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Cartilage T1ρ and T2 Relaxation Times in Patients With Mild-to-Moderate Radiographic Hip Osteoarthritis

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Objective. **To analyze region-specific T1ρ and T2 relaxation times of the hip joint cartilage in relation to presence or absence of radiographic hip osteoarthritis (OA) and presence or absence of magnetic resonance imaging (MRI)–detected cartilage defects.**

Methods. **Weight-bearing radiographs and 3T MRI studies of the hip were obtained from 84 volunteers. Based on Kellgren/Lawrence (K/L) scoring of the radiographs, 54 subjects were classified as healthy controls (K/L grade $\leq$1) and 30 were classified as having mild or moderate radiographic hip OA (K/L grades 2 or 3, respectively). Two-dimensional fat-suppressed fast spin-echo MRI sequences were used for semiquantitative clinical scoring of cartilage defects, and a T1ρ/T2 sequence was used to quantitatively assess the cartilage matrix. The femoral and acetabular cartilage was then segmented into 8 regions and the mean T1ρ/T2 values were calculated. Differences in T1ρ and T2 relaxation times were compared between subjects with and those without radiographic hip OA, and those with and those without femoral or acetabular cartilage defects.**

Results. **Higher T1ρ and T2 relaxation times in the anterior superior and central regions of the acetabular cartilage were seen in individuals with radiographic hip OA and those with acetabular cartilage defects compared to their respective controls ($P < 0.05$). In the femoral cartilage, the differences in T1ρ and T2 were not significant for any of the comparisons. Significant differences in the T1ρ and T2 values (each $P < 0.05$) were found in more subregions of the cartilage and across the whole cartilage when subjects were stratified based on the presence of MRI-detected cartilage defects than when they were stratified based on the presence of radiographic hip OA.**

Conclusion. **T1ρ and T2 relaxation parameters are sensitive to the presence of cartilage degeneration. Both parameters may therefore support MRI evidence of cartilage defects of the hip.**

One in 4 individuals has a lifetime risk of developing symptomatic hip osteoarthritis (OA) by the age of 85 years (1). Individuals with hip OA experience substantial pain and disability, suggesting an urgent clinical need for diagnosis and prevention of hip OA (2,3). Hip OA is typically diagnosed through the use of radiographs, and semiquantitative clinical scores, such as the Kellgren/Lawrence (K/L) scores for radiographic damage (4), are used to quantify the severity of OA. However, diagnosis of OA with the use of radiographs is mostly focused on osteophytes and joint space narrowing, features that are indicative of advanced disease, whereas radiography lacks sensitivity for early changes of the soft tissues, such as cartilage and labrum. Magnetic resonance imaging (MRI) can provide information on hip degeneration at an earlier stage, by allowing visualization of morphologic abnormalities of the cartilage, bone marrow, and labrum (5–8).

Early changes in OA consist of proteoglycan loss, changes in water content, and collagen disruption (9).

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However, clinical anatomic MRI cannot detect early compositional changes in the hip cartilage (6). The T1ρ relaxation time and T2 relaxation time provide indirect estimation of the proteoglycan content and collagen integrity, respectively, of the hip cartilage, and both parameters are sensitive to changes seen in early OA (10–13).

A number of studies have demonstrated that individuals with knee OA have elevated T1ρ and T2 relaxation times in comparison to healthy controls (14–16). However, T1ρ and T2 estimates have not been used to quantify the compositional changes associated with hip OA; the only published studies to date have focused on hip dysplasia and femoroacetabular impingement (FAI) (17–20). Although the potential usefulness of quantitative imaging techniques in hip cartilage has been demonstrated in these studies conducted in small samples, there is a need to analyze the effectiveness of these techniques in a larger cohort of subjects to prove their importance in a clinical setting. Furthermore, quantitative T1ρ and T2 imaging has yet to be evaluated in the context of presence of cartilage defects in the hip. The presence of defects is important to consider, since it has recently been shown that in individuals with mild-to-moderate radiographic hip OA, cartilage defects at the acetabulum have a stronger association with patient-reported pain and disability than defects at the femur (21).

If T1ρ and T2 relaxation times are found to be sensitive parameters in the detection of cartilage degeneration in hip OA, these quantitative tools could be used for early detection of the disease. Current interventions to halt the structural progression of OA are ineffective. Therefore, early detection before the onset of structural changes may allow for development of therapies that can prevent the progression of hip OA. The purpose of this study was to analyze T1ρ and T2 relaxation times in the femoral and acetabular cartilage of individuals with and those without mild-to-moderate radiographic hip OA.

PATIENTS AND METHODS

Subject recruitment. This study included data from 84 subjects enrolled as part of a longitudinal study on hip OA and FAI. Of 96 individuals originally enrolled, 12 had radiographic evidence (presence of cam-lesion) and symptomatic evidence (self-reported hip pain) of FAI but no radiographic evidence of hip OA (all had a K/L grade of <2). These 12 subjects were excluded from the study. All subjects were recruited using media and internet postings from September 2011 to December 2012. The study protocol was approved by our institution's Committee of Human Research, and written informed consent was acquired from all individuals before participation.

