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Local associations between knee cartilage T1ρ and T2 relaxation times and patellofemoral joint stress during walking: A voxel-based relaxometry analysis

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Abstract

Objective—This study aimed to utilize voxel-based relaxometry (VBR) to examine local correlations between patellofemoral joint (PFJ) stress during gait and PFJ cartilage relaxation times.

Methods—Eighty-three subjects with and without PFJ osteoarthritis (OA) underwent knee magnetic resonance (MR) images using fast spin-echo, $T_{1\rho}$ and T_2 relaxation time sequences. Patellar and trochlear cartilage relaxation times were computed for each voxel. Subjects also underwent three-dimensional gait analysis. Peak PFJ stress was computed during the stance phase. Statistical Parametric Mapping was used to perform VBR analyses. Pearson partial correlations were used to evaluate the associations between peak PFJ stress and cartilage relaxation times for the whole compartment, medial and lateral compartments, and in subjects with and without PFJ OA.

Results—A higher percentage of the trochlear cartilage (15.9–29.1%) showed significant positive correlations between PFJ stress and $T_{1\rho}$ and T_2 than the patellar cartilage (7.4–13.6%). Average correlation coefficient (R) of the voxels showing significant positive correlations ranged from 0.27 to 0.29. Subcompartment analysis revealed a higher percentage of lateral compartment

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Conflict of interest

The authors declare that they do not have any financial or personal relationships with other people or organizations that could have inappropriately influenced this study.

PFJ cartilage (trochlea: 30.2–34.7%, patella: 8.1–14.8%) showed significant correlations between peak PFJ stress and $T_{1\rho}$ and T_2 than the medial compartment PFJ cartilage (trochlea: 7.1–27.2%, patella: 5.5–5.9%). Subgroup analysis showed that there were larger percentages of PFJ cartilage that demonstrated significant positive correlations with PFJ stress in subjects with PFJ OA than those without PFJ OA.

Conclusions—The Findings of this study suggest that peak PFJ stress has a greater influence on the biochemical composition of the trochlear than patellar cartilage, and the lateral than medial PFJ compartment.

Keywords

Magnetic resonance imaging; Relaxation time; Gait; Patellofemoral joint

1. Introduction

Patellofemoral joint (PFJ) osteoarthritis (OA) is a highly prevalent knee condition [1–3] and an important source of pain and dysfunction in the knee joint [2,4–6]. While it remains controversial in the literature whether medial or lateral PFJ OA is more common [7–12], recent studies suggest that lateral PFJ OA is associated with more severe pain and dysfunction than medial PFJ OA [12,13]. This highlights the importance of identifying modifiable risk factors of lateral PFJ OA to promote prevention and intervention protocols of PFJ OA.

Increased mechanical loading in the sagittal plane during walking has been shown to be associated with PFJ OA [14–18]. Specifically, increased PFJ stress, knee flexion moment and impulse, and dynamic knee stiffness have been found to be associated with the presence, severity and progression of PFJ OA [14–18]. Nevertheless, there is limited knowledge regarding the relationship between these biomechanical risk factors and specific location of PFJ OA. Chang et al. [14] recently reported that higher knee sagittal dynamic joint stiffness was associated with morphological changes of OA, such as cartilage damage, in the lateral PFJ but not medial PFJ.

Quantitative magnetic resonance (MR) $T_{1\rho}$ and T_2 relaxation times provide non-invasive tools to evaluate cartilage biochemical changes related to degeneration. For example, higher cartilage $T_{1\rho}$ relaxation time is closely associated with a loss of glycosaminoglycan [19–21]; and higher T_2 relaxation time is related to an increase in water content and disorganization of the collagen matrix [20,22,23]. Together, higher cartilage $T_{1\rho}$ and T_2 times are indicative of more severe OA and have been used as imaging biomarkers of early-stage OA [24–26]. Although $T_{1\rho}$ and T_2 relaxation times are calculated for each voxel, it has traditionally been analyzed using a region of interest (ROI)-based approach. Using this approach, each ROI (compartment of cartilage) is described by the average $T_{1\rho}$ or T_2 of all the voxels within the ROI. As such, it may miss the local changes in cartilage relaxation times especially in cases of early stage OA. Furthermore, each ROI is typically segmented manually or semiautomatically, which is susceptible to user variations, potential for user bias, and requires extensive human resources and time. Voxel-based relaxometry (VBR), on the other hand, is a fully automatic technique that allows voxel-by-voxel analysis of cartilage

relaxation times [27]. It has recently been used to evaluate longitudinal changes and group differences in cartilage $T_{1\rho}$ and T_2 in subjects with knee OA [27,28], hip OA [29] and after anterior cruciate ligament reconstruction [27,30]. Nonetheless, VBR has not been used to evaluate the relationship between biomechanical factors and PFJ cartilage relaxation times.

PFJ stress represents the compressive (joint reaction) force applied to the PFJ per unit area and has been related to the presence of PFJ OA in our recent study [17]. In this recent study [18], an ROI-based approach was employed to assess the correlations between mechanical loadings on PFJ and PFJ cartilage relaxation times. As such, PFJ stress remains an unclear modifiable risk factor associated with location-specific degenerative changes in PFJ cartilage. The primary goal of this study was to utilize VBR analysis to further examine the location-specific correlations between peak PFJ stress during gait and patellar and trochlear cartilage $T_{1\rho}$ and T_2. The secondary goal was to evaluate separately these correlations in the medial and lateral compartments of the PFJ cartilage. The tertiary goal was to examine these correlations in individuals with and without PFJ OA. We hypothesized that peak PFJ stress would show similar correlations within trochlear and patellar cartilage. In addition, we hypothesized that lateral compartment would show stronger correlations with PFJ stress than the medial compartment. Lastly, stronger correlations between PFJ stress and PFJ cartilage relaxation times would be observed in subjects with PFJ OA than those without PFJ OA.

