



# Preliminary study on the assessment of early cartilage degeneration by quantitative ultrashort echo time magnetic resonance imaging *in vivo*

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**Background:** To investigate the feasibility of quantitative ultrashort echo time magnetic resonance imaging (UTE-MRI) techniques for assessing early cartilage degeneration *in vivo*.

**Methods:** A total of 46 patients with knee pain due to osteoarthritis (OA) as the main complaint were recruited into the study. We performed MRI examinations with different quantitative UTE-MRI techniques, including UTE-based magnetization transfer (MT), UTE-adiabatic T1ρ, and UTE-T2\* mapping on a 3.0T clinical magnetic resonance (MR) scanner (MR750; GE Healthcare, Milwaukee, WI, USA). Three regions of interest (ROIs) were manually drawn on the medial and lateral femoral condyles and the corresponding medial and lateral tibial plateaus, respectively. A total of 561 ROIs (12 ROIs for each knee) were finally included and divided into 3 groups according to the MRI Osteoarthritis Knee Score (MOAKS): normal (MOAKS 0, n=175), mild degeneration (MOAKS 1, n=283), and moderate degeneration (MOAKS 2, n=103). One-way analysis of variance (ANOVA) and Tamhane's T2 test were used to compare the differences of quantitative UTE-biomarkers among different groups. The analysis of Spearman's correlation was used to assess the correlation between the UTE-biomarkers and MOAKS grading. The diagnostic efficacy of different quantitative UTE-MRI techniques for detecting mild cartilage degeneration was evaluated using the receiver operating characteristic (ROC) curve.

**Results:** The UTE-MT ratio (UTE-MTR) and the UTE-adiabatic T1ρ values had a moderate correlation with the MOAKS grading ( $r=-0.523$ ,  $P<0.001$ ;  $r=0.531$ ,  $P<0.001$ , respectively), while the UTE-T2\* was weakly correlated with the MOAKS grading ( $r=-0.396$ ,  $P<0.001$ ). For the normal group (MOAKS 0) and the mild group (MOAKS 1), the UTE-MTR values were  $21.09\pm 3.03\%$  and  $17.30\pm 3.22\%$ , respectively. The UTE-adiabatic T1ρ values were  $30.43\pm 6.26$  ms and  $35.05\pm 8.78$  ms for the normal group (MOAKS 0) and the mild group (MOAKS 1), respectively. With respect to the UTE-T2\* values, the normal group (MOAKS 0) values were  $21.49\pm 3.96$  ms and the mild group (MOAKS 1) values were  $19.86\pm 3.08$  ms. All the differences between the 2 groups of the 3 UTE-MRI values were significant. The AUCs of the UTE-MTR, UTE-adiabatic T1ρ, and UTE-T2\* mapping were 0.794, 0.732, and 0.651, respectively.

**Conclusions:** The quantitative UTE-MRI techniques (UTE-MT, UTE-adiabatic T1ρ, and UTE-T2\* mapping) show great promise for assessing the early degeneration of articular cartilage *in vivo*, and the UTE-

MT and UTE-adiabatic T1 $\rho$  values show better diagnostic efficacy than UTE-T2\* mapping.

**Keywords:** Magnetic resonance imaging (MRI); ultrashort echo time (UTE); *in vivo*; cartilage degeneration

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## Introduction

Osteoarthritis (OA) is a common degenerative joint disease, characterized by degeneration of articular cartilage. Currently, there are no effective drugs to arrest the progression of OA, and total knee arthroplasty is recommended when OA has progressed to an advanced stage (1-3). Therefore, a noninvasive diagnosis of OA at an early stage is clinically important for implementing early intervention and alleviating symptoms. With an echo time (TE) of approximately 10–80 ms, the sensitivity of conventional magnetic resonance imaging (MRI) for detecting early cartilage degeneration is poor, partly due to the inability of MRI to obtain a signal from many short T2 tissues or tissue components in the knee joint, such as deep layer cartilage, subchondral bone, menisci, ligaments, and tendons (4). Ultrashort echo time (UTE) MRI techniques with TEs in the order of 10 ms allow for the direct imaging and quantitative assessment of the short T2 components in tissues (4-6).

