

Received: 2019.06.23
Accepted: 2019.10.08
Published: 2019.12.27

Histological Grade and Magnetic Resonance Imaging Quantitative T1rho/T2 Mapping in Osteoarthritis of the Knee: A Study in 20 Patients

Authors' Contribution:
Study Design A
Data Collection B
Statistical Analysis C
Data Interpretation D
Manuscript Preparation E
Literature Search F
Funds Collection G

ABEF 1 **Zhaowei Lin***
BCDE 1,2 **Zhijian Yang***
BCD 3 **Huashou Wang**
BCD 4 **Minning Zhao**
BCD 4 **Wen Liang**
AFG 1 **Lijun Lin**

1 Department of Orthopaedics, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, P.R. China
2 Department of Joint Surgery, The First Affiliated Hospital of Sun Yat-sen University, Guangzhou, Guangdong, P.R. China
3 Department of Pathology, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, P.R. China
4 Department of Radiology, Zhujiang Hospital, Southern Medical University, Guangzhou, Guangdong, P.R. China

* Zhaowei Lin and Zhijian Yang contributed equally to this study

Corresponding Authors: Wen Liang, e-mail: liangwendoc@163.com, Lijun Lin, e-mail: gost1@smu.edu.cn

Source of support: This study was funded by the Science and Technology Program of Guangzhou, China (No. 201704020129)

Background: Magnetic resonance imaging (MRI) of osteoarthritis (OA) of the knee is a preoperative method of joint assessment. Histology of the joint is invasive and performed after surgery. T1rho/T2 MRI mapping is a new preoperative method of quantifying joint changes. This study aimed to analyze and compare the histological changes in the joint cartilage with the use of quantitative T1rho/T2 MRI mapping in patients with OA of the knee.

Material/Methods: Twenty patients with OA of the knee (20 knees) underwent preoperative MRI with T1rho mapping, T2 mapping, T1-weighted, and T2-weighted fat-suppressed MRI sequences. The degree of OA of the knee on MRI was graded according to the Osteoarthritis Research Society International (OARSI) criteria and the Kellgren-Lawrence grading system. Histological grading of OA used the OARSI criteria. Four tibiofemoral condyles were assessed histologically, and the degree of cartilage destruction was determined using the OARSI criteria. Two investigators performed cartilage segmentation for T1rho/T2 values.

Results: Histology of the four knee joint condyles confirmed mild to severe OA. The histology of the cartilage thickness ($P < 0.001$) and the MRI findings of the distal medial condyle ($P < 0.00$) were significantly different from the other three knee joint condyles. The T2 and T1rho values of each condyle were significantly correlated with the histological grade (II–IV) of the joint condyles, including the cartilage volume, cartilage defects, thickness, and bone lesions ($P < 0.05$).

Conclusions: In 20 patients with OA of the knee, preoperative T2/T1rho MRI identified Grade II–IV OA changes in the joint.

MeSH Keywords: **Magnetic Resonance Imaging • Osteoarthritis, Knee • Pathology, Clinical**

Full-text PDF: <https://www.medscimonit.com/abstract/index/idArt/918274>

 2480

 5

 11

 23



Background

Magnetic resonance imaging (MRI) is a semi-quantitative method for evaluating the severity of osteoarthritis (OA) of the knee and is a valuable method for the assessment of the features that determine the functional integrity of the knee joint [1]. The histological assessment of the degree or grade of damage to the cartilage of the knee joint is an invasive procedure and is performed after surgery. The preoperative assessment of articular cartilage morphology, subchondral bone lesions, bone marrow lesions (BMLs), osteophyte and joint space narrowing is necessary for optimal surgical planning.

Recently, T1rho and T2 mapping, which differs from T1/T2 imaging, has been reported as a preoperative method of assessing the degree of degenerative cartilage in advanced OA of the knee [1–3]. Although previous studies have shown the association between histology and T1/T2 images, previous studies have investigated the association between T1rho/T2 mapping values and the histological grade of the degenerative changes. Therefore, this study aimed to analyze and compare the histological changes in the joint cartilage with the use of quantitative T1rho/T2 MRI mapping in patients with OA of the knee. This study included histological grading of OA involving cartilage volume, cartilage defects, thickness, and BMLs and T2 and T1rho values of the four tibiofemoral condyles, the medial femoral condyle (MFC), the lateral femoral condyle (LFC), the medial tibial plateau (MTP), and the lateral tibial plateau (LTP).

Material and Methods

Patients and X-ray imaging of the knee joints

Twenty patients with osteoarthritis (OA) of the knee who underwent total knee arthroplasty (TKA) in the inpatient Department of Orthopedics from January 2018 to October 2018 were enrolled in this study. Their age, gender, the affected knee, and the height and weight of the patients were recorded.

The visual analog scale (VAS) and the Knee Society Score (KSS) were used to evaluate the degree of pain and knee function. The X-ray images from 20 affected knees were obtained. The presence of osteophytes, joint space narrowing, and severity of OA were assessed using the Osteoarthritis Research Society International (OARSI) criteria [4] and the Kellgren-Lawrence Classification System. The local Institutional Review Board approved the protocol. All study participants provided written informed consent before the study procedures began.

Magnetic resonance imaging (MRI)

In the morning before surgery for total knee replacement (TKA), MRI was performed with a 3.0-T Achieva unit (Philips Healthcare, Eindhoven, The Netherlands). The MRI sequences used included the fat-suppressed (FS) proton density-weighted imaging (PDWI) sequence, the T2 mapping sequence, the T1rho mapping sequence, and the T1-weighted fat-saturated 3D spoiled gradient-echo (FSPGR) sequence. The acquisition parameters were consistent with the methods previously described [2]. The four tibiofemoral condyles evaluated were the medial femoral condyle (MFC), the lateral femoral condyle (LFC), the medial tibial plateau (MTP), and the lateral tibial plateau (LTP). T1rho and T2 mapping values were calculated. Cartilage volume, cartilage defects, and bone marrow lesions (BMLs) on MRI were quantified.