The inclusion criteria for this study were as follows: 1) age 18 years or older; 2) history of good health according to medical history review; and 3) willingness and ability to comply with study procedures. Subjects were excluded from the study if they had undergone hip surgery or had inflammatory arthritis, hematochromatosis, sickle cell disease, hemoglobinopathy, knee OA with a K/L score of >2, hip OA with a K/L score of 4, any condition other than OA that would limit lower extremity function and mobility, a positive test result for pregnancy, contraindications to MRI (e.g., implanted pacemaker or claustrophobia), or acquired MR images that were suboptimal in quality.

Radiographic protocol. Anteroposterior, weight-bearing frontal radiographs of the pelvis were obtained from all subjects, with each subject placed in a standing position. For positioning, the feet were aligned so that the toes were facing forward with slight internal rotation. Settings included a focus-film distance of 40 inches and voltage of 80 kVp with automatic exposure, using a GE Healthcare Discovery 650 X-ray system. A board-certified musculoskeletal radiologist (TML) with 25 years of experience performed the bilateral K/L grading of the hip radiographs and measured the center edge angle of the hip from these radiographs. Ten subjects were chosen at random, and a repeat reading of their radiographs was performed for intrareader reliability measurements, with the reliability calculated using the intraclass correlation coefficient (ICC).

MRI protocol. Unilateral hip MRI examinations were performed on a 3T scanner (MR750) using an 8-channel receive-only cardiac coil (GE Healthcare). For all scans, the subject's feet were internally rotated and forefeet were taped together to maintain a reproducible foot position and reduce hip movement. The hip side with the higher K/L grade was scanned if the grading was not the same for both sides. For subjects with equal K/L grades for both hips, the side scanned was selected at random. The MRI protocol included intermediate-weighted, fat-suppressed, fast spin-echo (FSE) sequences for semiquantitative clinical grading of the hip in 1) a sagittal orientation (time to recovery [TR] 3,678 msec, echo time [TE] 60 msec, slice thickness 4 mm, echo train length [ETL] 16, number of slices 24, field of view [FOV] 14 cm, matrix size 288 × 224 pixels, number of signals averaged 4, acquisition time 4 minutes); 2) an oblique coronal orientation along the femoral neck (TR 2,496 msec, TE 60 msec, slice thickness 4 mm, ETL 16, number of slices 16, FOV 20 cm, matrix size 288 × 224 pixels, number of signals averaged 6, acquisition time 4 minutes 40 seconds); and 3) an oblique axial orientation parallel to the femoral neck (TR 2,800 msec, TE 60 msec, slice thickness 3 mm, 18 slices, FOV 18 cm, matrix size 288 × 224 pixels, number of signals averaged 4, acquisition time 3 minutes 50 seconds).

Subjects were also scanned with a combined T1ρ/T2 sequence using a 3-dimensional (3-D), segmented spoiled gradient-recalled acquisition in the steady state (SPGR), in which the T2 echoes are acquired immediately after the T1ρ acquisitions, as detailed by Li et al (22). The scan was applied in the sagittal plane with the slab in the left/right direction. The parameters for the T1ρ/T2 sequence were as follows: time of spin lock (TSL) 0/15/30/45 msec, spin-lock frequency 300 Hz, views per segment (VPS) 64, and TR 1.2 seconds.

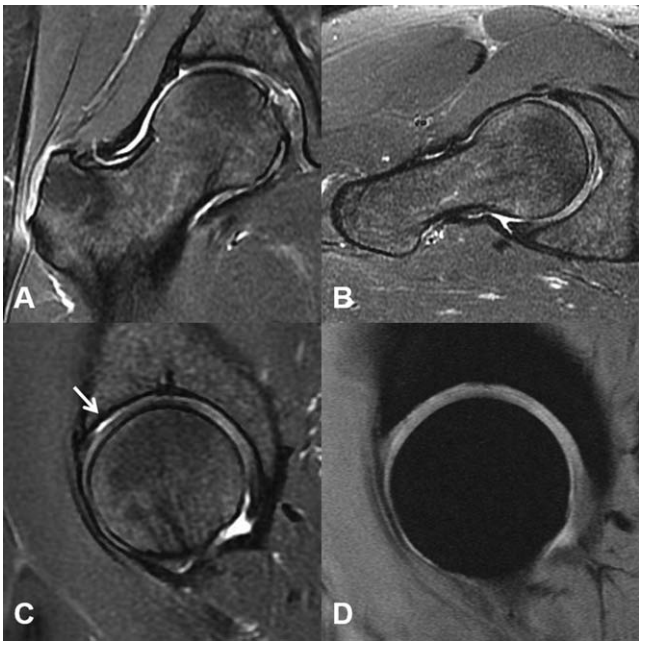

Figure 1. Examples of clinical images acquired from the right hip of a 52-year-old female subject with a Kellgren/Lawrence radiographic damage score of 2 and magnetic resonance imaging–detected acetabular and cartilage defects. The images represent the **A,** coronal fast spin-echo (FSE), **B,** axial FSE, **C,** sagittal FSE, and **D,** multiecho spoiled gradient-recalled acquisition in the steady-state acquisitions. **Arrow** indicates the location of an acetabular cartilage defect.

