

TECHNICAL NOTE

Quantitative T_2 Mapping of Knee Cartilage: Comparison between the Synthetic MR Imaging and the CPMG Sequence

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The purpose was to evaluate the feasibility of quantitative MRI T_2 mapping based on the quantitative MRI (QRAPMASTER) sequence for the quantitative assessment of knee cartilage. The T_2 values from the phantom study showed excellent correlation between the two techniques ($r^2 = 0.998$). The cartilage T_2 values exhibited strong correlations ($r^2 = 0.867$ – 0.982). Quantitative MRI (qMRI) T_2 mapping can be used as an alternative to multi-echo T_2 mapping, with relatively short scan time.

Keywords: cartilage, knee, quantitative magnetic resonance imaging, T_2 relaxation time

Introduction

Osteoarthritis (OA) is a musculoskeletal disorder of utmost concern,¹ which is characterized by synovial inflammation and progression of cartilage lesions.² The main pathophysiological process of OA involves development of cartilage lesions or loss of cartilage; therefore, radiological imaging studies focus on the visualization of cartilage. The articular cartilage is composed of approximately 70–80% water and 20–30% solid extracellular matrix.³ Articular cartilage can be assessed qualitatively and quantitatively using MRI including $T_{1\rho}$ and T_2 relaxation time and magnetization transfer ratio (MTR).⁴ T_2 relaxation mapping with MRI can help visualize and quantitatively evaluate the water content of cartilage, which is important since it serves as a biomarker of cartilage degeneration. The changes in T_2 values correlate with the variations in water content and collagen structure and organization, as well as changes in hyaline cartilage composition and its depletion, thus, reflecting the histological degeneration of cartilage.^{4,5} T_2 mapping such as CartiGram (GE Healthcare, Waukesha, WI, USA) have been used to non-invasively measure alterations in the water and collagen content of cartilage.⁶ T_2 mapping enables the prediction of early biochemical changes in cartilage degeneration, prior to morphological changes in early OA. In addition, T_2

mapping enables the demonstration of treatment response based on changes in T_2 values.⁷

Traditionally, T_2 mapping has been reformatted from multi-echo spin-echo pulse sequences, such as the Carr-Purcell-Meiboom-Gill (CPMG) sequence, which are generally time-consuming of multiple time points along T_2 decay for a complete T_2 decay curve. The long scan time could be impractical for cartilage imaging of the entire knee joint in a clinical setting. Focused scanning of a limited area of the knee and increasing slice thickness can reduce the scan time; however, these changes limit volumetric T_2 mapping and evaluation of the entire knee.

Quantitative MRI (qMRI) or synthetic MRI (SyMRI) was recently introduced to enable rapid acquisition and accurate quantification of MR images.⁸ The advantage of qMRI is the clinical feasibility of obtaining quantitative T_1 , T_2 , and proton density (PD) measurements during a single scan. The qMRI produces synthetic images by adjusting certain scanning parameters of TR, TE and inversion time (TI) from the computation of characteristic T_1 and T_2 times and PD values of tissues. We hypothesized that qMRI T_2 mapping could be used as an alternative to conventional multi-echo spin-echo CPMG T_2 mapping. However, no studies have compared the clinical performances of these two imaging methods for knee cartilage. Therefore, the purpose was to evaluate the feasibility of qMRI T_2 mapping based on the qMRI method (QRAPMASTER) pulse sequence as an alternative to conventional CPMG T_2 mapping for quantitative assessment of knee cartilage.

Material and Methods

Phantom study

A phantom study using agarose gels of various concentrations was performed to evaluate the correlation of T_2 relaxation times between qMRI and multi-echo spin-echo CPMG

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T₂ mapping. To simulate cartilage loss, phantoms comprised of agarose gels were prepared by boiling agarose powder at concentrations of 1%, 2%, 3%, 4%, and 5% in 3.75 mM sodium azide solution, then cooling the solutions to room temperature. Both CPMG and qMRI T₂ mapping of phantoms were acquired using a 3T MR system (Discovery 750w, GE Healthcare) with a 32-channel phased array head coil (GE Healthcare).

