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Diagnostic value of T1ρ and T2 mapping sequences of 3D fat-suppressed spoiled gradient (FS SPGR-3D) 3.0-T magnetic resonance imaging for osteoarthritis

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Abstract

Three-dimensional fat-suppressed spoiled gradient magnetic resonance imaging can be used to observe cartilages with high resolution.

To quantify and compare the T1ρ and T2 relaxation times of the knee articular cartilage between healthy asymptomatic adults and patients with osteoarthritis (OA).

This was a retrospective study of 53 patients with symptomatic OA (6 males and 47 females; aged 57.6 ± 10.0 years) and 26 healthy adults (11 males and 15 females; aged 31.7 ± 12.2 years) from the Ruijin Hospital. T1ρ and T2 relaxation times of knee cartilage were quantified using sagittal multi-echo T1ρ and T2 mapping sequences (3.0-T scanner) and analyzed by receiver operating characteristic (ROC) curve.

T1ρ and T2 relaxation times in the OA group were higher than in controls (both $P < .01$). The sensitivity, specificity, and critical value for differentiating normal from OA cartilage were respectively 92%, 85.6%, and 45.90 ms for T1ρ, and 93.6%, 93.3%, and 50.42 ms for T2. T2 mapping sequence showed a higher area under the ROC curve (AUC) than T1ρ (0.965 vs 0.927, $P = .02$). The AUC for differentiating normal from Noyes IIA cartilage was 0.922 for T1ρ (cut-off: 46.0; sensitivity: 87.7%; specificity: 89.7%) and 0.954 for T2 (cut-off: 49.5; sensitivity: 91.2%; specificity: 92.3%), with no significant difference between them ($P = .08$).

Both T1ρ and T2 mapping sequences could be used to assess OA cartilage lesions, with T2 mapping sequence demonstrating significant sensitivity for cartilage degeneration. These 2 sequences could also identify early-stage OA cartilage.

Abbreviations: AUC = area under the curve, BW = bandwidth, FOV = field of view, FSL = spin lock freq, FS SPGR-3D = three-dimensional fat-suppressed spoiled gradient, GAG = glycosaminoglycan, IFC = intercondylar fossa cartilage, KL = Kellgren–Lawrence, MRI = magnetic resonance imaging, NEX = number of excitation, OA = osteoarthritis, PG = proteoglycan, ROC = receiver operating characteristic, TR/TE = repetition time/echo time, TSL = time of spin-lock.

Keywords: articular cartilage, knee, MRI, osteoarthritis, T1ρ mapping, T2 mapping

1. Introduction

Knee osteoarthritis (OA) is a degenerative disease primarily characterized by the breakdown and loss of the cartilage matrix of the joint. It is typically diagnosed radiographically by the identification of bone changes and joint-space narrowing, and then evaluated using the Kellgren–Lawrence (KL) score.[1] Early changes in the articular cartilage may not be visible on plain X-ray films. Cartilage loss can only be indirectly inferred by the progression of the joint space narrowing, which is highly unreliable even with careful attention to proper technique.[2] In addition, plain X-ray films are insensitive for focal cartilage loss, and joint space widening despite significant cartilage loss may occur in 1 knee compartment simply as a result of narrowing in the other compartment.[3]

Articular cartilage consists of chondrocytes and extracellular matrix, which mainly contains collagen fibers, proteoglycan (PG) aggregates, and water. Cartilage matrix breakdown is characterized by changes in the content of glycosaminoglycan (GAG), type II collagen, and water.[4] Magnetic resonance imaging (MRI) can observe not only the destruction of the structural integrity but also the change of the components in articular cartilage. In particular, many studies showed that T1ρ mapping can detect the changes of PG,[5] while T2 mapping is able to identify the early changes of cartilage (mainly through evaluating the changes in water content).[6] In addition, the changes of T1ρ and T2 relaxation times, can be quantified.[7,8]

Arthroscopy is the gold standard for detecting cartilage lesions; however, it is an invasive operation. Besides, it only observes the surface structure of cartilage and cannot detect the changes of

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ZL and HW contributed equally to this work.

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cartilage tissue components. Therefore, it is unsuitable for the follow-up of OA patients. Compared with arthroscopy, three-dimensional (3D) spoiled gradient (SPGR) imaging has good diagnostic accuracy and is considered as the standard for the quantitative morphological evaluation of knee joint cartilage. Since 3D SPGR sequence has high spatial resolution and very high signal intensity in articular cartilage imaging, it has been widely used in cartilage segmentation technology and evaluation of cartilage morphology.[9–12] Nevertheless, this MRI technique still needs to be refined.

