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An Analysis of Changes in *In Vivo* Cartilage Thickness of the Healthy Ankle following Dynamic Activity

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Abstract

Abnormal cartilage loading after injury is believed to be an important factor leading to post-traumatic ankle osteoarthritis. Due to the viscoelastic behavior of cartilage, it is possible to measure localized cartilage strains from changes in thickness following dynamic activities. However, there are limited data characterizing *in vivo* cartilage mechanics under physiological loading conditions in the healthy ankle. Therefore, the objective of this study was to directly measure *in vivo* cartilage strains in the healthy ankle joint in response to a dynamic hopping exercise. Ten healthy subjects with no history of ankle injury underwent magnetic resonance imaging before and after a single-leg hopping exercise. Bony and articular cartilage surfaces were created from these images using solid modeling software. Pre-exercise and post-exercise models were then registered to each other, and site-specific cartilage strains (defined as the normalized changes in cartilage thickness) were calculated at grid points spanning the articular surfaces. The effects of both location and exercise on strain were tested using a two-way repeated measures analysis of variance. We did not detect any significant interaction effect between location and exercise for either tibial or talar cartilage. However, hopping resulted in significant decreases in tibial ($p < 0.05$) and talar ($p < 0.05$) cartilage thicknesses, corresponding to strains of 3% and 2%, respectively. Additionally, pre-exercise cartilage thickness varied significantly by location in the talus ($p < 0.05$), but not in the tibia. These strain data may provide important baseline information for future studies investigating altered biomechanics in those at high risk for the development of post-traumatic ankle osteoarthritis.

Keywords

Ankle; Stress test; Strain; Dynamic loading; MRI; Imaging; Mechanics; Contact; Joint

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Conflict of Interest Statement

The authors certify they have no commercial relationships which may lead to a conflict of interest.

Introduction

Mechanical loading is believed to play an important role in maintaining cartilage health (Griffin and Guilak, 2005). Though previous studies have used cadaveric models to measure cartilage loading in the ankle (Hirose et al., 2004; Omori et al., 2004; Tochigi et al., 2008), little is known regarding the *in vivo* loading environment of ankle cartilage (Bischof et al., 2010; Van Ginckel et al., 2011a; Van Ginckel et al., 2011b; Wan et al., 2008). Data characterizing normal *in vivo* ankle cartilage function may be critical to better understanding the mechanical factors contributing to the development of post-traumatic ankle osteoarthritis (OA).

With mechanical loading, cartilage is deformed and fluid is exuded from the cartilage matrix (Mow et al., 1984). Due to the low permeability of the cartilage matrix, time is required for the cartilage to equilibrate to its prior unloaded state (Eckstein et al., 1999; Mow et al., 1984). This time-dependent response (Mow et al., 1980; Zhang et al., 2015) allows for the measurement of cartilage deformation in response to loading. Specifically, this principle has allowed for the use of magnetic resonance (MR) imaging to measure cartilage volumetric changes (Eckstein et al., 2005; Van Ginckel et al., 2011a; Van Ginckel et al., 2011b) and site-specific cartilage strains (Coleman et al., 2013; Sutter et al., 2015; Widmyer et al., 2013) in response to *in vivo* loading conditions.

While previous studies have characterized localized cartilage strains in the knee (Sutter et al., 2015), there are limited data characterizing site-specific cartilage strains in response to dynamic loading in the ankle. Thus, the goal of this study was to measure *in vivo* localized cartilage strains in response to mechanical loading in the healthy ankle. We hypothesized that dynamic movement, specifically single-limb hopping, would result in compressive strains that vary with location in the tibial and talar cartilage of the healthy ankle joint.

Methods

Subject Recruitment

Following Institutional Review Board approval, 10 healthy subjects (7 male and 3 female; mean age: 27 years; age range: 22–31 years) with normal body mass index (BMI, mean: 22.9) were recruited for participation in this study. Subjects with a previous history of injury, surgery, or degeneration in either ankle joint were excluded.

Study Procedure

In order to minimize the effect of pre-exercise mechanical loading on baseline ankle cartilage thickness, subjects were tested in the morning (Coleman et al., 2013) and instructed not to perform any strenuous activities on the day prior to and morning of testing. Upon arrival, subjects lay supine for 45 minutes prior to the MR scan (Sutter et al., 2015). Subjects were then transported into the adjacent MR suite in a wheelchair. MR images of one ankle for each subject (5 right and 5 left) were obtained in the sagittal plane using a 3.0T MR scanner with an eight-channel knee coil (Trio Tim, Siemens Medical Solutions USA, Malvern, PA) and a 3-dimensional (3D) double-echo steady state (DESS) sequence (flip angle: 25°, TE: 6 ms, TR: 17 ms, field of view: 15×15 cm², resolution: 512×512 pixels, slice

thickness: 1 mm, sequence time: approximately 9 minutes) (Abebe et al., 2011; Bischof et al., 2010; Caputo et al., 2009; Taylor et al., 2013). Following pre-exercise imaging, subjects were wheeled to an adjacent hallway and asked to perform 60 single-limb hops spaced 2 feet apart on the imaged limb (Sutter et al., 2015). Subjects were also told to avoid touching the ground with their non-test limb and to perform the hopping exercise in a controlled manner. Following the hopping exercise, subjects were wheeled back to the MR suite, where a post-exercise scan of their test ankle was performed using identical acquisition parameters.