Study population

We retrospectively evaluated the images of 17 patients (men, 5; women, 12; mean age, 55.6 ± 15.7 years; range, 23–78 years) who underwent knee MRI (both multi-echo spin-echo CPMG T₂ mapping and qMRI T₂ mapping based on the QRAPMASTER pulse sequence), between March and June 2016. This retrospective study was approved by the institutional review board.

Magnetic resonance imaging protocol

The MRI was performed using a 3T MR system (Discovery 750w) with a 16-channel GEM Flex-medium flexible coil (NeoCoil, Pewaukee, WI, USA). The qMRI T₂ mapping was performed using the following imaging parameters: sagittal qMRI sequence; TR, 4,384 ms; TE, 21.952 and 98.784 ms; four inversion recovery (IR) times, 175, 700, 1,930, and 4,210 ms; FOV, 160 × 160 mm; acquisition matrix, 320 × 256; slice thickness, 3 mm (interslice gap, 1 mm); slice number, 25; flip angle, 90° and 110°; and echo train length, 14. The image acquisition time for the qMRI sequence was 6 min 20 s. Carr-Purcell-Meiboom-Gill T₂ mapping was performed using the following imaging parameters: T₂-weighted multi-echo spin-echo sequence; TR, 1,000 ms; TE, 17.108, 14.216, 21.324, 28.432, 35.54, 42.648, 49.756, and 56.864 ms; FOV, 160 × 160 mm; acquisition matrix, 256 × 160; slice thickness, 3 mm (interslice gap, 1 mm); slice number, 20; flip angle, 90°; and echo train length, 1. The image acquisition time for the T₂-weighted multi-echo spin-echo sequence was 7 min 7 s.

Conventional T₁-weighted and T₂-weighted MR images were used for image comparison evaluation. Conventional sagittal T₂-weighted fast spin echo (FSE) images with periodically rotated overlapping parallel lines with enhanced reconstruction (PROPELLER) technique was performed using the following imaging parameters: TR, 8,240–9,570 ms; TE, 139–141 ms; FOV, 140 × 140 mm; image matrix, 512 × 512; slice thickness, 3 mm (interslice gap, 0.3 mm); flip angle, 160°; slice number, 32; and echo train length, 24. The image acquisition time was 4 min 5 s. Conventional axial T₁-weighted FSE images was performed using the following imaging parameters: TR, 609–831 ms; TE, 10 ms; FOV, 140 × 140 mm; image matrix, 384 × 320; slice thickness, 3 mm (interslice gap, 1 mm); flip angle, 111°; slice number, 28; and echo train length, 3. The image acquisition time was 3 min and 39 s.

T₂ relaxation time analysis of cartilage

Two board-certified fellowship-trained musculoskeletal radiologists, with 1 year and 10 years of subspecialty clinical experience, who were blinded to the medical records of the patients, performed the image analyses. Any discrepancy between the two radiologists was settled by senior radiologist's decision. The T₂ relaxation times of conventional multi-echo T₂ mapping and qMRI T₂ mapping were evaluated using the CartiGram and Magnetic Resonance Image Compilation (MAGiC; GE Healthcare) utilities, respectively. Analyses were performed using the MRI console (Discovery 750w, GE Healthcare) with the Functool (version 14.3.03, GE Healthcare) and MAGiC (version 100.0.0.) modules. The radiologists manually drew ROI, in consensus, to be as large an area as possible within each of the three anterior, middle, and posterior subregions of the six regions of the knee cartilage, including the medial femoral condyle, medial tibial plateau, patellar facet, femoral trochlea, lateral femoral condyle, and lateral tibial plateau. Therefore, 18 ROIs were drawn for the multi-echo T₂ mapping and the qMRI T₂ mapping of each patient, except for the four patients whose lateral compartment of knee was not completely scanned due to limitation of time. For these four patients, only 12 ROIs were drawn within the cartilage of the medial femoral condyle, medial tibial plateau, patellar facet, and femoral trochlea. The average sizes ROIs were 2.5–4 mm².

