Title
Physical activity and spatial differences in medial knee T1rho and t2 relaxation times in knee osteoarthritis.

Journal
The Journal of orthopaedic and sports physical therapy, 44(12)

ISSN
0190-6011

Authors
Kumar, Deepak
Souza, Richard B
Singh, Justin
et al.

Publication Date
2014-12-01

DOI
10.2519/jospt.2014.5523

Peer reviewed

HHS Public Access
Author manuscript
J Orthop Sports Phys Ther. Author manuscript; available in PMC 2015 December 01.

Published in final edited form as:
J Orthop Sports Phys Ther. 2014 December ; 44(12): 964–972. doi:10.2519/jospt.2014.5523.

Physical Activity and Spatial Differences in Medial Knee T1rho and T2 Relaxation Times in Knee Osteoarthritis

DEEPAK KUMAR, PT, PhD[1], **RICHARD B. SOUZA, PT, PhD**[1,2], **JUSTIN SINGH, BS**[1], **NATHANIEL E. CALIXTO, BS**[1], **LORENZO NARDO, MD**[1], **THOMAS M. LINK, MD**[1], **XIAOJUAN LI, PhD**[1], and **SHARMILA MAJUMDAR, PhD**[1]

[1]Musculoskeletal Quantitative Imaging Research Group, Department of Radiology and Biomedical Imaging, University of California San Francisco, San Francisco, CA

[2]Department of Physical Therapy and Rehabilitation Science, University of California San Francisco, San Francisco, CA

Abstract

STUDY DESIGN—Cross-sectional.

OBJECTIVES—To investigate the association between knee loading–related osteoarthritis (OA) risk factors (obesity, malalignment, and physical activity) and medial knee laminar (superficial and deep) T1rho and T2 relaxation times.

BACKGROUND—The interaction of various modifiable loading-related knee risk factors and cartilage health in knee OA is currently not well known.

METHODS—Participants with and without knee OA (n = 151) underwent magnetic resonance imaging at 3 T for superficial and deep cartilage T1rho and T2 magnetic resonance relaxation times in the medial femur (MF) and medial tibia (MT). Other variables included radiographic Kellgren-Lawrence (KL) grade, alignment, pain and symptoms using the Knee injury and Osteoarthritis Outcome Score, and physical activity using the International Physical Activity Questionnaire (IPAQ). Individuals with a KL grade of 4 were excluded. Group differences were calculated using 1-way analysis of variance, adjusting for age and body mass index. Linear regression models were created with age, sex, body mass index, alignment, KL grade, and the IPAQ scores to predict the laminar T1rho and T2 times.

RESULTS—Total IPAQ scores were the only significant predictors among the loading-related variables for superficial MF T1rho (P = .005), deep MT T1rho (P = .026), and superficial MF T2 (P = .049). Additionally, the KL grade predicted the superficial MF T1rho (P = .023) and deep MT T1rho (P = .022).

Address correspondence to Dr Deepak Kumar, 1700 4th Street, Suite 203, Byers Hall, UCSF Mission Bay, San Francisco, CA 94158. krdeepak2pro@gmail.com.

The authors certify that they have no affiliations with or financial involvement in any organization or entity with a direct financial interest in the subject matter or materials discussed in the article.

The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Institutes of Health.

CONCLUSION—Higher physical activity levels and worse radiographic severity of knee OA, but not obesity or alignment, were associated with worse cartilage composition.

Keywords

cartilage; IPAQ; KL; magnetic resonance imaging

Approximately 5% of American adults over 25 years of age and 12% over 65 years have knee osteoarthritis (OA).[11,29] People with knee OA report significant knee pain and difficulties with activities of daily living, making knee OA a leading cause of disability in noninstitutionalized adults.[10,18,21] Knee OA most commonly affects the medial knee compartment,[9] and degenerative cartilage lesions have been reported more frequently at the medial knee compartment as well.[41,50] Early cartilage changes in knee OA consist of proteoglycan loss and an increase in water content, along with loosening, disorganization, and loss of collagen matrix.[34,40] These changes precede the structural damage that is commonly detected using radiography and anatomic magnetic resonance imaging (MRI). Recent advances in quantitative compositional MRI techniques have allowed for noninvasive estimation of tissue composition that may aid in early disease identification. Two magnetic resonance techniques commonly used for assessment of cartilage composition are T1rho and T2 relaxation time mapping.[2,31,44,45,47] An increase in T1rho relaxation times indicates a loss of proteoglycans, and an increase in T2 relaxation times indicates an increase in water and a disruption of collagen matrix.[2,14,30,31,36,37] A number of studies have demonstrated the utility of these imaging metrics as indicators of cartilage degeneration commonly seen in OA.[3,14,26,31,39,50,54,58]

Because cartilage structure is not homogeneous through the depth of the cartilage, T1rho and T2 relaxation times can also be calculated separately for the superficial and deep cartilage laminae. Laminar analysis of magnetic resonance relaxation time parameters has been shown to improve classification between individuals with and without knee OA, compared to global mean values.[7] Using laminar analyses in individuals with an anterior cruciate ligament reconstruction, degenerative changes have been found in the superficial (articular) cartilage layer and not in the deep (bone) layer 1 year after surgery.[52] Conversely, tears of the posterior horn of the medial meniscus were found to be associated with degenerative changes in the deep (bone) cartilage layer but not in the superficial (articular) layer.[28] These studies demonstrate the use of laminar analysis of T1rho and T2 relaxation times to understand the OA disease process.

Primary knee loading–related OA risk factors are obesity,[49,56] malalignment (varus or valgus),[16,17,49] and volume of physical activity. However, the association of these OA risk factors with laminar cartilage magnetic resonance relaxation times is currently not well understood. Such investigation could identify potentially modifiable risk factors that could be targeted in interventions to slow the cartilage degeneration seen in knee OA. Hence, the primary objective of this study was to investigate the association of medial femur (MF) and medial tibia (MT) laminar T1rho and T2 relaxation times with the knee loading–related OA risk factors of obesity, malalignment, and volume of physical activity.

METHODS

Participants

Participants were recruited from the community as part of a longitudinal study of knee OA. The inclusion criteria for those with knee OA were age greater than 35 years, OA knee symptoms (pain, aching, stiffness on most days during the past year, or use of medication for knee pain on most days during the past year), and definite radiographic evidence of knee OA (Kellgren-Lawrence [KL] grade greater than 1). The inclusion criteria for the comparison group were age greater than 35 years, no knee pain or stiffness in either knee or use of medications for knee pain in the last year, and no radiographic evidence of OA (KL grade 1 or less) on either knee. The exclusion criteria for all potential participants were concurrent use of an investigational drug, history of intra-articular fracture or surgical intervention in the study knee, conditions other than OA that limit lower extremity function and mobility and/or would confound the evaluation of function, and contraindications to MRI.

