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## Longitudinal Analysis of Tibiofemoral Cartilage Contact Area and Position in ACL Reconstructed Patients

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### Abstract

Patients who have suffered ACL injury are more likely to develop early onset post-traumatic osteoarthritis despite reconstruction. The purpose of our study was to evaluate the longitudinal changes in the tibiofemoral cartilage contact area size and location after ACL injury and reconstruction. Thirty-one patients with isolated unilateral ACL injury were followed with T<sub>2</sub> weighted Fast Spin Echo, T<sub>1p</sub> and T<sub>2</sub> MRI at baseline prior to reconstruction, and 6 months, 1 year, and 2 years after surgery. Areas were delineated in FSE images with an in-house Matlab program using a spline-based semi-automated segmentation algorithm. Tibiofemoral contact area and centroid position along the anterior-posterior axis were calculated along with T<sub>1p</sub> and T<sub>2</sub> relaxation times on both the injured and non-injured knees. At baseline, the injured knees had significantly smaller and more posteriorly positioned contact areas on the medial tibial surface compared to corresponding healthy knees. These differences persisted 6 months after reconstruction. Moreover, subjects with more anterior medial centroid positions at 6 months had elevated T<sub>1p</sub> and T<sub>2</sub> measures in the posterior medial tibial plateau at 1 year. Changes in contact area and centroid position after ACL injury and reconstruction may characterize some of the mechanical factors contributing to post-traumatic osteoarthritis.

### Keywords

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

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Anterior cruciate ligament (ACL) injuries are one of the most common injuries of the knee.

<sup>1,2</sup> Studies have shown a high incidence of early osteoarthritis (OA), or more specifically,

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#### AUTHORS' CONTRIBUTIONS

E.C. participated in data collection, processing, and analysis and also compiled the manuscript. K.A. and V.P. participated in data collection, data processing, and data analysis. Richard Souza provided guidance in data collection and data analysis. X.L. and C.B.M., Co-PI on this project, secured funding, provided guidance on data collection, analysis, and processing.

All authors have read and approved the final submitted manuscript.

posttraumatic OA (PTOA), following ACL injury.<sup>3,4</sup> Like idiopathic OA seen in older individuals, PTOA causes pain, impaired function, and overall decreased quality of life,<sup>5</sup> but PTOA secondary to ACL injuries can affect a much younger population who are otherwise healthy. Investigating how ACL injuries lead to PTOA may have important implications for these young individuals who may face significant cartilage degeneration as a sequelae in the future.<sup>2,6</sup>

Surgical treatment of ACL tears is one of the most common knee surgeries performed on young individuals in the United States.<sup>7</sup> Goals of ACL reconstruction (ACLR) and rehabilitation include restoring biomechanics and stability of the knee joint.<sup>1</sup> However, macroscopic restoration of knee functions may not address slight changes in kinematics that can overtime cause cartilage degeneration, leading to PTOA at a young age.<sup>8,9</sup> These changes have been shown to include the contact area (CA) between the femoral and tibial cartilage surfaces and its overall positioning defined as the centroid position (CP) in ACLR knees compared to contralateral non-injured knees.<sup>10–12</sup> As cartilage on the tibial plateau can vary in thickness and concavity depending on the location, small shifts in loading patterns and location may begin a cascade that can lead to cartilage loss and PTOA.<sup>13</sup>

Because studies have shown that CA and CP are altered in idiopathic OA knees,<sup>14,15</sup> investigating the changes in CA and CP after ACLR may offer more insight to the development of PTOA. Since ACLR is a known risk factor for PTOA, ACL reconstructed knees may develop similar kinematics as idiopathic OA but at a faster rate. Shin et al. showed that subjects with idiopathic OA had medial CA's that were 75–90 mm<sup>2</sup> larger compared to healthy subjects.<sup>14</sup> Also, Subburaj et al. observed similar CA differences as well as a more posterior positioning of CP in idiopathic OA subjects.<sup>15</sup> Interestingly, in ACL deficient knees and at early stages (6-month) after ACL reconstruction, investigators reported decreased CA, which may imply rigid and protective biomechanics for the joint and cause abnormal joint loading, accelerating the joint degeneration.<sup>10,11,16</sup> However, no previous studies reported longitudinal changes of CA and CP after ACL reconstruction. Thus, the ability to quantify longitudinal tibiofemoral contact changes after ACL injury and ACLR can be valuable in determining the potential pathophysiology of PTOA development.

Previous studies have shown magnetic resonance imaging (MRI) assessment of cartilage-to-cartilage contact area is comparable to the established pressure film technique.<sup>17,18</sup> Many researchers have also used advanced imaging techniques to develop 3D models of knees in order to measure the CA and CP.<sup>11,19</sup> However, to our knowledge, there is no technique to assess dynamic CA and CP without the use of cartilage models in vivo directly under load. Moreover, no study has assessed longitudinal information about ACLR knees and correlated their findings to cartilage health years after injury.

Since healthy bilateral knees should have almost identical alignments, we reason that a reliable method is one with margins of error that is below what was detected as the difference between left and right healthy knees. A similar study method performed previously found that the CP difference between healthy knees had a standard deviation of 1.1 mm at extension.<sup>20</sup> Thus, we believe that any deviation more than that can be due to pathology in the knee. We were unable to find reported reproducibility information for CA.

Furthermore, in general, the intra- and inter-user ICC's >0.9 are considered to be excellent reliability.<sup>21</sup> Thus, we believe that our methods can be considered reliable if our error is below 1.1 mm for CP measurement, and intra- and inter-user ICC for both CA and CP measures >0.9.

T<sub>1ρ</sub> and T<sub>2</sub> MRI techniques have been shown to be effective in detecting hydration and molecular changes in cartilage matrices.<sup>22</sup> Specifically, T<sub>1ρ</sub> relaxation times correlated with proteoglycan content while T<sub>2</sub> relaxation times correlated with collagen structure and water content.<sup>23–26</sup> These changes in cartilage composition may indicate early cartilage degeneration and result in elevated relaxation times. Thus, these MRI sequences can help assess whether kinematic changes after ACLR relate to cartilage damages before the clinical onset of PTOA.

The primary aim of this study is to establish a reproducible and reliable method to assess CA and CP in the tibiofemoral joint in vivo using T<sub>2</sub> weighted Fast Spin Echo (FSE) MRI scans of patients undergoing ACLR. We hypothesize that our image processing methodology will have excellent inter- and intra-user reliability. Our secondary aim is to track CA and CP changes over a period of 2 years after ACLR. We hypothesize a smaller CA and a more anterior CP in the injured knee 6 months after ACLR compared to baseline measurements, and increased CA and more posterior CP will be seen 1 year after ACLR. Lastly, this study aims to relate the CA and CP findings with cartilage MR T<sub>1ρ</sub> and T<sub>2</sub> relaxation times mapped to further elucidate potential interrelationship between CA and CP changes, and cartilage degeneration development after ACL injury and reconstruction. We hypothesize that early changes in CA and CP will relate to increased degeneration at later time points.