In addition, conventional T2 and T1 $\rho$  scans are subject to the magic angle effect, and so the values are significantly affected when the orientation of tissue fiber approaches 54.7° relative to the main magnetic field (7). Shao *et al.* claimed that T2 values increased by 231.8% and T1 $\rho$  values increased by 92% on average near the magic angle, and the changes due to the magic angle effect can be several times larger than those caused by cartilage degeneration (8), which may affect the accuracy of quantitative results. Ma *et al.* (9) showed that the ultrashort echo time-based magnetization transfer (UTE-MT) technique was resistant to the magic angle effect in a two-pool model by scanning 5 cadaveric Achilles tendon samples in which orientations ranged from 0 to 90° relative to the main static (B0) magnetic field. Wu *et al.* (10) investigated the greatly decreased magic angle effect of three-dimensional (3D) UTE-adiabatic T1 $\rho$  sequences compared to regular 3D UTE Cones-CW-T1 $\rho$  and Cones-T2\* sequences by repeating human patellar samples from different angular orientations. The feature of UTE-adiabatic T1 $\rho$  and UTE-MT showing less sensitivity to the magic angle effect than other conventional sequences is important for the quantitative

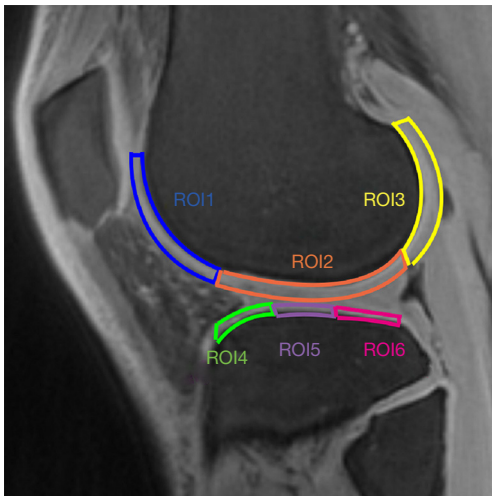
evaluation of cartilage degeneration. Previous studies have indicated that the UTE-T2\* values of deep articular cartilage typically decrease with more severe cartilage degeneration, and the UTE-T2\* values are susceptible to water content and collagen orientation in early OA (11-13). The T1 $\rho$  values may reflect changes to the extracellular matrix (ECM), such as proteoglycan (PG) loss. Many *in vitro* studies have shown that UTE-T1 $\rho$  enables the quantitative assessment of short T2 tissues in the musculoskeletal system, and UTE-T1 $\rho$  values increase with structural changes in short T2 tissues (14-18). The magnetization transfer ratio (MTR) provides a measure of the magnetization exchange rate of hydrogen protons bound to macromolecules such as collagen and free water (19). The UTE-MTR values have been used to evaluate the pools of protons indirectly by analyzing the interactions between the bound and pore water proton pools (20,21). However, the capability of these UTE-based quantitative techniques to evaluate cartilage degeneration at an early stage has not yet been systematically assessed *in vivo*.

The purpose of the study was to investigate the feasibility of quantitative UTE-MRI sequences (UTE-MT, UTE-adiabatic T1 $\rho$ , and UTE-T2\* mapping) for the assessment of early cartilage degeneration *in vivo* and to evaluate the diagnostic performance of these different UTE techniques. We present the following article in accordance with the STARD reporting checklist (available at <https://qims.amegroups.com/article/view/10.21037/qims-21-1181/rc>).