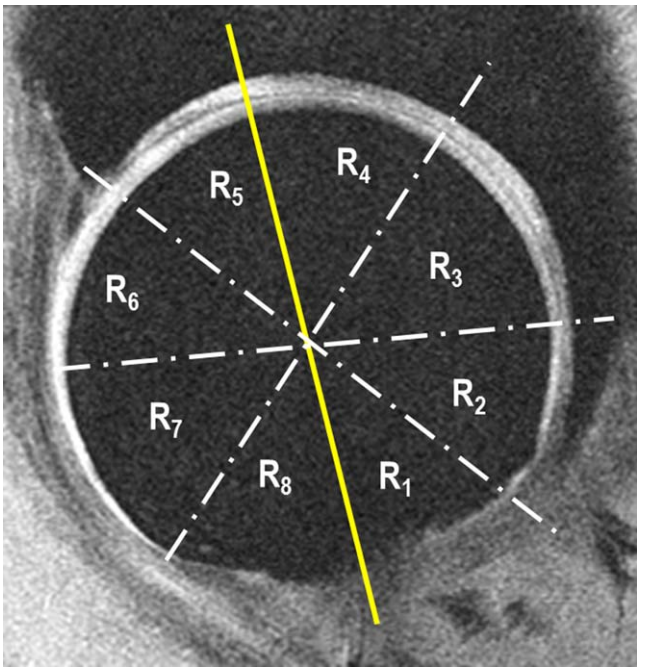

Figure 2. Division and numbering of the 8 subregions (R1–R8) of the hip cartilage on a representative magnetic resonance image acquired using multiecho spoiled gradient-recalled acquisition in the steady state. The solid yellow line represents a line parallel with the femoral neck that is drawn for each subject.

For T2 preparation, the TE was 0/10.4/20.8/41.7 msec, while for the T1ρ and T2 sequences, the parameters were as follows: FOV 14 cm, matrix size 256 $\times$ 128 pixels, VPS 64, bandwidth 62.5 kHz, TR 1.2 seconds, slice thickness 4 mm, no gap, in-plane resolution 0.5 mm, and acquisition time 13 minutes 47 seconds. Lastly, 70 of the subjects were scanned with a fat-suppressed, 3-D multiecho SPGR (MERGE) sequence with the following parameters: TR 30.4 msec, TE 5 msec (effective TE 12.4 msec), flip angle 15°, matrix size 512 $\times$ 512 pixels, 28 slices, slice thickness 4 mm, FOV 14 cm, bandwidth 62.5 kHz, number of signals averaged 1, and acquisition time 11 minutes 46 seconds. The MERGE sequence was scanned with the same prescription as the T1ρ/T2 sequence. Representative images, acquired from the hip joints of a patient with a K/L grade of 2, are shown in Figure 1.

MRI clinical grading. All MR images were reviewed by 2 fellowship-trained board-certified musculoskeletal radiologists (SL and LN) with 5 years and 7 years of musculoskeletal imaging experience, respectively. The clinical grading for each subject was performed independently on the oblique coronal, sagittal, and oblique axial MR images of the hip. If there were discrepancies between the 2 reviewers, a consensus review with a senior radiologist (TML) was performed.

First, the alpha angle of the hip was measured on the oblique axial MR images. A scoring system named SHOMRI (7,23), developed at our institution, was then used to evaluate the presence of cartilage defects. The femoral and acetabular segments of the hip cartilage were divided into 6 subregions (4 femoral, 2 acetabular) on the coronal FSE images, and 4 subregions (2 femoral, 2 acetabular) on the sagittal FSE images, for a total of 10 subregions (21). The mid portion of the femoral head was defined on the sagittal images and subdivided into 4 subregions on the coronal images, from lateral to medial. The landmark for division was the lateral acetabular rim for the lateral and superolateral, a vertical line from the center of the femoral head for the superolateral and