Image evaluation of the MAGiC knee images

Image analysis was performed using commercially available picture archiving and communication system (PACS) (Centricity Radiology, RA1000, GE Healthcare, Barrington, IL, USA) and the MRI console-installed MAGiC utility. 1) For quantitative evaluation of relaxation time, three parameters of T₁ relaxation time, T₂ relaxation time, and PD values were measured from one ROI simultaneously. 2) For qualitative comparative evaluation of the conventional and MAGiC images, the tissue contrast and image quality of T₁-weighting and T₂-weighting were evaluated. In the MAGiC utility, the TR and TE were adjusted to the same times. For T₁-weighted images, axial conventional T₁-weighted image and sagittal MAGiC T₁-weighted image were used because the T₁-weighted image is axial plane in our knee routine protocol. For T₂-weighted images, we selected one mid sagittal image from T₂-weighted images and one mid sagittal image from sagittal MAGiC T₂-weighted image.

For qualitative analysis, the image score in terms of tissue contrast and image quality, was determined on a three-point scale for MAGiC T₁-weighted and MAGiC T₂-weighted images as follows: tissue contrast (grade 1, poor tissue contrast with significant unclear contrast; grade 2, intermediate tissue contrast with some but insignificant unclear contrast; and grade 3, excellent tissue contrast with clear T₁- or T₂-weighted contrast) and image quality (grade 1, poor quality with significant dead pixels; grade 2, intermediate quality

with insignificant dead pixels; and grade 3, excellent image quality with no dead pixels on knee joint). Conventional FSE T_1 -weighted and T_2 -weighted images were used as references.

Statistical analysis

Correlation of the T_2 relaxation times between qMRI and multi-echo spin-echo CPMG T_2 mapping was assessed using the Pearson correlation coefficients. All statistical analyses were performed in the R (R package version 3.1.2, R Foundation of Statistical Imaging, Vienna, Austria; <http://cran.r-project.org>). P -values < 0.05 were considered statistically significant.

Discussion

In the phantom study (Fig. 1), the T_2 relaxation times increased with the increase in agarose gel concentration. The T_2 relaxation time measured by qMRI T_2 mapping using MAGiC showed excellent correlation with that measured by the conventional CPMG T_2 mapping using CartiGram ($r^2 = 0.998$, $P < 0.05$).

T_2 values of the cartilage in the medial/lateral tibiofemoral and patellofemoral joints measured by CPMG T_2 mapping and qMRI T_2 mapping were strongly correlated at all six regions of the knee (Fig. 2). The cartilage was clearly depicted on the T_2 maps that were reformatted using both techniques. While joint effusion was not suppressed i.e., visible on the qMRI T_2 maps, it was suppressed on the conventional CPMG T_2 maps (Fig. 3).

For the quantitative evaluation of qMRI, three parameters of T_1 relaxation time, T_2 relaxation time, and PD values could be measured from one ROI simultaneously. The averages and standard deviations of these parameters are reported in Table 1.

For the comparative qualitative evaluation (Fig. 3), the tissue contrast of both T_1 -weighting and T_2 -weighting were scored 2.88 ± 0.33 (mean \pm standard deviation) and 2.94 ± 0.24 , respectively, on all MAGiC images. The image quality scores of MAGiC T_1 -weighted images in bone marrow were 2.94 ± 0.24 . However, the image quality scores of MAGiC T_2 -weighted images were slightly low: 2.65 ± 0.49 and 2.59 ± 0.51 , respectively. Notably, the image quality of

