Sys Rev Pharm 2020;11(12):2024-2028
A multifaceted review journal in the field of pharmacy

Value of adding a T2 mapping sequence to a routine MR imaging protocol in evaluation of articular cartilage of the knee joint

Samar Shehata Mohamed El Sayed*, Mohamed Amin Nassef, Mennatallah Hatem Shalaby, Ali Haggag Ali

Radiodiagnosis Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt
Corresponding Author: Samar Shehata Mohamed El Sayed

ABSTRACT

Background: Magnetic resonance imaging (MRI) allows direct visualization of all tissues of the knee joint, including the articular cartilage with direct evaluation of chondral lesions. Beyond the morphological evaluation, MRI allows to characterize the structural organization (collagen network) and the matrix content of the cartilage. Such a quantitative approach may be performed in clinical practice by T2 mapping technique which can be used as early biomarker for knee osteoarthritis. T2 relaxation time measurements reflect these pathophysiological changes. T2 mapping technique had recently shown its potentiality to evaluate the quality of the cartilage composition since the transversal relaxation time (T2) reflects the ability of proton molecule to move and to exchange energy inside the cartilaginous matrix. Each variation of matrix content (water, proteoglycan and collagen) or each modification of the organization of the collagen network can induce T2 variations.

Objective: The primary purpose of this study was determine whether the addition of a T2 mapping sequence to a routine MR imaging protocol could or could not improve diagnostic performance in the detection of the articular cartilage lesions and early identification of the cartilage degeneration within the knee joint.

Methods: The current study is a cross sectional study that was conducted at private radiology centres in cairo.in the period between September 2019 and December 2020. The study included 20 patients. 13 Males and7 Females with age range from 25 to 65 years (mean age 41.53 years). Complaining from knee pain after direct trauma or twisting. Routine knee MR images from all patients were assessed for gross articular lesion. Then mean T2 values are obtained and the T2 maps are generated and reviewed. Comparative data of the overall Diagnostic indices of conventional MRI and T2 mapping are taken.

Results: The age of the study group ranged from 25 to 65 years (mean age 41.53 years). The male patients represented the majority of our cases. We noted that there was more affection of the left knee compared to the right one with regional differences in the T2 values were observed as higher T2 values in the medial compartments cartilage (weight-bearing) compared to lateral ones' cartilage (non-weight-bearing). Cases can be categorized according to the site of pain which was correlated later to the T2 values as: 15% anterior 35% medial, 15% lateral and 35% global. Out of the 20 cases, 12/20 (60 %) cases presented by knee pain following direct trauma, and 8/20 (40 %) cases presented by knee pain following knee twisting. All cases underwent conventional MRI with complementary T2 mapping sequence. In this study, the sensitivity, specificity, and accuracy of the conventional MRI results are 82.3%, 100 %, and 85 %, respectively. While the sensitivity, specificity, and accuracy of the T2 mapping finding

Keywords: Knee pain, Magnetic resonance imaging, T2 mapping, Cartilage degeneration.

Corresponding Author: Samar Shehata Mohamed El Sayed
Radiodiagnosis Department, Faculty of Medicine, Ain Shams University, Cairo, Egypt

results are 100 %, 100 %, and 100 %, respectively.
Conclusion: In this study The addition of a T2 mapping of the knee cartilage sequence to a routine MR knee protocol at 1.5 T improved sensitivity in the detection of cartilage lesions within the knee joint from 82.3 % to 100 %, with improvement of accuracy from 85 % to 100%. The improvement in sensitivity with use of the T2 maps was in the identification of early cartilage degeneration.

INTRODUCTION

Articular cartilage is a non-vascularized tissue where chondrocytes are surrounded by an extracellular matrix composed of two major constituents: proteoglycan, responsible for hydration and deformability, and collagen, responsible for stiffness. A primary function of articular cartilage is absorption and redistribution of biomechanical forces applied to the joint through activities of daily living. *(1).*

Osteoarthritis (OA) is the most common form of arthritis. It is characterized by progressive degeneration and eventual loss of cartilage tissue, and often accompanied by subchondral bone modifications and synovial inflammation. The most affected joints are the knee, hip, and hands. (OA) is mainly observed in older population. And in some cases, OA may also be secondary to focal cartilage lesions, especially in young sportive patients, related or not to direct trauma. *(2).*