Sample-size estimates in the parent study were performed using preliminary data on T1rho measurements in individuals with and without knee OA. Data from all participants enrolled in the parent study were included in this analysis, except those with KL grade equal to 4 (n = 5). In the final analyses, 151 individuals (control, n = 110; OA, n = 41) were included. Participant recruitment and data collection took place from October 2011 to February 2014. All participants signed written informed consent prior to participation in the study, and all protocols were approved by the University of California San Francisco Committee on Human Research.

Radiographs

All participants underwent a weight-bearing, posteroanterior, fixed-flexion radiograph[8] using the Synaflexer device (BioClinica, Inc, Newtown, PA). A musculoskeletal radiologist with more than 20 years of experience performed the KL grade scoring[27] of the tibiofemoral compartment from these radiographs. In the KL classification, grade 0 indicates no radiographic features of knee OA; grade 1 indicates doubtful joint-space narrowing (JSN) and possible osteophytic lipping; grade 2 indicates the presence of definite osteophytes and possible JSN; grade 3 indicates multiple osteophytes, definite JSN, sclerosis, and possible bony deformity; and grade 4 indicates large osteophytes, marked JSN, severe sclerosis, and definite bony deformity. Alignment was assessed using a standing, anterior/posterior radiograph in which the hip, knee, and ankle joints were visible. Alignment was determined by the angle (varus less than 180°, valgus greater than 180°) of the mechanical axes of the femur and tibia.[25]

Magnetic Resonance Acquisition

Magnetic resonance imaging was performed using a 3-T MR750w scanner (GE Healthcare, Waukesha, WI) and an 8-channel transmit/receive knee coil (Invivo, Gainesville, FL). For the participants with OA, the knee with more severe findings on the radiographs was imaged. If the KL grade was the same for both knees, the more symptomatic knee was imaged. For those in the control group, the extremity to be imaged was selected at random.

The following sequences were obtained for each participant: (1) high-resolution, 3-D, T2-weighted fast spin echo (FSE) cube sequence for cartilage segmentation (relaxation time/echo time [TE], 1500/26.69 milliseconds; field of view, 16 cm; matrix, 384 × 384; slice thickness, 0.5 mm; echo train length, 32; bandwidth, 37.5 kHz; number of excitations, 0.5; acquisition time, 10 minutes 30 seconds); (2) 3-D T1rho relaxation time sequence (relaxation time/TE, 9/2.6 milliseconds; time of recovery, 1500 milliseconds; field of view, 14 cm; matrix, 256 × 128; slice thickness, 4 mm; bandwidth, 62.5 kHz; time of spin lock [TSL], 0/2/4/8/12/20/40/80 milliseconds; frequency of spin lock, 500 Hz; acquisition time, 11 minutes); and (3) 3-D T2 relaxation time sequence (same as the T1rho quantification except for magnetization preparation: TE, 1.8/3.6/7.3/14.5/29.1/43.6/58.2; acquisition time, 11 minutes).

Magnetic Resonance Analysis

Articular Cartilage T1rho and T2 Relaxation Times—Sagittal high-resolution FSE cube images were downsampled so that the slice thickness was the same as the T1rho and T2 images. This was followed by rigid registration of the FSE cube and first echo of the T2 images to the first echo of the T1rho images. This ensured that all images were aligned and any differences between images (eg, due to movement of the participant) were minimized. To account for small movement during acquisition of the T1rho and T2 images, echoes 2 through 8 were each registered to the first echo of both the T1rho and T2 sequences. Additionally, all echoes from the T2 map sequence were registered to the first T1rho echo. The MF and MT cartilage compartments were segmented semi-automatically (automated edge detection and manual correction) on multiple slices of the high-resolution FSE cube images using in-house software developed with MATLAB (The MathWorks, Inc, Natick, MA), based on edge detection and Bézier splines.[6] The segmented cartilage regions of interest described above were then partitioned automatically into 2 equal laminae, the deep layer (closer to the subchondral bone) and superficial layer (closer to articular surface), using software developed in-house (FIGURE 1).[7] Voxels were assigned to only 1 layer, based on minimum Euclidean distances to the segmented splines. Relaxation time maps for T1rho and T2 were constructed by 3-parameter fitting of all 8 of the T1rho- and T2-weighted images, pixel by pixel, to the equations below using software developed in-house:

$$S(TSL) \propto A(\exp\left(-\frac{TSL}{T1\rho}\right)) + B \quad for\, T1\rho$$
$$S(TE) \propto A(\exp\left(-\frac{TE}{T2}\right)) + B \quad for\, T2,$$

where *S* is the image signal at a given time point (TSL for T1rho maps or TE for T2 maps), *A* is initial magnetization, and *B* is a constant.

The cartilage regions of interest were overlaid on the previously coregistered T1rho and T2 maps. The cartilage splines were adjusted manually to avoid synovial fluid or surrounding anatomy. To eliminate artifacts due to partial volume effects with synovial fluid, voxels with relaxation time greater than or equal to 130 milliseconds for T1rho or 100 milliseconds for T2 maps were excluded from the data used for quantification. Mean T1rho and T2 values were calculated for the MF and MT superficial and deep laminae.

Self-Reported Function

All participants completed the Knee injury and Osteoarthritis Outcome Score.[32,48] The Knee injury and Osteoarthritis Outcome Score pain and symptoms subscales were used in the analyses for the assessment of knee OA–related pain and symptoms. In these subscales, higher scores (0–100) represent better function.

Physical Activity Assessment

The International Physical Activity Questionnaire (IPAQ) short form was completed by all participants. The vigorous, moderate, walking, and total physical activity categories from the IPAQ were reported in metabolic equivalent of task (MET) minutes per week. The IPAQ is a commonly used and validated questionnaire to assess physical activity levels.[1,35] Scores on the IPAQ have been shown to be significantly correlated with objective accelerometry data.[35]

Statistical Analysis

Independent-sample *t* tests were used to compare age, body mass index (BMI), and alignment between control and OA groups. Group differences between control and OA participants for the Knee injury and Osteoarthritis Outcome Score, IPAQ, and laminar T1rho and T2 times were assessed using multivariate analysis of variance, with age and BMI as covariates. For the primary analyses, linear regression models were created with age, sex, BMI, alignment, KL grade, and the total IPAQ scores to predict the laminar T1rho and T2 times that were different between the control and OA participants.

