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$T_{1\rho}$ and T_2 Relaxation Times are Associated with Progression of Hip Osteoarthritis

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Abstract

Objective—To evaluate whether baseline $T_{1\rho}$ and T_2 relaxation times of hip cartilage are associated with magnetic resonance imaging (MRI) based progression of hip osteoarthritis (OA) at 18 months.

Methods—3T MRI studies of the hip were obtained at baseline and 18-month follow-up for 54 subjects without evidence of severe OA at baseline [Kellgren-Lawrence (KL) score of 0–3]. 2D fast spin-echo sequences were used for semi-quantitative morphological scoring of cartilage lesions and a combined $T_{1\rho}/T_2$ sequence was used to quantitatively assess cartilage composition.

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Data Collection and Coordination: CW, DK
Data Analysis and Results Interpretation: all authors
Statistical Expertise: DK
Manuscript Draft: MCG, CW, VP
Critical Review, Edit and Proof of Manuscript: all authors
Obtaining of funding: RBS, SM
MG and CW had full access to all of the data in the study and take full responsibility for the integrity of the data and the accuracy of the data analysis

Competing Interest Statement

The authors certify that there are no conflicts of interest to report.

Progression of hip OA was defined based on incident or progression of morphological semi-quantitative grade at 18 months. Baseline $T_{1\rho}$ and T_2 relaxation times were compared between progressors and non-progressors using one-way analysis of variance and Mann-Whitney U tests and used to predict progression with binary logistic regression after adjusting for age, gender, body mass index, and KL score. Additionally, a novel voxel-based relaxometry technique was used to compare the spatial distribution of baseline $T_{1\rho}$ and T_2 between progressors and non-progressors.

Results—Significantly higher baseline $T_{1\rho}$ and T_2 values were observed in hip OA progressors compared to non-progressors, particularly in the posterosuperior and anterior aspects of the femoral cartilage. Logistic regression showed that higher baseline $T_{1\rho}$ or T_2 values in the femoral cartilage were significantly associated with progression of femoral cartilage lesions at 18 months.

Conclusion—$T_{1\rho}$ and T_2 relaxation parameters are associated with morphological cartilage degeneration at 18 months and may serve as potential imaging biomarkers for progression of cartilage lesions in hip OA.

Keywords

Osteoarthritis; Hip; $T_{1\rho}/T_2$; Progression; Magnetic Resonance Imaging; Voxel Based Relaxometry

Introduction

One in four people has a lifetime risk of developing symptomatic hip osteoarthritis (OA) by the age of 85 and individuals with this disease experience substantial pain and disability[1,2]. Traditionally, hip OA is diagnosed using radiographs and disease severity is characterized with clinical scores such as the Kellgren-Lawrence (KL) score[3]. Criteria for radiographic diagnosis include osteophytes and joint space narrowing, features that are indicative of relatively advanced disease. Radiography lacks the soft tissue discrimination necessary to identify hip OA at the earliest stages and shows low sensitivity to changes[4]. Therefore, the identification and validation of imaging biomarkers related to early and subtle changes of hip OA are essential to improving clinical assessment and intervention strategies for this disease.

Early osteoarthritic changes include proteoglycan loss, changes in water content, and collagen disruption within the cartilage matrix[5]. While morphologic magnetic resonance imaging (MRI) can directly visualize cartilage abnormalities, it cannot detect compositional changes in the cartilage[6,7]. Quantitative MRI techniques including $T_{1\rho}$ and T_2 relaxation time measurements reflect the compositional changes seen in the early stages of OA, as detailed in previous review articles about OA imaging[8,9]. Thus, $T_{1\rho}$ and T_2 relaxation time measurements can show degenerative cartilage changes before these abnormalities are visualized with morphological MRI or radiographs.

Previous studies in the hip have used $T_{1\rho}$ and T_2 quantification to assess compositional changes in cartilage associated with hip OA, hip dysplasia and femoroacetabular impingement (FAI)[10–12]. However, these studies have only focused on a cross-sectional analysis of these populations, and it is unclear whether these measurements are associated

with longitudinal progression of degenerative changes in the hip. Several studies in the knee have shown associations between baseline $T_{1\rho}$ and T_2 values and knee OA progression, suggesting the possibility of using these values to predict disease progression[13–16]. Yet, the hip joint differs from the knee joint in its cartilage morphology, thickness, and mechanical properties[17–19]. Therefore, longitudinal analyses of hip relaxation times are needed to determine if similar relationships may be established. The purpose of this study was to examine whether baseline $T_{1\rho}$ and T_2 relaxation times are associated with the incidence or progression of morphological cartilage lesions in the hip at 18 months.

Methods

Subjects

Subjects were recruited from the local community as part of a longitudinal study on hip OA and FAI. Subjects with radiographic (presence of cam deformity) and symptomatic (determined by physical evaluation) evidence of FAI were excluded from this study due to the complex interaction of altered hip joint morphology and cartilage lesion development. All participants were above 18 years of age and did not have: (i) history of hip surgery, inflammatory arthritis, hemochromatosis, sickle cell disease, or hemoglobinopathy, (ii) knee OA with KL ≥ 2, (iii) hip KL score of 4, (iv) any condition other than OA which would limit lower extremity function and mobility, and (v) MRI contraindications (e.g. pregnancy, implanted pacemaker). As part of the procedure for this study, anterior-posterior, weight-bearing frontal radiographs of the pelvis were obtained for all subjects at baseline; a board-certified musculoskeletal radiologist (TML) with 25 years of experience performed bilateral KL grading and center edge angle measurement using these radiographs. Subjects also completed the Hip Disability and Osteoarthritis Outcome Score (HOOS)[20]. Percentage scores range from 0–100, with a higher HOOS score representing less pain and better function. Prior to inclusion, all subjects signed informed consent as approved by the Committee of Human Research at our institution.