Total knee arthroplasty (TKA)

TKA was performed by one professional surgeon in elective scheduled surgery. The four resected condyles, the MDC, LDC, MPC, and the LPC were examined histologically. Surgical tissue samples were obtained from bone and cartilage.

Histology

Samples of the four tibiofemoral condyles, the MDP, LDC, MPC, and LPC of the distal femur were fixed in 10% neutral buffered formalin. The condyles were decalcified with dilute hydrochloric acid using a Rapid Bone Decalcifier (American Master Tech Inc., Lodi, CA, USA) for 48 hours and fixed in formalin for at least 48 hours and then embedded in paraffin wax. Sagittal sections across the entire condyle were sectioned at 8 μ m in thickness. All sections were stained with hematoxylin-eosin (H&E) and Masson's trichrome stain. For each knee joint sample, the degree of cartilage destruction was evaluated histologically by the OARSI osteoarthritis cartilage assessment system [5] by two pathologists (Zhaowei Lin and Zhijian Yang) who were experienced in the histopathological analysis of bone and soft tissue. If there were differences in grading between the two pathologists, the histology was reviewed and discussed with a third pathologist to achieve consensus (Huashou Wang). Surgical artifacts generated by electric surgical knives were not assessed.

Image analysis

Image analysis was performed using OsiriX imaging software (OsiriX, Bernex, Switzerland). However, T2/T1rho values were analyzed using in-house developed and implemented software in MatLab (MathWorks, Natick, MA, USA). The cartilage of the femoral condyle was analyzed in both the T2 mapping and T1rho images by two experienced radiologists (Wen Liang and Minning Zhao). Images with echo time (TE)=26 in T2 and

Table 1. The clinical and demographic data of the 20 study participants.

General information	Total	Mean value	Range	95% CI
Affected Knee	Right knee: n=11 Left knee: n=9			
Gender	Female: n=18 Male: n=2			
Age (years)		67.50	52–77	64.70–70.30
Height (m)		1.58	1.45–1.68	1.55–1.599
Weight (kg)		57.10	45–66	53.55–60.65
BMI (kg/m ²)		35.53	26.31–41.25	33.38–37.68
Histological grade	MDC: n=20	3.65	2–6	3.19–4.12
	LDC: n=20	2.50	1–4	2.11–2.89
	MPC: n=20	2.10	1–4	1.70–2.50
	LPC: n=20	2.10	1–4	1.76–2.44

Each knee was divided into four parts: the medial distal condyle (MDC), the lateral distal condyle (LDC), the medial posterior condyle (MPC), and the lateral posterior condyle (LPC). BMI – body mass index; CI – confidence interval.

spin-lock pulse duration (TSL)=20 in T1rho were chosen for segmentation because of their higher signal-to-noise ratio compared with that of the other images [6,7]. T2 and T1rho values were measured in a range of –10 to 20 degrees for the distal condyle and 70 to 100 degrees for the posterior condyle. Two radiologists calculated the average T2 and T1rho values of each femoral condyle and the average thickness of the cartilage as pixel numbers in the four joint condyles.

Statistical analysis

Statistical analysis was performed using SPSS version 20.0 for Windows (SPSS, Chicago, IL, USA). Differences in the KSS scores, VAS scores, histological grades, X-ray results, the Kellgren-Lawrence grading score, and grading for osteophytes, joint space narrowing, MRI results of the grades of cartilage volume, cartilage defects, cartilage thickness, BMLs, and T2/T1rho values between the four tibiofemoral joint condyles were analyzed with the Mann-Whitney U test. Univariate logistic and binomial regression analysis were used to estimate relative risks of the association between histological grade and imaging results. A P-value of <0.05 (two-tailed) or a 95% confidence interval (CI) not including the null point (for linear regression) or 1 (for logistic regression) was considered to indicate statistical significance.

Results

Study participants

Twenty study participants who underwent T1rho magnetic resonance imaging (MRI) and total knee arthroplasty (TKA)

for osteoarthritis (OA) of the knee. MRI of four tibiofemoral condyles was examined in all 20 study participants, including the medial femoral condyle (MFC), the lateral femoral condyle (LFC), the medial tibial plateau (MTP), and the lateral tibial plateau (LTP). The study group included 18 women and two men. The mean age was 67.5 years (range, 52–77 years) (95% CI, 64.7–70.3) (Table 1). Eleven patients had OA of the right knee, and nine patients had OA of the left knee. Table 1 shows the clinical and demographic details of the patients and includes the mean height, weight, and body mass index (BMI).

The visual analog scale (VAS), Kellgren-Lawrence grading, the Knee Society Score (KSS), and the histological grade of severity of OA in the four joint condyles

Table 2 shows the average VAS and KSS scores of the involved knee of each patient, the Kellgren-Lawrence grading scores, and grades of osteophytes and joint space narrowing. Figure 1 shows the histological grade of the four joint condyles. There were significant differences in the distances between MFC and the LFC (P<0.001), the MTP (P<0.001), and the LTP (P<0.001).

Osteophytes and joint space narrowing

Differences in osteophyte grades and joint space narrowing grades of the medial and lateral tibiofemoral joints are shown in Figures 2 and 3. The tibiofemoral joint could be divided into two parts on X-ray imaging, the femoral condyle, and the tibial plateau. Osteophytes grades of femoral condyles or tibial plateaus are shown in Figure 4. Differences in osteophytes grades between medial and lateral tibiofemoral joints indicated no statistical significance, while differences in joint space narrowing

Table 2. The clinical findings of osteoarthritis (OA) in the 20 study participants.