2. Methods

2.1 Subjects

Subjects were recruited from the local community as a part of a longitudinal knee OA study [15,31]. All participants were above 35 years of age. The exclusion criteria include: (1) history of lower extremity or spine surgery, (2) self-reported inflammatory arthritis, (3) any conditions that limited the ability to walk without assistant device, and (4) contraindications to MR imaging [15]. All participants underwent a weight-bearing, posteroanterior, fixed-flexion radiograph of the tibiofemoral joints. The knee with higher Kellgren–Lawrence (KL) grade was chosen for gait analysis and MR imaging. When both knees presented the same KL grade, the test limb was determined randomly. All subjects completed the Knee injury and Osteoarthritis Outcome Score (KOOS) survey, which has a range from 0 to 100 [32]. A higher KOOS score represents less pain and better function [32]. The study was approved by the Committee of Human Research of our university. Prior to participation, all subjects signed a written informed consent.

2.2 Gait analysis

Three-dimensional (3D) lower extremity kinematics were recorded using a 10-camera motion capture system (Vicon, Oxford, UK) at a sampling rate of 250 Hz. Ground reaction force data were obtained using two embedded force platforms (Advanced Mechanical Technology, Watertown, MA) at a sampling rate of 1000 Hz. Marker and ground reaction force data were collected and synchronized using motion capture software (Nexus, Oxford, UK). Participants wore shorts and their personal sneakers during the evaluation.

Prior to the walking test, retro-reflective markers (14-mm spheres) were placed on the subjects' bilateral lower limbs and pelvis as previously described [16,17]. Subjects were instructed to walk at a self-selected speed, which was described as "you have some place to be, but you are not late." Five successful trials were obtained. A trial was considered successful when the foot of the tested limb fell within the borders of force platform from initial contact to toe-off. Walking speed of trial 2 to 5 was controlled to be within ± 5% of the first successful trial.

Kinematic and kinetic data were computed using Visual3D (C-Motion, Germantown, MD) and MATLAB software (The MathWorks, Natick, MA). Marker trajectory data were low-pass filtered using a fourth-order Butterworth filter with a cut-off frequency of 6 Hz. The hip, knee, and ankle joints were assigned three degrees of freedom for rotations. Joint kinematics were calculated using a Cardan rotation sequence in the order of flexion/extension, abduction/adduction, and internal/external rotation. Net joint moments were reported as external moments and normalized to each participant's body mass (kg) and height (m). Knee flexion moment and sagittal plane knee angle during the stance phase of gait were exported for PFJ stress computation. The stance phase of gait was defined during the time when the vertical ground reaction force was greater than 20 N [33–35].

PFJ stress was computed using a previously described sagittal plane biomechanical model [17,36,37]. This model used subject-specific knee flexion angles and net joint moments (obtained from inverse dynamics), and data from literature (i.e. quadriceps effective lever arm, ratio between quadriceps force and PFJ reaction force, and PFJ contact area) to estimate PFJ reaction force and contact area.

First, the model calculated the quadriceps effective lever arm as a function of knee flexion angle using cadaveric data reported by Eijden et al. [38]. Second, the quadriceps force was computed by dividing the knee flexion moment by the effective lever arm. Third, PFJ reaction force was estimated by multiplying the quadriceps force with a ratio reported by van Eijden et al. [39] that defines the relationship between quadriceps force and PFJ reaction force as a function of knee flexion angle. Fourth, PFJ contact area was estimated based on cadaveric data reported by Powers et al. [40]. A second-order polynomial curve was fitted to discrete data of PFJ contact area at seven knee flexion angles (0, 15, 30, 45, 60, 75, and 90°). PFJ contact area was then calculated as a function of knee flexion angle during the stance phase. Lastly, PFJ reaction force was divided by PFJ contact area to estimate PFJ stress during the stance phase of walking. Average peak PFJ stress from five successful trials were exported for statistical analyses.

2.3 MR acquisition

MR images of the knee were acquired using a 3-T MR 750w Scanner (General Electric, Milwaukee, WI, USA) and an eight-channel phased-array knee coil (Invivo, Orlando, FL, USA). All subjects were placed in a supine position with their knee in neutral rotation and full extension. To reduce movement, the test foot was secured in place, the study knee was stabilized with padding, and a belt was secured across the subject's waist. All subjects arrived at the imaging center and were unloaded (seated in a chair) for a 45-min period before imaging to prevent the effects of acute loading on cartilage relaxation time values

[41,42]. The following sequences were obtained for each participant: (1) high-resolution 3D intermediate-weighted fast spin-echo (FSE) CUBE sequence for clinical grading and cartilage segmentation (Repetition Time (TR)/ Echo Time (TE) = 1500/26.69 ms, Field of View (FOV) = 14 cm, matrix = 384 × 384, slice thickness = 0.5 mm, echo train length = 32, bandwidth = 50.0 kHz, Number of Excitations (NEX) = 0.5, acquisition time = 10.5 min); (2) 3D $T_{1\rho}$ relaxation time sequence (TR/TE = 9/2.6 ms, time of recovery = 1500 ms, FOV = 14 cm, matrix = 256 × 128, slice thickness = 4 mm, bandwidth = 62.5 kHz, TSL = 0/2/4/8/12/20/40/80 ms, Frequency of Spin-Lock (FSL) = 500 Hz, acquisition time = 11 min); and (3) 3D T_2 relaxation time sequence (same as the $T_{1\rho}$ quantification except for magnetization preparation TE = 1.8/3.67.3/14.5/29.1/43.6/58.2, acquisition time = 11 min).

2.4 MR image post-processing

Image processing was perfomed with in-house programs written in Matlab (MathWorks, Natick, MA), integrated with the elastix toolbox for non-rigid image registration [27,43,44]. All images were non-rigidly registered and aligned to a single reference image identified through an iterative process aimed to minimize the global image deformation using a technique previously described [27–30]. This fully automated technique allowed the calculation of association between cartilage relaxation time and biomechanical factor on a voxel basis.

