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Authors

Subburaj, Karupppasamy
Kumar, Deepak
Souza, Richard B
et al.

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The Acute Effect of Running on Knee Articular Cartilage and Meniscus Magnetic Resonance Relaxation Times in Young Healthy Adults

Karupppasamy Subburaj, PhD[*,†], **Deepak Kumar, PT, PhD**[†], **Richard B. Souza, PT, PhD**[†,‡], **Hamza Alizai, MD**[†], **Xiaojuan Li, PhD**[†], **Thomas M. Link, MD**[†], and **Sharmila Majumdar, PhD**[†]

[†]Musculoskeletal Quantitative Imaging Research, Department of Radiology and Biomedical Imaging, University of California–San Francisco, San Francisco, California

[‡]Department of Physical Therapy and Rehabilitation Science, University of California–San Francisco, San Francisco, California

Abstract

Background—Understanding the acute response of healthy knee cartilage to running may provide valuable insight into functional properties. In recent years, quantitative magnetic resonance (MR) imaging techniques ($T1_\rho$ and T2 relaxation measurement) have shown tremendous potential and unique ability to noninvasively and quantitatively determine cartilage response to physiologic levels of loading occurring with physiologic levels of exercise.

Purpose—To measure the short-term changes in MR $T1_\rho$ and T2 relaxation times of knee articular cartilage and meniscus in healthy individuals immediately after 30 minutes of running.

Study Design—Descriptive laboratory study.

Methods—Twenty young healthy volunteers, aged 22 to 35 years, underwent 3T MR imaging of the knee before and immediately after 30 minutes of running. Quantitative assessment of the cartilage and menisci was performed using MR images with a $T1_\rho$ and T2 mapping technique. After adjusting for age, sex, and body mass index, repeated-measures analysis of variance was used to determine the effects of running on MR relaxation times.

Results—The post-run $T1_\rho$ and T2 measurement showed significant reduction in all regions of cartilage except the lateral tibia when compared with the pre-run condition. The medial tibiofemoral ($T1_\rho$: 9.4%, $P < .0001$; T2: 5.4%, $P = .0049$) and patellofemoral ($T1_\rho$: 12.5%, $P < .0001$; T2: 5.7%, $P = .0007$) compartments experienced the greatest reduction after running. The superficial layer of the articular cartilage showed significantly higher change in relaxation times than the deep layer ($\Delta T1_\rho$: 9.6% vs 8.2%, $P = .050$; $\Delta T2$: 6.0% vs 3.5%, $P = .069$). The anterior and posterior horns of the medial meniscus (9.7%, $P = .016$ and 11.4%, $P = .001$) were the only meniscal subregions with significant changes in $T1_\rho$ after running.

Conclusion—Shorter $T1_\rho$ and T2 values after running suggest alteration in the water content and collagen fiber orientation of the articular cartilage. Greater changes in relaxation times of the medial compartment and patellofemoral joint cartilage indicate greater load sharing by these areas during running.

[*]Address correspondence to Karupppasamy Subburaj, PhD, Department of Radiology and Biomedical Imaging, University of California–San Francisco, 1700 4th St, Suite 203, San Francisco, CA 94158 (subburaj@radiology.ucsf.edu).

Investigation performed at the University of California–San Francisco, San Francisco, California

Keywords

knee cartilage; meniscus; running; MRI; relaxation times

Biomechanically, cartilage can be viewed as an intra-articular shock absorber that dampens physiologic loads, transfers the applied load to the subchondral bone, and reduces friction in the joint. The meniscus, fibrocartilaginous tissue found within the knee joint, is responsible for shock absorption, load transmission, and stability within the knee joint. Type I collagen and smaller amounts of type II collagen are the major fibrillar collagens in the meniscus. Type II collagen is the dominant fibrillar collagen in hyaline cartilage such as the articular cartilage of the knee joint. It is known that healthy cartilage requires compressive loading from physical activity to develop normally and to maintain cartilage integrity.[36] High-impact sports involving repetitive joint loading (such as running) have been reported to be a biomechanical risk factor for developing knee osteoarthritis.[11,30] Although a number of studies have examined the relationship between physical activity and knee osteoarthritis, the effects of physical activity on the healthy knee joint remain unclear.[7,11,30,35]

Quantitative studies on the effects of static loading on cartilage volume, thickness,[20,28] and water content in specimens (animal and human),[33] intact cadaveric joints, and in vivo human joints[20,28] have suggested that structural changes in the cartilage matrix occur with physical activity (physiologic loading). Although the partial recovery of the cartilage and meniscus after rest[12,13] has been reported, prolonged physical activity may affect the biochemistry of the cartilage. Neu et al[27] reported nonuniform deformations in cartilage of an intact cadaver knee joint under unconfined compression testing. Kaab et al[12] observed from in vitro rabbit cartilage specimens significantly higher deformation of the collagen structure throughout all cartilage zones under static loading conditions compared with cyclic loading conditions in which deformation was limited to the superficial regions. Knowledge of the acute response effects of physical exercise on healthy cartilage and meniscus in vivo may thus provide valuable insight into functional properties of knee cartilage in response to physiologic loading.