In this study, the fat-suppressed (FS) SPGR 3D sequence was used to evaluate the pathological changes of cartilage lesions in patients with knee OA. Many criteria are available for grading the knee cartilage morphology, but we used the Noyes classification standard, which is thought to be close to arthroscopic evaluation.[13] The aim of the present study was to quantify and compare the T1ρ and T2 relaxation times of the knee articular cartilage in healthy adults and OA patients.

2. Materials and methods

2.1. Study design and subjects

This was a retrospective study of healthy subjects and OA patients who underwent knee MRI between April 1, 2013 and October 31, 2013 at the Ruijin Hospital (Shanghai, China). The study was approved by the ethics committee of Ruijin Hospital. The need for individual consent was waived by the committee because of the retrospective nature of the study.

The study involved symptomatic OA patients and healthy volunteers. OA diagnosis was based on the AAOS clinical practice guideline: treatment of OA of the knee.[14] The inclusion criteria were:

1. ≥18 years of age;
2. without family history of OA or joint degenerative disease.

The exclusion criteria were:

1. osteosarcoma, giant cell tumor of bone, organic bone injury, or meniscus injury;
2. poor image quality;
3. any contraindication to MRI examination.

2.2. MRI

All MRI examinations were performed using a 3.0-T Signa HDxt MRI scanner (GE Healthcare, Waukesha, WI) and a knee dedicated coil (Quadknee, GE Healthcare, Waukesha, WI). Before examination, all subjects had to statically sit for 30 min outside the MRI room. The following sagittal FS SPGR sequence was used: repetition time/echo time (TR/TE) = 12.3/2.2 ms; field of view (FOV) = 16 cm; matrix = 288 × 256; slice thickness = 1.2 mm; bandwidth (BW) = 31.25 kHz; flip angle = 15°; and acquisition time = 4 min 30 s. Sagittal multi-echo T1ρ and T2 mapping sequences were used to quantify the T1ρ and T2 relaxation times. The T1ρ mapping sequence parameters were: repetition time/echo time (TR/TE) = 9.7/2.9 ms; recovery time = 1175 ms; FOV = 19 cm; matrix = 300 × 200; slice thickness = 4 mm; BW = 41.67 kHz, time of spin-lock (TSL) = 0/10/30/60 ms; spin lock freq (FSL) = 500 Hz; and acquisition time = 12 min 11 s. The 8-echo T2 mapping sequence parameters were: TR = 1000 ms; TE = 8.9–71.0 ms; slice thickness = 5 mm; slice gap = 2 mm; FOV = 16 × 16 cm; number of excitation (NEX) = 1; matrix = 320 × 192; and scan time = 3 min 30 s.

All images were reviewed retrospectively and independently by the 2 experienced musculoskeletal radiologists. In the event of disagreement, a consensus was reached by discussion.

2.3. Morphological analysis

Cartilage defects were graded using 3D FS SPGR images by the 2 experienced radiologists who were blinded to the clinical information and relaxation data of the subjects. The radiologists evaluated the images independently. The Noyes classification standard for evaluation of the knee cartilage morphology is presented in Table 1.[13]

2.4. Quantitative analysis

The knee articular cartilage was divided into 4 parts: patella cartilage, intercondylar fossa cartilage (IFC), and the medial and lateral femoral condyle cartilage (MFC and LFC, respectively). The tibial cartilage is very thin, so it was not considered in the present study. T1ρ and T2 images were reconstructed by fitting the image intensity pixel-by-pixel using the mono-exponential fitting algorithms:

$$S(TSL) = S0 \times \exp(-TSL/T1\rho)$$

where TSL is the time of spin-lock and S is the signal intensity of the T1ρ-weighted image with a given TSL; and

$$S(TE) = S0 \times \exp(-TE/T2)$$

where S is the signal intensity of the T2-weighted image with a given TE. The same pixel and the same ROI of the cartilage were used in the 2 groups.

2.5. Statistical analysis

Continuous data were presented as mean ± standard deviation and analyzed using the Student *t* test. Categorical data were presented as frequencies and analyzed using the chi-square test. The T1ρ and T2 relaxation times were compared using the paired *t* test. The diagnostic values of the 2 mapping sequences in detecting cartilage degeneration were evaluated using the receiver-operating characteristic (ROC) curve method. All statistical analyses were conducted using SPSS 16.0 (IBM, Armonk, NY) and MedCalc 12.2.0.0 (MedCalc Software bvba, Ostend, Belgium). Two-sided *P*-values < .05 were considered statistically significant.

Table 1

Noyes classification system of knee articular cartilage defects.[13].