Clinical information	Total	Mean value	Range	95% CI
VAS score	n=20	6.3	3–9	5.426–7.174
KSS	n=20	61.6	28–80	53.39–69.81
K-L grade	II: n=4 (20%) III: n=8 (40%) IV: n=8 (40%)			
Osteophytes grade	n=20	8.3	3–12	7.236–9.364
Grade of joint space narrowing	n=20	3.25	1–5	2.824–3.676

K-L – Kellgren-Lawrence; VAS – visual analog scale; KSS – Knee Society Score.

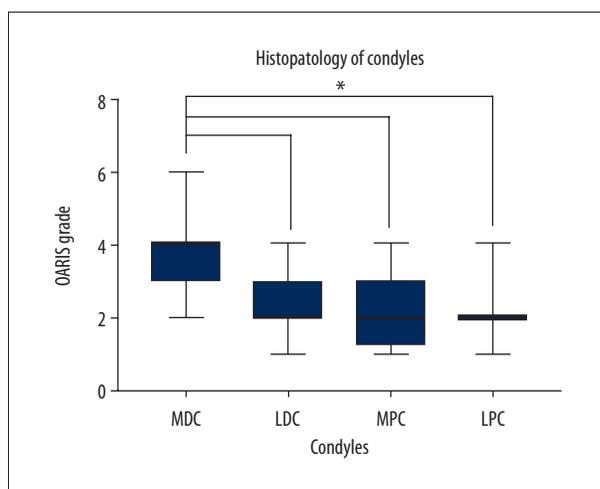


Figure 1. The Osteoarthritis Research Society International (OARSI) four histological grades of cartilage degeneration of the condyles of the knee joint. MDC – medial distal condyle; LDC – lateral distal condyle; MPC – medial posterior condyle; LPC – lateral posterior condyle. * P<0.001.

grades between medial and lateral tibiofemoral joints were statistically significant.

Grades of cartilage defects and bone marrow lesions (BMLs) using T1rho MRI

The grades of cartilage volume, cartilage defects, and BMLs are shown in Figures 5 and 6. Differences in the grades of cartilage defect between the medial and lateral tibiofemoral condyles were statistically significant. MRI showed that medial femoral condyle had less cartilage volume, more cartilage defects, and more BMLs than lateral the femoral condyles. MRI also showed that the MTP had less cartilage volume and more cartilage defects than the LTP. The tibial plateau had less cartilage volume than ipsilateral femoral condyles.

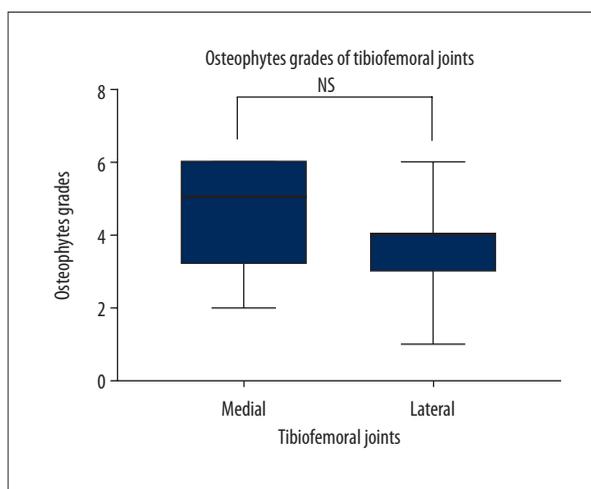


Figure 2. Osteophyte grades of the tibiofemoral joints. The differences in osteophytes grades between the medial and lateral tibiofemoral joints were not statistically significant.

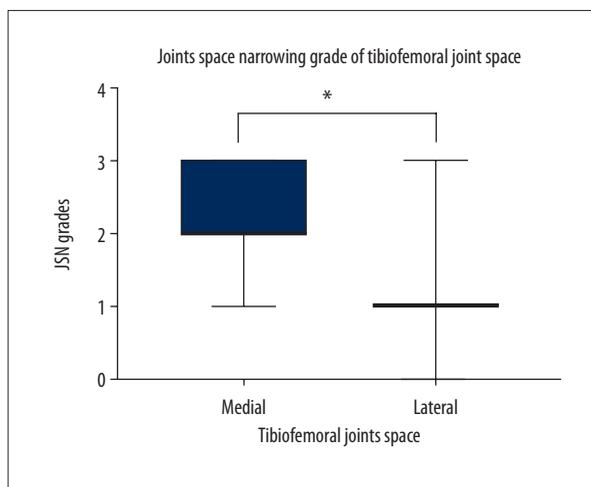


Figure 3. Grades of joint space narrowing of the tibiofemoral joint. * P<0.001

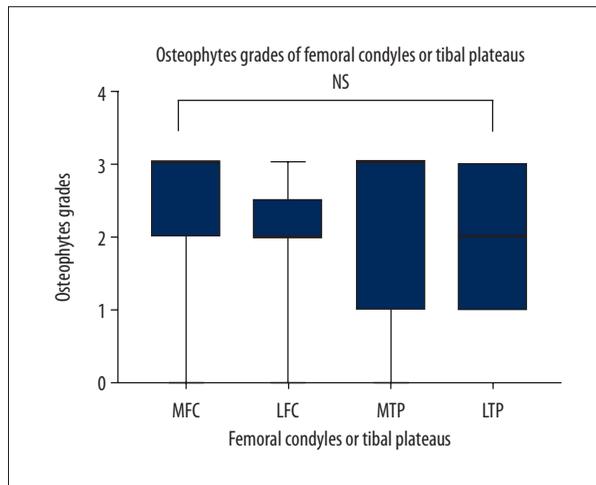


Figure 4. Osteophyte grades of the femoral condyle and tibial plateau. MFC – medial femoral condyle; LFC – lateral femoral condyle; MTP – medial tibial plateau; LTP – lateral tibial plateau. Differences in osteophyte grade between the four parts show no statistical significance.

