Evaluation of the Articular Cartilage of the Knee Joint: Value of Adding a T2 Mapping Sequence to a Routine MR Imaging Protocol[1]

Richard Kijowski, MD
Donna G. Blankenbaker, MD
Alejandro Munoz del Rio, PhD
Geoffrey S. Baer, MD
Ben K. Graf, MD

Purpose: To determine whether the addition of a T2 mapping sequence to a routine magnetic resonance (MR) imaging protocol could improve diagnostic performance in the detection of surgically confirmed cartilage lesions within the knee joint at 3.0 T.

Materials and Methods: This prospective study was approved by the institutional review board, and the requirement to obtain informed consent was waived. The study group consisted of 150 patients (76 male and 74 female patients with an average age of 41.2 and 41.5 years, respectively) who underwent MR imaging and arthroscopy of the knee joint. MR imaging was performed at 3.0 T by using a routine protocol with the addition of a sagittal T2 mapping sequence. Images from all MR examinations were reviewed in consensus by two radiologists before surgery to determine the presence or absence of cartilage lesions on each articular surface, first by using the routine MR protocol alone and then by using the routine MR protocol with T2 maps. Each articular surface was then evaluated at arthroscopy. Generalized estimating equation models were used to compare the sensitivity and specificity of the routine MR imaging protocol with and without T2 maps in the detection of surgically confirmed cartilage lesions.

Results: The sensitivity and specificity in the detection of 351 cartilage lesions were 74.6% and 97.8%, respectively, for the routine MR protocol alone and 88.9% and 93.1% for the routine MR protocol with T2 maps. Differences in sensitivity and specificity were statistically significant ($P <$ .001). The addition of T2 maps to the routine MR imaging protocol significantly improved the sensitivity in the detection of 24 areas of cartilage softening (from 4.2% to 62%, $P <$ .001), 41 areas of cartilage fibrillation (from 20% to 66%, $P <$ .001), and 96 superficial partial-thickness cartilage defects (from 71% to 88%, $P = .004$).

Conclusion: The addition of a T2 mapping sequence to a routine MR protocol at 3.0 T improved sensitivity in the detection of cartilage lesions within the knee joint from 74.6% to 88.9%, with only a small reduction in specificity. The greatest improvement in sensitivity with use of the T2 maps was in the identification of early cartilage degeneration.

[1] From the Departments of Radiology (R.K., D.G.B., A.M.d.R.), Statistics (A.M.d.R.), and Orthopedic Surgery (G.S.B., B.K.G.), University of Wisconsin School of Medicine and Public Health, 600 Highland Ave, Clinical Science Center-E3/311, Madison, WI 53792-3252. Received June 26, 2012; revision requested August 9; revision received September 6; accepted September 12; final version accepted September 27. **Address correspondence to** R.K. (e-mail: *rkijowski@uwhealth.org*).

The identification of early cartilage degeneration in symptomatic patients undergoing routine magnetic resonance (MR) imaging of the knee joint is clinically important (1–6). Intervention strategies, including weight loss, aerobic activity, and range of motion and strengthening exercises, may alleviate symptoms in patients with osteoarthritis and potentially slow the rate of joint degeneration (1). There has also been much recent effort in developing disease-modifying osteoarthritis drugs, with many promising new pharmacologic agents currently being investigated in clinical trials (2–6). 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 (4,7). Thus, successful treatment of patients with osteoarthritis requires early identification of cartilage degeneration within the knee joint.

Evaluation of articular cartilage in symptomatic patients undergoing routine MR imaging of the knee joint is typically performed by using sequences that assess cartilage morphology (8–18). The main limitation of morphologic cartilage imaging sequences is their relatively low sensitivity in the detection of early cartilage degeneration (8–18). Quantitative cartilage imaging techniques such as T2 mapping sequences have also been used to evaluate the articular cartilage of the knee joint (19–25). T2 mapping sequences are now commercially available on many MR vendor platforms and can help detect changes in the water and collagen content and the three-dimensional ultrastructure of cartilage (26–30). These sequences have been used extensively in osteoarthritis research studies to detect disease- and treatment-related changes in articular cartilage (19–25). However, few previous studies have investigated the ability of T2 mapping sequences to depict early cartilage degeneration in symptomatic patients (31,32). Thus, this study was performed to determine whether the addition of a T2 mapping sequence to a routine MR imaging protocol could improve diagnostic performance in the detection of surgically confirmed cartilage lesions within the knee joint at 3.0 T.

Advances in Knowledge

- A routine MR imaging protocol with T2 maps has significantly higher sensitivity ($P < .001$) in the detection of cartilage lesions within the knee joint at 3.0 T compared with a routine MR protocol alone, with the greatest improvement occurring in the identification of early cartilage degeneration.
- A routine MR imaging protocol with T2 maps has significantly lower specificity ($P < .001$) in the detection of cartilage lesions within the knee joint at 3.0 T compared with a routine MR imaging protocol alone and cannot depict all areas of cartilage degeneration.
- A routine MR imaging protocol with T2 maps has similar interobserver agreement as a routine MR imaging protocol alone for determining the presence or absence of cartilage lesions within the knee joint at 3.0 T.

Materials and Methods

Study Group

The study was performed in compliance with Health Insurance Portability and Accountability Act regulations and with the approval of our institutional review board. The requirement to obtain informed consent was waived. The study group consisted of 10 patients evaluated retrospectively and 150 patients evaluated prospectively at our institution by using MR imaging and arthroscopy of the knee joint.

Between April 1, 2010, and December 1, 2010, 136 symptomatic patients (70 male patients aged 16–74 years [average age, 44.1 years] and 66 female patients aged 15–76 years [average age, 44.7 years]) who underwent routine MR imaging of the knee at our institution were included in a retrospective study to qualitatively investigate the normal distribution of cartilage T2 relaxation time on each articular surface of the knee joint. All 136 patients underwent imaging with our routine knee MR imaging protocol and a T2 mapping sequence. Forty-nine patients (25 male patients aged 17–64 years [average age, 40.6 years] and 24 female patients aged 16–65 years [average age, 41.1 years]) underwent subsequent arthroscopic knee surgery and were identified retrospectively by means of a review of the orthopedic surgery schedule. The medical records and MR images from these 49 patients were reviewed to identify 10 patients who met the following inclusion criteria: *(a)* age less than 25 years; *(b)* body mass index of less than 30; *(c)* no history of previous knee surgery; *(d)* no history of inflammatory, crystalline, or infectious arthritis; *(e)* normal articular cartilage identified at arthroscopy; *(f)* no ligament tear identified at MR imaging or arthroscopy; and *(g)* no bone marrow edema identified at MR imaging. The retrospective study group consisted of these 10 patients (five male patients aged 17–25 years [average age, 23.1 years] and five female patients aged 18–25 years [average age, 23.5

Implication for Patient Care

- The addition of a T2 mapping sequence to a routine MR imaging protocol at 3.0 T can improve the detection of cartilage lesions within the knee joint and may be especially useful in certain patient populations where the identification of early cartilage degeneration is clinically important.

Published online before print
10.1148/radiol.12121413 **Content code:** MK

Radiology 2013; 267:503–513

Author contributions:
Guarantors of integrity of entire study, R.K., G.S.B.; study concepts/study design or data acquisition or data analysis/interpretation, all authors; manuscript drafting or manuscript revision for important intellectual content, all authors; manuscript final version approval, all authors; literature research, R.K.; clinical studies, R.K., D.G.B., G.S.B.; statistical analysis, R.K., A.M.d.R.; and manuscript editing, R.K., D.G.B., A.M.d.R., G.S.B.

