Adding MERGE Sequence to Routine MRI Examination of the Knee: Is it Valuable?

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Abstract

Background: Osteoarthritis is a leading cause of disability which has major implications in elderly and public health. Early detection is critical for understanding the disease progression which can contribute in development of new treatment strategies to stop or slow its progression. MRI has excellent soft tissue contrast and advanced techniques have improved its ability to evaluate cartilage morphology and macromolecular changes.

Aim of Study: To test the value of adding T2 MERGE sequence to the routine (MRI) protocol of the knee for early detection of cartilage changes around the knee.

Patients and Methods: We retrospectively evaluated the images of 107 patients (64 male and 43 female) age ranged between 23-52 years (mean 43.52) who underwent MRI examination of the knee at Menofia University Hospital between June 2019 and February 2020.

Results: Our study was a retrospective study done between June 2019 and Feb. 2020 on 107 patients. The patient's age ranged from 23 to 67 years with the mean age 45.6 ± 12.7 years. The study included 64 males and 43 females.

There was slight agreement between T2WI and surgical grading ($\kappa 0/172$, $p<0.001$), while there was total agreement between 3D merge and surgical grading ($\kappa 1.00$, $p<0.001$).

3D MERGE had 100% sensitivity, 100% PPV and 100% overall accuracy compared to Arthroscopic findings.

Conclusion: Adding MERGE sequence to the routine protocol of knee MRI has improved sensitivity for detection of early cartilage lesions.

Key Words: Osteoarthritis (OA) – Knee – MRI – 3D-MERGE (Multiple Echo Recombined Gradient Echo).

Introduction

OSTEOARTHRITIS (OA) is a leading cause of lower extremity disability among elderly. Its pathogenesis is based on changes in articular cartilage with progressive loss of its hyaline matrix and increase in water content [1-4].

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A sensitive method for detecting structural and functional changes of cartilage in the early stages of OA is required for assessing the progression of disease and monitoring the response to therapy [5].

MRI is able to assess OA related morphological abnormalities with evaluation of cartilage thickness. It also can be helpful in detecting changes in biochemical composition of the cartilage in early stages [6,7,8].

Many Standard sequences such as T2-weighted and proton density-weighted spin-echo and turbo spin-echo sequences with and without fat suppression can detect cartilagenous defects [9].

Dedicated sequences for cartilage evaluation improve the reliability of MRI in early detection of cartilage abnormalities such as 3D spoiled gradient echo (SPGR) or 3D fast low-angle shot (FLASH) sequences with fat saturation and 3D double-echo steady-state (DESS) sequences, which showed sensitivity and specificity as high as 96% and 95%, respectively [10,11].

These techniques provide T2 quantification of the cartilages, which can be a promising imaging biomarkers of osteoarthritis which can assess cartilage quality and susceptibility to injury with non-invasive way [12,13].

List of Abbreviations:

OA	: Osteoarthritis.
MRI	: Magnetic resonance imaging.
3D	: 3 Dimensional.
MERGE	: Multiple Echo Recombined Gradient Echo.
MEDIC	: Multi-echo Data Image Combination.
DESS	: Double Echo Steady State.
SPGR	: Spoiled Gradient Recalled Acquisition.
FLASH	: Fast Low Angle Shot.
PPV	: Positive predictive value.
NPV	: Negative predictive value.

T2 mapping techniques can measure alterations in the water and collagen content of cartilage. It enables early detection of biochemical changes in cartilage degeneration before morphological changes are evident in early OA. It also can follow treatment response based on changes in T2 values [14].

Newly developed (MERGE/MEDIC/M-FFE) combination sequence is another MRI sequence useful in imaging of articular cartilage [15].

MERGE ("Multiple Echo Recombined Gradient Echo") is a spoiled T2* weighted sequence for spinal and musculoskeletal imaging developed by GE Healthcare. The corresponding Siemens sequence is called MEDIC ("Multi-Echo Data Image Combination"), while the Philips sequence is called M-FFE ("Merged Fast Field Echo"). These sequences are useful for both volumetric and T2* relaxation time analyses of cartilage [16].

This sequence eliminates the main limitations of other gradient-echo sequences such as chemical shift, low signal-to-noise ratio and image degradation due to susceptibility gradients. This is achieved by acquiring and combining multiple echoes with a high receiver bandwidth instead of using a single low band width echo [17].

Aim of study: This study was performed to test the value of adding T2 MERGE sequence to the routine (MRI) protocol of the knee for early detection of cartilage changes around the knee.