Grade of articular cartilage defects	Description
0	Normal articular cartilage
I	Softening or discoloration of the articular cartilage
IIA	Partial defect <50% of the total thickness of articular cartilage
IIB	Partial defect >50% of the total thickness of articular cartilage
IIIA	Full thickness defect of articular cartilage with normal subchondral bone
IIIB	Full thickness defect of articular cartilage with erosive subchondral bone

Table 2

Characteristics of the patients.

	Control group (n = 26)	OA group (n = 53)	P
Age (years)	31.7 ± 12.2	57.6 ± 10.0	<.01
BMI (kg/m^2)	22.4 ± 3.1	23.4 ± 2.3	.09
Sex (male, %)	11, 42.3%	6, 11.3%	<.01
Location			.81
Left knees	14, 53.8%	27, 50.9%	
Right knees	12, 46.2%	26, 49.1%	
Noyes Grades (lesions)			–
IIA	–	57 (in 31 patients)	
IIB	–	35 (in 26 patients)	
IIIA	–	3 (in 3 patients)	
IIIB	–	30 (in 13 patients)	

OA = osteoarthritis.

3. Results

3.1. Subjects characteristics

Table 2 presents the characteristics of the subjects. Fifty-three OA patients were recruited as the OA group (6 males and 47 females), with 27 left knees and 26 right knees. Mean age was 57.6 ± 10.0 years and mean BMI was 23.4 ± 2.3 kg/m^2. Twenty-six healthy controls were involved (11 males and 15 females), with 14 left knees and 12 right knees. Mean age was 31.7 ± 12.2 years and mean BMI was 22.4 ± 3.1 kg/m^2. There were more females in the OA group than in the control group ($P < .01$). There was no significant difference in BMI ($P = .09$).

3.2. Morphological findings

In the control group, the 3D SPGR images showed that the knee cartilage was integrated and continuous, and there was no lesion to the subchondral bone. There was a laminated structure on the T1ρ and T2 color maps (Fig. 1). Images of cartilage lesions demonstrated that the cartilage was thin, the surface was not smooth and continuous, and there was subchondral bone edema (Figs. 2 and 3).

3.3. T1ρ and T2 relaxation times

A total of 125 cartilage lesions were found in the OA group, including 37 in patella cartilage, 30 in IFC, 30 in MFC, and 28 in LFC. There were 57 grade IIA lesions, 35 grade IIB lesions, 3 grade IIIA lesion, and 30 grade IIIB lesions.

The average T1ρ values of the OA group (58.21 ± 11.15 ms) were significantly higher than those of the control group (40.12 ± 7.25 ms; $P < .01$) (Table 3). The average T2 values of the OA group (62.87 ± 10.61 ms) were also significantly higher than those of the control group (41.23 ± 6.33 ms; $P < .01$) (Table 3).

Comparisons of T1ρ and T2 values of different grades of cartilage lesions of the OA group are shown in Table 4.

3.4. Comparison of T1ρ and T2 mapping sequences

The ROC curve analysis suggested that the sensitivity, specificity, and critical value for identifying normal and OA cartilage were 92%, 85.6%, and 45.90 ms for T1ρ, and 93.6%, 93.3%, and 50.42 ms for T2 (Table 5). The area under the curve (AUC) of the T2 mapping sequence (0.965) was significantly higher than for the T1ρ mapping sequence (0.927; $P = .02$) (Table 5 and Fig. 4A).

