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Abnormal Tibial Position is Correlated to Early Degenerative Changes Orene Year Following ACL Reconstruction

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Abstract

Altered knee kinematics following ACL reconstruction may predispose patients to the development of early onset posttraumatic osteoarthritis. The goal of our study was to examine the longitudinal interrelationship between altered tibial position relative to the femur and cartilage health measured by quantitative $T_{1\rho}$ MRI. Twenty-five patients with isolated unilateral ACL injury underwent kinematic and cartilage $T_{1\rho}$ MRI at baseline prior to ACL reconstruction and then at 1-year post-reconstruction. Tibial position relative to the femur in the anterior–posterior plane was calculated as well as cartilage $T_{1\rho}$ relaxation values in the injured and uninjured knee. At baseline prior to ACL reconstruction, the tibia was in a significantly more anterior position relative to the femur in the ACL deficient knee compared to the healthy contralateral knee. This difference was no longer present at 1-year follow-up. Additionally, the side–side difference in tibial position correlated to increased cartilage $T_{1\rho}$ relaxation values in the medial compartment of the knee 1-year post-reconstruction. Altered tibial position following ACL reconstruction is correlated with detectable cartilage degeneration as soon as 1 year following ACL reconstruction. © 2015 Orthopaedic Research Society. Published by Wiley Periodicals, Inc. J Orthop Res 33:1079–1086, 2015.

Keywords

ACL injury; post-traumatic osteoarthritis; knee kinematics; quantitative imaging

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Anterior cruciate ligament injuries are one of the most common ligamentous injuries of the knee, sustained by roughly 1 in 3,000 people per year in the United States.¹ Mostly affecting a young and healthy population, ACL injury leads to pain and instability and can predispose the patient to secondary damage to other structures in the knee such as cartilage and the meniscus.^{2,3} Previous studies have demonstrated that on average, 50% of patients will have radiological evidence of osteoarthritis 10–15 years following initial ACL injury.² Additionally, patients with post-traumatic osteoarthritis are on average 15–20 years younger than patients with primary degenerative osteoarthritis.⁴

Although the cause of this early onset post-traumatic osteoarthritis is not completely understood, altered knee kinematics following ACL injury and reconstruction may play a role in its development. Many different methods, including gait analysis, dual-plane fluoroscopy, and magnetic resonance (MR)-based kinematics, have been utilized to study kinematics in the ACL deficient and reconstructed knee.^{5–8} While ACL reconstruction has been shown to correct knee laxity, studies have demonstrated that tibiofemoral mechanics, such as tibial position, anterior tibial translation, and internal tibial rotation are not restored following ACL reconstruction.^{9–11}

Recent advancements in quantitative magnetic resonance imaging (MRI) provide the ability to reliably detect changes in cartilage structure and health far before radiographic evidence of cartilage damage occurs.^{12–14}Previous work has demonstrated that $T_{1\rho}$ is correlated to the concentration of proteoglycan in the cartilage matrix in histological analysis of bovine^{14,15} and human cartilage specimens.^{16,17} In vivo work has also shown that $T_{1\rho}$ values increase in animal models with cartilage damage,¹⁸ as well in human subjects with osteoarthritis. ^{12,13,19–23} In addition to these cross-sectional studies, a recent longitudinal study demonstrated that $T_{1\rho}$ is predictive of cartilage degeneration progression in knee osteoarthritis,²⁶ suggesting that $T_{1\rho}$ is an indicator of early cartilage degeneration. The goal of our study was to examine the longitudinal interrelationship between altered tibial position relative to the femur and cartilage health as measured by $T_{1\rho}$ MRI in the ACL injured and reconstructed knee. We hypothesize that abnormal tibial position in the ACL reconstructed knee will correlate with increased cartilage $T_{1\rho}$ relaxation times, suggesting decreased proteoglycan content, and thus, cartilage damage 1 year following ACL reconstruction.

METHODS

Subjects

Fifty-six subjects with isolated unilateral ACL injuries were recruited for this study and are currently being followed prospectively. A subset of 25 patients (Table 1) who had completed 1-year follow-up at the time of analysis was analyzed for this study. Patients with other ligamentous injuries, history of inflammatory or primary osteoarthritis, previous knee surgery, or those requiring meniscal repair at the time of reconstruction were excluded from this study. All patients underwent arthroscopic ACL reconstruction by one of three fellowship-trained orthopedic surgeons. Subjects were treated with a standardized post-operative rehabilitation protocol. At enrollment, patients were required to have a healthy contralateral knee with no history of traumatic injury, osteoarthritis, knee surgery, or

previous ligamentous injury. The Institutional Review Board approved this study, and all participants consented to take part.

