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IN VIVO TIBIAL CARTILAGE STRAINS IN REGIONS OF CARTILAGE-TO-CARTILAGE CONTACT AND CARTILAGE-TO-MENISCUS CONTACT IN RESPONSE TO WALKING

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Abstract

Background—There are currently limited human *in vivo* data characterizing the role of the meniscus in load distribution within the tibiofemoral joint.

Purpose—Our objective was to compare the strains experienced in regions of articular cartilage covered by the meniscus to regions of cartilage not covered by the meniscus. We hypothesized that in response to walking, tibial cartilage covered by the meniscus would experience lower strains than uncovered tibial cartilage.

Study Design—Magnetic resonance (MR) imaging of the knees of eight healthy volunteers was performed before and after walking on a treadmill. Using MR-generated 3D models of the tibia, cartilage, and menisci, cartilage thickness was measured in four different regions based on meniscal coverage and compartment — covered medial, uncovered medial, covered lateral, and uncovered lateral. Strain was defined as the normalized change in cartilage thickness before and after activity.

Results—Within each compartment, covered pre-activity cartilage was significantly thinner than uncovered pre-activity cartilage ($p<0.001$). Following 20 minutes of walking, all four regions experienced significant cartilage thickness decreases ($p<0.01$). The covered medial region experienced significantly less strain than the uncovered medial region ($p=0.04$). No difference in strain was detected between covered and uncovered regions in the lateral compartment ($p=0.4$).

Conclusion—In response to walking, cartilage that is covered by the meniscus experiences lower strains than uncovered cartilage in the medial compartment. These findings provide

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important baseline information on the relationship between *in vivo* tibial compressive strain response and meniscal coverage, which is critical to understanding normal meniscus function.

Keywords

articular cartilage; imaging; knee; meniscus; gait; MRI

INTRODUCTION

Articular cartilage health is believed to be maintained through normal, physiologic loads, while abnormal loads lead to alterations in the composition, metabolism, and mechanical properties of cartilage that predispose the knee to osteoarthritis (OA).[20] Since the meniscus plays a variety of roles in knee biomechanics, including distributing loads in the knee,[16, 44, 56] enhancing knee stability,[2, 55] and lubricating cartilage surfaces,[35] healthy menisci are critical for normal joint loading and maintaining joint health. This importance is highlighted by the severe consequences of meniscal tears, which can affect all age groups and are among the most common knee conditions.[42] Meniscal tears are associated with degenerative changes within the knee and increase the risk of developing radiographic and symptomatic OA.[17, 41] With surgical intervention, degenerative changes in the joint are observed as early as 3 months post-operatively on radiographs of total meniscectomy patients.[16] To limit these changes, more conservative treatment options, such as partial meniscectomy or meniscal repair,[25, 34, 37] are used when possible. Despite improvements in function, however, early onset OA remains a concern in these patients.[15, 37]

Due to the important role of the meniscus in load distribution within the normal joint,[4, 17, 29, 36] understanding how normal tibial cartilage and meniscal tissues function together is critical for elucidating how meniscal tears and meniscectomy may predispose the knee to OA. Many groups have utilized animal models to analyze the relationship between tibiofemoral cartilage and the meniscus.[35, 45, 46] These studies report that meniscectomy results in increased cartilage contact stresses and strains, as well as provide support to the hypothesis that altered mechanical loading contributes to cartilage degeneration associated with disruption of the meniscus.[35, 45, 46]

While these previous studies have provided valuable information regarding meniscus function, there are limited *in vivo* data characterizing the role of the meniscus in load distribution within normal human joints.[6] Previous work using biplanar fluoroscopy has shown that medial meniscal injury results in elevated cartilage deformation in regions of cartilage-to-cartilage contact.[6] However, there is a lack of *in vivo* data regarding regions of cartilage-to-meniscus contact. Utilizing magnetic resonance (MR) imaging and three-dimensional (3D) modeling techniques[9, 12, 13, 30, 32, 48, 54, 59] to measure cartilage deformation in response to a hopping activity, previous work from our lab found increased tibial cartilage strains near the tibial spine compared to the peripheral regions in both tibial compartments.[47] This pattern was thought to be a result of the meniscus distributing loads across the tibial plateau.[47] Therefore, in the present study, we sought to compare cartilage strains in regions covered by the meniscus to strains in regions not covered by the meniscus. We hypothesized that medial and lateral compartment tibial cartilage covered by the

meniscus would experience lower strains than uncovered tibial cartilage in response to walking.