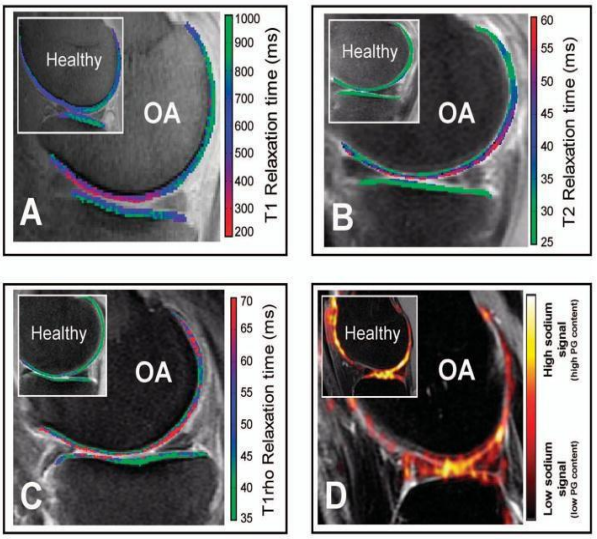
Before structural changes manifest, the cartilage tissue is subjected to biochemical alterations, including a loss of proteoglycans (PG) and deterioration of the collagen network within the cartilage, which cause increased mobility of water and a concomitant increase in water content. These early changes cannot be detected using classical methods such as radiography. *(2)* The prospects for slowing or even stopping early osteoarthritis are generally thought to be much stronger than those for slowing more advanced forms of the disease. Thus, successful treatment of patients with osteoarthritis requires early identification of cartilage degeneration within the knee joint. *(3).*

Quantitative MRI techniques including cartilage T2 relaxation time measurements reflect these pathophysiological changes. Such a quantitative MRI structural approach may be performed by MRI-based techniques that have been developed to allow characterization and quantification of the biochemical composition of cartilage. These include relaxometry measurements (T2, T2* mapping), sodium imaging, delayed gadolinium enhanced MRI of cartilage, glycosaminoglycan specific chemical exchange saturation transfer, diffusion weighted imaging (DWI), and diffusion tensor imaging (DTI). These compositional MRI techniques may have the potential to serve as quantitative, reproducible, non-invasive and objective methods to assess OA, particularly in early and pre-radiographic stages of the disease. DWI, DTI, T1rho and T2 relaxation time measurements do not require a contrast agent injection and can be performed on most clinical 1.5 and 3.0 T MRI systems. *(4) (Figure 1)*.

T2 mapping technique had recently shown its potentiality to evaluate the quality of the cartilage composition since the transversal relaxation time (T2) reflects the ability of proton molecule to move and to exchange energy inside the cartilaginous matrix. Each variation of matrix content (water, proteoglycan and collagen) or each modification of the organization of the collagen network can induce T2 variations. *(5).*

The following compartments of articular cartilage are usually investigated: patella (PAT), trochlea (TRO), medial femur (MF), lateral femur (LF), medial tibia (MT), and lateral tibia (LT). The LF/MF compartment can be subdivided in a central and posterior sub-region, the TRO and PAT in a medial, central, and lateral sub-region. The medial and lateral sub-regions of the TRO are often added to the MF and LF Compartment, respectively *(4).* Laminar analysis can be automatically performed and subdivides the segmented compartment, e.g., into a superficial and deeper cartilage layer, the superficial layer is orientated to the articular surface, the deeper layer to the cartilage bone interface. Significantly greater T2 relaxation times are noted in the superficial compared to the deep cartilage layer suggesting that laminar analysis could lead to better and probably earlier identification of cartilage matrix degeneration. *(6).*

Figure 1. (A, B, C and D) A) Delayed gadolinium-enhanced magnetic resonance imaging (MRI) of cartilage (dGEMRIC), B) T2 mapping, C) T1rho mapping, and D) Sodium imaging differentiate between healthy and early-stage knee osteoarthritis (OA) ***(7).***



AIM/ OBJECTIVES

The primary purpose of this study was determine whether the addition of a T2 mapping sequence to a routine MR imaging protocol could or could not improve diagnostic performance in the detection of the articular cartilage lesions and early identification of the cartilage degeneration within the knee joint.

PATIENTS AND METHODS

This study was conducted at private radiology centres in cairo.in the period between September 2019 and December

2020. The study included 20 patients. 13 Males (65%) and7 Females (35%), with age range from 25 to 65 years (mean age 41.53 years). Complaining from knee pain after direct trauma or twisting.

Patients were subjected to full clinical history including the patient's name, age, sex, residence, phone number, complaint, duration of illness and past history.