Conflicts of interest are listed at the end of this article.

years]) with arthroscopically normal articular cartilage.

Between December 15, 2010, and February 1, 2012, 290 symptomatic patients (148 male patients aged 15–71 years [average age, 43.9 years] and 142 female patients aged 16–75 years [average age, 44.8 years]) undergoing routine MR imaging of the knee at our institution were included in a prospective study investigating the ability of a T2 mapping sequence to evaluate the articular cartilage of the knee joint. All 290 patients underwent imaging with our routine knee MR protocol and a T2 mapping sequence. One hundred fifty of these 290 patients underwent subsequent arthroscopic knee surgery and were identified prospectively by means of a review of the orthopedic surgery schedule. The prospective study group consisted of these 150 consecutive patients (76 male patients aged 17–63 years [average age, 41.2 years] and 74 female patients aged 18–64 years [average age, 41.5 years]) who were evaluated with MR imaging and arthroscopy. No patient was excluded from the study on the basis of any factor including age, weight, severity of knee injury, history of previous knee surgery, or quality of the MR images.

MR Examination

The 10 patients in the retrospective study group and the 150 patients in the prospective study group underwent imaging with the same 3.0-T MR unit (Sigma Excite HDx; GE Healthcare, Waukesha, Wis) by using an eight-channel phased-array extremity coil (Precision Eight TX/TR High Resolution Knee Array; Invivo, Orlando, Fla). All MR examinations consisted of an axial frequency-selective fat-suppressed T2-weighted fast spin-echo sequence, a coronal intermediate-weighted fast spin-echo sequence, a coronal frequency-selective fat-suppressed intermediate-weighted fast spin-echo sequence, a sagittal intermediate-weighted fast spin-echo sequence, a sagittal frequency-selective fat-suppressed T2-weighted fast spin-echo sequence, and a sagittal T2 mapping sequence (Cartigram, GE Healthcare). The imaging parameters of all sequences are summarized in Table 1. T2 maps of the articular cartilage of the knee joint, with a color scale ranging between 25 and 75 msec, were created from the T2 mapping source data. The T2 maps were created in less than 5 minutes by a technologist immediately following the MR examination with use of postprocessing software (AW MR Func Tool, GE Healthcare) on the imager workstation.

Image Evaluation

Retrospective study group.—The T2 maps from the 10 patients in the retrospective study group were reviewed in consensus by two fellowship-trained musculoskeletal radiologists with 10 and 13 years of clinical experience with use of a picture archiving and communication system workstation (Horizon Medical Imaging; McKesson, San Francisco, Calif). The radiologists qualitatively assessed the normal distribution of cartilage T2 relaxation time on each articular surface of the knee joint. The articular cartilage was divided into superficial and deep layers, and the range of T2 relaxation times within each layer on each articular surface was determined by using the color scales. Patterns of regional variations in T2 relaxation time were also assessed by measuring the percentage thickness of the deep layer of cartilage in various regions on each articular surface by using electronic calipers on the picture archiving and communication system workstation.

Prospective study group.—The MR images from all 150 patients in the prospective study group were reviewed in consensus by the same two fellowship-trained musculoskeletal radiologists with use of a picture archiving and communication system workstation (Horizon Medical Imaging) before arthroscopic knee surgery. All sequences in the routine MR imaging protocol were first used together to grade the articular cartilage on the patella, trochlea, medial femoral condyle, lateral femoral condyle, medial tibial plateau, and lateral tibial plateau according to a modified Noyes classification system, as follows: grade 0 = normal cartilage, grade 1 = increased T2 signal intensity within

Table 1

Summary of MR Imaging Parameters

Parameter	Axial Fat-saturated T2-weighted FSE	Coronal Intermediate-weighted FSE	Coronal Fat-saturated Intermediate-weighted FSE	Sagittal Intermediate-weighted FSE	Sagittal Fat-saturated T2-weighted FSE	Sagittal T2 Mapping
Repetition time (msec)	4300	1800	2000	2000	5300	1500
Echo time (msec)	77	20	20	20	80	9, 18, 27, 36, 44, 53, 62, 71
Flip angle (degrees)	90	90	90	90	90	90
Matrix size	448 × 224	384 × 224	384 × 224	384 × 224	384 × 224	320 × 192
Field of view (cm)	18	14	14	14	14	16
Section thickness (mm)	3	2	2	2	3	3
Bandwidth (kHz)	41.7	31.2	31.2	31.2	41.7	31.3
Echo train length	21	4	4	4	20	N/A
No. of signals acquired	4	2	2	2	3	1
Imaging time	3 min 30 sec	3 min 25 sec	3 min 26 sec	3 min 26 sec	3 min16 sec	5 min

Note.—FSE = fast spin echo.

morphologically normal cartilage, grade 2A = superficial partial-thickness cartilage lesion less than 50% of the total thickness of the articular surface, grade 2B = deep partial-thickness cartilage lesion greater than 50% of the total thickness of the articular surface, and grade 3 = full-thickness cartilage lesion (18,33,34). The T2 maps were then used to detect areas of increased T2 relaxation time on articular surfaces that appeared normal with the routine MR imaging protocol (19,31,32,35,36). Articular cartilage that appeared normal with the routine MR imaging protocol but showed increased T2 relaxation time on the T2 maps was classified as a grade 1A cartilage lesion. The location and grade of all cartilage lesions were documented on a knee map provided in the International Knee Document Committee Knee Evaluation Form (37).

When a grade 2A or 2B cartilage lesion was identified with the routine MR imaging protocol, the T2 maps were used to determine whether the partial-thickness cartilage lesion had a normal, increased, or decreased T2 relaxation time. When a grade 1A cartilage lesion was identified on the T2 maps, the presence or absence of four features of the area of increased T2 relaxation time was determined. These features included whether the area of increased T2 relaxation time *(a)* was two or more color scales higher than normal, *(b)* was more than 1 cm in maximal diameter, *(c)* was present on at least two consecutive images, and *(d)* involved the entire thickness of the deep cartilage layer.

The MR images from 40 randomly chosen patients from the prospective study group were reviewed a second time independently by the same two fellowship-trained musculoskeletal radiologists, who were blinded to the arthroscopic findings. To prevent recall bias, the second review was performed a minimum of 4 months after the initial review. The second review of the MR images was performed in the same manner as the initial review and was used to assess interobserver agreement for determining the presence and absence of cartilage lesions within the knee joint.

Arthroscopic Knee Surgery

Arthroscopic knee surgery was performed within 3 months of the MR examination in all 10 patients in the retrospective study group (average interval between MR imaging and surgery, 34.3 days; range, 10–79 days) and all 150 patients in the prospective study group (average interval between MR imaging and surgery, 36.3 days; range, 3–89 days). All arthroscopic knee surgeries were performed by one of two orthopedic surgeons at our institution who specialized in sports medicine (G.S.B. and B.K.G., with 10 and 25 years of clinical experience, respectively). All articular surfaces of the knee joint were carefully inspected both visually and with a surgical probe at arthroscopy and graded by using a modified Noyes classification system, as follows: grade 0 = normal, grade 1A = cartilage softening, grade 1B = cartilage fibrillation, grade 2A = superficial partial-thickness cartilage defect less than 50% of the total thickness of the articular surface, grade 2B = deep partial-thickness cartilage defect greater than 50% of the total thickness of the articular surface, and grade 3 = full-thickness cartilage defect (38). The orthopedic surgeons were aware of the MR findings of all patients at the time of arthroscopy. For patients in the prospective study group, the orthopedic surgeons also had a copy of the knee map showing the location and grade of cartilage lesions on each articular surface, which was based on the findings on both the routine MR images and the T2 maps.