Magnetic resonance imaging (MRI) usage in studying cartilage structure (volume and thickness) and alterations (lesions) has received considerable interest in recent years.[13] Cartilage magnetic resonance (MR) relaxation times ($T1_\rho$ and T2) are highly sensitive to alterations in the structural integrity of the collagen/proteoglycans (PG) matrix as well as corresponding change in water, collagen, and PG content.[6,22] $T1_\rho$ relaxation time, which is the spin-lattice relaxation in the rotating frame, probes the interaction between motion-restricted water molecules and the macromolecular environment.[18] It has been shown in the literature that $T1_\rho$ relaxation is negatively correlated with PG content.[1,17] T2 reflects the ability of energy exchange between free water proton molecules and is dominated by the collagen matrix structure and water content.[22] The functional response of the articular cartilage (change in $T1_\rho$ and T2) to physiologic loading depends on its biochemical composition (PG content, water, and collagen structure) and may serve as a more sensitive biomarker than the morphological markers such as volume and thickness.[7,24] These studies indicate that MR relaxation times ($T1_\rho$ and T2) can be used as noninvasive measures to quantify and monitor the change in biochemical and biomechanical properties of cartilage and meniscus after physical activity or exercise. Significant decreases in T2 values of the articular cartilage (tibiofemoral joint) immediately after running[24] and knee-bending[20] activities also have been reported. Elevated cartilage $T1_\rho$ and T2 values in long-distance runners in the days after a marathon run when compared with age-matched controls also has been reported.[21] The acute effect on $T1_\rho$ values in the knee articular cartilage and menisci immediately after running has not been studied yet.

The goals of this study were (1) to analyze MR relaxation time ($T1_\rho$ and T2) change in various regions of knee articular cartilage (tibiofemoral and patellofemoral joints) and menisci in healthy controls before and immediately after a 30-minute run and (2) to determine which regions of articular cartilage and menisci are most affected by running (regional variations and spatial heterogeneity). We hypothesized that running reduces the water content and disturbs the collagen/PG matrix of the cartilage, which will be reflected in shorter MR relaxation ($T1_\rho$ and T2) values. This study exploits the unique ability of MR imaging techniques to noninvasively and quantitatively determine articular cartilage response to physiologic levels of loading occurring with physiologic levels of exercise. The study results would be valuable in various fields of sports medicine such as cartilage repair, functional biomechanics, exercise, and posttraumatic osteoarthritis.

MATERIALS AND METHODS

Participants

Twenty young healthy volunteers between ages 22 and 35 years (10 men and 10 women, with a mean age of 28.75 years; median, 29 years) and with a mean body mass index (BMI) of 22.7 kg/m^2 (range, 19.9–26.6 kg/m^2; median, 23.1 kg/m^2), with no knee pain or stiffness, no prior knee trauma, no joint disorders, and no history of orthopaedic surgery that affects the cartilage and meniscus of the knee joint, were recruited. A maximum age of 35 years was selected to reduce the likelihood of undiagnosed osteoarthritis (OA), as well as the age effect. In addition, volunteers were screened to exclude individuals with a known contraindication to MR safety guidelines (implanted pacemaker, metal clips, etc). Six participants (2 men, 4 women) were regular participants of long-distance running competitions. The nature of the procedure and aim of the study were explained to each participant, and an informed consent to participate in the study, approved by the Committee for Human Research at our institution, was signed.

Procedures

On the day of MRI acquisition, demographic data of the participants (age, height, weight, BMI, and frequency and duration of routine exercise) were collected. The short-form International Physical Activity Questionnaire (IPAQ) was administered to assess the physical activity levels among the participants. Participants were instructed not to deviate from their typical physical activity level on the day before their MRI. During all imaging, participants were positioned in the MR scanner in the supine position and their lower extremity in neutral rotation with the knee in full extension. The pre-run MR images were acquired after a 30-minute rest period, during which the participants were positioned supine. This period of rest was used to reduce the influence of preceding physical activities on MR relaxation times of cartilage and meniscus in the pre-run scan. According to the new American College of Sports Medicine (ACSM)/American Heart Association (AHA) guidelines, adults aged 18 to 65 years should continue to accumulate at least 30 minutes of moderate-intensity aerobic physical activity 5 days per week (a minimum of 150 minutes/wk) to gain advanced protection against “inactivity-related chronic diseases.”[10] Participants were instructed to run for 30 minutes (distance and speed were recorded but not controlled). Immediately after completion of running, post-run scanning was performed (Figure 1). Approximate time between cessation of running and initiation of the MR scan was less than 1 minute. All participants performed 30 minutes of running on a treadmill with a mean speed of 6.7 miles per hour (mph) (range, 5.6–8.0 mph; median, 6.3 mph) and maintained a mean stride frequency of 82.8 strides/min (median, 83.0 strides/min; range, 75–89 strides/min). Mean activity level of the volunteers was 3624 metabolic equivalents (MET)/wk measured by IPAQ score (median, 3543 MET/wk; range, 1056–7212 MET/wk).

