strong, due to its highly organized structure [13]. Thus far, T2 mapping and UTE-T2* mapping in the human meniscus have not been compared in vivo and therefore it is not clear whether UTE-T2* mapping could replace T2 mapping.

Our study aimed to assess the feasibility of UTE-T2* mapping for quantitative evaluation of meniscal degeneration compared with the standard T2 mapping of the meniscus and hyperintensity subregion within the meniscus. Our final goal was to investigate whether UTE-T2* mapping could be a suitable substitute for standard T2 mapping, because UTE-T2* mapping has advantages over standard T2 mapping such as

shorter acquisition time.

MATERIALS AND METHODS

Patients

This retrospective study was approved by the Institutional Review Board of Asan Medical Center (IRB No. 2021-0342). The requirement for written informed consent was waived. We searched consecutive patients who had undergone knee joint MRI in our institution due to knee pain between July 2015 and September 2015 with the institutional picture archiving and communication system (PACS). We included the patients aged >15 years if they had completed a full sequence knee MRI with conventional T1, T2, proton density-weighted sequences and T2 mapping, and T2* mapping sequences without gadolinium enhancement. We searched the electronic medical records of the patients and excluded patients who 1) had a previous surgical history, acute trauma, infectious arthritis, rheumatoid arthritis, gouty arthritis, or other inflammatory arthritis of the ipsilateral knee joint; 2) had Kellgren-Lawrence grade IV OA. In total, 208 menisci were collected from 99 patients with knee OA: 49 right and 55 left knees, 104 medial and 104 lateral menisci (61 knees from 59 women and 43 knees from 40 men). The median patients' age was 52 years (range 16-80).

MRI Acquisition

All the imaging was performed on a 3-T clinical MRI scanner equipped with a 16-channel dedicated knee coil (Ingenia 3.0T CX, Philips Medical Systems Nederland B.V., Best, the Netherlands). All the patients underwent a routine morphological knee MRI sequence. In the 3D UTE acquisition and reconstruction, we used a 3D Stack of Stars type of k-space trajectory. Although the 3D Kooshball technique has a higher signal-to-noise ratio, the 3D Stack of Stars technique has the advantage of reducing TE to a shorter time than the 3D Kooshball technique, and relatively reducing the overall scan time (JW Hwang, personal communication, 2022). The full imaging parameters of T2 mapping, UTE-T2* mapping, T2 weighted, and proton density-weighted sequence used are summarized in Table 1.

Image Analysis

A radiologist with experience in musculoskeletal radiology interpreted and quantified the images. On T2-weighted sagittal images and proton density-weighted sagittal images, the meniscus degeneration was graded according to the morphological classification scheme proposed by Crues et al. [14] (Table 2).

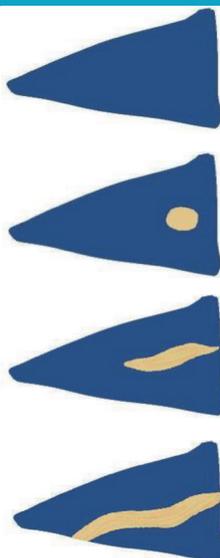
Table 1. MRI Parameters for the Standard T2, UTE-T2*, T2WI, and PDWI Sequences

Parameter	Standard T2 Mapping	UTE-T2* Mapping	T2WI	PDWI
	2D Fast Spin-Echo Sagittal	3D UTE Variable TEs Sagittal	Sagittal	Sagittal
TE (ms)	13.0, 26.0, 39.0, 52.0, 65.0, 78.0	0.1, 2.5, 4.8, 7.2, 9.5, 11.8, 14.2	100	30
TR (ms)	2600	20.2	2600	2600
FOV (mm)	160 × 160	180 × 180	180 × 180	180 × 180
Matrix (RO × PE)	320 × 320	268 × 268	360 × 343	360 × 343
Interpolated resolution (mm)	0.5	0.67 × 0.67	0.5 × 0.52	0.5 × 0.52
Slice thickness (mm)	3	3	3	3
Scan time	11 min 18 seconds	7 min 21 seconds	4 min 30 seconds	4 min 30 seconds

All the imaging was performed on a 3-T clinical MRI scanner equipped with a 16-channel dedicated knee coil (Ingenia 3.0T CX, Philips Medical Systems). UTE, ultrashort echo time; T2WI, T2-weighted imaging; PDWI, proton density-weighted imaging; TE, echo time; TR, repetition time; FOV, field of view; PE, phase encoding; RO, readout