Statistical Analysis

Statistical analysis was performed by using the R programming environment (version 2.3.1; R Foundation of Statistical Imaging, Vienna, Austria; *http://www.R-project.org*). For all tests, $P < .05$ was indicative of a statistically significant difference.

With use of arthroscopy as the standard of reference, the sensitivity and specificity of the routine MR protocol alone and with T2 maps in the detection of each arthroscopic grade and all arthroscopic grades combined were calculated for each surface and all surfaces combined. When calculating sensitivity and specificity for the routine MR protocol alone, the cartilage grades assigned at MR imaging were classified as either negative for disease (ie, MR grade 0 and 1A) or positive for disease (ie, MR grades 1, 2A, 2B, and 3). When calculating sensitivity and specificity for the routine MR protocol with T2 maps, the cartilage grades assigned at MR imaging were classified as either negative for disease (ie, MR grade 0) or positive for disease (ie, MR grades 1, 1A, 2A, 2B, and 3). A generalized estimating equation model was used to compare differences between the sensitivity and specificity of the routine MR protocol alone and the routine MR protocol with T2 maps. The model used a binomial family with logit link and independence working correlation structure. Standard errors were calculated by using robust sandwich covariance estimates.

Nonweighted Cohen κ statistics were used to measure interobserver agreement for determining the presence or absence of cartilage lesions within the knee joint by using the routine MR protocol alone and with T2 maps. Standard errors were calculated by using a bootstrapping method for patients. The null hypothesis that the κ values of the routine MR protocol alone and the routine MR protocol with T2 maps were equal would be rejected at the $P < .05$ level if the 95% confidence interval for the difference between κ values did not contain zero.

Posthoc multivariable analysis with use of a generalized estimating equation model was performed to determine whether certain features of the area of increased T2 relaxation time of MR grade 1A cartilage lesions could help differentiate between true-positive lesions (ie, lesions that corresponded to abnormal articular cartilage at arthroscopy) and false-positive lesions (ie, lesions that corresponded to normal articular cartilage at arthroscopy). The variables in the model included whether the area of increased T2 relaxation time *(a)* was two or more color scales higher than normal, *(b)* was more than 1 cm in maximal diameter, *(c)* was present on

two or more consecutive images, and *(d)* involved the entire thickness of the deep cartilage layer. The model used a binomial family with logit link and independence working correlation structure. Standard errors were calculated by using robust sandwich covariance estimates.

Results

T2 Relaxation Time of Normal Articular Cartilage

The T2 maps from the 10 patients in the retrospective study group had a similar appearance (Fig 1). Arthroscopically normal articular cartilage had a striated appearance, with a lower T2 relaxation time in the deep layer, a higher T2 relaxation time in the superficial layer, and a smooth transition between the two layers. The T2 relaxation time and thickness of the deep and superficial layers varied from one articular surface to another and in different regions on the same articular surface.

The deep layer of cartilage on the medial and lateral femoral condyles and the medial and lateral tibial plateaus had a T2 relaxation time between 20 and 30 msec, whereas the superficial layer had a T2 relaxation time between 40 and 50 msec. The deep layer comprised 75% of the thickness of the anterior and central weight-bearing surfaces and less than 20% of the thickness of the posterior weight-bearing surface of the femoral condyles. The deep layer comprised 50%–75% of the thickness of the central weight-bearing surface of the tibial plateau and less than 10% of the thickness in the peripheral regions beneath the body and horns of the menisci.

The deep layer of cartilage on the patella had a T2 relaxation time between 20 and 30 msec, whereas the superficial layer had a T2 relaxation time between 40 and 50 msec. The deep layer comprised 50% of the thickness of the middle and inferior portions of the patella and less than 10% of the thickness of the superior portion of the patella. The deep layer of cartilage on the trochlea had a T2 relaxation time between 20 and 40 msec, whereas the superficial layer had a T2 relaxation time between 50 and 60 msec. The deep layer comprised 50% of the thickness of the superior and inferior portions of the trochlea and less than 10% of the thickness of the middle portion of the trochlea.

Figure 1

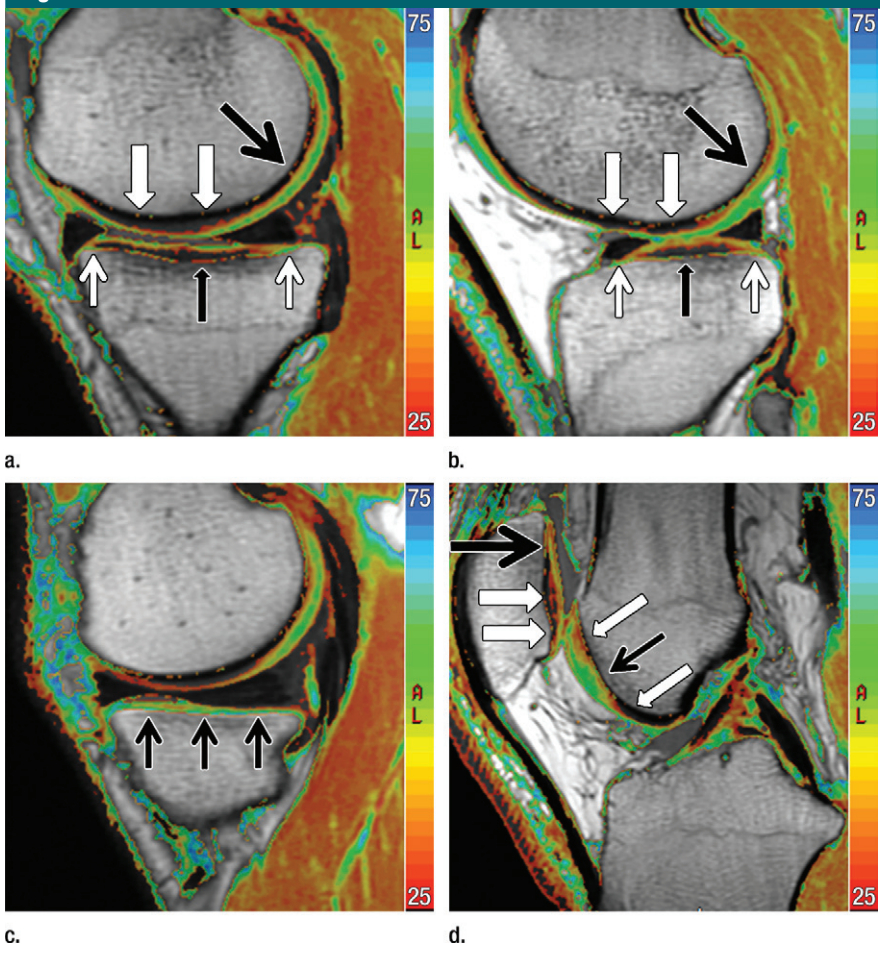

Figure 1: Images in 21-year-old man with arthroscopically normal articular cartilage within knee joint. **(a, b)** Sagittal T2 maps through **(a)** central portion of medial femoral condyle and tibial plateau and **(b)** central portion of lateral femoral condyle and tibial plateau show deep layer (black and/or red) and superficial layer (yellow and/or green) of cartilage. The deep cartilage layer is much thicker on anterior and central weight-bearing surfaces (thick white arrows) than on posterior weight-bearing surface (large black arrow) of femoral condyles and much thicker on central weight-bearing surface (small black arrow) of tibial plateau than on peripheral surface (thin white arrows) beneath horns of the menisci. **(c)** Sagittal T2 map through far medial portion of medial femoral condyle and tibial plateau shows thin deep cartilage layer on peripheral surface (arrows) of tibial plateau beneath body of meniscus. **(d)** Sagittal T2 map through patella and trochlea shows deep layer (black and/or red on patella and black and/or red and/or yellow on trochlea) and superficial layer (yellow and/or green on patella and green on trochlea) of cartilage. The deep cartilage layer is thicker in middle and inferior portions (thick white arrows) than in superior portion (large black arrow) of patella and is thicker in superior and inferior portions (thin white arrows) than in middle portion (small black arrow) of trochlea.