METHODS

Subjects

Eight healthy adult subjects (4 males and 4 females; age: 22–30 years; body mass index: 20–25) were recruited for this Institutional Review Board approved study. Written, informed consent was obtained prior to participation. Subjects had no history of surgery or injury in either knee. Limb alignment was determined by the anatomic femorotibial angle[5, 27, 33], as measured from 3D models created from the MR images (described below). The average femorotibial angle was 174° (95% confidence interval: 173–175°), which is within the range of normal subjects without lower limb injuries.[5, 27, 33, 39, 40]

Protocol and Image Analysis

In order to ensure minimal baseline cartilage compression, the study was conducted in the morning.[9] Subjects were asked to minimize load-bearing activity prior to testing. Upon arrival, subjects rested in a supine position for 45 minutes to allow for cartilage equilibration.[13, 30] Each subject subsequently had one knee (4 right knees and 4 left knees) imaged, using a 3.0T MR scanner with an eight-channel knee coil (Trio Tim, Siemens Medical Solutions USA, Inc.), while lying in a relaxed, supine position. Sagittal plane images (field of view: 16 cm × 16 cm; resolution: 512 × 512 pixels; thickness: 1 mm) were generated using a double-echo steady state (DESS) sequence (flip angle: 25°; repetition time: 17 ms; echo time: 6 ms, scan time: 9 min).[1, 50, 53] After initial MR imaging, subjects walked unsupported on a level treadmill (F80, Sole Fitness Equipment) for 20 minutes at approximately 1.12 m/s in a room adjacent to the MR scanner. The walking speed was chosen so that it could be comfortably performed by most subjects.[18, 30] After completing the walking activity, subjects immediately underwent a post-activity MR scan of the same knee. The elapsed time from the end of the walk to the start of the DESS scan was less than 4 minutes.

Using solid modeling software (Rhinoceros; Robert McNeel & Associates; Seattle, WA), the outer margins of the bones, cartilage surfaces, and menisci were manually segmented by a single investigator in the pre- and post- activity MR images (Figure 1a). Contours from all slices in a single scan were used to generate 3D mesh models of the tibia, cartilage, and menisci (Figure 1b and 1c). Using an iterative closest point technique in a solid modeling software program (Geomagic Studio; Geomagic, Inc.; Cary, NC), pre- and post-activity bone models were registered to each other by aligning the model of the post-activity tibial surface to the entire pre-activity tibial surface.[9, 30, 47, 59]

Next, cartilage thickness was measured at various points selected to span regions of tibial cartilage covered and not covered by the meniscus, resulting in four separate regions of tibial cartilage – covered medial, uncovered medial, covered lateral, and uncovered lateral (Figure 2). Specifically, thickness was measured at five sampling points in each of the four cartilage regions for a total of 20 points of measurement.

Cartilage thickness at each point was calculated by determining the distance from each mesh vertex on the cartilage model surface to the nearest point on the bone model surface (Figure 3). All cartilage thicknesses within a 2 mm radius of each sampling point were averaged to calculate the mean thickness at that sampling point. Within each sampling point, the local compressive strain was then calculated as the normalized change in cartilage thickness before and after activity. This method has been shown to accurately reflect tibiofemoral cartilage thickness to within 1%.[9, 54] Additionally, to evaluate repeatability, three segmentation trials of the meniscus were performed on a single subject. The coefficient of repeatability for quantifying the meniscus surface area corresponded to less than 1% of the total area.

Statistical Analyses

Data were summarized using routine descriptive statistics. A Friedman ANOVA and the Wilcoxon Signed Rank test were performed to compare pre-activity cartilage thicknesses by region. Pre- and post-activity cartilage thicknesses in each region were compared using a Wilcoxon Signed Rank test. A matched-pairs t-test was used to determine whether strains in regions of meniscal coverage were significantly different than those in uncovered regions. Differences were considered statistically significant where $p < 0.05$. Bonferroni corrections for multiple comparisons were used as appropriate.

