How to Cite:

Ghoneim, S. E. A., Younis, R. L., Eltomey, M. A., & Elshafey, K. E. (2022). Role of MRI and T2 mapping in osteoarthritis of knee joint. *International Journal of Health Sciences*, *6*(S5), 4710–4722. https://doi.org/10.53730/ijhs.v6nS5.9599

Role of MRI and T2 mapping in osteoarthritis of knee joint

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Abstract --- Introduction: osteoarthritis is the most common joint disease and the leading cause of long-term disability, placing tremendous financial burdens at the individual and societal levels. Indeed, the onset of biochemical changes leading to irreversible cartilage loss. Objective: to clarify the role of conventional MRI anT2 mapping in patients with osteoarthritis of knee joint. Materials and methods: This prospective study was conducted between June 2019 and July 2021, on 40 cases; 30 patients clinically presented with knee pain and 10 healthy volunteers as a control group. They were referred from outpatient clinics and orthopedic surgery department to Radiodiagnosis and Medical Imaging Department of Tanta university hospitals for assessment by MRI. This study was approved by the ethics committee of Tanta University. Results: The mean and standard deviation for T2 values of cartilage that measured at 4 compartments of the knee joint were elevated in patients clinically suspected to have osteoarthritic changes than healthy volunteers with statistically significant P values (<0.001) at 4 compartments. Conclusions: MRI is a powerful non-invasive tool for both diagnosis and characterization of cartilage degeneration. T2 mapping is potential MR imaging techniques that reflect changes in the biochemical composition of articular cartilage; this non-invasive method helps in assessing early cartilage degenerative changes in patients with early OA changes of the knee joint. T2 mapping also help in initiating early treatment, monitoring the disease progression and follow-up of operative cartilage repair procedures.

International Journal of Health Sciences ISSN 2550-6978 E-ISSN 2550-696X © 2022.

Manuscript submitted: 27 Feb 2022, Manuscript revised: 9 April 2022, Accepted for publication: 18 June 2022 4710

Introduction

Knee osteoarthritis (OA) is a chronic joint disease affecting one-third of elderly people. Nevertheless, joint injury also contributes to acute and long-term cartilage degradation in the younger population (Musumeci, 2017). The knee joint is one of the regions of the body that is most commonly prone to injury during sports and everyday activities, joint injuries frequently lead to cartilage degeneration, which ultimately results in OA (Soellner, Goldmann, Muelheims, Welsch, & Pachowsky, 2017). Osteoarthritis is a multifactorial, slowly progressive degenerative disorder of the joints leading to irreversible damage of the cartilage, sclerosis of subchondral bone and synovial inflammation, as a consequence of increasing longevity and obesity, the cost of OA to the health care system rapidly grows (Pers et al., 2016).

The traditional imaging tool for OA is plain radiography, with joint space narrowing offering an indirect measure of cartilage loss and meniscal tears. However, Magnetic resonance imaging (MRI) is now widely used for the evaluation of osteoarthritis because it allows the visualization of intra-articular pathologies that are not evident on plain radiography (Yoon et al., 2016). The capacity for cartilage self-repair is limited due to its unique structure, as it lacks blood supply, nerves and lymphangion; cartilage absorbs supplements mainly from the synovial fluid (Zeckser, Wolff, Tucker, & Goodwin, 2016). Characteristic changes in the cartilage macromolecular matrix occur with OA, including a decrease in proteoglycan content and disruption of the highly organized collagen fiber network; various quantitative MRI techniques have been used to identify changes in the composition and ultrastructure of articular cartilage in patients with OA (Liu et al., 2015).

The T2 of cartilage is one of the most commonly used MRI parameters and has been shown to be sensitive for detection of cartilage degeneration. However, cartilage T2 is a complex measurement that is influenced by multiple factors including water and macromolecular content, organization of the collagen fiber network, cartilage loading and orientation of cartilage relative to the main magnetic field (Liu et al., 2015). T2 relaxation time measurements have been proven useful with respect to prediction of cartilage loss and early onset of OA at the knee, T2 relaxation time measurements have been reported to correlate with collagen disruption, collagen orientation and increasing intra-cartilaginous water contents (Jungmann et al., 2015). Mean T2 relaxation times significantly increased with increasing morphological cartilage defect (Soellner et al., 2017).