## Methods

### Participants

A total of 46 OA patients, including 26 males (age range: 30 to 71 years; 48.3±11.1 years) and 20 females (age range: 37 to 72 years; 51.0±7.9 years) with complaints of knee joint discomfort and no contraindication to MRI examination were recruited within a year. Among them, 5 patients were scanned bilaterally. The exclusion criteria included previous knee surgery or traumatic knee injury, tumor, or infectious lesion. The study was conducted in accordance with the



**Figure 1** Based on the mid-sagittal section of the UTE-adiabatic T1 $\rho$  (TSL = 0 ms) sequence, ROIs were manually drawn at the lateral femoral condyle and the corresponding cartilage intermediate levels of the tibial plateau, respectively. UTE-adiabatic T1 $\rho$ , ultrashort echo time-based adiabatic T1 $\rho$ ; ROIs, regions of interest.

Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee at the Shanghai Tenth People's Hospital of Tongji University (approval number: shsy-iec-ky-3964). All participants provided written informed consent before the examination.

### **MRI protocol**

The whole knee joint was scanned using a transmit/receive 8-channel knee coil (Chenguang Medical Technologies, Shanghai, China) on a 3.0 T clinical magnetic resonance (MR) scanner (MR750; GE Healthcare, Milwaukee, WI, USA). The following 4 imaging protocols were continuously performed without any clinical interventions: (A) proton density (PD) fat-suppressed (FS): repetition time (TR) = 3,000 ms, TE = 32 ms, scan time = 3.37 min; (B) 3D UTE-MT: off-resonance frequency = 2 kHz, saturation power = 750 degrees, TR/TE = 100/0.032 ms, scan time = 6.4 min; (C) 3D UTE-adiabatic T1 $\rho$ : spin-locking times = 0, 24, 48, and 96 ms, scan times = 16.53 min; (D) UTE-T2\* mapping: TEs = 0.032, 4.9, 9.8, and 14.7 ms, TR = 30.9 ms, scan time = 5.2 min. Other imaging parameters included: field of view (FOV) = 16 cm<sup>2</sup>, acquisition matrix = 256 × 256 pixels, slice thickness = 3 mm, and slices = 32. The total scan time was 31.5 min.

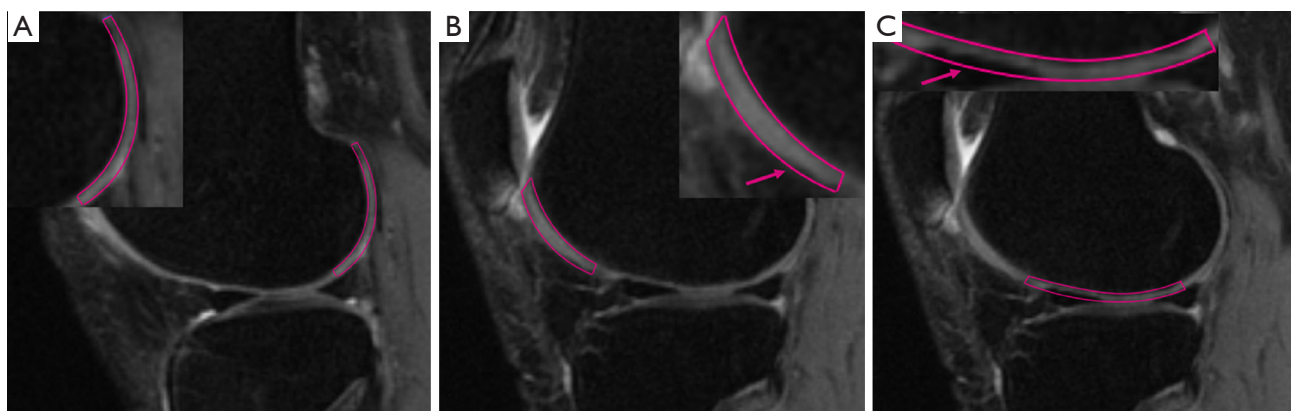
### **Post-processing and image analysis**

Digital Imaging and Communications in Medicine (DICOM) images obtained from the MR protocol mentioned above were analyzed in MatLab (Mathworks Inc., Natick, MA, USA). The UTE-T2\* and UTE-adiabatic T1 $\rho$  values were calculated in MatLab (Mathworks Inc., USA) using the Levenberg–Marquardt method for nonlinear least-squares curve fitting problems, while the UTE-MTR was obtained using the 2-pool effect MT model with saturation powers of 750° (MT on) and 0° (MT off).