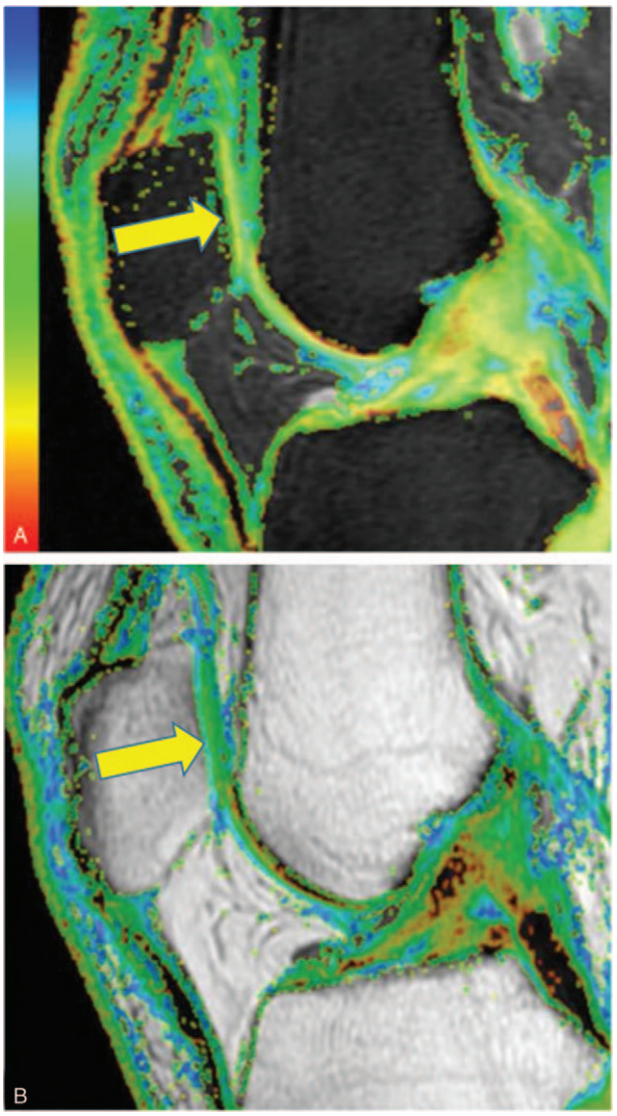

Figure 1. T1ρ (A) and T2 (B) color maps of a representative subject from the control group showing that the patella cartilage (yellow arrow) was integrated, continuous, and has a laminated structure. The T1ρ and T2 relaxation times of patella cartilage were 47.64 ms and 46.25 ms, respectively.

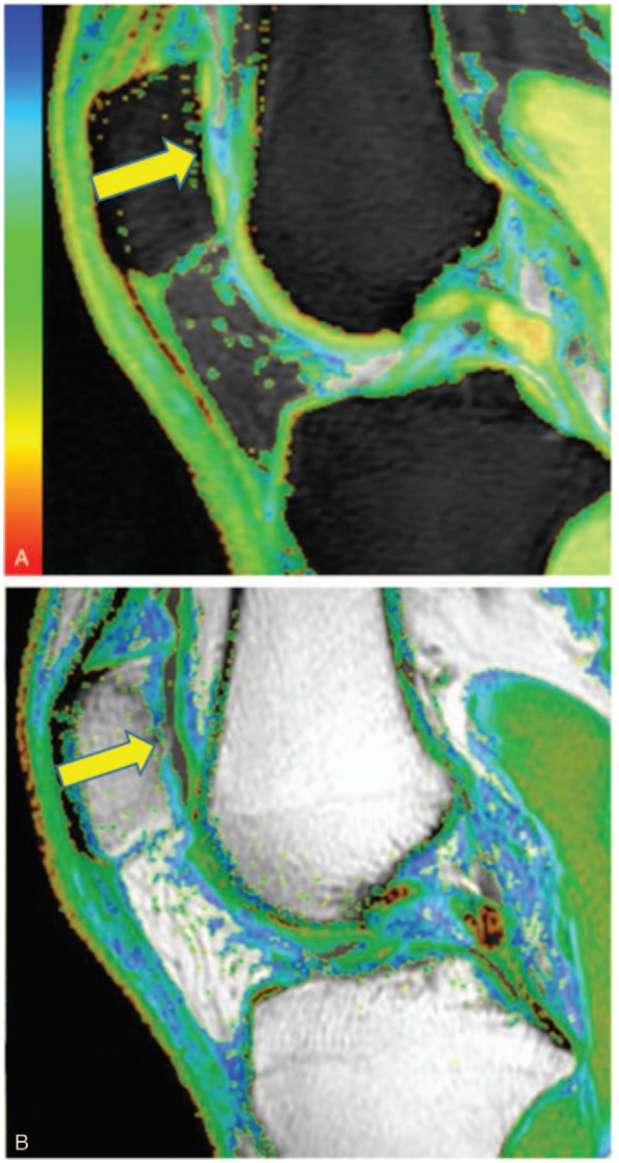

Figure 2. T1ρ (A) and T2 (B) color maps of a representative patient from the OA group showing that the central region of the patella cartilage was thin (yellow arrow). T1ρ and T2 relaxation times of the middle region (71.58 ms and 78.93 ms, respectively) were higher than the surrounding region. OA = osteoarthritis.

We also performed ROC curve analysis of these 2 mapping sequences for different Noyes classes. The AUC for differentiating normal and Noyes IIA cartilage was 0.922 for T1ρ (cut-off value of 46.0, sensitivity of 87.7%, and specificity of 89.7%) and 0.954 for T2 (cut-off value of 49.5, sensitivity of 91.2%, and specificity of 92.3%), indicating that the T1ρ and T2 mapping sequences could effectively differentiate healthy from early-stage OA cartilage, and with no significant difference between them ($P = .08$) (Table 5 and Fig. 4B). The AUC of differentiating Noyes IIA from IIB and Noyes III (IIIA and IIIB) cartilage was 0.615 for T1ρ (cut-off value of 51.4, sensitivity of 83.8%, and specificity of 38.6%) and 0.656 for T2 (cut-off value of 65.6, sensitivity of 48.5%, and specificity of 84.2%), with no significant difference between them ($P = .45$) (Table 5 and Fig. 4C). When differentiating Noyes IIB and Noyes III cartilage, the AUC was 0.534 ($P = .628$) for T1ρ, and for 0.552 ($P = .458$) for T2, indicating that T1ρ and T2 mapping sequences could not differentiate Noyes IIB from Noyes III cartilage (Table 5 and Fig. 4D). These results suggest that T1ρ and T2 mapping sequences were not able to differentiate different Noyes classes of cartilage.