MRI Protocol

Unilateral hip MR images were obtained at baseline and 18 months on a 3T scanner (GE MR750; GE Healthcare, Waukesha, WI) using an 8-channel receive-only cardiac coil (GE Healthcare, Waukesha, WI). For all scans, the subject's feet were internally rotated and their forefeet were taped together to achieve a reproducible hip joint position. At baseline, the hip side with greater KL score was scanned if the score differed between sides or the side was chosen at random for subjects with an equal KL score for both hips. At follow-up, the hip scanned at baseline was re-scanned for each subject. The MRI protocol included intermediate-weighted fat-suppressed fast spin-echo (FSE) sequences in sagittal, oblique coronal, and oblique axial orientations, following the protocol described by Wyatt et al[10]. These sequences were used for semi-quantitative clinical grading of OA-related abnormalities. For use in quantitative cartilage analysis, subjects were scanned with a combined $T_{1\rho}/T_2$ mapping sequence using a 3D segmented SPGR acquisition in which the T_2 echoes were acquired immediately after the $T_{1\rho}$ acquisitions, as detailed by Li et al[21]. The sagittal plane scan was acquired with the slab in the left/right direction. The parameters for the $T_{1\rho}/T_2$ sequence were time of spin lock (TSL) = 0/15/30/45 ms, spin-lock frequency

= 300 Hz, views per segment (VPS) = 64, time of recovery = 1.2 sec; for T_2 preparation: TE = 0/10.4/20.8/41.7 ms; for both $T_{1\rho}$ and T_2: FOV = 14 cm, matrix size = 256 × 128, views per segment (VPS) = 64, BW = 62.5 kHz, time of recovery = 1.2 sec, slice thickness = 4 mm, no gap, in-plane resolution = 0.5 mm, and acquisition time = 13:47 minutes. A 300 Hz spin lock pulse was used due to specific absorption rate (SAR) concerns in patients with higher body mass index (BMI). Lastly, subjects were scanned with a fat-suppressed 3D multi-echo SPGR (MERGE) sequence, with TR = 30.4 ms, 5 echo times (effective TE = 12.4 ms), flip angle = 15°, matrix size = 512×512, number of slices = 28, slice thickness = 4 mm, FOV = 14 cm, BW = 62.5 kHz, signal averages = 1, and acquisition time = 11:46 minutes. The MERGE sequence was scanned with the same prescription as the $T_{1\rho}/T_2$ sequence and was used for semi-automatically segmenting the cartilage.

MR Clinical Assessment

Two fellowship-trained, board-certified musculoskeletal radiologists (SL, LN), with 7 and 5 years of musculoskeletal imaging expertise, respectively, independently reviewed all baseline and 18 month MR images. Reviewers were blinded to clinical and radiographic findings for all subjects, and discrepancies between the two reviewers were resolved by a consensus review with a senior radiologist (TML). First, the SHOMRI scoring system was used to evaluate the presence of articular cartilage lesions using the three FSE MRI series[4,7]. This semi-quantitative scoring system has been shown to have high intra-rater and inter-rater reliability (ICC > 0.91) and demonstrated strong agreement with radiographic grading and clinical parameters[7]. For scoring cartilage, the hip joint was divided into 10 anatomical subregions – 6 femoral and 4 acetabular – that are based on a simplified geographic zone method introduced by the Arthroscopy Society of North America[22]. Cartilage defects were graded separately in each of the 10 subregions on a three-point scale: 0 (no defect), 1 (partial thickness cartilage loss), and 2 (full thickness cartilage loss). The SHOMRI cartilage score was then calculated for each subject for the femur and acetabulum by adding the scores in the corresponding six and four subregions, respectively. After SHOMRI scoring, the alpha angle of the hip was measured using the oblique axial MR images in accordance with the method described by Notzil et al[23].

Hip OA Progression

Subjects were stratified into progressors and non-progressors based on changes in SHOMRI cartilage lesion score over 18 months. Progression was defined as an increase in SHOMRI of at least 1 on the cartilage lesion score, including from 0 to 1. Two different classifications of OA progression were examined in this study: any increase in the cartilage lesion score in the femoral cartilage and any increase in the cartilage lesion score in the acetabular cartilage.

Quantitative Cartilage Analysis

All image post processing was performed using an in-house software program developed in MATLAB (Mathworks Inc, El Segundo, CA)[24]. MERGE images as well as all the $T_{1\rho}$- and T_2-weighted images were rigidly registered to the first $T_{1\rho}$-weighted image (TSL=0) using the VTK CISG Registration Toolkit (Kitware Inc, Clifton Park, NY). $T_{1\rho}$ and T_2 relaxation maps were then computed by using a voxel-based two-parameter exponential fit. The femoral and acetabular cartilage compartments were segmented separately on the MERGE

image using a semi-automated segmentation algorithm that relies on Bezier splines and edge detection[25,26]. The two compartments were segmented on approximately four slices near the center of the hip, as slices affected by severe partial volumes were excluded from the segmentation. The segmentations were then divided into eight subregions to allow for more localized analysis, similar to the method described by Karupppasamy et al (Figure 1)[12]. $T_{1\rho}$ and T_2 relaxation times in each subregion were computed as an average of all voxels in that subregion. A representative $T_{1\rho}$ color map of a subject with femoral cartilage lesion progression is shown in Figure 2. For each subject, subregions were not analyzed if they contained fewer than 50 pixels over all segmented slices.

