Section: Radiodiagnosis

Original Research Article

T2* CARTILAGE RELAXOMETRY AT 3T AS A BIOMARKER OF KNEE OA SEVERITY: COMPARTMENT-SPECIFIC ASSOCIATIONS WITH KELLGREN–LAWRENCE GRADING

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ABSTRACT

Background: Knee osteoarthritis (OA) is a common degenerative disorder influenced by modifiable factors such as body weight. Early radiological detection is important for grading and management.

Aim: To assess the correlation between radiographic Kellgren–Lawrence (KL) grades and MRI findings, including morphological changes and T2* relaxometry of articular cartilage and bone marrow.

Materials and Methods: Patients ≥40 years with clinically diagnosed knee OA were included. The cohort comprised 55% males and 45% females, with left knee dominance in 55%. BMI analysis showed 58% overweight, 40% obese, and 2% normal. Weight-bearing anteroposterior radiographs were graded using the KL system: 62% grade II, 28% grade III, and 10% grade IV. MRI assessed osteophytes, bone marrow edema (BME), and T2* relaxation values. Only cartilage with normal or grade I–IIA degeneration was analyzed for T2* values.

Results: KL grade showed significant correlation ($p < 0.05$) with osteophytes at medial and lateral femoral condyles, medial and lateral tibial plateaus and both superior and inferior patellar poles. BME correlated significantly with KL grade at medial ($p < 0.05$) and lateral femoral condyles ($p < 0.01$), but not at tibial, trochlear or patellar sites. T2* relaxometry correlated significantly with KL grade at medial tibial, lateral femoral, and lateral tibial cartilage ($p < 0.05$), with no significant association at medial femoral cartilage. **Conclusion:** KL grading correlates strongly with osteophytes and femoral BME. T2* relaxometry serves as a promising early quantitative biomarker for cartilage degeneration in OA.

Keywords: Osteoarthritis knee, KL grade, T2* relaxometry, MRI, bone marrow edema, BMI.

INTRODUCTION

Osteoarthritis (OA) is a chronic degenerative joint disorder involving progressive structural damage to cartilage, bone, menisci, ligaments, synovium and is the most prevalent form of arthritis, particularly in individuals over 60 years of age.[1] OA may be primary or secondary to abnormal joint mechanics or stress. Although traditionally considered cartilage-centric, emerging evidence shows that synovium and subchondral bone may also initiate disease, and the exact primary site remains uncertain.[2] Obesity is a major modifiable risk factor with mechanical overload accelerating cartilage breakdown.[3] Before age 50, OA is more common in men; after 50, prevalence is higher in women.[4] Malalignment further accelerates compartment-specific degeneration—varus deformity is linked to medial tibiofemoral narrowing, whereas valgus is associated with lateral compartment involvement.[5]

Conventional diagnosis relies on clinical assessment and radiography, demonstrating joint space narrowing, osteophytes and subchondral changes. However, radiographic findings correlate poorly with

symptoms and underestimate early disease.[6] This supports the view of OA as a "whole-organ" pathology, for which MRI offers superior soft tissue and bone evaluation.[7] Multicomponent MRI-based semi-quantitative systems such as WORMS, KOSS, and BLOKS evaluate cartilage, bone marrow lesions, menisci, ligaments and osteophytes.[8-10]

Given that degeneration begins with biochemical changes—loss of proteoglycan and disruption of the collagen matrix leading to increased water content—quantitative MRI such as T2* relaxometry can detect pre-morphologic alterations in cartilage extracellular matrix. T2* mapping reflects collagen integrity, water content and fiber orientation, typically showing elevated T2* values in early OA. Layer-specific T2* analysis further provides compartmental insight, supporting its role as a non-invasive biomarker for early OA severity assessment.

MATERIALS AND METHODS

The present study was conducted in the Institute of Nuclear Medicine and Allied Sciences, Delhi, India. Ethical clearance was obtained from the institutional review board, and written informed consent was taken from all patients or their legally authorized representatives prior to inclusion in the study. The study was carried out over a six-month period from December 2015 to May 2016.

A total of forty patients were prospectively enrolled for the study. All participants provided informed consent to be included after detailed explanation of the study protocol and imaging procedures.

All adult patients with clinically diagnosed osteoarthritis fulfilling the American Rheumatism Association criteria were included. These criteria required the presence of osteophytosis and knee pain along with either age greater than 40 years, joint stiffness lasting less than 30 minutes or palpable crepitus. Diagnosis of osteoarthritis was considered confirmed in the presence of criteria 1 and 2 and at least one among criteria 3, 4, or 5. Both recently diagnosed untreated cases and those on symptomatic management but not receiving disease-modifying agents were included. In cases where both knees met inclusion criteria equally, the self-reported dominant knee was selected for evaluation.