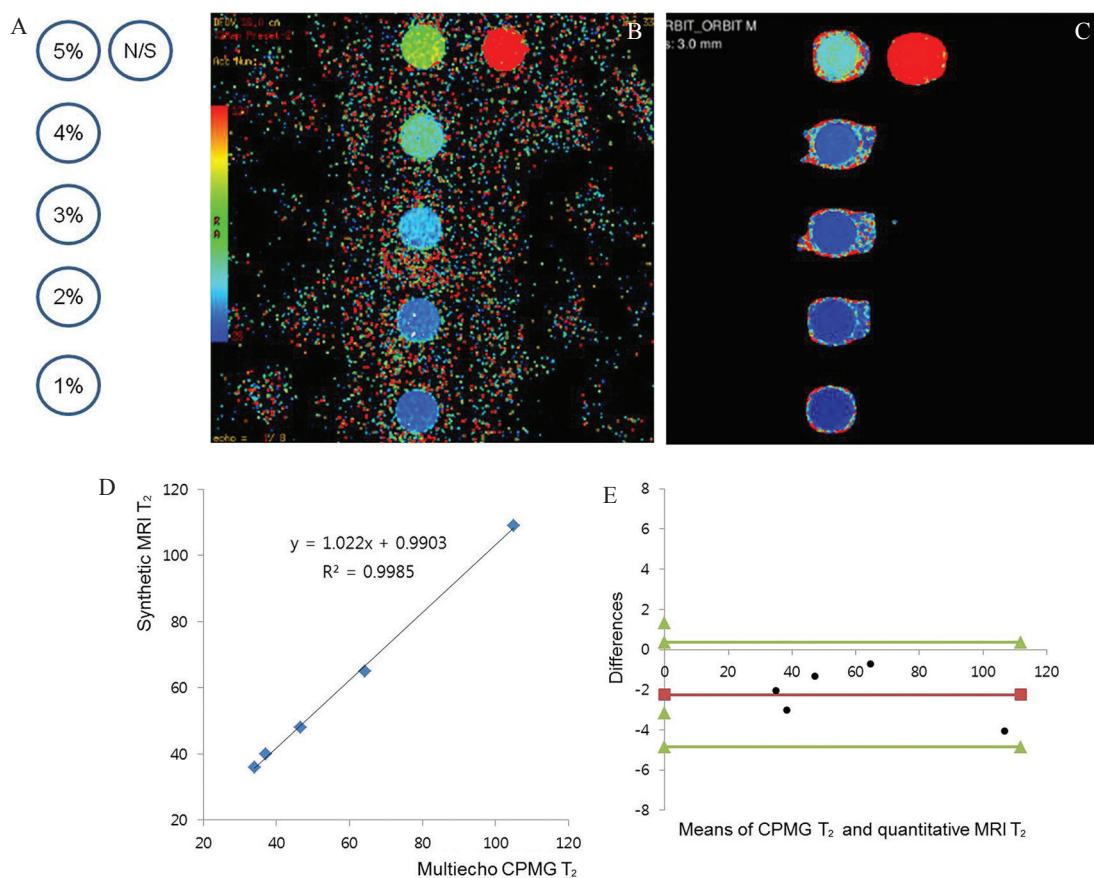


Fig. 1 Phantom images of agarose gel of five different concentrations and normal saline. (A) Six 20 mL tubes containing agarose gels of varying agarose percentage—1%, 2%, 3%, 4%, 5%, and 0% (normal saline). Multi-echo Carr-Purcell-Meiboom-Gill (CPMG) T_2 maps (B) and quantitative MRI (qMRI) T_2 maps (C) of the tubes with different concentrations of agarose gel. (D) Scatter plot of T_2 relaxation times acquired from multi-echo CPMG and qMRI T_2 mapping of the phantoms. (E) Bland-Altman plot comparing the T_2 relaxation times of the multi-echo CPMG T_2 and qMRI T_2 maps.