MR Image Acquisition

All imaging was performed with a 3-Tesla GE Signa HDx (GE Healthcare, Waukesha, Wisconsin) MR scanner, using an 8-channel phased-array transmit/receive knee coil (In Vivo, Orlando, Florida). The imaging protocol included sagittal T2-weighted fat-saturated fast spin-echo (FSE) images (repetition time [TR]/echo time [TE] = 4300/51 ms, field of view [FOV] = 14 cm, matrix = 512 × 256, slice thickness = 2.5 mm, gap = 0.5 mm, echo train length [ETL] = 9, band-width = 31.25 kHz, number of excitations [NEX] = 2) and sagittal 3-dimensional (3D) fat-saturated high-resolution spoiled gradient-echo (SPGR) images (TR/TE = 15/6.7 ms, flip angle = 18, FOV = 14 cm, matrix = 512 × 512, slice thickness = 1 mm, bandwidth = 31.25 kHz, NEX = 1), and a combined $T1_\rho$/T2 quantification sequence[19] that allows for creation of both $T1_\rho$ and T2 maps during postprocessing. The combined sequence is composed of 2 parts: magnetization preparation for either $T1_\rho$ or T2 weighting, followed by a 3D SPGR acquisition during transient signal evolution immediately after magnetization preparation. A flag is defined in the pulse sequence to switch between $T1_\rho$ and T2 preparation according to the number of time of spin-lock (TSL) and TE defined (for $T1_\rho$ preparation: TSL = 0/10/40/80 ms, spin-lock frequency = 500 Hz; for T2 preparation: TE = 0/13.67/27.34/54.68 ms, FOV = 14, matrix = 256 × 128, views per segment [VPS] = 64, time of recovery = 1.2 s, slice thickness = 3 mm, number of slices = 30, pixel size = 0.5469 mm, no gap, acquisition time = 9 min). Concatenation of the 2 measurements in a single scan allows us to perform direct (voxel-by-voxel) comparison between $T1_\rho$ and T2 maps by removing potential quantification variations by minimizing chances of motion between these 2 quantifications. The total acquisition time for each knee was approximately 25 minutes. Post-run $T1_\rho$ and T2 images were acquired immediately after running (completed within 10 minutes of cessation of running).

MR Image Analysis

All MR images were reviewed by a senior musculoskeletal radiologist (T.M.L.) to evaluate and grade knee cartilage and meniscus focal abnormalities. The MR images were transferred to an HP workstation (Hewlett-Packard, Palo Alto, California) for off-line quantification of MR relaxation times ($T1_\rho$ and T2). Cartilage and meniscus were segmented in sagittal SPGR images using a software program developed in-house based on a spline-based semiautomated (automated edge detection and manual correction) segmentation algorithm in MATLAB (Math-works, Inc, El Segundo, California). Cartilage segmentation was divided into 6 regions: medial and lateral femoral condyle (MFC and LFC), medial and lateral tibial plateau (MTP and LTP), patella (PAT), and trochlea (TRO). The MFC and LFC regions were further divided into 2 subregions: central weightbearing (CMFC/CLFC) and posterior weightbearing (PMFC/PLFC) using the posterior boundary of the meniscus as a landmark, as shown in Figure 2. All these cartilage regions of interest were further partitioned into 2 equal layers: deep (closer to the subchondral bone) and superficial (closer to the articular surface). Cartilage voxels were classified to only 1 layer based on minimum Euclidean distances to the transferred splines. With typical imaging parameters, matrix size, and resolution, there may be only 3 to 7 pixels across the cartilage. Six regions of meniscus were also segmented: medial and lateral posterior horns (MPHN and LPHN), anterior horns (MAHN and LAHN), and body (MBOD and LBOD).

Quantification of $T1_\rho$ and T2

The $T1_\rho$ and T2 maps were reconstructed by fitting the image intensity (voxel by voxel) to the following equation using a Levenberg-Marquardt monoexponential fitting algorithm developed in-house: $S(TSL) = S_0 \exp(-TSL/T1_\rho)$ for $T1_\rho$ fitting, where S_0 is the signal intensity when TSL = 0 ms, and $S(TE) = S_0 \exp(-TE/T2)$ for T2 fitting, where S_0 is the signal intensity when preparation TE = 0 ms. All 4 $T1_\rho$ - or T2-weighted images were used

to reconstruct the cartilage maps. For the menisci only the first 3 $T1_\rho$ - or T2-weighted images were used as $T1_\rho$ -weighted images with TSL = 80 ms and T2-weighted images with TE = 54.8 ms had a very low signal-to-noise ratio (SNR; <5) for meniscus due to short $T1_\rho$ and T2 in meniscus, respectively, and therefore were not used during map reconstruction.[29] To minimize the error due to knee motion between the scans, $T1_\rho$ - and T2-weighted images with the shortest TSL or TE (therefore with highest SNR) were rigidly registered to high-resolution SPGR images acquired in the same examination using the VTK CISG Registration Toolkit (Kitware Inc, Clifton Park, New York). The transformation matrix was applied to the reconstructed $T1_\rho$ and T2 maps. The original splines of segmented cartilage and meniscus contours from the high-resolution SPGR images were superimposed on the corresponding reconstructed $T1_\rho$ and T2 maps to define the regions of interest for $T1_\rho$ and T2 assessment. To reduce artifacts caused by partial volume effects with synovial fluid, regions with relaxation time greater than 130 ms for $T1_\rho$ or 100 ms for T2 maps were removed from the data used for quantification.