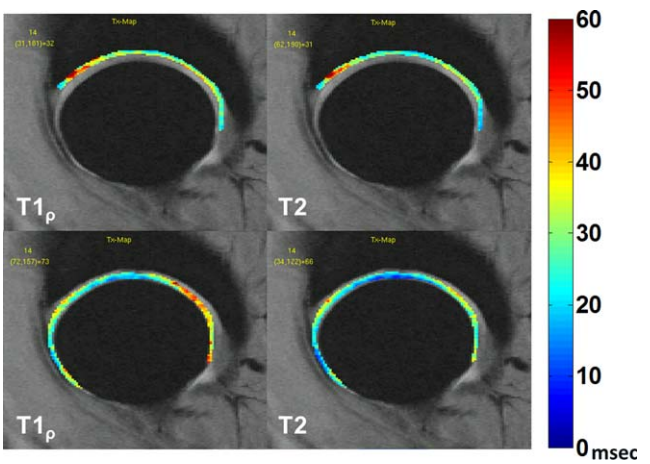

Figure 3. T1ρ and T2 maps overlaid on magnetic resonance images acquired using multiecho spoiled gradient-recalled acquisition in the steady state, showing femoral cartilage (top) and acetabular cartilage (bottom) of the right hip of a subject with a Kellgren/Lawrence radiographic damage score of 2 (same subject as in Figure 1). The color map corresponds to the range of relaxation times (in msec).

superomedial, and ligamentum teres for the superomedial and inferior subregions. On the sagittal MRI study, the anterior subregion represented the anterior 1 cm of the femoral head, and the posterior subregion represented the posterior 1 cm of the femoral head. The division was based on a simplified version of the geographic zone method described by Ilizaliturri et al (24) for hip arthroscopy, which showed superior interobserver reproducibility compared to the clock-face method. Cartilage defects were graded as 0 (no defect), 1 (partial thickness), and 2 (full thickness), and total scores were calculated for the entire joint. Consensus readings were performed in cases of disagreement.

Quantitative cartilage analysis. Due to the occasional movement of some subjects during the examination, the T1ρ- and T2-weighted images, as well as the high-resolution MERGE images acquired in the same examination (if available), were rigidly registered to the T1ρ image with the shortest TSL (therefore with the highest signal-to-noise ratio) using the Kitware VTK CISG Registration Toolkit. Using the registered images, the T1ρ and T2 relaxation maps were created by applying a nonlinear 2-parameter fit. The femoral cartilage and acetabular cartilage were then semiautomatically segmented separately (on the MERGE images when available, on the T1ρ images with a TSL of 0 when MERGE images were not available), using a software program developed in-house based on a spline-based semiautomated (automated edge detection and manual correction) segmentation algorithm in MatLab (Mathworks). The cartilage layers were segmented on ~4 slices near the center of the hip, as these were typically the only slices without severe partial volume effects. The segmentations were then divided into subregions to allow for more localized analysis.

To account for small variations in the internal rotation of the hip between subjects, a line was drawn parallel to the femoral neck on 1 slice of the T1ρ image (TSL 0). The cartilage was divided into 8 subregions around the line, as shown in Figure 2. The mean T1ρ and T2 values in the resulting subregions containing cartilage (~5 subregions for the acetabulum, 6 subregions for the femur) were quantified. For each subject, segmentation regions were not analyzed if they contained <50 pixels over all segmented slices. The resultant T1ρ and T2 maps after analysis are shown in Figure 3, using images from the same subject as in Figure 1 (a representative subject with a K/L grade of 2).

Statistical analysis. The subjects were then stratified 3 different ways for statistical analysis: 1) those with radiographic hip OA (K/L grades 2 or 3) and those without radiographic hip OA (K/L grades 0 or 1); 2) those with femoral cartilage defects in any subregion (femoral cartilage score >0) and those without femoral cartilage defects in any subregion (femoral cartilage score 0); and 3) those with acetabular cartilage defects in any subregion (acetabular cartilage score >0) and those without acetabular cartilage defects in any subregion (acetabular cartilage score 0). Age, body mass index (BMI), alpha angle of the hip, and center edge angle of the hip were compared between the groups using independent-sample *t*-tests. Multivariate analyses of variance, adjusted for age, were performed using SPSS software, to compare the T1ρ and T2 values in each subregion between the control and OA groups, as well as between the groups with and those without cartilage defects. Region 6 in the acetabulum had data from fewer subjects (23 of the original 84 subjects) compared to the other regions, since the region was too small in some subjects to satisfy our 50-pixel threshold. Spearman's correlation coefficients were calculated to assess correlations between T1ρ and T2 values in each of the subcompartments and for the whole cartilage. *P* values less than 0.05 were considered significant.

