Is cartilage thickness different in young subjects with and without patellofemoral pain?


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Summary

Objective: To determine the differences in load-bearing patellofemoral joint cartilage thickness between genders. To determine the differences in load-bearing cartilage thickness between pain-free controls and individuals with patellofemoral pain.

Methods: The articular cartilage thickness of the patella and anterior femur was estimated from magnetic resonance images in 16 young, pain-free control subjects (eight males, eight females) and 34 young individuals with patellofemoral pain (12 males, 22 females). The average age of all subjects was 28 ± 4 years. The cartilage surfaces were divided into regions approximating the location of patellofemoral joint contact during knee flexion. The mean and peak cartilage thicknesses of each region were computed and compared using a repeated-measures Analysis of Variance.

Results: On average, males had 22% and 23% thicker cartilage than females in the patella (P < 0.01) and femur (P < 0.05), respectively. Male control subjects had 18% greater peak patellar cartilage thickness than males with patellofemoral pain (P < 0.05); however, we did not detect differences in patellar cartilage thickness between female control subjects and females with patellofemoral pain (P = 0.45). We detected no significant differences in femoral cartilage thickness between the control and pain groups.

Conclusions: Thin cartilage at the patella may be one mechanism of patellofemoral pain in male subjects, but is unlikely to be a dominant factor in the development of pain in the female population.

Key words: Cartilage thickness, Patellofemoral joint, Magnetic Resonance Imaging.

Introduction

Patellofemoral pain is a common and debilitating disorder.1,2 Unfortunately, the cause of pain is unclear, making treatment challenging1,2. One common hypothesis is that pain is caused by increased stress in the subchondral bone1,3 associated with increased stress in the overlying cartilage2,4. Finite-element models have shown that cartilage stress increases with decreasing articular cartilage thickness5, indicating that cartilage thickness may play a role in the mechanism of pain. To test this hypothesis, in vivo measurements of cartilage thickness must be obtained in subjects with and without patellofemoral pain.

Articular cartilage thickness has been directly measured in cadavers using a variety of techniques5,7; however, these methods are invasive and do not permit measurements to be made in vivo. Magnetic resonance imaging (MRI) allows one to visualize articular cartilage and non-invasively measure its morphology. Many studies have developed and validated techniques to measure cartilage volume and thickness at the knee joint using high-resolution magnetic resonance (MR) images.8-20 These techniques have been shown to provide repeatable and accurate estimates of patellar, femoral, and tibial cartilage thicknesses.

A number of studies have used MR-based techniques to estimate in vivo cartilage thickness distributions in young, healthy subjects.8,11,18,21-23 These techniques have also been used to assess the degree of cartilage thinning with disease progression in the osteoarthritic population.21-24-26 Cartilage thickness may also play a role in patellofemoral pain because of the dependence of cartilage stress on articular cartilage thickness. Subjects with this disorder can experience pain in the absence of cartilage degeneration, and may have thinner than normal cartilage on the patella and anterior femur. No previous studies have examined articular cartilage thickness in young subjects with patellofemoral pain.

The incidence of patellofemoral pain is higher in females than in males27. Differences in cartilage thickness with gender may provide one explanation for this disparity. Jones et al. reported that young males have significantly thicker articular cartilage at the tibia than females of the same age28 and Eckstein et al. found that males had thicker mean femoral22,29 and patellar22 cartilage than females;
however, the data of Faber et al. did not reveal significant differences in cartilage thickness at the knee between non-athletic males and females\(^29\). These discrepancies suggest that further research must be performed to evaluate the dependence of cartilage thickness on gender.

To quantify the cartilage thickness distribution, most previous studies have examined the peak and mean cartilage thickness of the entire surface. Other studies have divided the femur into regions separating the two condyles and the trochlea\(^29,30,31\). In evaluation of patellofemoral pain, it may be more relevant to quantify the thickness distribution by dividing the cartilage surface according to the locations of joint contact between the patella and femur. Previous studies have not selectively examined cartilage thickness in these load-bearing regions.

The goals of this study are to (1) assess whether males have thicker cartilage than females in regions of articular contact, and (2) determine whether pain-free control subjects have thicker cartilage in these regions than individuals with patellofemoral pain.