Quantitative T2 mapping has been investigated in a considerable number of studies and has some major advantages compared to other quantitative MR sequences, such as gagCEST imaging, dGEMRIC or sodium imaging, as it is technically less demanding, it also does not require intravenous administration of contrast agent compared to dGEMRIC and can also be performed at lower field strengths compared to the gagCEST and sodium imaging (which both highly

benefit from ultra-high field strength) (Apprich et al., 2020). T2 mapping has been used in numerous studies to assess repair tissue after different cartilage repair procedures (Apprich et al., 2020).

The traditional OA drugs are effective in reducing pain and inflammation but insufficient to slow, stop or reverse the joint damage and are frequently associated with adverse effects, new OA drugs such as biologic agents and chemotherapeutic drugs show more marked effects, fewer side effect and look more promising than traditional OA drugs (Zhang, Ouyang, Dass, & Xu, 2016). The aim of this work is to evaluate the role of conventional MRI and T2 mapping in patients with osteoarthritis of knee joint.

Materials and Methods

This prospective study was conducted between June 2019 and July 2021, on 40 cases; 30 patients (12 males & 18 females) clinically presented with knee pain and 10 healthy volunteers (3 males & 7 females) as a control group. The patient's ages ranged from 25-56 years with a mean age of 38.30 ± 6.49 years and the healthy volunteer's ages ranged from 23-44 years with a mean age of 34.70 ± 4.99 years. They were referred from outpatient clinics and orthopedic surgery department to Radio-diagnosis and Medical Imaging Department of Tanta university hospitals for assessment by MRI. This study was approved by the ethics committee of Tanta University.

Inclusion criteria: patients complaining of knee pain, decreased range of movement of knee joint and unremarkable X-ray findings.

Exclusion criteria: patients with deformities or mal-alignment of the lower extremity, patients contraindicated for MRI e.g., cardiac pacemaker, aneurysmal clips, orthopedic implants, intravascular stents, coils and filters and patients suffering from claustrophobia.

All patients were assessed for Thorough history taking (personal history, complaint, present history, past history and the presences of any other disease or previous operation were recorded), Clinical examination including (general examination, body weight was recorded and BMI was calculated (BMI= weight (kg)/height2(m2)); as BMI (18.5 – 24.9 kg/m²) of normal weight cases and BMI \geq 30 kg/ m² of obese cases and local examination of knee joint., radiological examination including (plain x-ray of the knee joint AP and lateral views, routine MRI sequences of knee joint (sagittal proton density FAT SAT, sagittal T1 weighted image, sagittal T2 weighted image, coronal proton density FSE, coronal STIR and axial T2 weighted image) and T2 mapping of cartilage), and MRI examination(The study was performed using 1.5 Tesla MRI scanner signa explorer, GE (General Electric) health care machine (closed magnet)).

Patient preparation:

Metallic objects in patient's body or clothes like keys and teeth prosthesis will be removed prior to entrance to magnetic area.

Patient positioning:

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Patient was made to lay down in Supine position with the knee in the center of the coil with the external rotation of 150 to 200, flexed to 50 to 100 and the coil was closed after adequate immobilization and the landmark was set in the center of the coil.

Utilized parameters

T1WI sequence repetition time (TR) of 600 ms, TE of 15 ms, field of view (FOV) = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness), T2WI sequence (TR/TE = 4000/90 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness), Proton density sequence (TR/TE = 2000/10-20 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness), STIR sequence (TR/TE = 4000/120 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness), a sagittal PD-weighted FSE series (TR/TE = 4000/13 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 3 mm slice thickness), a sagittal T2-weighted FSE series (TR/TE = 3700/91 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness), a sagittal T2-weighted FSE series (TR/TE = 3700/91 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness), a sagittal T2-weighted FSE series (TR/TE = 3700/91 ms, FOV = 160 mm, matrix 512×512 , 0.31 mm in-plane resolution, 4 mm slice thickness). Sagittal T2 maps were displayed by using this sequence TR1000 ms, TE=8.3msec, slice thickness: 3mm, slice interval of 0.6mm, Matrix: 256 X 256, FOV: 160 mm.