Before the examination, patients were routinely questioned about any contraindication for MRI examination and instructed to remove any metal objects.

TECHNIQUE

The patients will undergo MR examination using a 1.5 T machine (Achieva and Ingenia, Philips medical system, Eindhoven, Netherlands) using 8 channel dedicated phased array knee coil.

The standard knee protocol (sagittal proton density-SPIR or PD-FS, coronal proton density-SPIR or PD-FS, axial proton density-SPIR or PD-FS, axial T2 weighted image, sagittal T2 weighted image and coronal T1 weighted image) was done. Complementary sagittal or axial T2 maps were displayed by using the available software tools provided by the MR scanner manufacturer.

ETHICAL STATEMENT

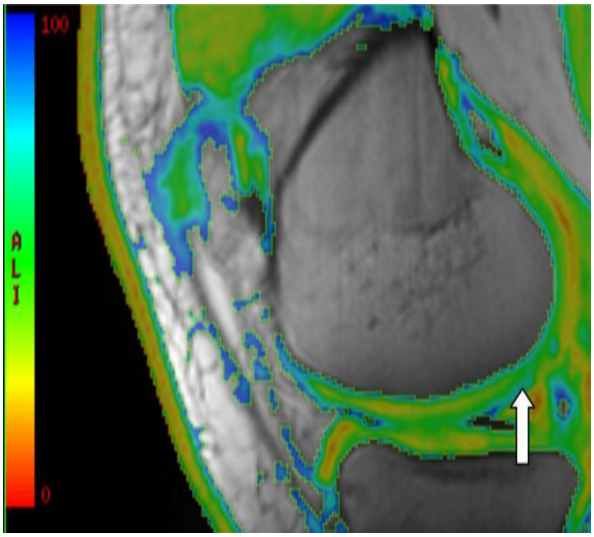
The study was approved by the scientific and ethical committee of the hospital. Written consents were obtained from all patients.

IMAGE ANALYSIS

An intact articular cartilage on conventional MRI was the one with uniform thickness and bright hyper intense signal on PD-SPIR sequence, while affected articular cartilage in OA appears as an area with non- uniform thickness, or of altered signal intensity.

An intact articular cartilage on T2 maps was the one with normal T2 values not exceeding 40 milliseconds delineated by colour coded map (red, yellow or green) *(Figure 2)* represented on a colour coded scale. And cartilage affection on T2 maps in early OA can be delineated as it takes a certain colour (aqua or blue) *(Figure3)* corresponding to high T2 value on the colour coded scale.

Figure 2. Normal articular cartilage by T2 maps.



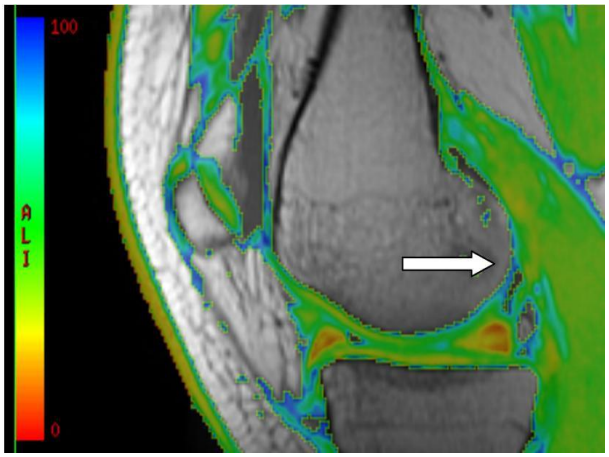


Figure 3. Affected articular cartilage by T2 maps.

STATISTICAL ANALYSIS

Data were collected, revised, coded and entered to the Statistical Package for Social Science (SPSS) version 25.

Data were statistically described in terms of range, mean standard deviation (SD), frequencies (number of cases) and percentages when appropriate.

Accuracy was represented using the terms sensitivity, specificity, positive predictive value, negative predictive value, and overall accuracy.

RESULTS

This study included 20 patients, with an age range from 25 to 65 years (mean age 41.53 years). They presented with knee pain after trauma or twisting. The patients are 13 Males (65%) and7 Females (35%), Cases were classified according to the clinical presentation as 12/20 (60 %) cases presented by knee pain following direct trauma.and 8/20 (40 %) cases presented by knee pain following knee twisting. Cases can be categorized according to the site of pain which was correlated later to the T2 values as: 15% anterior 35% medial, 15% lateral and 35% global. All cases underwent conventional MRI with complementary T2 mapping sequence.