Regions of interests (ROIs) were manually drawn on the mid-sagittal section of the image of UTE-adiabatic T1 $\rho$  (TSL = 0 ms) and then copied to each of the other sequence images. We mapped 3 ROIs on the medial and lateral femoral condyles and their corresponding medial and lateral tibial plateaus, respectively, as shown in *Figure 1*. Each ROI was measured in MatLab by one of the authors with a special interest in musculoskeletal radiology who was blinded to the MRI Osteoarthritis Knee Score (MOAKS) gradings, and this process was repeated in the same region 3 times, with the average signal intensity used for statistical analysis. All ROIs were graded according to the MOAKS by 2 musculoskeletal radiologists (each with 6 and 10 years of work, respectively) based on the sagittal (Sag)-proton density-weighted imaging (PDWI)/fat saturation (FS) sequence, as shown in *Figure 2*: normal cartilage (MOAKS 0); mild degeneration (MOAKS 1) = <10% defect of regional cartilage surface area; moderate degeneration (MOAKS 2) = 10–75% defect of regional cartilage surface area; and severe degeneration (MOAKS 3) = >75% defect of regional cartilage surface area. The ROIs for which 2 musculoskeletal radiologists held different opinions were excluded. Since the main purpose of this study was to investigate the feasibility of UTE techniques for the diagnosis of OA at an early stage *in vivo*, ROIs with severe degeneration (MOAKS 3) were excluded. A total of 561 ROIs were finally included in this study.

### **Statistical analysis**

The software SPSS 20.0 (IBM Corp, Armonk, NY, USA) was used for the statistical analysis. Quantitative UTE-MRI values were normally distributed using the Kolmogorov–Smirnov normality test. The intra-class correlation coefficient (ICC) was used to describe the reliability of the measurements of UTE-MRI values. One-way analysis of variance (ANOVA) was used to compare



**Figure 2** Gradings of the ROIs according to MOAKS based on the mid-sagittal section of PDWI. (A) MOAKS 0: normal cartilage. (B) MOAKS 1: <10% defect of regional cartilage surface area. (C) MOAKS 2: 10–75% defect of regional cartilage surface area. PDWI, proton density-weighted image; ROIs, regions of interest; MOAKS, MRI Osteoarthritis Knee Score.

**Table 1** The values (mean  $\pm$  SD) and 95% CI of different quantitative UTE-MRI sequences in different MOAKS Grading, and correlations with MOAKS Grading

Quantitative UTE-MRI sequences	MOAKS Grading	N	Mean $\pm$ SD	95% CI	P value		Spearman correlation coefficient	
					vs. grade 1	vs. grade 2	r	P value
T1 $\rho$ (ms)	0	175	30.43 $\pm$ 6.26	29.50–31.36	<0.001	<0.001	0.531	<0.001
	1	283	35.05 $\pm$ 8.78	34.03–36.07		<0.001		
	2	103	45.98 $\pm$ 4.75	45.06–46.90				
MTR (%)	0	175	21.09 $\pm$ 3.03	20.64–21.54	<0.001	<0.001	–0.523	<0.001
	1	283	17.30 $\pm$ 3.22	16.23–18.37		<0.001		
	2	103	14.64 $\pm$ 3.34	14.00–15.29				
T2* (ms)	0	175	21.49 $\pm$ 3.96	20.76–22.23	0.002	<0.001	–0.396	<0.001
	1	283	19.86 $\pm$ 3.08	19.27–20.45		<0.001		
	2	103	15.15 $\pm$ 2.84	14.60–15.70				

SD, standard deviation; CI, confidence interval; UTE-MRI, ultrashort echo time magnetic resonance imaging; MOAKS, MRI Osteoarthritis Knee Score; MTR, magnetization transfer ratio; T2\*, UTE-T2\* mapping value.