In addition to a traditional semi-automatically segmented, ROI-based analysis, a voxel-based relaxometry (VBR) analysis was also performed. All images were non-rigidly registered on a single reference image identified through an iterative process aimed to minimize the global image deformation using a technique previously presented for knee applications[27]; reference ROIs for the femur and acetabulum were then applied on the morphed images. This fully automated technique allowed for a comparison of $T_{1\rho}$ and T_2 values between progressors and non-progressors on a voxel basis.

Statistical Analysis

All statistical analyses were performed for both the femoral and acetabular progression classifications described earlier. One-way analysis of variance (ANOVA), Mann-Whitney U tests, and Chi-squared tests were used to compare demographic, symptom, and clinical data between progressors and non-progressors.

Baseline $T_{1\rho}$ and T_2 relaxation times were compared between progressors and non-progressors using one-way ANOVA, or Mann-Whitney U tests for nonparametric distributions. These analyses were performed for each subregion and for global averages of the whole cartilage region (femoral or acetabular).

Binary logistic regression was used to identify whether baseline $T_{1\rho}$ and T_2 values (subregional and whole cartilage) predicted progression of hip cartilage lesions at 18 months. Models were performed with and without adjustment for age, gender, BMI and KL score at baseline. All interval and ordinal data were converted to standardized scores before entering the logistic regression models.

All analyses described above were performed using SPSS software (IBM SPSS 22.0.0, Armonk, NY USA) with a significance level set at .05. Note that the following regions were excluded from all subregional statistical analyses: femur subregions 1,7,8 and acetabulum subregions 1,6,7,8 (Figure 1). These subregions did not have data for all subjects because the region was too small in some subjects to satisfy our 50-pixel requirement.

Lastly, the results of the VBR technique were used to compare the spatial distributions of baseline $T_{1\rho}$ and T_2 values between progressors and non-progressors at the voxel level. Average $T_{1\rho}$ and T_2 maps for progressors and non-progressors were computed and differences between these maps were calculated using unpaired t-tests; the resulting p values for each voxel were used to create volumetric statistical parametric maps (SPM).

Results

Subject Characteristics

Table 1 shows subject characteristics stratified by the two progression classifications. Overall, the study population with 18-month follow-up consisted of 54 subjects (25 females and 29 males), with a mean age of 46.5 ± 13.2 years (24–72 years) and mean BMI of 23.7±3.0 kg/m^2 (15.7–30.0 kg/m^2). At baseline, 16 subjects (29.6%) were diagnosed with mild or moderate hip OA (KL = 2,3). At 18-month follow-up, 9 of the 54 subjects [16.7% overall, 5 females (20%) and 4 males (14%)] demonstrated progression of hip OA. Among the progressors, 4 subjects demonstrated progression of femoral cartilage lesions, 1, subject demonstrated progression of acetabular cartilage lesions, and 4 subjects demonstrated progression of both femoral and acetabular lesions. No statistically significant differences ($P > .05$) were noted in age, gender, presence of baseline hip OA, HOOS scores, alpha angle, or center edge angle between progressors and non-progressors. However, BMI was significantly elevated in acetabular cartilage lesion progressors ($P = .05$). Although not significant, age showed a positive trend for both femoral and acetabular cartilage progressors, and BMI showed a positive trend for femoral cartilage progressors, meaning increased values were associated with lesion progression. HOOS scores showed a negative trend with progression, but no significant associations were found.

Morphological Findings: SHOMRI Analysis

At baseline, the average SHOMRI femoral cartilage scores were 2.9 and 1.3 ($P = .07$) for femoral lesion progressors ($n = 8$) and non-progressors, respectively. The average SHOMRI acetabular cartilage scores were 1.6 and 0.9 ($P = .30$) for acetabular lesion progressors ($n = 5$) and non-progressors, respectively. In total, 16 new or progressive lesions were found, and the anatomical locations of these lesions are shown in Table 2. In the femoral progression cohort, a total of 10 progressive lesions were found: 7 of the 10 lesions were new lesions characterized by partial thickness cartilage loss and the other 3 were characterized by progression of a pre-existing lesion. In the acetabular progression cohort, a total of 6 progressive lesions were found: 5 of the 6 lesions were new lesions and 1 lesion was characterized by progression of a pre-existing lesion. An example of a progressive lesion at 18-month follow-up is shown in Figure 3.

Baseline $T_{1\rho}$ and T_2 relaxation times between progressors and non-progressors

Baseline $T_{1\rho}$ and T_2 relaxation times for the two progression classifications are shown in Table 3. ANOVA and Mann-Whitney U tests revealed significantly higher T_2 values in femoral region 6, and significantly higher $T_{1\rho}$ and T_2 values in femoral region 3 and in the whole femoral cartilage for subjects with femoral cartilage lesion progression over 18 months. There were no significant differences between acetabular cartilage lesion progressors and non-progressors when examining the $T_{1\rho}$ and T_2 values of the acetabular cartilage.