In this study, the sensitivity, specificity, and accuracy of the conventional MRI results are 82.3%, 100 %, and 85 %, respectively (Table 1). While the sensitivity, specificity, and accuracy of the T2 mapping finding results are 100 %, 100 %, and 100 %, respectively (table 2). Comparison of the overall Diagnostic indices of conventional MRI and T2 mapping were done so as 17/20 (85 %) cases were correctly diagnosed by conventional MRI. and 20/20 (100 %) cases were correctly diagnosed by T2 mapping. (Table 3).

Table 1. Diagnostic indices of conventional MRI:

Sensitivity	82.3 %
Specificity	100 %
Accuracy	85 %

Table 2. Diagnostic indices of T2 mapping:

Sensitivity	100 %
Specificity	100 %
Accuracy	100 %

Table 3. Comparative indices of conventional MRI and T2 mapping:

	Sensitivity	Specificity	Positive predictive value	Negative predictive value	Accuracy

Conventional MRI	82.3%	100 %	100%	50%	85 %
T2 mapping	100 %	100 %	100 %	100 %	100 %

DISCUSSION

Radiological imaging are commonly used to evaluate decreased joint space associated with cartilage thinning, but this approach is limited to moderate to severe diffuse cartilage loss, Current clinical MRI evaluation of articular cartilage relies primarily on identification of morphological changes in damaged cartilage. These include determination of cartilage thickness and volume using T1-weighted fat-suppressed gradient-echo imaging and detection of superficial cartilage lesions, primarily with proton density-weighted fast spin-echo sequences. But this is less sensitive to the biochemical changes associated with early OA. *(6)*

In addition to these anatomic techniques, Compositional MR imaging such as cartilage T2 mapping, are being developed to clarify the sensitivity of MRI to biophysical properties of tissue. They play an important role in the assessment of early and potentially reversible cartilage damage. *(8)*

The main clinical application for T2 mapping involves the detection of early cartilage damage prior to the onset of symptoms and prior to detection using conventional screening techniques. *(9)*

Combining the anatomical and functional information may enhance our ability to detect early cartilage degeneration, and to distinguish between different stages of degeneration. *(10)*

T2 mapping has been used to describe the composition of hyaline articular cartilage in the knee joint on the basis of collagen structure and hydration. Analysis of T2 relaxation times in the knee have been performed, usually at 1.5 T or, more recently, 3.0 T, demonstrating the ability to depict abnormalities before there are evident morphologic changes. *(11)*

Among quantitative MRI techniques, T2 mapping and dGEMRIC are currently the most widely used in the clinical setting. Compared with other quantitative MRI techniques, T2 mapping has the advantage that it can be performed non-invasively without the injection of contrast agents; also this sequence and its post-processing software are available in many commercial MRI scanner systems. *(6)*

this study included 20 cases; 14/30 (70 %) of which were diagnosed by conventional MRI as having cartilage abnormalities and 3/20 (15 %) were missed to be accurately diagnosed, this false negative result was considered to be due to minimal alteration of cartilage composition denoting early arthritic changes that were detected by T2 mapping findings.

This agrees with *Chang et al., 2014 (12)* who reported that the potential value of T2 mapping as a biomarker for early cartilage degeneration is highlighted by its inclusion in the MRI protocol for the early osteoarthritis.

A study by *Hesper et al., 2014 (13)* concluded that "Biochemically sensitive" MRI techniques as T2 mapping, are able to add biomarkers for osteoarthritis onset and progression with varying degrees of sensitivity and specificity, and therefore could be meaningful assessment tools for the diagnosis and follow-up of cartilage abnormalities.

The age of presentation in this study ranged from 25- to 65-year-old, with a mean age 41.5 ± 10.4 (mean ± SD).

Out of the 20 cases, 12/20 (60 %) cases presented by knee pain following direct trauma, 8/20 (40 %) cases presented by knee pain following knee twisting. All cases underwent conventional MRI with complementary T2 mapping sequence.

Cases can be categorized according to the site of pain which was correlated later to the T2 values as: 15% anterior 35% medial, 15% lateral and 35% global.