## METHODS

This is a prospective cohort study (Level of Evidence: II). The Institutional Review Board approved this study and written consent was obtained from all subjects.

### Subjects

Thirty-one adults (Table 1) with unilateral ACL injury with or without concurrent meniscal or other ligamentous injuries were included in this study. Included subjects had healthy contralateral non-injured knees with no history of osteoarthritis, inflammatory diseases, or other knee trauma. The exclusion criteria were concurrent meniscal injury that required repairs, concurrent other ligamentous injuries requiring surgical treatment, prior injury, or surgery to either knee, known history of rheumatoid arthritis or other inflammatory joint diseases, and diagnosis of any form of OA

All subjects underwent arthroscopic single-bundle ACL reconstruction surgery using soft tissue grafts, such as hamstring autograft, hamstring allograft, or posterior tibial allograft. Surgeries were performed by one of four sports medicine fellowship trained orthopaedic surgeons at a single institution, and all subjects underwent standardized rehabilitation post-operation. On average, patients received surgery 54 days after the date of injury.

## Imaging Protocol

Subjects' baseline MRI scans were obtained after acute ACL injury prior to surgery. Follow-up scans were obtained at 6 months, 1 year, and 2 years post ACLR. Subjects' injured and non-injured knees were scanned with a three Tesla MRI scanner (GE Healthcare, Milwaukee, WI) with an 8-channel phased array knee coil (Invivo, Gainesville, FL). Three MR sequences were obtained including (i) high-resolution 3D FSE (CUBE) (TR/TE = 1500/26.69 ms slice thickness of 0.5 mm, field of view of 16 cm,  $384 \times 384$  matrix size, and echo train length 32); (ii) quantitative combined  $T_{1\rho}/T_2$  ( $T_{1\rho}$  Time of Spin Lock [TSL] = 0/10/40/80 ms, slice thickness 4 mm, field of view of 14 cm, matrix size  $256 \times 128$ , spin-lock frequency 500 Hz;  $T_2$  preparation TE, 0/12.87/25.69/51.39 ms); and (iii) sagittal  $T_2$ -weighted non-fat-saturated FSE images (TR/TE = 4000/49.3 ms, slice thickness of 1.5 mm, field of view of 16 cm,  $512 \times 512$  matrix size and echo train length 9). All sequences were obtained with subjects in a full supine position. Sequences (i) and (ii) were obtained first with knee at extension without loading. Then, sequence (iii) was obtained with knees loaded axially with 25% total body weight using a custom apparatus where the weight was applied to the plantar surface of the subject's foot.<sup>27</sup>

## Image Processing

The femur, tibia, and cartilage-on-cartilage CA were segmented on  $T_2$ -weighted FSE images with an in-house MATLAB program (MathWorks, Natick, MA) using a spline-based semi-automated segmentation algorithm.<sup>27,28</sup> Tibiofemoral cartilage CA was defined as the weight bearing regions on the tibial surface where the tibial and femoral articular cartilages were in direct contact. Intra-articular fluid, indicated by regions of hyper-intensity, and cartilage-on-menisci contact regions were excluded from the CA (Fig. 1a). Regions close to the tibial spine were also excluded due to concerns for increased partial volume effects and their little contribution to weight bearing (Fig. 1b). A single observer processed all MR images and delineated the measurements used for longitudinal and cross sectional comparisons.

A tibia-based three-dimensional (3D) coordinate system was established to evaluate CP. The origin was set at the midpoint of the medial-lateral axis draw by the MATLAB program between the two most posterior points in the medial and lateral tibial cortical borders. The superior-inferior axis was set based on the long axis of the tibia, which was also orthogonal to the medial-lateral axis. Lastly, the anterior-posterior axis was set orthogonal to these axes, and negative direction was set toward the anterior position. The 3D coordinate system was set once for each subject based on the non-injured knee at baseline, and all subsequent injured and non-injured knee scans of the same subject were registered onto this baseline scan. Previous study that used this coordinate system's ability to detect anterior tibial translation observed excellent interclass correlations coefficients of 0.89–0.94.<sup>29</sup> Changes along the medial-lateral and superior-inferior axes were not investigated. CP was defined as the distance in the anterior-posterior direction between the centroid of the CA and the origin (Fig. 2). A more negative CP denoted a more anterior position. The centroid was the geometric center of the CA generated from sagittal slice segmentations.

A 3D model of the femur was also established to calculate the femoral inter-condyle distance to estimate the relative bone size. Based on the segmentation of the femoral condyles, spheres were fitted to model the lateral and medial femoral condyles. Two points were defined as the centers of these spheres, and the distance between them were defined as the inter-condyle distance. Subsequent CA and CP measurements were normalized to their relative bone size using this inter-condyle distance.

The  $T_{1\rho}$  and  $T_2$  relaxation times were calculated with methods previously shown to be reliable.<sup>30,31</sup> Briefly, sagittal CUBE images were registered onto the cartilage  $T_{1\rho}$ -weighted images ( $TSL = 0$ ) and used for cartilage segmentation. Using a semiautomatic segmentation program, two major compartments were identified: Medial femoral condyle (MF) and medial tibia (MT). Additionally, each of these compartments were divided into three smaller anterior, central, and posterior regions. Cartilage regions of interest (ROIs) were used to constrain piecewise rigid registration along the different  $T_{1\rho}$ -weighted and  $T_2$ -weighted images. Additionally, all  $T_{1\rho}$  and  $T_2$  echoes of the contralateral and follow-up images were registered to the first  $T_{1\rho}$  echo sequence of the injured knee using an intensity-based method using an elastix ITK library (Open Source Initiative).<sup>32,33</sup> This process was performed to ensure that the same anatomical regions of cartilage were compared during longitudinal analysis.  $T_{1\rho}$  and  $T_2$  relaxation times were determined with a pixel-by-pixel, 2-parameter mono exponential-fitting curve. The  $T_{1\rho}$  and  $T_2$  values of each compartment were computed as the mean of all pixels belonging to the ROI.

### Reliability Assessment

Two researchers (EC) and (KA) served as independent observers. The observers met prior to segmentation to establish a standard operating procedure as stated in the “Image Processing” section. Intra-user reproducibility was assessed by comparing original measurements of 10 cases made by EC with measurements EC yielded from re-processing after at least 2 weeks. To assess inter-user reproducibility, KA re-processed these same 10 cases and KA’s results were compared to EC’s second trial of measurements.