**Methods**

We examined the patellofemoral joints of 16 healthy, pain-free control subjects (eight males and eight females) and 34 individuals with patellofemoral pain (12 males and 22 females). All subjects were between the ages of 18 and 37 and had their MR images screened by a radiologist to ensure there were no ligament or meniscal tears, no evidence of bone marrow edema, and no evidence of cartilage damage (modified Outerbridge scale, grade 0)\(^32\). Subjects with patellofemoral pain were diagnosed by a sports medicine clinician and were included in the study if they experienced anterior knee pain during physical activity. In subjects with bilateral pain, the more symptomatic knee was studied. Furthermore, subjects who met any of the following criteria were excluded from the study: knee ligament instability, patellar tendonitis, joint line tenderness or knee effusion, previous knee trauma or surgery, patellar dislocation, and neurological disorders that would affect jogging or squatting. There were no differences in age between subject groups and no differences in height or weight between subject groups of the same sex (Table I). Each subject’s score on the anterior knee pain scale (AKPS)\(^33\) was measured (a score of 100 indicates no anterior knee pain or disability). There was no difference in the AKPS score between the male and female patellofemoral pain subjects of our study (Table I). Prior to participation, subjects were informed about the nature of the study and provided consent according to the policies of the Stanford University Institutional Review Board.

Sagittal plane images were acquired with a 1.5 T MR scanner (GE Healthcare, Milwaukee, WI) while subjects were supine with the knee in full extension (Fig. 1). This position minimized cartilage deformation and load at the patellofemoral joint. A three-dimensional (3D) fat-suppressed spoiled gradient echo (SPGR) MR sequence was used with a transmit/receive extremity coil and the following scan parameters: TR: 40 ms, TE: 5 ms, flip angle: 30°, matrix size: 256 x 256, field-of-view: 12 cm x 12 cm, slice thickness: 1.5 mm, slices: 60, receive bandwidth: 122 Hz per pixel, and acquisition time: 15 min.

The distal femoral and patellar cartilage surfaces were segmented from the MR images as described previously\(^34\). Briefly, the subchondral bone and articular cartilage boundaries of each bone were manually segmented using custom software to generate 3D point clouds. Using solid modeling software, 3D triangulated surfaces of both the subchondral bone and articular cartilage boundaries were created from the point clouds (Geomagic, Raindrop Geomagic, NC). Cartilage thickness was estimated by computing the minimum distance between the subchondral bone surface and the articular cartilage surface for every point on the articular cartilage surface (approximately 500 points per cm\(^2\)). This algorithm results in a distribution map of the cartilage thickness of the patella and anterior femur (Fig. 2). In our experience, cartilage thickness based on manual segmentation of SPGR images acquired using a 1.5 T MRI scanner can be determined to be within ±0.2–0.3 mm\(^35\).

To provide a quantitative analysis of the thickness distribution map, we divided the patellar and femoral cartilage surfaces into three regions (Fig. 3). This division was motivated by the change in relative position of the femur and patella, and therefore the change in location of load-bearing cartilage, during knee flexion. Cartilage stress is higher in regions of joint contact; thus, it may be more relevant to measure the thickness specifically in these regions. Using a GE Signa 0.5 T SP/i MR scanner, we obtained images of loaded knee flexion\(^36\). From these images, we defined the location of contact between the patella and femur at 0°, 30°, and 60° of knee flexion for a typical healthy subject [Fig. 3(A)]. Generic regions on each bone were then created to approximate the locations of contact at these flexion angles [Fig. 3(B)].

The mean and peak cartilage thicknesses were computed in each region. The mean thickness was computed using all data points in the region. The peak thickness of each region was defined as the mean of the top 10% of the data points in the region.

We performed a repeatability study to assess the precision of the image segmentation technique and cartilage thickness measurement algorithm. One subject was segmented by two independent observers to assess the inter-observer repeatability. The intra-observer repeatability was assessed by a single examiner segmenting the images of a single knee on three separate occasions and performing the thickness measurements on each set of surfaces.