Diagnostic Performance with and without T2 Maps

There were 351 surgically confirmed cartilage lesions within the knee joint in the 150 patients in the prospective study group. The sensitivity and specificity in the detection of all arthroscopic grades of cartilage lesions were 74.6% (262 of 351 lesions) and 97.8% (537 of 549 lesions), respectively, for the routine MR imaging protocol alone and 88.9% (312 of 351 lesions) and 93.1% (511 of 549 lesions) for the routine MR

Table 2

Sensitivity and Specificity of the Routine MR Imaging Protocol Alone and with T2 Maps according to Arthroscopic Grade

Arthroscopic Grade	Sensitivity (%)		Specificity (%)	
	Routine MR Protocol	Routine MR Protocol with T2 Maps	Routine MR Protocol	Routine MR Protocol with T2 Maps
0	Not applicable	Not applicable	97.8 (537/549) [96.2, 98.8] {<.001}	93.1 (511/549) [90.6, 94.9] {<.001}
1A	4.2 (1/24) [0.0, 20.1] {<.001}	62 (15/24) [42.7, 78.8] {<.001}	Not applicable	Not applicable
1B	20 (8/41) [10.2, 34.0] {<.001}	66 (27/41) [50.6, 78.4] {<.001}	Not applicable	Not applicable
2A	77 (74/96) [67.7, 77.1] {.004}	88 (84/96) [79.4, 92.7] {.004}	Not applicable	Not applicable
2B	93.0 (146/157) [87.9, 96.0] {.023}	97.5 (153/157) [93.6, 99.0] {.023}	Not applicable	Not applicable
3	100 (33/33) [89.6, 100.0] {.999}	100 (33/33) [89.6, 100.0] {.999}	Not applicable	Not applicable
All grades	74.6 (262/351) [69.8, 78.9] {<.001}	88.9 (312/351) [85.2, 91.8] {<.001}	97.8 (537/549) [96.2, 98.8] {<.001}	93.1 (511/549) [90.6, 94.9] {<.001}

Note.—Numbers in parentheses are numbers of lesions, numbers in brackets are 95% confidence intervals, and numbers in braces are *P* values. Where "not applicable," sensitivity or specificity could not be calculated.

Figure 2

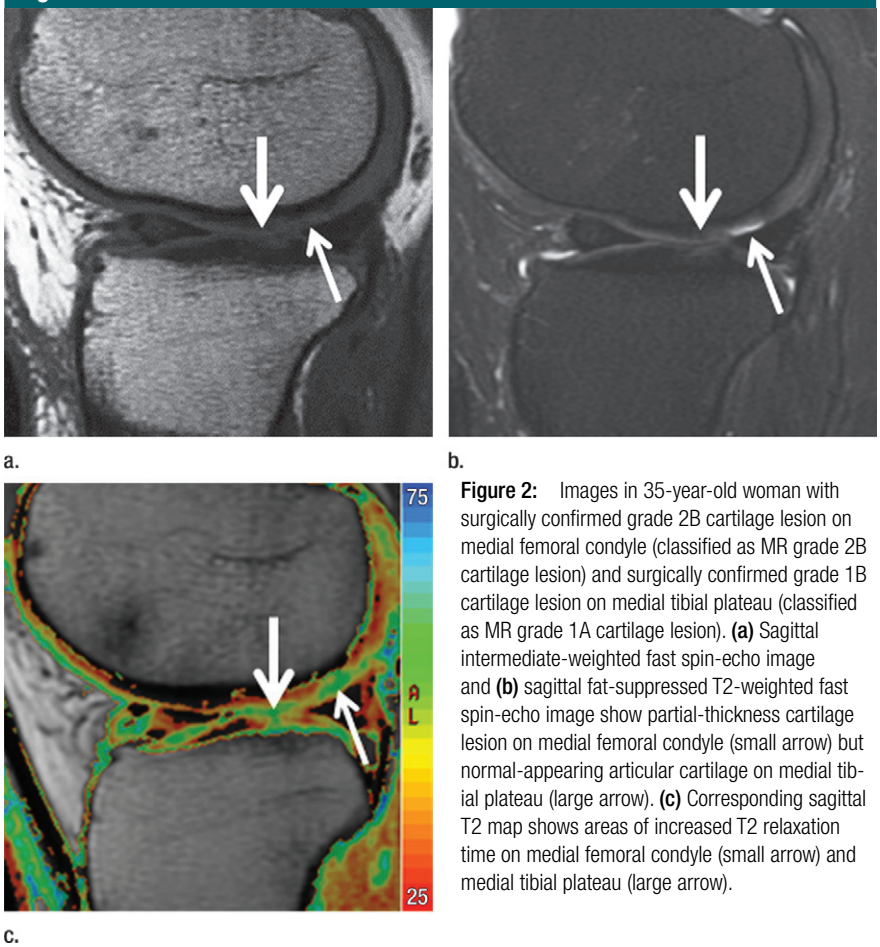

Figure 2: Images in 35-year-old woman with surgically confirmed grade 2B cartilage lesion on medial femoral condyle (classified as MR grade 2B cartilage lesion) and surgically confirmed grade 1B cartilage lesion on medial tibial plateau (classified as MR grade 1A cartilage lesion). **(a)** Sagittal intermediate-weighted fast spin-echo image and **(b)** sagittal fat-suppressed T2-weighted fast spin-echo image show partial-thickness cartilage lesion on medial femoral condyle (small arrow) but normal-appearing articular cartilage on medial tibial plateau (large arrow). **(c)** Corresponding sagittal T2 map shows areas of increased T2 relaxation time on medial femoral condyle (small arrow) and medial tibial plateau (large arrow).

imaging protocol with T2 maps (Table 2). The addition of the T2 maps to the routine MR imaging protocol improved the sensitivity in the detection of arthroscopic grade 1A cartilage lesions from 4.2% (one of 24 lesions) to 62% (15 of 24 lesions), improved the sensitivity in the detection of arthroscopic grade 1B cartilage lesions from 20% (eight of 41 lesions) to 66% (27 of 41 lesions), and improved the sensitivity in the detection of arthroscopic grade 2A lesions from 77% (74 of 96 lesions) to 88% (84 of 96 lesions) (Figs 2–6). Of the 76 MR grade 1A cartilage lesions identified on the T2 maps but not on the routine MR images, 26 corresponded to normal articular cartilage, 14 were grade 1A cartilage lesions, 19 were grade 1B cartilage lesions, 10 were grade 2A cartilage lesions, and seven were grade 2B cartilage lesions at arthroscopy. The routine MR imaging protocol with T2 maps had significantly higher sensitivity for detecting arthroscopic grade 1A ($P < .001$), arthroscopic grade 1B ($P < .001$), arthroscopic grade 2A ($P = .004$), arthroscopic grade 2B ($P = .023$), and all arthroscopic grades of cartilage lesions ($P < .001$) and significantly lower specificity for detecting all arthroscopic grades of cartilage lesions ($P < .001$) compared with the routine MR imaging protocol alone (Table 2). The routine MR imaging protocol with T2 maps had significantly higher sensitivity for detecting all arthroscopic grades of cartilage lesions on the patella ($P < .001$), trochlea ($P < .001$), medial tibial plateau ($P = .013$), and lateral tibial plateau ($P = .004$) and significantly lower specificity for detecting all arthroscopic grades of cartilage lesions on the patella ($P = .004$) and lateral tibial plateau ($P = .002$) compared with the routine MR imaging protocol alone (Table 3).