RESULTS

Figure 4 presents results of pre- and post- walking cartilage thicknesses for both compartments by region of meniscal coverage. Prior to the walking activity, cartilage thickness varied significantly by region. The covered medial region was significantly thinner than the other three regions ($p<0.001$). The cartilage in the uncovered lateral region was significantly thicker than the cartilage in all other regions ($p<0.001$). While uncovered medial cartilage thickness was similar to covered lateral cartilage thickness, covered cartilage was significantly thinner than uncovered cartilage in both medial and lateral compartments ($p<0.001$). Following 20 minutes of walking, all four regions experienced significant cartilage thickness decreases ($p<0.01$).

Figure 5 presents compressive strain results for both compartments by meniscal coverage. In the medial compartment, the covered region experienced a mean compressive strain of 2%, while compressive strain in the uncovered medial cartilage averaged 5%; a 3% increase in strain magnitude ($p=0.04$). In the lateral compartment, the covered cartilage experienced mean compressive strain of 3%, while compressive strain in the uncovered cartilage averaged 4%; a 1% increase in strain magnitude ($p=0.40$). While the uncovered medial region had a significantly higher cartilage strain response than its covered counterpart ($p=0.04$), no difference was detected between strains in covered and uncovered regions in the lateral compartment ($p=0.40$).

DISCUSSION

In this study, we used MR imaging and 3D modeling techniques to measure site-specific cartilage strains, which allowed for the comparison of tibial cartilage mechanical response

between regions that are covered and uncovered by the meniscus. Our results indicate that following 45 minutes of supine rest, tibial cartilage covered by the meniscus is thinner than its uncovered counterpart in both the medial and lateral compartments. Twenty minutes of walking resulted in significant decreases in tibial cartilage thickness, with average compressive strains ranging between 2% and 6% in each of the four defined tibial regions. Within the four regions studied, there was significantly greater strain in the uncovered medial region when compared to the covered medial region. No such difference was found for the lateral compartment.

Our study observed significantly thicker tibial cartilage in the lateral compartment compared to the medial compartment, which is consistent with the findings of previous MR imaging studies.[8–10, 14, 26, 59] Furthermore, our findings of covered cartilage being thinner than uncovered cartilage is consistent with the findings of an *ex vivo* human cadaver study,[51] which found that covered cartilage was significantly thinner than cartilage not covered by the meniscus, in both the medial and lateral compartments. Finally, our observation that covered cartilage is thinner than uncovered cartilage in both the medial and lateral compartments is in agreement with previous work that evaluated *in vivo* cartilage thickness in regions of cartilage-to-cartilage contact, as estimated using biplanar fluoroscopy and MR imaging techniques.[31] Specifically, tibial cartilage in regions of cartilage-to-cartilage contact were significantly thicker than regions further away from cartilage-to-cartilage contact,[31] which may reflect the ability of cartilage to adapt to its loading conditions.[3] While other studies have observed cartilage thickness trends consistent with the present study, in this study we provide localized *in vivo* measurements of cartilage thickness and strain resulting from the compressive forces of walking in regions that are covered and not covered by the meniscus.

Other studies have also utilized MR imaging to quantify cartilage strain responses to different forms of activity.[9, 30, 48, 59] While these studies evaluated strain based on compartment (medial or lateral), and the present study evaluated strain based on region (covered medial, uncovered medial, covered lateral, uncovered lateral), our regional strains for each compartment were comparable to the overall compartment strains previously reported. For example, Coleman *et al.* evaluated tibiofemoral cartilage strain in response to general diurnal activity (between 8am and 4pm) and observed 5% strain in medial tibial cartilage and 3% strain in lateral tibial cartilage,[9] and Sutter *et al.* observed 5% strain in response to single-legged hops in both medial and lateral tibial compartments.[48] While our measurements of strain values (2–6%) are on the same order of magnitude as strains experienced during diurnal activity[9] and dynamic hopping,[48] variations in our findings may be explained by differences in the chosen activity,[12, 19] as well as in the age[24] and sex[7, 28] of the subject populations.

