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The Effects of Femoral Graft Placement on Cartilage Thickness after Anterior Cruciate Ligament Reconstruction

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Abstract

Altered joint motion has been thought to be a contributing factor in the long-term development of osteoarthritis after ACL reconstruction. While many studies have quantified knee kinematics after ACL injury and reconstruction, there is limited *in vivo* data characterizing the effects of altered knee motion on cartilage thickness distributions. Thus, the objective of this study was to compare cartilage thickness distributions in two groups of patients with ACL reconstruction: one group in which subjects received a non-anatomic reconstruction that resulted in abnormal joint motion and another group in which subjects received an anatomically placed graft that more closely restored normal knee motion. Ten patients with anatomic graft placement (mean follow-up: 20 months) and 12 patients with non-anatomic graft placement (mean follow-up: 18 months) were scanned using high-resolution MR imaging. These images were used to generate 3D mesh models of both knees of each patient. The operative and contralateral knee models were registered to each other and a grid sampling system was used to make site-specific comparisons of cartilage thickness. Patients in the non-anatomic graft placement group demonstrated a significant decrease in cartilage thickness along the medial intercondylar notch in the operative knee relative to the intact knee (8%). In the anatomic graft placement group, no significant changes were observed. These findings suggest that restoring normal knee motion after ACL injury may help to slow the progression of degeneration. Therefore, graft placement may have important implications on the development of osteoarthritis after ACL reconstruction.

Keywords

Kinematics; MRI; imaging; osteoarthritis; mechanics; ACL

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Conflict of Interest Statement

The authors have no other disclosures related to this work.

Introduction

ACL reconstruction is a commonly performed procedure that improves functional outcomes and allows many patients to return to recreational activities (Brophy et al., 2012; Feller and Webster, 2013; Koutras et al., 2013; Kvist, 2004). However, despite encouraging short-term clinical results, the development of post-traumatic osteoarthritis is an important concern in the long-term after ACL reconstruction (Delince and Ghafil, 2012; Lohmander et al., 2007). Specifically, numerous studies with follow-up times beyond ten years have reported radiographic evidence of degenerative changes in more than half of patients (Holm et al., 2012; Janssen et al., 2013; Salmon et al., 2006). While these changes are generally more severe in subjects with a concurrent meniscal injury, cartilage degeneration remains a problem even in patients with intact menisci at the time of surgery (Kessler et al., 2008; Salmon et al., 2006). Since ACL injury generally afflicts a relatively young population, preventing the development of osteoarthritis in these patients is an important clinical problem (Lohmander et al., 2007; Renstrom et al., 2008).

The precise mechanisms contributing to degenerative changes after ACL reconstruction are not well understood. Although a number of factors potentially contribute to the development of osteoarthritis after ACL injury, altered joint motion is believed to be one important factor (Andriacchi et al., 2004; Chen et al., 2012; Papannagari et al., 2006; Tashman and Araki, 2013; Tochigi et al., 2011). In particular, recent studies have suggested that some ACL reconstruction techniques may not restore normal tibiofemoral joint motions under physiological loading conditions (Abebe et al., 2011b; Gao and Zheng, 2010; Papannagari et al., 2006; Tashman and Araki, 2013). These abnormal joint motions are believed to alter normal cartilage contact mechanics (Andriacchi et al., 2004; Hosseini et al., 2012). Abnormal cartilage loading potentially disrupts normal cartilage homeostasis (Griffin and Guilak, 2005; Halloran et al., 2012), which could ultimately influence the initiation and progression of joint degeneration in these patients. Since a number of recent studies have indicated that abnormal knee kinematics persist after ACL reconstruction (Deneweth et al., 2010; Gao and Zheng, 2010; Papannagari et al., 2006; Scanlan et al., 2010; Tashman et al., 2004), understanding the relationship between altered joint motion and changes in cartilage morphology could provide critical information for improving long-term outcomes after ACL reconstruction.