Relaxation maps were acquired by fitting the morphed images from different TSLs, employing Levenberg–Marquardt mono-exponentials applied to each voxel where S is the image signal at a given time point, A is initial magnetization, and B is a constant [28].

$$S(\mathrm{TSL}) \propto A\left[\exp\left(-\frac{\mathrm{TSL}}{\mathrm{T1\rho}}\right)\right] + B \quad \text{for } \mathrm{T_{1\rho}}$$

$$S(\mathrm{TE}) \propto A\left[\exp\left(-\frac{\mathrm{TE}}{\mathrm{T2}}\right)\right] + B \quad \text{for } \mathrm{T_2}$$

Subcompartements of medial and lateral cartilage were defined. Medial and lateral patellar cartilage was separated by the sagittal MR image that showed the greatest cross-sectional area of the patella. Medial and lateral trochlear cartilage was divided by the sagittal MR image that showed the shortest anterior–posterior distance of the femoral trochlea (trochlear groove).

2.5 PFJ OA identification (clinical cartilage lesion assessment)

A board-certified, fellowship-trained musculoskeletal radiologist performed gradings of articular cartilage lesions using the modified Whole Organ Magnetic Resonance Imaging Score (WORMS) [3,45]. Cartilage lesions were graded using a scale from 0 to 6 as described previously [3,16,45]. Scoring was performed at the articular cartilage overlying six regions: patella, trochlea, medial and lateral femoral condyle, and medial and lateral tibia plateau. WORMS cartilage lesion score was used to define the presence of OA in this study. PFJ OA was defined as present when the WORMS score was 2 or higher for cartilage lesion

of the patella or trochlea [3]. TFJ OA was defined when the WORMS score was 2 or higher for cartilage lesion of the tibia or femur (excluding the trochlear area of the femur) [3].

2.6 Statistical Analyses

Statistical Parametric Mapping (SPM) was used to perform VBR analyses [28,30]. Student's *t*-tests were used to compare differences in $T_{1\rho}$ and T_2 times between PFJ OA and control subjects. Percentage of voxels showing significant group difference, average percentage difference of voxels showing significant difference, and average *P*-values of voxels showing significant difference were summarized by SPMs.

Pearson partial correlations were used to evaluate the associations between peak PFJ stress and cartilage relaxation times. Percentage of voxels showing significant correlation, average correlation coefficient (R) of voxels showing significant correlation, and average *P*-values of voxels showing significant correlation were reported by SPMs. Age, sex and body mass index (BMI) were considered as adjusting factors in statistical analyses. Random Field Theory correction was used to take into account possible false positives due to multiple comparison [46]. All analyses were performed for whole, medial, and lateral compartments, as well as for $T_{1\rho}$ and T_2. The significance level was set at 0.05.

For visualization, an in-house developed program was used to construct a 3D bone mesh segmented from the first echo MR images (TSL = 0). The patellar and trochlea compartments were stitched together and interpolated from the 2D sagittal images, creating a color map of the desired statistical parameter or relaxation time and then overlaid on the 3D bone mesh.

3. Results

3.1 Subject characteristics

A total of 83 subjects were included in this study (Table 1). Among which, 49 subjects had PFJ OA (18 having mixed PFJ and TFJ OA). Thirty-four control subjects had no PFJ OA (six had TFJ OA). Compared to the control group, subjects in the PFJ OA group were older (P=0.003) and there were more females in the PFJ OA group (P=0.009). Independent *t*-tests showed that PFJ OA subjects had worst scores in KOOS-pain (P=0.03), sports (P=0.02), and quality of life (P=0.04) compared to controls. There was no significant group difference in walking speed (P=0.21) and peak PFJ stress (P=0.24).

Results of VBR analysis comparing $T_{1\rho}$ and T_2 time between PFJ OA and control groups are presented in Table 2 and Figure 1. In general, 46.4–53.4% of trochlear cartilage showed significant difference in $T_{1\rho}$ between the two groups regardless of whole, lateral, or medial compartments (Table 2). The voxels showed significant group difference demonstrated 12.7–13.5% average elevation in $T_{1\rho}$ in PFJ OA subjects. Additionally, 21.7–44.3% of trochlear cartilage showed significant group difference in T_2, with an average elevation of 14.4–15.1% in the PFJ OA group compared to the control group (Table 2). In patellar cartilage, 8.3–35.4% of cartilage showed significant group difference in $T_{1\rho}$ depending on the compartments (Table 2). On average, these voxels showed 15.3–16.5% elevation in $T_{1\rho}$ in PFJ OA subjects compared to controls. Lastly, 31.3–38.1% of patellar cartilage showed

significant group difference in T_2, with an average elevation of 14.5–17.6% in PFJ OA group. Figure 1(c) shows that, overall, the PFJ OA group had higher $T_{1\rho}$ and T_2 with the greatest difference located in the central region of the trochlear cartilage.

3.2 VBR analysis: Correlations between PFJ stress and cartilage $T_{1\rho}$ and T_2

3.2.1 Whole compartment analysis—Results of VBR analysis evaluating correlations between peak PFJ stress and cartilage relaxation times for whole compartments are presented in Table 3. Overall, a higher percentage of trochlear cartilage (15.9–29.1%) showed significant positive correlations with PFJ stress compared to the patellar cartilage (7.4–13.6%) regardless of $T_{1\rho}$ or T_2 (Table 3, Figures 2(a), (b), 3(a), (b)). Average R of the voxels showing significant positive correlations ranged from 0.27 to 0.29.

There were limited percentages of voxels showing significant negative correlations between PFJ stress and PFJ cartilage $T_{1\rho}$ and T_2 (Table 3). In trochlea, significant negative correlations were observed in less than 1% of cartilage. In patella, significant negative correlations were observed in 1–2.6% of cartilage, with average R of around −0.25.