Texture Analysis

Cartilage flattening was performed, with the aid of Bezier splines and warping to extract textural information that had correspondence to the natural laminar organization of cartilage as described by Carballido-Gamio et al.[4] Texture analysis of cartilage relaxation maps ($T1_\rho$ or T2) was performed using a gray-level co-occurrence matrix (GLCM).[9] The GLCM extracts information related to the spatial distribution of voxel intensities by analyzing their co-occurrences at a certain orientation and offset. The GLCM texture parameters, including contrast, entropy, and variance, were calculated in each cartilage region.[5] These texture parameters were selected as representative parameters from each of the 3 texture groups (contrast, order, and statistics, respectively) and also based on results from previous studies demonstrating their elevation in patients with OA.[3,5] An offset of 1 voxel was chosen based on the fact that approximately 3 to 4 voxels span the cartilage thickness. Texture parameters were quantified for 2 orientations: 0° or horizontal, corresponding to the anterior-posterior axis (parallel to the natural cartilage layers), and 90°, or vertical, corresponding to the superior-inferior axis (perpendicular to the natural cartilage layers) in sagittal images.

Statistical Analysis

Mean, standard deviation, and median $T1_\rho$ and T2 values and texture parameters were calculated for different regions of the cartilage and menisci. After adjusting for potential confounders (age, sex, and BMI) in the general linear regression model, repeated-measures analysis of variance (ANOVA) was used to determine the main effects of running on the changes in MR relaxation times (global mean, deep and superficial layers, and texture parameters) of both cartilage and menisci from the pre-run to the post-run measurement. To assess the effect of exercise on femorotibial and patellofemoral joints, we merged the regions of interest to create larger units: Patella and trochlea were combined to create the *patellofemoral* compartment, trochlea and medial and lateral femoral condyle were called *femur*, lateral and medial tibial plateaus yielded the *tibia* compartment, medial femoral and medial tibial plateau together represented the *medial* compartment, and the *lateral* compartment resulted from merging the lateral femoral and lateral tibial plateau. The initial compartments together were referred to as *all*. The relative changes in $T1_\rho$ and T2 were measured within these groups. All statistical analysis was performed using JMP 7.0 (SAS Institute, Cary, North Carolina), with a significance level of $P < .05$.

RESULTS

Effect of Running on Cartilage Relaxation Times ($T1_\rho$ and T2)

Collated data show a significant decrease in $T1_\rho$ (9.0%, $P < .0001$) and T2 (4.2%, $P = .0007$) times of articular cartilage after running. Regional analysis showed significant reduction in $T1_\rho$ values ranging from 4.1% to 14.3% in all regions, except the LTP. The medial tibia showed the largest reduction (14.3%, $P < .0001$), followed by the trochlea (13.5%, $P < .0001$) and the patella (11.7%, $P < .0001$) cartilage regions. Regional analysis of T2 relaxation times showed reduction in the same order (range, 3.0%–9.3%) but did not reach significance in lateral tibia and patella regions of cartilage. When we pooled the data, the patellofemoral region showed the highest reduction in $T1_\rho$ (12.5%, $P < .0001$) and T2 (5.7%, $P = .0007$), followed by the medial ($T1_\rho$: 9.4%, $P < .0001$; T2: 5.4%, $P = .0049$) and the lateral ($T1_\rho$: 6.5%, $P = .0001$; T2: 2.1%, $P = .2878$) compartments of the tibiofemoral joint. The tibial cartilage region showed the highest reduction in $T1_\rho$ (9.3%, $P = .0001$), whereas T2 (4.1%, $P = .066$) showed the lowest reduction and failed to reach statistical significance. Of note, $\Delta T1_\rho$ values in all regions of interest were consistently larger than $\Delta T2$ values. The central weightbearing regions of the femoral cartilage showed a higher reduction in relaxation times after running than the posterior regions (10.1% vs 4.5% for $T1_\rho$; 6.5% vs 2.6% for T2). When we stratified the data into 2 equal groups (low IPAQ group and high IPAQ group) at the median value of the IPAQ score, to assess the effect of regular physical activity on change in relaxation times, the low IPAQ group showed a higher change than did the high IPAQ group (9.8% vs 7.5%, $P = .113$ for $T1_\rho$; 4.5% vs 3.9% for T2, $P = .382$). When data were grouped based on sex, average $\Delta T1_\rho$ and $\Delta T2$ values for women were lower than those for men but did not reach statistical significance.