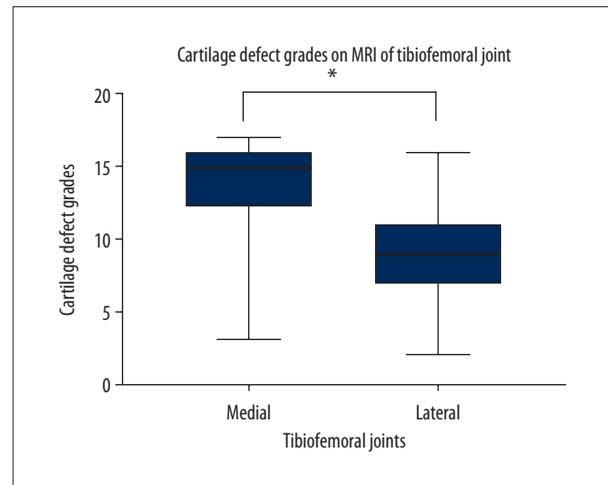


Figure 5. Grades of cartilage defects of the tibiofemoral joints. * The differences in the grades of the cartilage defects between the medial and lateral tibiofemoral joints are statistically significant ($P < 0.001$).

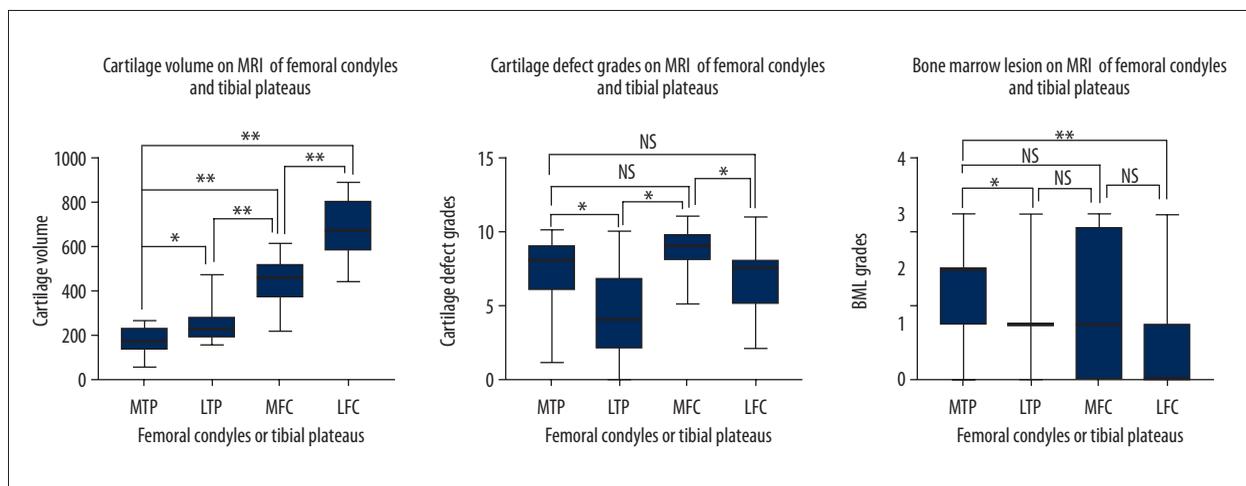


Figure 6. Cartilage volume, cartilage defects, and bone lesions of the femoral condyle and tibial plateau. MFC – medial femoral condyle; LFC – lateral femoral condyle; MTP – medial tibial plateau; LTP – lateral tibial plateau. * The differences in cartilage volumes (cm^2) between the two parts are statistically significant ($P < 0.001$). ** Differences in cartilage volumes (cm^2) between the medial tibial plateau and lateral tibial plateau are statistically significant ($P < 0.05$).

Histological grades and the grade of the cartilage defect using T1rho MRI

Figure 7 shows the correlation between the scores for histological grade and the grade of cartilage defect. There was a significant difference in the grade of cartilage defect between histological Grade II and Grade III ($P = 0.009$). Cartilage damage was found to increase with increasing histological grade. Tables 3 and 4 show the relationship between the histological grade and the grade of cartilage defect.

Figure 8 shows the correlation between the MRI T1rho values and the histological grading scores. The relationship between the T2 mapping values and the histological grading scores is shown in Figure 9. There were significant differences in the T1rho and T2 mapping values between histological Grade II–III and Grade III–IV (Table 5). Figure 10 shows differences in the T1rho MRI findings in eight patients who had histological grade OA changes of between Grade II–IV. Figure 11 shows the histological findings in the four tibiofemoral condyles of two patients who were included in the study.

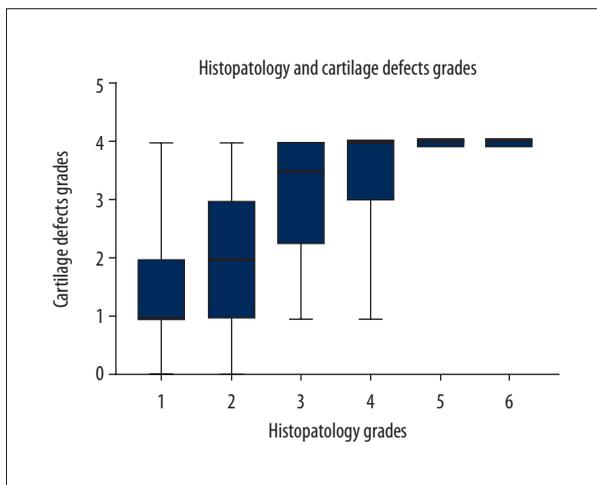


Figure 7. Scatter plot of the correlation between the histological grade and the grade of the cartilage defect.