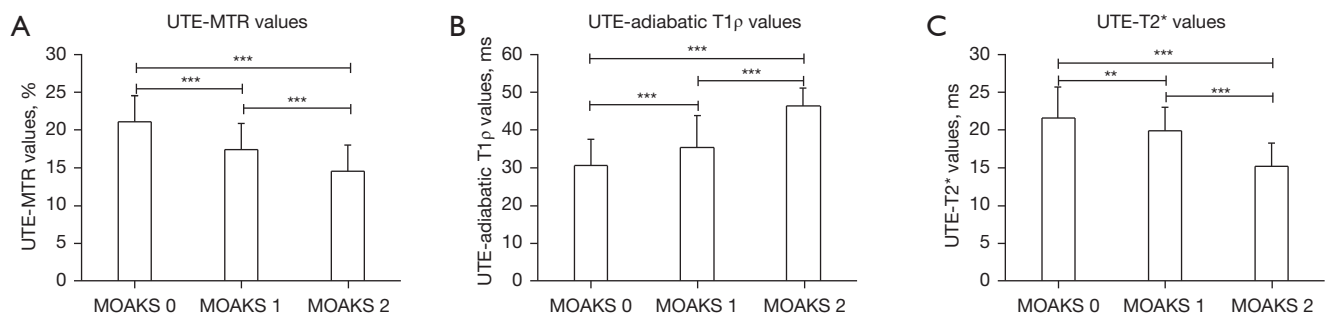
the differences of different groups based on MOAKS scores, and the Tamhane-T2 test was performed for post hoc multiple comparisons when a significant difference existed. Spearman's correlation analysis was used to test the correlation between different quantitative UTE-MRI values and MOAKS scores. Finally, receiver operating characteristic (ROC) curves were used to compare the diagnostic efficacy of different quantitative UTE-MRI techniques for mild cartilage degeneration (MOAKS 1). The area under the curve (AUC) values of different UTE-MRI values for mild cartilage degeneration (MOAKS 1)

were calculated according to the ROC curves. A P value less than 0.05 was considered statistically significant.

## Results

### *Comparison of quantitative UTE-MRI values among different groups of cartilage degeneration*

The quantitative results of different UTE-biomarkers are shown in *Table 1* and *Figure 3*. The UTE-MTR and UTE-T2\* values in the normal group (MOAKS 0) were significantly higher than those in both the



**Figure 3** Differences between the UTE-MTR, UTE-adiabatic T1ρ, and UTE-T2\* values of the 3 groups. (A) UTE-MTR values were compared among different MOAKS gradings (\*\*\*,  $P < 0.001$ ). (B) UTE-adiabatic T1ρ values were compared among different MOAKS gradings (\*\*\*,  $P < 0.001$ ). (C) UTE-T2\* values were compared among different MOAKS gradings (\*\*,  $P = 0.002$ , \*\*\*,  $P < 0.001$ ). UTE-MTR, ultrashort echo time-based magnetization transfer ratio; UTE-adiabatic T1ρ, ultrashort echo time-based adiabatic T1ρ; UTE-T2\*, ultrashort echo time-based T2\*; MOAKS, MRI Osteoarthritis Knee Score.

**Table 2** Comparison of the diagnostic efficacy of three quantitative UTE-MRI sequences for mild cartilage degeneration (MOAKS 1)

UTE-MRI sequences	AUC	95% CI	P value	Sensitivity	Specificity
UTE-MT	0.794	0.751–0.837	0.001	0.754	0.732
UTE-adiabaticT1ρ	0.732	0.685–0.779	0.001	0.522	0.903
UTE-T2* mapping	0.651	0.600–0.702	0.002	0.746	0.403

UTE-MRI, ultrashort echo time magnetic resonance imaging; MOAKS, MRI Osteoarthritis Knee Score; AUC, area under the curve; CI, confidence interval.