3.2.2 Subcompartment analysis: Lateral and medial compartments—Results of subcompartment analysis of all subjects revealed that a higher percentage of the lateral trochlear and patellar cartilage showed significant positive correlations with PFJ stress compared to the medial compartment (Table 3, Figures 2(b), 3(b)). A proportion of 30.2–34.7% of the lateral trochlear cartilage, versus 7.1–27.2% of the medial trochlear cartilage, showed significant positive correlations with peak PFJ stress (Table 3). Moreover, 8.1–14.8% of the lateral patellar cartilage, versus 5.5–5.9% of the medial patellar cartilage, demonstrated significant positive associations with peak PFJ stress (Table 3). The average R of voxels showing significant positive correlations ranged from 0.26 to 0.30 across the medial and lateral patellar and trochlear cartilage.

Similar to the whole compartment analysis, less than 1% of medial and lateral trochlear cartilage and medial patellar cartilage showed significant negative correlations with PFJ stress. There were 2.8% and 6.7% of lateral patellar cartilage showing significant negative correlations with PFJ stress in $T_{1\rho}$ and T_2, respectively.

3.2.3 Subgroup analysis: PFJ OA and control groups—Results of VBR analysis evaluating correlations between peak PFJ stress and cartilage relaxation times in the PFJ OA group showed similar findings as all subjects (Table 4, Figures 2(c), (d), 3(c), (d). A higher percentage of trochlear cartilage (10.7–18.3%) showed significant positive correlations with peak PFJ stress compared to the patellar cartilage (2.2–6.0%). Additionally, there are higher percentages of the lateral trochlear and patellar cartilage showed significant positive correlations with peak PFJ stress compared to the medial trochlear and patellar cartilage, with the exception of patella T2 relaxation time (1.4% vs. 2.0%) (Table 4). Overall, the average R of voxels showing significant positive correlations ranged from 0.34 to 0.41 (Table 4). Significant negative correlations between peak PFJ stress and cartilage relaxation times were observed in less than 1% of trochlear cartilage regardless of compartments, and $T_{1\rho}$ or T_2. Approximately 5% of the whole patellar cartilage showed significant negative

correlations with PFJ stress, with 8.3–10.2% of lateral compartment and 1.2–5.3% of medial compartment showing significance (Table 4).

Table 5 and Figures 2(e), (f) and 3(e), (f) display the results of VBR analysis evaluating correlations between peak PFJ stress and cartilage relaxation times in the control group. Overall, less than 5% of patellar and trochlear cartilage showed significant positive correlations with PFJ stress, with the exception of medial trochlear cartilage $T_{1\rho}$ (8.2%). In addition, significant negative correlations between PFJ stress and cartilage relaxation times were shown in less than 1% of patellar and trochlear cartilage, except for trochlea whole (3.1%) and medial (5.1%) compartments T_2.

4. Discussion

This study aimed to use a novel approach, VBR, to evaluate the local associations between peak PFJ stress and PFJ cartilage $T_{1\rho}$ and T_2. Findings of this study have identified location-specific relationships between biomechanical factors and cartilage composition. Overall, our results revealed that a higher percentage of trochlear cartilage showed significant correlation with peak PFJ stress during walking compared to the patellar cartilage. In addition, a higher percentage of lateral compartment PFJ cartilage showed significant correlations with peak PFJ stress in $T_{1\rho}$ and T_2 than the medial compartment PFJ cartilage. Together, this suggests that peak PFJ stress has a greater influence on the biochemical composition of the trochlear than patellar cartilage, and the lateral than the medial PFJ compartment. Given that the lateral compartment PFJ OA is related to more severe pain and dysfunction [12,13], it provides support for peak PFJ stress as an important risk factor of PFJ OA.

Consistent with Chang et al. [14], this current study provides further support that increased sagittal plane mechanical loading is associated with worse cartilage health in the lateral compartment of the PFJ. PFJ stress and dynamic sagittal knee stiffness are used to quantify mechanical loading at the PFJ in this and the previous study [14], respectively. Both of these biomechanical factors increase with higher external knee flexion moment. Higher external knee flexion moment during walking is indicative of greater quadriceps contractions [47]. Due to the valgus alignment of the quadriceps femoris, during its contraction, its resultant force is oriented laterally, superiorly, and posteriorly [48]. This leads to a greater compressive force on the lateral compartment of the PFJ than the medial compartment. As such, it is reasonable that a higher percentage of lateral PFJ cartilage showed a significant positive correlation with peak PFJ stress during walking than lateral compartment PFJ cartilage.

Using a VBR approach, this study revealed a small percentage of the medial trochlear and patellar cartilage showed significant correlations between peak PFJ stress and $T_{1\rho}$ and T_2. This finding is in contrast to the previous study by Chang et al. [14] that showed no significant association between dynamic sagittal knee stiffness and progression of cartilage lesions in the medial compartment of the PFJ. In the previous study [14], cartilage lesions were defined by morphological changes using semi-quantitative methods on MR images, and the same percentage of knees showed progression on medial and lateral cartilage lesions. In this current study, quantitative $T_{1\rho}$ and T_2 relaxation times were used to evaluate

OA-related biochemical changes in cartilage and VBR analysis was employed to assess voxel-specific correlations between knee biomechanics and cartilage relaxation times. Therefore, although small in percentage, our study was able to reveal that a small portion of the medial patellar and trochlear cartilage showed significant correlation with peak PFJ stress.

The findings of this study add information to the previous study that reported positive associations between knee flexion moment and PFJ cartilage relaxation times using an ROI approach [15]. Using a VBR approach, this study uncovered not only significant positive correlations between PFJ stress and cartilage relaxation times, but also the percentage of PFJ cartilage that showed significant correlations and their locations (Figures 2, 3). Moreover, the findings of this study revealed that a small percentage of patellar cartilage showed significant negative correlations between PFJ stress and relaxation times. This indicates that a greater PFJ stress is associated with lower $T_{1\rho}$ and T_2 in a small portion of patellar cartilage. In children and healthy young adults, mechanical loading has been shown to have a positive effect on knee cartilage health [49–51]. However, higher physical activity level has been reported to lead to greater T_2 progression in older adults [52]. Further studies are needed to investigate why increased PFJ stress is related to lower cartilage $T_{1\rho}$ and T_2 in certain areas of patellar cartilage.