MRI post processing

The T2 mapping data was transferred to a workstation to be qualitatively and quantitatively assessed. The vendor-provided GE Functool software was used to determine T2 relaxation maps, color-coding with a color scale from 25 ms to 75 ms with 2 ms interval was used.

Image interpretation and lesion characterization

All sequences in the routine MR imaging protocol were first used to evaluate the articular cartilage on the medial femoral condyle, lateral femoral condyle, medial tibial plateau and lateral tibial plateau and to document any lesion on the articular cartilage, osseous lesions, bone marrow edema and soft-tissue lesions. Intact articular cartilage on conventional MRI sequences was the one with uniform thickness and a homogeneous signal on T2 or PD FAT SAT sequences covering the tibial and femoral articular surfaces.

A cartilage lesion was defined as an area of non-uniform thickness and a focal change in the signal intensity of the articular cartilage on T2 or PD FAT SAT sagittal images. Cartilage lesions containing a hyperintense signal representing synovial fluid were defined as defects. In each joint compartment, the number of chondral lesions and T2-value of the chondral lesion using ROI was recorded. The lesions were compared to the color scale, which had steps every 2ms. Cartilage lesions location were manually detected at different topographical locations of the femur and tibia, The knee joint cartilage was assessed according to the following regional compartments: 1- medial femoral, 2- medial tibial, 3- lateral femoral, 4- lateral tibial, any associated meniscal, ligamentous, muscular or bony abnormalities in the knee were reported. The T2 map acquisition is displayed in

Functool where the T2 relaxation time color map is coded and color scale is used. A data point for each echo is plotted when ROI is deposited

- Short T2 structures = Orange to Red
- Intermediate T2 structures = Yellow
- Long T2 structures = Green to Blue

Statistical analysis

Statistical analysis of the present study was conducted, using the mean, standard deviation, student t- test, Chi-square by SPSS V20.

Results

From Table I we found that the average T2 values of articular cartilage at MFc ranged from 31 to 75 ms in patients clinically suspected to have OA changes and from 29 to 42 ms in healthy volunteers which is statistically significant with p value <0.001, The average T2 values of articular cartilage at MTc ranged from 28 to 75 ms in patients and from 28 to 47 ms in volunteers which is statistically significant with p value <0.001, The average T2 values of articular cartilage at LFc ranged from 32 to 74 ms in patients and from 27 to 49 ms in volunteers which is statistically significant with p value <0.001 and The average T2 values of articular cartilage at LFc ranged from 33 to 72 ms in patients and from 26 to 44 ms in volunteers which is statistically significant with p value <0.001 and The average T2 values of articular cartilage at LFc ranged from 33 to 72 ms in patients and from 26 to 44 ms in volunteers which is statistically significant with p value <0.001.

Table II showed that the elevation of T2 values of articular cartilage in the patients who diagnosed as having OA changes by conventional MRI was more than those firstly discovered to have OA by T2 mapping with statistically significant p values of the cartilage at MFc (0.042), at MTc (0.015) and at LFc (0.015). Table III showed that T2 values of articular cartilage at four compartments were elevated in obese than average weight individuals with statistically significant p value (0.007) of cartilage at medial tibial condyle. Table IV showed ROC analysis for the cutoff point for T2 mapping of cartilage was analyzed according to each compartment with >35 ms of cartilage at medial femoral, medial tibial, lateral femoral condyles and >33 ms at lateral tibial condyle with sensitivity ranged between (90% -95%) and specificity of 90% at four compartments; MFc, MTc, LFc and LTc.

Case I:

Clinical presentation: Female patient aged 42 years old, presented with chronic LT knee joint pain.