Imaging ProtocolMR imaging methods previously developed and validated by our group were utilized to evaluate knee kinematics as well as cartilage health.²⁷⁻³⁰ Images were obtained on a 3 T GE MR scanner (General Electric, Milwaukee, WI) using an eightchannel phased array knee coil (Invivo, Orlando, FL). Patients were instructed to rest for 30 min prior to image acquisition in a seated, unloaded state. Both the injured and uninjured knees were scanned prior to ACL reconstruction, and then at 6 months and 1 year following surgery. Cartilage imaging including high resolution 3D fast spin-echo (FSE) images (CUBE) and T_{10} mapping were acquired bilaterally prior to kinematic sequences. The cube imaging parameters included: repetition time (TR)/echo time (TE) 1500/25 ms, field of view (FOV) 16 cm, matrix =384 ×384, slice thickness =1mm. Quantitative cartilage $T_{1\rho}$ parameters included: TR/TE= 9 ms/min full, FOV = 14 cm, matrix = 256×128, slice thickness 4 mm, views per segment = 64, time of recovery 1.2 s, number of slices = 26; time of spin-lock (TSL) 0/10/40/80 spin-lock frequency = 500 Hz.³¹ For kinematic sequences, patients were placed in a previously described custom loading device with an axial load of 25% of the patient's total body mass applied to the plantar surface of the patient's foot (Fig. 1).^{28,30}Patients were scanned in full extension and approximately 30° of knee flexion using T₂-weighted fast spin echo (TR/TE=4000/50.96 ms, FOV cm, 512×256 matrix, slice thickness of 1.5 mm) sequences to assess kinematics. Total scan time including bilateral cartilage $T_{1\rho}$ mapping and T_2 FSE images in extension and flexion was one hour and 30 min and included time to reposition the patient between scan sequences.

Kinematic Data Analysis

In-house software run in MATLAB (MathWorks, Natick, MA) was used to calculate knee kinematic measurements as previously described.^{28,29} Briefly, image segmentation was performed using a spline-based semi-automated segmentation algorithm in MATLAB. Regions of interest, including the tibia and femur were segmented with Bezier splines for each subject in flexion and extension. An automated process was then used to define an arc along the posterior aspect of the medial and lateral condyles of the extended femur. The tibia and femur in the extended position were registered to the tibia and femur in the flexed position using an iterative closest point algorithm. Tibial position relative to the femur in both the extended and flexed states was calculated as the difference between the position of the posterior tibial and epicondylar axis. Aside-to-side difference (SSD) in tibial position defined as the difference between the tibial position in the injured knee and the patient's healthy contralateral knee was calculated to account for physiological variations in tibial position between patients. In order to group all patients together for further analysis, the absolute value of this side-to-side difference (absSSD) was then calculated to measure the distance from the normal tibial position to evaluate the difference in cartilage loading between the reconstructed and normal knees. Previous studies have demonstrated that kinematic measures with these procedures show excellent inter-observer and intra-observer reproducibility of about 0.6–0.9 mm for translational measurements.³⁰

Quantitative Cartilage Analysis

Cartilage $T_{1\rho}$ relaxation times were calculated using previously validated and published methods.²⁹ CUBE images were registered to the $T_{1\rho}$ images with a TSL 0. Cartilage in the medial and lateral compartments was semi-automatically segmented from high-resolution CUBE images using in house software run in MATLAB. Cartilage was further divided into subcompartments to examine the effects of differential loading on cartilage health in weight bearing regions versus non-weight bearing regions (Fig. 2). To ensure consistency in division of subcompartments, the anterior and posterior aspects of the menisci were used as borders to determine cartilage subcompartments. $T_{1\rho}$ relaxation times were calculated with a pixel-by-pixel exponential decay fit of the signal from four registered TSLs. Mean $T_{1\rho}$ relaxation times were calculated for each subcompartment as well as each global compartment. $T_{1\rho}$ quantification has excellent reproducibility with an average coefficient of variation ranging from 1.7% to 8.7% for repeated measures of mean $T_{1\rho}$ values in cartilage. 43

Statistical Analysis

Statistical analysis was completed using Microsoft Excel (Microsoft, Richmond, WA) and SPSS (IBM, Armonk, NY). Spearman's Rho correlation coefficients were calculated between kinematic measurements and cartilage $T_{1\rho}$ values. Paired Student's *t*-test were used to compare the kinematic values and cartilage $T_{1\rho}$ values between baseline and 1 year for the patient's injured/reconstructed knee and normal, contralateral knee. For all statistical analyses, the level of significance was defined as p < 0.05.