Discussion

Recently, T1rho/T2 magnetic resonance imaging (MRI) mapping has been reported as a rapid preoperative method for the quantitative assessment of joint changes in osteoarthritis (OA) of the knee [2,3,8–13]. Kester et al. [2] showed that T2 and T1rho values of cartilage in patients with OA were significantly higher in patients with advanced OA ($P=0.043$). However, no significant difference in cartilage thickness was shown by MRI between controls and patients with advanced OA [2]. The study by Li et al. [3] showed T2/T1rho values were significantly associated with the Kellgren-Lawrence grading scores. Studies by Mahar et al. and Wu et al. [8,9] showed that T1rho/T2 contributed to the clinical diagnosis of trauma-induced OA. Monu et al. [10] found that patients with injury to the anterior cruciate ligament (ACL) resulted in increased T1rho/T2 relaxation times compared with healthy volunteers. William et al. [11] showed that the mean T2 assessments could

Table 3. Correlation between the histological grade and the grade of the cartilage defect in the knee joints of the 20 study participants.

Histological grade	Grade of the cartilage defect				
	0	1	2	3	4
I	0	4	2	2	1
II	4	8	13	7	4
III	1	1	2	5	10
IV	0	1	0	4	8
V	0	0	0	0	2
VI	0	0	0	0	1

Each knee was divided into four parts: the medial distal condyle (MDC), the lateral distal condyle (LDC), the medial posterior condyle (MPC), and the lateral posterior condyle (LPC). All 80 histological tissue sections from the 20 affected knees are included ($P<0.001$).

Table 4. Correlation between the histological grade and the grade of the cartilage defect in the knee joints of the 20 study participants.

Comparison between different histological grades	P-value of correlation between histological grade and the grade of cartilage defect
I and II	0.818
II and III	0.009*
III and IV	0.983
IV and V	0.956
V and VI	0.999

* The correlation between the histological grade and the magnetic resonance imaging (MRI) value is statistically significant ($P<0.05$).

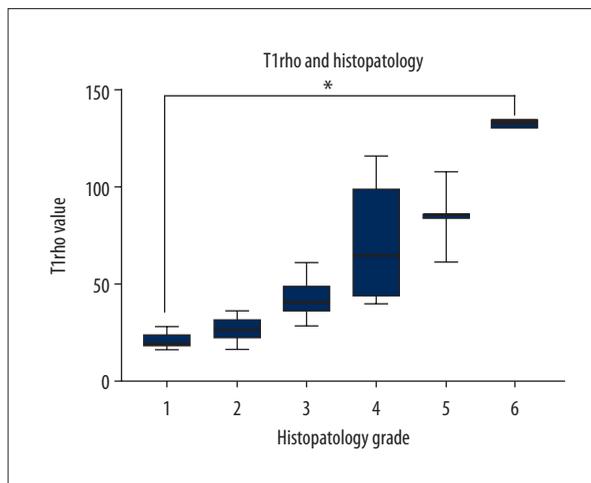


Figure 8. Scatter plot of the correlation between the histological grade and the T1rho value on magnetic resonance imaging (MRI).

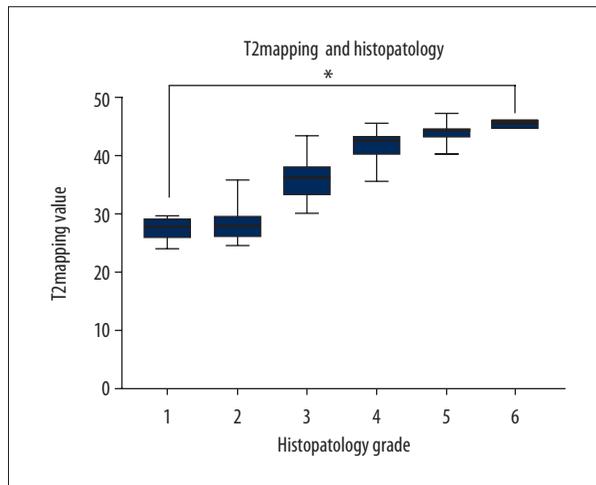


Figure 9. Scatter plot for correlation between the histological grade and the T2 mapping value on magnetic resonance imaging (MRI).

indicate damage to the cartilage after ACL reconstruction and could predict the progression of symptomatic OA. Urish et al. and Zhong et al. [12,13] used the T2 texture index and T2 mapping signal variation to predict the progression of symptomatic OA. However, few previous studies have investigated the correlation between T1rho/T2 mapping values and the histological findings of the joint cartilage in OA. The findings of the present study showed a significant correlation between the T2/T1rho results and histological Grade II–IV. To our knowledge, this study was the first to investigate the association between the MRI T2/T1rho values and the histological grade, according to the Osteoarthritis Research Society International (OARSI) criteria. Also, this study was the first to investigate whether T2/T1rho MRI was an improved method for the preoperative assessment of OA of the knee.