Some studies have used a combination of MR and fluoroscopic imaging to evaluate cartilage deformation in regions of cartilage-to-cartilage contact.[6, 22, 32] These studies reported higher deformation values than the present study, which can be attributed to differences in methodology. The previous studies used fluoroscopic imaging, which quantifies cartilage deformation in regions of cartilage-to-cartilage contact. The present study has the ability to evaluate regions of cartilage-to-cartilage contact as well as cartilage-to-meniscus contact.

Furthermore, prior studies measured deformation that reflected the instantaneous strain response during the selected activity,[6, 22, 32] while the present study measured the cumulative strain response after multiple gait cycles.

The differences in strain response between regions of covered and uncovered cartilage in the medial compartment may be explained by the heterogeneity of tibial cartilage composition and organization, the loading environment during gait, or both. Mechanical testing of cadaveric specimens has indicated that regions of covered tibial cartilage are significantly stiffer than uncovered tibial cartilage.[11, 51] The increased stiffness may result in significantly less deformation in regions of covered tibial cartilage than its uncovered counterpart, as we observed. This may be attributed to differences in the composition and organization of the cartilage extracellular matrix, which may influence the mechanical response of cartilage.[21, 49, 57, 58]

Previous studies have suggested that the medial compartment bears more weight than the lateral compartment during gait.[23, 38, 43] Increased medial compartment loading during gait may result in differences between covered and uncovered regions to be more easily detectable in the medial compartment than the lateral compartment. Since the strain response of cartilage is likely dependent on the magnitude, frequency, and duration of the loading experienced, other *in vivo* activities may result in different cartilage strain responses. For example, as described above, the average compartmental strain values after hopping[47] were roughly one and a half times higher than what we found after walking. Thus, further work is needed to characterize the role of the meniscus in distributing loads across the joint during different activities.

Clinically, the medial compartment has a higher prevalence of OA than the lateral compartment.[60] The role of the meniscus in load distribution across the joint may provide several reasons why the medial compartment is more susceptible to OA. For example, Gilbert *et al.* utilized cadaveric knees to determine the location of peak contact stresses in the tibial plateau during gait.[19] They demonstrated that high peak contact stresses in the medial compartment occurred in regions of cartilage-to-cartilage contact, which is consistent with our observation of significantly larger strains in the medial uncovered region. The elevated strains may make this region more susceptible to degenerative changes than the lateral compartment. In contrast in the lateral compartment, equal load distribution was observed between covered and uncovered cartilage regions throughout the simulated gait cycle,[19] consistent with the findings of the present study.

The static position of the meniscus during MR imaging was used in the present study to determine the regions of cartilage that were covered and not covered by the meniscus. Therefore, our observation that lateral covered and uncovered strains were similar may be explained by the lateral meniscus motion that occurs during gait. A cadaveric study found that the lateral meniscus has a significantly larger posterior displacement (11.2 mm) than the medial meniscus (4.1 mm) during flexion.[52] The large lateral meniscal motion during flexion may provide more coverage and thus load support to the lateral tibial cartilage throughout gait, which may explain the relatively small difference in strain response within the lateral compartment.

Due to the cartilage equilibration time prior to data acquisition, these measurements of cartilage strain may be conservative. Though subjects were asked to refrain from strenuous activity and rested in a supine position for 45 minutes the morning of data collection, it is possible that cartilage did not recover to its full thickness prior to the initial MR scan. This potential lack of full cartilage thickness recovery would lead to lower baseline thickness values and lower calculated strain values. Additionally, approximately nine minutes were required to complete the DESS scan. Less than four minutes were required for the patient to move from the treadmill to the scanner before the beginning of the post-activity DESS scan. Cartilage recovery during this time also may have resulted in an underestimate of the calculated strain levels. While it has been shown that patellar cartilage recovers 50% of its volume in 45 minutes following a knee bend activity,[13] cartilage recovery during this period likely resulted in an underestimation of the cartilage strain immediately after exercise.

