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MR T2 values of the knee menisci in the healthy young population: zonal and sex differences

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Summary

Objective: The magnetic resonance (MR) T2 value of the cartilage, which has been shown in the articular cartilage to correlate with collagen fiber orientation and water content, may be helpful for early detection of chondropathy. However, the measurement and significance of MR T2 value for knee meniscus have not been well established. The purpose of this study was to investigate whether the MR T2 values in the diverse zones of the posterior horn of the knee meniscus differ between sexes in a young healthy population.

Method: Twenty healthy volunteers, 10 men and 10 women (aged from 22 to 32 years), were enrolled for MR imaging of the right knee menisci. The T2 values of the posterior horns of the medial and lateral knee menisci were measured for the white zone, red/white zone, and red zone on images acquired with fat-suppressed multislice turbo spin-echo sequence at 3.0 T.

Results: The T2 value, with medial and lateral menisci considered together, increased significantly from the inner white zone (T2 = 8.02 ± 0.60 ms), to the red/white zone (T2 = 8.78 ± 0.99 ms), and to the outer red zone (T2 = 12.22 ± 0.92 ms) of the posterior horns of the menisci ($P < 0.001$). A generalized estimating equation method and multiple linear regression model showed that the T2 values averaged for the medial and lateral menisci together in the red and red/white zones were significantly lower in men than in women by 1.320 ms ($P = 0.002$) and 0.865 ms ($P < 0.001$), respectively, while the white zone showed no significant difference ($P = 0.694$) between men (8.08 ± 0.63 ms) and women (7.98 ± 0.60 ms).

Conclusion: Zonal and sex differences in the MR T2 values in the posterior horns of the knee menisci exist in the young healthy population. These differences may be associated with sex differences in the occurrence of knee osteoarthritis.

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Key words: MR, T2 value, Meniscus, Cartilage, Osteoarthritis, Knee, Sex difference.

Introduction

Osteoarthritis (OA) of the knee is primarily a disorder of cartilage and is one of the most frequent illness in the musculoskeletal system for older people¹. OA appears to result from serious damage to the anterior cruciate ligament, meniscus tears, or spontaneous degeneration of knee cartilage as a result of overloading^{2–4}. These pathologies lead to progressive inflammation and edema of the synovial

membrane and subchondral bone, triggering the release of pain factors and resulting in arthralgia. Using noninvasive means to learn about the effects of OA on knee cartilage and to provide early detection of the structural changes in knee cartilage is imperative for effective diagnosis and treatment of OA^{5–7}. For this purpose, quantitative magnetic resonance (MR) imaging techniques have been proposed to evaluate cartilage damage in early OA^{8,9}. Specifically, the MR T2 value provides important information about the changes of collagen fibers and water content in the articular cartilage, as demonstrated in human studies and animal models of OA^{8,10,11}.

Besides the articular cartilage whose damage serves as an important index for estimating the severity of knee OA¹², the meniscus which plays a critical role in the normal biomechanics of the knee joint in load bearing, load distribution, and other functions, may also be related to the

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developments of OA¹³. A few reports have demonstrated that the meniscal pathologies, such as meniscal degeneration and meniscal tear, may be associated with change of the articular cartilage in patients in early or late stages of OA^{7,12,14,15}. The imaging features investigated in these studies for the menisci, however, remain morphological in nature. By the analogy of the articular cartilage, it is possible that a quantitative measurement of the MR T2 value in the meniscus may provide additional information to help in understanding the evolution of meniscal degeneration and its potential relationship with articular cartilage and OA of the knee.

To our knowledge, there are relatively few articles describing the use of MR T2 value to assess the biomechanical changes and degradation of the menisci in the knee¹⁶, likely due to the rapid signal decay in menisci causing difficulty in experimental measurements. Occasional reports have mentioned that the T2* value of the menisci ranges from 5 to 8 ms at 1.5 T when estimated with an ultrashort echo-time (UTE) pulse sequence¹⁷. In addition to the difficulty from short T2, the human knee meniscus is not a homogeneous and isotropic substance because the orientation and the types of collagen fibers in and the blood supply to the menisci vary substantially between different zones^{18,19}. Furthermore, the mobility of the anterior and posterior horns of the knee menisci, as well as that of the medial and lateral knee menisci, is quite diverse²⁰. Possible zonal variations of T2 in the menisci, therefore, need to be investigated before quantitative T2 measurements can be used to assist clinical evaluation of OA.