Diagnosis: Osteoarthritic changes of cartilage at the medial tibio-femoral condyles and lateral femoral condyle of the left knee joint with posterior horn medial meniscus and posterior horn lateral meniscus degeneration. Figure I

Case II:

Clinical presentation: Female patient aged 48 years old, presented with chronic RT knee joint pain.

Diagnosis: Osteoarthritic changes at the medial tibio-femoral & lateral tibio-femoral condyles of the right knee joint with popliteal cyst and mild joint effusion. Figure II

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Discussions

This study included 40 cases, 30 patients clinically presented with knee pain and 10 healthy volunteers as a control group. The patient's ages ranged from 25-56 years with a mean age of 38.30 ± 6.49 years and healthy volunteers ages ranged from 23-44 years with a mean age of 34.700 ± 4.99 years, but in El-Liethy, N. E., & Kamal, H. A. (2021) study included 60 patients, where divided into two groups; control group (20 volunteers) with age range from 19 to 41 years old 26.80 ± 8.05 (mean \pm SD)and patients (40 candidates) with age range from 13 to 57 years old with a mean age 33.00 ± 14.1 (mean \pm SD) (Nebelung et al., 2019). However, the difference noticed between the two studies is a consequence of discrepancy in number of cases and range of their ages.

In our study T2 map acquisition is displayed in functool software to determine T2 relaxation maps and colour coding with a colour scale from 25 ms to 75 ms with 2 ms interval was used, that is in agreement with Bazaldua-Cheda, Héctor M.,(2019) study at which Post-processing of mapping acquisition with the Functool software in the work station was used to determine the average relaxation time, a color scale with values of 20 ms-80 ms was used, with 2 ms intervals to evaluate the cartilage (Bazaldua-Cheda, Onofre-Castillo, & Torres-Gómez, 2019).

In our study the cartilage lesions location were manually detected at different topographical locations of the femur and tibia, and map of T2 relaxation time was analyzed in four knee cartilage compartments (medial femoral condyle, lateral femoral condyle, medial tibial condyle and lateral tibial condyle), This is in agreement with the study of Xie, Yuxue, et al (2021) that showed the cartilage regions of interest (ROI) were manually contoured on T2 mapping images, The femoral cartilage and the tibial cartilage were divided into four compartments (medial femur (MF), medial tibia (MT), lateral femur (LF), and lateral tibia (LT)) (Xie et al., 2021).

Our study showed that significantly higher T2 values in patient with knee pain and clinically suspicted to have osteoarthritic changes than volunteers this is in agreement with Liu, Fang, et al. (2015) study at which cartilage T2 Single was significantly higher in patients with osteoarthritis of the knee than in volunteers (Liu et al., 2015).

In our study we found that significant elevation of T2 values in all four compartments of knee joint in cases suspected to have osteoarthritic changes than the control group, which is in agreement with Mittal, Shruti, et al. (2019) study that showed the average T2 relaxation times of articular cartilage were statistically significantly higher values in all the compartments of knee joint in OA patients as compared to healthy volunteers (Mittal, Pradhan, Singh, & Batra, 2019).

In our study the lateral femoral condyle showed slightly higher T2 values (its mean value = 52.73 ± 10.74) than medial femoral condyle (52.67 ± 9.33) and medial tibial condyle had higher values (51.166 ± 10.07) than the lateral tibial condyle (48.500 ± 8.68) that is in agreement with Hannila, Ilkka (2016) who

reported that the lateral femoral condyle had statistically significantly higher T2 values as compared to the corresponding segments in the medial femoral condyle. In the tibial condyles, MT had significantly higher values as compared to LT (Hannila, Lammentausta, Tervonen, & Nieminen, 2015). And also is in agreement with Abdelaziz, Hussein, et al. (2019) study that showed the medial joint compartment was the most commonly affected compartment than the lateral compartment (Abdelaziz et al., 2019).