Although many studies have quantified altered kinematics after ACL reconstruction, there is limited data relating these altered knee kinematics to early degenerative changes in cartilage. In particular, there is a lack of *in vivo* data relating altered knee joint motion to site-specific measurements of cartilage thickness in patients with ACL reconstruction. Thus, the objective of this study was to compare cartilage thickness distributions in two groups of patients with ACL reconstruction (Abebe et al., 2011a; Abebe et al., 2009; Abebe et al., 2011b): one group in which subjects received a non-anatomic reconstruction that resulted in abnormal joint motion and another group in which subjects received an anatomically placed graft that more closely restored normal knee motion. We hypothesized that the abnormal knee motions that were observed with non-anatomic graft placement would result in an increased loss of cartilage thickness compared to anatomically placed grafts.

Materials and Methods

Patient Recruitment and Inclusion Criteria

Twenty two patients (16 men and 6 women, 19-49 years old) between 6 and 36 months after unilateral ACL reconstruction and with healthy contralateral knees participated in this IRB approved study. Patients were recruited from the clinics of two surgeons at the Duke University Sports Medicine Center and completed the same post-surgery rehabilitation

protocol. Study participants were excluded if they exhibited any of the following features: varus-valgus deformity, osteoarthritis, tibiofemoral articular cartilage defects, removal of more than 10% of meniscus in the operated knee, or any other history of trauma or surgery to either knee. All participants had stable knees under Lachman and pivot-shift examinations. At the time of testing, all study participants had returned to sports activity without restriction. All patients meeting these recruitment criteria were sorted by operative date, and invited to participate in chronological order.

At the time of the study, twelve subjects (9 men, 3 women; mean age: 32 years; mean follow-up: 20 months) had received a procedure performed by one surgeon resulting in non-anatomic placement of the graft on the femur (Abebe et al., 2011a). Five patients had intact menisci, and the remaining seven had tears requiring removal of less than 10% of the meniscus (five lateral tears and two medial tears). These subjects had a graft placed using a transtibial technique, where the femoral tunnel was placed through the tibial tunnel (Abebe et al., 2009; Kaseta et al., 2008). This technique resulted in anteroproximal graft placement on the femur, an average of 9mm from the center of the original ACL attachment (Abebe et al., 2011a). These subjects had significantly increased anterior translation, medial translation, and internal tibial rotation in their reconstructed knee relative to their normal knee during a quasi-static weight-bearing lunge (Abebe et al., 2011b).

The remaining ten subjects (7 men, 3 women; mean age: 30 years; mean follow-up: 18 months) had received a procedure from another surgeon resulting in anatomic graft placement (Abebe et al., 2011a). Four patients had intact menisci, and the remaining six had tears requiring removal of less than 10% of the meniscus (three lateral tears and three medial tears). In these subjects, the femoral tunnel was placed independently of the tibial tunnel (RetroDrill, Arthrex, Naples, FL) (Abebe et al., 2009; Kaseta et al., 2008). Graft placement was within an average of 3mm from the center of the ACL (Abebe et al., 2011a). In these subjects, no differences in kinematics were detected between the intact and reconstructed knee during a quasi-static weight-bearing lunge (Abebe et al., 2011b).

MR Imaging

The subjects were seated in a non-weight bearing position for 30 minutes (Bischof et al., 2010) before the start of the investigation in order to minimize compression of the cartilage prior to imaging. Each subject's operative and intact contralateral knees were imaged at the Center for Advanced Magnetic Resonance Development using a 3T MR scanner (Trio Trim, Siemens, Germany) while positioned in a supine, relaxed position. Sagittal MR images were acquired using a double-echo steady state sequence (DESS, field of view: 15x15 cm, matrix: 512x512 pixels, slice thickness: 1mm, flip angle: 25°, TR: 17ms, TE: 6ms) and an eight-channel knee coil (In Vivo, Orlando, FL) (Abebe et al., 2009; Taylor et al., 2011). Total scan time was approximately 9 minutes for each knee. All MR images were imported into solid modeling software (Rhinoceros, Robert McNeel and Associates) for further processing.