Gender dependence is another factor that may have an effect on the diagnostic value of quantitative T2 measurements in the menisci. The prevalence and severity of knee OA are higher in women than in men, which has been thought to be related to the different mechanical loading associated with the walking pattern^{20,21}. These may influence the probability of meniscal degeneration²⁰. On the other hand, compressive loading is believed to lead to alterations in collagen organization and water content in the cartilage, which results in T2 changes at MR imaging as demonstrated at least for the articular cartilage^{22,23}. As

a consequence, it appears that the sex-related differences in meniscal structure and in the prevalence of OA may be reflected in variations in the T2 values of knee menisci.

The aim of this study was to determine whether the MR T2 values of the knee menisci are variable and whether these variations are related to the different zones of the medial and lateral menisci in healthy men and women aged below 35. Specifically, we hypothesized that the MR T2 values of knee menisci measured in the clinical setting would exhibit zonal and sex differences, with elevated T2 possibly related to increased vascularity and OA occurrence. Since the posterior horn of the medial meniscus is the most frequent location of meniscal degeneration and tears in primary OA of the knee^{24,25}, the posterior horns of the medial and lateral menisci were selected as the focus of this study.

Materials and methods

SUBJECTS

This study was approved by the local institutional review board, and informed consent was obtained from each subject. Twenty normal young adult volunteers, 22–32 years of age (10 men, 10 women; mean age, 26.50 ± 2.74 years; mean body mass index, 21.48 ± 3.04) were enrolled in this study. They were recruited from the community and were screened to exclude subjects with a known contraindication for MR imaging. All subjects were healthy, as defined by a lack of pain, stiffness, or losing stability of the knee joint. None reported a history of injury or OA of the knee.

DATA ACQUISITION

All volunteers were scanned in a supine position using a 3.0 T MR system (Achieva, Philips, Best, Netherlands). The right knee joint of each subject was centered in an eight-channel SENSE knee coil (Philips Medical System, Best, Netherlands). To minimize the "magic angle" effect on the meniscus T2 measurement²⁶, the imaged leg was positioned straight with the long axis parallel to the main magnetic field (B_0), and immobilized with MR-compatible plastic pads.

As the posterior horn of the medial meniscus is the most frequent location of meniscal degeneration and tear in primary OA of the knee^{24,25}, the posterior horns of the medial and lateral menisci were selected as the focus of this study. MR images in the nearly sagittal plane were acquired to cover these regions using the procedure described below. After three-plane tripilot imaging, 20 contiguous axial T1-weighted images for the purpose of later slice positioning were acquired using a spin-echo sequence with repetition time (TR) = 600 ms, echo time (TE) = 14 ms, number of excitation (NEX) = 1,

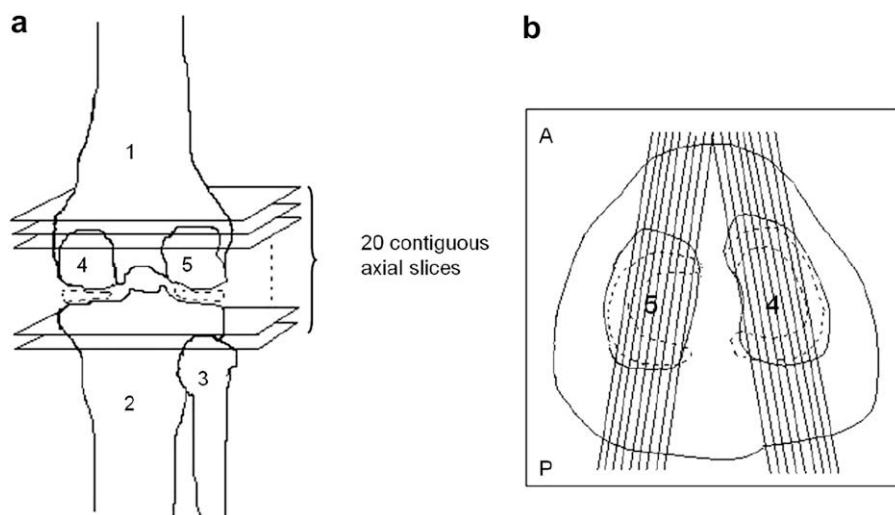


Fig. 1. (a) Schematic representation of a posterior view of the knee joint and 20 contiguous axial slices acquired for positioning of the nearly sagittal slices. Dotted areas: menisci. (b) For the axial slice showing the largest width of femoral condyles on both the medial and lateral sides of the knee joint, nine nearly sagittal slices with the orientation parallel to the anteroposterior long axis of the femoral condyle were prescribed for both the medial and lateral sides. Dotted areas: menisci projected onto this axial plane. 1: Femur; 2: tibia; 3: fibula; 4: medial condyle; 5: lateral condyle; A: anterior; P: posterior.