RESULTS

Group Characteristics

Age, BMI, and sex distribution are shown in TABLE 1. Individuals in the OA group were significantly older ($P<.001$) and had a higher BMI ($P = .097$). The distribution of men and women was not significantly different between the groups ($P = .740$). In the control group, there were 57 participants with KL grade 0 and 53 with KL grade 1. In the OA group, there were 21 participants with KL grade 2 and 20 with KL grade 3. The participants in the OA group had significantly more pain ($P = .004$) and symptoms ($P = .012$), but their lower extremity alignment ($P = .360$) and physical activity level ($P>.05$) were not significantly different from those in the control group.

Group Differences for Magnetic Resonance Parameters

The mean and 95% confidence intervals for the T1rho and T2 relaxation times for each KL grade are shown in TABLE 2. Laminar T1rho and T2 relaxation times for the 2 groups are shown in FIGURE 2. After adjusting for age and BMI, the OA group had higher superficial MF T1rho ($P = .009$), and the difference in deep MF T1rho was nearly significant ($P = .054$) (FIGURE 2A). The OA group had higher deep MT T1rho ($P = .017$), but the difference in superficial MT T1rho ($P = .195$) was not significant (FIGURE 2A). The OA group also had higher superficial MF T2 ($P = .038$). The differences in deep MF ($P = .154$), superficial MT ($P = .458$), and deep MT ($P = .820$) T2 were not significant.

Association of Magnetic Resonance Parameters With OA Risk Factors

Regression models were created with dependent variables of superficial MF and deep MT T1rho and superficial MF T2. Results from the regression analyses are shown in TABLE 3. For superficial MF T1rho, of the loading-related variables, only the total IPAQ score (*P* = .005) made a significant contribution to the outcome. Additionally, radiographic KL grade (*P* = .023) was significant in the model. For deep MT T1rho, of the loading-related variables, the contribution of total IPAQ score (*P* = .026), in addition to KL (*P* = .022), was significant. For superficial MF T2, only the total IPAQ score (*P* = .049) made a significant contribution to the outcome.

DISCUSSION

The results show that of the loading-related risk factors of obesity, malalignment, and volume of physical activity, only physical activity was associated with MF and MT laminar T1rho and T2 relaxation times. Additionally, radiographic severity of knee OA assessed with the KL classification was associated with higher magnetic resonance relaxation times. These results suggest that, with worsening radiographic severity of knee OA, careful recommendations on participation in physical activity may be needed for people with this condition.

We observed that an increase of 213 to 445 MET minutes per week of physical activity was associated with a 1-millisecond increase in MF superficial layer T1rho and T2. An increase in T1rho and T2 indicates cartilage degeneration. Previous studies in healthy adults without knee pain have shown that greater amounts of physical activity are related to better cartilage morphology, including greater knee cartilage volume and reduced risk of cartilage lesions.[19,43] However, data from the large Osteoarthritis Initiative (OAI) show that in 128 individuals with knee OA risk factors and 33 normal controls, those who engaged in frequent knee-bending activities had higher T2 and worse cartilage lesions compared to those who did not engage in frequent knee-bending activities.[24] In the same cohort, women with OA risk factors who participated in moderately strenuous physical activity had higher cartilage T2 relaxation times when compared to those who performed light physical activities and sedentary women.[24] Other studies from the OAI report greater prevalence of meniscus, cartilage, bone marrow, and ligament lesions in individuals with medium and high scores on the physical activity scale for the elderly,[51] and greater increase in cartilage T2 over 4 years in individuals with very high and very low scores on the physical activity scale for the elderly.[33] Our results are consistent with these findings. However, further longitudinal studies are needed to ascertain whether the physical activity levels observed in our study are related to the progression of laminar T1rho and T2 over time.

We observed that both greater physical activity levels and worse radiographic knee OA were related to worse cartilage composition. People with knee OA have an increased risk of mortality (standardized mortality ratio = 1.55; 95% confidence interval: 1.41, 1.70), if all causes of death are considered.[22,38] Furthermore, people with knee OA who have walking disability are more likely to die than people with knee OA who do not have walking disability (hazard ratio = 1.93; 95% confidence interval: 1.59, 2.36) due to the association between walking disability and cardiovascular disease.[38] Studies report that increasing physical activity in people with knee OA is associated with improvements in pain and function.[15,42] In spite of these benefits, objective assessment of physical activity levels using accelerometers shows that only about 11% of individuals with knee OA meet the physical activity guidelines.[13] In fact, a third of the men and more than half of the women with knee OA were considered completely inactive.[13] Therefore, recommendations for management of knee OA include measures to increase physical activity and to reduce body weight.[23,59] However, the results from this study suggest that, as knee OA progresses, care may be needed when prescribing the volume of physical activity for these individuals. This is supported by a recent longitudinal study showing that in people with pre-existing knee OA, walking more than 10 000 steps per day was predictive of worsening cartilage, meniscus, and bone marrow lesions.[12]

The results demonstrate that other knee loading–related OA risk factors, including BMI and frontal plane alignment, did not make significant contributions toward explaining the variance in the laminar T1rho and T2 parameters. Obesity leads to a greater risk of knee OA incidence and progression,[50,57] and varus and valgus malalignment leads to a greater progression of medial knee OA and lateral knee OA, respectively.[16,17,49] Data from the OAI show that in asymptomatic adults and those with OA risk factors, obese individuals had the highest T2 values and normal-weight individuals had the lowest mean T2 values.[4] In cohorts of less than 30 individuals, people with medial knee OA who had varus alignment were found to have higher cartilage T1rho and T2 than those with valgus alignment.[20,55] Most of these studies either were in healthy cohorts or had a small sample size. Longitudinal studies in larger samples, like the OAI cohort, are needed to understand the effect of these OA risk factors on cartilage degeneration over time.