<table>
<thead>
<tr>
<th>Subject group</th>
<th>Age (years)</th>
<th>Weight (kg)</th>
<th>Height (m)</th>
<th>Pain score (AKPS)(^33)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Control</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>28 ± 3</td>
<td>71.8 ± 4.0</td>
<td>1.78 ± 0.08</td>
<td>—</td>
</tr>
<tr>
<td>Female</td>
<td>29 ± 5</td>
<td>57.4 ± 5.1</td>
<td>1.65 ± 0.05</td>
<td>—</td>
</tr>
<tr>
<td>Patellofemoral pain</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>30 ± 4</td>
<td>75.9 ± 11.7</td>
<td>1.80 ± 0.07</td>
<td>71.3 ± 11</td>
</tr>
<tr>
<td>Female</td>
<td>28 ± 5</td>
<td>61.3 ± 9.1</td>
<td>1.67 ± 0.07</td>
<td>71.1 ± 13.8</td>
</tr>
</tbody>
</table>
The coefficients of variation (CV) between the resulting thickness estimates were computed.

The high degree of inter-subject variability in cartilage thickness has prompted investigations into the correlation of these measurements with anthropometric parameters\(^{23,25,37}\). Simon determined a significant scaling relationship between body mass and cartilage thickness for animals spanning a four-decade range of body mass\(^{37}\). His results show that cartilage thickness is proportional to body mass raised to the 0.45 power (mass\(^{0.45}\))\(^{37}\). Therefore, to account for potential differences in the subject mass, we scaled the thickness measurements by mass\(^{0.45}\), to calculate a “scaled thickness”.

Differences between subject groups were evaluated using a two factor Analysis of Variance (gender \times pain) to assess differences with gender and with pain.

**Results**

Male control subjects had 22% thicker cartilage on the patella \((P < 0.01)\) and 23% thicker cartilage on the femur \((P < 0.05)\) than female control subjects when averaged over all regions of contact. The mean patellar cartilage of the male control subjects was significantly thicker than that of the female controls in both the superior and middle contact regions \((P < 0.01)\) (Fig. 4). The mean femoral cartilage of the male controls was significantly thicker than that of the female controls in the inferior region \((P < 0.01)\). The mean scaled thickness of both the patella and femur was not different between genders. However, we detected differences in the peak patellar cartilage thickness between the male and female control subjects both before and after scaling by mass\(^{0.45}\) \((P < 0.05)\). Therefore, in our subsequent analyses of cartilage thickness differences in the patellofemoral pain population we examined males and females separately.

Male control subjects had 18% greater peak patellar cartilage thickness than male subjects with patellofemoral pain when averaged over all regions of joint contact \((P < 0.05)\). The specific locations of greater peak cartilage thickness were in the superior and middle regions of the patella.

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**Fig. 1.** Sample sagittal MR image (fat-suppressed 3D SPGR) of knee used to estimate articular cartilage thickness.

**Fig. 2.** Sample map of cartilage thickness distribution of femur and patella for one pain-free male subject.

**Fig. 3.** Locations of contact between patella and femur during loaded knee flexion (0°, 30°, and 60°) for a typical subject (A). Generic regions (superior, middle, and inferior) on femur and patella based on locations of contact during loaded knee flexion (B).
These differences in peak thickness were also significant when scaled by mass. We did not detect any differences in patellar cartilage thickness between female control subjects and female subjects with patellofemoral pain ($P = 0.45$) (Fig. 6). We were also unable to detect differences in femoral cartilage thickness between control subjects and individuals with patellofemoral pain for either males ($P = 0.2$) or females ($P = 0.3$) (Fig. 7).

Cartilage thickness measurements from the two independent observers showed good inter-observer agreement (CV of 0.2% for the patella and 5.9% for the femur). Additionally, the measurements showed good intra-observer repeatability (CV of 2.8% and 2.4% for the patella and femur, respectively).