Patients and Methods

Study population:

We retrospectively evaluated the images of 107 patients (64 male and 43 female) age ranged between 23-52 years (mean 43.52) who underwent MRI examination of the knee at Menofia University Hospital between June 2019 and February 2020.

Inclusion criteria were patient who underwent both knee MRI and MRI arthroscopy of the knee.

Exclusion criteria were patient with rheumatoid arthritis or other inflammatory arthritis, bilateral advanced joint space narrowing, and children.

MRI technique:

The MRI was performed on GE Optima MR450w 1.5 T MR system:

- The 3D MERGE sequence was performed using the following imaging parameters: TR 500-950, TE5-20, FOV16, Slice thickness 2.4mm (inter-slice gap 2mm) Flip angle 20°, matrix 256x224, Echo train length 4, band width 31.25. Number of slices about 30. The image acquisition time was 4min and 38sec.

- Conventional sagittal T2-weighted fast spin echo (FSE) images was performed using the following imaging parameters: TR 8.24-9,57ms; TE 139-141ms; FOV140 x 140mm; image matrix 512 x 512; slice thickness, 3mm (inter-slice gap, 0.3mm), flip angle 160°; slice number about 30, and echo train length 24. The image acquisition time was 4min and 5sec.

- Conventional axial T1 weighted FSE images was performed using the following imaging parameters: TR, 609-831ms, TE 10ms, FOV,140 x 140mm, image matrix 384 x 320, slice thickness 3mm (inter-slice gap 1mm), flip angle 111°; slice number about 30, and echo train length 3. The image acquisition time was 3min and 39sec.

Surgical grading of cartilage Lesions: [17]

A 5 point scale grading system; modification of the system originally described by Outerbridge [17] used by the surgeons to categorize cartilage damage as follow:

• Grade 0, normal;

• Grade 1, softening or swelling;

• Grade 2, partial thickness defect;

• Grade 3, fissuring to the level of the subchondral bone; or

• Grade 4, exposed subchondral bone.

In the original Outerbridge classification system, grades 2 and 3 lesions are defined as fragmentation or fissuring with a diameter of less (grade 2) or more (grade 3) than 1 inch.

Imaging evaluation and scoring system: [3]

• Grade 0, normal thickness and signal intensity;

• Grade 1, increased signal intensity without cartilage deformity or cartilage swelling

• Grades 2, partial thickness defect

• Grade 3, fissuring to the level of subchondral bone, less than 1cm in width

• Grade 4, focal (more than 1cm width) or diffuse complete loss of retropatellar cartilage with exposed bone.

The retropatellar cartilage (medial and lateral facets) was analyzed as a single entity. The highest grade of cartilage abnormality was used in cases of multiple retro-patellar cartilage defects.

Statistical analysis:

Data were analyzed by SPSS statistical package version 23 (SPSS Inc. Released 2015. IBM SPSS statistics for windows, version 23.0, Armnok, NY: IBM Corp.). Cohen's κ (or interrater classification) was run to determine the agreement between two surgical grading and each imaging technique. Two sided *p*-value was considered statistically significant.

Kappa agreement:
• <0 Less than chance agreement.
• 0.01-0.20 Slight agreement.
• 0.21-0.40 Fair agreement.
• 0.41-0.60 Moderate agreement.
• 0.61-0.80 Substantial agreement.
• 0.81-0.99 Almost perfect agreement.

Results

There were 107 patients (64 male and 43 female) studied with M/F ratio 1.48/1. Their ages ranged between 23-52 years (mean age 43.52).

The cause for performing MRI examination was knee trauma in 64 patients, knee swelling in 32 patients, continuous pain not responding to analgesic in 11 patients.

Most of studied patients in our study had low-grade cartilage lesions. Surgery identified grade 0 (n=50), grade 1 (n=26), grade 2 (n=8), grade 3 (n=19), and grade 4 (n=4). As most of the patients were young age and underwent knee MRI after trauma to evaluate Cruciate ligaments injury (n=64).

Table (1) showed that There was slight agreement between T2WI and surgical grading (κ 0/172, *p*<0.001), while there was total agreement between 3D merge and surgical grading (κ 1.00, *p*<0.001).

Routine T2WI sequence detected fifteen patients to have grade I cartilage lesion, fourteen patients had grade II lesion, six patients had grade 3 lesion and four patients had grade 4 lesion.

3D MERGE sequence detected twenty six patients to have grade I cartilage lesion, eight patients had grade 2, nineteen patients had grade 3 and four patients had grade 4 cartilage lesion.