Superficial MF layer T1rho and T2 and deep MT layer T1rho were higher in the OA group compared to the control group. Additionally, the difference in deep MF T1rho was nearly significant. An increase in T1rho and T2 is indicative of worsening cartilage composition, with proteoglycan loss and collagen disruption. A number of earlier studies have reported higher T1rho and T2 relaxation times in people with radiographic knee OA,[31,46,58] cartilage lesions,[3,50] meniscal lesions,[28,58] and bone marrow lesions.[60] Earlier studies have also shown that in individuals post–anterior cruciate ligament reconstruction, it was the superficial layer that had higher T1rho and T2 a year after surgery and not the deep layer.[52] Conversely, tears of the posterior horn medial meniscus were associated with higher T1rho and T2 of the deep but not the superficial layer.[28] Hence, it is possible that cartilage degeneration may have spatial differences with different mechanisms of onset. Recent animal work supports these hypotheses, where centroid paths at the knee were increased after an anterior cruciate ligament transection and reduced after meniscal excision.[5] The authors concluded that the mechanism of cartilage damage may be related to increased magnitude and velocity of surface motion in the anterior cruciate ligament transection model and to increased contact stress in the meniscectomy model. These studies highlight the importance of investigating the superficial and deep cartilage layers separately to understand the knee OA disease process.

Both T1rho and T2 are measures of cartilage composition. They are considered complementary techniques because T1rho is sensitive to proteoglycan composition and T2 is sensitive to collagen integrity and cartilage hydration. Early OA changes consist of loss of proteoglycans, disruption of the collagen matrix, and change in water content of the articular cartilage. However, it has been suggested in the literature that T1rho may be superior to T2 in its ability to detect various grades of cartilage degeneration.[31] This is attributed to its higher dynamic range and sensitivity to early changes.[45,53] On the other hand, T2 is a more widely available technique and has also been used in the OAI data sets.[57] In our study, we observed that 2 of the T1rho parameters and 1 of the T2 parameters were significantly higher in the OA group, suggesting greater sensitivity of the T1rho metric. However, these techniques are currently difficult to use in the clinical setting due to the technical challenges and resource-intensive nature of the data processing. Hence, work needs to be done to make these techniques more widely available, and also to standardize them so that they can be used across different MRI scanners and sites.

The present study has limitations that need to be taken into consideration. The cross-sectional nature of the study does not allow determination of causality. A longitudinal study design is needed to isolate the effect of physical activity levels on laminar magnetic resonance relaxation times in individuals with progressive knee OA. Our cohort had 110 control participants and 41 participants with knee OA, leading to unbalanced groups. However, 22% of our control cohort had medial cartilage lesions (results not shown), suggesting that the prevalence of OA was higher than that determined by KL grading. We also excluded individuals with a KL grade of 4. Hence, the results may not be generalizable to these populations. However, the strength of these magnetic resonance techniques lies in their ability to diagnose early OA. Furthermore, the importance of physical activity for prevention of OA progression is more relevant in individuals with mild to moderate disease. Finally, we used a self-report questionnaire for assessment of physical activity levels. The questionnaire only asks about activities over the past week, and thus only captures information over a brief period. In chronic degenerative conditions like knee OA, activity levels over longer periods may provide better information. However, such information is difficult to obtain with currently available tools.

CONCLUSION

Greater volume of self-reported physical activity and worse radiographic knee OA were associated with worse cartilage composition. Other loading-related OA risk factors, including obesity and malalignment of the lower extremity, did not contribute to explaining the variance of the magnetic resonance relaxation times.

Acknowledgments

This work was supported in part through funding by National Institutes of Health-National Institute of Arthritis and Musculoskeletal and Skin Diseases grants R01 AR046905 and R01 AR062370. The protocol for this study was approved by the University of California San Francisco Committee on Human Research (Institutional Review Board approval number 10-04724).

The authors would like to thank Melissa Guan for assistance with patient recruitment, Aldric Chau and Joseph Schooler for assistance with data acquisition and processing, and K. Subburaj and Megan Marsh for software support.

References

1. Ainsworth BE, Bassett DR Jr, Strath SJ, et al. Comparison of three methods for measuring the time spent in physical activity. Med Sci Sports Exerc. 2000; 32:S457–S464. [PubMed: 10993415]
2. Akella SV, Regatte RR, Gougoutas AJ, et al. Proteoglycan-induced changes in $T_{1\rho}$-relaxation of articular cartilage at 4T. Magn Reson Med. 2001; 46:419–423. http://dx.doi.org/10.1002/mrm.1208. [PubMed: 11550230]
3. Baum T, Joseph GB, Arulanandan A, et al. Association of magnetic resonance imaging-based knee cartilage T2 measurements and focal knee lesions with knee pain: data from the Osteoarthritis Initiative. Arthritis Care Res (Hoboken). 2012; 64:248–255. http://dx.doi.org/10.1002/acr.20672. [PubMed: 22012846]
4. Baum T, Joseph GB, Nardo L, et al. Correlation of magnetic resonance imaging-based knee cartilage T2 measurements and focal knee lesions with body mass index: thirty-six-month followup data from a longitudinal, observational multicenter study. Arthritis Care Res (Hoboken). 2013; 65:23–33. http://dx.doi.org/10.1002/acr.21741. [PubMed: 22623435]
5. Beveridge JE, Heard BJ, Shrive NG, Frank CB. Tibiofemoral centroid velocity correlates more consistently with cartilage damage than does contact path length in two ovine models of stifle injury. J Orthop Res. 2013; 31:1745–1756. http://dx.doi.org/10.1002/jor.22429. [PubMed: 23832294]
6. Carballido-Gamio J, Bauer JS, Stahl R, et al. Inter-subject comparison of MRI knee cartilage thickness. Med Image Anal. 2008; 12:120–135. http://dx.doi.org/10.1016/j.media.2007.08.002. [PubMed: 17923429]
7. Carballido-Gamio J, Stahl R, Blumenkrantz G, Romero A, Majumdar S, Link TM. Spatial analysis of magnetic resonance $T_{1\rho}$ and T_2 relaxation times improves classification between subjects with and without osteoarthritis. Med Phys. 2009; 36:4059–4067. http://dx.doi.org/10.1118/1.3187228. [PubMed: 19810478]
8. Charles HC, Kraus VB, Ainslie M, Hellio Le Graverand-Gastineau MP. Optimization of the fixed-flexion knee radiograph. Osteoarthritis Cartilage. 2007; 15:1221–1224. http://dx.doi.org/10.1016/j.joca.2007.05.012. [PubMed: 17977754]
9. Dearborn JT, Eakin CL, Skinner HB. Medial compartment arthrosis of the knee. Am J Orthop (Belle Mead NJ). 1996; 25:18–26. [PubMed: 8722125]
10. Dekker J, van Dijk GM, Veenhof C. Risk factors for functional decline in osteoarthritis of the hip or knee. Curr Opin Rheumatol. 2009; 21:520–524. http://dx.doi.org/10.1097/BOR.0b013e32832e6eaa. [PubMed: 19550331]
11. Dillon CF, Rasch EK, Gu Q, Hirsch R. Prevalence of knee osteoarthritis in the United States: arthritis data from the Third National Health and Nutrition Examination Survey 1991–94. J Rheumatol. 2006; 33:2271–2279. [PubMed: 17013996]
12. Dore DA, Winzenberg TM, Ding C, et al. The association between objectively measured physical activity and knee structural change using MRI. Ann Rheum Dis. 2013; 72:1170–1175. http://dx.doi.org/10.1136/annrheumdis-2012-201691. [PubMed: 22896739]
13. Dunlop DD, Song J, Semanik PA, et al. Objective physical activity measurement in the Osteoarthritis Initiative: are guidelines being met? Arthritis Rheum. 2011; 63:3372–3382. http://dx.doi.org/10.1002/art.30562. [PubMed: 21792835]
14. 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; 232:592–598. http://dx.doi.org/10.1148/radiol.2322030976. [PubMed: 15215540]
15. Ettinger WH Jr, Burns R, Messier SP, et al. A randomized trial comparing aerobic exercise and resistance exercise with a health education program in older adults with knee osteoarthritis. The Fitness Arthritis and Seniors Trial (FAST). JAMA. 1997; 277:25–31. http://dx.doi.org/10.1001/jama.1997.03540250033028. [PubMed: 8980206]
16. Felson DT, Goggins J, Niu J, Zhang Y, Hunter DJ. The effect of body weight on progression of knee osteoarthritis is dependent on alignment. Arthritis Rheum. 2004; 50:3904–3909. http://dx.doi.org/10.1002/art.20726. [PubMed: 15593215]