Figure 3

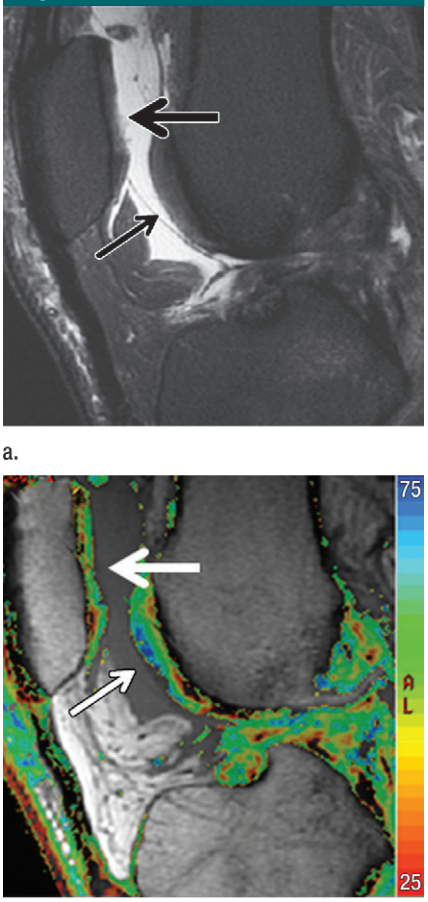

Figure 3: Images in 46-year-old woman with surgically confirmed grade 2B cartilage lesion on patella (classified as MR grade 2B cartilage lesion) and surgically confirmed grade 1A cartilage lesion on trochlea (classified as MR grade 1A cartilage lesion). **(a)** Sagittal fat-suppressed T2-weighted fast spin-echo image shows partial-thickness cartilage lesion on patella (large arrow) but normal-appearing articular cartilage on trochlea (small arrow). **(b)** Corresponding sagittal T2 map shows areas of increased T2 relaxation time on patella (large arrow) and trochlea (small arrow).

Figure 4

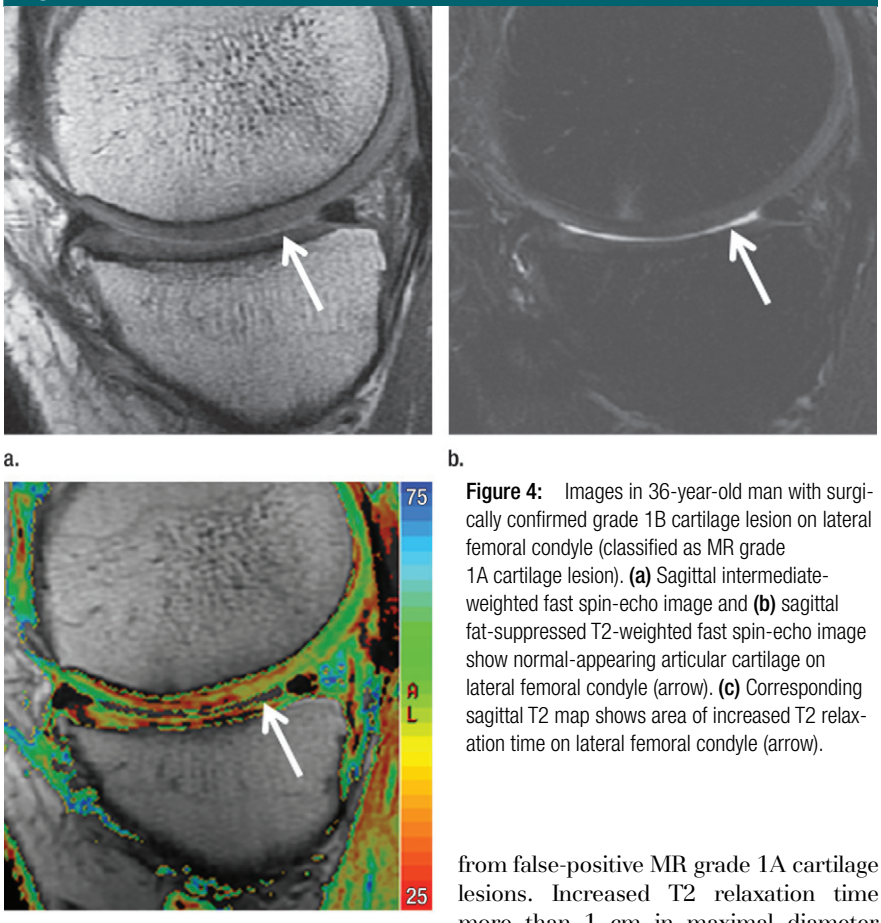

Figure 4: Images in 36-year-old man with surgically confirmed grade 1B cartilage lesion on lateral femoral condyle (classified as MR grade 1A cartilage lesion). **(a)** Sagittal intermediate-weighted fast spin-echo image and **(b)** sagittal fat-suppressed T2-weighted fast spin-echo image show normal-appearing articular cartilage on lateral femoral condyle (arrow). **(c)** Corresponding sagittal T2 map shows area of increased T2 relaxation time on lateral femoral condyle (arrow).

Of the 228 partial-thickness cartilage lesions identified with the routine MR imaging protocol and confirmed at arthroscopy, 204 (89.5%) showed an increased T2 relaxation time, 21 (9.2%) showed a normal T2 relaxation time, and three (1.3%) showed a decreased T2 relaxation time on the T2 maps.

The κ value for interobserver agreement for determining the presence and absence of cartilage lesions within the knee joint was 0.843 (95% confidence interval: 0.767, 0.908) for the routine MR imaging protocol alone and 0.827 (95% confidence interval: 0.756, 0.890) for the routine MR imaging protocol with T2 maps. There was no significant difference in κ values (difference of 0.016; 95% confidence interval of difference: −0.051, 0.014).

Increased T2 relaxation time two or more color scales higher than normal (estimate of 2.74 with standard error of 1.02, $P = .007$) and increased T2 relaxation time that involved the entire thickness of the deep cartilage layer (estimate of 1.86 with standard error of 0.52, $P < .001$) were features that could significantly help differentiate true-positive from false-positive MR grade 1A cartilage lesions. Increased T2 relaxation time more than 1 cm in maximal diameter (estimate of −0.18 with standard error of 0.48, $P = .716$) and increased T2 relaxation time present on two or more consecutive images (estimate of −0.94 with standard error of 0.53, $P = .074$) were features that could not significantly help differentiate true-positive from false-positive MR grade 1A cartilage lesions.

Discussion

In our study, the addition of a T2 mapping sequence to a routine MR imaging protocol significantly increased the sensitivity for detecting cartilage lesions within the knee joint, with the greatest improvement occurring in the identification of early cartilage degeneration. Our low sensitivity for detecting early cartilage degeneration by using the morphologic cartilage imaging sequences in the routine MR protocol is similar to the findings of previous

studies, which have reported sensitivity values for detecting cartilage fibrillation and superficial partial-thickness cartilage defects ranging from 9% to 62% at both 1.5 T and 3.0 T (8–16) Superficial changes in cartilage morphology can only be differentiated from the smooth surface of normal articular cartilage when using an in-plane spatial resolution of 0.3 mm, which is beyond the spatial resolution of most morphologic cartilage imaging sequences used in clinical practice (39). T2 mapping sequences do not rely on spatial resolution to identify superficial changes in cartilage morphology but instead depict areas of increased water content and altered collagen matrix ultrastructure in degenerative cartilage (26–30). As shown in our study, T2 mapping sequences can also depict areas of cartilage softening with moderate sensitivity and thus can help detect changes in the composition and three-dimensional ultrastructure of degenerative cartilage even before changes in cartilage morphology occur.