Histology of the tibiofemoral condyles is considered to be the gold standard to evaluate cartilage degeneration and inflammation in the cartilage and subchondral bone marrow

lesions (BMLs) [14,15]. The OARSI system is the most used method to evaluate the histopathology of OA of the knee [5]. The OARSI system includes the combined grade and stage for the total score. The OARSI grade is defined as the depth of involvement of the cartilage and the severity of the progression of OA, as the deeper the involvement of the cartilage indicates more advanced OA and can be a good indicator of progressive disease [5]. The OARSI stage includes the horizontal extent of the injury to the cartilage surface and is presented as the percentage of involvement. However, the assessment of the severity of OA by MRI T1rho/T2 mapping and histopathology [2] compared with the assessment of the four tibiofemoral condyles following total knee arthroplasty (TKA) ensures that each condyle is assessed optimally. Therefore, in the present study, the OARIS grading system was used to evaluate the pathology of the cartilage in OA of the knee. In this study, cartilage degeneration was more severe in the medial distal condyle and distal condyle than that in other condyles, including the posterior condyle. These findings add to the current knowledge of the pathogenesis and mechanism of OA [14,16–18]. Although preoperative X-ray imaging can show changes of OA in the knee, the findings from the present study identified a significant correlation between the histological changes in the knee joint and the Kellgren–Lawrence grading scores. In this study, damage in the medial distal condyle was more severe than the three other condyles in terms of Kellgren–Lawrence scores and grades of cartilage volume, cartilage defects, and bone marrow lesions (BMLs). X-ray and non-functional MRI showed no significant difference in damage between the distal medial and the other three condyles. However, functional MRI showed a significant difference in damage between the medial distal condyle and the other three condyles, and the severity of damage shown by histology was significantly correlated with high T2/T1rho values and functional MRI showed differences between Grades I–V.

Dunn et al. [19] found that when compared with healthy controls, patients with mild OA had high T2 values. In the present

Table 5. Comparison of the histological grade and the T1rho/T2 magnetic resonance imaging (MRI) mapping value in the knee joints of the 20 study participants.

Comparison between the histological grades	P-value of correlation between the histological grade and the T1rho value	P-value of correlation between histology and the T2 mapping value
I and II	0.752	0.950
II and III	0.002*	<0.001*
III and IV	<0.001*	<0.001*
IV and V	0.7105	0.8767
V and VI	0.033*	0.9980

* Comparison between the histological grade and the magnetic resonance imaging (MRI) value is statistically significant ($P < 0.05$).