Patients were excluded if they refused consent, were pregnant or had suspected inflammatory arthritis, septic arthritis or crystal-induced arthritis. Additional exclusion criteria included severe comorbid illness disproportionate to the presenting complaint, prior intra-articular injection or aspiration within one month, history of knee surgery, inability to stand for radiography, claustrophobia or the presence of metallic prostheses, cardiac pacemakers or ferromagnetic or haemostatic clips within the central nervous system.

Radiographic imaging of the affected knee was performed using a digital radiographic system ('DRX Evolution X Factor', 500 mA). Anteroposterior radiographs were acquired in a weight-bearing, fully extended position using a standard technique.

After obtaining informed consent and applying all necessary safety precautions, patients were positioned supine with the knee placed in approximately 10 degrees of external rotation. MRI of the knee joint was performed using a 3T MRI scanner (Siemens Magnetom Skyra) with a dedicated surface coil. Imaging was acquired in sagittal, axial, and coronal planes using the following sequences and parameters: T1 TSE sagittal (slice thickness 3 mm, TR/TE 750/8.5 ms), PD TSE FS sagittal (3 mm, 700/24 ms), T2 TSE FS sagittal (3 mm, 5150/91 ms), T1 IRM coronal (3 mm, TR/TE 4860/33 ms, TI 200), 2D T2 MEDIC axial (3.5 mm, 853/16 ms), 3D T2 DESS sagittal (0.6 mm, 14.8/5.0 ms) and ME-GRE sagittal for T2* mapping (3 mm, 486/4.36 ms). MEDIC and DESS sequences were primarily utilized for detailed cartilage evaluation.

Anteroposterior radiographs obtained in weight-bearing extension were evaluated and graded using the Kellgren–Lawrence scoring system, which assesses osteophyte formation, joint space narrowing, subchondral sclerosis, and joint deformity. The scale includes five grades: Grade 0 (normal), Grade 1 (doubtful OA), Grade 2 (minimal OA), Grade 3 (moderate OA), and Grade 4 (severe OA). Only the medial and lateral tibiofemoral compartments were assessed; the patellofemoral compartment was not included.

MRI evaluation included assessment of cartilage defects, subchondral bone marrow edema, osteophytes, subchondral cysts, sclerosis, meniscal abnormalities, ligamentous injuries (anterior cruciate, posterior cruciate, medial collateral, and lateral collateral ligaments), joint effusion, synovial cysts, synovitis and T2* relaxometry. Each knee was evaluated for twelve imaging parameters across the medial and lateral femoral and tibial articular surfaces, medial and lateral patellar facets and the trochlear region. Cartilage defects were assessed by location, severity and approximate size across the medial femorotibial, lateral femorotibial and patellofemoral compartments, using a modified Noyes arthroscopic grading system: Grade 0 (normal), Grade I (signal alteration only), Grade IIA (<50% thickness loss), Grade IIB (50–99% loss), Grade IIIA (full-thickness loss without bone ulceration), and Grade IIIB (full-thickness loss with adjacent bone ulceration). T2* relaxation time of cartilage, an indirect marker of microstructural integrity, was measured using gradient-echo T2* mapping in the sagittal plane by manually placing regions of interest over the medial and lateral articular surfaces of the femur and tibia.

Data were statistically described in terms of mean (±SD), frequencies (number of cases) and percentages when appropriate. Comparison of quantitative variables between two study groups was done using Student t test and by one way ANOVA for more than 2 groups. For comparing categorical data, Chi square test was performed. Exact test was used

instead when the expected frequency is less than 5. A probability value (p value) less than 0.05 was considered statistically significant. All statistical calculations were done using computer programs Microsoft Excel 2007 (Microsoft Corporation, NY, USA) and SPSS (Statistical Package for the Social Science; SPSS Inc., Chicago, IL, USA) version 17.