In our study, the addition of a T2 mapping sequence to a routine MR protocol resulted in a small but significant decrease in specificity for detecting cartilage lesions within the knee joint. The decrease in specificity may be due to spurious increases in cartilage T2 relaxation time secondary to the magic angle effect or regional variations in the collagen matrix ultrastructure or to early cartilage degeneration, which was unable to be detected with use of arthroscopy. The size of the area of increased T2 relaxation time was not a useful feature for differentiating between abnormalities on the T2 maps that corresponded to cartilage lesions at arthroscopy and those that corresponded to normal articular cartilage. However, increased T2 relaxation time two or more color scales higher than normal and increased T2 relaxation time that involved the entire thickness of the deep cartilage layer were features that could significantly help differentiate between true-positive and false-positive abnormalities. Identification of these features on T2 maps could provide greater confidence that an area of increased T2 relaxation time corresponds to an arthroscopically detectable cartilage lesion.

Our general impression from the literature is that cartilage degeneration increases T2 relaxation time owing to increased water content and disruption of the collagen matrix ultrastructure (19,31,32,35,36). The increased T2 relaxation time can occasionally be identified as areas of increased signal intensity within articular cartilage on T2-weighted fast spin-echo images, but these areas are much more difficult to detect when compared with use of quantitative T2 mapping techniques (40,41). However, previous studies have also reported unchanged or decreased T2 relaxation time with in vitro cartilage degeneration (42,43) and decreased signal intensity within surgically confirmed cartilage lesions on T2-weighted fast spin-echo images (44,45). It has been hypothesized that the decrease in T2 relaxation time is caused by collagenase-induced collagen cleavage, which creates additional sites of interaction

Figure 5

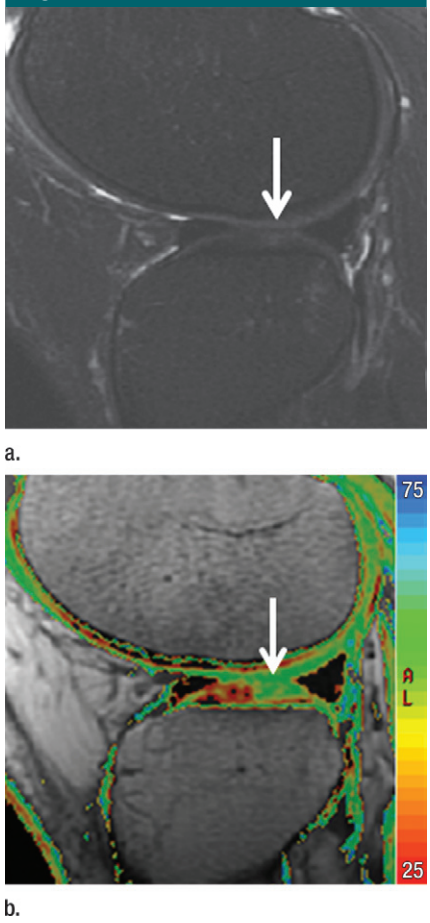

Figure 5: Images in 40-year-old man with arthroscopically normal articular cartilage on lateral femoral condyle (classified as MR grade 1A cartilage lesion). **(a)** Sagittal fat-suppressed T2-weighted fast spin-echo image shows normal-appearing articular cartilage on lateral femoral condyle (arrow). **(b)** Corresponding sagittal T2 map shows area of increased T2 relaxation time on lateral femoral condyle (arrow).

Figure 6

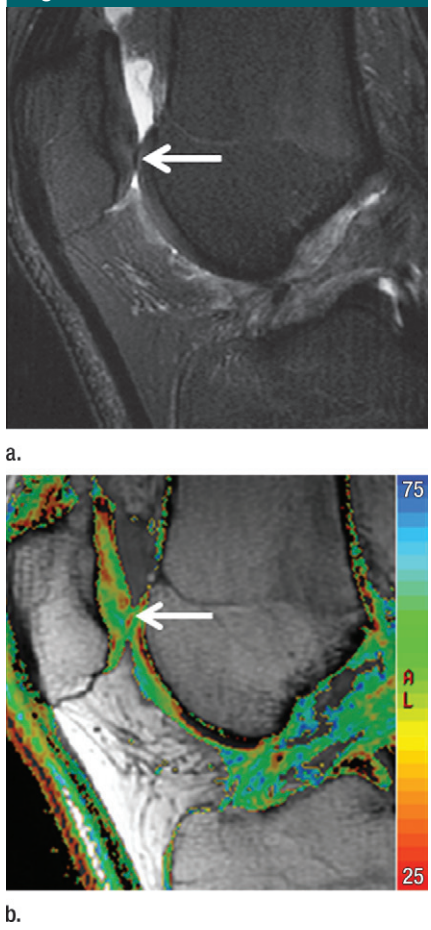

Figure 6: Images in 37-year-old man with arthroscopically normal articular cartilage on patella (classified as MR grade 1A cartilage lesion). **(a)** Sagittal fat-suppressed T2-weighted fast spin-echo image shows normal-appearing articular cartilage on patella (arrow). **(b)** Corresponding sagittal T2 map shows area of increased T2 relaxation time on patella (arrow).

Table 3

Sensitivity and Specificity of the Routine MR Imaging Protocol Alone and with T2 Maps according to Articular Surface

	Sensitivity (%)		Specificity (%)	
Articular Surface*	Routine MR Protocol	Routine MR Protocol with T2 Maps	Routine MR Protocol	Routine MR Protocol with T2 Maps
Patella	83 (75/90) [74.3, 89.6] {.001}	98 (88/90) [92.3, 99.4] {.001}	98 (59/60) [91.1, 99.7] {.004}	82 (49/60) [70.0, 89.4] {.004}
Trochlea	71 (47/66) [59.4, 80.7] {.001}	91 (60/66) [81.6, 95.8] {.001}	98 (82/84) [91.2, 99.3] {.0248}	94 (79/84) [86.8, 97.4] {.0248}
MFC	81 (61/75) [71.1,88.5] {.074}	88 (66/75) [78.7, 93.6] {.074}	100 (75/75) [95.1, 100.1] {.999}	100 (75/75) [95.1, 100.1] {.999}
LFC	81 (26/32) [64.7, 91.1] {.999}	84 (27/32) [68.3, 93.1] {.999}	95.8 (113/118) [90.5, 98.2] {.999}	95.8 (113/118) [90.5, 98.2] {.999}
MTP	63 (26/41) [48.1, 76.4] {.013}	83 (34/41) [68.7, 91.5] {.013}	100 (109/109) [96.6, 100.0] {.999}	99.1 (108/109) [95.0, 99.9] {.999}
LTP	57 (27/47) [43.3, 70.5] {.004}	79 (37/47) [65.1, 88.0] {.004}	96.1 (99/103) [90.4, 98.5] {.002}	94.2 (97/103) [76.3, 90.2] {.002}

Note.—Numbers in parentheses are numbers of lesions, numbers in brackets are 95% confidence intervals, and numbers in braces are *P* values.

* LFC = lateral femoral condyle, LTP = lateral tibial plateau, MFC = medial femoral condyle, MTP = medial tibial plateau.

between water and the collagen molecule (43). In our study, normal or decreased T2 relaxation time within degenerative cartilage was relatively uncommon. However, the fact that some surgically confirmed cartilage lesions did not show increased T2 relaxation time suggests that T2 mapping sequences should not be used alone to evaluate articular cartilage in clinical practice or osteoarthritis research studies.