The site-specific technique employed in this study allows for control in sampling multiple regions throughout the tibial cartilage, providing both average strain values characterizing medial and lateral compartments, as well as demonstrating more localized changes to the covered and the uncovered regions of each compartment. This site-specific technique provided the ability to measure cartilage changes in both regions of cartilage-to-cartilage contact and meniscus-to-cartilage contact. This method is complementary to biplanar fluoroscopy, which we have previously used to evaluate changes in regions of cartilage-to-cartilage contact due to a meniscus tear.[6] Therefore, this site-specific technique can be employed in future studies to identify changes caused by meniscus pathology in both regions of cartilage-to-cartilage and cartilage-to-meniscus contact. In addition, this method can be used to characterize the overall strains experienced by cartilage on the tibial plateau, as well as to identify variations in strain response within each compartment. This knowledge is crucial to understanding the *in vivo* function of the meniscus and tibial cartilage as well as mechanisms of cartilage degeneration in patients with meniscus tears.

In conclusion, the present study described baseline data for demonstrating normal meniscus and cartilage mechanical responses to walking. We found that walking resulted in significant decreases in tibial cartilage thickness in regions covered and uncovered by the meniscus in both the medial and lateral compartments. In the medial compartment, significantly greater strain was observed in regions not covered by the meniscus compared to covered regions, while no significant differences in strain were detected between covered and uncovered cartilage in the lateral compartment. These observations provide important baseline information regarding the influence of the meniscus on cartilage strain during walking. By comparing the normal baseline data collected in this study to data from populations at risk of developing OA, such as ligament-deficient and post-meniscectomy patients, the mechanisms contributing to OA development may be further elucidated. Furthermore, this baseline information can be utilized to evaluate meniscal function in patients as well as the efficacy of meniscal replacements and treatments.

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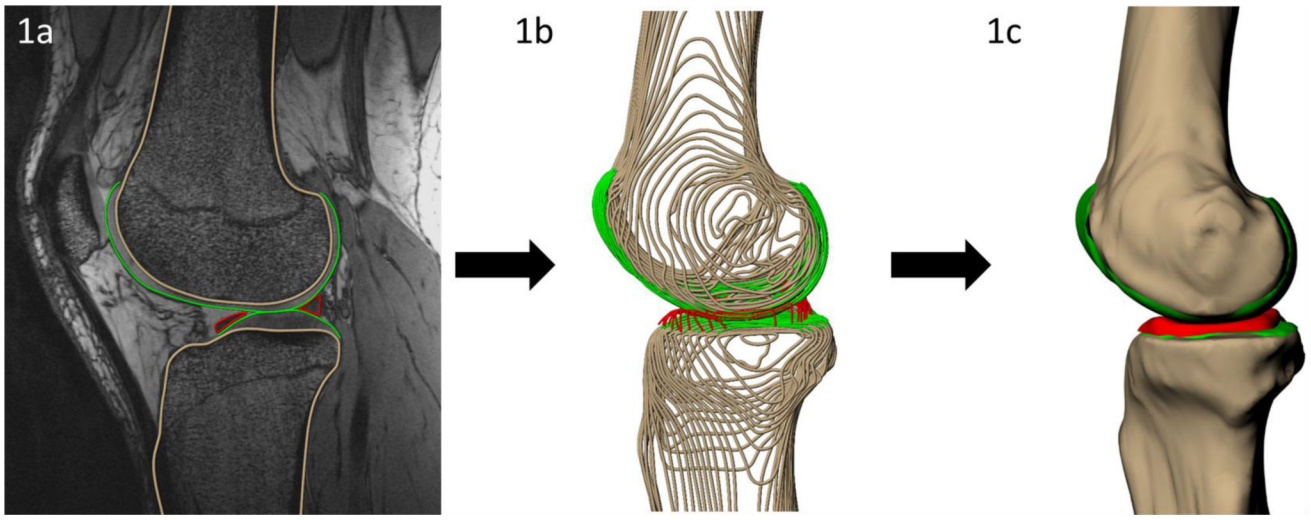

Figure 1.

(a) Human knees were imaged in the sagittal plane using a 3.0T MR scanner. Tibial and femoral cortices, articular cartilage surfaces, and menisci were segmented. (b) Segmented surfaces were combined to form a wireframe model that was (c) converted into a 3D surface mesh model.

