



# Double-inversion recovery with synthetic magnetic resonance: a pilot study for assessing synovitis of the knee joint compared to contrast-enhanced magnetic resonance imaging

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Received: 16 June 2018 / Revised: 10 September 2018 / Accepted: 25 September 2018 / Published online: 28 November 2018

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## Abstract

**Objectives** To investigate the agreement between double-inversion recovery (DIR) with synthetic magnetic resonance imaging (MRI) and T1-weighted contrast-enhanced (CE)-MRI for the assessment of knee synovitis.

**Methods** T1-weighted CE-MRI and synthetic MRI of 30 patients were compared. Synthetic DIR image reconstruction was performed with two inversion times (280–330 ms and 2800–2900 ms). Subjective image quality, visibility of synovium, detection of synovitis, and total synovitis score in the knee joint were evaluated on both MR images. The relative signal intensity (SI) and relative contrast of synovium, joint effusion, and bone marrow for two imaging were assessed. Differences in data between two imaging were assessed by using Wilcoxon's signed-rank test and chi-square test/Fisher's exact test. Interobserver agreement was expressed as weighted kappa value. Accuracy of synthetic DIR image was calculated by using CE-MRI as reference standard.

**Results** T1-weighted CE-MRI yielded better image quality than synthetic DIR imaging ( $p < 0.001$ ). Interobserver agreements for detecting synovitis diagnosis/sum of the synovitis score were moderate to almost perfect ( $\kappa = 0.58/0.44$ , synthetic DIR;  $\kappa = 0.83/0.65$ , T1-weighted CE-MRI). There were no statistical differences in visibility of synovium ( $p = 0.058–0.190$ ), detection of synovitis ( $p < 0.001$ ), and relative SI of structures between two imaging ( $p = 0.086–0.360$ ). Synovium-to-effusion contrast was higher in synthetic DIR ( $p = 0.003$ ) and synovium-to-bone marrow contrast was higher in CE-MRI ( $p < 0.001$ ).

**Conclusion** Synthetic DIR imaging showed a moderate degree of interobserver agreement and good accuracy for detecting synovitis. Though it has limitations, it may play a role in imaging of degenerative joint disease or larger cohort scientific studies where gadolinium application is not feasible.

## Key Points

- Synthetic double-inversion recovery (DIR) imaging avoids the use of contrast agent.
- There was no significant difference between T1-weighted CE-MRI and synthetic DIR imaging in evaluating presence of synovitis in knee joint.
- Synthetic DIR imaging showed moderate degree of interobserver agreement and good accuracy for detecting synovitis compared to CE-MRI, and it may facilitate evaluation of some regions of peripatellar synovitis.

**Keywords** Knee · Synovitis · Magnetic resonance imaging · Contrast media

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## Abbreviations

DIR Double-inversion recovery  
FS Fat-suppressed  
MDME Multiple-dynamic multiple echo

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## Introduction

The synovium is a thin specialised membrane lining the joint surfaces, bursae, and tendon sheaths [1]. The knee is a

synovial joint that consists of a condylar joint (tibiofemoral joint) and a saddle joint (patellofemoral joint), and the inner surface of this joint is lined by synovium [2]. Inflammation of the synovium is called synovitis and may occur in association with conditions such as inflammatory arthritis and osteoarthritis (OA) [3]. Inflammation itself appears to play a role in increasing input from peripheral nociceptors [4], and the synovium contains nociceptive fibres [5]. A histopathological study of synovial tissue inflammation in both early and late knee OA has shown the production of pro-inflammatory cytokines by synovium [6]. Thus, the synovium can be a source of pain in knee OA [7]. Synovitis is visualised on magnetic resonance imaging (MRI) as synovial thickening on T2-weighted images (due to water accumulation) and contrast enhancement on T1-weighted images [8].

Gadolinium contrast-enhanced (CE)-MRI is regarded as the gold standard for evaluating synovitis, as it can distinguish the synovium from joint effusion [9, 10]. Ideally, direct imaging assessment of synovitis should be performed using CE-MRI [7–9], but it is not routinely used in clinical practice due to the increased cost and scan time and the potential side effect of the contrast agent including nausea or vomiting, urticaria, bronchospasm, tachycardia, loss of consciousness, nephrogenic systemic fibrosis, and storage of gadolinium in the brain [11–14]. Thus, some studies have compared unenhanced fluid-sensitive fat-suppressed (FS) sequences and fluid-attenuated inversion recovery sequences with CE-MRI for evaluation of synovitis and have shown moderate to good agreement [15, 16]. The inversion recovery (IR) sequence can be applied to void the signal of a single tissue, by selecting the inversion time (TI) during preparation of inversion recovery, by applying a 180° inversion radio frequency pulse before signal acquisition [17, 18]. A double-inversion recovery (DIR) sequence uses two inversion pulses, with two different TIs, and can simultaneously suppress signals from two different tissues, thereby improving imaging contrast [17, 19, 20]. By suppressing joint effusion and fat tissue, the DIR sequence may hold potential for replacing CE-MRI in assessing knee joint synovitis [18, 21].