**Discussion**

In this study, we found that male control subjects had thicker load-bearing cartilage than females on both the patella and anterior femur. In our experiments, the mean patellar and femoral cartilage thicknesses showed significant differences between genders; however, once scaled to account for subject mass, we did not detect differences in the scaled mean thickness between genders. This is consistent with the study by Eckstein et al.\textsuperscript{22}, which reported no differences in mean cartilage thickness between males and females once they were matched for body weight. In our study, males had greater peak patellar cartilage thickness than females both before and after scaling. These results imply that one reason for the differences in cartilage thickness between genders is the difference in body mass; however, there may be some gender differences in peak cartilage thickness due to factors other than body mass.

Our results show that in some regions of the patella, the peak cartilage thickness in male subjects with patellofemoral pain was less than that in male subjects without pain. We know that thinner cartilage results in higher stress for the same applied load. Li et al.\textsuperscript{5}, found that a 10% reduction in cartilage thickness results in an 8% increase in peak von Mises stress and a 10% increase in peak hydrostatic pressure. Therefore, the thin cartilage observed in the male patellofemoral pain subjects of our study may result in a sufficient increase in cartilage stress and lead to pain in these individuals.
We were unable to detect differences in the patellar cartilage thickness of our female subjects. To assess our ability to detect differences in cartilage thickness between the female subjects in this study, we performed a power analysis using the inherent resolution of the MRI data as the expected effect size. Using a resolving threshold of 0.68 mm based on an estimated isotropic voxel size of the MR images, the power for detecting a difference of this magnitude between the cartilage thickness of females with and without pain was 0.71. Therefore, any potential difference in cartilage thickness between the females in this study would likely be smaller than 0.68 mm, suggesting that other factors may play a role in the development of pain in the female population.

We did not detect differences in femoral cartilage thickness between the control and the patellofemoral pain subjects. Our power analysis suggests that any potential difference in cartilage thickness would likely be smaller than 0.68 mm and that femoral cartilage thickness may not be the primary factor in the development of patellofemoral pain in the young subjects we examined.

Our articular cartilage thickness measurements are comparable to those obtained in prior studies (Fig. 8). Both the peak and mean values of the patellar and femoral cartilage thickness of pain-free control subjects obtained in this study were similar to those estimated previously using MRI.

Previous studies have examined the cartilage thickness of males and females separately and have assessed the effects of gender on articular cartilage morphology, however, the results of these studies are conflicting. Our results are consistent with the findings of Eckstein et al., that males have greater mean femoral and patellar cartilage thicknesses than females. Faber et al. did not find significant differences in cartilage thickness at the knee between genders. One possible explanation for the inconsistency between our results and previous measurements is that, in our study, we only examined the load-bearing cartilage regions. The differences in cartilage thickness may be accentuated in the load-bearing areas, whereas any differences in thickness may not be preserved when measurements are averaged over the entire cartilage plate. Furthermore, in contrast to the study of Faber et al., all of the subjects in our study engaged in regular physical activity.

A limitation of this study is that the regions used to define load-bearing cartilage were not specific to individual subjects. It is likely that the location of contact between the patella and femur varies among subjects, especially those with abnormal patellar tracking. It may be possible that, in some subjects, the true load-bearing cartilage regions were different from the generic regions defined in this study. Another possible limitation may be the accuracy of our cartilage thickness maps. However, we observed differences in cartilage thickness of approximately 1 mm which is larger than the accuracy of our measurements using this technique (0.2–0.3 mm). A final consideration is the effect of subject age on cartilage thickness. Studies have found that cartilage thickness decreases with age. However,
there were no differences in age between any of our subject groups, and we did not find a correlation between cartilage thickness and age in our subjects \( (P > 0.24) \). Our limited age range (18–37 years) and the absence of cartilage degeneration in our subjects likely eliminated any effects of age in our study.

Cartilage thickness is only one possible factor associated with patellofemoral pain. There are other factors that influence cartilage stress, such as joint loads, joint contact area, joint kinematics, and cartilage material properties. Any combination of these mechanisms might play a role in the development of patellofemoral pain. Our results suggest that different subgroups of the patellofemoral pain population may experience pain because of different biomechanical factors. The implication of these findings is that patients may require different treatment protocols depending on the mechanism of pain. It is necessary to identify and understand all factors that cause pain so that treatments can be tailored to address the specific cause of pain in each patient.

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