RESULTS

Kinematic Analysis

At baseline, prior to ACL reconstruction, the tibia in the injured knee was in a more anterior position relative to the femur in both the extended (by 1.18 ± 2.58 mm; p = 0.019) and flexed states (by 1.63 ± 1.86 mm; p = 0.007) in the ACL deficient knee when compared to the healthy, contralateral knee (Fig. 3). At 6 months post-ACL reconstruction, the tibia was in a more anterior position relative to the femur in both the extended and flexed states in the ACL reconstructed knee, albeit this result was not statistically significant. Similarly at 1 year following ACL reconstruction there was no statistically significant difference in the tibial position on average in the ACL reconstructed knee as compared to the healthy contralateral knee (Fig. 3); however, there was a wide distribution in tibial position (Fig. 5). There was no significant difference in the tibial position in the contralateral knee from baseline, 6 months to 1 year.

Cartilage $T_{1\rho}$ Quantification Analysis

Following acute ACL injury at baseline, $T_{1\rho}$ relaxation times were significantly elevated in the posterior lateral femoral condyle (pLF) and posterior lateral tibial cartilage (pLT) compared to the healthy contralateral knee. The medial tibial (MT) cartilage overall, and the central medial tibial (cMT) and posterior medial tibial cartilage (pMT) subcompartments, showed elevated $T_{1\rho}$ relaxation times in the contralateral knee when compared to the ACL

injured knee (Table 2). At 6 months after ACL reconstruction, $T_{1\rho}$ values continued to be significantly elevated in the pLF and pLT of the injured knee compared to the healthy, contralateral knee. Additionally, there is a significant elevation in the $T_{1\rho}$ value of the posterior medial femoral condyle (pMFC) in ACL reconstructed knee compared to the healthy contralateral knee. At 1 year following ACL reconstruction, $T_{1\rho}$ relaxation values remained elevated in the pLF and pLT when compared to the contralateral side, while there was no significant difference in global MT, cMT, or pMT between sides (Table 2). $T_{1\rho}$ relaxation values were also elevated in the global medial femoral condyle (MFC) and posterior medial femoral condyle cartilage when compared to the contralateral side. At baseline, there was an elevation in $T_{1\rho}$ in the MT compartment of the healthy contralateral knee, although at 1-year post-reconstruction, this significant difference was no longer present.

Correlation Between Kinematics and Cartilage T₁₀ Values

One year following ACL reconstruction the absSSD in tibial position during knee extension correlates with the SSD in cartilage $T_{1\rho}$ values in the MFC cartilage (Rho = 0.446, p = 0.033). This effect was driven by the central medial femoral condyle cartilage subcompartment (cMFC) (Rho = 0.437, p = 0.037) and the pMFC (Rho = 0.422, p = 0.04) (Fig. 4).

When considering the SSD of the tibial position in the extended state, a more posteriorly positioned tibia correlated with a SSD in $T_{1\rho}$ values in the pMFC (Rho = -0.636, p = 0.048). There was a trend towards a significant correlation with an anteriorly position tibia and the SSD of $T_{1\rho}$ in the pMFC (Rho = $0.468 \ p = 0.091$) (Fig. 5). Additionally, an anterior tibial position was correlated to increased cartilage $T_{1\rho}$ in the cMFC (Rho = 0.662, p = 0.01), while there was no relationship between a more posterior tibial position and cartilage health for this compartment. There were no significant correlations between the extended tibial position and the lateral cartilage compartments, or the flexed position with any cartilage compartments. There were no significant correlations between kinematic measurements at 6 months and cartilage $T_{1\rho}$ values at 6 months or 1-year post-ACL reconstruction.

DISCUSSION

The purpose of this study was to evaluate the relationship between knee kinematics and cartilage health using quantitative imaging. Significant correlations were observed between an abnormal position of the tibia following ACL reconstruction and cartilage damage in the MFC. While, on average, the tibial position is restored following ACL reconstruction, those patients with an abnormal position are at higher risk of developing degenerative cartilage changes in the medial compartment of the knee. These findings support our hypothesis, demonstrating a link between abnormal kinematics and osteoarthritis development in the ACL reconstructed knee.

Kinematic changes have been hypothesized as a mechanism to explain the acceleration of degenerative cartilage changes in the ACL injured and reconstructed knee.^{5,32–35} However,

there have been no prospective longitudinal studies that have shown a relationship between altered kinematics and early quantifiable cartilage changes following ACL reconstruction.