We observed a higher percentage of the PFJ cartilage that showed significant correlations between PFJ stress and relaxation times in subjects with PFJ OA than controls without PFJ OA. This finding may explain why a previous study found a stronger association between knee flexion moment and PFJ $T_{1\rho}$ and T_2 in subjects with PFJ OA than controls using an ROI-based approach [15]. Given that PFJ OA was defined by cartilage morphological lesions, these findings suggest that in the presence of morphological lesions, the cartilage is more susceptible to mechanical overloading than those without lesion [53].

Taken together the findings of this current study and previous studies [14–18], suggest that increased sagittal plane mechanical loading at the knee joint during walking is related to worse PFJ cartilage health. Future studies may focus on developing intervention programs that reduce sagittal plane mechanical loadings at the knee joint during walking and evaluate the effects of these programs on the progression and symptoms of PFJ OA.

There are several limitations in this study. First, PFJ stress was calculated using a previously described sagittal plane model. As such, it did not provide location-specific information as to PFJ stress distribution on the patellar and trochlear cartilage. Using finite element model, Farrokhi et al. reported higher PFJ stress on the lateral than medial compartment of the PFJ in healthy controls and individuals with patellofemoral pain [54]. Future studies may utilize finite element models along with VBR to better understand location-specific correlations between PFJ stress and cartilage relaxation times. Second, 24 out of 83 subjects in this study have TFJ OA (18 in the PFJ OA and six in the control groups) as identified by cartilage lesions in the tibia or femoral condyle. A recent study reported that individuals with TFJ or combined TFJ and PFJ cartilage deficits demonstrated lower PFJ mechanical loading during walking [55]. It is possible that the observed correlations may differ in this subgroup of subjects with TFJ OA. However, given the small number of subjects with TFJ OA (n = 24), a

separate analysis was not performed. Third, a relatively small group of subjects were included in the PFJ OA and control groups. A larger number of subjects would provide better representation of distribution of cartilage $T_{1\rho}$ and T_2 and allow more advanced analysis using VBR. Lastly, given the cross-sectional design of the study, it is unclear how peak PFJ stress affects the progression of PFJ cartilage $T_{1\rho}$ and T_2. Future study may include the longitudinal changes of $T_{1\rho}$ and T_2 to further examine the influence of increased PFJ stress on PFJ cartilage health.

In conclusion, this study showed that VBR can be used to evaluate location-specific associations between biomechanical factors and cartilage health. Our findings revealed that peak PFJ stress during walking has a greater influence on the biochemical composition of the trochlear than patellar cartilage, and the lateral than the medial PFJ compartment. Prevention and rehabilitation programs for PFJ OA, especially lateral compartment PFJ OA, may consider reducing PFJ stress during walking.

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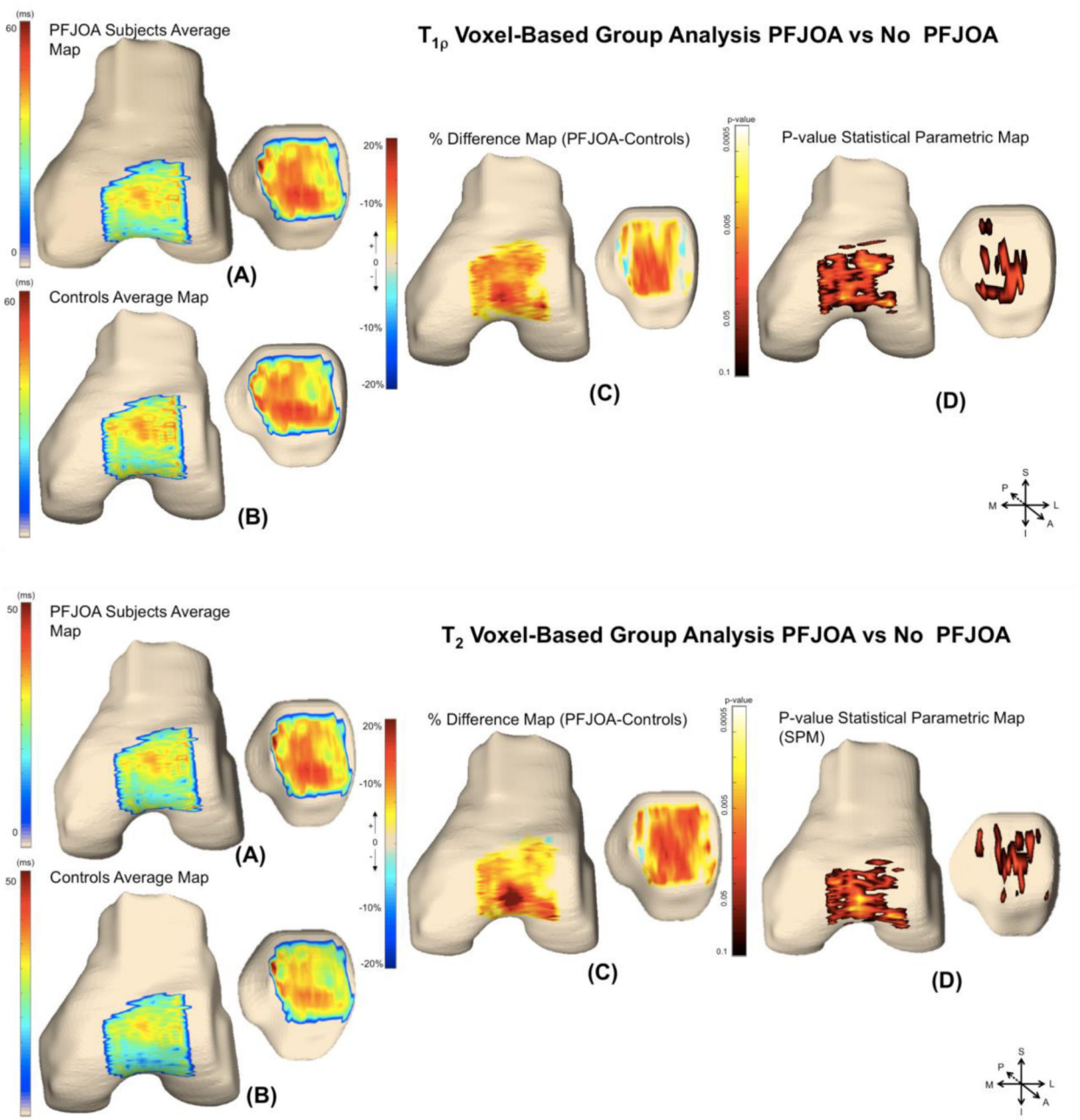