### Statistical Analysis

Statistical analyses were performed using SPSS v23 (IBM, Armonk, NY). Intra and inter-user reliability was measured using the intra-class correlation coefficient (ICC) and coefficients of variation (CV). CA and CP measurements were all normalized based on each subject’s bone size as suggested by their inter-condyle distance before calculations were made (i.e., normalized CA = measured CA/inter-condyle distance). Normalized values were used for all statistical analyses to take into account individual bone size. The averages of absolute differences were also report for comparison to the reproducibility data. A Two-Way repeated measures Analysis of Variance (ANOVA) was performed with injured and non-injured knees as one factor and time as the second factor. Then, a paired Student’s t-test was performed for cross-sectional (injured vs. non-injured contralateral knees) and longitudinal (between different time points) CA and CP differences if the ANOVA was found to be significant. Linear regression models controlled for multiple comparisons were applied to evaluate if CA and CP at 6-month will predict cartilage  $T_{1\rho}$  and  $T_2$  at 1-year, after adjusting for gender, age and BMI. An ad-hocs sub-analyses on subjects with partial lateral

meniscectomies were also performed because it has been reported as a contributor to increased CA.<sup>34</sup> Significance was defined as  $p < 0.05$  for all analyses.

## RESULTS

Fifteen females and 16 males were included in this study with an average age of 29 years (range 16–45). Among them, 21 subjects had hamstring autograft, 1 had hamstring allograft, and 9 had posterior tibialis allograft. Ten subjects had concurrent partial meniscectomies, of which eight subjects had lateral meniscectomy and one had medial meniscectomy, and one subject with both. Table 1 summarizes the demographic and clinical information of the patients at baseline. Due to the small number of medial partial meniscectomy, sub-analysis was performed only for patient with and without lateral partial meniscectomy.

### Reliability of Contact Area (CA) and Centroid Position (CP) Measures

Intra-user and inter-user ICC's were above 0.900 for all measures with averages of coefficients of variance (CV) less than 10% (Tables 2 and 3). The average absolute difference of CA on both sides for intra- and inter-user was less than 10 mm<sup>2</sup> and less than 17 mm<sup>2</sup> (0.201 mm and 0.360 mm normalized), respectively. The average absolute difference of CP on both sides was equal to or less than 1 mm (0.02 normalized) for both intra- and inter-user.

### Contact Area

**Medial**—At baseline, side-to-side comparisons showed that injured knees had significantly smaller CA compared to non-injured knees ( $p = 0.022$ ) (Fig. 3 and Table 4). The injured knees CA at 6 months were also significantly smaller compared to corresponding non-injured knees ( $p = 0.003$ ). The injured and non-injured knees did not have significant changes longitudinally.

**Lateral**—At 1 year, side-to-side comparisons showed injured knees had significantly larger CA compared to non-injured knees ( $p = 0.002$ ). The injured knees CA at 2 years were also significantly smaller compared to corresponding non-injured knees ( $p = 0.027$ ). Longitudinally, the injured knee had significantly larger CA at 1 year compared to baseline ( $p < 0.001$ ) and 6 months ( $p = 0.003$ ) (Table 5). At 2 years, the injured knee CA was also significantly larger than what was observed at baseline ( $p = 0.007$ ) and 6 months ( $p = 0.037$ ). The non-injured knee did not have significant changes throughout the four time points.

Sub-analysis for patients with and without lateral partial meniscectomy showed that the longitudinal changes in the lateral CA was primarily driven by the patients who had lateral partial meniscectomy (Fig. 4). However, the trends between the two groups are parallel. No significant difference was observed in medial CA change pattern between patients with and without lateral partial meniscectomy.

### Centroid Position

**Medial**—The CP of the injured side was more posteriorly positioned at baseline compared to non-injured knees ( $p = 0.001$ ) (Fig. 5 and Table 6). At 6 months, the injured knee CP was

also more posteriorly positioned compared to the non-injured knee ( $p = 0.009$ ). The injured knee did not have significant changes longitudinally. The CP of the non-injured knee was significantly more posterior at 2 years compared to baseline ( $p = 0.031$ ) (Table 7).

**Lateral**—There were no significant differences found in lateral CP between injured and non-injured knees. There were no significant changes longitudinally on either knee.

Sub-analysis for patients with and without partial lateral meniscectomy showed no significant difference in the longitudinal changes of the lateral and medial CP between patients with and without lateral partial meniscectomy.

### T<sub>1ρ</sub> and T<sub>2</sub>

Linear regression analysis showed that subjects with more anteriorly positioned CP on the medial plateau of the injured knee at 6 months had significantly elevated T<sub>1ρ</sub> in the posteromedial tibial compartment (pMT) at 1 year ( $p = 0.044$ ) (Table 8 and Fig. 6). Linear regression also showed that elevated T<sub>2</sub> relaxation times in pMT at 1 year was also seen in subjects with more anteriorly positioned medial CP at 6 month although significance was not reached ( $p = 0.098$ ).

## DISCUSSION

This study aimed to establish a method to reliably measure and track changes in tibiofemoral cartilage CA and CP in ACL injured and subsequently reconstructed patients over a period of 2 years using T<sub>2</sub> weighted FSE MRI. The intra- and inter-user ICC's met standard thresholds of data analysis studies, which consider >0.9 to be excellent reliability.<sup>21</sup> Thus, CA and CP can be measured by outlining cartilage contact region on sagittal MRI images with reproducible results. Moreover, our CP intra- and inter-user average absolute differences were below 1.1 mm, which was the detected standard deviation between opposite healthy knees reported by other studies.<sup>20</sup>

Moreover, we believe that our method measures the tibiofemoral cartilage contact more precisely compared to 3D models using fluoroscopic methods as it directly extrapolated from MR images of in vivo knee joints under weight. A number of 3D cartilage models defined cartilage-to-cartilage contact points based on surface intersections,<sup>11,16,35</sup> but, these models did not consider the cartilage morphology changes under strain and weight bearing, which can alter the amount of cartilage contact.<sup>36</sup> Our current method derived the contact region from direct visualization under dynamic loading, which may describe a more accurate area of the tibiofemoral cartilage contact. This direct visualization also enabled us to consider the irregularities of the contact area to discern a centroid position that may better describe the region where the knee bears the most weight.<sup>13</sup>

Our findings partially supported our second hypothesis that the CA and CP in the injured knee will change after ACLR compared to pre-surgical (baseline) measurements. The lack of significant longitudinal changes in medial or lateral CA and CP between baseline and 6 month after surgery suggests that ACLR did not correct tibiofemoral contact region abnormalities developed after injury. Thus, altered load bearing on tibial cartilage may



continue to be present even after ACLR. Given that the medial CA was significantly smaller in the injured knee compared to the contralateral knee at both baseline and 6 months, it is possible that load was more concentrated on particular sections of the cartilage.<sup>37</sup> This increased pressure on cartilage that may not be adapted to sustain increased load could damage the integrity of the articular cartilage.<sup>38</sup>

Though not statistically significant, we also found that the medial CA of the injured knee had an increasing trend at one year compared to 6 months. A possible reason for the increase may be an increased compressibility of the articular cartilage. Studies have shown that idiopathic OA knees with cartilage degeneration lose cartilage stiffness and increase compression compliance.<sup>39,40</sup> It is possible that ACLR knees are exhibiting increased cartilage compressibility at 1 year after surgery to result in an enlarged CA under loading.