Logistic regression unadjusted for demographic variables demonstrated that higher baseline $T_{1\rho}$ and T_2 values in the whole femoral cartilage were significantly associated with progression of hip OA at 18 months (Table 4). When adjusted for age, gender, BMI, and KL

score, higher baseline T_2 values in the femoral cartilage, specifically the whole femoral cartilage, region 3, and region 6 were significantly associated with hip OA progression at 18 months. Baseline $T_{1\rho}$ and T_2 values of the acetabular cartilage were not significantly associated with acetabular lesion progression at 18 months.

Voxel-Based Relaxometry

The results of the VBR technique are shown in Figure 4. Figure 4a–4d show maps of the average $T_{1\rho}$ and T_2 relaxation times for progressors and non-progressors. Figure 4e, 4f show the SPM obtained when progressors were compared to non-progressors through a voxel-based unpaired t-test. For femoral progressors, significant local $T_{1\rho}$ and T_2 elevation were observed in the posterior, posterosuperior, superior, and anterior femoral cartilage; for acetabular progressors, significant local $T_{1\rho}$ and T_2 elevations were observed in the anterosuperior acetabular cartilage, and $T_{1\rho}$ was elevated in the superior acetabular cartilage.

Discussion

This study demonstrates that quantitative $T_{1\rho}$ and T_2 relaxation times are associated with progression of cartilage degeneration in the hip, assessed with 3T MRI. In particular, we found that individuals who demonstrated hip cartilage lesion progression at 18 months exhibited higher baseline $T_{1\rho}$ and T_2 values in the whole femoral cartilage, and in femoral regions 3 and 6 (Figure 1). Moreover, our findings using a ROI-based approach were consistent with the results of a voxel-based analysis. After adjusting for age, gender, BMI, and KL score, baseline T_2 values were predictive of hip OA progression at 18 months. $T_{1\rho}$ and T_2 relaxation time measurements in the acetabular cartilage were not related to hip OA progression at 18 months.

Results of our study add to current knowledge regarding $T_{1\rho}$ and T_2 relaxation time measurements as potential biomarkers of OA-related degeneration[28–30]. Previously, higher $T_{1\rho}$ and T_2 relaxation measurements have been identified as predictors of progression of cartilage lesions in knee OA[13,14]. The findings of our study indicate a similar relationship exists in the hip. Therefore, our study extends previous work done in the knee and supports $T_{1\rho}$ and T_2 relaxation time measurements as biomarkers of cartilage degeneration in the hip, a joint with markedly different structure, physiology, and MR technical challenges[4,17,31]. Additionally, our study is the first to identify regional increases in $T_{1\rho}$ and T_2 relaxation time measurements that are associated with hip OA progression; we have accomplished this using both a traditional, semi-automated ROI-based approach as well a novel, fully automated voxel-based approach.

Based on the results of the adjusted ORs, every one standard deviation increase in T_2 relaxation time over the whole femoral cartilage was related to an 11.91 (95% confidence interval (CI) 1.46–96.95) times greater likelihood of hip OA progression at 18 months. Similarly, a one standard deviation increase in T_2 of femoral region 3 or region 6 was related to a 6.89 (95% CI 1.55–30.61) or 2.68 (95% CI 1.00–7.22) times greater likelihood of progression at 18 months, respectively (Table 4). While the results of our logistic regression analysis suggest that T_2 relaxation times may be better suited for predicting progression, $T_{1\rho}$ values in the whole femoral cartilage and in femoral region 3 showed a positive statistical

trend in the adjusted models, and may have been significant with a larger cohort of progressors. Regions of $T_{1\rho}$ and T_2 elevation – reflecting biochemical changes in cartilage know to precede degeneration – were also qualitatively associated with the location of progressive lesion development. The majority of progressive lesions were found in the posterior, superior and anterior regions of the femoral cartilage (Table 2). Progressors demonstrated elevated $T_{1\rho}$ and T_2 values in these regions, which are clearly visualized in Figure 4. Four progressive lesions were also detected in the inferior medial femur, but this region was not included in the cartilage volume used for quantitative assessment. Overall, the areas of cartilage lesion progression seen in our study are in agreement with the literature regarding the regional prevalence of cartilage lesions in individuals with hip OA compared to healthy controls[32].

Based on the findings of this study, $T_{1\rho}$ (OR 95% CI 0.46–3.83, P = 0.58) and T_2 (OR 95% CI 0.45–4.23, P = 0.57) relaxation time measurements in the acetabular cartilage were not associated with progression of acetabular cartilage lesions at 18 months. However, acetabular progressors did show higher $T_{1\rho}$ and T_2 values in the whole cartilage and in all subregions compared to non-progressors and progressive cartilage lesions were found primarily in the anterior and superior portions of the acetabulum (Table 2, Table 3). These findings are concurrent with previous studies that reported a high prevalence of cartilage lesions in the anterosuperior acetabulum in subjects with hip OA[32,33]. The lack of significance in our study may be a result of the small cohort size (n = 5), which makes it difficult to draw conclusions about the role of $T_{1\rho}$ and T_2 relaxation time measurements as biomarkers of acetabular cartilage lesion progression. Further studies with a larger group of subjects and/or longer follow-up periods will be needed to more accurately assess the role of acetabular cartilage degeneration in hip OA progression.