Synthetic MRI was recently introduced to facilitate accurate quantification, similar to that of tissue-contrast MRI. Synthetic MRI uses quantitative probing of multiple physical properties within a single scan and can generate T1-weighted, T2-weighted, proton density-weighted, and inversion recovery images by modifying the repetition time (TR), echo time (TE), and TI [22]. Additionally, synthetic DIR MRI can be generated from synthetic MRI scans by employing two TIs, which can simulate T1-weighted CE-MRI. Synthetic DIR imaging could, thus, possibly replace CE-MRI for assessing knee joint synovitis. However, to date, knee joint synovitis has not been evaluated using synthetic DIR MRI. Therefore, the purpose of this study was to investigate the agreement of synthetic DIR imaging and T1-weighted CE-MR imaging for the assessment of knee joint synovitis.

## Materials and methods

### Subjects

This study was approved by the relevant institutional review board, and the need for obtaining informed consent was waived due to the retrospective nature of the study. Between March 2016 and January 2017, 34 consecutive adult patients underwent both conventional knee MRI with contrast enhancement and synthetic MRI at this institution. Among them, four patients were excluded: one patient with hemarthrosis in the knee joint due to fracture of the femur, one patient with quadriceps tendon rupture, and two patients with severe motion artefacts and poor synthetic DIR image quality. In total, 30 patients were included in this study, comprising 15 men (aged 22–74 years; mean age, 44.9 years) and 15 women (aged 21–80 years; mean age, 41.1 years). The reasons for knee MR imaging with contrast enhancement were as follows: non-specific knee pain with ( $n = 9$ ) or without ( $n = 13$ ) history of trauma, degenerative osteoarthritis ( $n = 5$ ), rheumatoid arthritis ( $n = 1$ ), limited range of knee motion ( $n = 1$ ), and osteoid osteoma ( $n = 1$ ).

### Imaging study

MRI was performed using a 3.0-T magnetic resonance system (Discovery 750w, GE Healthcare) with a 16-channel GEM Flex-medium flexible coil (NeoCoil).

For synthetic MRI, a multiple-dynamic multiple echo (MDME) sequence was acquired in the sagittal orientation, with the following imaging parameters for synthetic reconstruction: TR, 4384 ms; TE, 21.952 and 98.784 ms; four different TIs, 175, 700, 1930, and 4210 ms; field of view (FOV), 160 × 160 mm; acquisition matrix, 320 × 256; reconstructed voxel size, 0.312 mm; slice thickness, 3 mm (interslice gap, 1 mm); two flip angles, 90° and 110°; and echo train length, 14. The image acquisition time was 6 min 20 s. Synthetic DIR images were generated by one radiologist (J.Y.), by adjusting TR, TE, and TI, and the TI that effectively suppressed the signal from joint fluid and fat was set: TR, 8000 ms; TE, 100 ms; TI1, 280–330 ms; TI2, 2800–2900 ms.

For conventional T1-weighted MRI, an FS three-dimensional spoiled gradient-recalled (3D SPGR) acquisition in the steady-state sequence was used in the sagittal plane, within 1 min after administration of intravenous gadolinium-based contrast agent (Dotarem; Guerbet) at a dose of 0.2 mL (0.1 mmol per kilogramme of body weight). The following parameters were used: TR, 10.448 ms; TE, 4.676 ms; FOV, 160 × 160 mm; acquisition matrix, 320 × 320; reconstructed voxel size, 0.312 mm; slice thickness, 1 mm; slab thickness 116 mm; number of excitations, 0.8026; flip angle, 10°; and echo train length, 1. The image acquisition time was 4 min 5 s.