Since normal knee loading is mostly concentrated on the medial side,<sup>19</sup> it was not surprising that the lateral CA of the injured knee did not differ significantly from the non-injured knee at the time of injury and 6 months after ACLR. Beyond the initial 6 months, quadriceps weakness after ACLR had been seen to be related to joint space narrowing, which may increase the cartilage contact on the lateral side.<sup>41</sup> Tourville et al. also found significant joint space narrowing in patients who had deficient knee extension strength after ACL injury and reconstruction.<sup>41</sup> This may explain why risk of lateral cartilage loss doubles 1 year after ACL injury regardless of surgical intervention.<sup>42</sup> However, increases in lateral CA can also be partly attributed to the fact that a subset of subjects also underwent partial lateral meniscectomy. Since partial meniscectomies are known to also change the articular cartilage and knee biomechanics,<sup>43</sup> we cannot definitively discern the primary cause for the CA increase.

We also found that injured knees had more posteriorly positioned medial CP on the tibial surface compared to corresponding non-injured knees. This is consistent with previous studies that investigated tibiofemoral contact area after ACLR.<sup>11,28</sup> Coupled with longitudinally increasing medial CA, the posterior medial tibia may have abnormal stress, possibly resulting in the wearing of the cartilage surface. It is known that cartilage topography varies on the tibial surface.<sup>44</sup> Moreover, Li et al. showed that healthy cartilage contact points are often in regions with thicker cartilage, which can decrease the contact stress.<sup>45</sup> Thus, changes to the position and size of the tibiofemoral cartilage contact can place stress on vulnerable cartilage regions that are not meant for bearing load and cause degeneration.<sup>46</sup>

An unexpected finding was that the medial CP of the non-injured knee was more posterior 2 years after ACLR compared to baseline. It appeared that the injured knee's abnormal kinematics is influencing the non-injured knee. Subjects were perhaps favoring the non-injured knee more after ACLR, and using it in a different manner than before. This finding may be consistent with studies that have found that non-injured knees have increased risk of ACL injury after ACLR of the opposite knee.<sup>47-49</sup>

Our last hypothesis that early changes in CA and CP are related to cartilage degeneration later on was only partially confirmed and in an unexpected manner. Since a more posterior

medial CP provides a direct explanation for cartilage wearing in the posterior tibial plateau, we were surprised to find that subjects with more anterior medial CP at 6 months had worse cartilage health in the posterior medial tibial plateau at 1 year as seen in  $T_{1\rho}$  and  $T_2$  measures. Our data showed a large range of CP at 6 months, suggesting some subjects may have large, clinically relevant changes, while others do not; and its significant correlation with  $T_{1\rho}$  (and  $T_2$  reaching significance) at 1 year could suggest that anterior CP at 6 months was a possible predictor for worse cartilage health at 1 year.

This study has some limitations. First, we had limited power (ranged 0.41–0.68) due to our small sample size. Thus, the statistically significant findings may not be clinically significant. Also, the non-injured contralateral knee may not be the most ideal control, since it would not account for inherent knee characteristics that could increase the chance of ACL injury and PTOA.<sup>5,7</sup> Thus, similarities between injured and non-injured knees cannot be truly defined as being “normal.” However, using non-injured knees can account for between subject variations to provide more robust longitudinal and cross-sectional comparisons. Moreover, this study used static loaded MRI, which is not a complete true representation of walking or other more complex motions.<sup>50</sup> However, it is very difficult to take accurate motion MRI measurements due to decreased resolution.<sup>51</sup> Instead, we scanned the knees at extension to capture them at midstance with loading in attempt to simulate the natural weight bearing aspect of walking. Our CA measurements were also derived from segmentations from the sagittal plane alone, where the medial and lateral borders of the CA could be affected by volume averaging. Also, the CP analyzed in this study is limited to the anterior-posterior axis, which neglects the medial-lateral changes that influence cartilage degeneration. The cartilage contact area changes can be additionally examined by scanning the knee at various knee flexion angles, which were not characterized in this study. Additionally, the current algorithm allowed only the evaluation of tibiofemoral contact biomechanics and we did not investigate concurrent changes in other areas such as femoral patella contact, which could also inform contact changes and will be explored in the future. Lastly, we could only achieve an accuracy of up to 10 mm<sup>2</sup> due to our slice thickness of 1.5 mm. Thus, measurements may be improved by the use of coronal images and decreasing our slice thickness.

Overall, altered CA and CP after ACL injury and reconstruction may be readily measured and assessed using quantitative MR techniques. Our study suggests that changes in CP may represent some of the possible mechanical factors that lead to PTOA. However, it is difficult to conclude exactly how these alterations are affecting the articular cartilage. It appears that factors additional to the CA and CP are contributing to the cartilage wear. Nonetheless, our ability to reliably measure contact area provides the opportunity to advance the investigation into the influence of cartilage contact area and centroid position on PTOA development. As subjects return for their 3 year follow up, we will continue to monitor the effects of acute ACL injury despite reconstruction and see how our current CA and CP results will correlate with the cohort’s future cartilage health.