The results of the VBR technique, which had previously only been used in the knee, are promising[27]. The algorithm showed the capability to detect local areas of $T_{1\rho}$ and T_2 increase between progressors and non-progressors. For femoral progressors, the areas of greatest significance on the $T_{1\rho}$ and T_2 SPM maps (Figure 4e, 4f) are seen in the posterosuperior and anterior regions of the femoral cartilage, which are consistent with subregions 3 and 6 and confirm the findings the ROI-based analysis (Figure 1). Additional areas of local significant difference can bee seen for both progression classifications, and these areas are consistent with the locations of progressive lesions. These findings suggest that the VBR technique may be more sensitive for detecting local changes in cartilage composition, which are obscured by the averaging of a ROI-based method. Further, this technique is fully automatic and the morphing of the images to a reference allows for comparisons of the same anatomical areas across subjects, thereby accounting for local spatial variations due to the normal heterogeneity of the cartilage matrix, common loading pattern, or technical issues such as magic angle effect. Additional studies comparing voxel-based and ROI-based approaches are clearly warranted.

We believe that the results of this study are most informative in the context of subtle progression of hip OA. Progression of hip OA, defined as new or increased severity of cartilage lesions between baseline and 18 months, was assessed using an MR-based semiquantitative scoring system (SHOMRI). In contrast to radiographs, which have been

used in previous studies to define OA severity and progression, SHOMRI can reliably identify subtle morphologic changes associated with hip OA[7,10,34,35]. This sensitivity is shown reflected by the difference in SHOMRI cartilage scores between progressors and non-progressors. Despite no significant differences in the presence of baseline radiographic hip OA, average SHOMRI cartilage scores were higher for femoral and acetabular progressors compared to non-progressors, and the lack of significance may be explained by the study's small sample size or short follow-up period. However, in this same sample, $T_{1\rho}$ and T_2 were able to differentiate these two groups and predict morphological progression with statistical significance, which highlights the importance of these imaging biomarkers.

The decision to use an MR-based definition of progression and the lack of longitudinal studies in cohorts with hip OA makes it difficult to assess whether progression rates seen in this study (16.7% overall) are valid. Previous studies have examined radiographic OA progression, with reported values varying widely based on criteria for progression, patient population, and follow-up period chosen[35–37]. While rates of progression were generally lower in our study, this may be due to the fact that our cohort was composed of younger, healthier (as determined by baseline KL and HOOS scores) subjects, and had a short follow-up period (Table 1). As age and OA severity are risk factors for progression, it is reasonable that subjects in our study experienced lower rates of progression[35]. Despite the lower progression rate, age, BMI, presence of baseline hip OA, and female gender showed a positive trend for progression in our study (Table 1), which is consistent with the literature on risk factors for incident hip OA[35,38]. Patient reported outcomes including pain and symptoms were not significantly associated with morphologic progression in our study (not reported), but previous cross sectional studies have shown an association between these parameters[34,39]. The lack of clinical progression in our study may be explained by the small sample size, but it may also indicate that morphological MR imaging is more sensitive for detecting early or subtle changes in OA.

Despite the promising results, there are several limitations of this study, including a relatively small study population and a short follow-up period. Future studies with a larger cohort and/or follow-up periods beyond 18 months can substantiate the results obtained in this study. Second, a variety of disease states ranging from normal hips to hips with moderate OA were included, as well as a large range of ages. The small number of subjects did not permit the exclusion of higher KL grades or narrowing the age range for inclusion. Third, the adjusted ORs obtained in this study should be interpreted with caution, as gender exhibited a suppressor effect in the logistic regression models. As such, the unadjusted ORs may provide a more accurate representation of the predictive capacity of these quantitative parameters. Fourth, progression was defined based on MR clinical grading and not clinical findings. Further studies are warranted that incorporate clinical metrics of OA progression. Finally, it must be kept in mind that slices with severe partial volume effects limited the volume of cartilage used for quantitative analysis.

In conclusion, we observed significantly higher baseline $T_{1\rho}$ and T_2 relaxation times in the femoral cartilage of individuals who experienced femoral cartilage lesion progression using both ROI-based and voxel-based approaches. Logistic regression analysis showed that higher $T_{1\rho}$ and T_2 values in the whole femoral cartilage, and in the posterosuperior and

anterior femoral cartilage were associated with progression at 18-month follow-up. No significant differences were found in subjects who experienced acetabular cartilage lesion progression. These findings support the role of $T_{1\rho}$ and T_2 relaxation times as biomarkers for cartilage degenerative disease progression in the hip.

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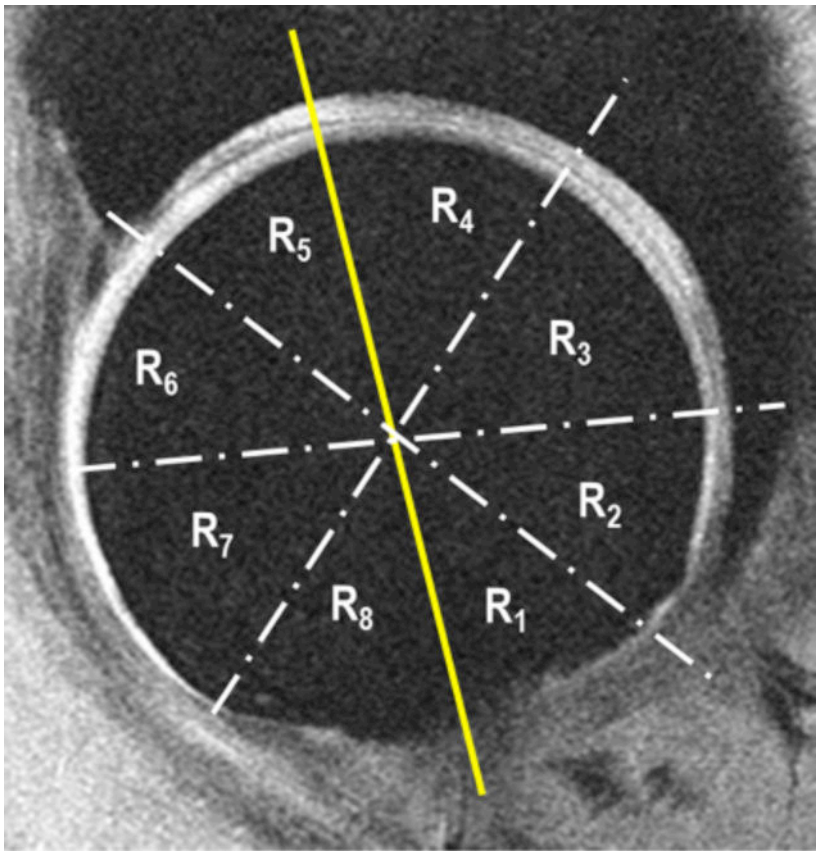