## Imaging interpretation

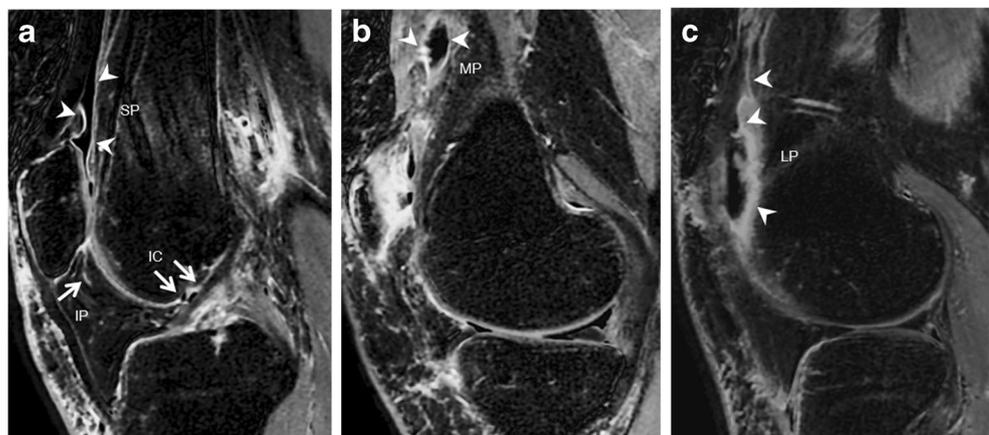
Image analysis was performed independently and in random order by two musculoskeletal radiologists (Y.H.L. and J.Y. with 10 and 2 years of experience, respectively), who were blinded to the electronic medical records of the patients, including the radiology report and the final diagnosis. The images were digitally assessed with a commercially available PACS workstation (Centricity<sup>®</sup> Radiology RA1000; GE Healthcare). One reader (J.Y.) selected three planes of sagittal images in which the T1-weighted CE-MRI and synthetic DIR images were best matched, i.e. (1) the medial margin of the patella, (2) the central portion that showed the anterior cruciate ligament as straight, and (3) the lateral margin of the patella (Fig. 1). Visualisation of the synovium and synovitis was evaluated in these three sagittal sections of images in five peripatellar areas (suprapatellar area, intercondylar area, infrapatellar area, medial parapatellar area, and lateral parapatellar area).

## Image quality and visibility of synovium

Subjective image quality assessment of T1-weighted CE and synthetic DIR images was performed by both readers, using a 4-point grading scale: excellent (4), good (3), sufficient (2), poor (1). The scores of both readers were summed for both sequences for comparison.

A high signal intensity line between the suppressed joint effusion and intra-articular fat regions on synthetic DIR images was considered the synovium. The visibility of the synovium on T1-weighted CE-MRI and synthetic DIR images was rated on a 4-point grading scale by both readers: grade 1 (poorly visualised synovium), grade 2 (partially visualised synovium), grade 3 (synovium was fully delineated but at low contrast as compared to the intra-articular fat or joint effusion), and grade 4 (synovium was sharply delineated with good contrast as compared to both of the intra-articular fat and joint effusion) [16].

**Fig. 1** Sagittal synthetic double-inversion recovery magnetic resonance imaging of the knee joint. The synovium was evaluated in five peripatellar areas on three sections of sagittal images. **a** The suprapatellar (SP), infrapatellar (IP), and intercondylar (IC) areas were assessed where the anterior cruciate ligament is fully visualised. **b** The medial peripatellar (MP) area. **c** The lateral peripatellar (LP) area



## Assessment of synovitis

Synovitis was defined as synovial thickening of more than 2 mm on both types of images [15, 23]. Both readers rated the presence (1) or absence (0) of synovitis in five peripatellar areas, individually. The sum of the scores (scores ranging from 0 to 5 points) in the five peripatellar areas was calculated for each patient to represent the severity of synovitis. After independent evaluation of synovitis, both readers reached a consensus about the interpretation of T1-weighted CE images, and these consensus results were considered the reference standard.

## The relative signal intensity and the relative contrast

The relative signal intensity (SI) and the relative contrast of synovium, joint effusion, and bone marrow for T1-weighted CE-MRI and synthetic DIR images were assessed in the level of central portion that showed the anterior cruciate ligament as straight (Fig. 1a) by one reader (J.Y.). For the signal measurement, 1–2-mm<sup>2</sup>-sized circular regions of interest (ROIs) were drawn for each structure in the same region in both imaging sequences. The relative SI of each structure was calculated with the equation, SI/SD. And the relative contrast of structure A to structure B was calculated with the equation  $(SI_A - SI_B) / (SD_A^2 + SD_B^2)^{1/2}$  [24].