## Grant sponsor:

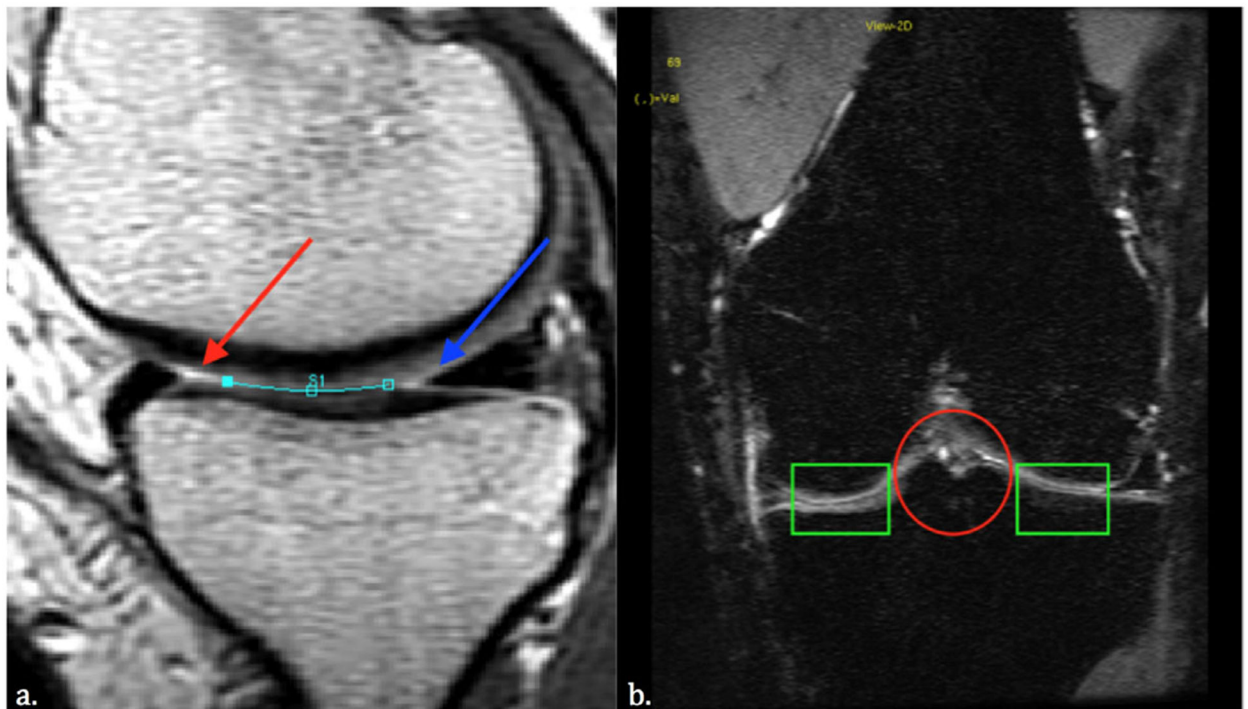
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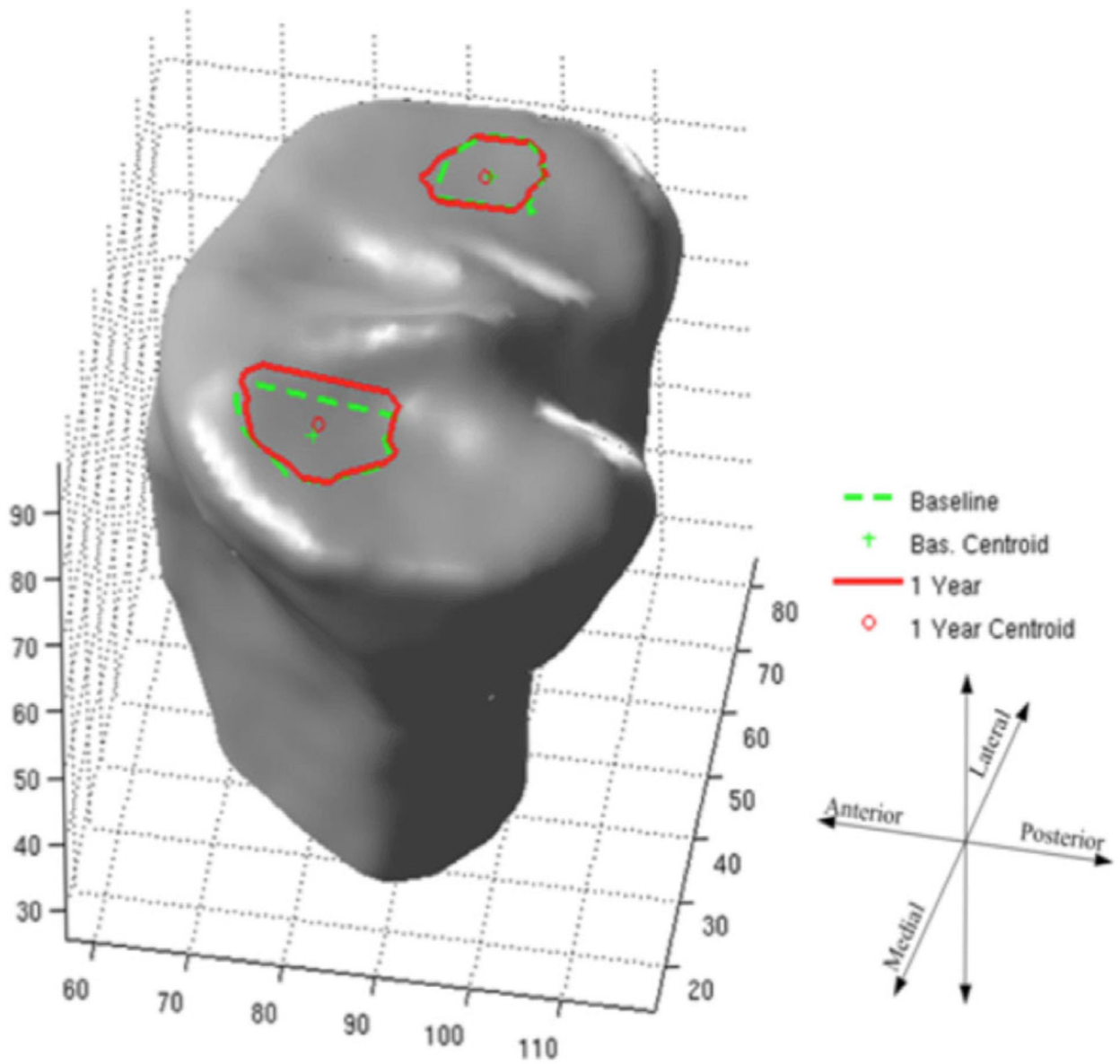
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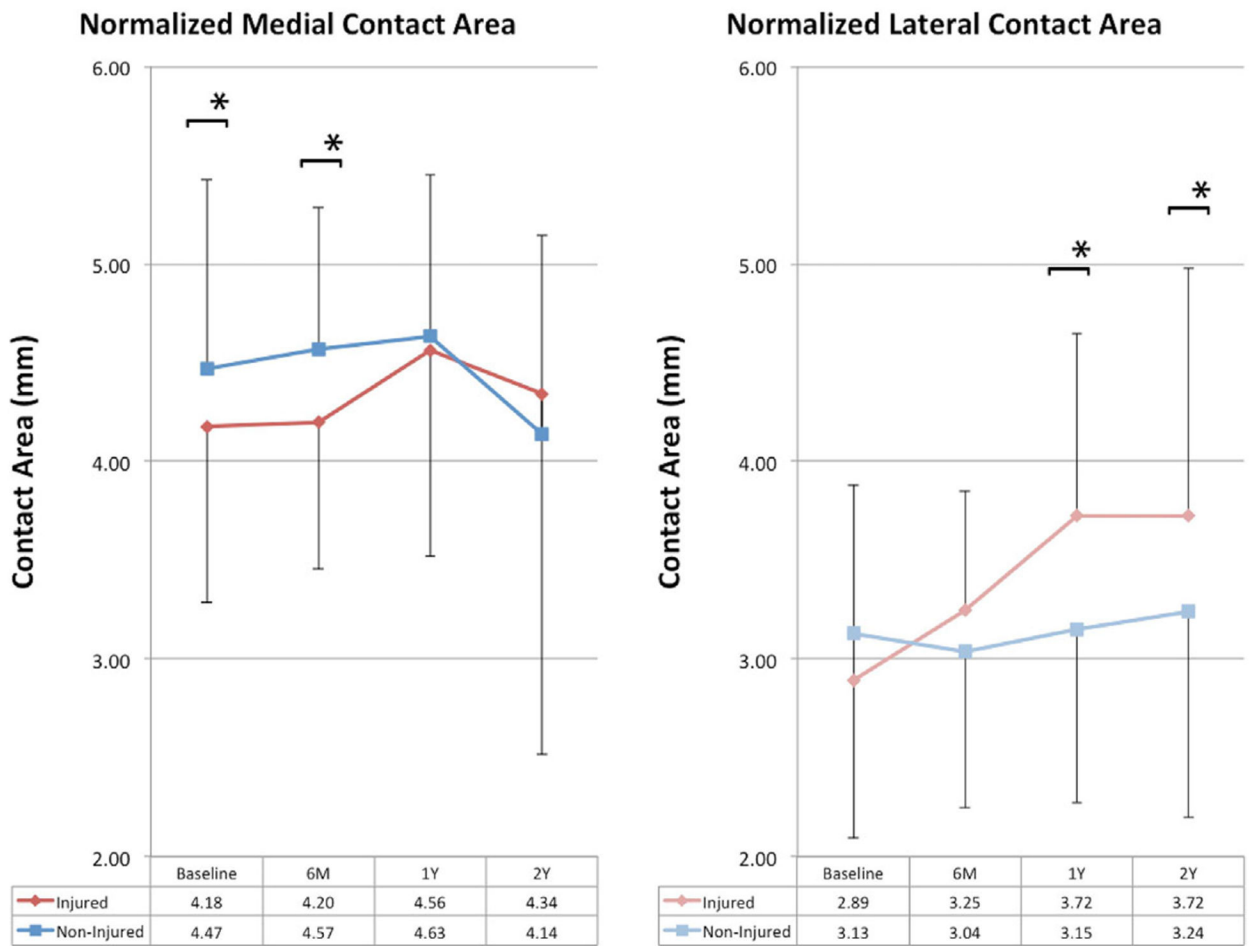
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**Figure 1.** Sagittal and coronal images of knee joint with defined segmented and non-segmented regions. (a) Left arrow: Hyperintensity indicating intra-articular fluid; Right arrow: Cartilage-on-menisci contact. (b) Rectangles: Segmented regions; Circle: Non-segmented region.