4. Discussion

FS SPGR-3D MRI can be used to image cartilages with high resolution. The aim of the present study was to quantify and compare the T1ρ and T2 relaxation times of the knee articular cartilage between healthy asymptomatic adults and OA patients. The results demonstrated that both T1ρ and T2 cartilage values were significantly increased in patients with OA. Thus, T1ρ and T2 mapping sequences could be used to assess OA cartilage lesions, and T2 mapping sequence was superior to T1ρ mapping sequence when detecting cartilage degeneration. Moreover, we also found that T1ρ and T2 mapping sequences could differentiate normal from Noyes IIA cartilage, indicating that these 2 sequences could be used to diagnose early-stage OA. In addition, ROC curve analysis of different Noyes classes indicated that these 2 sequences could not effectively identify different Noyes classes of cartilage.

OA is thought to be the most prevalent chronic joint disease and its incidence is rising because of the ageing population and obesity epidemic.[15] Indeed, OA becomes more common with age, and more women are affected than men after 50 years of age.[15] McAlindon et al[16] revealed a higher prevalence of OA in women, especially for the PAT-femur compartment, with a prevalence of 8% in women >55 years of age and of 2% in men of the same age group. Accordingly, we also found that female patients accounted for the majority of the patients with OA, and the mean age of the OA group was 57.6 ± 10.0 years.

Arthroscopy is the gold standard for detecting cartilage lesions, but it is invasive, while X-rays are unsuitable to detect cartilage lesions. Therefore, in order to compare OA cartilage with normal cartilage, younger controls were selected in our study. Although some previous studies demonstrated that aging is a major factor in cartilage degeneration, Hirose et al showed that the T1ρ and T2 values of proximal tibiofibular and femorotibial joint cartilages were not affected by aging in the femorotibial joint.[17,18] Therefore, the difference of age between the 2 groups should not introduce a significant bias.

T1ρ relaxation time has recently been proposed as an attractive alternative modality to detect biochemical changes in cartilage.[7,19–22] Indeed, the T1ρ parameter describes the spin-lattice relaxation in the rotating frame. It probes the slow-motion interactions between motion-restricted water molecules and their local macromolecular environment. Extracellular matrix in articular cartilage provides a motion-restricted environment to water molecules. Thus, changes to the extracellular matrix (such as PG loss) may be reflected by measuring T1ρ.[23] Accordingly, early studies in human subjects had shown elevated T1ρ values in patients with OA.[23–25]

Cobb et al[26] suggested that significant differences were found in T1ρ values between epiphyseal and articular cartilage layers, and that T1ρ measurement is a feasible method for differentiating epiphyseal and articular cartilage in a pediatric population. Before cartilage morphology changes, T1ρ value can be sensitive to show age-related cartilage degeneration and the extent of cartilage degeneration.[27] Therefore, T1ρ is able to display the hierarchical structure of normal cartilage in children and can be used to evaluate the natural degeneration of cartilage.

Some studies suggested that the T1ρ values of patella and femoral cartilages in OA patients were higher than that of