Table 1. Demographic and clinical characteristics of the 84 subjects*

	Radiographic hip OA			Femoral defects on hip MRI			Acetabular defects on hip MRI		
	Healthy controls (n = 54)	Hip OA (n = 30)	*P*	Without (n = 32)	With (n = 52)	*P*	Without (n = 49)	With (n = 35)	*P*
Age, mean (range) years	43.7 (40.1–48.3)	50.8 (46.0–55.6)	0.018	41 (36.6–45.4)	49.6 (45.9–53.3)	0.004	42.4 (38.6–46.2)	52 (47.9–56.1)	0.001
BMI, mean (range) kg/m^2	23.8 (22.9–24.7)	23.9 (22.8–25.0)	0.869	23.4 (22.1–24.7)	24 (23.4–24.6)	0.339	23.3 (22.3–24.3)	24.5 (23.6–25.4)	0.06
Sex, no. male/no. female	25/29	19/11		15/17	29/23		2 2/27	22/13	
K/L grade, no. of subjects									
Grade 0	21	NA		11	10		15	6	
Grade 1	33	NA		13	20		22	11	
Grade 2	NA	19		6	13		9	10	
Grade 3	NA	11		2	9		3	8	
Hip side evaluated, no. of subjects									
Right	25	17		15	27		19	23	
Left	29	13		17	25		30	12	
Alpha angle, mean (range) degrees	55 (51–59)	61 (57–65)	0.028	53 (47–59)	60 (57–63)	0.04	52 (49–55)	64 (59–69)	<0.001
Center edge angle, mean (range) degrees	32 (30–34)	32 (29–35)	0.644	31 (28–34)	32 (29–35)	0.359	31 (29–33)	33 (29–37)	0.365

* OA = osteoarthritis; MRI = magnetic resonance imaging; BMI = body mass index; K/L = Kellgren/Lawrence; NA = not applicable.

Table 2. T1ρ and T2 relaxation times of the cartilage subregions and whole cartilage of subjects with or without radiographic hip OA and subjects with or without MRI-detected femoral and acetabular cartilage defects*

	Cartilage subregion					
	Region 2	Region 3	Region 4	Region 5	Region 6	Whole cartilage
T1ρ relaxation time						
Femoral cartilage						
Radiographs						
Healthy controls	36.7 ± 4.7	40.3 ± 3.6	33.8 ± 4.5	37.6 ± 3.4	34.1 ± 3.6	36.3 ± 2.8
Hip OA	36.4 ± 4.5	40.0 ± 4.3	33.5 ± 5.4	36.8 ± 4.7	34.5 ± 2.9	36.1 ± 2.9
P	0.895	0.968	0.911	0.588	0.986	0.871
MRI						
Without femoral defects	36.5 ± 5.0	40.6 ± 4.6	34.7 ± 4.1	37.9 ± 4.3	34.2 ± 3.0	36.6 ± 2.7
With femoral defects	36.6 ± 5.4	40.0 ± 4.4	33.1 ± 5.2	36.9 ± 3.6	34.3 ± 3.6	36.0 ± 2.9
P	0.582	0.829	0.205	0.454	0.604	0.421
Acetabular cartilage						
Radiographs						
Healthy controls	30.5 ± 4.6	36.7 ± 4.3	32.8 ± 4.7	33.4 ± 4.1		33.7 ± 3.2
Hip OA	33.1 ± 6.0	38.8 ± 3.6	32.2 ± 3.9	34.5 ± 5.5		34.6 ± 3.0
P	0.067	0.010	0.784	0.286		0.18
MRI						
Without acetabular defects	30.6 ± 5.6	36.9 ± 4.3	32.2 ± 4.4	33.4 ± 4.8		33.5 ± 3.3
With acetabular defects	32.6 ± 4.4	38.2 ± 3.9	33.2 ± 4.4	34.2 ± 4.4		34.8 ± 2.9
P	0.217	0.056	0.104	0.320		0.039
T2 relaxation time						
Femoral cartilage						
Radiographs						
Healthy controls	30.4 ± 4.1	35.8 ± 4.5	31.6 ± 4.3	33.4 ± 3.4	29.3 ± 3.6	32.2 ± 3.2
Hip OA	30.4 ± 4.9	35.6 ± 4.9	30.3 ± 5.7	32.4 ± 4.4	29.4 ± 2.5	31.6 ± 3.3
P	0.856	0.944	0.329	0.502	0.865	0.555
MRI						
Without femoral defects	29.9 ± 4.5	35.5 ± 5.1	32.4 ± 4.5	33.7 ± 4.0	29.5 ± 3.0	32.4 ± 3.3
With femoral defects	30.7 ± 4.3	35.9 ± 4.4	30.4 ± 5.0	32.7 ± 3.6	29.2 ± 3.4	31.8 ± 3.2
P	0.288	0.480	0.100	0.560	0.539	0.584
Acetabular cartilage						
Radiographs						
Healthy controls	24.4 ± 5.0	28.1 ± 4.2	26.0 ± 3.5	29.1 ± 3.6		27.3 ± 2.7
Hip OA	25.7±3.9	30.0 ± 5.5	26.1 ± 4.0	30.6 ± 5.0		28.1 ± 3.5
P	0.278	0.040	0.616	0.119		0.175
MRI						
Without acetabular defects	24.1 ± 4.7	28.0 ± 4.2	25.3 ± 3.5	28.8 ± 4.1		26.8 ± 2.8
With acetabular defects	25.9±4.5	29.8 ± 5.4	27.0 ± 3.7	30.8 ± 4.0		28.6 ± 3.2
P	0.109	0.033	0.005	0.024		0.003

* Data from region 6 and region 7 of the acetabular cartilage and femoral cartilage, respectively, are not shown due to a low number of subjects for statistical comparison. Values are the mean ± SD relaxation times (in msec). OA = osteoarthritis; MRI = magnetic resonance imaging.