Our study has shown that a T2 mapping sequence can be used to detect surgically confirmed cartilage lesions within the knee joint. Previous studies have also demonstrated the feasibility of using T2 mapping sequences to evaluate articular cartilage in symptomatic patients. Hannila et al (31) compared a T2 mapping sequence with a routine MR imaging protocol for evaluating patellar cartilage in 20 patients at 3.0 T and found that eight areas of increased T2 relaxation time corresponded to normal-appearing cartilage identified by using the routine MR protocol. Apprich et al (32) evaluated the articular cartilage of the medial femoral condyle in 43 patients at 3.0 T by using a T2 mapping sequence and a routine MR imaging protocol and found a significant association between the T2 relaxation time and the morphologic grade of the cartilage lesion. However, neither study included patients with surgical correlation and thus did not assess the diagnostic performance of T2 mapping sequences in the evaluation of articular cartilage by using the established reference standard of arthroscopy.

Our study has several limitations. One limitation was that a qualitative analysis was performed in the 10 patients in the retrospective study group to investigate the normal distribution of cartilage T2 relaxation time on each articular surface of the knee joint. However, the main objective of this retrospective analysis was to allow the musculoskeletal radiologists to gain a better understanding of the appearance of arthroscopically normal articular cartilage on the T2 maps before beginning the prospective portion of the study. A more quantitative assessment of the normal distribution of cartilage T2 relaxation time was beyond the scope of this investigation and has been described in detail in previous studies (22,46). Additional limitations of our study include the sequential use of the routine MR imaging protocol and T2 maps to evaluate articular cartilage, the use of the T2 maps only to evaluate articular surfaces that were classified as normal with the routine MR imaging protocol, and the consensus interpretation of the MR images by the two fellowship-trained musculoskeletal radiologists. In addition, the orthopedic surgeons were aware of the MR findings of all patients at the time of arthroscopic knee surgery, which may have biased their evaluation of the articular cartilage. Our study also did not include an assessment of reader confidence for determining the presence or absence of cartilage lesions when using the routine MR imaging protocol with and without the T2 maps. In addition, no attempt was made to standardize the degree of joint loading in patients in the retrospective and prospective study groups. The degree of joint loading before MR examination may have varied from individual to individual, which may have influenced the T2 relaxation time of articular cartilage and the detection of cartilage lesions on the T2 maps (32,47). A final limitation of our study was that arthroscopy, and not histologic examination, was used as the standard of reference for evaluating articular cartilage. Although arthroscopy is the best available minimally invasive reference standard, its ability to depict early cartilage degeneration, especially in the deep layers of articular cartilage, has been questioned (48).

In conclusion, our study has demonstrated the feasibility of using a commercially available T2 mapping sequence with a relatively short imaging time to evaluate the articular cartilage of the knee joint at 3.0 T. The addition of a T2 mapping sequence to a routine MR imaging protocol increased the sensitivity for detecting surgically confirmed cartilage lesions, with the greatest improvement occurring in the identification of early cartilage degeneration. However, limitations of using the T2 mapping sequence included the lower specificity for evaluating articular cartilage, the need to purchase

dedicated imager and postprocessing software, the increase in MR examination time, and the learning curve needed to interpret the T2 maps. Nevertheless, the addition of a T2 mapping sequence to a routine MR imaging protocol can improve the detection of early cartilage degeneration within the knee joint in symptomatic patients. A T2 mapping sequence may be especially useful for evaluating articular cartilage in certain patient populations where the identification of early cartilage degeneration is clinically important (eg, individuals with knee pain and no meniscal tear or cartilage lesions detected with the routine MR imaging protocol or individuals with persistent knee pain after meniscal resection or anterior cruciate ligament reconstruction surgery).

Disclosures of Conflicts of Interest: R.K. Financial activities related to the present article: none to disclose. Financial activities not related to the present article: owns stock/stock options in Flex Biomedical. Other relationships: none to disclose. **D.G.B.** No relevant conflicts of interest to disclose. **A.M.d.R.** Financial activities related to the present article: none to disclose. Financial activities not related to the present article: is a paid consultant for Lippincott, Williams, and Wilkins. Other relationships: none to disclose. **G.S.B.** No relevant conflicts of interest to disclose. **B.K.G.** Financial activities related to the present article: none to disclose. Financial activities not related to the present article: receives payment for patents and royalties for orthopedic devices from Smith & Nephew. Other relationships: none to disclose.

References

1. Altman RD. Early management of osteoarthritis. Am J Manag Care 2010;16(Suppl Management):S41–S47.
2. Pelletier JP, Martel-Pelletier J, Raynauld JP. Most recent developments in strategies to reduce the progression of structural changes in osteoarthritis: today and tomorrow. Arthritis Res Ther 2006;8(2):206.
3. Pelletier JP, Martel-Pelletier J. DMOAD developments: present and future. Bull NYU Hosp Jt Dis 2007;65(3):242–248.
4. Qvist P, Bay-Jensen AC, Christiansen C, Dam EB, Pastoureau P, Karsdal MA. The disease modifying osteoarthritis drug (DMOAD): is it in the horizon? Pharmacol Res 2008;58(1):1–7.
5. Hellio Le Graverand-Gastineau MP. OA clinical trials: current targets and trials for OA. Choosing molecular targets: what have we learned and where we are headed? Osteoarthritis Cartilage 2009;17(11):1393–1401.
6. Hunter DJ, Hellio Le Graverand-Gastineau MP. How close are we to having structure-modifying drugs available? Med Clin North Am 2009;93(1):223–234, xiii.
7. Burstein D, Hunter DJ. "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.
8. Bachmann GF, Basad E, Rauber K, Damian MS, Rau WS. Degenerative joint disease on MRI and physical activity: a clinical study of the knee joint in 320 patients. Eur Radiol 1999;9(1):145–152.
9. Irie K, Yamada T, Inoue K. A comparison of magnetic resonance imaging and arthroscopic evaluation of chondral lesions of the knee. Orthopedics 2000;23(6):561–564.
10. Kijowski R, Davis KW, Woods MA, et al. Knee joint: comprehensive assessment with 3D isotropic resolution fast spin-echo MR imaging—diagnostic performance compared with that of conventional MR imaging at 3.0 T. Radiology 2009;252(2):486–495.
11. Kijowski R, Blankenbaker DG, Klaers JL, Shinki K, De Smet AA, Block WF. Vastly undersampled isotropic projection steady-state free precession imaging of the knee: diagnostic performance compared with conventional MR. Radiology 2009;251(1):185–194.
12. Kijowski R, Blankenbaker DG, Davis KW, Shinki K, Kaplan LD, De Smet AA. Comparison of 1.5- and 3.0-T MR imaging for evaluating the articular cartilage of the knee joint. Radiology 2009;250(3):839–848.
13. Kijowski R, Blankenbaker DG, Woods MA, Shinki K, De Smet AA, Reeder SB. 3.0-T evaluation of knee cartilage by using three-dimensional IDEAL GRASS imaging: comparison with fast spin-echo imaging. Radiology 2010;255(1):117–127.
14. Macarini L, Murrone M, Marini S, Mariano M, Zaccheo N, Moretti B. MR in the study of knee cartilage pathologies: influence of location and grade on the effectiveness of the method. Radiol Med (Torino) 2003; 105(4):296–307.
15. von Engelhardt LV, Schmitz A, Pennekamp PH, Schild HH, Wirtz DC, von Falkenhausen F. Diagnostics of degenerative meniscal tears at 3-Tesla MRI compared to arthroscopy as reference standard. Arch Orthop Trauma Surg 2008;128(5):451–456.
16. von Engelhardt LV, Kraft CN, Pennekamp PH, Schild HH, Schmitz A, von Falkenhausen M. The evaluation of articular cartilage lesions of the knee with a 3-Tesla magnet. Arthroscopy 2007;23(5):496–502.
17. Quatman CE, Hettrich CM, Schmitt LC, Spindler KP. The clinical utility and diagnostic performance of magnetic resonance imaging for identification of early and advanced knee osteoarthritis: a systematic review. Am J Sports Med 2011;39(7):1557–1568.
18. Bredella MA, Tirman PF, Peterfy CG, et al. Accuracy of T2-weighted fast spin-echo MR imaging with fat saturation in detecting cartilage defects in the knee: comparison with arthroscopy in 130 patients. AJR Am J Roentgenol 1999;172(4):1073–1080.
19. Dunn TC, Lu Y, Jin H, Ries MD, Majumdar S. T2 relaxation time of cartilage at MR imaging: comparison with severity of knee osteoarthritis. Radiology 2004;232(2):592–598.
20. Mosher TJ, Collins CM, Smith HE, et al. Effect of gender on in vivo cartilage magnetic resonance imaging T2 mapping. J Magn Reson Imaging 2004;19(3):323–328.
21. Mosher TJ, Smith H, Dardzinski BJ, Schmithorst VJ, Smith MB. MR imaging and T2 mapping of femoral cartilage: in vivo determination of the magic angle effect. AJR Am J Roentgenol 2001;177(3):665–669.
22. Smith HE, Mosher TJ, Dardzinski BJ, et al. Spatial variation in cartilage T2 of the knee. J Magn Reson Imaging 2001;14(1):50–55.
23. Stahl R, Blumenkrantz G, Carballido-Gamio J, et al. MRI-derived T2 relaxation times and cartilage morphometry of the tibio-femoral joint in subjects with and without osteoarthritis during a 1-year follow-up. Osteoarthritis Cartilage 2007;15(11):1225–1234.
24. Peterfy CG, Schneider E, Nevitt M. The osteoarthritis initiative: report on the design rationale for the magnetic resonance imaging protocol for the knee. Osteoarthritis Cartilage 2008;16(12):1433–1441.
25. Pan J, Pialat JB, Joseph T, et al. Knee cartilage T2 characteristics and evolution in relation to morphologic abnormalities detected at 3-T MR imaging: a longitudinal study of the normal control cohort from the Osteoarthritis Initiative. Radiology 2011; 261(2):507–515.
26. Fragonas E, Mlynárik V, Jellús V, et al. Correlation between biochemical composition and magnetic resonance appearance of articular cartilage. Osteoarthritis Cartilage 1998; 6(1):24–32.
27. Nieminen MT, Rieppo J, Töyräs J, et al. T2 relaxation reveals spatial collagen architecture in articular cartilage: a comparative quantitative MRI and polarized light microscopic study. Magn Reson Med 2001; 46(3):487–493.