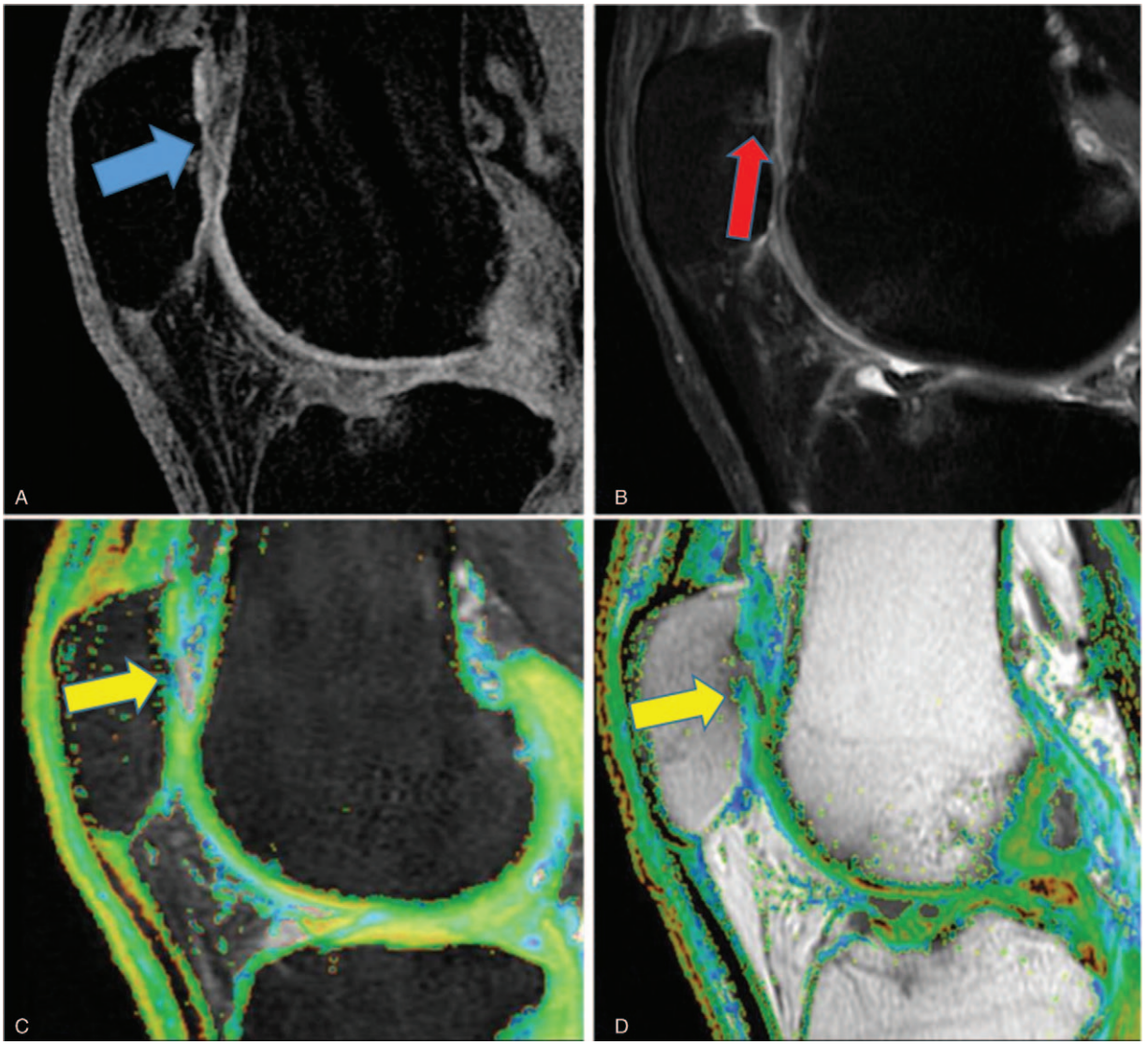

Figure 3. 3D SPGR image (A), PD (B), T1ρ color map (C), and T2 color map (D) of a representative OA patient. The central region of the patella cartilage was thin and worn (blue arrow) (A), and there was bone edema (red arrow) under the cartilage lesion (B). T1ρ and T2 relaxation times of the middle region (yellow arrow) (77.77 ms and 78.86 ms, respectively) were higher than the surrounding region. 3D SPGR = 3D fat-suppressed spoiled gradient, OA = osteoarthritis.

Table 3

Comparison of the T1ρ and T2 average values between the 2 groups.

	Control group	OA group	*P*
T1ρ			
Patella	39.84 ± 6.33	58.88 ± 10.85	<.01
IFC	48.28 ± 5.52	59.82 ± 8.42	<.01
MFC	36.51 ± 4.58	55.75 ± 12.18	<.01
LFC	35.84 ± 4.94	58.23 ± 12.96	<.01
Average of total	40.12 ± 7.25	58.21 ± 11.15	<.01
T2			
Patella	40.31 ± 5.37	65.06 ± 10.08	<.01
IFC	47.53 ± 5.26	64.33 ± 9.42	<.01
MFC	37.86 ± 5.81	59.93 ± 12.07	<.01
LFC	39.22 ± 4.08	61.56 ± 10.49	<.01
Average of total	41.23 ± 6.33	62.87 ± 10.61	<.01

T1ρ and T2 values with mean ± standard deviation, unit: ms.
IFC = intercondylar fossa cartilage, LFC = lateral femoral condyle cartilage MFC = medial femoral condyle cartilage, OA = osteoarthritis.

controls,[23,28] indicating that T1ρ can be used to detect early cartilage degeneration before morphological changes and may allow the monitoring of the course of OA and injury progression, as well as evaluating treatment success. These results are consistent with the results of our study.