RESULTS

Characteristics of the subjects. The age, BMI, sex, K/L score, study hip, alpha angle, and center edge angle are shown for each group in Table 1. There were 40 women and 44 men, with a mean ± SD age of 44.6 ± 13.5 years (range 23–72) and mean ± SD BMI of 23.7 ± 3.0 kg/m^2 (range 16.5–31.0). Women had a mean ± SD age of 45.3 ± 14.3 years (range 23–68) and mean ± SD BMI of 22.4 ± 2.7 kg/m^2 (range 16.5–27.5), while in men, these values were a mean ± SD of 46.9 ± 12.9 years (range 23–72) and 24.9 ± 2.9 kg/m^2 (range 18.6–31.0), respectively. There was a significant difference in age between subjects with and those without hip OA, as well as between subjects with and those without cartilage defects. There were no significant differences in the BMI between groups, although the difference in BMI between those with and those without acetabular cartilage defects approached significance. The alpha angle of the hip was significantly greater in subjects with OA and in subjects with cartilage defects (both femoral and acetabular) compared to their control counterparts. There were no significant differences between groups with regard to the center edge angle. Finally, the ICC for K/L scoring of radiographic damage was 0.649.

Comparison between subjects with radiographic hip OA and healthy controls. The T1ρ and T2 relaxation times in the hip cartilage of subjects with radiographic hip OA compared to healthy controls, both in

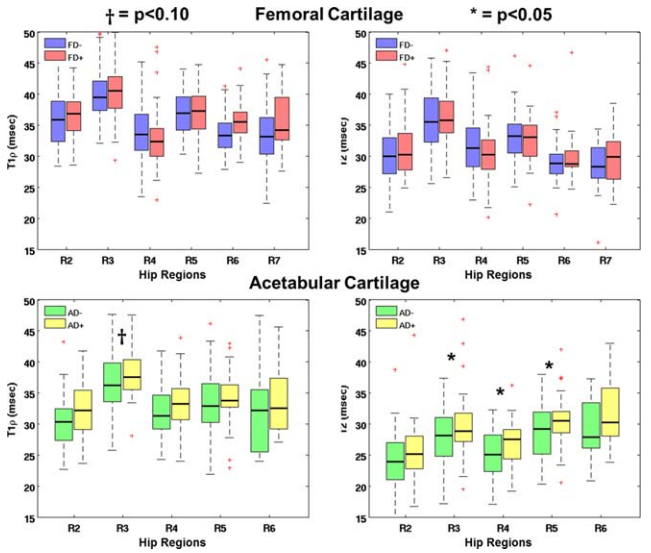

Figure 4. Mean T1ρ and T2 relaxation times in the femoral and acetabular cartilage of healthy control subjects without cartilage defects compared to subjects with femoral (FD+) or acetabular (AD+) cartilage defects, stratified by subregions of the hip. Values are presented as box plots, where the boxes represent the 25th to 75th percentiles, the lines within the boxes represent the median, and the lines outside the boxes represent the 1st and 99th percentiles. Crosses indicate outliers. Color figure can be viewed in the online issue, which is available at http://onlinelibrary.wiley.com/doi/10.1002/art.39074.abstract.

the femoral compartment and in the acetabular compartment, are shown in Table 2. The OA group had higher T1ρ and T2 relaxation times in acetabulum region 3 compared to controls (for T1ρ, mean 38.8 msec versus 36.7 msec [$P = 0.010$]; for T2, mean 30.0 msec versus 28.1 msec [$P = 0.04$]), and the difference in T1ρ approached significance in acetabulum region 2 (mean 33.1 msec versus 30.5 msec; $P = 0.067$). No significant differences were seen in the femoral compartments. The differences in whole-compartment femoral T1ρ and T2 values and whole-compartment acetabular T1ρ and T2 values between subjects with radiographic hip OA and healthy controls were not statistically significant.

Comparison between subjects with and those without cartilage defects. The T1ρ and T2 relaxation times of the femoral and acetabular cartilage in subjects with and those without cartilage defects are shown in Table 2 and Figure 4. There were no significant differences seen in the femoral cartilage regions. The T2 relaxation time was significantly higher in subjects with acetabular cartilage defects compared to control subjects without acetabular cartilage defects, in acetabulum regions 3, 4, and 5 (for region 3, mean 29.8 msec versus 28.0 msec [$P = 0.033$]; for region 4, mean 27.0 msec versus 25.3 msec [$P = 0.005$]; for region 5, mean 30.8 msec versus 28.8 msec [$P = 0.024$]). The difference between the groups in the T1ρ relaxation time of acetabulum region 3 was close to significant (mean 38.2 msec in those with acetabular cartilage defects versus 36.9 msec in controls; $P = 0.056$). In analyses of the whole cartilage, significantly higher T2 relaxation times were seen in the whole acetabular compartment in subjects with femoral cartilage defects compared to controls without femoral cartilage defects (data not shown). Subjects with acetabular cartilage defects had both significantly higher T1ρ relaxation times and significantly higher T2 relaxation times in the whole acetabular compartment compared to controls (Table 2).