In our study the cutoff point for T2 mapping of cartilage was analyzed according to each compartment as >35 ms at medial femoral, medial tibial, lateral femoral condyles and >33 ms at lateral tibial condyle with sensitivity of 95% and specificity of 90%., this is in agreement with Yang, Zhijian, et al. (2021) study that showed that the cutoff point for T2 mapping was suggested as 35.04 ms with a sensitivity of 88.24 (95% CI: 72.5–96.7) and specificity of 97.83 (95% CI: 88.5–99.9) (Yang, Xie, Ou, Zhao, & Lin, 2021).

In our study 73.33% of patients were obese with BMI \geq 30 kg/m², showed increased incidence of osteoarthritic changes with elevated T2 values at all four knee compartments, at MFc (54.067±7.741) , MTc (54.067±9.075) ,LFc (53.600±10.006) and LTc (47.933±7.035) compared to non-obese individuals which showed lower T2 values than obese cases at the same four knee compartments; at MFc (46.600±9.965) ,MTc (39.800±9.121) ,LFc (50.200±8.289) and LTc (44.000±8.031), that is in agreement with Liebl, Hans, et al. (2015) study that showed that subjects with incident TFOA had higher BMIs and knees with incident TFOA had higher mean T2 values in each compartment (Liebl et al., 2015), Also this is in agreement with Bazaldua-Cheda, Héctor M.,(2019) study that provided valuable information in asymptomatic patients, especially in case of overweight where there is a greater axial force in the different compartments covered with joint cartilage in the knee (Bazaldua-Cheda et al., 2019).

The above results showed that quantitative T2 mapping is sensitive even to minor cartilage changes and is able to detect the onset of early-stage OA in knee joints, As T2 relaxation times increase with increasing cartilage defect, so addition of a T2 mapping sequence to a routine MR imaging protocol can improve the detection of early cartilage degeneration within the knee joint.

However, this study has some limitations that consist of a small amount of patients in addition to lack of histological information or arthroscopic correlation, As we investigated full thickness cartilage values and did not consider zonal variation, That different biochemical compositions and orientation of collagen fibrils in different layers may yield different results. On the other hand, we hypothesized that values of full thickness cartilage obtained using the ROI measurement method may be more practical and accessible in clinical use

Conclusions

MRI is a powerful non-invasive tool for both diagnosis and characterization of cartilage degeneration than other imaging modality. T2 mapping is potential MR imaging techniques that reflect changes in the biochemical composition of articular cartilage; This non-invasive method helps in assessing early cartilage

degenerative changes in patients with early OA changes of the knee joint. T2 mapping also help in initiating early treatment, monitoring the disease progression and follow-up of operative cartilage repair procedures.

Acknowledgements: Nil

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Tables:

Table (I):	dis	tributio	n of the	studied	cases a	accordin	ig to T2 v	value	s of art	icular
cartilage	at	medial	femoral,	medial	tibial,	lateral	femoral	and	lateral	tibial
condyles										

		Group								
T2 map findings			Patient			Control			P- valu e	
Cartilage at medial femoral	Range	31 -		75	29	-	42	22	<0.0	
condyle (ms)	Mean ±SD	52.6 7	±	9.3 3	33.9 00	Ŧ	3.4 4	38	<0.0 01*	
Cortilage at medial tibial	Range	28	-	75	28	-	47	11	<0.0	
condyle (ms)	Mean ±SD	51.1 66	±	10. 07	34.0 0	Ŧ	5.1 85	90	<0.0 01*	
Cartilage at lateral femoral	Range	32	-	74	27	-	49	63	<0.0	
condyle (ms)	Mean ±SD	52.7 3	±	10. 71	32.9 00	Ŧ	6.1 73	35	<0.0 01*	
Cartilago at lateral tibial	Range	33	33 -	72	26	-	44	2.6	<0.0	
condyle (ms)	Mean ±SD	48.5 00	±	8.6 8	32.0 00	±	4.6 67	30	<0.0 01*	

Table (II): relation between T2 mapping values of patients with OA changes and others not have OA changes by conventional MRI