Figure 1.
Division and numbering of the eight subregions of hip cartilage on the MERGE image. The solid yellow line represents a reference line parallel with the femoral neck that is drawn for each subject.

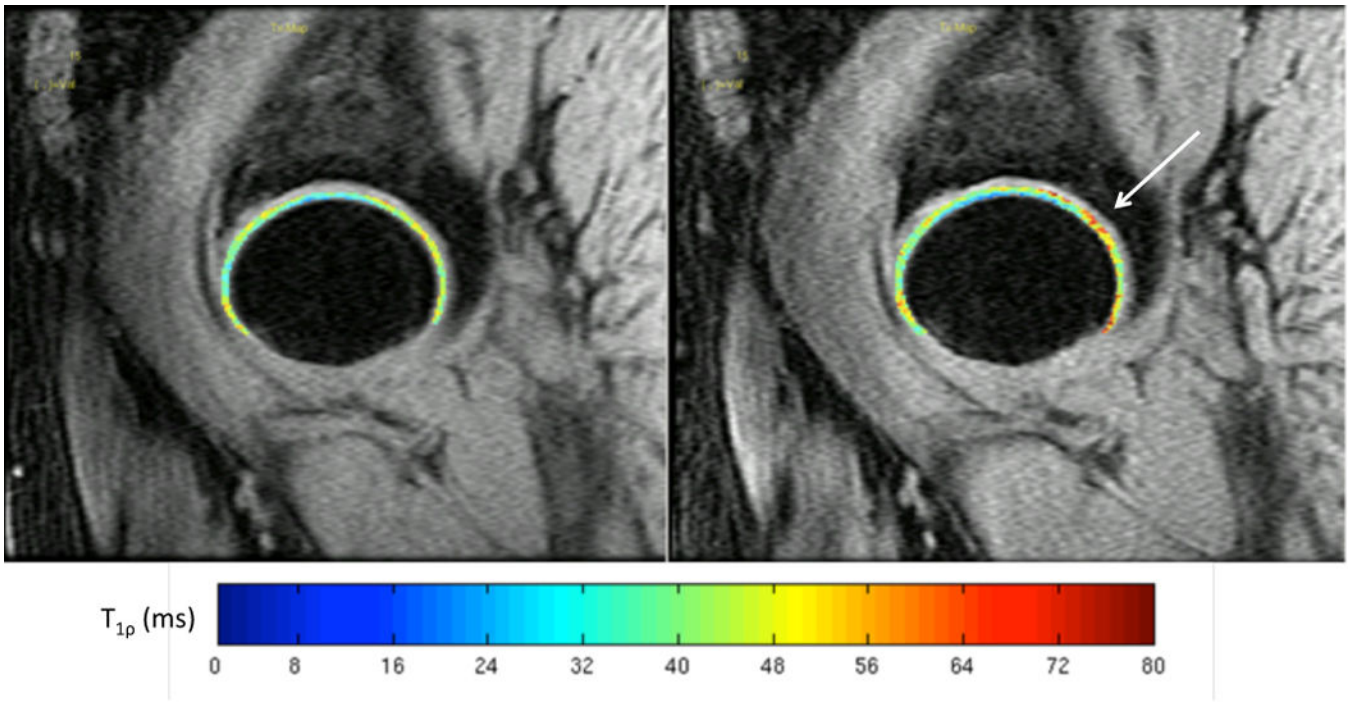

Figure 2.

$T_{1\rho}$ relaxation map overlay of baseline (Left) and 18-month follow-up (Right) for a femoral cartilage lesion progressor with baseline KL=0 (Female, Age 65). Note the marked increase in relaxation time in the posterosuperior femoral cartilage (arrow), which corresponds to subregion 3.