T2 relaxation reflects the free water proton molecules moving and exchanging energy inside the cartilaginous matrix.[28] Damage to the collagen–PG matrix and increase of water content in degenerating cartilage may increase T2 relaxation times. In an effort to correlate the T2 relaxation times with

Table 4

Comparison of the T1ρ and T2 average values in different Noyes classes.

	IIA	IIB	IIIA	IIIB	*P*
T1ρ	55.91 ± 11.23	60.58 ± 11.00	70.55 ± 3.08	58.57 ± 10.58	.050
T2	59.74 ± 10.23	64.85 ± 10.59	70.25 ± 6.41	65.76 ± 10.34	.018

Table 5

Value of the T1ρ and T2 mapping sequences for identifying different OA stages.

	AUC	Cut-off value	Sensitivity	Specificity	95%CI	*P*
OA cartilage vs normal						
T1ρ	0.927 ($P<.01$)	45.9	0.92	0.856	0.885–0.957	.02
T2	0.965 ($P<.01$)	50.4	93.60%	93.30%	0.932–0.985	
Noyes IIA cartilage vs normal						
T1ρ	0.922 ($P<.01$)	46	0.877	0.897	0.880–0.965	.08
T2	0.954 ($P<.01$)	49.5	0.912	0.923	0.922–0.987	
Noyes IIB and III vs Noyes IIA						
T1ρ	0.615 ($P<.05$)	51.4	0.838	0.386	0.516–0.713	.45
T2	0.656 ($P<.01$)	65.6	0.485	0.842	0.560–0.753	
Noyes III (IIIA and IIIB) vs Noyes IIB						
T1ρ	0.534 ($P=.628$)	/	/	/	/	/
T2	0.552 ($P=.458$)	/	/	/	/	

AUC = area under the curve, OA = osteoarthritis.

biochemical changes in cartilage, previous in vitro studies have reported that T2 correlated poorly with PG content,[29,30] and PG cleavage did not affect T2 values.[31] Instead, T2 can be affected by collagen content and orientation and/or water content.[19,32] It has been observed that loss of PG is an initiating event in early OA, while neither the content nor the type of collagen is altered in early OA.[33] Increased T2 values were reported previously in degenerated cartilage in both animal models and human