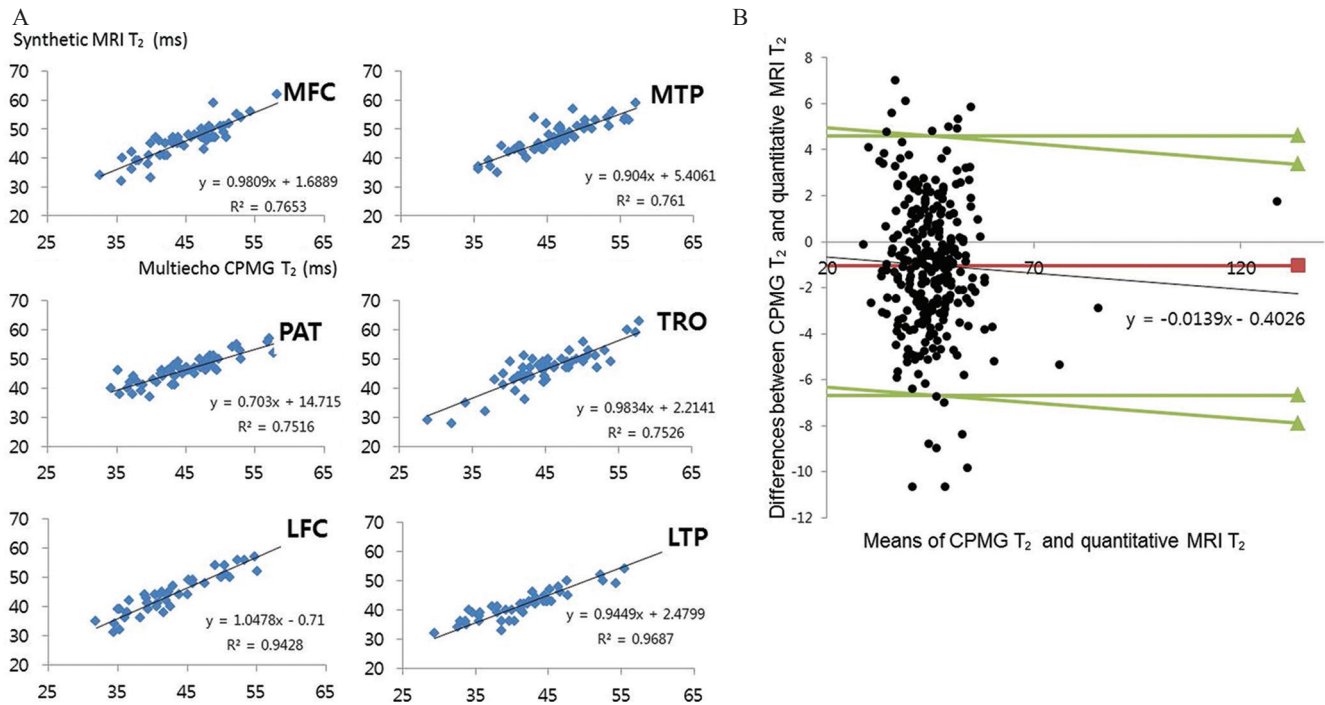


Fig. 2 Agreements of T₂ values. (A) Correlation between the cartilage T₂ relaxation acquired using the multi-echo Carr-Purcell-Meiboom-Gill (CPMG) T₂ mappings and that of the synthetic MRI T₂ mapping, for six different regions in the medial/lateral tibiofemoral and patellofemoral joints of the knee. (B) Bland–Altman plot comparing the cartilage T₂ relaxations times of the entire knee acquired using the multi-echo CPMG and with those acquired using the qMRI T₂ mapping. The y-axis represents the differences between the T₂ relaxation times from CPMG mapping and quantitative MRI (qMRI). The x-axis represents the means of the T₂ values from the CPMG T₂ maps and the qMRI T₂ maps. The regression line is presented as a center parallel line, and 95% confidence interval limits are presented as a continuous line. MFC, medial femoral condyle; MTP, medial tibial plateau; LFC, lateral femoral condyle; LTP, lateral tibial plateau; PAT, patellar facet; TRO, femoral trochlea.

the muscles of both MAGiC T₁-weighted and MAGiC T₂-weighted images was excellent score: 3.00 ± 0.0 .

The qMRI is utilized for the quantitative mapping of T₁, T₂, and PD values, as well as the reformatting of images equivalent to those acquired by conventional T₁- or T₂-weighted techniques.^{9,10} These MR images with variable weighting and quantitative mapping can be reformatted during a single acquisition, without additional scanning. The qMRI was initially used for rapid quantitative imaging of the brain.^{9,10} In the present study, this technique was applied for the quantitative assessment of articular cartilages of the knee. To the best of our knowledge, this is the first to apply qMRI for the evaluation of the knee joint and quantitatively compare the performances of qMR and CPMG T₂ mapping.