matrix size = 256×256 , slice thickness = 5 mm, and acquisition time = 2 min 35 s. From the total of 20 axial slices, the single axial plane with the largest width of femoral condyles on both the medial and lateral sides of the knee joint was selected manually as the reference plane [Fig. 1(a)]. Based on the selected axial reference plane, the sagittal planes for the posterior horns of the knee menisci were then prescribed by placing nine contiguous slices with orientation parallel to the anteroposterior long axes of the femoral condyles [Fig. 1(b)], which covered most of the posterior horns of both the medial and lateral menisci. A total of 18 slices of the medial and lateral menisci were acquired for each subject. Following the slice positioning, T2-weighted images with four different echoes were obtained by using multi-slice turbo spin-echo sequence with TR = 2500 ms; TE = 6.4, 9.4, 12, and 15 ms; echo train length = 3; slice thickness = 1 mm; slice gap = 1 mm; matrix size = 258×324 (zero-filled to 560×560); NEX = 2; and acquisition time = 14 min 40 s. Fat suppression was used to improve the tissue contrast of the images such that the derived T2 value is less prone to inaccuracy due to fat signal contamination from partial volume effects.

IMAGE PROCESSING

Motion correction

After imaging acquisition was completed, all data were transferred to a stand alone personal computer. These images were corrected for motion using a two-dimensional auto-correlation method, in which the first image, i.e., the one acquired with TE = 6.4 ms, was used as a reference image to coregister the remaining three echo images, i.e., TE = 9.4, 12, 15 ms, by calculating two-dimensional correlation coefficients at different spatial "shifts". Since the signal intensities of all tissues except the menisci were similar at these TEs, the spatial shift corresponding to that yielding the maximum correlation coefficient was regarded as having optimal coregistration. In this manner, all images were coregistered with the first-echo image with minimal in-plane motion.

Region of interest (ROI) definition

The ROIs for measurements of the T2 values in the posterior horns of the medial and lateral menisci were identified on the sagittal MR images of the first echo, including the entire region of meniscus and the regions of three different zones of meniscus. The three different zones of meniscus were defined by dividing the meniscus into three different parts with each part occupying one-third the width of the meniscus (Fig. 2). Based on the anatomical division with respect to vascularization (Fig. 3)^{19,27}, the red zone (i.e., the outer zone) is the outer one-third of the meniscus, which receives a full blood supply (10–30% for the medial meniscus)^{19,27,28}. The white zone (i.e., the inner zone) is the inner one-third of the meniscus and includes mainly fibrocartilage and is completely avascular^{3,19,27}. The red/white zone (i.e., the middle zone) represents the transition between the outer vascular and inner avascular zones^{19,27}. To avoid partial volume effects, the upper and lower borders of the meniscus were not selected in the ROIs. The selection of ROIs was performed by two experienced assistants (PHT and MCC) who worked on ROI selection for three randomly selective subjects separately, discussed the disagreements together, and achieved a consensus on the

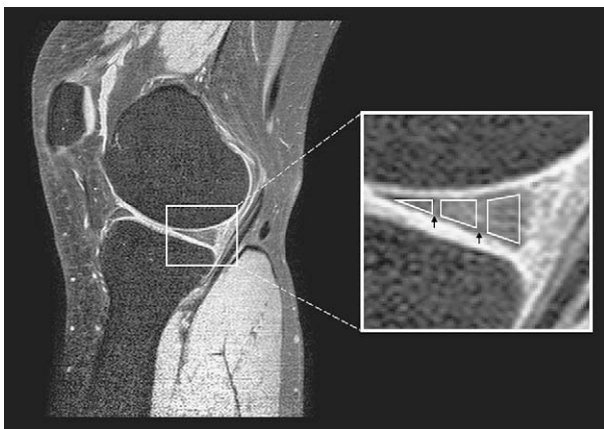


Fig. 2. Example of an ROI placement on a nearly sagittal slice of the knee menisci is shown. The selection of ROIs is performed on the first-echo image, which is enlarged on the right side. The black arrows indicate the separation between the three zones, and each zone occupies about one-third the width of the meniscus.