17. Felson DT, Niu J, Gross KD, et al. Valgus malalignment is a risk factor for lateral knee osteoarthritis incidence and progression: findings from the Multicenter Osteoarthritis Study and the Osteoarthritis Initiative. Arthritis Rheum. 2013; 65:355–362. http://dx.doi.org/10.1002/art.37726. [PubMed: 23203672]

18. Fitzgerald GK, Piva SR, Irrgang JJ. Reports of joint instability in knee osteoarthritis: its prevalence and relationship to physical function. Arthritis Rheum. 2004; 51:941–946. http://dx.doi.org/10.1002/art.20825. [PubMed: 15593258]

19. Foley S, Ding C, Cicuttini F, Jones G. Physical activity and knee structural change: a longitudinal study using MRI. Med Sci Sports Exerc. 2007; 39:426–434. http://dx.doi.org/10.1249/mss.0b013e31802d97c6. [PubMed: 17473768]

20. Friedrich KM, Shepard T, Chang G, et al. Does joint alignment affect the T2 values of cartilage in patients with knee osteoarthritis? Eur Radiol. 2010; 20:1532–1538. http://dx.doi.org/10.1007/s00330-009-1689-7. [PubMed: 20013272]

21. Guccione AA, Felson DT, Anderson JJ, et al. The effects of specific medical conditions on the functional limitations of elders in the Framingham Study. Am J Public Health. 1994; 84:351–358. [PubMed: 8129049]

22. Hochberg MC. Mortality in osteoarthritis. Clin Exp Rheumatol. 2008; 26:S120–S124. [PubMed: 19026154]

23. Hochberg MC, Altman RD, April KT, et al. American College of Rheumatology 2012 recommendations for the use of nonpharmacologic and pharmacologic therapies in osteoarthritis of the hand, hip, and knee. Arthritis Care Res (Hoboken). 2012; 64:465–474. http://dx.doi.org/10.1002/acr.21596. [PubMed: 22563589]

24. Hovis KK, Stehling C, Souza RB, et al. Physical activity is associated with magnetic resonance imaging-based knee cartilage T2 measurements in asymptomatic subjects with and those without osteoarthritis risk factors. Arthritis Rheum. 2011; 63:2248–2256. http://dx.doi.org/10.1002/art.30419. [PubMed: 21538328]

25. Hsu RW, Himeno S, Coventry MB, Chao EY. Normal axial alignment of the lower extremity and load-bearing distribution at the knee. Clin Orthop Relat Res. 1990:215–227. [PubMed: 2347155]

26. Joseph GB, Baum T, Alizai H, et al. Baseline mean and heterogeneity of MR cartilage T2 are associated with morphologic degeneration of cartilage, meniscus, and bone marrow over 3 years – data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2012; 20:727–735. http://dx.doi.org/10.1016/j.joca.2012.04.003. [PubMed: 22503812]

27. Kellgren JH, Lawrence JS. Radiological assessment of osteo-arthrosis. Ann Rheum Dis. 1957; 16:494–502. [PubMed: 13498604]

28. Kumar D, Schooler J, Zuo J, et al. Trabecular bone structure and spatial differences in articular cartilage MR relaxation times in individuals with posterior horn medial meniscal tears. Osteoarthritis Cartilage. 2013; 21:86–93. http://dx.doi.org/10.1016/j.joca.2012.09.014. [PubMed: 23047010]

29. Lawrence RC, Felson DT, Helmick CG, et al. Estimates of the prevalence of arthritis and other rheumatic conditions in the United States. Part II. Arthritis Rheum. 2008; 58:26–35. http://dx.doi.org/10.1002/art.23176. [PubMed: 18163497]

30. Li X, Cheng J, Lin K, et al. Quantitative MRI using $T_{1\rho}$ and T_2 in human osteoarthritic cartilage specimens: correlation with biochemical measurements and histology. Magn Reson Imaging. 2011; 29:324–334. http://dx.doi.org/10.1016/j.mri.2010.09.004. [PubMed: 21130590]

31. Li X, Ma CB, Link TM, et al. In vivo $T_{1\rho}$ and T_2 mapping of articular cartilage in osteoarthritis of the knee using 3 T MRI. Osteoarthritis Cartilage. 2007; 15:789–797. http://dx.doi.org/10.1016/j.joca.2007.01.011. [PubMed: 17307365]

32. Liang MH, Larson MG, Cullen KE, Schwartz JA. Comparative measurement efficiency and sensitivity of five health status instruments for arthritis research. Arthritis Rheum. 1985; 28:542–547. [PubMed: 4004963]

33. Lin W, Alizai H, Joseph GB, et al. Physical activity in relation to knee cartilage T2 progression measured with 3 T MRI over a period of 4 years: data from the Osteoarthritis Initiative. Osteoarthritis Cartilage. 2013; 21:1558–1566. http://dx.doi.org/10.1016/j.joca.2013.06.022. [PubMed: 23831632]