Differences between femoral cartilage and acetabular cartilage T1ρ and T2. Across all subjects, the T1ρ relaxation time of the whole femoral cartilage was significantly higher than that of the whole acetabular cartilage (mean 36.3 msec versus 33.7 msec; $P < 0.001$). Similarly, the T2 relaxation time of the whole femoral cartilage was significantly higher than that of the whole acetabular cartilage (mean 32.0 msec versus 27.3 msec; $P < 0.001$).

Correlation between T1ρ and T2. Correlations between the T1ρ and T2 relaxation times within the same region in the femur and acetabulum ranged from 0.493 to 0.817 in the femoral cartilage subregions, with a correlation of 0.576 in the whole femoral cartilage. In the acetabulum subregions, the correlations ranged from 0.542 to 0.738. The correlation for the whole acetabular cartilage was 0.743. All correlations were highly significant ($P < 0.001$) and the correlations were, on average, higher in the acetabulum than in the femoral cartilage.

DISCUSSION

The purpose of this study was to evaluate differences in T1ρ and T2 relaxation times between those with and those without radiographic hip OA and those with and those without hip cartilage defects. We observed higher T1ρ and T2 values in the acetabular cartilage of subjects with radiographic hip OA and subjects with cartilage defects as compared to healthy controls. We also found that the differences in T1ρ and T2 relaxation times were more prominent when subjects were stratified based on the presence of cartilage defects than when they were stratified based on the presence of radiographic OA. These findings demonstrate the utility of techniques that rely on estimations of the T1ρ and T2 relaxation times for quantification of cartilage degeneration at the hip. They also

demonstrate that cartilage degeneration at the hip is heterogeneous, with some regions being more affected than others.

Previous quantitative studies that were focused on the hip have been limited in scope, mainly focusing on patients with FAI or hip dysplasia. Delayed gadolinium-enhanced MRI (dGEMRIC) was used in earlier studies to assess individuals with FAI and those with hip dysplasia (25–29). Both the subjects with FAI and those with hip dysplasia were found to have lower dGEMRIC values compared to healthy controls, thereby indicating that the glycosaminoglycan content was lower in these subjects. However, the dGEMRIC technique has not been evaluated in a large cohort of patients with hip OA. In addition, dGEMRIC scans can result in long wait times for the patient, often involving exercise and 90 minutes of rest to allow the contrast agent to infiltrate the joint.

Although MRI studies of T1ρ and T2 relaxation times in the hip cartilage have been performed, the only published studies have involved subjects with hip dysplasia or FAI, and mixed results have been reported. In studies by Rakhra et al (30) and Nishii et al (17), lower T1ρ and T2 values have been reported in the hip cartilage of patients with hip dysplasia and those with FAI compared to controls. In contrast, in a study by members of our group (19), an increase in T1ρ was demonstrated in the anterior superior portions of the hip cartilage of patients with FAI compared to controls. Furthermore, Apprich and colleagues (31) demonstrated that the T2* value was lower in subjects with FAI compared to healthy controls. Discrepancies in these results may be related to differences in the study populations and severity of OA across the different studies.

In the current study, the whole acetabular cartilage T1ρ and T2 values were significantly higher in subjects with acetabular cartilage defects compared to those without cartilage defects. The T2 relaxation time of the whole acetabular cartilage was also significantly higher in subjects with femoral cartilage defects compared to those without femoral cartilage defects. No significant differences were seen in the femoral cartilage for any of the comparisons. When the cartilage was divided into subregions, the acetabular regions with the most elevated T1ρ and T2 values (regions 3, 4, and 5) were located at the anterior superior acetabulum, which was the region in which the majority of the acetabular cartilage defects were located according to the findings on clinical grading. The anterior superior region of the acetabulum has also been associated with increased contact stress in the hip, as determined in a finite element analysis performed by Harris et al (32). Moreover, in another study performed on this cohort, increased disability and pain were associated with the presence of acetabular cartilage defects, but not femoral defects (21). Combined with the results from this study, the data suggest that acetabular cartilage defects may have greater significance for structural and symptomatic presentation of hip OA compared to femoral cartilage defects. Furthermore, the increased significance of acetabular lesions could also suggest that acetabular lesions are more complex than femoral lesions, with more changes in protein content as the disease progresses. However, longitudinal studies are needed to investigate this further.