## Statistical analysis

To compare subjective image quality, visibility of the synovium, the total synovitis score, the relative SI, and the relative contrast of structures between the two imaging sequences, Wilcoxon's signed-rank test was used. Weighted kappa ( $\kappa$ ) statistics was used for interobserver agreement. Also, Bland-Altman plots were drawn to demonstrate the interobserver agreement in evaluating summed score of synovitis. Chi-square test or Fisher's exact test was used to compare T1-weighted CE-MRI and synthetic DIR imaging in detection of synovitis for both readers. The accuracy, sensitivity, and

specificity for detecting synovitis in knee joint of synthetic DIR imaging were calculated by using T1-weighted CE-MRI as a reference standard.

All statistical analyses were performed using SPSS software (version 23; IBM Corp.).  $P$  values  $< 0.05$  were deemed to indicate statistically significant differences.

## Results

The mean score of subjective image quality in T1-weighted CE-MRI and synthetic DIR imaging demonstrated sufficient to excellent image quality (Table 1). However, the T1-weighted CE imaging has higher scores of subjective image quality than synthetic DIR imaging ( $p < 0.001$ ). The fat suppression was not homogeneous on synthetic DIR imaging as compared to that of T1-weighted CE-MRI. Table 2 lists the mean score of both sequences for the visualisation of synovium; the synovium was well visualised with both sequences by both readers. The score for T1-weighted CE imaging was higher than that for synthetic DIR imaging, for both readers. There was no significant difference in the visualisation of the synovium on either sequence between readers ( $p = 0.190$  and  $p = 0.058$ , respectively) (Table 2).

Peripatellar synovitis on synthetic DIR imaging was detected in 19 patients by reader 1 and in 18 patients by reader 2. On T1-weighted CE imaging, peripatellar synovitis was found in 18 patients by reader 1 and in 17 patients by reader 2. Table 3 lists the comparison of T1-weighted CE-MRI and synthetic DIR imaging for both of the readers in evaluating the detection of synovitis in five peripatellar areas. There was no significant difference in detecting synovitis on both MR imaging in both of the readers at suprapatellar area, intercondylar area, and medial peripatellar area (Fig. 2). Both of the readers show difference in detecting synovitis between two MRI sequences when evaluating lateral peripatellar area (reader 1,  $p = 0.245$ ; reader 2,  $p = 0.078$ ). After a second viewing of the MR images, (1) the cartilage of the lateral articular facet (Fig. 3), (2) uneven fat suppression of the suprapatellar fat pad, and (3) a

**Table 1** Subjective image quality of the two imaging techniques

Subjective image quality	CE T1-weighted FSPGR imaging	Synthetic DIR imaging
Grade 1	0 (0/0)	0 (0/0)
Grade 2	2 (2/0)	11 (4/7)
Grade 3	13 (7/6)	33 (11/22)
Grade 4	45 (21/24)	16 (15/1)

Data are the sum of the scores for readers 1 and 2. Data in parentheses are the sum of scores for readers 1 and 2, respectively

CE contrast-enhanced, FSPGR fat-suppressed spoiled gradient-recalled, DIR double-inversion recovery

**Table 2** Comparison of contrast-enhanced T1-weighted fat-suppressed spoiled gradient-recalled imaging and synthetic double-inversion recovery images for the evaluation of synovitis

Parameter and reader	CE T1-weighted FSPGR imaging	Synthetic DIR imaging	$p$ value
Synovium visibility (grades 1–4)			
Reader 1	3.77 $\pm$ 0.43	3.60 $\pm$ 0.68	0.190
Reader 2	3.83 $\pm$ 0.38	3.53 $\pm$ 0.38	0.058
Sum of synovitis score (scores 0–5)			
Reader 1	1.63 $\pm$ 1.85	1.63 $\pm$ 1.83	0.962
Reader 2	1.40 $\pm$ 1.63	1.37 $\pm$ 1.50	0.952

Data are presented as means  $\pm$  standard deviation.  $P$  values are based on Wilcoxon's signed-rank test

CE contrast-enhanced, FSPGR fat-suppressed spoiled gradient-recalled, DIR double-inversion recovery

partial volume effect due to thick slice thickness (4 mm) were found to lead to misdiagnosis of lateral peripatellar synovitis. And it was similar to previous study reported hyperintense SI of synovial lining of articular cartilage on fluid-attenuated inversion recovery sequence [16].