Table (2) showed that T2WI had 33% sensitivity, 100.0 positive predictive value (PPV), 57% negative predictive value (NPV) and 64% overall accuracy, while 3D MERGE had 100.0 sensitivity, 100.0% PPV and 100.0 overall accuracy in comparison to surgical findings.

Table (1): *p*-value and κ agreement of used sequences with surgical findings.

Image grading	Surgical grading					κ *p*-value
	0 (n=50)	I (n=26)	II (n=8)	III (n=19)	IV (n=4)	
T2W1:						
Grade 0	50 (100.0)	18 (69.2)	0 (0.0)	0 (0.0)	0 (0.0)	0.172
Grade I	0 (0.0)	8 (30.8)	7 (87.5)	0 (0.0)	0 (0.0)	0.002
Grade II	0 (0.0)	0 (0.0)	1 (12.5)	13 (68.4)	0 (0.0)	
Grade III	0 (0.0)	0 (0.0)	0 (0.0)	6 (31.6)	0 (0.0)	
Grade IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	
3D merge:						
Grade 0	50 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	1.00
Grade I	0 (0.0)	26 (100.0)	0 (0.0)	0 (0.0)	0 (0.0)	<0.001
Grade II	0 (0.0)	0 (0.0)	8 (100.0)	0 (0.0)	0 (0.0)	
Grade III	0 (0.0)	0 (0.0)	0 (0.0)	19 (100.0)	0 (0.0)	
Grade IV	0 (0.0)	0 (0.0)	0 (0.0)	0 (0.0)	4 (100.0)	

Table (2): Sensitivity, specificity, and accuracy for various diagnostic thresholds.

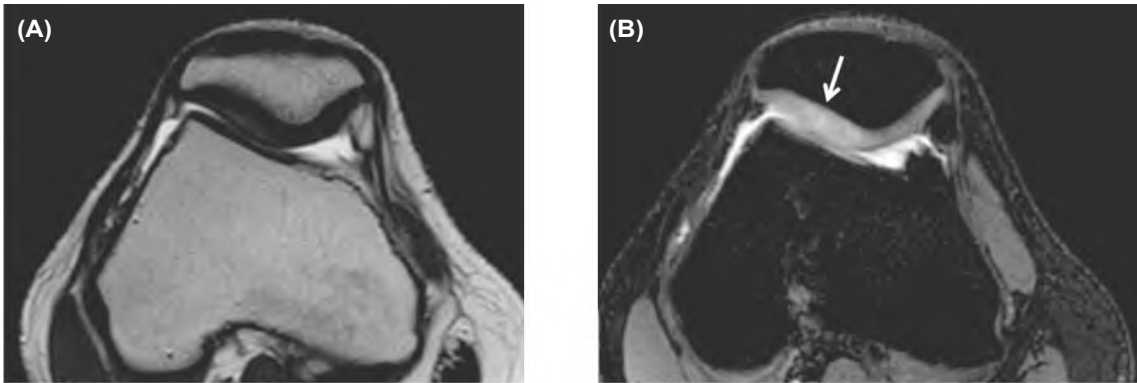|	Sensitivity	Specificity	PPV	NPV	Accuracy
T2W1	33.0	100.0	100.0	57	64
3D MERGE	100.0	100.0	100.0	100.0	100.0

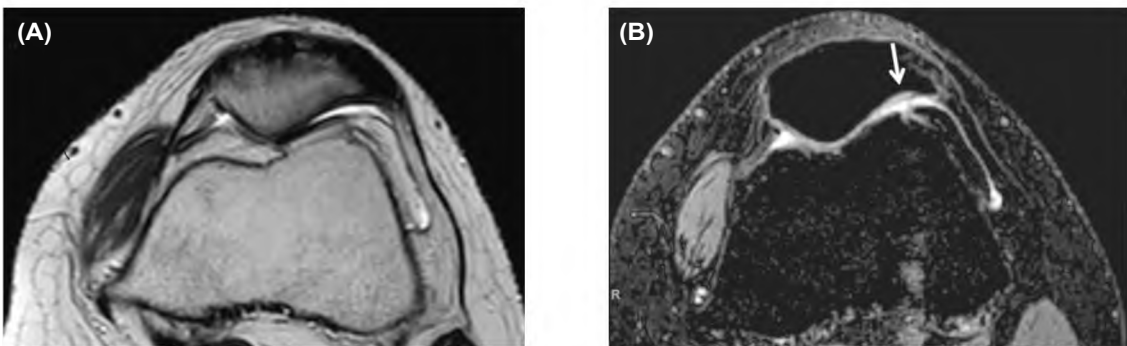Fig. (1): Grade I cartilage lesion clearly visible in 3D MERGE not detected in T2WI.