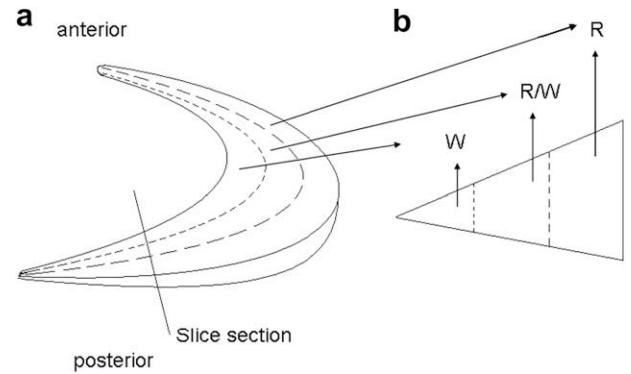


Fig. 3. (a) A schematic diagram representing the three diverse zones of the meniscus, including the red (R), red/white (R/W), and white (W) zones. (b) The cross-section of the posterior horn of the meniscus along the nearly sagittal image slice.

ROI selection procedure stated above to minimize the manual discrepancies. After unification of the ROI selection procedure, disagreement in the area of ROI was less than 6%, leading to less than 4% discrepancies in the resulting T2 estimation for the three subjects. One set of image data was discarded from the statistical analysis because of low image quality caused by severe involuntary motion. The total of 20 volunteers reflects the number of subjects after excluding the single data set.

T2 CALCULATION

To improve the signal-to-noise ratio (SNR) of the meniscus image, analysis of the T2 values of knee menisci was conducted on a zone-by-zone basis. The mean signal intensities were calculated first in the ROIs of the posterior horns of the medial and lateral menisci on each slice of the motion-corrected images. Then, the T2 values were derived using the least-square single-exponential curve-fitting method on the MATLAB 7.0 software platform (Mathworks, Natick, MA, USA). Two parameters, M_0 (spin density) and T2 (transverse relaxation time), were determined by fitting the signal magnitude from echoes of the multislice multiecho experiment to the spin–spin relaxation signal decay equation:

$$S(\text{TE}) = M_0 \exp\left(-\frac{\text{TE}}{T_2}\right),$$

where $S(\text{TE})$ represents the known signal intensity values measured at the prescribed TE. For fast convergence of this curve fitting, initial guesses were set at $T_2 = 10$ ms and $M_0 = 1.4$ times the mean signal intensity of the first echo (i.e., signal at TE = 6.4 ms). The T2 values derived from each single image were then averaged over all slices to obtain mean T2 values for the entire red zone, white zone, and red/white zone in the posterior horns.

STATISTICAL ANALYSIS

After the manual selection of ROIs on the first-echo image, i.e., TE = 6.4 ms, the mean and standard deviation (SD) of the T2 values in the different zones of the posterior horns of medial and lateral menisci were calculated. Paired-*t* tests were used to compare the differences in T2 values between the medial and lateral menisci for those aforementioned total region and the three different zones. The generalized estimating equation (GEE) methods' multiple linear regression models were used to compare the gender effect on T2 values in the three different zones of the posterior horns and the total region selected, after adjusting for the side effect of the meniscus (medial vs lateral)^{29,30}. The GEE method of regression was also used to check the tendency for an increased T2 value through the three zones of the knee meniscus. The results were done under the SPSS v15.0 for windows system (SPSS Inc., Chicago, IL, USA). Statistical significance was defined as $P < 0.05$.

Results

T2 VALUE OF THE POSTERIOR HORNS IN THE MEDIAL VS LATERAL MENISCI

The T2 value of the posterior horns of both the medial and lateral menisci of the total region selected was

9.59 ± 0.92 ms. There was no significant difference in any T2 value between the medial and lateral menisci in the three different zones in the posterior horn or in the total region selected (Table I).

T2 VALUES IN DIFFERENT ZONES OF THE POSTERIOR HORNS OF THE MENISCI

The T2 values differed significantly between different zones in the posterior horns of the medial and lateral menisci, including the white zone (T2 value = 8.02 ± 0.60 ms), red/white zone (T2 value = 8.78 ± 0.99 ms), and red zone (T2 value = 12.22 ± 0.92 ms) (Fig. 4). The GEE method and linear regression showed that, after adjusting for the side effect of the meniscus (medial or lateral), the T2 values were 0.759 and 4.118 ms higher in the red/white and red zones, respectively, than in the white zone (both $P < 0.001$) (Table II).