MR Imaging-Based 3D Modeling and Cartilage Thickness Analysis

For each sagittal MR image slice, the outer margins of the femoral and tibial cortices as well as the surface contours of articular cartilage were outlined (Figure 1). These traced curves were then used to generate anatomic 3D mesh models of the tibiofemoral joint using solid modeling software (Geomagic Studio, Geomagic Inc., Raleigh, NC) (Figure 1). In order to measure the cartilage thickness on both the operative and intact knee models using the same coordinate system, all operative knee models were mirrored to create two models with the same orientation. Next, the mirrored operative knee models were aligned to the intact knee models using an iterative closest point technique (Caputo et al., 2009). This registration was performed to allow for site-specific comparisons of cartilage thickness. A grid sampling

system was then created on both the operative and intact knee models to quantify variations in cartilage thickness by location (Figure 2). Both the lateral and medial femoral condyles were subdivided into 3x6 grids. Additionally, three points were sampled in the medial aspect of the intercondylar notch because this is a region where elevated cartilage contact strains have been observed in patients with ACL injury (Sutter et al., 2013; Van de Velde et al., 2009). Furthermore, this is also a region where early evidence of degeneration has been observed clinically in patients with ACL deficiency (Fairclough et al., 1990). A total of 18 evenly-spaced points were also sampled on the lateral and medial tibial plateaus. Using mathematical analysis software (Mathematica, Wolfram, Champaign, IL), thickness measurements were calculated by finding the smallest Euclidian distance between the vertex of the articular surface to the cartilage-bone interface of the 3D surface mesh models (Coleman et al., 2013). This thickness information was color encoded on the cartilage surface to generate a thickness map (Figure 3). These calculations were then followed by averaging thickness at each vertex on the mesh model within a 2.5 mm radius of the grid sampling point for each joint (Coleman et al., 2013). Finally, at each point, the percent change in cartilage thickness was calculated relative to the intact contralateral knee. This MR imaging technique for measuring cartilage thickness has been previously validated in the literature (Van de Velde et al., 2009). Additionally, a recent study from our laboratory indicated that this technique has a coefficient of repeatability of 0.03mm for measuring tibial, femoral, and patellar cartilage thickness (Coleman et al., 2013), which corresponds to a difference in cartilage thickness of 1% (Coleman et al., 2013; Widmyer et al., 2013).

Statistical Methods

The Yates corrected chi-squared test was used to compare the proportion of males and females between groups and t-tests were used to compare differences between follow-up time and age between groups. A two-way repeated measures analysis of variance (ANOVA) was performed to determine whether knee state (intact versus reconstructed) and location had significant effects on cartilage thickness. The Tukey post-hoc test was used to detect differences between means, as appropriate. Differences were considered statistically significant where $p < 0.05$.

Results

No statistically significant differences were observed between groups for proportion of males to females ($p = 0.82$), age ($p = 0.19$), or follow-up time ($p = 0.39$).

In knees with an anatomic reconstruction, there was a statistically significant effect of location on cartilage thickness ($p < 0.001$, Figure 4). Cartilage in the lateral tibia was thicker than all other regions ($p < 0.001$). No differences in cartilage thickness were observed between the medial femur, lateral femur, medial tibia, and the medial aspect of the intercondylar notch. No statistically significant effects of knee state (intact versus reconstructed, $p = 0.30$) or interactions between knee state and location were observed ($p = 0.27$). In the medial intercondylar notch, there was a mean difference of just 1% in cartilage thickness between intact and reconstructed knees.

In knees with the non-anatomic graft placement, there was a statistically significant interaction between knee state (intact versus reconstructed) and location on cartilage thickness ($p = 0.002$, Figure 5). In particular, cartilage in the medial aspect of the intercondylar notch in reconstructed knee was significantly thinner than intact cartilage by 8% ($p = 0.02$). No statistically significant differences in cartilage thickness were observed between intact and reconstructed knees in any other region ($p > 0.61$). In both intact and reconstructed knees, cartilage in the lateral tibia was thicker than all other regions ($p < 0.001$).

Discussion

The long-term development of cartilage degeneration remains a concern after ACL reconstruction (Janssen et al., 2013; Salmon et al., 2006). This study used MR imaging and 3D modeling techniques to make site-specific comparisons of femoral and tibial articular cartilage thickness between reconstructed and intact contralateral knees in two ACL reconstruction groups. Our data demonstrates that in the anatomic graft placement group, where kinematics were restored (Abebe et al., 2011b), cartilage thickness was maintained. In the non-anatomic graft placement group, where altered joint kinematics were observed (Abebe et al., 2011b), cartilage thickness significantly decreased on the lateral aspect of the medial femoral condyle.