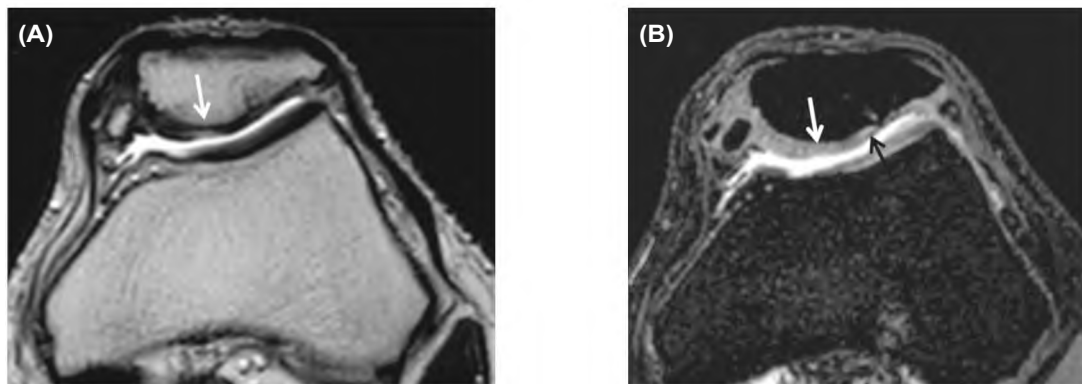Fig. (2): 3D MERGE show grade 1 cartilage lesion of the medial facet not seen at T2WI.

Fig. (3): Cartilage lesion appeared in T2WI as abnormal signal intensity (grade 2) while 3D MERGE partial thickness defect is seen (grade 3) (white arrow). Another area of abnormal signal intensity is seen in 3D MERGE not visible in T2WI. (black arrow).
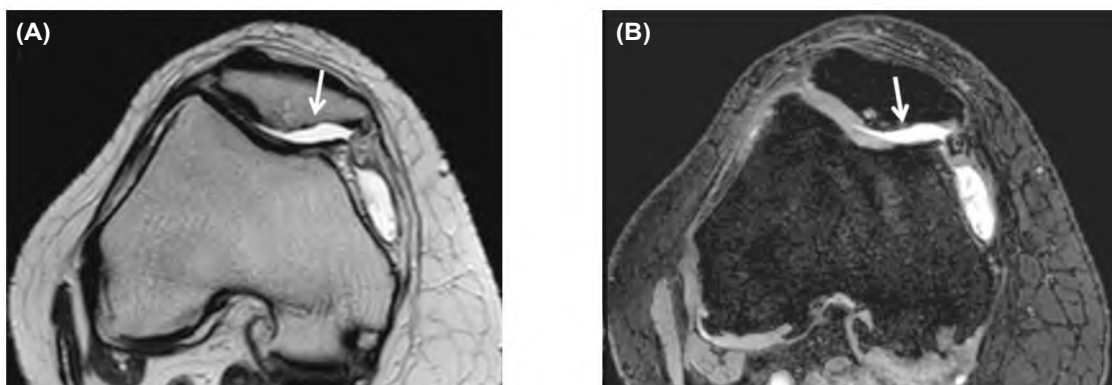

Fig. (4): Grade 4 lesion. Diffuse complete loss of retropatellar cartilage with exposed bone seen in T2WI & 3D MERGE.

Discussion

Early detection of osteoarthritis before the presence of symptoms and radiographic changes is necessary in order to optimize preventive and therapeutic strategies [18].

It was though that the limited efficacy of OA treatment strategies was attributed to the presence of irreversible disease at time of implementation. Therefore, early identification of reversible cartilage changes will enhance treatment effect and slow the disease progression [19].

Radiography is the gold standard for diagnosing OA using the Kellgren-Lawrence (KL) grading system. This system measuring OA severity on a scale of 0 to 4, but it has limitations in assessment of early OA changes involving only cartilages [20,21].

CT arthrography was not routinely used in diagnosis of articular cartilage abnormalities. In a study done by Vande Berg BC et al., [22] they stated that CT arthrography had sensitivity and specificity slightly superior to those of standard MRI (80-88% vs 78-86%) in lesions involving less than half of the cartilage thickness. This method, however, requires an intraarticular contrast injection and is associated with radiation exposure.