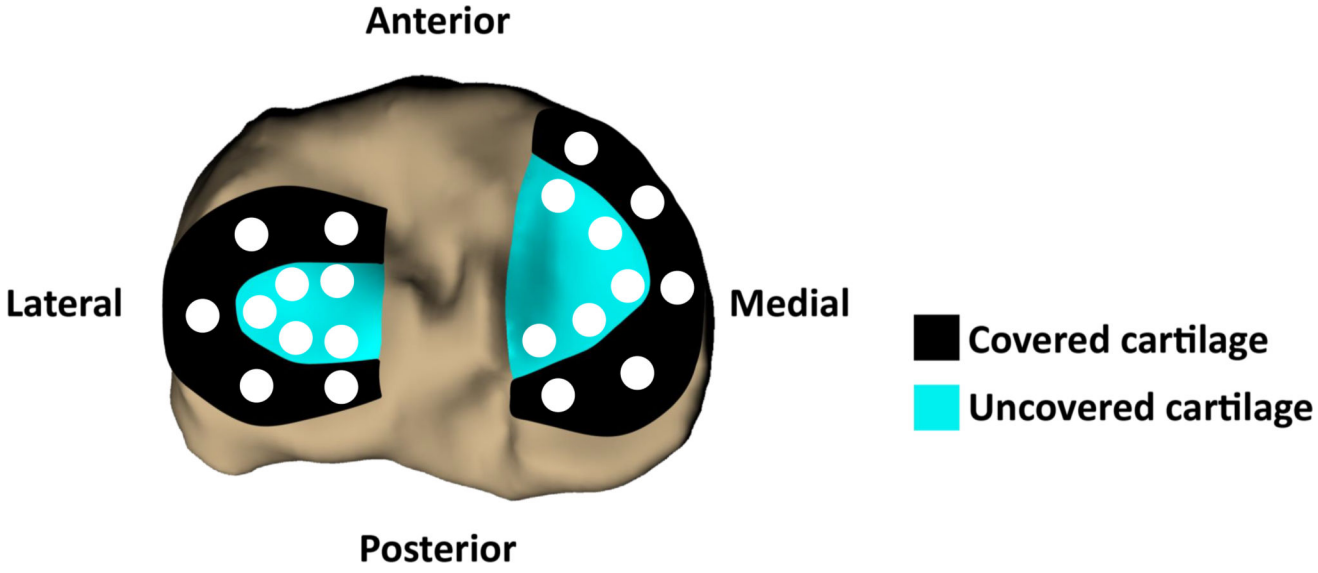

Figure 2.

A sampling system spanning the tibial plateau was constructed to provide site-specific measurements of thickness before and after a 20-minute walking activity. Twenty points were created with 10 placed in the medial compartment and 10 placed in the lateral compartment. In each compartment, 5 points were placed on regions of cartilage covered by the meniscus, while the other 5 were placed on uncovered cartilage.

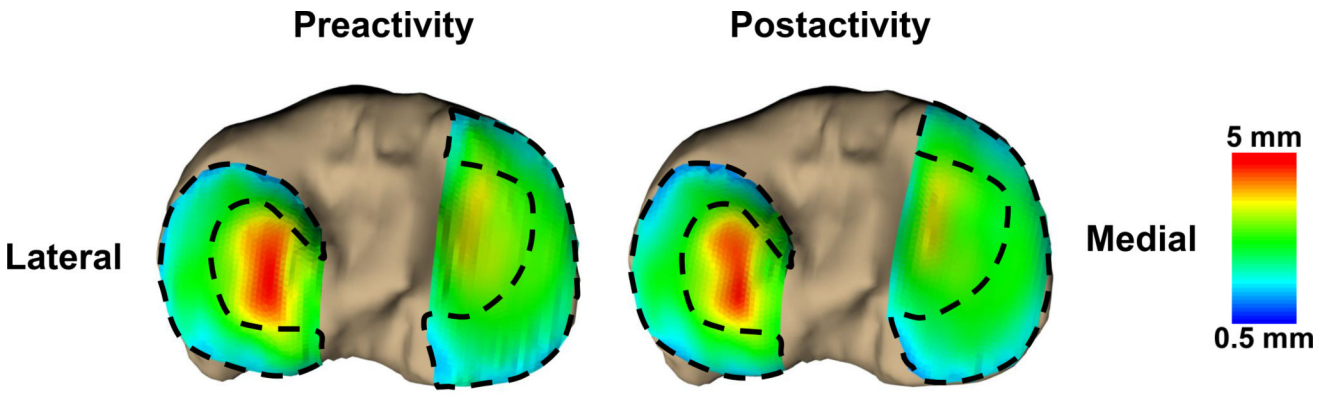

Figure 3.