mild degeneration group (MOAKS 1) and moderate degeneration group (MOAKS 2) ( $P < 0.001$ ,  $P < 0.001$  and  $P = 0.002$ ,  $P < 0.001$ , respectively). The UTE-adiabatic T1ρ values in the normal group (MOAKS 0) were significantly lower than those in the mild degeneration group (MOAKS 1) and moderate degeneration group (MOAKS 2) ( $P < 0.001$ ). Meanwhile, the UTE-MTR values in the mild degeneration group (MOAKS 1) were significantly higher than those in the moderate degeneration group (MOAKS 2) ( $P < 0.001$ ), and the UTE-adiabatic T1ρ values in the mild degeneration group (MOAKS 1) were significantly lower than those in the moderate degeneration group (MOAKS 2) ( $P < 0.001$ ). The UTE-adiabatic T1ρ [ICC = 0.984, 95% confidence interval (CI): 0.937 to 0.996], UTE-MTR (ICC = 0.977, 95% CI: 0.912 to 0.994), and UTE-T2\* values (ICC = 0.988, 95% CI: 0.952 to 0.997) all showed good reliability and reproducibility.

#### Correlation between different quantitative UTE-MRI values and MOAKS gradings

There was a moderate positive correlation between UTE-

adiabatic T1ρ values and MOAKS gradings ( $r = 0.531$ ;  $P < 0.001$ ). The UTE-MTR values showed a moderate negative correlation with MOAKS gradings ( $r = -0.523$ ;  $P < 0.001$ ), and UTE-T2\* values showed a weak negative correlation with MOAKS gradings ( $r = -0.396$ ;  $P < 0.001$ ).

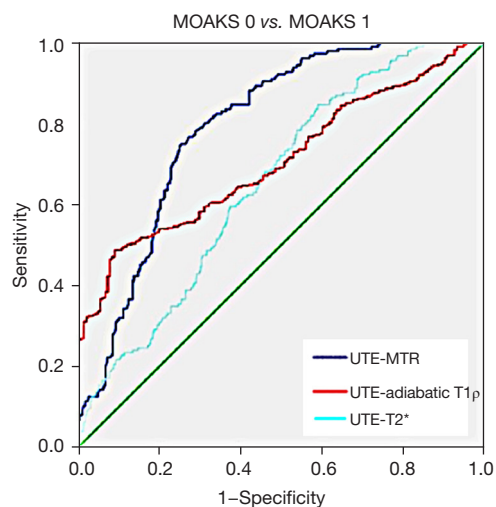
#### Diagnostic efficacy of 3 quantitative UTE-MRI techniques using the ROC curve

As shown in Table 2 and Figure 4, the AUC values of UTE-MTR (AUC = 0.794, 95% CI: 0.751 to 0.837;  $P < 0.001$ ) and UTE-adiabatic T1ρ (AUC = 0.732, 95% CI: 0.685 to 0.779;  $P < 0.001$ ) were higher than that of UTE-T2\* (AUC = 0.651, 95% CI: 0.600 to 0.702;  $P < 0.002$ ). Of these, UTE-MTR exhibited the highest diagnostic sensitivity (0.754), and UTE-adiabatic T1ρ exhibited the highest diagnostic specificity (0.903).

#### Discussion

This study systematically investigated the feasibility and potential of 3 different UTE-MRI techniques (UTE-MT,





**Figure 4** ROC curves of 3 quantitative UTE-MRI sequences for the diagnosis of mild cartilage degeneration (MOAKS 1). The AUC of UTE-MTR (AUC =0.794, 95% CI: 0.751 to 0.837;  $P < 0.001$ ) and UTE-adiabatic T1 $\rho$  (AUC =0.732, 95% CI: 0.685 to 0.779,  $P < 0.001$ ) were higher than that of UTE-T2\* (AUC =0.651, 95% CI: 0.600 to 0.702;  $P < 0.002$ ). AUC, area under the curve; CI, confidence interval; ROC, receiver-operating characteristic; UTE-MRI, ultrashort echo time magnetic resonance imaging; UTE-MTR, ultrashort echo time-based magnetization transfer ratio; UTE-adiabatic T1 $\rho$ , ultrashort echo time-based adiabatic T1 $\rho$ ; UTE-T2\*, ultrashort echo time-based T2\*.