Few studies have compared the diagnostic value of standard MRI sequences and MR arthrography in detecting articular cartilage defects in the knee joint. Alparslan et al., [23] stated that the instilled intraarticualr contrast outlines cartilage defects and their contours which increase the image sensitivity to detect cartilage abnormalities.

In a study done by Schmid et al., [16] they find that 2D MEDIC sequence is comparable to the established 3D DESS sequence that has already been described by several authors [24,25]. Kijowki R and Gold G [26] stated that 3D DESS sequence allow obtaining high quality multi-planar reformat images following a single acquisition, thereby eliminating the need to repeat sequences with identical tissue contrast in different planes.

In another study done by Disler et al., [27] they found higher sensitivity for cartilage lesion detection in fat-suppressed SPGR images compared to standard spin-echo MRI sequences (75-85% vs 29-38%). However the specificities of fat-suppressed SPGR and spin-echo sequences were nearly identical about 97%. According to our results, the 3D MERGE sequence had sensitivity similar to that obtained by arthroscope (100% sensitivity). However standard T2WI had 33% sensitivity.

Previous study done by Stehling C et al., [28] showed a high prevalence of OA-related cartilage and meniscal abnormalities in middle-aged, asymptomatic individuals. This is in agreement of our study where Low-grade cartilage lesions predominate in asymptomatic patients who are free of OA symptoms and performed MRI examination for other symptoms (64 patients for knee trauma).

Our study population included a larger proportion of low-grade lesions, which are more difficult to detect, however comparison of the MERG sequence with the routinely performed T2WI in relation to surgical grading obtained from arthroscope showed that T2WI had 67% sensitivity, 64% overall accuracy, while 3D merge had 100.0 sensitivity, 100.0% PPV and 100.0 overall accuracy.

Reviewing the literature and comparing our results with arthroscopy we concluded that the 3D MERG sequence is comparable to previously described sequences optimized for cartilage imaging such as the 3D DESS or 3D SPGR sequences with high sensitivity, and excellent specificity in detecting low to intermediate degrees of cartilage defects compared to surgical findings.

Conclusion:

Adding MERG sequence to routine MRI protocol improved sensitivity for detection of early cartilage lesions within the knee joint. That will allow early diagnosis and management of osteoarthritis and can contribute in decreasing morbidity and complications.

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إختبار إضافة T2 MERGE إلى البروتوكول الروتينى
لتصوير الركبة بالرنين المغناطيسى
هل هى قيمة ؟

خشونة المفاصل هى سبب رئيسى للإعاقة عند كبار السن ولها آثار كبيرة على الصحة العامة.

يعد الاكتشاف المبكر أمراً بالغ الأهمية لفهم تطور المرض حيث أنه يساهم فى تطوير استراتيجيات العلاج مما يساعد على إيقاف المرض أو إبطاء تقدمه.

يتميز التصوير بالرنين المغناطيسى على قدرته على تصوير الأنسجة الرخوة مثل الغضاريف بتباين عالى وقد حسنت التقنيات المتقدمة من قدرته على تقييم شكل الغضروف والتغيرات الجزيئية التى تحدث فيه.

تهدف هذه الدراسة إلى إختبار قيمة إضافة T2 MERGE إلى البروتوكول الروتينى لتصوير الركبة بالرنين المغناطيسى للكشف المبكر عن تغيرات الغضاريف حول الركبة.

شملت هذه الدراسة ١٠٧ مريض خضعوا لفحص الركبة بالرنين المغناطيسى فى الفترة من يونيو ٢٠١٩ إلى فبراير ٢٠٢٠.

تم إجراء التصوير بالرنين المغناطيسى بإستخدام جهاز ١.٥ تسلا وتم فحص جميع الصور لكشف وجود تغيرات بغضاريف الركبة وتقييم درجة تأثر هذه الغضاريف ومقارنتها بالنتائج الجراحية التى ظهرت بمنظار الركبة.

أظهر تحليل البيانات بإستخدام التحليل الإحصائى تطابق كلى بين نتائج المنظار الجراحى وصور فحص الرنين بإستخدام MERGE T2.

توصى هذه الدراسة بإضافة T2 MERGE إلى الفحص الروتينى للركبة بإستخدام الرنين المغناطيسى حيث يساعد على كشف التغيرات الأولية التى تحدث بالغضاريف حول الركبة مما يساعد فى التدخل المبكر لعلاج خشونة الركبة وإبطاء تطور المرض.