When we divided the cartilage regions into 2 layers (deep and superficial), longer relaxation values were observed in the superficial layer than in the deep layer of the cartilage (43.9 ± 5.2 vs 34.2 ± 5.9 ms for $T1_\rho$ and 31.7 ± 3.9 vs 24.5 ± 4.8 ms for T2). Collated data showed that a reduction in mean relaxation times of the superficial layer was trending larger than that of the deep layer after exercise ($\Delta T1_\rho$: 9.6% vs 8.2%, $P = .0506$; $\Delta T2$: 6.0% vs 3.5%, $P = .0688$) but was not significant. The tibial cartilage region showed the highest reduction in $T1_\rho$ and T2 values in the superficial layer, followed by patella and femur. $T1_\rho$ analysis of the superficial layer showed that the patellofemoral cartilage region had the highest reduction compared with the medial and the lateral compartments of the tibiofemoral joint, whereas $\Delta T2$ showed a different order (medial > patellofemoral > lateral). A larger reduction in relaxation times was observed in the central weightbearing regions than in the posterior nonweightbearing regions of the cartilage (10.4% vs 3.6% for $T1_\rho$ and 7.3% vs 2.5% for T2 in the superficial layer; 9.7% vs 5.6% for $T1_\rho$ and 5.5% vs 3.1% for T2 in the deep layer). Both layers of central weightbearing regions showed a significant reduction in $T1_\rho$ and T2 values after running, whereas posterior nonweightbearing regions did not reach significance. A higher reduction in $T1_\rho$ values in the superficial layer of CLFC than CMFC (10.9% vs 9.9% for $T1_\rho$; 8.5% vs 6.1% for T2) was observed but was not significant. The reduction in relaxation times (both $T1_\rho$ and T2) of the central weightbearing regions was higher than in the whole-femur cartilage regions (detailed results are available in Appendix Figures A1 and A2, available online at http://ajs.sagepub.com/supplemental/).

Overall, values of the texture parameters were decreased after running. Appendix Figure A4 (available online) illustrates the GLCM texture analysis results (GLCM contrast, GLCM entropy, and GLCM variance) of both $T1_\rho$ and T2 maps before and after running. Changes in texture parameters of the cartilage in the horizontal orientation (anterior-posterior direction) were higher than in the vertical orientation (superior-inferior direction). The GLCM entropy in the anterior-posterior orientation showed significant reduction after

exercise in both $T1_\rho$ and T2 maps, whereas GLCM contrast and GLCM variance followed the same trend but were not significant.

Effects of Running on Meniscus Relaxation Times ($T1_\rho$ and T2)

After running, a significant decrease in $T1_\rho$ values was observed in the anterior and posterior horn regions of the medial meniscus (9.7%, $P = .016$ and 11.4%, $P = .001$, respectively). When we pooled the data into medial and lateral menisci, the medial meniscus showed significantly shorter $T1_\rho$ after running compared with the baseline measurement (17.8 ± 2.1 vs 16.5 ± 1.9 ms, $P = .018$). Decreases in $T1_\rho$ values were observed after running exercise in all regions of both medial and lateral menisci, except the lateral posterior horn, whereas T2 quantification showed an increasing trend in all regions, except the medial posterior horn. Appendix Figure A3 (available online) provides detailed results of $T1_\rho$ and T2 values in different regions of the menisci before and after running exercise.

Cartilage Thickness

There were no significant differences observed in cartilage thickness after running in this study. The mean cartilage thicknesses for femoral, tibial, and patellar cartilage were 1.57 ± 0.3 mm, 1.52 ± 0.3 mm, and 1.98 ± 0.3 mm, respectively. After running, tibial cartilage showed the highest decrease in thickness (4.5%, $P = .31$), followed by femoral (2.1%, $P = .51$) and patellar (1.31%, $P = .31$) cartilage regions. Within the tibiofemoral joint, the medial compartment (3.6%, $P = .29$) showed a larger change in thickness when compared with the lateral compartment (2.6%, $P = .51$). Larger decreases in thickness were observed in the central weightbearing region (4.6%, $P = .25$) of the femoral cartilage than in the posterior non-weightbearing region (0.16%, $P = .94$).

DISCUSSION

This study investigated the changes in biochemical composition of knee articular cartilage and meniscus in young healthy adults after a 30-minute bout of running, using MR relaxation times. Our finding confirms that running has acute effects on the articular cartilage and menisci, with fluid shifts in the extracellular collagen matrix, which was demonstrated by shorter cartilage relaxation times ($T1_\rho$ and T2) in all regions after running. Changes in cartilage $T1_\rho$ and T2 values were greatest in the medial compartment and the patellofemoral joints. Both global and laminar analysis showed that the central weightbearing region of the femoral condyle had a significantly larger change in relaxation times after running. After running, a significant decrease in $T1_\rho$ values was observed in the anterior and posterior horns of the medial meniscus.