34. Lohmander LS. Articular cartilage and osteoarthrosis. The role of molecular markers to monitor breakdown, repair and disease. J Anat. 1994; 184(pt 3):477–492. [PubMed: 7928637]
35. Mäder U, Martin BW, Schutz Y, Marti B. Validity of four short physical activity questionnaires in middle-aged persons. Med Sci Sports Exerc. 2006; 38:1255–1266. http://dx.doi.org/10.1249/01.mss.0000227310.18902.28. [PubMed: 16826022]
36. Menezes NM, Gray ML, Hartke JR, Burstein D. T_2 and $T_{1\rho}$ MRI in articular cartilage systems. Magn Reson Med. 2004; 51:503–509. http://dx.doi.org/10.1002/mrm.10710. [PubMed: 15004791]
37. Mosher TJ, Dardzinski BJ. Cartilage MRI T2 relaxation time mapping: overview and applications. Semin Musculoskelet Radiol. 2004; 8:355–368. http://dx.doi.org/10.1055/s-2004-861764. [PubMed: 15643574]
38. Nüesch E, Dieppe P, Reichenbach S, Williams S, Iff S, Jüni P. All cause and disease specific mortality in patients with knee or hip osteoarthritis: population based cohort study. BMJ. 2011; 342:d1165. http://dx.doi.org/10.1136/bmj.d1165. [PubMed: 21385807]
39. 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; 261:507–515. http://dx.doi.org/10.1148/radiol.11102234. [PubMed: 21900614]
40. Pearle AD, Warren RF, Rodeo SA. Basic science of articular cartilage and osteoarthritis. Clin Sports Med. 2005; 24:1–12. http://dx.doi.org/10.1016/j.csm.2004.08.007. [PubMed: 15636773]
41. Pelletier JP, Raynauld JP, Berthiaume MJ, et al. Risk factors associated with the loss of cartilage volume on weight-bearing areas in knee osteoarthritis patients assessed by quantitative magnetic resonance imaging: a longitudinal study. Arthritis Res Ther. 2007; 9:R74. http://dx.doi.org/10.1186/ar2272. [PubMed: 17672891]
42. Penninx BW, Messier SP, Rejeski WJ, et al. Physical exercise and the prevention of disability in activities of daily living in older persons with osteoarthritis. Arch Intern Med. 2001; 161:2309–2316. [PubMed: 11606146]
43. Racunica TL, Teichtahl AJ, Wang Y, et al. Effect of physical activity on articular knee joint structures in community-based adults. Arthritis Rheum. 2007; 57:1261–1268. http://dx.doi.org/10.1002/art.22990. [PubMed: 17907212]
44. Rauscher I, Stahl R, Cheng J, et al. Meniscal measurements of $T1_{\rho}$ and T2 at MR imaging in healthy subjects and patients with osteoarthritis. Radiology. 2008; 249:591–600. http://dx.doi.org/10.1148/radiol.2492071870. [PubMed: 18936315]
45. Regatte RR, Akella SV, Lonner JH, Kneeland JB, Reddy R. $T_{1\rho}$ relaxation mapping in human osteoarthritis (OA) cartilage: comparison of $T_{1\rho}$ with T_2. J Magn Reson Imaging. 2006; 23:547–553. http://dx.doi.org/10.1002/jmri.20536. [PubMed: 16523468]
46. Regatte RR, Akella SV, Wheaton AJ, et al. 3D-$T_{1\rho}$-relaxation mapping of articular cartilage: in vivo assessment of early degenerative changes in symptomatic osteoarthritic subjects. Acad Radiol. 2004; 11:741–749. http://dx.doi.org/10.1016/j.acra.2004.03.051. [PubMed: 15217591]
47. Roemer FW, Hunter DJ, Winterstein A, et al. Hip Osteoarthritis MRI Scoring System (HOAMS): reliability and associations with radiographic and clinical findings. Osteoarthritis Cartilage. 2011; 19:946–962. http://dx.doi.org/10.1016/j.joca.2011.04.003. [PubMed: 21550411]
48. Roos EM, Roos HP, Lohmander LS, Ekdahl C, Beynnon BD. Knee Injury and Osteoarthritis Outcome Score (KOOS)—development of a self-administered outcome measure. J Orthop Sports Phys Ther. 1998; 28:88–96. http://dx.doi.org/10.2519/jospt.1998.28.2.88. [PubMed: 9699158]
49. Sharma L, Chmiel JS, Almagor O, et al. The role of varus and valgus alignment in the initial development of knee cartilage damage by MRI: the MOST study. Ann Rheum Dis. 2013; 72:235–240. http://dx.doi.org/10.1136/annrheumdis-2011-201070. [PubMed: 22550314]
50. Souza RB, Feeley BT, Zarins ZA, Link TM, Li X, Majumdar S. $T1_{\rho}$ MRI relaxation in knee OA subjects with varying sizes of cartilage lesions. Knee. 2013; 20:113–119. http://dx.doi.org/10.1016/j.knee.2012.10.018. [PubMed: 23159719]
51. Stehling C, Lane NE, Nevitt MC, Lynch J, Mc-Culloch CE, Link TM. Subjects with higher physical activity levels have more severe focal knee lesions diagnosed with 3 T MRI: analysis of a non-symptomatic cohort of the osteoarthritis initiative. Osteoarthritis Cartilage. 2010; 18:776–786. http://dx.doi.org/10.1016/j.joca.2010.02.008. [PubMed: 20202488]

52. Stull JD, Philippon MJ, LaPrade RF. "At-risk" positioning and hip biomechanics of the Peewee ice hockey sprint start. Am J Sports Med. 2011; 39(suppl):29S–35S. http://dx.doi.org/10.1177/0363546511414012. [PubMed: 21709029]

53. Takayama Y, Hatakenaka M, Tsushima H, et al. $T1_{\rho}$ is superior to T2 mapping for the evaluation of articular cartilage denaturalization with osteoarthritis: radiological-pathological correlation after total knee arthroplasty. Eur J Radiol. 2013; 82:e192–e198. http://dx.doi.org/10.1016/j.ejrad.2012.11.031. [PubMed: 23265927]

54. Wang L, Chang G, Xu J, et al. T1rho MRI of menisci and cartilage in patients with osteoarthritis at 3T. Eur J Radiol. 2012; 81:2329–2336. http://dx.doi.org/10.1016/j.ejrad.2011.07.017. [PubMed: 21908122]