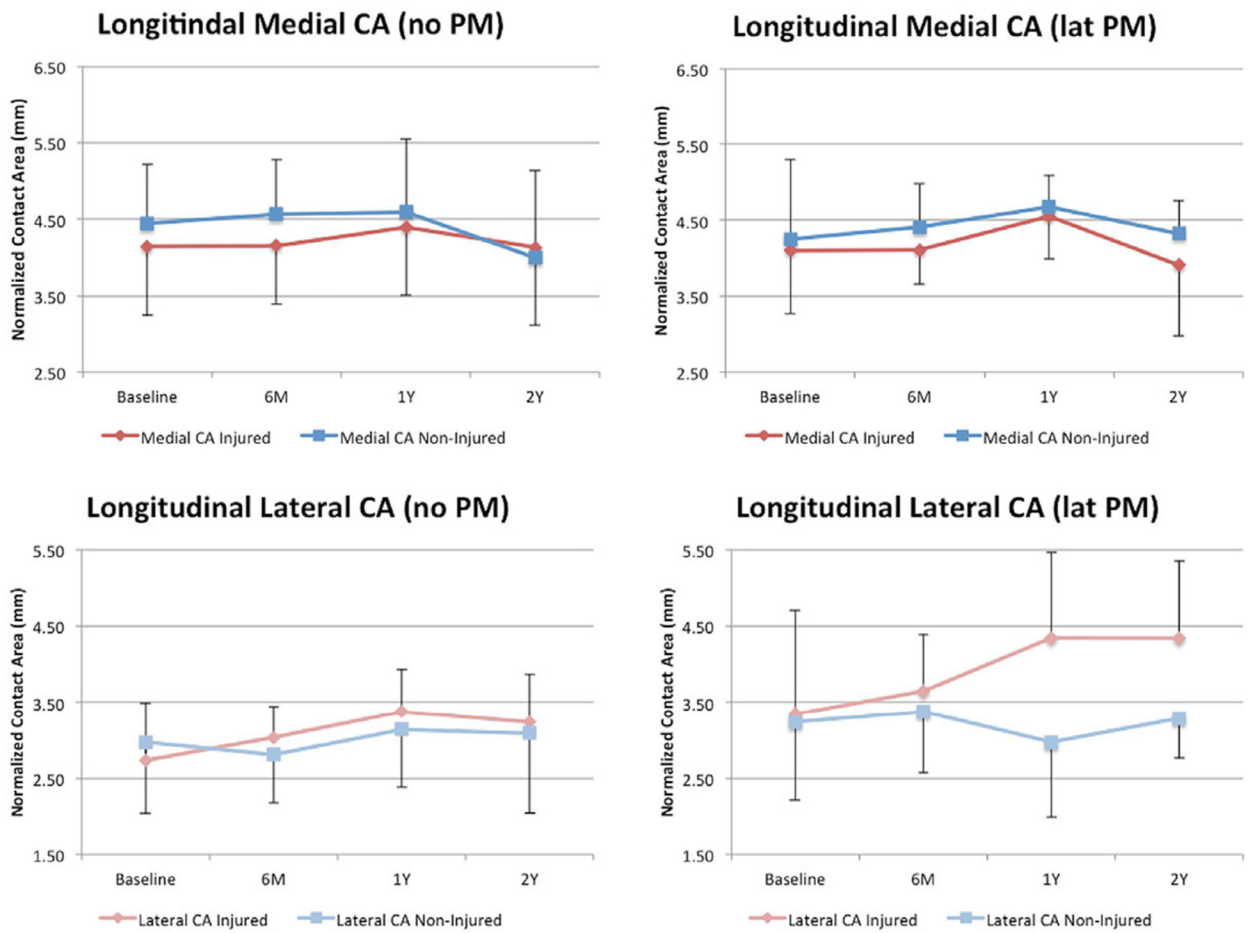


**Figure 2.**  
Contact area and centroid position located on tibial plateau.

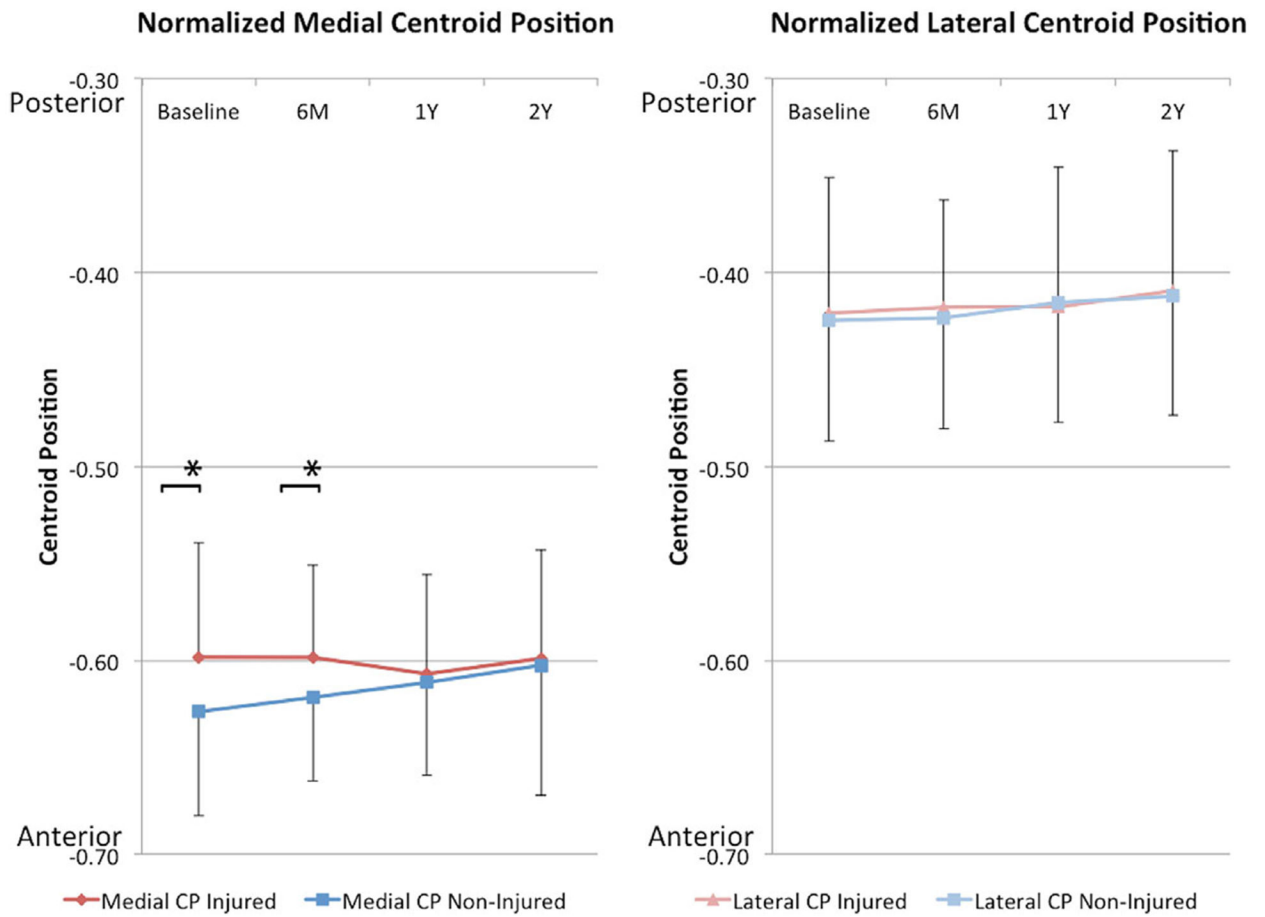


**Figure 3.** Longitudinal changes in tibiofemoral cartilage contact area (statistically significant [ $p < 0.05$ ] between injured [diamond] and non-injured [square] knee). Bars on graph show standard deviation.