ZONAL T2 VALUES OF THE POSTERIOR HORNS IN THE MEDIAL VS LATERAL MENISCI

The T2 values of the posterior horns did not differ significantly between the medial and lateral menisci for the entire region (T2 = 9.65 ± 1.16 ms for medial and T2 = 9.58 ± 0.63 ms lateral meniscus, respectively; $P = 0.873$), for the white zone (T2 = 8.06 ± 0.71 vs 7.91 ± 0.49 ms; $P = 0.492$), for the red/white zone (T2 = 9.01 ± 1.07 vs 8.63 ± 0.85 ms; $P = 0.414$), or for the red zone (T2 = 12.27 ± 1.45 vs 11.64 ± 1.37 ms; $P = 0.227$) (Fig. 5). The GEE regression model showed that the T2 values tended to increase from the inner white zone to the outer red zone of the posterior horn of both the medial and lateral menisci ($P < 0.001$).

SEX DIFFERENCES IN T2 VALUES IN THE POSTERIOR HORNS OF THE MENISCI

As shown in Table III, the T2 values in the white zone of the posterior horns of menisci did not differ between men and women ($P = 0.694$). The GEE multiple linear regression model showed that, in women, the T2 values were significantly higher in the total (1.956 ms), red (4.740 ms), and red/white (1.150 ms) zones than in the white zone ($P < 0.001$). The T2 value in the total meniscus was 0.864 ms lower in men than in women ($P < 0.001$). Similarly, the T2 values in the red and red/white zones were 1.320 and 0.865 ms lower in men than in women ($P = 0.002$ and $P < 0.001$, respectively) (Fig. 6).

Table I
Comparison of the T2 values of the three zones and the total region of the posterior horns in the medial and lateral menisci

Zone	Medial meniscus, T2 (ms)		Lateral meniscus, T2 (ms)		t value	P value
	Mean	SD	Mean	SD		
White zone	8.062	0.711	7.907	0.492	0.709	0.492
Red/white zone	9.012	1.067	8.628	0.863	0.846	0.414
Red zone	12.266	1.454	11.641	1.366	1.287	0.227
Total region	9.645	1.163	9.580	0.628	0.163	0.873

Data were analyzed by paired-t test.

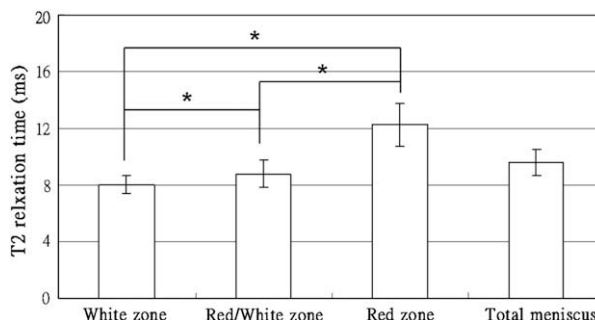


Fig. 4. T2 values of the posterior horn of the medial and lateral menisci at the different zones selected. The bar chart shows that the T2 value tended to increase from the inner white zone to the outer red zone of the posterior horns.

Discussion

Our findings show the feasibility of using high-resolution MR imaging to assess the regional T2 value for the posterior horn of the knee menisci. We found significant zonal differences in the T2 values of the posterior horns in the medial and lateral menisci. The highest T2 value of the red zone is expected to reflect the abundant blood vessels within this vascular zone. The lowest signal intensity of the white zone is presumably related to the main substance of circumferential fibers³¹. The red/white zone has an intermediate T2 value, which could be attributed to the larger radial "tie" of collagen fibers³², which generate a stronger signal intensity. Although it has been reported that the vasculature exists in 10–30% of the outer portion of the medial meniscus²⁸, the possibility that the difference in T2 values between the red/white zone and white zone probably reflects the existence of minor extent of blood contents within the red/white zone cannot be ruled out. However, our results show no significant differences between the medial and lateral menisci for any T2 values for the three different zones or in the total region of the posterior horns selected in this young healthy population.