28. Xia Y, Moody JB, Alhadlaq H. Orientational dependence of T2 relaxation in articular cartilage: a microscopic MRI (microMRI) study. Magn Reson Med 2002;48(3):460–469.

29. Liess C, Lüsse S, Karger N, Heller M, Glüer CC. Detection of changes in cartilage water content using MRI T2-mapping in vivo. Osteoarthritis Cartilage 2002;10(12):907–913.

30. Goodwin DW, Wadghiri YZ, Zhu H, Vinton CJ, Smith ED, Dunn JF. Macroscopic structure of articular cartilage of the tibial plateau: influence of a characteristic matrix architecture on MRI appearance. AJR Am J Roentgenol 2004;182(2):311–318.

31. Hannila I, Nieminen MT, Rauvala E, Tervonen O, Ojala R. Patellar cartilage lesions: comparison of magnetic resonance imaging and T2 relaxation-time mapping. Acta Radiol 2007;48(4):444–448.

32. Apprich S, Welsch GH, Mamisch TC, et al. Detection of degenerative cartilage disease: comparison of high-resolution morphological MR and quantitative T2 mapping at 3.0 Tesla. Osteoarthritis Cartilage 2010; 18(9):1211–1217.

33. Potter HG, Linklater JM, Allen AA, Hannafin JA, Haas SB. Magnetic resonance imaging of articular cartilage in the knee: an evaluation with use of fast-spin-echo imaging. J Bone Joint Surg Am 1998;80(9):1276–1284.

34. Sonin AH, Pensy RA, Mulligan ME, Hatem S. Grading articular cartilage of the knee using fast spin-echo proton density-weighted MR imaging without fat suppression. AJR Am J Roentgenol 2002; 179(5):1159–1166.

35. Regatte RR, Akella SV, Lonner JH, Kneeland JB, Reddy R. T1rho relaxation mapping in human osteoarthritis (OA) cartilage: comparison of T1rho with T2. J Magn Reson Imaging 2006;23(4):547–553.

36. Mosher TJ, Dardzinski BJ, Smith MB. Human articular cartilage: influence of aging and early symptomatic degeneration on the spatial variation of T2—preliminary findings at 3 T. Radiology 2000;214(1):259–266.

37. Irrgang JJ, Anderson AF, Boland AL, et al. Development and validation of the international knee documentation committee subjective knee form. Am J Sports Med 2001; 29(5):600–613.

38. Noyes FR, Stabler CL. A system for grading articular cartilage lesions at arthroscopy. Am J Sports Med 1989;17(4):505–513.

39. Rubenstein JD, Li JG, Majumdar S, Henkelman RM. Image resolution and signal-to-noise ratio requirements for MR imaging of degenerative cartilage. AJR Am J Roentgenol 1997;169(4):1089–1096.

40. McCauley TR, Kier R, Lynch KJ, Jokl P. Chondromalacia patellae: diagnosis with MR imaging. AJR Am J Roentgenol 1992;158(1):101–105.

41. De Smet AA, Monu JU, Fisher DR, Keene JS, Graf BK. Signs of patellar chondromalacia on sagittal T2-weighted magnetic resonance imaging. Skeletal Radiol 1992;21(2):103–105.

42. Regatte RR, Akella SV, Borthakur A, Kneeland JB, Reddy R. Proteoglycan depletion-induced changes in transverse relaxation maps of cartilage: comparison of T2 and T1rho. Acad Radiol 2002;9(12): 1388–1394.

43. Menezes NM, Gray ML, Hartke JR, Burstein D. T2 and T1rho MRI in articular cartilage systems. Magn Reson Med 2004;51(3):503–509.

44. Hodler J, Berthiaume MJ, Schweitzer ME, Resnick D. Knee joint hyaline cartilage defects: a comparative study of MR and anatomic sections. J Comput Assist Tomogr 1992;16(4):597–603.

45. Stephens T, Diduch DR, Balin JI, Gaskin CM. The cartilage black line sign: an unexpected MRI appearance of deep cartilage fissuring in three patients. Skeletal Radiol 2011; 40(1):113–116.

46. Hannila I, Räinä SS, Tervonen O, Ojala R, Nieminen MT. Topographical variation of T2 relaxation time in the young adult knee cartilage at 1.5 T. Osteoarthritis Cartilage 2009;17(12):1570–1575.

47. Apprich S, Mamisch TC, Welsch GH, et al. Quantitative T2 mapping of the patella at 3.0T is sensitive to early cartilage degeneration, but also to loading of the knee. Eur J Radiol 2012;81(4):e438–e443.

48. Hodler J, Resnick D. Chondromalacia patellae. AJR Am J Roentgenol 1992; 158(1):106–107.