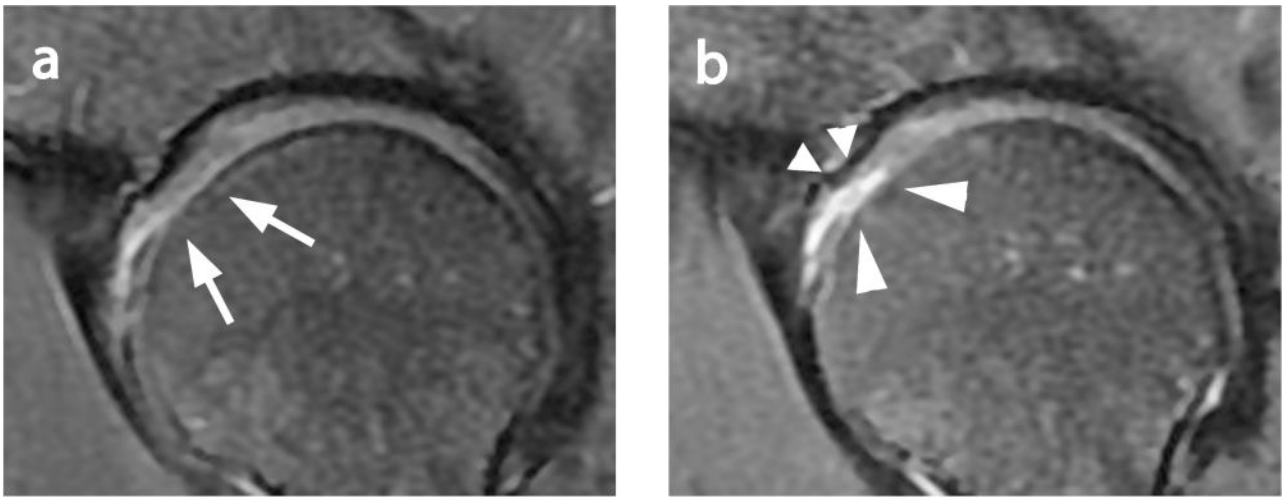

Figure 3.

Sagittal intermediate-weighted MR images demonstrate progression of cartilage loss: at baseline (a) anterior femoral cartilage partial-thickness lesion (arrows) and at 18 month-follow-up (b) full-thickness cartilage lesion at the same site (long arrowheads). Opposing anterior acetabular cartilage that was intact on baseline shows new partial thickness cartilage lesion (short arrowheads) at follow up.

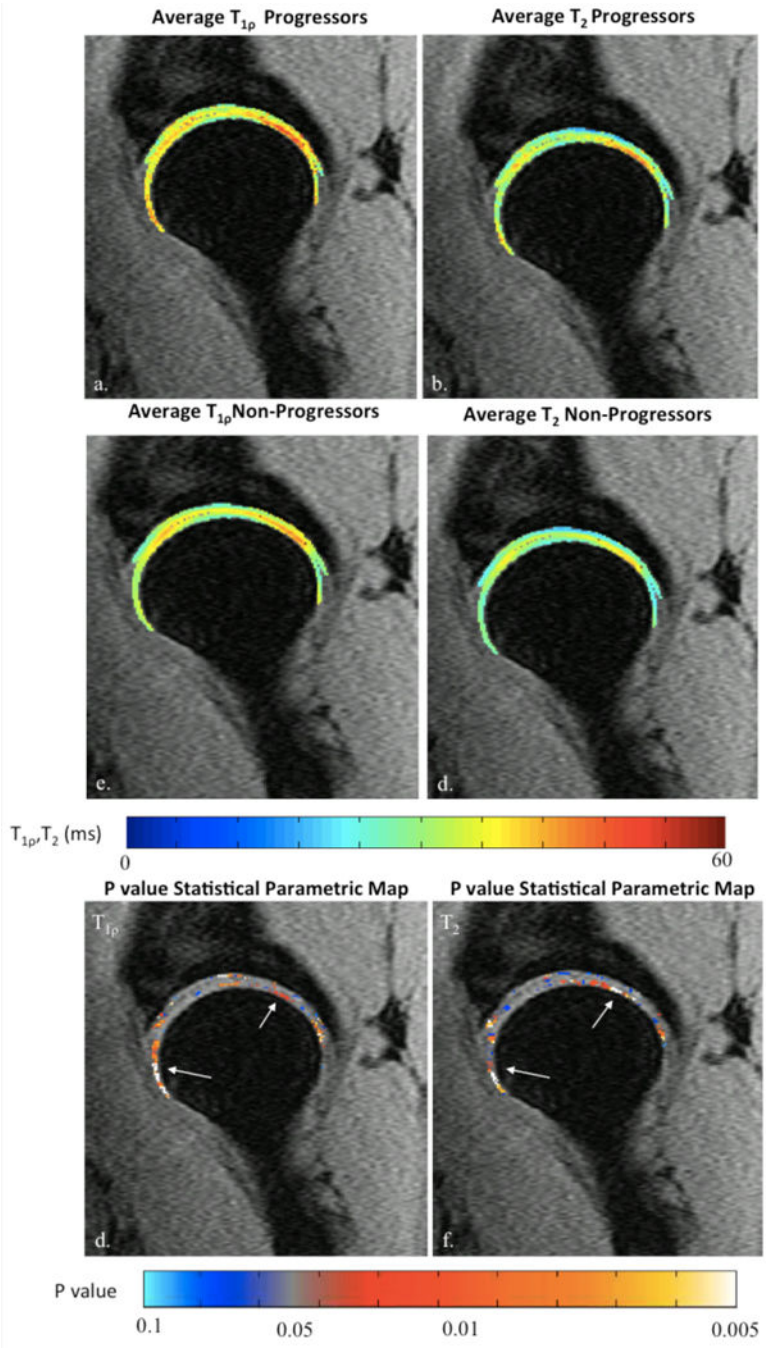

Figure 4.

Average $T_{1\rho}$ and T_2 relaxation time maps for progressors (a,b) and non-progressors (c,d) in the atlas coordinate system. (e,f) P value statistical parametric maps comparing local differences between progressors and non-progressors.

Table 1

Baseline demographic, symptom, and clinical data for hip OA progressors and non-progressors. Progression criteria include femoral cartilage lesion progression and acetabular cartilage lesion progression.