The zonal difference in T2 for the meniscus strongly suggests that quantitative T2 measurements for the evaluation of meniscus diseases should be conducted on a regional basis, in order for the results to be objective. Rauscher *et al.* recently documented meniscus T2 values of

Table II
Comparison of the T2 values of the three zones and the total region of the posterior horns in the medial and lateral menisci after adjusting for the side effect of the meniscus (medial or lateral)

Parameter	B	SE	95% Confidence interval		Wald chi-square	P
Lateral M vs medial M	-0.290	0.2968	-0.872	0.291	0.957	0.328
Total region vs white zone	1.566	0.1254	1.320	1.812	155.864	<0.001
Red zone vs white zone	4.118	0.2713	3.586	4.649	230.362	<0.001
Red/white zone vs white zone	0.759	0.1403	0.484	1.034	29.308	<0.001

The white zone was used as the reference group. Data were analyzed by GEE linear regression. M, meniscus; B, regression coefficient; SE, standard error.

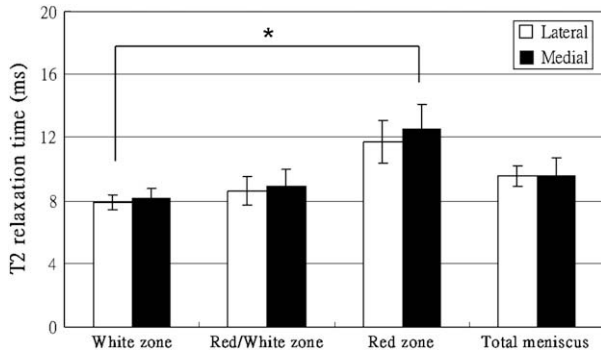


Fig. 5. T2 values of the posterior horn compared between the medial and lateral of the menisci in the different ROIs selected.

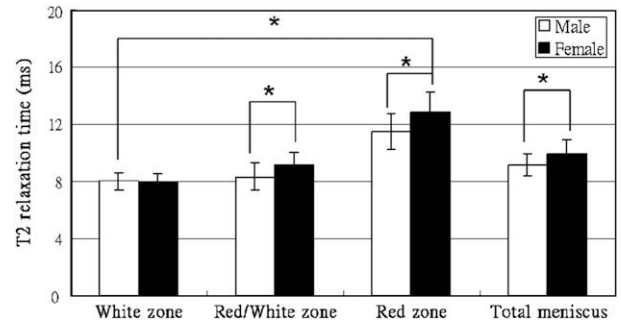


Fig. 6. T2 values of the posterior horn of medial and lateral menisci compared between men and women in the different ROIs selected.

11.4 ± 3.9 ms at 3.0 T for healthy subjects¹⁶, falling between the white zone T2 (8.02 ± 0.60 ms) and the red zone T2 (12.22 ± 0.92 ms) found in our subjects. Therefore it is possible that the T2 values reported by Rauscher *et al.* reflected the averaged estimates from regional zones with various degrees of vascularity. Performing regional T2 analysis may be potentially advantageous in enhancing disease detection sensitivity, in that alterations in vascularity or the collagen fibers might, for instance, affect the red or the white zones to different extents. The finding that gender dependence of zonal T2 exists in only the red/white and red zones but not the white zone is another example that regional analysis should be the preferred method for meniscus T2 measurements.

Changes in T2 values of the menisci are thought to reflect disruption of the cartilage architecture and consequent changes in water content in a way similar to the articular cartilage^{33,34}. With its restricted water mobility, the meniscus has a relatively short T2 relaxation time because of its anisotropic collagen matrix, which provides an efficient mechanism for the transverse relaxation³⁵. Previous studies revealed the T2* value of the meniscus obtained by UTE pulse sequence which can overcome the low SNR of the meniscus caused by the short T2 relaxation time¹⁷. Gatehouse *et al.* also demonstrated the imaging of the red and white zones with the UTE pulse sequence³⁶. However, only the T2* value of the meniscus, which depends on both the effect of spin-spin interactions and the homogeneity of the external field, was calculated, and this may not reflect precisely the change in biochemical architecture and water content of cartilage. In addition, the UTE pulse

sequence is not generally available in clinical application. Our study suggests that the measurement of pure T2 value of the knee menisci is feasible and may be helpful for evaluating the status of knee meniscus in the future clinical studies.