Table 1: Study variables

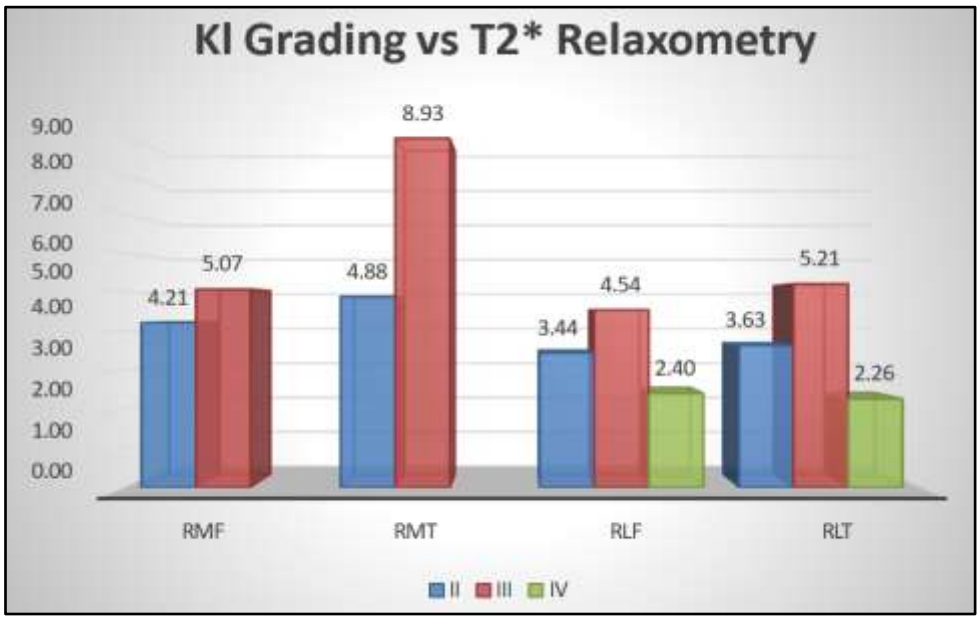
Parameter	Category	Number of Patients (%)
Age Group (years)	40–50	55%
	51–60	30%
	≥61	15%
Gender	Male	55%
	Female	45%
BMI Category	Normal (≤25)	2%
	Overweight (25.1–30)	58%
	Obese (>30)	40%
Dominant Knee	Left Knee	55%
	Right Knee	45%
Kellgren–Lawrence Grade	Grade II	62%
	Grade III	28%
	Grade IV	10%

Table 2: KL score and osteophyte grading

Osteophyte Grading		KL Grade			Total	p- value
		II (n- 25)	III (n- 11)	IV (n- 4)		
oMF*	I	16	2	0	18	
	II	9	9	4	22	< 0.05
oMT*	I	22	6	0	28	
	II	3	5	4	12	< 0.05
oLF*	O	3	0	0	3	
	I	16	2	2	20	
	II	6	9	2	17	< 0.05
oLT	O	4	0	0	4	<0.05

Table 3: T2* relaxometry value of cartilage

KL grading		rMF	rMT	rLF	rLT
II	Mean	32.39	21.41	27.52	19.15
	SD	4.21	4.88	3.44	3.63
III	Mean	32.40	30.02	30.22	21.96
	SD	5.07	8.93	4.54	5.21
IV	Mean			32.70	23.98
	SD			2.40	2.26
Total	Mean	32.39	23.13	29.15	19.94
	SD	4.20	6.67	3.87	4.16
p- value		0.998	< 0.05	<0.05	<0.05