A significant decrease in $T1_\rho$ and T2 relaxation times indicates the change in composition of the cartilage after running. Running disturbs the collagen matrix structure (deformation and change in orientation of collagen fibers) and composition (expulsion of water molecules within the matrix), resulting in a reduction in T2 relaxation times. It has been shown in the literature that $T1_\rho$ relaxation is negatively correlated with PG content.[1] Reduction in $T1_\rho$ after running in this study likely indicates a relative increase in PG concentration due to water loss and deformation, rather than an actual increase in PG content. A higher change in $T1_\rho$ and T2 values of the medial compartment compared with the lateral compartment is in agreement with previous suggestions that a larger share of the contact stress while running is experienced by this compartment. Larger $\Delta T1_\rho$ and $\Delta T2$ values were observed in the patellofemoral compartment, indicating that greater traction of the patella during running results in lower hydration of cartilage tissue. These results are supported by a study, conducted by Eckstein et al,[8] that demonstrated that patellar cartilage deforms more under high-impact loading (jumping). Liess et al[20] also demonstrated a significant reduction in

patellar cartilage T2 following 60 deep knee bends. Souza et al[34] showed a decrease in cartilage $T1_\rho$ and T2 values with simulated static loading during in vivo image acquisition. Luke et al[21] observed elevated cartilage $T1_\rho$ and T2 values in long-distance runners in the days after a marathon run when compared with age-matched controls. These studies demonstrated the importance of understanding the behavior of cartilage under various day-to-day physical activities. Based on the literature available on T2,[23] deformation,[8] volume change,[14] and recovery after exercise,[13] it was anticipated that the changes in cartilage composition due to running would lead to shorter $T1_\rho$ and T2 relaxation times compared with the baseline measurement. Larger reduction in relaxation times in the low IPAQ group than in the high IPAQ group may suggest that the regular physical activity conditioned the articular cartilage, which experienced little change in biochemical composition after running. A larger dynamic range was observed for $T1_\rho$ compared with T2 between pre- and post-run relaxation time measurements in this study, which is in accordance with earlier studies on patients with OA and healthy controls.[16] The acute effect on $T1_\rho$ values in the articular cartilage and menisci immediately after running has not been studied yet. This study demonstrates that $T1_\rho$ may be a valuable biomarker in quantifying changes in PG concentration after various levels of physical activity (eg, running).

A significantly larger reduction in relaxation times ($T1_\rho$ and T2) in the central weightbearing region of the femoral condyle than in the posterior nonweightbearing region (see Appendix Figure A2, available online) clearly suggests that running had a greater effect on the central region. Similar results were found by Mosher et al,[24] who showed significant shortening in the superficial 40% of the cartilage T2 in the weightbearing region of the femoral condyle after running. It has been shown in the literature that variations in cartilage shape are associated with regional variations in the loading at the knee during functional activities.[2,15] A larger reduction in relaxation times ($T1_\rho$ and T2) and cartilage thickness clearly indicates that the weightbearing region experiences more changes during running. Also, the greater change in $T1_\rho$ and T2 in the superficial layer of the cartilage suggests that running altered more of the tangential fiber orientation in the layer than the deep layer's radial fibers. Our results also indicate that running affects less of the posterior nonweightbearing cartilage region of the femoral condyle. It is known that the biomechanical response of cartilage to compression load is not uniform and varies across the cartilage from the articular surface to the bone-cartilage interface.[15,25,27] Hence, the ability to spatially localize the effect of exercise on cartilage becomes necessary to understand the mechanism behind cartilage degeneration.

The change in relaxation times of the superficial layer was significantly larger than in the deep layer of cartilage in all cartilage regions of interest. In addition, the observed longer cartilage relaxation times in the superficial cartilage layers compared with the deep layers are consistent with published results. There is also evidence of nonuniform deformation in cartilage, with larger compression in the superficial layer. Koo and Andriacchi[15] suggested that the loading patterns in the knee are region specific and responsible for nonuniform cartilage degeneration observed clinically. Carballido-Gamio et al[5] demonstrated use of laminar and texture analysis of relaxation times, instead of global means, in improving subjects' classification. Schinagl et al[32] observed increased compressive modulus from the articular surface to the surface close to the bone-cartilage interface. Earlier studies on cartilage samples and intact cadaveric joints observed that the response of cartilage relaxation time is nonuniform, with initial changes occurring near the articular surface.[22,25,31] These studies suggest that the superficial layer of the cartilage will have a larger deformation (more water displacement and collagen fiber disorientation, resulting in shorter $T1_\rho$ and T2 values) than the deep layer, under compressive loading. The change in relaxation times is due to a combination of loss of water content, change in PG concentration, and alteration in collagen architecture (orientation). In terms of comparing

laminar analysis to global (full-thickness) mean values, although the global mean $T1_\rho$ or T2 times were significantly shorter after running, laminar analysis showed greater change, suggesting better sensitivity. Although a larger difference was expected for the superficial than for the deep layers, this was not observed in T2. However, in $T1_\rho$ laminar analysis, layers were found to be significantly different from each other. This may be due to the fact that in the combined $T1_\rho$/T2 sequence, $T1_\rho$ data were always acquired first and then the T2 data. Lower values of texture parameters (GLCM contrast, GLCM entropy, and GLCM variance) after running suggest lower dispersion and more uniform co-occurrence of neighboring voxels in the cartilage. They also suggest that the spatial changes occurred in extracellular matrix of the articular cartilage during running.