Interobserver agreement for detecting synovitis was almost perfect for T1-weighted CE-MRI and moderate for synthetic DIR imaging (Table 4). The respective agreement rate between readers per peripatellar area was also determined. The intercondylar area and lateral peripatellar area showed relatively lower interobserver agreements in both sequences than the other three peripatellar areas. For interobserver agreement related to sum score of peripatellar synovitis, it was substantial for T1-weighted CE-MRI and moderate for synthetic DIR imaging. Figure 4 shows the Bland-Altman plots to demonstrate the degree of agreement between readers in evaluating summed score of peripatellar synovitis in both sequences. The accuracy of synthetic DIR imaging for detecting synovitis was 80% (95% CI, 72.7–86.1%) for reader 1 and 82% (95% CI, 74.9–87.8%) for reader 2. The sensitivity of synthetic DIR imaging for detecting synovitis was 87.0% (95% CI, 78.8–92.9%) for reader 1 and 85.3% (95% CI, 77.3–91.4%) for reader 2. The specificity of synthetic DIR imaging for detecting synovitis was 66% (95% CI, 51.2–78.8%) for reader 1 and 73.2% (95% CI, 57.1–85.8%) for reader 2.

Table 5 lists the relative SI of synovium, joint effusion, and bone marrow of knee joint and relative contrast of synovium-to-effusion and synovium-to-bone marrow in both MR images. There were no statistically significant differences in relative SI of structures between two imaging (synovium,  $p = 0.086$ ; effusion,  $p = 0.360$ ; bone marrow,  $p = 0.178$ ). Synthetic DIR imaging shows higher synovium-to-effusion ratio than T1-weighted CE-MRI (11.36  $\pm$  11.06 versus 5.46  $\pm$  4.47,  $p = 0.003$ ). T1-weighted CE-MRI shows higher synovium-to-bone marrow ratio than synthetic DIR imaging (13.59  $\pm$  7.92 versus 3.72  $\pm$  1.78,  $p < 0.001$ ).

**Table 3** Comparison between the two MR sequences evaluated in the detection of synovitis in each of peripatellar area

	CE T1-weighted FSPGR imaging		Synthetic DIR imaging		<i>p</i> value
	Presence	Absence	Presence	Absence	
<b>All areas</b>					
Reader 1	41 (27.3%)	109 (72.7%)	50 (33.3%)	100 (66.7%)	< 0.001
Reader 2	42 (28.0%)	108 (72.0%)	41 (27.3%)	109 (72.7%)	< 0.001
<b>Suprapatellar area</b>					
Reader 1	8 (26.7%)	22 (73.3%)	10 (33.3%)	20 (66.7%)	< 0.001
Reader 2	8 (26.7%)	22 (73.3%)	10 (33.3%)	20 (66.7%)	< 0.001
<b>Intercondylar area</b>					
Reader 1	4 (13.3%)	26 (86.7%)	9 (30.0%)	21 (70.0%)	0.005
Reader 2	8 (26.7%)	22 (73.3%)	4 (13.3%)	26 (86.7%)	0.048
<b>Infrapatellar area</b>					
Reader 1	8 (26.7%)	22 (73.3%)	6 (20.0%)	24 (80.0%)	0.175
Reader 2	6 (20.0%)	24 (80.0%)	8 (26.7%)	22 (73.3%)	0.029
<b>Medial peripatellar area</b>					
Reader 1	11 (36.7%)	19 (63.3%)	10 (33.3%)	20 (66.7%)	0.001
Reader 2	10 (33.3%)	20 (66.7%)	11 (36.7%)	19 (63.3%)	< 0.001
<b>Lateral peripatellar area</b>					
Reader 1	10 (33.3%)	20 (66.7%)	15 (50.0%)	15 (50.0%)	0.245
Reader 2	10 (33.3%)	20 (66.7%)	8 (26.7%)	22 (73.3%)	0.078