55. Wang L, Vieira RL, Rybak LD, et al. Relationship between knee alignment and $T1_{\rho}$ values of articular cartilage and menisci in patients with knee osteoarthritis. Eur J Radiol. 2013; 82:1946–1952. http://dx.doi.org/10.1016/j.ejrad.2013.05.010. [PubMed: 23769189]

56. Wluka AE, Lombard CB, Cicuttini FM. Tackling obesity in knee osteoarthritis. Nat Rev Rheumatol. 2013; 9:225–235. http://dx.doi.org/10.1038/nrrheum.2012.224. [PubMed: 23247649]

57. Wong CS, Yan CH, Gong NJ, Li T, Chan Q, Chu YC. Imaging biomarker with $T1_{\rho}$ and T2 mappings in osteoarthritis – in vivo human articular cartilage study. Eur J Radiol. 2013; 82:647–650. http://dx.doi.org/10.1016/j.ejrad.2012.11.036. [PubMed: 23333531]

58. Zarins ZA, Bolbos RI, Pialat JB, et al. Cartilage and meniscus assessment using $T_{1\rho}$ and T_2 measurements in healthy subjects and patients with osteoarthritis. Osteoarthritis Cartilage. 2010; 18:1408–1416. http://dx.doi.org/10.1016/j.joca.2010.07.012. [PubMed: 20696262]

59. Zhang W, Nuki G, Moskowitz RW, et al. OARSI recommendations for the management of hip and knee osteoarthritis: part III: changes in evidence following systematic cumulative update of research published through January 2009. Osteoarthritis Cartilage. 2010; 18:476–499. http://dx.doi.org/10.1016/j.joca.2010.01.013. [PubMed: 20170770]

60. Zhao J, Li X, Bolbos RI, Link TM, Majumdar S. Longitudinal assessment of bone marrow edema-like lesions and cartilage degeneration in osteoarthritis using 3 T MR $T_{1\rho}$ quantification. Skeletal Radiol. 2010; 39:523–531. http://dx.doi.org/10.1007/s00256-010-0892-6. [PubMed: 20195865]

Author Manuscript
Author Manuscript
Author Manuscript

KEY POINTS

FINDINGS

Greater volume of self-reported physical activity and worse radiographic knee OA were associated with worse cartilage composition. Other loading-related OA risk factors, including obesity and malalignment of the lower extremity, did not contribute to explaining the variance of the magnetic resonance relaxation times.

IMPLICATIONS

These results show that physical activity levels may need careful monitoring as the disease progresses.

CAUTION

Cross-sectional analyses limit interpretations about causality. These results would need to be replicated in larger samples and the participants followed longitudinally to ascertain the long-term effect of physical activity on OA progression.

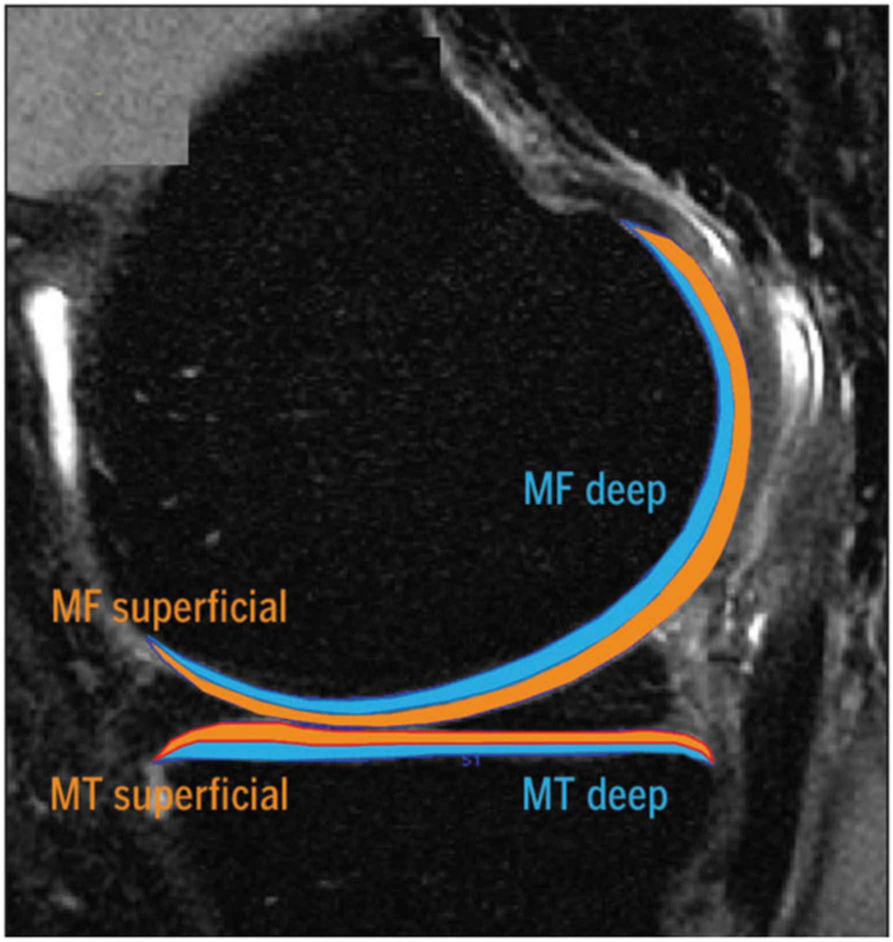

FIGURE 1.
Superficial and deep MF and MT cartilage layers. Abbreviations: MF, medial femur; MT, medial tibia.