The largest change in $T1_\rho$ and T2 was observed in the posterior horn of the medial meniscus. The literature shows that the posterior horn of the medial meniscus has the highest prevalence of meniscus degeneration.[37] The anterior horn of the medial meniscus showed a significant decrease in $T1_\rho$ relaxation but not in T2 relaxation. The meniscus is macroscopically a fibrous cartilage that is formed from water (74%), type I collagen, PG, and other proteins. The concentration of PG in hyaline cartilage is much higher than the PG amount in the meniscus. Also, the factors that contribute to $T1_\rho$ changes in the meniscus are not clear and need further investigation. Although earlier studies have shown that in the menisci T2 values were more useful than $T1_\rho$ values for differentiating patient populations with and without osteoarthritis,[29] this study's results suggest that $T1_\rho$ values were more sensitive to acute loading of the meniscus than were T2 values. Greater change in $T1_\rho$ values with loading may be related to meniscus biomechanical characteristics and could potentially be a more sensitive biomarker of meniscus than morphological measures in the early phase of degeneration or change due to microdamage.

Change in thickness of the tibial cartilage was double the amount of deformation (% change in thickness) in the femoral cartilage, but the difference in change was not significant. The similar trend of cartilage deformation was also observed by Mosher et al.[23] This may indicate that compressive stiffness of the femoral cartilage may be relatively higher than tibial cartilage and probably recovers faster than tibial cartilage. However, we did not observe the same trend in change in relaxation times; only $\Delta T1_\rho$ of the tibial cartilage showed a significant change and the largest but not ΔT2. Mosher et al[24] also observed the same trend in relating change in cartilage thickness and T2. The biochemical response of the articular cartilage to functional loading could potentially be a more sensitive biomarker of cartilage than morphological measures.

The results of this study demonstrated that advanced quantitative MR imaging techniques (such as relaxation times and morphological measures) could be used to noninvasively and quantitatively determine articular cartilage and meniscus response to physiologic loading occurring with physiologic level of exercise. The feasibility of using MR relaxation time (T2) in measuring changes in biochemical composition in articular cartilage of the tibiofemoral joint after running has been demonstrated by Mosher and colleagues[23,24] in young male participants, and their study provided the foundation for the present study. The present study, which included 20 participants (10 men and 10 women), confirmed the T2 measurement in tibiofemoral cartilage and was extended to include the patellofemoral cartilage region, studied the change in $T1_\rho$ measurement in both tibiofemoral and patellofemoral cartilage regions, and measured $T1_\rho$ and T2 changes in the meniscus after running. These MR relaxation times ($T1_\rho$ and T2) may act as a noninvasive measure in addition to the existing qualitative clinical measures (pain and functional performance) to monitor the effect of exercise on cartilage and meniscus in longitudinal studies. The results from this study would be valuable in various fields of sports medicine such as cartilage repair, functional biomechanics, exercise, and posttraumatic osteoarthritis.

Limitations of our study have to be considered while interpreting the findings. The number of participants recruited to our study is relatively low (n = 20), which may have led to statistical power issues for some of the variables studied. The physical activity levels of the participants were self-reported, and the running speed and total distance were not controlled. Because the quantified measures are in "relative % change," the results are still valid even if a participant had a larger-than-normal knee or thicker cartilage (larger deformation). Six of the 20 volunteers were regular participants in long-distance running competitions; the time interval between previous competition and MR examination was not controlled. Varying physical activity levels between the participants also needs to be considered while interpreting the results of this study. A smaller pixel can better resolve individual subtissue layers, better differentiate topographical variations, and better identify local tissue changes. In this study, one has about 7 pixels across the entire depth of the cartilage; in other words, each pixel represents approximately 15% of the total thickness of the tissue (at the thickest section of the cartilage). This may be one of the reasons why some of the regions did not reach significance. But careful attention must be paid to optimizing image resolution, acquisition time, and SNR (high-motion artifacts in long scans). Another limitation is that the alignment of the lower limb was not measured, which is an important element in analyzing biomechanics of the limb. An experimental study on rodents with induced arthritis (either run on a treadmill daily for 21 days or subject to cage activity) showed that treadmill running initiated 1 day after arthritis induction significantly slowed progression of arthritis, whereas treadmill running initiated 5 or 9 days after arthritis induction, when cartilage destruction was more severe, was less effective in protecting articular cartilage from destruction.[26] Studies need to establish and characterize the effects of specific loading behavior of different types of exercise on various regions of cartilage and meniscus, using biomechanical loading of a physical activity to stimulate cartilage in patients at risk for OA as a nonsurgical treatment to slow or reverse the pathological process.

CONCLUSION

This study demonstrates that running has an acute effect on knee articular cartilage and meniscus composition, quantified with $T1_\rho$ and T2 relaxation time measurements in young healthy adults. Running has considerable biomechanical and acute biochemical effects on the articular cartilage and meniscus, resulting in shorter cartilage relaxation times ($T1_\rho$ and T2) in all regions after running. Further research including patients with OA as well as normal participants is needed to demonstrate that a specific form of exercise (eg, running) may be used to stimulate a target region of the cartilage, without disturbing other regions.