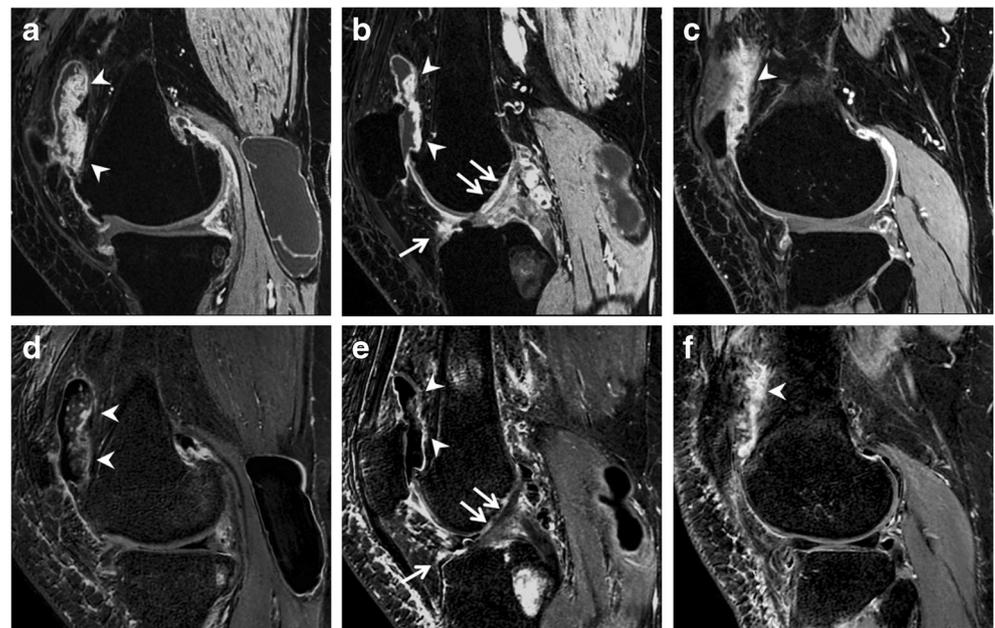
Data in all area mean numbers of joint sites in 30 subjects, with the percentage of the total sample of 150 peripatellar areas in parentheses. Data in each of five peripatellar area mean numbers of subjects, with the percentage of the total sample of 30 in parentheses. *P* values are based on chi-square test or Fisher’s exact test  
*CE* contrast-enhanced, *FSPGR* fat-suppressed spoiled gradient-recalled, *DIR* double-inversion recovery

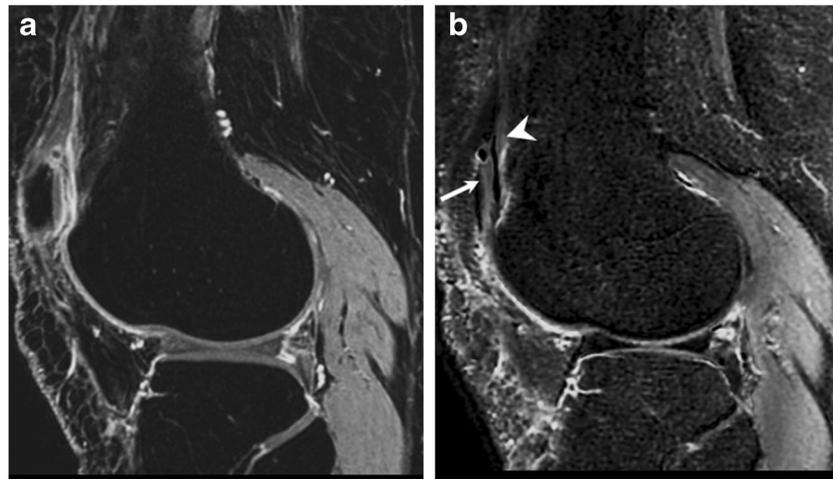
**Discussion**

Synthetic MRI is one of the advances in MR techniques that produces multi-contrast images within a single scan, based on MR quantification, and includes T1-weighted, T2-weighted, PD-

weighted, and inversion recovery images [25]. It has been applied to brain imaging and some studies have shown acceptable image quality in clinical practice [25–27]. Synthetic DIR MRI could be reformatted by applying two TI times, and the oedematous thickened tissue was visible after the two

**Fig. 2** Images from a 54-year-old man with left knee pain. Both the three-dimensional fat-suppressed contrast-enhanced T1-weighted image (a–c) and synthetic double-inversion recovery image (d–f) show synovitis in the medial peripatellar area (arrowheads in a and d), suprapatellar area (arrowheads in b and e), intercondylar area (arrows in b and e), and lateral peripatellar area (arrowheads in c and f), as assessed by both readers. Less effectively suppressed bone marrow fat in synthetic DIR





**Fig. 3** Images from a 59-year-old woman who underwent knee magnetic resonance imaging due to left knee pain. **a** The synovium is well visualised on the three-dimensional fat-suppressed contrast-enhanced T1-weighted image, and the thickness of the synovium is less than 2 mm. Both readers considered this as an absence of synovitis in this

area. **b** The synovium (arrowhead) is well visualised, although with low contrast, on synthetic double-inversion recovery images, and both readers misinterpreted the cartilage of the lateral articular facet of the patella (arrow) as thickening of the synovium

suppressions. Although the overall image quality of T1-weighted CE-MRI was superior to that of synthetic DIR imaging, synthetic DIR imaging provided sufficient to excellent imaging quality. Previous investigation by Jahng et al. first showed potential of DIR sequence replacing CE-MRI in assessing knee joint synovitis [18]. Herein, by applying synthetic MR to knee synovitis, we investigated synthetic DIR MRI for evaluation of knee synovitis, and it has not been reported previously.