In this study, the tibia in the ACL deficient knee was in a significantly more anterior position at baseline compared to that of the healthy contralateral knee. This finding is in agreement with Kvist et al. who demonstrated anterior positioning of the tibia during weight bearing in the ACL deficient knee.³⁶ The restoration of the injured knee's tibial position to that of the patient's healthy contralateral knee following ACL reconstruction was also consistent with previous studies.^{7,37,38} Almekinders et al. demonstrated, that ACL-reconstructed patients who had an irreducible anterior subluxation of the tibia were more likely to have radiographic osteoarthritic changes, possibly suggesting a relationship between an abnormal tibial position and the development of post-traumatic osteoarthritis.¹¹ Furthermore, Andriacchi et al. proposed that altered kinematics initiate a degenerative cascade that leads to a shift in loading to areas where the cartilage cannot accommodate this new loading.³⁴ These reports may explain the relationship between altered tibial position and degenerative changes in the medial compartment of the knee as seen in this study, with a more altered tibial position leading to a pronounced shift in loading patterns. It is likely that any shift in tibial position, whether anterior or posterior as compared to the healthy contralateral knee with an anterior position suggesting laxity while a posterior position suggesting an overconstrained knee, would contribute to altered loading in the knee. From our data we have demonstrated that an abnormal tibial position correlates to quantifiable cartilage degeneration at 1-year post-ACL reconstruction.

While in our analysis we used the absolute value of the side-to-side difference as a means of describing any patients with a shift in tibial position away from normal, there may be a difference in a posterior versus anterior tibial position. The slope of the best-fit line in Figures 4 and 5 for a posterior tibia is steeper as compared to the line for the anterior group, although this was not statistically significant. This trend suggests that patients with an over-constrained knee experience a larger degree of cartilage damage as compared to a neutral or anterior placement of the tibia. Suggs et al. concluded that over-constrained knee kinematics could lead to an increase in contact forces within in the joint, possibly offering an explanation to the differential slopes.³⁹

Using $T_{1\rho}$ MRI, a reliable method to detect early changes in articular cartilage proteoglycan content and hydration, degenerative changes in cartilage health are detectable as soon as 1 year following ACL reconstruction. Following acute ACL injury, $T_{1\rho}$ relaxation values are elevated in the pLT subcompartment, consistent with the bone bruise pattern seen following acute ACL injury.^{40,41,42,44} Previous studies have demonstrated that $T_{1\rho}$ relaxation values are elevated over areas of bone marrow edema, consistent with our results.⁴¹

At 6 months and 1-year post-reconstruction, a significantly elevated side-to-side difference in the $T_{1\rho}$ relaxation values in the medial compartment of the injured knee is observed, specifically in the medial femoral condyle cartilage. This difference was not present prior to ACL reconstruction. These results are consistent with the isolated medial-sided osteoarthritis pattern seen following ACL reconstruction.⁴⁵ The persistence of an abnormal tibial position following ACL reconstruction may explain why rates of post-traumatic osteoarthritis remain

elevated, even after corrective surgery. Although T_{ρ} values were elevated in the lateral compartment of the injured knee at 1 year, these values did not correlate with kinematic measurements. These elevated values may be as a result of the cartilage injury sustained at the time of ACL rupture, while the development of the increased $T_{1\rho}$ in the medial compartment may be as a result of altered postsurgical kinematics.

This study does not come without limitations. The use of the healthy contralateral knee as a control may not represent a truly healthy knee as there may be compensatory changes in this contralateral knee as a result of injury and surgery to their other knee. This may explain the elevated $T_{1\rho}$ values at baseline in the medial tibial cartilage in the healthy contralateral knee, although at 1 year we no longer see this difference. We propose that a temporary compensatory shift in load to the healthy contralateral knee at baseline may explain these elevated $T_{1\rho}$ values. This is further supported by the finding that $T_{1\rho}$ values decreased in the healthy contralateral knee from baseline to 1 year in the medial tibial compartment. However, the use of the contralateral knee may account for physiological variations in cartilage health and knee kinematics that allowed us to measure change from an individual's baseline. In regards to our kinematic measurements, although patients are scanned in a loaded extended and flexed state, this is not a true dynamic kinematic measurement.

The strengths of our study include a longitudinal prospective cohort study design. Additionally, our methods utilize non-invasive techniques to measure both knee kinematic and cartilage health longitudinally. Furthermore, both our kinematic and cartilage $T_{1\rho}$ measurements show good reproducibility. Lastly, the use of quantitative cartilage MRI allows us to detect cartilage changes as soon as 1 year following ACL reconstruction, far before any radiographic evidence of osteoarthritis becomes obvious.