T₂ relaxation mapping using the multi-echo spin-echo technique has been used to evaluate the water and collagen content of cartilage in order to predict the early biochemical changes of cartilage degeneration in early OA, prior to the onset of morphological changes.^{11,12} However, conventional multi-echo T₂ mapping requires a relatively long acquisition time, thus, limiting the clinical application of this technique, especially for imaging of articular cartilage covering the entire knee. This preliminary study indicated that the results of qMRI T₂ mapping are clinically comparable to those of conventional multi-echo T₂ mapping, with

the added advantage of reduced scan time. While the multi-echo CPMG sequence required 7 min 7 s to obtain full coverage of the knee joint, the MAGiC T₂ mapping required only 6 min 20 s for the same, which corresponds to a 23% decrease in scan time.

In technical views, the qMRI module in MAGiC is not yet optimized for cartilage imaging. It does not allow the suppression of joint fluid in the current version. Therefore, joint effusion is visible with high T₂ values on T₂ mapping. In contrast, in the CartiGram software, joint effusion is automatically suppressed in T₂ mapping, which can help differentiate fluid filled cartilage defects from cartilage lesion with increased T₂ times. And the current version of qMRI T₂ mapping does not support overlaying the transparent T₂ map on the conventional T₂-weighted or PD-weighted images. We expect the release of a dedicated cartilage module with this transparency and overlay option included.

The present study had several limitations. First, because of the retrospective nature of this study, we were unable to evaluate the interval change of T₂ values by follow-up examination. Second, we cannot modify the scan parameter of the qMRI because the TE values were fixed in current version. The second TE (98.784 ms) may be too long to calculate the T₂ value for cartilage because the cartilage has a short T₂ value. Third, limitation is the increased slice gap in