Abnormal knee motion is believed to be an important factor contributing to the development of OA after ACL reconstruction (Gao et al., 2012; Papannagari et al., 2006; Tashman and Araki, 2013; Tashman et al., 2004). Specifically, recent studies have theorized that abnormal knee motion alters cartilage stress and strain distributions, thus initiating a cascade of degenerative changes (Andriacchi et al., 2004; DeFrate et al., 2006; Li et al., 2006; Tashman et al., 2007; Tochigi et al., 2011). In particular, previous studies have indicated that the medial femoral condyle is a region where degeneration is commonly observed after ACL injury and reconstruction. For example, quantitative MR imaging studies have indicated that ACL reconstructed knees may demonstrate compositional evidence of cartilage degeneration in the medial femoral condyle (Haughom et al., 2012; Li et al., 2011). In this study, we examined a region on the lateral aspect of the medial femoral condyle because it may be at high risk for early degenerative changes (Fairclough et al., 1990; Feagin et al., 1982; Maffulli et al., 2003). One previous study noted the presence of osteophytes on the medial side of the intercondylar notch adjacent to the medial tibial spine in ACL deficient knees (Fairclough et al., 1990). The appearance of osteophytes in this area was thought to be the earliest radiographic sign of ACL deficiency and was hypothesized to be the result of impingement of the medial tibial spine on the medial femoral condyle (Fairclough et al., 1990). In support of this finding, recent studies have identified this area to be a region where high cartilage contact strains were observed in ACL deficient patients (Sutter et al., 2013; Van de Velde et al., 2009). In particular, cartilage contact was shifted closer to the medial tibial spine. This shift was attributed to the altered anterior tibial translation, medial tibial translation, and internal tibial rotations observed in ACL deficient patients (DeFrate et al., 2006; Li et al., 2006; Van de Velde et al., 2009).

The results of the present study are in agreement with these kinematic changes and regions of clinically observed cartilage degeneration. Specifically, in subjects with non-anatomic graft placement, where subjects had abnormal anterior tibial translation, medial tibial translation, and internal tibial rotation (Abebe et al., 2011b), we detected decreased cartilage thickness in the lateral aspect of the medial femoral condyle. In patients who had reconstructions that more closely mimicked normal ACL function (Abebe et al., 2011a) and restored normal knee motion (Abebe et al., 2011b), no changes in cartilage thickness were observed. These findings provide important evidence that abnormal joint motion may contribute to the cartilage degeneration that is frequently observed after ACL reconstruction. Furthermore, these findings suggest that achieving anatomic graft placement may help to restore normal knee function and, ultimately, may help to slow long-term knee degeneration compared to non-anatomic reconstructions. However, these subjects were evaluated at only one time point relatively close to the time of surgery (averages of 18 and 20 months in the non-anatomic and anatomic placement groups, respectively). In this regard, long-term follow-up studies measuring site specific changes in cartilage thickness, as well as MR-based measurements of changes in cartilage composition (Li et al., 2011), would provide

important information regarding the development and progression of post-traumatic osteoarthritis in these patients.

In this study, we used MR imaging to assess localized *in vivo* cartilage morphology after ACL reconstruction. Conventional radiographs of the tibiofemoral joint have been the principal method for quantifying joint space narrowing associated with knee osteoarthritis (Altman and Gold, 2007; Foucher et al., 2012; Kellgren and Lawrence, 1957; Wu et al., 2013). Although radiographic assessments provide important information regarding the progression and severity of osteoarthritis in later stages of the disease, they may be limited in their ability to detect early stages of osteoarthritis due to an inability to directly visualize cartilage (Eckstein et al., 2006). Therefore, directly assessing changes in cartilage morphology using MRI might provide a more sensitive measure of osteoarthritis progression compared to radiographic methods (Raynald et al., 2006). Additionally, the present study suggests that performing site-specific measurements of changes in cartilage thickness might be more sensitive to detecting changes in cartilage morphology than volumetric measurements. For example, we noted a significant decrease of 8% in cartilage thickness in the medial aspect of the intercondylar notch in the reconstructed knees of patients with non-anatomic graft placement. If the thickness of the medial portion of the intercondylar notch were averaged together with that of the rest of the medial femoral condyle, a decrease of only 2% would be detected.