Table 2. Morphological Meniscal Degeneration Classes According to Morphologic Criteria on the Intermediate-Weighted Sequence by Crues [14]

Grade	MR Morphological Criteria
0	Normal, no abnormal hyperintensity within the meniscus
1	Small focal area of the hyperintensity within the meniscus
2	Linear or wedge-shaped areas of the hyperintensity without extension to the articular surface
3	Abnormal hyperintensity extending to the articular surface, indicated tear



T2 and T2* mapping images were analyzed using Intellispace Portal 9.0 (Royal Philips, Amsterdam, the Netherlands). Manually drawn regions of interest (ROIs) were placed along the outline of each meniscus, and the intra-meniscal high signal intensity area [14], defined as the hyperintensity subregion, in the same location with sagittal image of each T2 and UTE-T2* mapping sequences by the radiologist (Fig. 1). ROI was directly drawn on T2 mapping images and T2* mapping images, however, in very confusing cases, we drew ROIs using the single centrally positioned slice of the optimal contrast between meniscus and surrounding tissues and the drawn ROIs were copied and pasted into the T2, T2* mapping images of the

same location. The meniscal T2 and T2* values (T2m and T2*m) and T2, T2* values of hyperintensity subregion (T2h, T2*h) were calculated automatically in the program. If there was no definite hyperintensity subregion, there were two ROIs.

Statistical Analysis

Descriptive statistics for continuous variables were reported as means with standard deviations. For statistical analyses, one-way analysis of variance (ANOVA) with Tukey's honestly significant difference post hoc test were done with multiple comparisons of T2m, T2*m, T2h, and T2*h with the morphological grades (Table 2). Pearson's correlation coefficients were calculated to determine the correlation between the T2m and T2*m, and T2h and T2*h, of T2 and T2* mapping images. Statistical analyses were performed using IBM SPSS Statistics v25 software (IBM Corp., Armonk, NY, USA). A p-value of less than 0.05 was considered to be statistically significant.

RESULTS

Morphological Grade of Meniscal Degeneration

Among the 208 menisci, 50, 52, 50, and 56 menisci were diagnosed as degeneration grade 0, 1, 2, and 3, respectively, according to the morphological classification scheme (Table 2). A total of 208 ROIs for meniscus were drawn while 158 ROIs for hyperintensity subregions were drawn because there were no hyperintensity subregions in grade 0 meniscus (Table 3).

T2 Relaxation Time in Standard T2 Mapping Images and T2* Relaxation Time in UTE-T2* Mapping Images

T2m was 19.7 ± 12.4 ms (mean ± standard deviation, range 5.2–59.0). T2*m was 12.1 ± 4.8 ms (range 4.7–29.2). T2h was 28.1 ± 9.4 ms (range 13.3–65.7). T2*h was 15.9 ± 3.4 ms (range

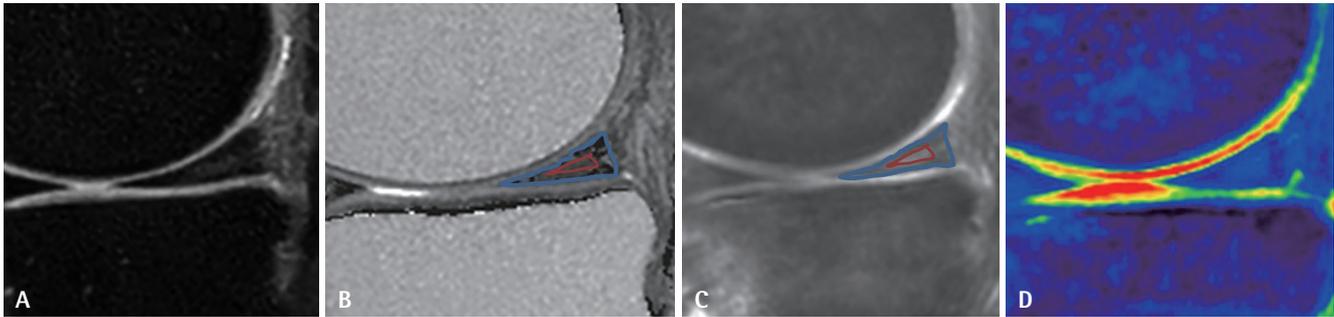


Fig. 1. Manually drawn regions of interest on each meniscus (blue line) and intra-meniscal hyperintensity subregion (red line) on both T2 and UTE-T2* mapping MRI. The mean T2 and T2* values were calculated. A: Proton density-weighted fat suppression image. B: Fast spin echo T2 mapping image. C: UTE-T2* mapping image without color-coding. D: UTE-T2* mapping image with color-coding. UTE, ultrashort echo time.