CONCLUSION

Altered tibial position in the ACL reconstructed knee correlates to degenerative cartilage changes in the contacting regions of the medial compartment of the knee as early as 1 year following ACL reconstruction. This relationship suggests that alterations in tibial position following ACL reconstruction is one of the mechanisms for the accelerated degenerative cartilage changes commonly seen following ACL reconstruction. As a part of this longitudinal study, we plan to follow patients out to 3 years post-reconstruction to further characterize the effects of altered kinematics on cartilage health during these time points as well.

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Figure 1.

MR kinematic loading device. The patient is positioned supine on the MR table with an axial load of 25% of body weight through a foot plate.



Figure 2.

The medial and lateral tibial and femoral condyle cartilage was divided into subcompartments to examine regional variations in cartilage health.



Figure 3.

Average tibial position in knee extension and flexion (mm) at baseline, 6 months, and 1-year post-ACL reconstruction. At baseline prior to ACL reconstruction, the tibia is in a more anterior position in both flexion and extension. At 1-year post-ACL reconstruction, there is no significant difference in tibial position in either the flexed or extended states. *p*-value of less than 0.05 denoted with a *.

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Absolute Value of Side to Side Difference in Extended Tibial Position (mm)

Figure 4.

Absolute value of the side to side difference in extended tibial position versus side to side difference in cartilage $T_{1\rho}$ values of the medial femoral condyle (MFC) 1 year following ACL reconstruction (Rho = 0.446, p = 0.033).

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Side to Side Difference in Extended Tibial Position (mm)

Figure 5.

Side-to-side difference in extended tibial position (mm) versus side-to-side difference in cartilage T_{1p} in the posterior medial femoral condyle cartilage (pMFC) 1-year post-reconstruction. Tibial position left of the origin suggests an over constrained knee, while tibial position on the right suggests knee laxity. Patients with a posterior tibial position (Rho=-0.636, *p*=0.048) were more likely to have a larger side-to-side difference in cartilage T_{1p} compared to an anterior tibial position (Rho=0.468, *p*=0.091).

Table 1.

Patient Demographics

	<i>n</i> = 25
	Mean (± SD)
Age	27.7 (7.4)
BMI	23.8 (2.9)
Time to scan (days)	61 (54.5)
Sex	n (%)
Male	12 (48)
Female	13 (52)
Graft type	
Hamstring autograft	17 (68)
Posterior tibial allograft	8 (32)

Table 2.

 $T_{1\rho}$ Relaxation Values (ms) at Baseline, 6 Months, and 1-Year Post-Reconstruction

	LFC		MFC	
	global	pLF	global	pMF
Baseline				
Injured	40.50 ± 3.19	41.05 ± 3.32	40.98 ± 2.62	41.92 ± 3.23
Healthy	40.20 ± 3.21	39.69 ± 2.80	40.31 ± 2.83	41.45 ± 3.06
<i>p</i> -value	0.577	0.036	0.168	0.231
6 month				
Injured	41.02 ± 3.28	41.32 ± 4.16	42.00 ± 3.23	43.06 ± 3.17
Healthy	39.90 ± 2.40	39.46 ± 3.09	40.69 ± 2.91	41.38 ± 2.94
<i>p</i> -value	0.064	0.014	0.062	0.008
1 year				
Injured	41.39 ± 3.31	42.11 ± 3.77	42.04 ± 3.25	43.03 ± 3.85
Healthy	39.42 ± 3.01	38.97 ± 3.56	40.00 ± 3.16	40.70 ± 3.25
<i>p</i> -value	0.014	0.001	0.00	0.004
	LT	Ш		
	pLT	Global	cMT	pMT
Baseline				
Injured	40.62 ± 3.01	35.05 ± 3.99	34.37 ± 4.58	36.10 ± 4.24
Healthy	39.16 ± 3.43	37.05 ± 2.79	36.84 ± 3.72	37.64 ± 3.17
<i>p</i> -value	0.035	0.002	0.003	0.047
6 month				
Injured	41.51 ± 3.05	35.50 ± 3.19	34.71 ± 4.15	36.40 ± 3.31
Healthy	38.93 ± 2.83	36.86 ± 2.91	36.52 ± 4.45	37.31 ± 3.66
<i>p</i> -value	0.002	0.057	0.058	0.249
1 year				
Injured	41.31 ± 2.99	36.73 ± 3.65	36.12 ± 4.21	37.41 ± 4.24
Healthy	38.86 ± 3.25	35.44 ± 3.52	35.01 ± 4.28	35.90 ± 3.85
<i>p</i> -value	0.003	0.127	0.288	0.077