Data Analysis

For each MR image, bony and articular surfaces of the tibiotalar joint were manually segmented using solid modeling software (Rhinoceros 4.0, Robert McNeel and Associates, Seattle, WA; Figure 1) (Bischof et al., 2010; Utturkar et al., 2013). These outlines were subsequently compiled to create 3D polygonal mesh models of the tibia, talus, and corresponding articular cartilage surfaces (Geomagic Studio, Geomagic Inc., Raleigh, NC; Figure 1). Pre- and post-exercise models for each subject were then registered to each other using an iterative closest point technique (Okafor et al., 2014), allowing for site-specific measurements of cartilage thickness (Coleman et al., 2013; Sutter et al., 2015). Cartilage thickness was calculated as the distance between each vertex on the cartilage mesh surface and the nearest vertex on the bony mesh surface (Figure 2). Site-specific measurements of cartilage thickness and strain (defined as the normalized change in cartilage thickness in response to exercise) were conducted using grid sampling systems created on both the tibial and talar cartilage surfaces. These grid systems were designed to uniformly span both articular surfaces, with 11 points spaced evenly across the tibial surface and 12 across the talar surface (Figure 3). Thickness measurements were made within a 2 mm radius around each grid point. The methodology used in the present study has been previously validated to measure cartilage strains in the tibiofemoral (Van de Velde et al., 2009) and tibiotalar joints (Bischof et al., 2010). Additionally, we calculated the coefficient of repeatability of the tibiotalar segmentations to be 0.02 mm by measuring cartilage thickness at five different locations on both the tibial and talar cartilage (Coleman et al., 2013).

Statistical Analysis

Statistical analysis was performed using STATISTICA (Statsoft, Inc., Tulsa, OK). The effects of location and exercise on tibiotalar cartilage thicknesses were assessed using a two-way repeated measures ANOVA on both the tibial and talar cartilage. Post-hoc statistical analysis was performed using the Fisher's least significant difference test. Statistical significance was determined at $p < 0.05$.

Results

No statistically significant location-exercise interaction effects were observed for either tibial or talar cartilage. However, cartilage thickness decreased significantly after exercise in both tibial and talar cartilage surfaces (Figure 4). Specifically, the tibial cartilage experienced an overall compressive strain of 3% ($p = 0.013$), while the talar cartilage experienced a compressive strain of 2% ($p = 0.001$).

No statistically significant variations in pre-exercise tibial cartilage thickness by location were detected, with thickness values ranging from 1.3 mm to 1.5 mm (Figure 5). However, location was found to have a significant effect on pre-exercise talar cartilage thickness ($p < 0.0001$). The posterolateral region (grid point 4) of the talar cartilage was the thickest with an average value of 1.6 ± 0.1 mm (mean $\pm$ standard error) across subjects. The thinnest baseline cartilage thickness was in the anterolateral region (grid point 1) of the talar cartilage, which averaged to 1.0 ± 0.1 mm across subjects (Figure 6).

Discussion

Currently, there are limited data quantifying ankle cartilage strain distributions in response to physiological loading conditions. Such data are important for understanding the role of altered biomechanics in the development of OA. Thus, the objective of this study was to measure *in vivo* tibiotalar cartilage strain distributions in response to a dynamic exercise. We found an overall statistically significant decrease in both tibial and talar cartilage thicknesses in response to single-limb hopping. Additionally, we found that pre-exercise cartilage thickness varied significantly by location in the talus but not in the tibia.

Compared to the compressive strains observed in the articular cartilage of the knee (Coleman et al., 2013; Sutter et al., 2015), the strains in the ankle observed in the present study were lower and more uniform. For example, in a study investigating a similar dynamic hopping exercise on articular cartilage of the knee (Sutter et al., 2015), the authors found that some areas of tibiofemoral cartilage experienced significant strains, reaching a local maximum of 8%, while other areas of cartilage did not experience significant strains (Sutter et al., 2015). One potential explanation for the difference in strain distributions between the knee and ankle may be that the articular surfaces of the ankle are relatively congruent (Wynarsky and Greenwald, 1983), perhaps accounting for less variation in ankle cartilage strains with location. Greater cartilage strain magnitudes in the knee compared to the ankle may be attributed in part to differences in the properties of tibiofemoral and tibiotalar cartilage. Compared to the knee, ankle cartilage has been described as having a higher dynamic stiffness and a lower hydraulic permeability due to greater proteoglycan content (Fetter et al., 2006; Kuettner and Cole, 2005; Treppo et al., 2000), which may result in decreased deformations in the ankle cartilage under loading. Together, these varying properties may influence the response of the ankle and knee joints to load (Fetter et al., 2006; Kuettner and Cole, 2005).