7.0–37.6). T2* values were lower with smaller standard deviations than T2 values. All T2 and T2* values increased with an increase in morphological grades. A strong correlation was found between T2m, T2*m, T2h, and T2*h, and morphological grades (correlation coefficient 0.793–0.943, 95% CI). T2m, T2*m, T2h, and T2*h of the meniscus according to each grade are shown in Tables 4 and 5 and Figures 2 and 3. The one-way ANOVA test showed statistically significant differences among the morphological grades (Table 6).

DISCUSSION

In our study T2 values and T2* values of the meniscus showed a strong correlation. T2m, T2*m, T2h, and T2*h values were significantly different among the morphological groups. All T2 and T2* values increased with an increase in morphological grades.

T2 mapping is a technique of pixelwise illustrations of absolute T2 transverse relaxation times on a map [15]. T2 mapping allows direct T2 quantification using the grayscale intensity of each voxel, which is the output of a calculation performed independently at each corresponding spatial pixel from a series of input images [15]. T2* mapping is a parametric imaging technique of T2* relaxation time, which is the time of inherent decay of transverse magnetization caused by a combination of spin-spin relaxation (T2) and magnetic field inhomogeneity (T2*) [15,16]. In general, T2* imaging requires a strong magnetic field and radiofrequency signals from a gradient [16].

T2 relaxation time has been used widely to evaluate meniscal tissue composition and is regarded as a reliable reference test for meniscal degeneration [11]. We investigated the T2* relaxation times of meniscal tissue with a reference to T2 relaxation times and the correlation between T2 values and T2* values. The results were statistically significant and reliably correlated. Therefore, we concluded that T2* relaxation time was also a feasible method for evaluating meniscal tissue.

Table 3. Meniscal Numbers and Morphological Grades

Grade	Number of Meniscus (n)	Hyperintensity Subregion (n)
Right knee		
Medial meniscus (n = 49)		45
Grade 0	4	
Grade 1	13	
Grade 2	14	
Grade 3	18	
Lateral meniscus (n = 49)		37
Grade 0	12	
Grade 1	17	
Grade 2	12	
Grade 3	8	
Left knee		
Medial meniscus (n = 55)		42
Grade 0	13	
Grade 1	8	
Grade 2	11	
Grade 3	23	
Lateral meniscus (n = 55)		34
Grade 0	21	
Grade 1	14	
Grade 2	13	
Grade 3	7	
Total knee (medial/lateral meniscus: n = 208)		158
Grade 0	50	
Grade 1	52	
Grade 2	50	
Grade 3	56	

There were no hyperintensity subregions in grade 0 meniscus.

T2 mapping has a limitation in meniscal imaging due to the very short T2 components and the heterogeneity of the meniscal tissue itself [8]. Multi-TEs for T2 mapping sequences are between 10 ms and 100 ms in a usual knee MRI; however, the mean T2 value of a normal meniscus has been reported as 11 ±

Table 4. T2 and T2* Relaxation Times of the Meniscus in Different Degeneration Grades

	Grade 0 (n = 50)	Grade 1 (n = 52)	Grade 2 (n = 50)	Grade 3 (n = 56)	Sig. (n = 208)
T2m (ms)	10.78 ± 2.91	15.81 ± 2.99	20.26 ± 3.19	30.80 ± 7.38	p < 0.0001
T2*m (ms)	7.10 ± 1.12	9.64 ± 1.27	12.01 ± 1.58	18.98 ± 4.67	p < 0.0001

Both mean T2 and T2* values of the menisci were significantly different among all the grades and tended to be higher in the more severely degraded meniscus (mean ± standard deviation).

Table 5. T2 and T2* Relaxation Times of Hyperintense Subregion Within the Meniscus

	Grade 1 (n = 52)	Grade 2 (n = 50)	Grade 3 (n = 56)	Sig. (n = 158)
T2h (ms)	20.05 ± 3.67	24.39 ± 4.73	38.92 ± 9.49	p = 0.002 (grade 1 vs. grade 2) p < 0.0001 (otherwise)
T2*h (ms)	10.94 ± 1.65	13.67 ± 2.41	22.36 ± 5.20	p < 0.0001

Mean T2 and T2* values of the hyperintense subregion in grades 1 to 3 meniscus were significantly different among all the grades and tended to be higher in the more degraded meniscus (mean ± standard deviation).