More recently, several studies have used MRI to quantify changes in cartilage volume after ACL injury or reconstruction (Andreisek et al., 2009; Li et al., 2012; Van Ginckel et al., 2013). For example, one recent study compared cartilage volumes and thicknesses in subjects 6 months after ACL reconstruction to matched controls with no injury (Van Ginckel et al., 2013). Although differences in cartilage composition and function were observed between groups, no differences in volume or cartilage thickness were detected. Another study performed quantitative analysis of cartilage thickness using regional cartilage surface segmentation approach and side-to-side comparisons of each knee (Andreisek et al., 2009). Average cartilage thickness was measured on a number of different regions on both the femur and tibia (Andreisek et al., 2009). This study also found no differences in cartilage thickness seven years after ACL reconstruction. However, there are some methodological differences between these studies and the present study that make a direct comparison of results difficult. Specifically, these previous studies performed volumetric or regional cartilage thickness analyses (as opposed to site-specific thickness measurements) and did not report where the graft was placed relative to the ACL footprint.

This study used the contralateral limb as a control rather than healthy limbs from matched subjects. The use of the contralateral limb as a control is supported by a previous study that advocated the use of cartilage parameters from the contralateral limb for retrospectively estimating cartilage loss in patients with unilateral osteoarthritis (Eckstein et al., 2002). Inter-subject variability has been noted to be substantially larger than side-to-side differences in a number of parameters including volume, mean thickness, maximum thickness, and joint surface area (Eckstein et al., 2002). However, to further address this issue, we compared left to right differences in cartilage thickness along the medial intercondylar notch in a group of four male control subjects with no history of knee injury (age range: 20-40 years old). Using an identical methodology as described above, 3D models of both knees were created and registered to each other. Side to side differences in cartilage thickness averaged less than 2% between sides ($p=0.45$, paired t-test). Based on these findings, we believe the contralateral knee to be an appropriate control for site-specific measurements of cartilage thickness in this population.

In conclusion, this study performed site-specific comparisons of femoral and tibial articular cartilage thickness distributions in two groups of patients with ACL reconstructions. Our data demonstrates that in the anatomic graft placement group, where kinematics were restored (Abebe et al., 2011b), no changes in cartilage thickness were detected. In the non-anatomic graft placement group, where altered joint kinematics were observed (Abebe et al., 2011b), cartilage thickness was significantly decreased in the medial aspect of the intercondylar notch. These findings suggest that restoring normal knee motion after ACL injury may help to slow the progression of degeneration. Thus, graft placement may have important implications on the development of osteoarthritis after ACL reconstruction. In the future, long-term follow-up studies are needed to evaluate site-specific changes in cartilage thickness at multiple time points in this patient population.

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Figure 1. Sagittal plane MR images were segmented to create 3D models of the femur, tibia, and articular cartilage.

Figure 2.

A uniform grid of points was created to span the articular surfaces of the femur and tibia. In addition, three points were sampled along the medial intercondylar notch, a region where degeneration is observed clinically after ACL injury (Fairclough et al., 1990).

Figure 3.

Thickness maps of the femur for representative subjects in the anatomic graft placement group (top) and the non-anatomic graft placement group (bottom). In the non-anatomic group, there is thinner cartilage along the medial intercondylar notch in the reconstructed knee compared to the intact knee. In the anatomic group, similar cartilage thickness is observed in this region.

Figure 4.

In the anatomic graft placement group, cartilage thickness was greatest in the lateral tibial plateau. No statistically significant differences in thickness were observed between intact and reconstructed knees. Bars represent mean $\pm$ sem.

Figure 5.

In the non-anatomic graft placement group, cartilage thickness varied with location in the joint, with the lateral tibia (LT) significantly thicker than the medial tibia (MT), medial intercondylar notch (MIN), lateral femur (LF) and medial femur (MF). Significant differences in cartilage thickness were observed along the medial intercondylar notch between intact and reconstructed knees (a decrease of 8%). Bars represent mean $\pm$ sem. (* $p < 0.05$)