Figure 1.

3D renderings showing average cartilage $T_{1\rho}$ and T_2 for patellofemoral joint osteoarthritis (PFJ OA) (n = 49) and Control (n = 34) groups overlaid onto a bone mesh constructed from the first echo (a, b). Voxel-based statistics, the average percentage difference (c) and average *P*-value (d), are also shown.

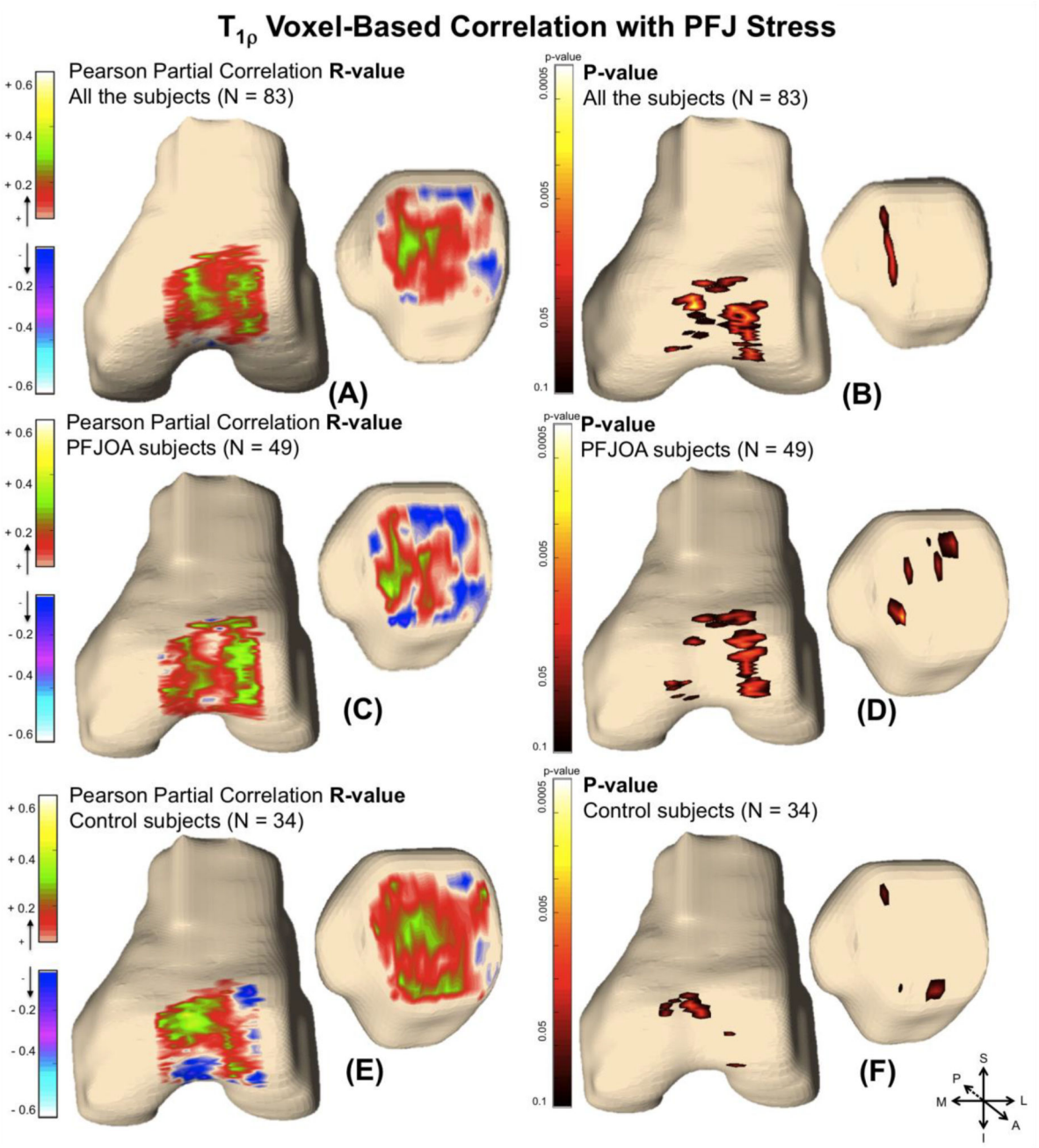

Figure 2.

3D renderings showing voxel-based statistics of Pearson partial correlations between peak patellofemoral joint stress and $T_{1\rho}$ of trochlear and patellar cartilage while controlling for age, sex, and body mass index (a, c, e), as well as voxels showed *P*-values <0.1 (b, d, f). PFJOA, patellofemoral joint osteoarthritis.