Regional differences in the T2 values were observed. T2 values in the medial compartments (MF, MT) cartilage (weight-bearing) regions were higher than those in the lateral ones (LF, LT) cartilage (non-weight-bearing) regions. And this agrees with *Hesper et al., (2014). (13)*

T2 mapping may provide the basis for diagnosis and follow-up evaluation of cartilage injury and response to cartilage treatment and repair. Once a set of standardized protocols are developed and proposed, subsequent studies are needed to determine specific values or distribution of values, which are associated with healthy and damaged cartilage. *(6)*

T2 mapping has proven to be a useful predictor of cartilage degeneration and repair tissue following surgical intervention in the knee. *(6)*

Among quantitative MRI techniques, T2 mapping and dGEMRIC are currently the most widely used in the clinical setting. The specific values associated with healthy and damaged cartilage remain variable and not well understood. The lack of understanding of factors that contribute to the variable values in the literature has hindered the inclusion of these techniques as part of standard clinical care. *(6)*

T2 mapping despite all the advantages, and its contribution to enhancing cartilage status assessment, is still in its limited role, as its values are based on several factors, including the biochemical status of the cartilage, physics variables involved in obtaining the mapping, and the physiology of the individual patient. So the current literature still lacks clinical correlation.

A study by *Surowiec et al., 2013 (6)* reported that the potential clinical applications of quantitative mapping are vast, but, before the clinical community can take full advantage of this tool, it must be automated, standardized, validated, and have proven reproducibility prior to its implementation into the standard clinical care routine.

CONCLUSION

In conclusion this study confirms that addition of T2 maps to standard views of the MR knee protocol improved accuracy in diagnosing early cartilage degeneration in knee pain and it provides a useful addition to standard MR imaging when cartilage degeneration is suspected especially among the young population. Helping the target of the future to early diagnose the cartilage degeneration and hopefully to prevent the disease process as well.

REFERENCES

1. Baum T., Joseph G.B., Karampinos D.C. et al.: Cartilage and meniscal T2 relaxation time as non-invasive biomarker for knee osteoarthritis and cartilage repair procedures. Osteoarthritis and Cartilage. (2013); 23:1474-1484.
2. Liess C., Lusse S., Heller M. et al.: Detection of changes in cartilage water content using MRI T2-mapping in vivo. Osteoarthritis and Cartilage. (2002); 10:907–913.
3. Kijowski., Donna G., Geoffrey S. et al.: Addition of a T2 Mapping Sequence to a Routine MR Imaging Protocol. Evaluation of the Articular Cartilage of the Knee. (2013);

267(2):503-513.
4. Guermazi A., Alizai H., Crema M.D. et al.: Compositional MRI techniques for evaluation of cartilage degeneration in osteoarthritis. Osteoarthritis and Cartilage. (2015); 23:1639-1653.
5. Stehling C., Baum T., Mueller-Hoecker C. et al.: A novel fast knee cartilage segmentation technique for T2 measurements at MR imaging data from the Osteoarthritis Initiative. Osteoarthritis and Cartilage. (2011); 19:984-989.
6. Surowiec R. K., Lucas E. P., Fitzcharles E. K. et al.: T2 values of articular cartilage in clinically relevant subregions of the asymptomatic knee. Knee Surg Sports Traumatol Arthrosc. (2013); 16:421-426.
7. Regatte RR, Akella SV, Lonner JH, Kneeland JB, Reddy R. et al.: T1rho relaxation mapping in human osteoarthritis (OA) cartilage: Comparison of T1rho with T2. J Magn Reson Imaging. (2016); 23:547–53.
8. Altman RD, Am J. et al.: Early management of osteoarthritis. Manag Care; 16(SupplManagement) (2010); S41–S47.
9. Burstein D, Hunter DJ. et al.: “Why aren’t we there yet?” Re-examining standard paradigms in imaging of OA: summary of the 2nd annual workshop on imaging based measures of osteoarthritis. Osteoarthritis Cartilage (2009); 17(5):571–578.
10. Poh CL and Sheah K. et al.: Visualization of Articular Cartilage Using Magnetic Resonance Imaging Data. ICBME 2008, Proceedings (2009); 23: 386–389.
11. Crema MD, Roemer FW, Marra MD, Burstein D, Gold GE, Eckstein F, et al.: Articular cartilage in the knee: current MR imaging techniques and applications in clinical practice and research. Radiographics (2011); 31:37–61.
12. Chang G. and Regatte R. et al.: Advanced MRI of Cartilage and SubchondralBone in Osteoarthritis.Springer-Verlag Berlin Heidelberg. (2014); 177:191.
13. Hesper T, Harish SH, Daniela B, Götz HW, Rüdiger K, Christoph Z, Bernd B. et al.: T2* mapping for articular cartilage assessment: principles, current applications, and future prospects, # ISS (2014).