UTE-adiabatic T1 $\rho$ , and UTE-T2\* mapping) for detecting early cartilage degeneration *in vivo*. It showed that UTE-MT and UTE-adiabatic T1 $\rho$  have a moderate correlation with MOAKS grading. Meanwhile, both techniques have higher diagnostic efficacy than UTE-T2\* mapping, which indicates that UTE-MT and UTE-adiabatic T1 $\rho$  may have more potential for clinical applications than UTE-T2\* mapping.

Williams *et al.* used UTE-T2\* mapping to scan the tibial plateaus of human cadaveric specimens and suggested that UTE-T2\* mapping has the sensitivity required to detect changes in the sub-surface matrix microstructure of articular cartilage (22,23). Wan *et al.* supported this by demonstrating the potential of 3D UTE-MT and UTE-adiabatic T1 $\rho$  to reflect matrix changes corresponding to early cartilage degeneration in an *in vitro* study (24). However, the variation of values may result from tissue degeneration after a freeze-thaw cycle, potentially impacting tissue MR properties and hydration as well as

the temperature of samples during imaging (25). Besides, measurements taken in the controlled conditions of studies performed *in vitro* (e.g., extracellular pH, at room temperature) are not the same as the measurements taken *in vivo* in the real physiological environment, which may impact tissue MR properties (25,26). Williams *et al.* (27) demonstrated the feasibility and intersession repeatability of UTE-T2\* mapping of articular cartilage *in vivo*, and Xue *et al.* (28) investigated the feasibility of 3D UTE-MT-derived macromolecular fraction (MMF) by scanning volunteers with and without OA. In the current study, the feasibility of 3 different quantitative UTE-MRI sequences for detecting early cartilage degeneration was investigated *in vivo*, thus promoting the clinical application of quantitative UTE-MRI techniques and facilitating the early detection and intervention of OA.

The onset of OA is mainly characterized by the loss of macromolecules, including PG and collagen, followed by the structural destruction of collagen fibers, reduction of bound water, and increase of free water (29-31). Therefore, the early detection of PG and collagen loss is important for identifying early cartilage degeneration and timely clinical intervention. Grey *et al.* showed reduced MTR values in trypsin-degraded bovine cartilage, suggesting that MTR values can reflect the reduction in the content of matrix macromolecules (e.g., collagen, PG) during cartilage degeneration (32). Fang *et al.* measured the UTE-MTR and UTE-T2\* values of tendon in runners at different times and believed that UTE-MTR values can reflect the biochemical changes of the Achilles tendons (33). In this study, we found that the UTE-MTR values decreased with the increase of MOAKS gradings, which has a similar tendency to the results of our group's previous *in vitro* study in which UTE-MTR values decreased with the degree of cartilage degeneration (34,35). The technology of UTE-MT is proving to be promising in a clinical setting, although there are still some further optimizations needed, such as the selection of frequency offsets and the MT powers.

Shen *et al.* found that T1 $\rho$  values increased with PG loss in the femoral condylar cartilage of OA rabbits (36). However, Menezes *et al.* found no direct correlation between changes of glycosaminoglycan (GAG) content and T1 $\rho$  values in mature human tissues at 8.5 T (37). The results of our study demonstrated that UTE-adiabatic T1 $\rho$  values of normal cartilage were significantly lower than those of the mildly and moderately degenerated cartilage groups, and there was a moderate positive correlation between UTE-adiabatic T1 $\rho$  values and MOAKS grading,

which is consistent with the results of the study conducted by Shen *et al.* (36). This may relate to the magic angle-insensitivity of the UTE-adiabatic T1 $\rho$  sequence and its sensitivity in detecting short T2 tissues, allowing better observation of the deep cartilage and calcified layers that are first affected during early cartilage degeneration (10,16).