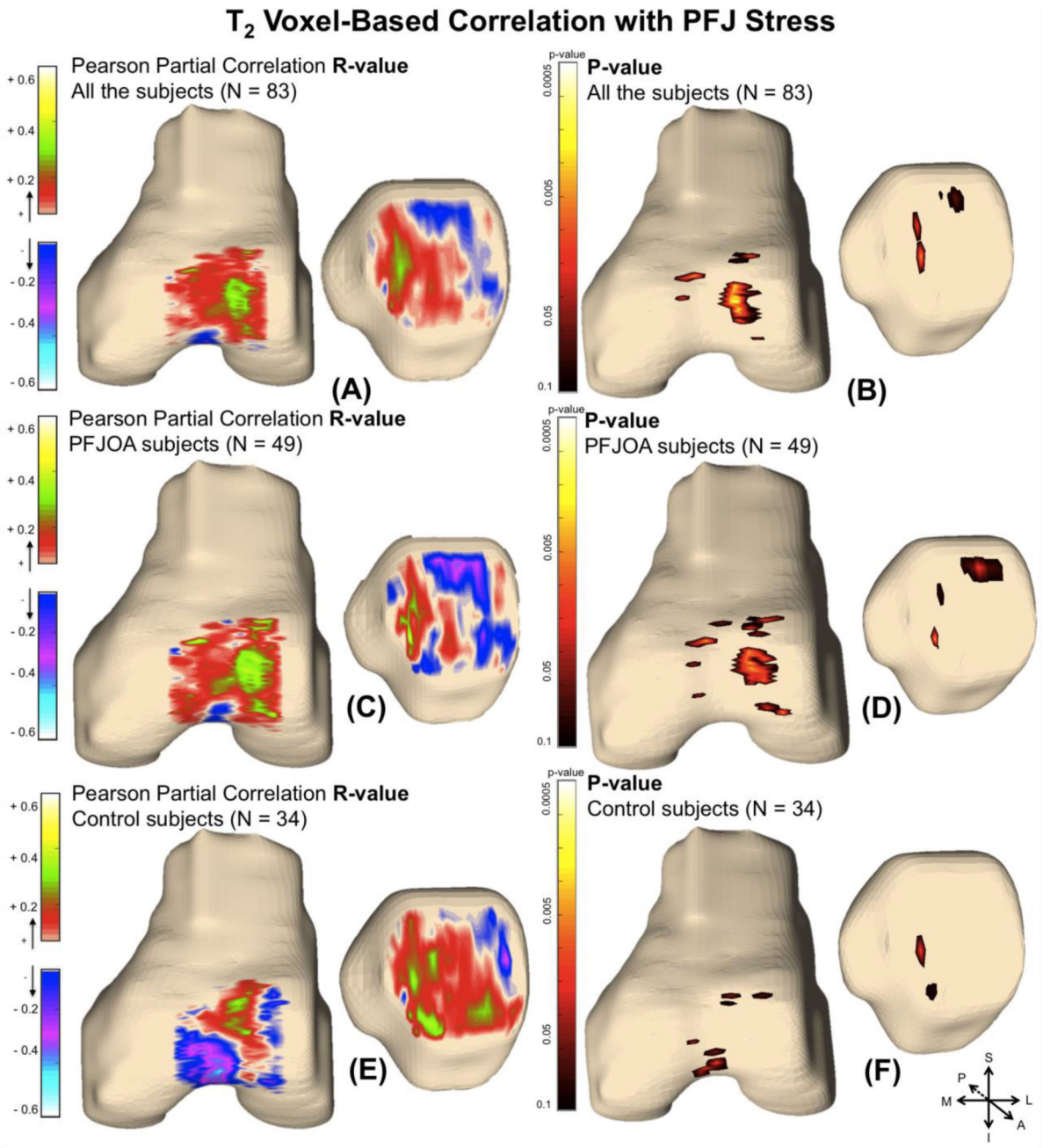

Figure 3.

3D renderings showing voxel-based statistics of Pearson partial correlations between peak patellofemoral joint stress and T_2 of trochlear and patellar cartilage while controlling for age, sex, and body mass index (a, c, e), as well as voxels showed *P*-values <0.1 (b, d, f). PFJOA, patellofemoral joint osteoarthritis.

Table 1

Subject descriptive statistics.

	All n = 83 Mean (95% CI)	PFJ OA n = 49 Mean (95% CI)	Control n = 34 Mean (95% CI)
Sex, Male/Female *	28/55	11/38	17/17
Age (years) *	52.5 (50.3, 54.7)	55.2 (52.3, 58.1)	48.6 (45.4, 51.9)
BMI (kg/m^2)	24.7 (23.9, 25.4)	24.5 (23.4, 25.6)	24.9 (23.8, 26.0)
TFJ OA, n	24	18	6
KOOS (0–100)			
Pain *	86.9 (83.5, 90.3)	83.8 (79.0, 88.7)	91.3 (87.0, 95.7)
Symptoms	86.6 (83.2, 90.0)	84.0 (79.2, 88.9)	90.3 (85.8, 94.8)
Activities of daily living *	92.1 (89.4, 94.7)	89.6 (85.6, 93.7)	95.6 (92.9, 98.3)
Sports *	82.4 (77.8, 87.0)	78.1 (71.2, 85.0)	88.7 (83.7, 93.7)
Quality of life *	76.0 (70.7, 81.2)	71.6 (64.2, 78.9)	82.4 (75.6, 89.1)
Walking biomechanics			
Walking speed (m/s)	1.52 (1.47, 1.58)	1.50 (1.42, 1.58)	1.56 (1.49, 1.63)
Peak PFJ stress (MPa)	3.3 (2.9, 3.6)	3.1 (2.7, 3.5)	3.5 (2.9, 4.1)

BMI, body mass index; CI, confidence interval; KOOS, Knee injury and Osteoarthritis Outcome Score; PFJ OA, patellofemoral joint osteoarthritis.

* Significant differences between PFJ OA and control groups revealed by Chi-squared and independent *t*-tests ($P<0.05$).

Table 2

Voxel-based relaxometry (VBR) comparison of cartilage $T_{1\rho}$ and T_2 between patellofemoral joint osteoarthritis (PFJ OA) (n = 49) and control (n = 34) groups.