Graph 1: T2* relaxometry value of cartilage

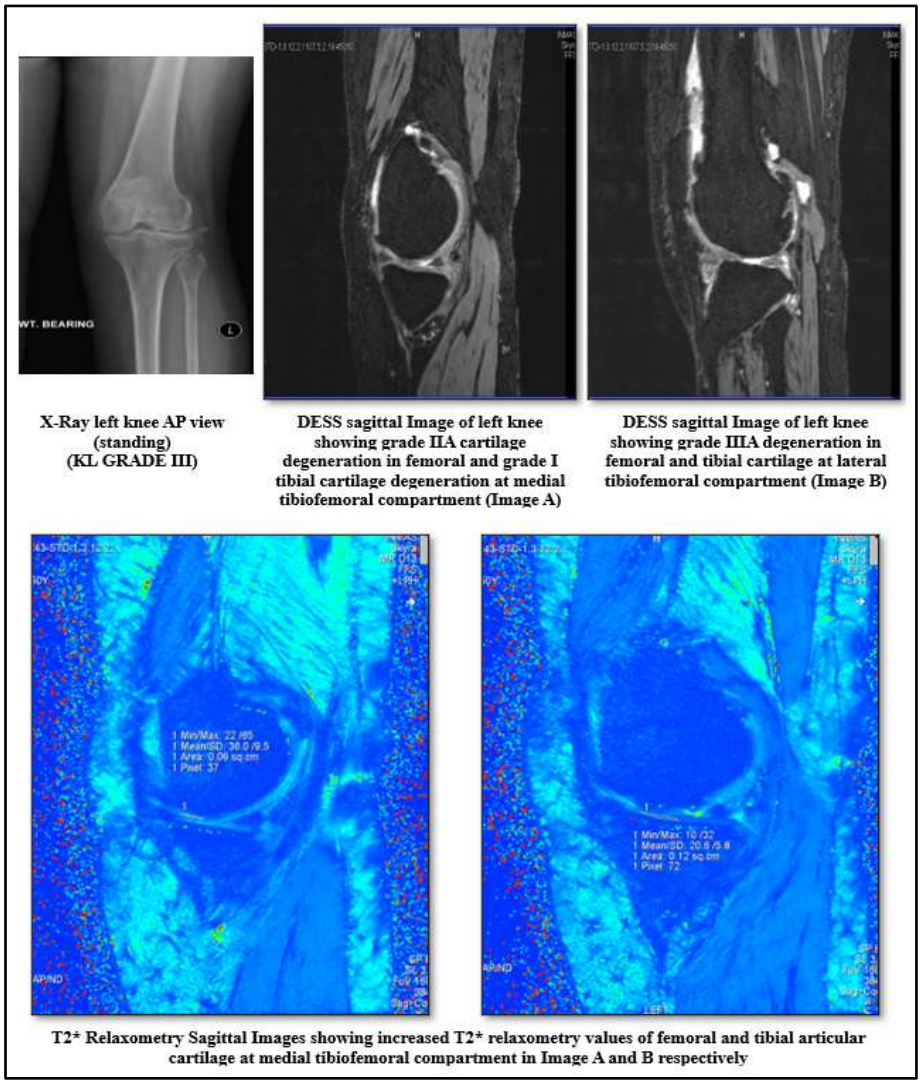


Fig 1: Case 1

RESULTS

Patient included in study were having age equal to or more than 40 years. Most of the patients (55%) were between 40-50 years age, 30% patients were between 51-60 years of age and 15% of patients were more than 61 years of age. The study includes 45% female and 55% of male patients. Increased weight is the strongest modifiable risk factor in pathogenesis of osteoarthritis of knee. In my study 58% patients were overweight having BMI between 25.1-30 and 40% patients were obese having BMI more than 30 and only 2% of patient were having normal weight. 55% of the patients were having complaint dominating in left knee and 45% on right side.

In my study the X-ray of self-described dominating knee was done in weight bearing antero-posterior view and then graded by Kellgren-Lawrence score. There were 62% patients having KL grade II, 28% patients having KL grade III and 10% patients were having KL grade IV.

There was significant correlation (p value <0.05) found between KL score and osteophytes at medial femoral condyle, lateral femoral condyle, medial tibial, lateral tibial condyle, superior and inferior pole of patella.

There was significant correlation seen between bone marrow edema and KL score in medial and lateral femoral condyles (p value < 0.05 and 0.01 respectively); however 'p' values in medial tibial, lateral tibial, femoral trochlea, medial and lateral articulating facets of patella was 0.243, 0.081, 0.745, 0.938 and 0.532 respectively.

In the present study the T2* relaxometry value of cartilage was calculated from articular cartilage surface. The cartilage which was adjacent to bony surface i.e. osteochondral interface was not included in study. The T2* relaxometry value of cartilage which were normal in appearance and having grade I and IIA degeneration were taken only in my study. Cartilage having degeneration grade IIB and above were not determined for T2* value. The statically significant correlation was seen with KL score in medial tibial, lateral femoral and lateral tibial cartilage (p value <0.05 in each); however, in medial femoral cartilage 'p' value was 0.998, which was not found statically significant.

DISCUSSION

Radiography has been the primary method for diagnosing and monitoring the progression of osteoarthritis in the knee. Unfortunately, early osteoarthritic changes may not be detected on radiographs. KL classification criteria is the most widely used radiographic classification of osteoarthritis knee; moreover, it is also the most criticized criteria due to the lack of agreement with clinical criteria of osteoarthritis, then also the KL criteria are also widely criticized due to the differences in the descriptions of the grades.

MRI is an excellent modality for evaluation of patients of osteoarthritis of knee joint. In my study MRI was compared with a plain radiograph of knee joint and MRI was found to be a much better diagnostic tool for evaluating the changes in bones and soft tissues in osteoarthritis of knee. In my study it was found that the frequency and severity of MRI changes in various tissues strongly correlated with Kellgren Lawrence grade of osteoarthritis of the knee at radiography. It was found that tibiofemoral compartment was more frequently involved than patellofemoral compartment in most of the patients. T2* relaxation time of cartilage was found to be a potential, clinically feasible parameter for the evaluation of early articular cartilage degeneration.