Representative color thickness maps of pre- and post-activity tibial cartilage. Thicker cartilage is indicated by red and thinner cartilage is indicated by blue. Meniscus footprint is outlined in black.

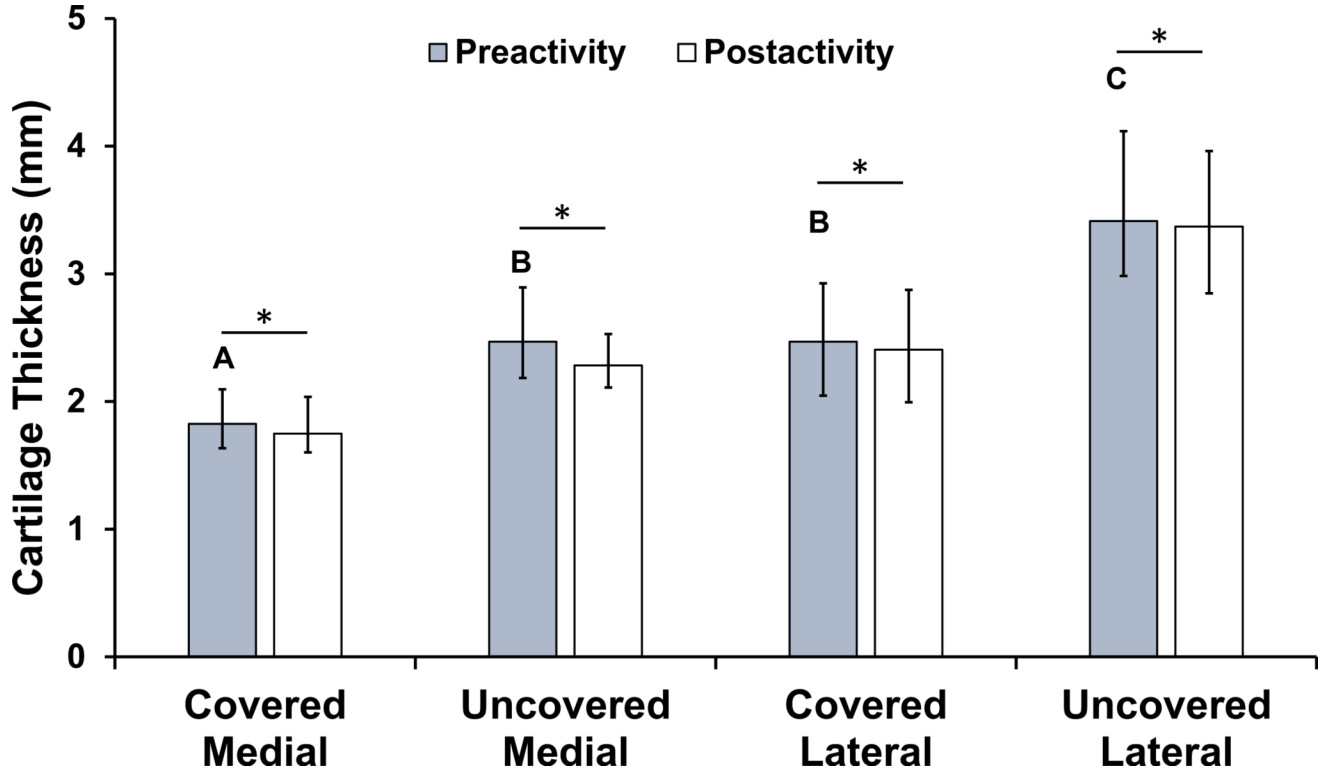

Figure 4.