		Whole compartment analysis		Subcompartment analysis			
		Trochlea	Patella	Trochlea		Patella	
		Whole	Whole	Lateral	Medial	Lateral	Medial
T1ρ	% Voxels showing significant difference	52.5%	26.7%	46.4%	53.4%	8.3%	35.4%
	% Difference of voxels showing significant difference*	13.2%	16.3%	12.7%	13.5%	15.3%	16.5%
	Average *P*-value of voxels showing significant difference	0.020	0.022	0.019	0.021	0.030	0.020
T2	% Voxels showing significant difference	35.9%	36.1%	21.7%	44.3%	38.1%	31.3%
	% Difference of voxels showing significant difference*	14.6%	16.3%	14.4%	15.1%	14.5%	17.6%
	Average *P*-value of voxels showing significant difference	0.022	0.023	0.028	0.021	0.027	0.023

Lateral, lateral compartment; Medial, medial compartment; Whole, whole compartment.

*Positive means the value is higher in the PFJ OA group than in the control group.

Table 3

Results of voxel-based relaxometry (VBR) analysis examining correlation between cartilage relaxation time and peak patellofemoral joint stress for all subjects (n = 83)[a].

	Whole compartment analysis				Subcompartment analysis							
	Trochlea T1ρ	Patella T1ρ	Trochlea T2	Patella T2	Trochlea T1ρ		Patella T1ρ		Trochlea T2		Patella T2	
	Whole	Whole	Whole	Whole	Lateral	Medial	Lateral	Medial	Lateral	Medial	Lateral	Medial
% Voxels showing significant positive correlation	29.1%	13.6%	15.9%	7.4%	34.7%	27.2%	14.8%	5.9%	30.2%	7.1%	8.1%	5.5%
Average R of voxels showing significant positive correlation	0.28	0.29	0.28	0.27	0.27	0.29	0.30	0.26	0.28	0.27	0.28	0.27
Average *P*-value of voxels showing positive significant correlation	0.019	0.018	0.018	0.025	0.021	0.017	0.018	0.023	0.019	0.024	0.019	0.028
% Voxels showing significant negative correlation	<1%	1.0%	<1%	2.6%	<1%	<1%	2.8%	<1%	<1%	<1%	6.7%	<1%
Average R of voxels showing significant negative correlation	—	−0.24	—	−0.27	—	—	−0.24	—	—	—	−0.27	—
Average *P*-value of voxels showing significant negative correlation	—	0.031	—	0.022	—	—	0.031	—	—	—	0.022	—

Lateral, lateral compartment; Medial, medial compartment; Whole, whole compartment.

[a]Correlations controlled for age, sex, and body mass index.

Table 4

Results of voxel-based relaxometry (VBR) analysis examining correlation between cartilage relaxation time and peak patellofemoral joint stress for subjects with patellofemoral joint osteoarthritis (n = 49)[a].

	Whole compartment analysis				Subcompartment analysis							
	Trochlea T1ρ	Patella T1ρ	Trochlea T2	Patella T2	Trochlea T1ρ		Patella T1ρ		Trochlea T2		Patella T2	
	Whole	Whole	Whole	Whole	Lateral	Medial	Lateral	Medial	Lateral	Medial	Lateral	Medial
% Voxels showing significant positive correlation	18.3%	6.0%	10.7%	2.2%	29.4%	10.9%	7.6%	2.0%	21.1%	3.9%	1.4%	2.0%
Average R of voxels showing significant positive correlation	0.35	0.38	0.36	0.38	0.35	0.35	0.38	0.36	0.36	0.34	0.38	0.41
Average *P*-value of voxels showing positive significant correlation	0.024	0.014	0.023	0.022	0.023	0.023	0.023	0.025	0.022	0.029	0.018	0.019
% Voxels showing significant negative correlation	<1%	5.5%	<1%	4.5%	<1%	<1%	8.3%	5.3%	<1%	<1%	10.2%	1.2%
Average R of voxels showing significant negative correlation	—	−0.35	—	−0.39	—	—	−0.37	−0.33	—	—	−0.40	−0.34
Average *P*-value of voxels showing significant negative correlation	—	0.023	—	0.020	—	—	0.017	0.032	—	—	0.018	0.028

Lateral, lateral compartment; Medial, medial compartment; Whole, whole compartment.

[a]Correlations controlled for age, sex, and body mass index.

Table 5

Results of Voxel-Based Relaxometry (VBR) analysis examining correlation between cartilage relaxation time and peak PFJ stress for control subjects (n = 34)[a].

	Whole compartment analysis				Subcompartment analysis							
	Trochlea T1ρ	Patella T1ρ	Trochlea T2	Patella T2	Trochlea T1ρ		Patella T1ρ		Trochlea T2		Patella T2	
	Whole	Whole	Whole	Whole	Lateral	Medial	Lateral	Medial	Lateral	Medial	Lateral	Medial
% Voxels showing significant positive correlation	4.5%	3.6%	<1%	3.3%	<1%	8.2%	4.6%	3.7%	2.1%	1.0%	4.0%	4.7%
Average R of voxels showing significant positive correlation	0.41	0.40	—	0.41	—	0.41	0.41	0.39	0.38	0.38	0.40	0.42
Average *P*-value of voxels showing positive significant correlation	0.027	0.029	—	0.027	—	0.026	0.023	0.034	0.040	0.037	0.031	0.025
% Voxels showing significant negative correlation	<1%	<1%	3.1%	<1%	<1%	<1%	<1%	<1%	<1%	5.1%	<1%	<1%
Average R of voxels showing significant negative correlation	—	—	−0.40	—	—	—	—	—	—	−0.40	—	—
Average *P*-value of voxels showing significant negative correlation	—	—	0.033	—	—	—	—	—	—	0.033	—	—

Lateral, lateral compartment; Medial, medial compartment; Whole, whole compartment.

[a]Correlations controlled for age, sex, and body mass index.