In western population, the patellofemoral compartment is more frequently and more severely involved in osteoarthritis, however in my study the tibiofemoral compartment was more frequently and more severely involved than the patellofemoral compartment. This difference could be due to sitting in squatting posture in Indian population. Prolonged squatting has been associated with development of osteoarthritis of knee joint in tibiofemoral compartment but only slightly associated with development of osteoarthritis in patellofemoral compartment.

Increased body weight is the strongest modifiable risk factor. Three to six times the body weight is transferred across the knee joint during walking. Increasing weight also increase the risk of contralateral osteoarthritis of the knee in women with established osteoarthritis of one knee. In my study 57% patients were having overweight (BMI 25.1-30), 40% patients were obese (BMI>30) and only 3% patients were having normal weight. This signifies that overweight and obese persons are more prone to develop osteoarthritis knee than persons having normal weight.

In my study most frequent site of osteophytosis was medial tibiofemoral joint (100%) while in Hayes CW et al[11] study patellofemoral compartment was most frequent site of osteophyte. The incidence of Grade II osteophytes was highest in medial condyle of femur (55%) of the study patients. The next most common site where Grade II osteophytes were seen was inferior pole of patella (50%) followed by lateral condyle of femur (42%) of the study patients.

The most common site of bone marrow edema in my study was tibiofemoral compartment with the highest incidence in medial condyle of femur (77.5%) and medial tibial condyle (57%) followed by lateral tibial condyle (37.5%). In Hayes et al.[11] study the patellofemoral compartment was most common site showing bone marrow edema. This difference could be due to squatting posture adopted by Indian population.

Frequent defects of focal cartilage, BME and other soft-tissue abnormalities may be critical in consideration of the clinical expression of early OA of the knee. Defects of cartilage of grade IIA or higher and BME lesions were seen on MR images, even when the radiography appears normal. In my study population the majority of the advanced defects of cartilage and BME lesions were located in the tibiofemoral compartment. In my study almost all patients shows cartilage defect in tibiofemoral compartment, grade IIIA defect was seen largest in medial femoral condyle cartilage (30%) followed by medial tibial condyle (15%). While Hayes et al[11] study shows larger number of cartilage defect in patellofemoral compartment.

T2* mapping technique use the relaxation constant as an indirect marker of cartilage structure and the T2* relaxation time is a feasible parameter for the biochemical evaluation of articular cartilage. The advantage of T2* mapping of cartilage is faster imaging times, 3D acquisition and its greater spatial resolution. Apart from assessment of articular cartilage T2* values can also be used in other body regions like in liver for monitoring of hepatic iron content. The T2* values of cartilage were recorded consistently less than the corresponding T2 values because of the additional contribution of microscopic susceptibility fields to relaxation of the transverse relaxation in the MS-GRE sequence.

T2* method offers significant improvement in scan time and signal to noise ratio, but it also have some limitations due to its greater sensitivity to susceptibility induced artifacts. It has limitation in the setting of metallic implants or when metallic particles were present as a result of surgery. Other limitation is the use of shorter TR for time optimization which can cause a significant T1-weighting on the data.

In my study the mean T2* relaxometry value of superficial healthy cartilage in medial femoral condyle was 26.2 and in focal cartilage defect with grade I and grade IIA cartilage degeneration was 27.5 and 35.8 respectively. The mean T2* value of superficial healthy cartilage in medial tibial condyle was 17.84 and in focal cartilage defect with grade I and grade IIA cartilage degeneration was 20.5 and 35.9 respectively. Similarly mean T2* value in superficial lateral femoral and lateral tibial condyles was 25.2 and 18.1 respectively and in focal cartilage defect with grade I and grade IIA degeneration was 28.3,35.7 and 20.9,35.9 respectively. The mean T2* values of medial tibial, lateral femoral and tibial condyles, which I found in my study was slightly

higher than the values of study done by Newbould et al[12] and Mamisch TC et al.[13]

CONCLUSION

T2* cartilage relaxometry at 3T MRI demonstrates significant compartment-specific correlation with radiographic Kellgren–Lawrence grades in knee osteoarthritis, supporting its role as a quantitative imaging biomarker of disease severity. In the present study, elevated T2* values—reflecting early biochemical disruption of cartilage collagen architecture—were strongly associated with higher KL grades specifically in the medial tibial, lateral femoral, and lateral tibial compartments, even before advanced morphologic cartilage loss. In contrast, medial femoral cartilage did not exhibit a statistically significant relationship, reinforcing the asymmetric and biomechanically driven progression pattern of knee OA. Significant associations were also observed between KL grade and bone marrow edema and osteophyte formation at femoral compartments, confirming their role as markers of disease progression.

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