Men and women exhibit gait differences. Kerrigan *et al.* demonstrated that, compared with men, women have significantly greater hip flexion and less knee extension before initial contact, greater knee flexion moment in pre-swing, and greater peak mechanical joint power absorption at the knee in pre-swing during walking³⁷. The difference in natural mechanical properties may be related to the observation that OA affects women more than men in the ratio of 3 to 2²¹. Our preliminary results demonstrate that women have higher T2 values of the red and red/white zones of the posterior horns of the medial and lateral menisci than men. Since patients with OA also show increased T2 in the meniscus¹⁶, the gender dependence of T2 in the meniscus reported in our study may be of important clinical significance. We postulate that the finding of relatively higher T2 value of menisci in young females than in young males could be related to the mechanical loading associated with the walking pattern. Possible increase of water content or disorganization of collagen substance in the vascular zone of the menisci under the chronic mechanical loading may be a possible explanation for the relatively higher T2 value of the menisci in young females. Nevertheless, whether the higher T2 value of the posterior horns of the knee menisci in young women implies early changes or degradation of the menisci and whether this is related to the later development of knee OA need to be further investigated.

Table III

Comparison of the T2 values of the three zones and the total region of the posterior horns in the medial and lateral menisci between men and women

Parameter	B	SE	95% Confidence interval		Wald chi-square	P value
Sex*	0.092	0.2342	-0.367	0.551	0.155	0.694
Total region	1.956	0.1045	1.751	2.161	350.127	<0.001
Red zone	4.740	0.3598	4.035	5.445	173.590	<0.001
Red/white zone	1.150	0.1410	0.874	1.427	66.532	<0.001
Total region × sex†	-0.864	0.1452	-1.148	-0.579	35.414	<0.001
Red zone × sex†	-1.320	0.4330	-2.168	-0.471	9.290	0.002
Red/white zone × sex†	-0.865	0.1898	-1.237	-0.493	20.785	<0.001

The white zone was used as the reference group. Data were analyzed by GEE linear regression. B, regression coefficient; SE, standard error.

*Sex = 1 is male; sex = 0 is female (reference group).

†The interaction terms between sex and zone.

One issue currently unsolved by magnetic resonance imaging (MRI) T2 measurements is the lack of statistically significant difference between the medial and lateral menisci. Degeneration of the medial meniscus is affected by OA more frequently and this may be caused by less mobility of the medial meniscus²⁰. However, in the young healthy population of our study, we found no significant differences in T2 values between the different zones of the posterior horns of the medial and lateral menisci. This is also in agreement with the results found in a recent study¹⁶.

There are several limitations of our study. First, we investigated only a small number of subjects, and this small number may have caused selection bias in the T2 value and its related sex differences observed in the menisci. Second, the images of the knee menisci obtained by our 3 T MR system had a relatively low SNR ratio because of the short T2 value of the meniscus, which causes a rapid decay of the signal. With the progression of MR hardware, higher SNR images of knee menisci could potentially be acquired by using much shorter TE, and T2 mapping could then be conducted on a pixel-by-pixel basis. Third, because of the "magic angle" effect, the signal intensity and T2 value may vary depending on the fiber orientation. When $3\cos^2\theta - 1 = 0$ ($\theta = 55^\circ, 125^\circ$, etc.), where θ is the angle between the fiber orientation and the magnet field B_0 , the dipolar interactions are minimized leading to higher T2 values and high signal intensity^{38,39}. Therefore, there is some deviation of T2 values between the different slices because of the different "magic angle" effect. This was compensated in our setup by unifying the MR imaging with the acquisition of more slices. We investigated only the posterior horns of the knee menisci in this study because the posterior horn is most susceptible to injury and degradation based on its anatomic and biomechanical architecture^{24,25}. Comprehensive investigation of the MR T2 value in the different segments of the knee meniscus, including the body and the anterior horn, would be crucial in a more advanced study.

To our knowledge, our study is the first to apply the quantitative measurement of MR T2 value to demonstrate zonal and sex differences in the diverse zones of the knee menisci in the young healthy population. Future studies of larger numbers of individuals are needed to evaluate the usefulness of the MR T2 value in assessing the evolution of changes in the knee menisci at different ages, in men and women, and its relationship to knee trauma and OA.

Conclusion

The results of this study confirm the feasibility of quantitatively measuring the T2 value in the diverse zones of human knee menisci. The zonal and sex differences in the T2 values in the posterior horns of the knee menisci in young healthy adults may be helpful for evaluating the biomechanical status of the knee menisci and for identifying the role of changes in the meniscus in knee OA.

Conflict of interest

We declare that we have no conflict of interest.

Acknowledgments

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