When comparing the relaxation values between the whole cartilage of the femur and whole cartilage of the acetabulum, the femoral cartilage T1ρ and T2 values were significantly higher than those in the acetabular cartilage. The same result was found when analyzing only subjects who had no cartilage defects in any compartment. Therefore, this result suggests an inherent difference between the femoral and acetabular cartilage. Similar trends in T2 have been reported in healthy controls and patients with hip dysplasia (18,33). In previous research involving ex vivo samples of hip cartilage, the compressive modulus has been shown to be higher in the acetabulum compared to the femur, which would result in lower T1ρ (34,35). When combined with our results, it may suggest that there is an increase in proteoglycan or collagen structure in the acetabulum compared to the femoral cartilage.

In our comparisons of the different groups (those with radiographic hip OA, those with femoral cartilage defects, and those with acetabular cartilage defects), a greater number of significant differences were seen when the cohort was stratified by cartilage defects graded by MRI compared to when the cohort was stratified by radiographic K/L scores. This is most likely attributable to the lack of soft tissue contrast in the radiographic images and the multiple imaging planes of the joint provided by the MRI. There were several subjects whose hip joints did not exhibit radiographic OA (K/L grades 0 or 1) and who had minimal joint space reduction, but who exhibited MRI evidence of cartilage defects. There were also several subjects with radiographic OA (K/L grades 2 or 3) who had no cartilage defects present. However, the same trends are seen with either technique, in that more significant increases in T1ρ and T2 are evident in the acetabulum. This finding is consistent with previous research showing that the SHOMRI cartilage lesion score has correlates significantly with the radiographic K/L score.

Strong correlations between T1ρ and T2 were found in all of the subcompartments of the hip joints and across the entire joint. The magnitude of the correlations was similar to those seen between T1ρ and T2 in a study of the knee joint performed by members of our group (36). This may suggest that both proteoglycan and collagen losses were occurring in damaged regions of the hip cartilage. However, T1ρ and T2 relaxation both respond to changes in proteoglycan and collagen, as shown in a study by Menezes et al (11), which could account for some of the correlation. Moreover, the low spin-lock frequency used in this study could also contribute to some of the correlation, since T1ρ will approach T2 as the frequency is lowered.

Magic angle effects are a confounding factor in the accurate measurement of T1ρ and T2, especially with the large amount of curvature in the hip. A study by Watanabe et al (18) showed a 10–20% change in T2 across 60° of curvature in the hip, demonstrating the potential severity of the effect. As shown by Du et al (37) in the tendons, T1ρ appears to be more affected by magic angle effects than T2, due to dipole–dipole interactions that are not fully understood. This potential increased dependence could be an explanation for the less significant increases in the T1ρ measurements compared to the T2 measurements. In addition, the spin-lock frequency will affect the magic angle dependence of T1ρ, as has been shown by Akella et al (38). The spin-lock frequency used in this study (300 Hz) was set relatively low due to considerations of specific absorption rates, and therefore this could have led to increased dependence on the magic angle. However, any magic angle effects in these measurements could have been abrogated by the regional analysis of the cartilage, since the angle did not change drastically within one region as compared to that when averaging across the entire hip.

There are some limitations to this study. Because of the large slice thickness, which resulted in partial volume effects, only a portion of the hip cartilage could be segmented and analyzed. This could result in areas of the cartilage with cartilage defects not being segmented, which would result in less significant increases in the T1ρ or T2. More work is needed to localize defects and compare the T1ρ and T2 relaxation times in those areas.

Furthermore, the hip cartilage of 14 subjects was only segmented on the T1ρ images, due to the lack of a MERGE sequence, and therefore there is the possibility that in some of the subjects, the separation of femoral and acetabular cartilage was not adequate. In addition to segmentation limitations, the in-plane spatial resolution of the T1ρ/T2 sequence was limited due to time and signal-to-noise constraints. The resolution used, 0.569 mm $\times$ 1 mm, provided at least 2–3 pixels in each layer of cartilage, but still could have resulted in averaging of the surrounding tissue.

Finally, the possible presence of fluid within the joint could have resulted in artificially high T1ρ and T2 values. The T1ρ/T2 sequence used does not include fluid suppression. However, areas of fluid were avoided while segmenting on the MERGE images, and a threshold (100 msec for T1ρ, 80 msec for T2) was applied to the T1ρ and T2 values to prevent high values from fluid.

In conclusion, we observed higher T1ρ and T2 relaxation times in the acetabular cartilage of subjects with radiographic hip OA and those with acetabular cartilage defects. These findings demonstrate the utility of T1ρ and T2 relaxation time techniques for quantification of cartilage degeneration at the hip. They also demonstrate that cartilage degeneration at the hip is heterogeneous, with some regions being more affected than others.

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AUTHOR CONTRIBUTIONS

All authors were involved in drafting the article or revising it critically for important intellectual content, and all authors approved the final version to be published. Dr. Wyatt had full access to all of the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis.

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