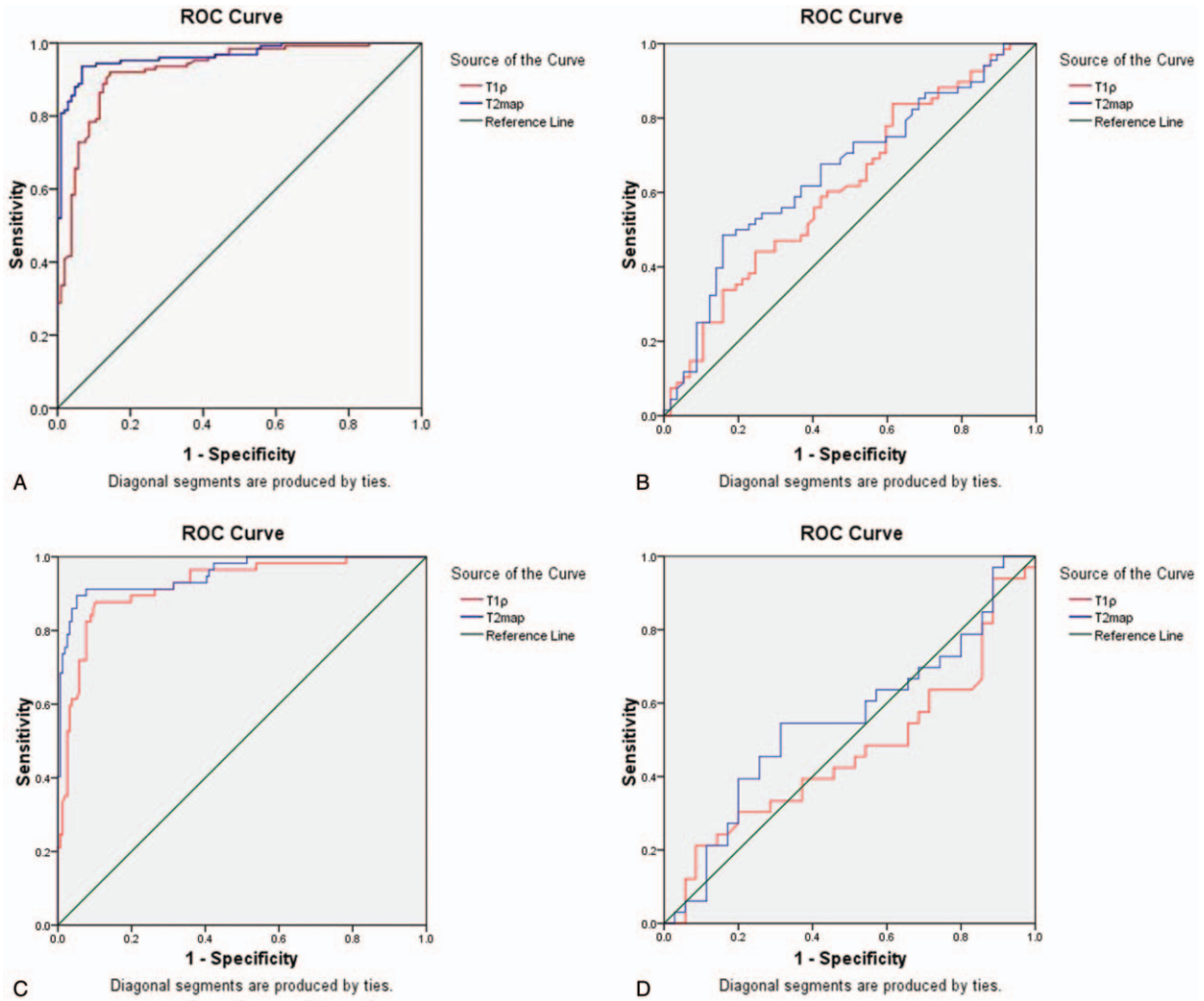

Figure 4. (A) ROC curve analysis of T1ρ and T2 mapping sequence in identifying normal and OA cartilage. (B) ROC curve analysis of T1ρ and T2 mapping sequence in identifying normal and Noyes IIA cartilage. (C) ROC curve analysis of T1ρ and T2 mapping sequence in differentiating Noyes IIA from IIB and Noyes III (IIIA and IIIB) cartilage. (D) ROC curve analysis of T1ρ and T2 mapping sequence in identifying Noyes IIB and Noyes III (IIIA and IIIB) cartilage. ROC = receiver operating characteristic.

subjects.[34–36] The values obtained in the present study are consistent with the reported values.

Previous studies showed that T1ρ and T2 relaxation times can display the biochemical changes of the knee joint cartilage.[37,38] Li et al[28] demonstrated that the average T1ρ and T2 values were significantly higher in patients with OA compared with controls. Increased T1ρ and T2 values were correlated with increased severity in plain X-ray imaging and MRI grading of OA. T1ρ has a larger range and higher effect size than T2, suggesting that the T1ρ relaxation time may be a more sensitive indicator for early cartilage degeneration than T2. Takayama et al[39] suggested that T1ρ mapping was superior to T2 mapping for evaluating the denatured articular cartilage of the knee in OA, supporting the present study.

In previous studies, T1ρ and T2 mappings were compared after correlating them to radiological scaling of severity or clinical severity scoring, and it was concluded that T1ρ mapping was more sensitive than T2 mapping for depicting articular cartilage degeneration.[28,40] Articular cartilage is composed of 90% type II collagen, 5% to 10% PG, and water.[41] It is known that the T1ρ value is inversely correlated to PG content and that T2 value is proportionally correlated to collagen orientation and water content, but not to PG content.[19,42,43] In the early stage of OA, PG depletion occurs before decrease in collagen.[44–46] Therefore, it is presumed that T1ρ mapping is sensitive enough to detect PG depletion in the early stage of OA. Results of our study showed that T2 change was more obvious than T1ρ change, and that the sensitivity and specificity of T2 are higher than that of T1ρ. Nevertheless, the results suggest that T1ρ and T2 mapping sequences were not able to differentiate different Noyes classes of cartilage. In addition, T1ρ and T2 mappings have similar values to differentiate between moderate and severe OA. Discrepancies between studies may be explained, at least in part, by the fact that T1ρ is more sensitive to early cartilage lesions, while the lesions assessed in the present study were more advanced lesions, leading to higher T2 sensitivity.

Of course, the present study is not without limitations. The sample size was small and from a single center. In addition, age and gender distribution were different between the 2 groups. Further study is still necessary to assess adequately the value of T1ρ and T2 FS SPGR 3D MRI for OA. In addition, SPGR should be compared with other advanced MRI sequences such as FLAIR, FIESTA, and 2D cine PC-MRI, which have been shown to be valuable for the observation of fine soft tissue structures.[47,48] The value of computer-assisted diagnostic tools and radionomics should also be explored.[49–51] Indeed, such sequences and tools are used in a variety of diseases and conditions, and they should be assessed in knee OA.

5. Conclusion

Both T1ρ and T2 mapping sequences could be used to assess OA cartilage lesions, with T2 mapping sequence being superior to T1ρ mapping sequence in detecting cartilage degeneration. These 2 sequences could also effectively identify healthy and early-stage OA cartilage.

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