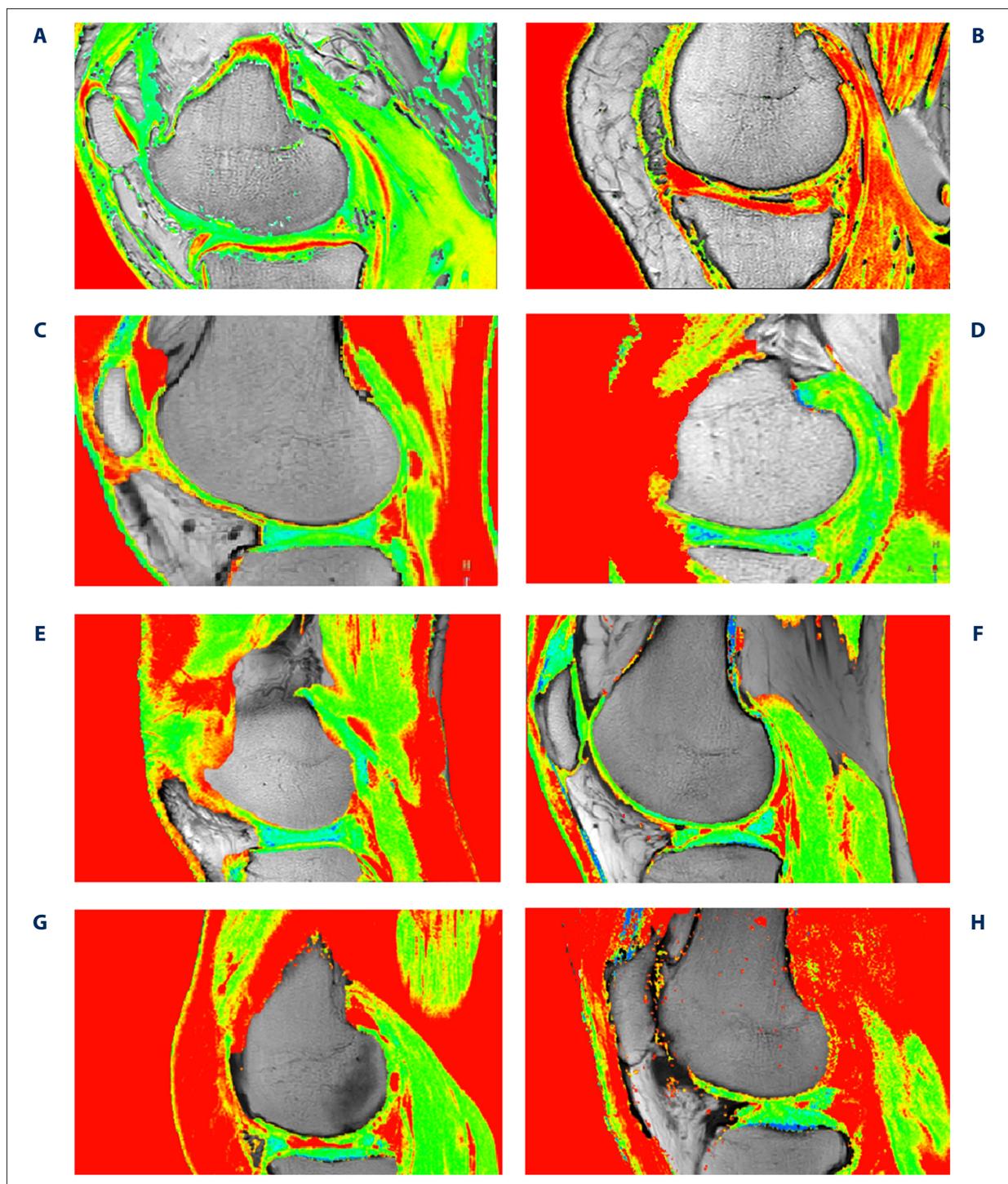


Figure 10. Macroscopic images of the histological Grades II–IV of femoral condylar cartilage and tibial cartilage in the knee joints of eight patients. (A) Femoral condyle cartilage, histological Grade II. Tibial condyle cartilage, histological Grade IV. (B) Femoral condyle cartilage, histological Grade III. Tibial condyle cartilage, histological Grade V. (C) Femoral condyle cartilage, histological Grade II. Tibial condyle cartilage, histological Grade II. (D) Femoral condyle cartilage, histological Grade II. Tibial condyle cartilage, histological Grade III. (E) Femoral condyle cartilage, histological Grade II. Tibial condyle cartilage, histological Grade III. (F) Femoral condyle cartilage, histological Grade II. Tibial condyle cartilage, histological Grade I. (G) Femoral condyle cartilage, histological Grade V. Tibial condyle cartilage, histological Grade III. (H) Posterior femoral condyle cartilage, histological Grade IV. Tibial condyle cartilage, histological Grade III. Figure 10 shows the differences in magnetic resonance imaging (MRI) between histological Grade II–IV.

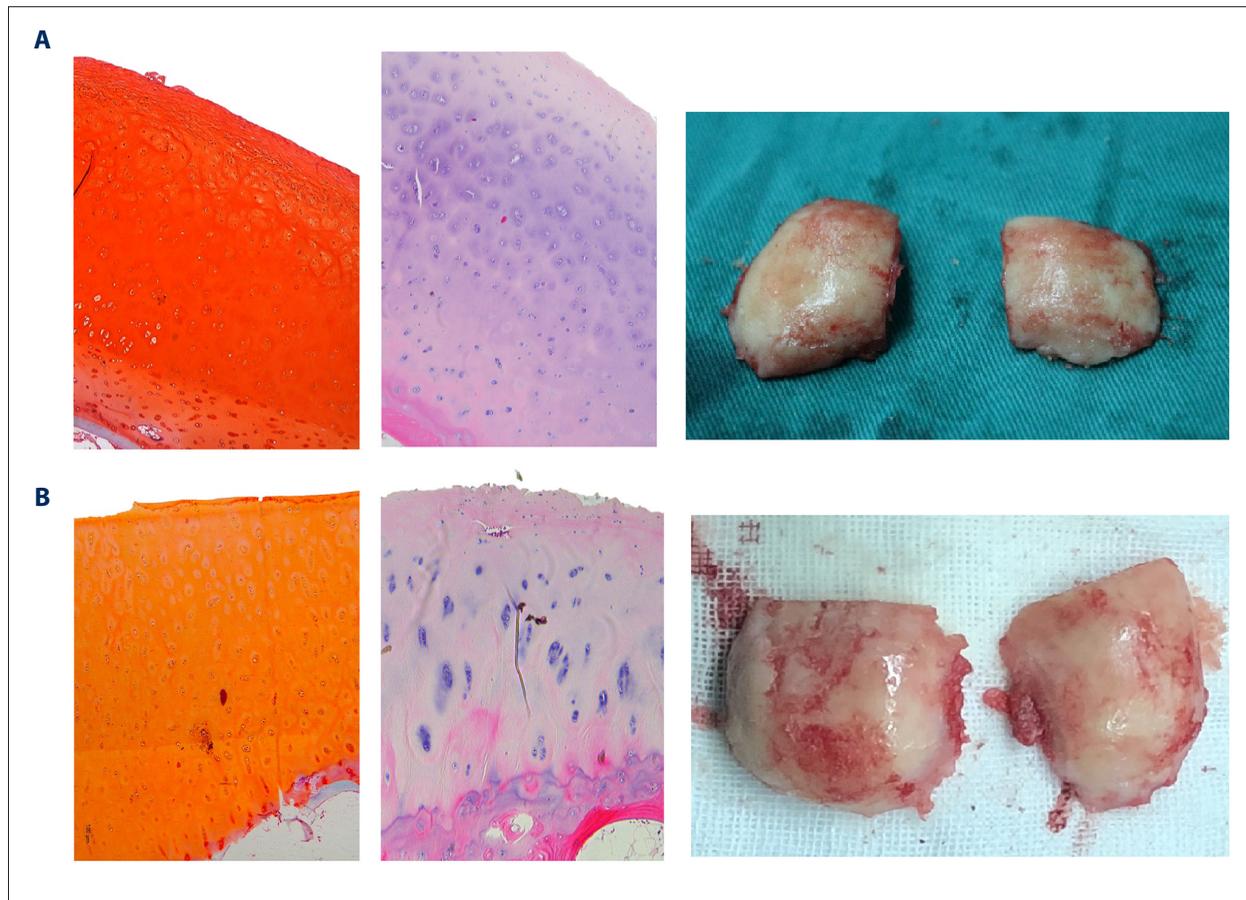


Figure 11. The femoral condyles and the histopathology from the knee joints of two patients with osteoarthritis (OA). **(A)** Femoral condylar cartilage. Histological Grade II. The surface is rough. Severe cell proliferation is shown. **(B)** Femoral condylar cartilage. Histological Grade III. The surface is rough. Mild cell proliferation is shown.

study, as the severity of OA increased, the T2 value also increased. However, the difference between histological Grade V and Grade VI was not statistically significant. No significant differences were found between histological grade and the grade of cartilage defect in MRI in the 20 affected knees of the study participants. However, T2 mapping showed a significant difference between Grade I to V, which may contribute to the role of T2 mapping in identifying subtle zonal variation in matrix constituents with depth [20]. Also, differences between histopathology Grade II and Grade III were significantly different.

It has been previously assumed that T2 and T1rho values could be used to determine whether articular cartilage degeneration has occurred or not [3,19–22]. However, previous studies have shown that there was no linear correlation between T2 values and the degree of articular cartilage degeneration [23]. The findings from the present study showed that there was a significant correlation between the histological changes in the joint cartilage and quantitative T1rho/T2 MRI mapping in patients with OA of the knee. However, this study had several limitations. This study was conducted at a single center, and

the study findings were reported by the study investigators, which could have introduced study bias. The average T1rho and T2 values were quantified within the entire cartilage surface, which might have been too generalized. Also, only 20 knees were included in this study.