Comparison of pre- and post-activity cartilage thicknesses in different regions of the tibial plateau. Bars show median and interquartile range. Pre-activity bars sharing the same letter are not statistically different from one another. * indicates a statistically significant decrease in cartilage thickness with activity ($p<0.01$).

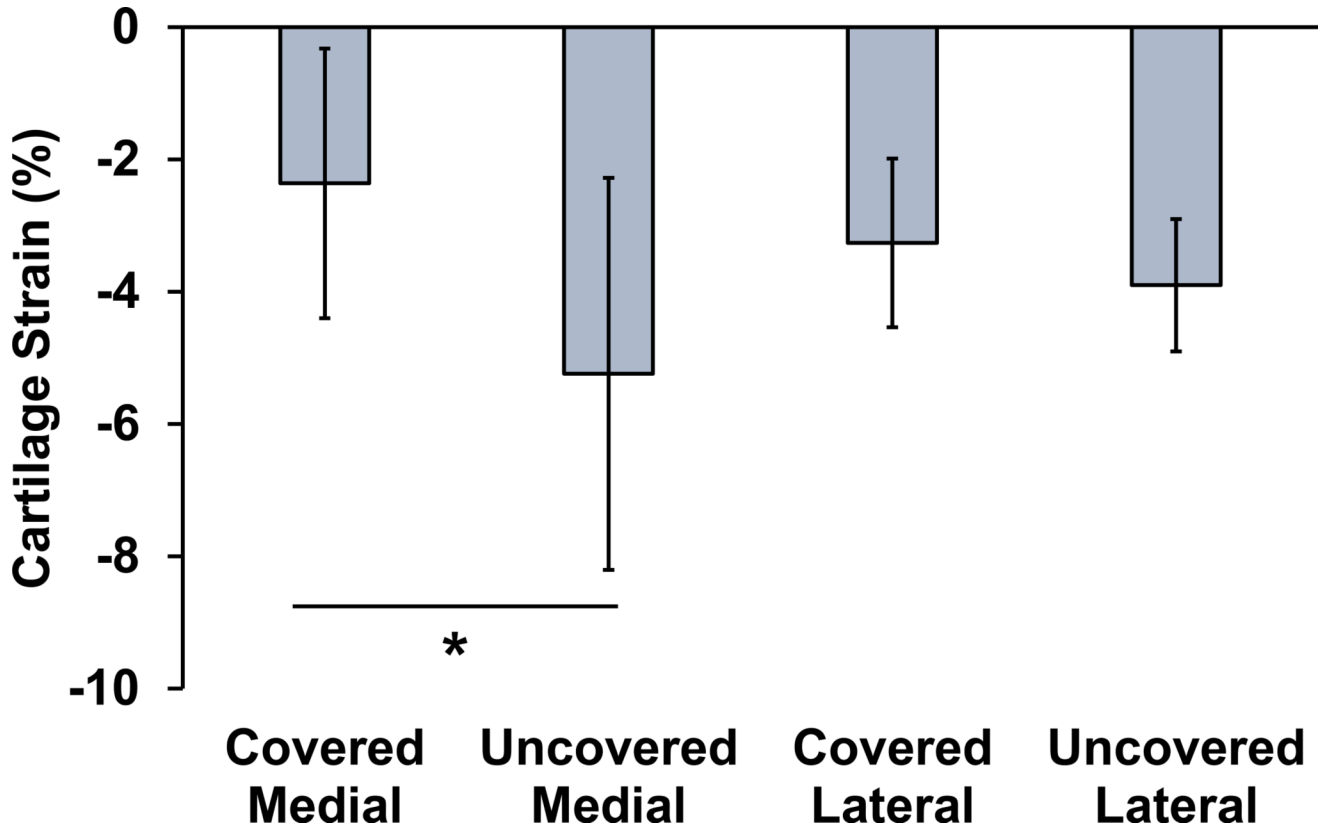

Figure 5.

Comparison of strains in covered regions of the tibial plateau to strains in uncovered regions within both medial and lateral compartments. Bars show mean and 95% confidence intervals. * indicates significant differences between covered and uncovered regions ($p < 0.05$).