	FC-NP	FC-P	P value*	AC-NP	AC-P	P value*
Age, years	45.8± 12.7	53.5±14.4	0.10	46.2±13.1	49.2±15.4	0.63
Sex, Male/Female, n	26/20	3/5	0.32	26/23	3/2	0.77
BMI, kg/m^2	23.6±2.9	24.8±3.7	0.31	23.5±2.8	26.3±3.9	0.05
KL Score						
0	14	1		14	1	
1	20	3		21	2	
2	8	2		9	1	
3	4	2		5	1	
Hip OA**, yes/no, n	12/ 34	4/ 4	0.17	14/ 35	2/ 3	0.59
HOOS						
Pain, %	93.0±13.5	90.9±12.5	0.11	92.8±13.2	91.5±16.3	0.76
Symptoms, %	92.7±11.1	86.3±17.3	0.43	91.9±11.5	90.0±19.7	0.65
Activities of Daily Livi	94.7±12.3	95.6±9.0	0.49	94.9±11.9	94.4±11.7	0.95
Alpha Angle, (°)	57.3±14.8	52.9±12.4	0.43	56.9±14.9	54.0±10.7	0.67
Center Edge Angle, (°)	32.3±6.8	31.3±6.3	0.68	31.9±6.9	35.2±3.7	0.29

Abbreviations: BMI, body mass index; OA, osteoarthritis; FC, femoral cartilage; AC, acetabular cartilage; P, progressor; NP, non-progressor; HOOS, Hip Disability and Osteoarthritis Outcome Score.

*One-way analysis of variance or Mann-Whitney U test for interval variables and Chi-Square for categorical variables

**Radiographic Definition based on Kellgren-Lawrence Score > 1 at baseline

Values are means ± SD

Table 2

Summary of lesion location and lesion type within the femoral and acetabular progression cohorts. Anatomical locations correspond to regions scored by SHOMRI, a semi-quantitative grading system.

Compartment	# of lesions	New Lesions	Increase of pre-existing lesions
Femoral Progression			
Femur Lateral	0	0	0
Femur Superior Lateral	1	1	–
Femur Superior Medial	2	2	–
Femur Inferior Medial	4	3	1
Femur Anterior	2	1	1
Femur Posterior	1	–	1
Total	10	7	3
Acetabular Progression			
Acetabulum Superior Lateral	2	2	–
Acetabulum Superior Medial	2	2	–
Acetabulum Anterior	2	1	1
Acetabulum Posterior	0	0	0
Total	6	5	1

Abbreviations: SHOMRI, Scoring Hip Osteoarthritis with MRI

Table 3

Baseline $T_{1\rho}$ and T_2 relaxation times for progressors and non-progressors. Progression criteria include femoral cartilage lesion progression and acetabular cartilage lesion progression.

		R2	R3	R4	R5	R6	Whole Cartilage
T1ρ Baseline	**Femoral**						
	FC-NP	36.3±5.0	39.8±4.5	33.4±4.5	37.7±4.0	33.5±2.9	36.0±2.8
	FC-P	37.8±4.1	43.4±4.0	35.3±2.7	37.6±3.2	36.8±4.6	38.1±2.3
	P value	0.25	0.02	0.11	0.99	0.08	0.04
	Acetabular						
	AC-NP	31.3±5.5	36.7±3.7	32.0±4.1	33.5±4.0	–	33.5±2.9
	AC-P	32.3±5.8	38.5±5.7	32.8±3.3	34.9±2.1	–	35.1±2.6
	P value	0.88	0.32	0.67	0.43	–	0.25
T2 Baseline	**Femoral**						
	FC-NP	29.6±4.1	35.0±4.1	30.5±4.1	33.0±3.8	28.7±2.4	31.5±2.8
	FC-P	32.0±4.3	39.0±3.5	32.7±2.9	33.7±3.4	31.1±2.5	33.8±1.9
	P value	0.13	0.01	0.12	0.60	0.02	0.03
	Acetabular						
	AC-NP	24.7±4.3	28.0±3.7	25.3±3.5	29.1±4.0	–	27.1±2.7
	AC-P	25.2±6.0	28.8±6.9	25.7±4.2	31.5±2.2	–	28.5±2.9
	P value	0.83	0.67	0.82	0.18	–	0.28

Abbreviations: FC, femoral cartilage; AC, acetabular cartilage; P, progressor; NP, non-progressor.

Values are means (in ms) +/− SD

Table 4

Odds ratios (OR), 95% confidence interval (CI), and P value of logistic regression analysis. All analysis shown corresponds to femoral cartilage lesion progression at 18 months.

	Univariable Analysis		Multivariable Analysis*	
	OR (95% CI)	**P value**	**OR (95% CI)**	**P value**
T1ρ femoral global	2.27 (1.00–5.12)	0.05	2.68 (0.93–7.74)	0.07
T1ρ femoral region 3	2.11 (0.99–4.50)	0.05	2.51 (0.97–6.51)	0.06
T1ρ femoral region 6	2.56 (1.11–5.88)	0.03	2.42 (0.80–7.33)	0.12
T2 femoral global	2.79 (1.03–7.57)	0.04	11.91 (1.46–96.95)	0.02
T2 femoral region 3	2.89 (1.18–7.08)	0.02	6.89 (1.55–30.61)	0.01
T2 femoral region 6	2.85 (1.11–7.32)	0.03	2.68 (1.00–7.22)	0.05

*Adjusted for age, gender, body mass index, and Kellgren-Lawrence score at baseline.