	OA cl MRI	han	T-Test					
T2 mapping	Yes				No			
	Mean	±	SD	Mean	±	SD	t	P- value
Cartilage at medial femoral condyle (msc)	58.1 67	±	4.49 1	49.6 43	±	8.94 1	2.19 5	0.042
Cartilage at medial tibial condyle (msc)	59.1 67	±	9.19 6	46.7 86	±	9.53 7	2.68 7	0.015 *
Cartilage at lateral femoral condyle (msc)	60.3 33	±	5.85 4	49.5 00	±	9.01 1	2.68 9	0.015 *
Cartilage at lateral tibial condyle (msc)	49.0 00	±	7.37 6	46.0 71	±	7.34 3	0.81 6	0.425

	Weigh	t	T Test						
	Average			Obese			1-1690		
	Mea n	±	SD	Mea n	±	SD	t	P- value	
Cartilage at medial femoral condyle (msc)	46.6 00	±	9.9 65	54.0 67	H	7.74 1	- 1.74 5	0.09 8	
Cartilage at medial tibial condyle (msc)	39.8 00	±	9.1 21	54.0 67	±	9.07 5	- 3.04 1	0.00 7*	
Cartilage at lateral femoral condyle (msc)	50.2 00	±	8.2 89	53.6 00	±	10.0 06	- 0.68 2	0.50 4	
Cartilage at lateral tibial condyle (msc)	44.0 00	±	8.0 31	47.9 33	±	7.03 5	- 1.04 8	0.30 9	

Table (III): relation between the weight of patients and the affected condyle

Table (IV): ROC curve

ROC curve											
	Cutoff	Sens.	Spec.	PPV	NPV	Accuracy					
Cartilage at medial femoral condyle (msc)	>35	95.0	90.0	95.0	90.0	95%					
Cartilage at medial tibial condyle (msc)	>35	90.0	90.0	94.7	81.8	89.3%					
Cartilage at lateral femoral condyle (msc)	>35	95.0	90.0	95.0	90.0	95.3%					
Cartilage at lateral tibial condyle (msc)	>33	95.0	90.0	95.0	90.0	95.2%					

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Figure (I): (A)X-ray AP standing view showed unremarkable signs of osteoarthritic changes.)B)&(C) Sagittal FAT SAT MRI along the plain of medial (B)and lateral(C) femoral condyles showed intrasubstance area of abnormal high SI not reaching to meniscal articular surfaces of posterior horn of medial meniscus (PHMM degeneration)(green arrow) and of posterior horn of lateral meniscus (PHLM degeneration)(blue arrow). And preserved SI of cartilage at medial and lateral tibio-femoral condyles with uniform cartilage thickness. Post processing sagittal colored T2 mapping MRI: (D)&(E) Sagittal colored post processing T2 mapping MRI, along the plain of medial femoral condyle (D) and lateral femoral condyle (E) Four ROIs are placed on knee joint cartilage (MF, MT, LF & LT condyles posteriorly); showed elevated color coded T2 value of cartilage at MFc (55 msc) blue arrow, MTc (48 msc) red arrow and LFc (47 msc) orange arrow. (F) The associated histogram curve showing drop of the curve at the site of elevated T2 values.



Figure (II): (A) Axial T2WI, (B) Sagittal FAT SAT MRI & (C) Sagittal T2WI MRI along the plain of medial femoral condyle showed well-defined lesion of fluid signal intensity displaying high SI between semimembnosus and semitendinosus muscles (cyst) (blue arrow) with mild knee joint effusion (green arrow), And increased SI of articular cartilage at both medial tibio-femoral condyle with decreased cartilage thickness and irregularity at the cartilage (red arrow). Post processing sagittal colored T2 mapping MRI: (D)&(E) Sagittal colored post processing T2 mapping MRI, along the plain of medial femoral condyle (E) and lateral femoral condyle (F) showed elevated color-coded values of cartilage at MF condyle (74 msc) blue arrow, at MTc (71 msc) red arrow, at LTc (70 msc) orange arrow and at LFc (69 msc) green arrow. (F) The associated histogram curve showing drop of the curve at the site of elevated T2 values.