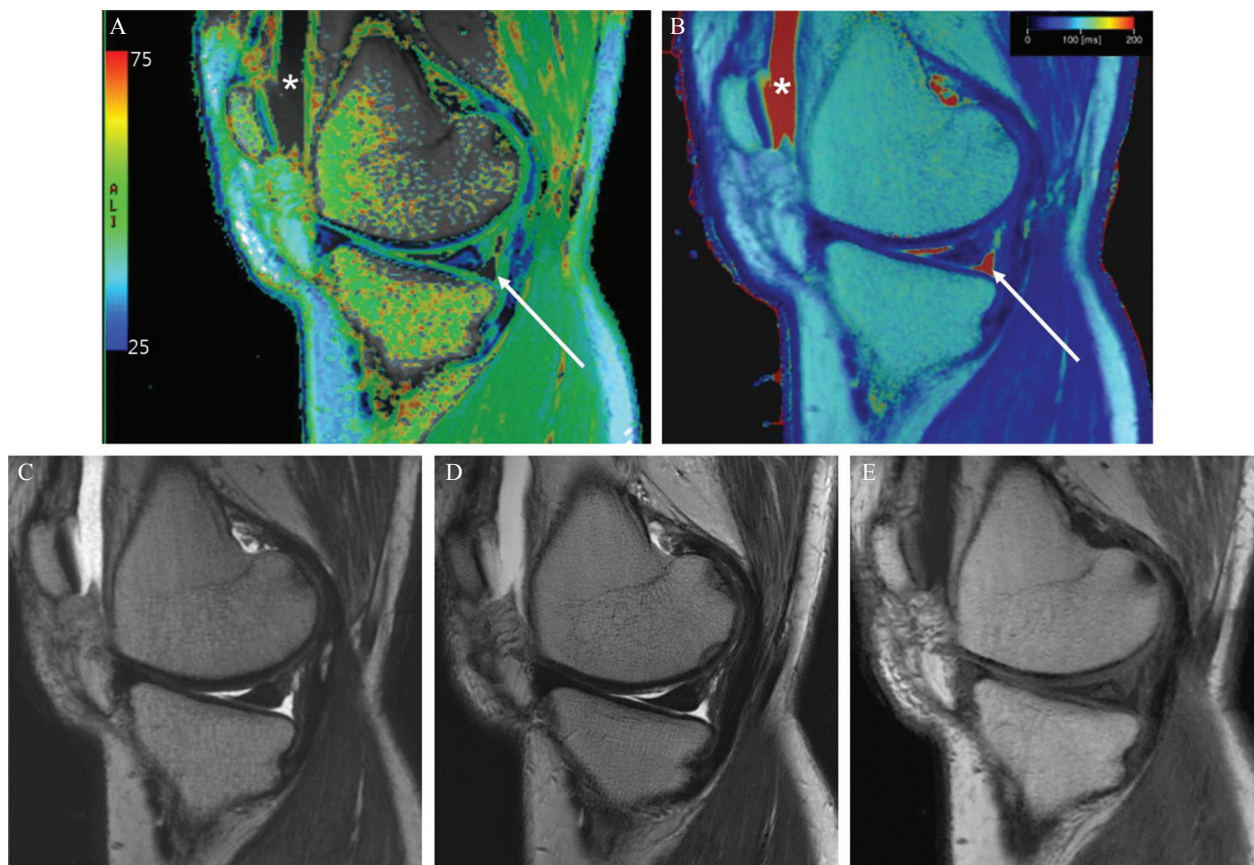


Fig. 3 A 69-year-old woman with knee pain. The knee cartilage was well-depicted on the multi-echo Carr-Purcell-Meiboom-Gill (CPMG) T_2 maps (A) and the quantitative MRI (qMRI) T_2 maps (B). Synovial fluid in the suprapatellar pouch (asterisks) and around the posterior horn of the medial meniscus (arrows), which is indicated by the red color on the qMRI T_2 map, is suppressed on the CPMG T_2 map. Portions of CPMG T_2 maps show the color suppression of the bone marrow and synovial fluid. The MAGiC T_2 weighted image (C) with a TR of 8,820 ms and TE of 138 ms have excellent soft tissue T_2 -weighted contrast with good image quality compared with the conventional T_2 -weighted images (D) with a TR of 8,818 ms and TE of 138 ms. The MAGiC T_1 weighted image (E) with a TR of 620 ms and a TE of 10 ms have excellent soft tissue T_1 -weighted contrast with good image quality.

Table 1 Three parameters of T_1 relaxation time, T_2 relaxation time, and proton density (PD) values of Quantitative MRI T_2 mapping and T_2 values of multi-echo CPMG

Region	qMRI			Multi-echo CPMG
	Proton density value (ms)	T_1 relaxation time (ms)	T_2 relaxation time (ms)	T_2 relaxation time (ms)
MFC	56.24 ± 11.69	965.71 ± 166.99	46.00 ± 6.01	45.17 ± 7.16
MTP	56.91 ± 11.12	993.33 ± 202.76	47.22 ± 6.08	46.25 ± 7.57
PAT	79.63 ± 10.93	931.78 ± 263.43	46.29 ± 5.25	44.92 ± 7.00
TRO	57.12 ± 11.00	843.02 ± 291.22	46.61 ± 5.57	45.14 ± 7.00
LFC	51.45 ± 11.06	958.85 ± 260.50	45.92 ± 5.10	44.15 ± 7.59
LTP	53.02 ± 12.89	976.15 ± 206.21	42.61 ± 5.14	43.40 ± 6.96

The data are presented as the mean ± standard deviation. CPMG, Carr-Purcell-Meiboom-Gill; MFC, medial femoral condyle; MTP, medial tibial plateau; LFC, lateral femoral condyle; LTP, lateral tibial plateau; PAT, patellar facet; TRO, femoral trochlea, qMRI, quantitative MRI.

qMRI T_2 mapping. We acquired images using a section thickness of 3 mm with a 1 mm gap due to limited scan time. We expect future research to be conducted on high-resolution, three-dimensional, unfolded cartilage mapping, which is

gaining importance in cartilage imaging. Given the relatively short total scan time of qMRI T_2 mapping, acquisition of unfolded maps of the articular cartilage covering the entire knee in a clinically acceptable scan time should be feasible.

Conclusion

In conclusion, qMRI T₂ mapping can be used as an alternative to multi-echo T₂ mapping of knee cartilage, with a relatively short scan time, in a clinical setting. The qMRI may enable T₂ mapping of cartilage covering the entire knee within a clinically acceptable time. T₂ maps acquired with this technique may serve as reliable imaging biomarkers for treatment monitoring, including the evaluation of the response to OA medications.

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Conflicts of Interest

The authors declare that they have no conflicts of interest.

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