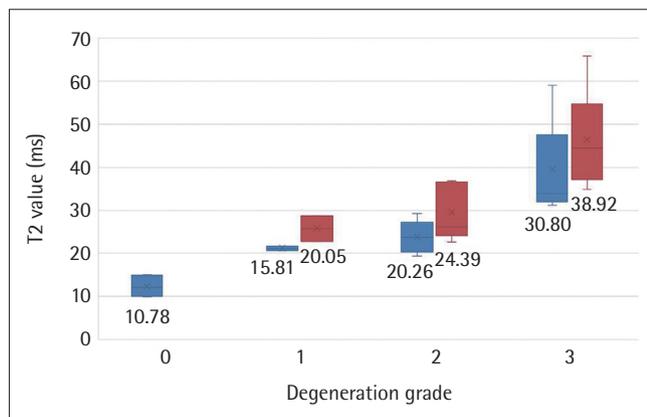


Fig. 2. Mean T2 relaxation time of the meniscus and hyperintensity subregion in T2 mapping. This bar graph demonstrates the mean T2 relaxation time of the meniscus and hyperintensity subregion on T2 mapping MRI. The blue bar indicates the T2 relaxation time of the meniscus (T2m) and the red bar indicates the T2 relaxation time of the hyperintensity subregion (T2h). The mean T2 relaxation time of the hyperintensity subregion was significantly higher than the values of the meniscus (p < 0.0001).

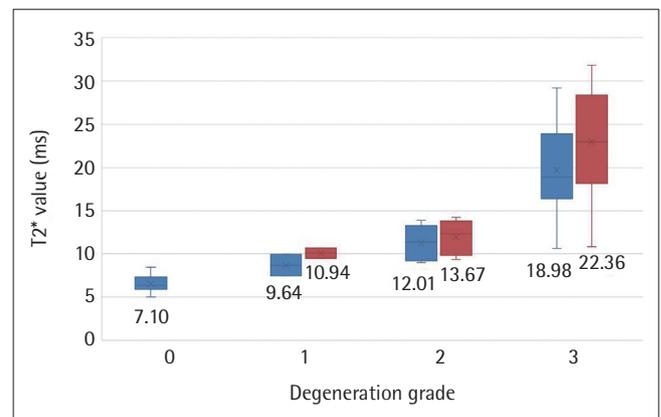


Fig. 3. Mean T2* relaxation time of the meniscus and hyperintensity subregion in UTE-T2* mapping. The blue bar indicates the T2* relaxation time of the meniscus (T2*m) and the red bar indicates the T2* relaxation time of the hyperintensity subregion (T2*h). The mean T2* relaxation time of the hyperintensity subregion was significantly higher than the values of the meniscus (p < 0.0001).

4 ms [17]. Therefore, quantitative MRI techniques with extremely short TEs, such as UTE-T2* or zeroTE-T2*, have been suggested as better methods of quantifying menisci than standard spin-echo-based T2 mapping [8,9,18]. Meniscal T2* can also respond to the extracellular matrix of collagen, glycoproteins, and proteoglycans, and be affected by myxoid changes, fibrocartilaginous separation of the matrix, extensive fraying, and tears that increase the heterogeneity of meniscal tissue [12].

UTE-T2* imaging has several advantages over T2 imaging; however, it also has a few disadvantages. UTE-T2* mapping has been reported to show different results among meniscal zones depending on the circumferential fibers [13]. Using UTE sequences with sub-millisecond TEs, the fibrillar network of the meniscus substructures is better depicted [19]. However, UTE-T2* imaging studies have revealed significant artifacts in im-

ages and the orientation dependency of T2* values: the magic angle orientation showed the highest T2* values and at a fiber-to-field angle of 0° the T2* values were lowest [13]. The relation between mono-exponential decay and bi-exponential decay in terms of fiber-to-field angle is still unclear [13]. This study was performed with standard 2D fast spin echo T2-weighted images and 3D UTE-T2* images with variable TEs.