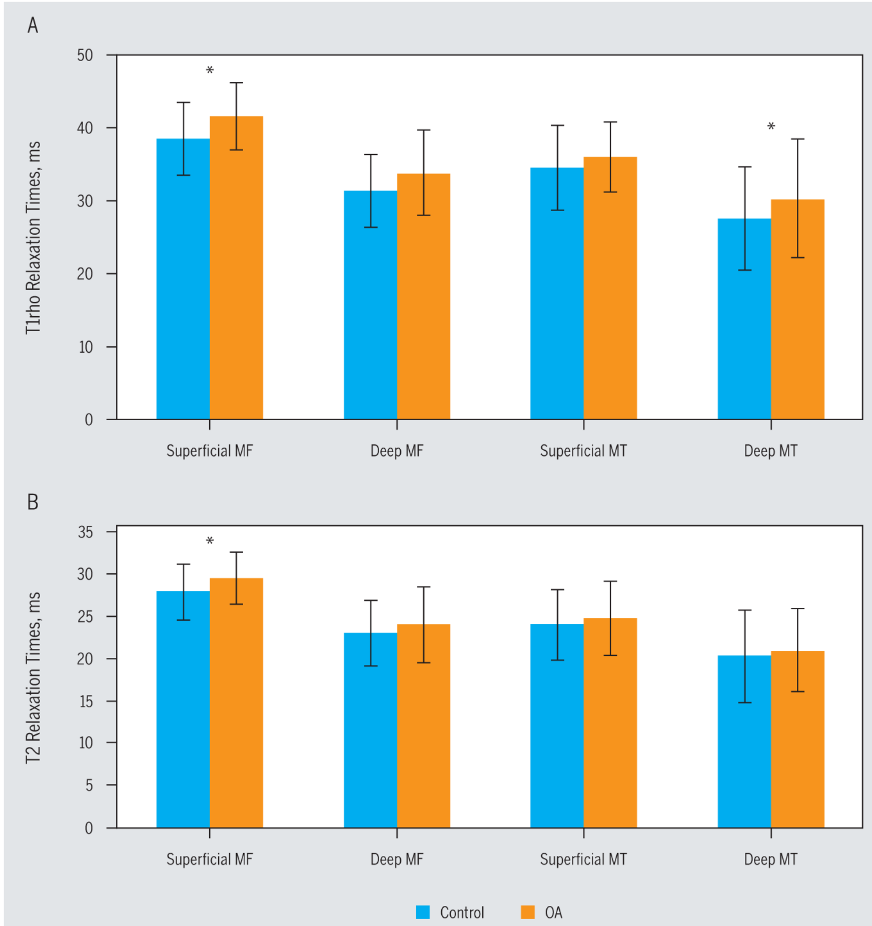

FIGURE 2.

(A) T1rho and (B) T2 laminar magnetic resonance relaxation times for the OA and control groups for the MF and MT. *Statistically significant difference (P<.05). Superficial MF T1rho, P = .009; deep MT, P = .017; superficial MF T2, P = .038. Abbreviations: MF, medial femur; MT, medial tibia; OA, osteoarthritis.

TABLE 1

Participant Demographic Data*

	Control (n = 110)	Osteoarthritis (n = 41)	*P* Value
Age, y	50.1 ± 8.9	57.9 ± 9.6	<.001
Body mass index, kg/m^2	24.0 ± 3.5	25.0 ± 3.4	.097
Sex, n			.740
Men	45	18	
Women	65	23	
Alignment, deg	179.2 ± 2.8	178.7 ± 3.2	.360
KOOS			
Symptoms	88.5 ± 11.8	81.6 ± 17.2	.012†
Pain	89.8 ± 13.7	80.2 ± 17.5	.004†
IPAQ, MET min/wk			
Vigorous	1719.0 ± 2337.5	1741.1 ± 2389.3	.934†
Moderate	836.7 ± 1065.9	1080.5 ± 1508.8	.353†
Walking	1467.1 ± 1289.0	1574.4 ± 1292.3	.670†
Total	4013.4 ± 3207.4	4396.0 ± 4201.8	.674†

Abbreviations: IPAQ, International Physical Activity Questionnaire; KOOS, Knee injury and Osteoarthritis Outcome Score; MET, metabolic equivalent of task.

*Values are mean ± SD unless otherwise indicated.

†Adjusted for age and body mass index.

TABLE 2

Laminar Magnetic Resonance Relaxation Times by Kellgren-Lawrence Grade*

MR Parameter/Body Region	KL Grade†	Value
T1rho		
Superficial medial femur	0	38.0 (36.7, 39.3)
	1	38.8 (37.4, 40.2)
	2	40.8 (38.9, 42.7)
	3	42.2 (39.8, 44.5)
Deep medial femur	0	31.0 (29.5, 32.5)
	1	31.7 (30.4, 32.9)
	2	33.2 (30.6, 35.8)
	3	34.4 (31.5, 37.2)
Superficial medial tibia	0	34.5 (33.0, 35.9)
	1	34.4 (32.7, 36.2)
	2	34.2 (32.1, 36.3)
	3	37.7 (35.4, 39.9)
Deep medial tibia	0	28.4 (26.2, 30.5)
	1	26.6 (24.9, 28.2)
	2	28.6 (23.9, 33.2)
	3	32.0 (29.3, 34.7)
T2		
Superficial medial femur	0	27.5 (26.7, 28.3)
	1	28.1 (27.2, 29.1)
	2	29.7 (28.4, 31.0)
	3	29.3 (27.6, 31.0)
Deep medial femur	0	22.4 (21.5, 23.3)
	1	23.6 (22.4, 24.7)
	2	23.4 (20.9, 25.8)
	3	24.6 (22.8, 26.3)
Superficial medial tibia	0	23.7 (22.7, 24.8)
	1	24.2 (22.9, 25.4)
	2	24.2 (22.1, 26.4)
	3	25.2 (23.4, 27.1)
Deep medial tibia	0	19.8 (18.6, 21.0)
	1	20.7 (19.0, 22.5)
	2	20.0 (17.3, 22.7)
	3	21.8 (20.0, 23.7)

Abbreviations: KL, Kellgren-Lawrence; MR, magnetic resonance.

*Values are mean (95% confidence interval) milliseconds.

†Grade 0, n = 57; grade 1, n = 53; grade 2, n = 21; grade 3, n = 20.

TABLE 3

Regression Analysis for Outcomes of Magnetic Resonance Relaxation Times

	Superficial MF T1rho				Deep MT T1rho				Superficial MF T2			
	B	SE	β	*P* Value	B	SE	β	*P* Value	B	SE	β	*P* Value
Age	0.049	0.045	.095	.283	−0.104	0.067	−.139	.127	0.032	0.031	.097	.293
Body mass index	−0.538	0.924	−.053	.561	0.467	1.380	.032	.735	−0.429	0.628	−.065	.496
Sex	−0.053	0.120	−.038	.659	0.092	0.179	.046	.607	0.038	0.081	.042	.640
Kellgren-Lawrence	1.016	0.443	.212	.023	1.538	0.662	.220	.022	0.409	0.299	.131	.174
Alignment	−0.157	0.158	−.088	.323	0.274	0.236	.106	.247	−0.012	0.108	−.011	.909
Total physical activity*	0.329	0.116	.231	.005	0.392	0.174	.189	.026	0.155	0.078	.171	.049

Abbreviations: B, unstandardized regression coefficient; β, standardized regression coefficient; MF, medial femur; MT, medial tibia; SE, standard error.

* International Physical Activity Questionnaire scores were rescaled to 1000 MET minutes per week.