Previous *in vitro* studies have confirmed that UTE-T2\* mapping is a potential method for evaluating the quality of cartilage, as it is sensitive to the destruction of deep cartilage (12,38,39). Williams *et al.* (22) claimed that UTE-T2\* mapping has lower values in severely degraded cartilage compared to healthy cartilage. However, Chu *et al.* (40) found that the medial femoral condyle (MFC) deep cartilage MRI UTE-T2\* value of anterior cruciate ligament (ACL)-injured patients was elevated compared to that of uninjured controls and UTE-T2\* mapping can be used for the follow-up of clinical disease states. That may result from subchondral edema, an acute phase change after ACL injury, which leads to the increase of the long T2\* (free water) components in cartilage (41). In this study, we found that UTE-T2\* values of normal cartilage were significantly higher than those of the mild and moderate degenerated cartilage groups, which was consistent with our previous studies (34). However, UTE-T2\* values have a weak negative correlation with MOAKS grading.

The diagnostic efficacy of UTE-MT and UTE-adiabatic T1 $\rho$  for detecting early cartilage degeneration is higher than that of UTE-T2\* mapping. The variability in diagnostic efficacy of different UTE-MRI sequences may be due to the different biochemical basis of cartilage. The loss of PG and collagen content occurs before the changes of collagen fiber structure and water content (42). Loss of collagen and PG leads to a decrease of bound water, causing a decrease in T2\* values, while collagen fiber destruction increases the exposed surface area of collagen, which may also lead to an increase of bound water (43). The simultaneous presence of both pathophysiological processes which cause contrary change of bound water certainly will affect the diagnostic efficacy of UTE-T2\* values. In addition, UTE-T2\* values are more susceptible to magic angle effects and magnetic field inhomogeneities than UTE-MT and UTE-adiabatic T1 $\rho$ , which can lead to an excessive increase in measured values (44).

There were several limitations to this study. Firstly, we did not perform scans on healthy volunteers comprising a control group. The normal quantitative UTE-MRI measured in the OA patients may not have been accurate. However, in the current study, both the trend of UTE-

MRI values with increasing cartilage degeneration and the correlation between UTE-MRI values and cartilage degeneration were similar to previous studies (22,24,34), which means our results still have some degree of credibility. Secondly, the scan time was longer than the PDWI (3.37 min), especially for the 3D UTE-adiabatic T1 $\rho$  sequence (16.53 min), and this could be shortened by reducing the number of spin-lock times or advanced image reconstruction techniques, such as parallel imaging and compressed sensing (45). Thirdly, MOAKS scores instead of pathological histology were used as grouping criteria. The relationship between different quantitative UTE-MRI values and pathological histology will be further investigated in our future work, which might be beneficial for demonstrating the intrinsic mechanisms at play. Fourthly, although we enlarged the sample size by expanding the number of ROIs, the sample size was relatively small. Furthermore, the longest echo acquired in this experiment was only 14.7 ms, and long T2 components, such as free water, may not have been well-captured by this sequence; hence, the measured profile values may have been underestimated.

## Conclusions

Quantitative UTE-MRI techniques (especially UTE-adiabatic T1 $\rho$  and UTE-MT) have the potential for detecting the degeneration of articular cartilage at an early stage *in vivo*. The diagnostic performance of UTE-based biomarkers, including UTE-adiabatic T1 $\rho$ , UTE-MT, and UTE-T2\* mapping, for the assessment of mild degeneration of cartilage is good; thus, these UTE-based biomarkers may facilitate the noninvasive diagnosis of early OA in clinical practice.

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## Footnote

*Reporting Checklist:* The authors have completed the STARD

reporting checklist. Available at <https://qims.amegroups.com/article/view/10.21037/qims-21-1181/rc>

*Conflicts of Interest:* All authors have completed the ICMJE uniform disclosure form (available at <https://qims.amegroups.com/article/view/10.21037/qims-21-1181/coif>). The authors have no conflicts of interest to declare.

*Ethical Statement:* The authors are accountable for all aspects of the work in ensuring that questions related to the accuracy or integrity of any part of the work are appropriately investigated and resolved. The study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee at the Shanghai Tenth People's Hospital of Tongji University (approval number: shsy-iec-ky-3964), and written informed consent was provided by all participants.

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