In the current study, we used synthetic DIR MRI, applying two different inversion times that suppressed fat signal intensity of the fat pad and water signal intensity of the joint effusion. We hypothesised that the synovium would be accentuated and synovitis could be evaluated without the need for contrast agent on MRI. The synovial scoring we used in was modified from that used in a previous study [28]. Our study demonstrated that the high signal intensity and thickening seen on synthetic DIR

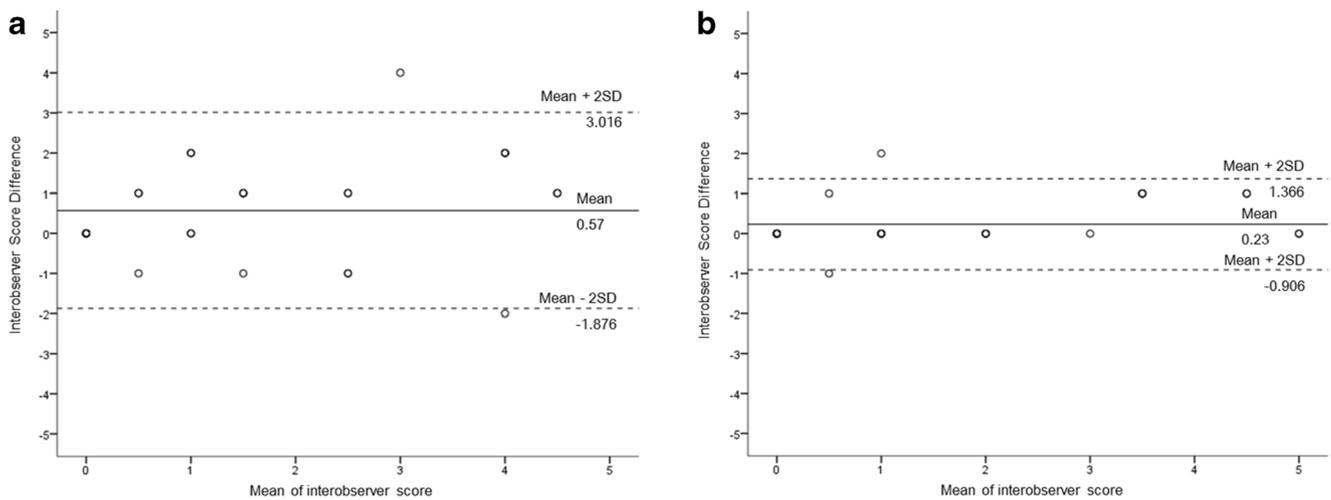
MRI correlated directly with those observed on T1 CE-MRI and indicated synovial enhancement due to synovitis.

There was no statistical significant difference in detecting synovitis in both MR imaging by both readers. And the accuracy of synthetic DIR imaging for detecting synovitis compared to that of T1-weighted CE-MRI was relatively good (80–82%). The interobserver agreement in detecting synovitis (Table 4), the readers showed moderate agreement on synthetic DIR image. For suprapatellar area and the medial patellar area, where other structures (ligament, cartilage, vascular structure) are relatively far from the synovium, the respective interobserver agreement was better than intercondylar and lateral peripatellar areas. Recognition of these limitations may help in interpreting synovitis on synthetic DIR imaging. We found a tendency of higher relative signal intensity of synovium, effusion, and bone marrow in T1-weighted CE-MRI compared to synthetic DIR imaging, without statistical significance. The relative SI of synovium-to-bone marrow ratio was higher in T1-weighted CE-MRI than in synthetic DIR imaging, and that of synovium-to-effusion ratio was higher in synthetic DIR imaging than in T1-weighted CE-MRI. It was inconsistent with previous investigation using conventional DIR imaging to evaluate the synovitis of knee which reported both of relative contrast were higher in DIR imaging than in CE-MRI [21]. There were similar results of synovium-to-effusion ratio (T1-weighted CE-MRI,  $0.86 \pm 0.64$ ; synthetic DIR imaging,  $26.58 \pm 52.14$ ;  $p < 0.001$ ) and synovium-to-bone marrow ratio (T1-weighted CE-MRI,  $19.51 \pm 9.39$ ; synthetic DIR imaging,  $6.53 \pm 7.34$ ;  $p < 0.001$ ) even by using the same equation of previous study [21]. This might be due to less effectively suppressed bone marrow fat in synthetic DIR imaging than in T1-weighted CE imaging, but it does not significantly affecting evaluation of the synovium (Figs. 2 and 3).