UTE-T2* values have been higher in torn or degenerated menisci and significantly different between normal meniscus, degenerated meniscus, and torn meniscus [9]. Biexponentially fitted T2* relaxation time has demonstrated a greater ability to distinguish normal and degenerated menisci in other investigations [20]. Another study revealed that both T2 and T2* values were higher in abnormally thick meniscal lamellar layers compared with the values in normal lamellar layers, and only the T2* value was statistically significant [21]. Interestingly, in an ex vivo study, there were significant increases in T2

Table 6. One-Way ANOVA Test of T2m and T2*m, T2h and T2*h

Value	Groups	Sum of Squares	Degree of Freedom	Mean Square	F	Sig.
T2m	Between groups	11680.267	3	3893.422	181.619	< 0.001
	Within groups	4373.218	204	21.437		
	Total	16053.485	207			
T2*m	Between groups	4220.990	3	1406.997	195.280	< 0.001
	Within groups	1469.828	204	7.205		
	Total	5690.817	207			
T2h	Between groups	22015.308	3	7338.436	208.822	< 0.001
	Within groups	7168.987	204	35.142		
	Total	29184.295	207			
T2*h	Between groups	6775.419	3	2258.473	233.135	< 0.001
	Within groups	1976.233	204	9.687		
	Total	8751.652	207			

The One-Way ANOVA test showed statistically significant differences among the morphological grades.

and UTE-T2* with increasing histology grades and high sensitivity and variable specificity but not in T2* [6].

In this study, we assessed the feasibility of UTE-T2* mapping to detect meniscal degeneration in comparison with T2 mapping. Both mean T2m and T2*m and mean T2h and T2*h, were significantly different among all the grades ($p < 0.001$) except for T2h grade 1 vs. T2h grade 2 ($p = 0.002$) and tended to be higher in the meniscus that was more degraded ($p < 0.001$ for both). These results suggest that UTE-T2* mapping was feasible in the evaluation of meniscal degeneration as a standard T2 mapping, and the focal hyperintensity subregions within the menisci depicted higher grades of degeneration. The results of our study suggest that both T2 mapping and UTE-T2* mapping are effective noninvasive diagnosing and monitoring methods for early degenerative changes within the meniscal tissue.

In previous studies, quantification of MRI mapping demonstrated a highly heterogeneous distribution of T2 and T2* values with focal regions of elevated values in degenerated or torn menisci [6,9,21]. These findings implied an inadequacy in measuring mean T2 and T2* values of menisci calculated by averaging across all voxel values within the whole meniscus. Therefore, in this study, we measured T2 and UTE-T2* values of hyperintensity subregion within the menisci (T2h, T2*h) as well as the cross-sectional area of menisci (T2m, T2*m). However, both T2m and T2*m, and T2h and T2*h values were statistically significant.

The mean values of meniscus reported in previous studies with different imaging acquisition parameters were 8–12 ms for the T2 value [17,22], and 5–8 ms for the UTE-T2* value [7,20], respectively. In this study, our values were in excellent agreement with previous values.

This study has several limitations. First, there was no histologic correlation of the meniscus. Our meniscal degeneration grading relied fully on the evaluation of morphologic MRI. His-

tologic validation as a marker for biochemical structures of the meniscus would be confirmative to verify T2 and UTE-T2* values. Second, we analyzed the entire meniscus without considering zonal variations. Degenerative changes within the meniscus can occur unevenly according to the zonal distribution. Further studies analyzing T2 and T2* values in each anatomic zone of the menisci are required. Third, we did not consider the possible confounding factors such as age, sex, and articular cartilage degeneration. Moreover, we did not correlate with OA clinical findings. Fourth, because only one radiologist analyzed the images, we could not evaluate the reproducibility of our measurements.

In conclusion, UTE-T2* relaxation time is feasible for the quantitative evaluation of meniscus degeneration. With a few improvements UTE-T2* mapping is a potential substitute for the standard T2 mapping, with improved efficacy.

Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

Conflicts of Interest

The authors have no potential conflicts of interest to disclose.

Author Contributions

Conceptualization: Sang Hoon Lee. Data curation: Sang Hoon Lee. Formal analysis: Sang Hoon Lee, JeongAh Ryu. Funding acquisition: Sang Hoon Lee. Supervision: Myung Jin Shin. Validation: Min Hee Lee, Hye Won Chung. Writing—original draft: Soo Yeon Choi, JeongAh Ryu. Writing—review & editing: JeongAh Ryu. Approval of final manuscript: all authors.

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