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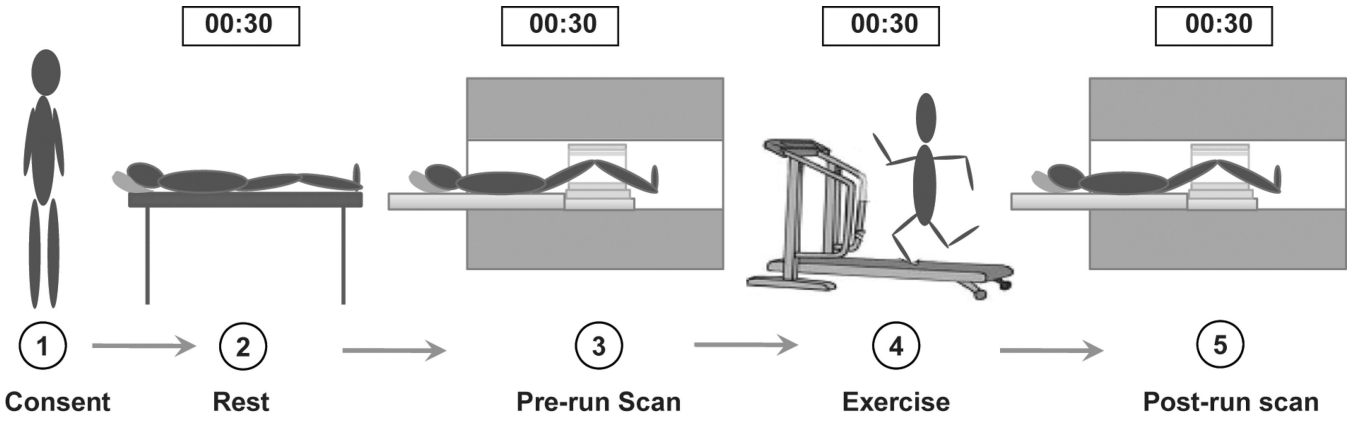

Figure 1.
Schematic representation of sequence of data acquisition.

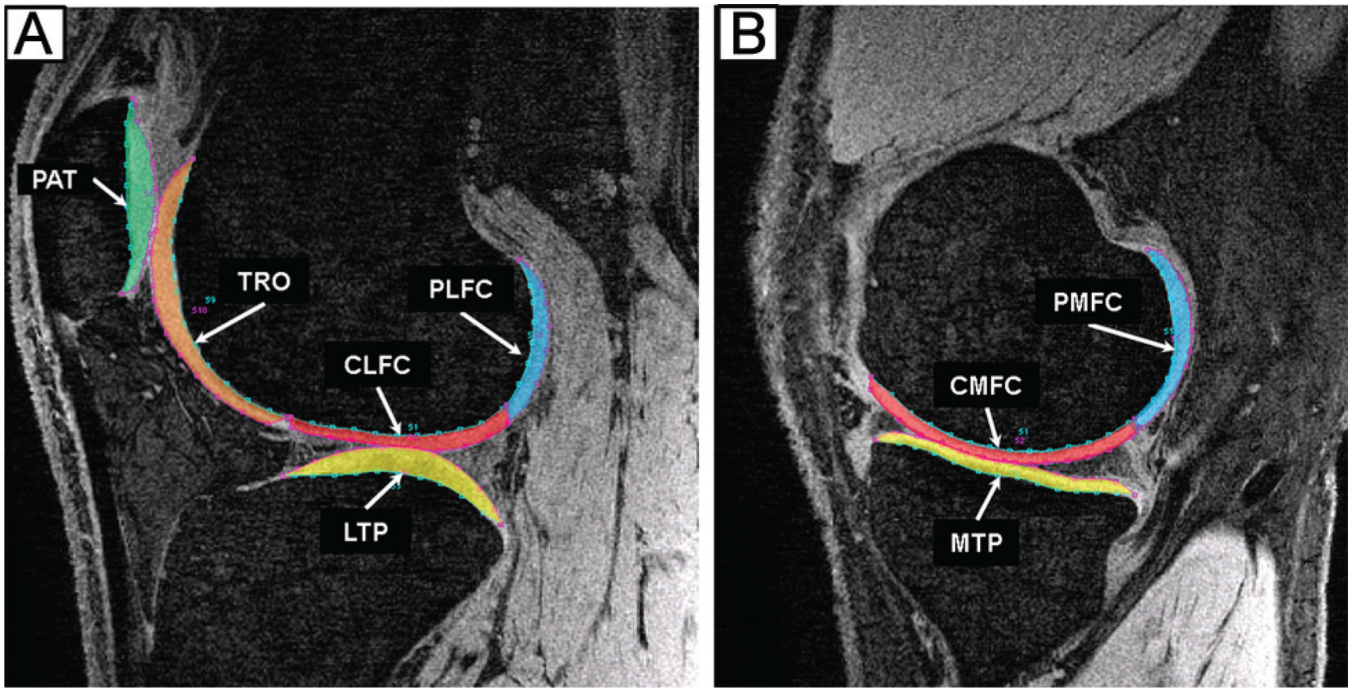

Figure 2. Cartilage regions of interest

(A) Lateral compartment (CLFC, central lateral femoral condyle; LTP, lateral tibial plateau; PLFC, posterior lateral femoral condyle) and patellofemoral compartment (PAT, patella; TRO, trochlea). (B) Medial compartment (CMFC, central medial femoral condyle; MTP, medial tibial plateau; PMFC, posterior medial femoral condyle).