**Table 4** Interobserver agreement in the evaluation of synovitis

Parameter	Weighted $\kappa$ value	
	CE T1-weighted FSPGR imaging	Synthetic DIR imaging
Detection of synovitis	0.83 (0.73–0.92)	0.58 (0.43–0.72)
Suprapatellar area	0.92 (0.76–1.00)	0.62 (0.31–0.92)
Intercondylar area	0.62 (0.32–0.91)	0.53 (0.20–0.86)
Infrapatellar area	0.81 (0.57–1.00)	0.63 (0.30–0.96)
Medial peripatellar area	0.93 (0.79–1.00)	0.71 (0.45–0.97)
Lateral peripatellar area	0.85 (0.65–1.00)	0.40 (0.11–0.69)
Sum of synovitis score	0.65 (0.55–0.75)	0.44 (0.34–0.53)

Data are presented with 95% confidence interval in parentheses  
 CE contrast-enhanced, FSPGR fat-suppressed spoiled gradient-recalled,  
 DIR double-inversion recovery



**Fig. 4** Bland-Altman plots to show levels of interobserver agreement in evaluating the degree of peripatellar synovitis for synthetic DIR sequence (a) and CE-MRI (b). Solid lines indicate the mean difference and dashed lines the 95% confidence interval around the mean difference of the repeated measures

To the best of our knowledge, our study represents the first to evaluate the synovitis of knee using synthetic DIR imaging compared to T1-weighted CE-MRI. Synthetic MR imaging is one of the accelerating MR techniques which can automatically generate variable sequences by single scan and also can provide quantified maps that showing absolute values of physical properties of patient [25, 29]. In the current study, no quantitative measurements were made to evaluate the synovium. Further study evaluating the absolute value of synovium using synthetic MR imaging is expected to evaluate synovitis more objectively. There are some limitations to this study. First, this study was a pilot study with retrospective design and small number of patients for assessing synovitis of knee joint using synthetic DIR sequence. Further study with prospective non-inferiority design is necessary to assess the clinical feasibility of this new imaging technique. Second, the

actual number of patients with synovitis was small. Further studies that include a large number of patients suffering from inflammatory or infectious synovitis of the knee are needed to generalise the results of this study. Third, we did not use a 2D spin-echo T1-weighted CE sequence, but a 3D SPGR CE sequence. According to a previous study [30], the 3D SPGR CE sequence showed accuracy and specificity comparable to that of MR arthrography for evaluating synovitis of the ankle joint. We also use 3D SPGR CE imaging in daily practice. Visualisation of the synovium and the image quality of 3D SPGR CE imaging were excellent in our study. Fourth, the reference standard of synovitis was not a pathology result. However, the aim for this study was to evaluate the agreement of synthetic DIR sequence and T1-weighted CE-MRI (which is a non-invasive sensitive and accurate method for diagnosing synovitis) in evaluation of synovitis of knee.

**Table 5** Comparing relative signal intensity and relative contrast of measurements in two imaging

	CE T1-weighted FSPGR imaging	Synthetic DIR imaging	<i>p</i> value
<b>Relative signal intensity</b>			
Synovium	15.81 ± 9.86	12.39 ± 11.50	0.086
Effusion	22.64 ± 19.18	17.73 ± 17.21	0.360
Bone marrow	3.35 ± 0.95	3.07 ± 1.98	0.178
<b>Relative contrast</b>			
Synovium to effusion	5.46 ± 4.47	11.36 ± 11.06	0.003
Synovium to bone marrow	13.59 ± 7.92	3.72 ± 1.78	<0.001

Data are presented with mean value ± standard deviation. *P* values are based on Wilcoxon’s signed-rank test

CE contrast-enhanced, FSPGR fat-suppressed spoiled gradient-recalled, DIR double-inversion recovery

In conclusion, synthetic DIR imaging showed a moderate degree of interobserver agreement and good accuracy for detecting synovitis. Though it has limitations, it may play a role in imaging of degenerative joint disease or larger cohort scientific studies where gadolinium application is not feasible.

**Funding** This work was supported by a National Research Foundation (NRF) grant funded by the Korea government, Ministry of Science and ICT (MSIP, 2018R1A2B6008076).

**Compliance with ethical standards**

**Guarantor** The scientific guarantor of this publication is Young Han Lee.

**Conflict of interest** The authors of this manuscript declare no relationships with any companies, whose products or services may be related to the subject matter of the article.

**Statistics and biometry** No complex statistical methods were necessary for this paper.

**Informed consent** Written informed consent was waived by the Institutional Review Board.

**Ethical approval** Institutional Review Board approval was obtained.

#### Methodology

- Retrospective
- Diagnostic or prognostic study
- Performed at one institution

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