Conclusions

This study aimed to analyze and compare the histological changes in the joint cartilage with the use of quantitative T1rho/T2 magnetic resonance imaging (MRI) mapping in patients with osteoarthritis (OA) of the knee. In 20 patients with OA of the knee, preoperative T2/T1rho MRI identified Grade II–IV OA cartilage degeneration. The use of preoperative T2/T1rho MRI may help to diagnose the degree of OA so that treatment can begin at an earlier stage to reduce disease progression and severity.

References:

1. Acebes C, Roman-Blas JA, Delgado-Baeza E et al: Correlation between arthroscopic and histopathological grading systems of articular cartilage lesions in knee osteoarthritis. *Osteoarthritis Cartilage*, 2009; 17(2): 205–12
2. Kester BS, Carpenter PM, Yu HJ et al: T1rho/T2 mapping and histopathology of degenerative cartilage in advanced knee osteoarthritis. *World J Orthop*, 2017; 8(4): 350–56
3. Li X, Benjamin Ma C, Link TM et al: *In vivo* T(1rho) and T(2) mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. *Osteoarthritis Cartilage*, 2007; 15(7): 789–97
4. Altman RD, Gold GE: Atlas of individual radiographic features in osteoarthritis, revised. *Osteoarthritis Cartilage*, 2007; 15(Suppl. A): A1–56
5. Pritzker KP, Gay S, Jimenez SA et al: Osteoarthritis cartilage histopathology: Grading and staging. *Osteoarthritis Cartilage*, 2006; 14(1): 13–29
6. Kaneko Y, Nozaki T, Yu H et al: Normal T2 map profile of the entire femoral cartilage using an angle/layer-dependent approach. *J Magn Reson Imaging*, 2015; 42(6): 1507–16
7. Nozaki T, Kaneko Y, Yu HJ et al: T1rho mapping of entire femoral cartilage using depth- and angle-dependent analysis. *Eur Radiol*, 2016; 26(6): 1952–62
8. Mahar R, Batool S, Badar F, Xia Y: Quantitative measurement of T2, T1p and T1 relaxation times in articular cartilage and cartilage-bone interface by SE and UTE imaging at microscopic resolution. *J Magn Reson*, 2018; 29(7): 76–85
9. Wu Y, Yang R, Jia S et al: Computer-aided diagnosis of early knee osteoarthritis based on MRI T2 mapping. *Biomed Mater Eng*, 2014; 24(6): 3379–88
10. Monu UD, Jordan CD, Samuelson BL et al: Cluster analysis of quantitative MRI T(2) and T(1p) relaxation times of cartilage identifies differences between healthy and ACL-injured individuals at 3T. *Osteoarthritis Cartilage*, 2017; 25(4): 513–20
11. Williams A, Winalski CS, Chu CR: Early articular cartilage MRI T2 changes after anterior cruciate ligament reconstruction correlate with later changes in T2 and cartilage thickness. *J Orthop Res*, 2017; 35(3): 699–706
12. Urish KL, Keffalas MG, Durkin JR et al: T2 texture index of cartilage can predict early symptomatic OA progression: Data from the osteoarthritis initiative. *Osteoarthritis Cartilage*, 2013; 21(10): 1550–57
13. Zhong H, Miller DJ, Urish KL: T2 map signal variation predicts symptomatic osteoarthritis progression: Data from the osteoarthritis initiative. *Skeletal Radiol*, 2016; 45(7): 909–13
14. Waldstein W, Perino G, Gilbert SL et al: OARSI osteoarthritis cartilage histopathology assessment system: A biomechanical evaluation in the human knee. *J Orthop Res*, 2016; 34(1): 135–40
15. Nebelung S, Sondern B, Oehrl S et al: Functional MR imaging mapping of human articular cartilage response to loading. *Radiology*, 2017; 282(2): 464–74
16. Berenbaum F: Osteoarthritis as an inflammatory disease (osteoarthritis is not osteoarthrosis!). *Osteoarthritis Cartilage*, 2013; 21(1): 16–21
17. Klein-Wieringa IR, de Lange-Brokaar BJ, Yusuf E et al: Inflammatory cells in patients with endstage knee osteoarthritis: A comparison between the synovium and the infrapatellar fat pad. *J Rheumatol*. 2016; 43(4): 771–78
18. Weber A, Chan PMB, Wen C: Do immune cells lead the way in subchondral bone disturbance in osteoarthritis? *Prog Biophys Mol Biol*, 2017 [Epub ahead of print]
19. Dunn TC, Lu Y, Jin H et al: T2 relaxation time of cartilage at MR imaging: comparison with severity of knee osteoarthritis. *Radiology*, 2004; 232(2): 592–98
20. Watrin A, Ruard JP, Olivier PT et al: T2 mapping of rat patellar cartilage. *Radiology*, 2001; 219(2): 395–402
21. Carballido-Gamio J, Stahl R, Blumenkrantz G et al: Spatial analysis of magnetic resonance T1rho and T2 relaxation times improves classification between subjects with and without osteoarthritis. *Med Phys*, 2009; 36(9): 4059–67
22. David-Vaudey E, Ghosh S, Ries M, Majumdar S: T2 relaxation time measurements in osteoarthritis. *Magn Reson Imaging*, 2004; 22(5): 673–82
23. Jungmann PM, Kraus MS, Nardo L et al: T(2) relaxation time measurements are limited in monitoring progression, once advanced cartilage defects at the knee occur: Longitudinal data from the osteoarthritis initiative. *J Magn Reson Imaging*, 2013; 38(6): 1415–24