A previous study used MR imaging and biplanar fluoroscopy to investigate tibiotalar cartilage strains in response to static loading with full body weight (Wan et al., 2008). Specifically, MR imaging techniques were used to create 3D models of the tibia, talus, and corresponding cartilage layers. These models were then registered to biplanar x-ray images to reproduce the motion of the tibiotalar joint and approximate the cartilage strains. Cartilage strain over the entire tibiotalar contact area averaged 7.5% (Wan et al., 2008). This strain measurement is greater than the 2% to 3% strain recorded in the present study, but these differences may be explained by the differences in measurement techniques. The combination of MR imaging and biplanar fluoroscopy enables the approximation of cartilage strains at the time of loading (Wan et al., 2008). However, while the present study

provides direct measurements of cartilage strains in response to dynamic exercise, strain measurements after the completion of exercise (Coleman et al., 2013; Sutter et al., 2015) would be expected to be less than strain values approximated in the joint while it is being loaded (Bischof et al., 2010; Wan et al., 2008).

Though subjects arrived early in the morning to minimize potential diurnal changes in baseline cartilage thickness (Coleman et al., 2013), were asked to refrain from strenuous exercise the day prior to and morning of testing, and rested for 45 minutes in a supine position (Sutter et al., 2015), it is possible that their cartilage was not fully relaxed to its baseline, unloaded thickness during pre-exercise MR imaging. Furthermore, although imaging was performed in a room adjacent to the MR scanner as soon as possible after completion of the exercise, an average of 4 minutes and 43 seconds was required to position the subject within the scanner, to run the localizing scans, and to initiate imaging. Given this time and the average scan time for the MR sequence (approximately 9 minutes), the cartilage may have recovered to some extent following the exercise. Thus, the measurements observed in the present study may underestimate ankle cartilage strains. Additionally, while cartilage strain values found in the present study (2%–3%) are not as large as those previously found in the knee (5%) (Coleman et al., 2013; Sutter et al., 2015), they are above the error threshold of 0.02 mm as determined by our repeatability analyses.

Baseline data characterizing the *in vivo* strain response of tibiotalar cartilage are critical to understanding the role of altered biomechanics in the development of post-traumatic ankle OA. Though previous studies have suggested that altered cartilage loading after joint injury may predispose the ankle to degeneration (Bischof et al., 2010; Caputo et al., 2009; Golditz et al., 2014; Harrington, 1979; Hirose et al., 2004), additional data are needed to fully characterize the changes in the mechanical environment of the joint in response to dynamic, physiological loading conditions. In this regard, the data and methodology used in this study may be subsequently used to evaluate the effects of injury on ankle cartilage strain distributions in response to activities of daily living. Specifically, this approach could be used to evaluate the effects of injuries such as lateral ankle instability on cartilage loading (Bischof et al., 2010). Such information may provide new insights into the role of altered mechanical loading in the development of degenerative changes associated with OA.

In conclusion, this study found significant cartilage strains of 3% and 2% in tibial and talar cartilage, respectively, in response to a dynamic hopping exercise. We also found that pre-exercise talar cartilage thickness varied significantly by location. This study provides useful baseline data for comparison against and evaluation of the effects of injury or instability on ankle joint mechanics. Future studies could use a similar approach to evaluate cartilage response in the pathological joint to better understand mechanical factors contributing to post-traumatic ankle OA.

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Figure 1.

Bony and articular cartilage surfaces of the ankle joint were segmented on each MR image using solid modeling software (a). Outlines of all image slices were compiled (b) to generate a surface model of the ankle joint (c).

Figure 2.

In a representative subject, cartilage thickness decreased on both the tibia and talus assessed pre- and post-exercise (A=Anterior, P=Posterior, M=Medial, L=Lateral).

Figure 3.

3D models of a left tibia and talus showing the grid scheme for computing cartilage thickness and strains. The grid system was designed to span both articular surfaces and allow for regional analyses of cartilage thickness changes.

Figure 4. Mean ($\pm$ standard error) cartilage thickness decreased significantly with exercise in both tibial and talar cartilage (ANOVA, $p < 0.05$). * indicates significant differences at $p < 0.05$.

Figure 5. Mean ($\pm$ standard error) cartilage thickness at each grid point on the pre-exercise tibial cartilage surface. No statistically significant differences in tibial cartilage thickness were detected with location, with thickness values ranging from 1.3 ± 0.1 mm to 1.4 ± 0.1 mm.

Figure 6.

Mean ($\pm$ standard error) cartilage thickness at each grid point on the pre-exercise talar cartilage surface. Location had a statistically significant effect on talar cartilage thickness ($p < 0.0001$). Grid point 1, corresponding to the anterolateral region, exhibited the lowest pre-exercise cartilage thickness (1.0 ± 0.1 mm), and grid point 4, corresponding to the posterolateral region, exhibited the highest pre-exercise cartilage thickness (1.6 ± 0.1 mm).