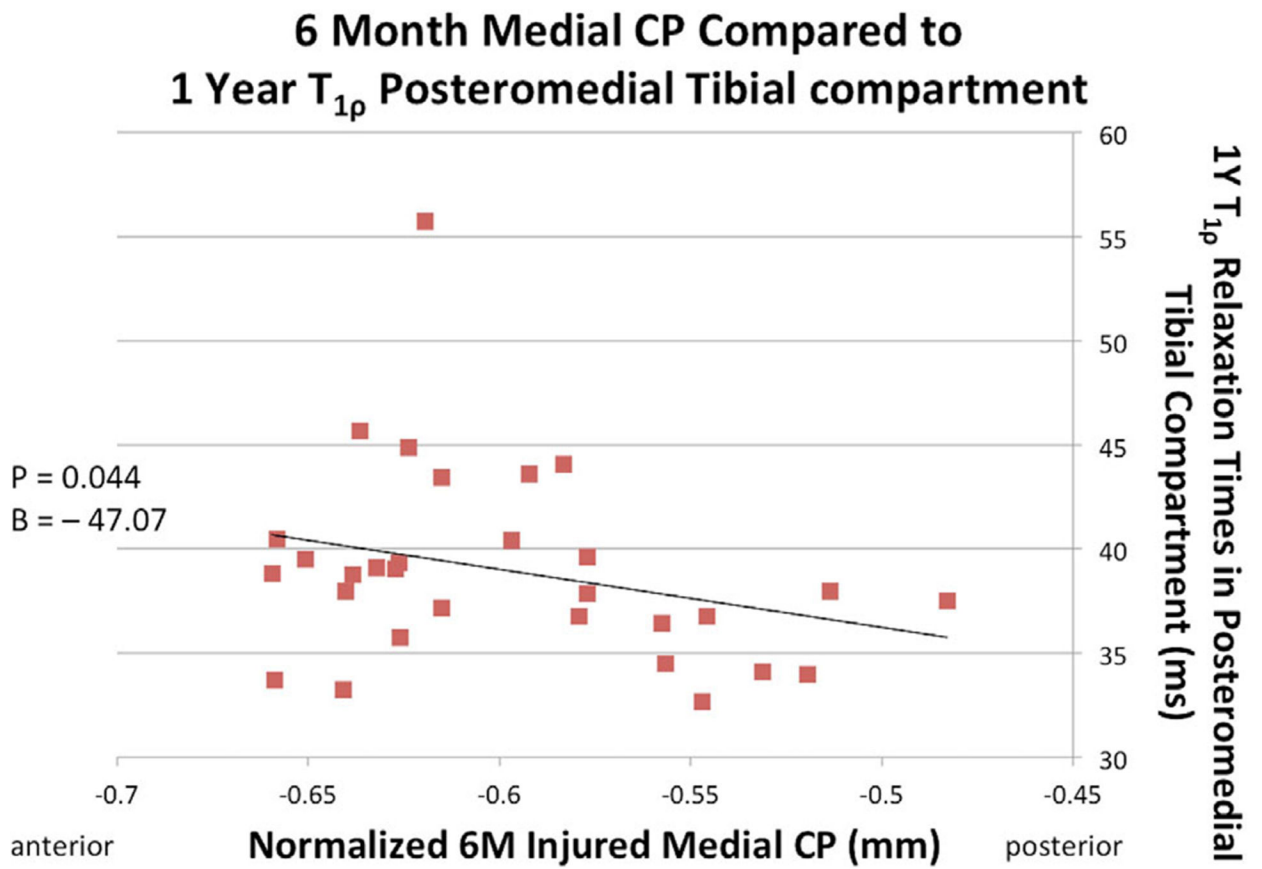




**Figure 4.** Comparison of longitudinal changes in tibiofemoral cartilage CA and CP between subjects with and without Partial Meniscectomy (PM) on the Lateral Side (Bars on graph show standard deviation).



**Figure 5.** Longitudinal changes in tibiofemoral cartilage centroid position (statistically significant [ $p < 0.05$ ] between injured [diamond] and non-injured [square] knee). Bars on graph show standard deviation.



**Figure 6.** Scatterplot of 6 month medial CP compared to 1 year  $T_{1\rho}$  relaxation times in the posteromedial tibial compartment.

Table 1.

## Subject Demographics and Surgical Findings

	Age (Mean $\pm$ SD) years	BMI (Mean $\pm$ SD) kg/m <sup>2</sup>	Hamstring Autograft	Graft Type ( <i>n</i> )			Partial Meniscectomy ( <i>n</i> )		
				Hamstring	Allograft	Posterior Tibial Allograft	Medial	Lateral	Both
Male ( <i>n</i> = 16)	30.06 $\pm$ 8.79	24.90 $\pm$ 2.98	13	0	3	1	6	1	
Female ( <i>n</i> = 15)	28.00 $\pm$ 6.90	22.83 $\pm$ 1.81	8	1	6	0	2	0	
All ( <i>n</i> = 31)	29.06 $\pm$ 7.64	23.90 $\pm$ 2.75	21	1	9	1	8	1	

Table 2.

## Intra-User Reliability

	Contact Area		Centroid Position	
	Medial	Lateral	Medial	Lateral
ICC	0.973	0.973	0.996	0.905
CV <sup>a</sup> (%)	3.1%	6.3%	0.3%	3.3%
Avg. absolute diff.	9.704 mm <sup>2</sup>	9.536 mm <sup>2</sup>	0.144 mm	0.943 mm
Avg. absolute diff. (normalized)	0.202 mm	0.207 mm	0.003	0.010

<sup>a</sup>CV is the average of individual coefficients of variance for each knee.

**Table 3.**

## Inter-User Reliability

	Contact Area		Centroid Position	
	Medial	Lateral	Medial	Lateral
ICC	0.900	0.920	0.991	0.909
CV <sup>a</sup> (%)	5.5%	8.3%	0.6%	3.2%
Avg. absolute diff.	17.064 mm <sup>2</sup>	14.710 mm <sup>2</sup>	0.264 mm	0.922 mm
Avg. absolute diff. (normalized)	0.351 mm	0.311 mm	0.005	0.020

<sup>a</sup>CV is the average of individual coefficients of variance for each knee.

**Table 4.**

## Significant Cross-Sectional CA Changes

	Medial	Lateral
Baseline	-0.29 mm (-0.55 to -0.05)* [-14.30 mm <sup>2</sup> (-26.51 to -2.10)]	-0.23 mm (-0.62 to 0.15) [-12.04 mm <sup>2</sup> (-31.47 to 7.37)]
6 month	-0.37 mm (-0.60 to -0.14)* [-18.32 mm <sup>2</sup> (-29.54 to -7.10)]	0.20 mm (-0.05 to 0.47) [10.33 mm <sup>2</sup> (-2.85 to 23.53)]
1 year	-0.06 mm (-0.50 to 0.36) [-2.69 mm <sup>2</sup> (-24.28 to 18.89)]	0.57 mm (0.23 to 0.92)* [27.95 mm <sup>2</sup> (10.64 to 45.26)]
2 year	0.20 mm (-0.42 to 0.83) [11.22 mm <sup>2</sup> (-21.50 to 43.95)]	0.48 (0.06 to 0.91)* [24.50 m <sup>2</sup> (3.22 to 45.79)]

\* Statistically significant  $p < 0.05$ . Note: Values are reported as normalized average difference (95% confidence interval) followed by (absolute average difference [95% confidence interval]).

**Table 5.****Significant Longitudinal Changes in Lateral CA of Injured Knee**

	<b>6 Months</b>	<b>1 Year</b>	<b>2 Years</b>
Baseline	0.35 mm (0.03 to 0.67)	0.83 mm (0.52 to 1.14)*	0.83 mm (0.036 to 1.30)*
6 months	[17.28 mm <sup>2</sup> (1.93 to 32.62)]	[40.72 mm <sup>2</sup> (24.78 to 56.67)]	[41.12 mm <sup>2</sup> (16.13 to 66.11)]
1 year		0.48 mm (0.23 to 0.73)*	0.48 mm (0.15 to 0.81)*
		[23.44 mm <sup>2</sup> (10.75 to 36.13)]	[23.84 mm <sup>2</sup> (6.03 to 41.64)]
		-0.00 mm (-0.31 to 0.31)	-0.00 mm (-15.56 to 16.35)]

\* Statistically significant  $p < 0.05$ . Note: Values are reported as normalized average difference (95% confidence interval) followed by (absolute average difference [95% confidence interval]).



**Table 6.**

## Significant Cross-Sectional CP Changes

	Medial	Lateral
Baseline	0.03 (0.01 to 0.04)*	0.00 (-0.01 to 0.01)
6 months	0.02 (0.01 to 0.04)*	0.01 (0.00 to 0.02)
1 year	0.00 (-0.01 to 0.02)	0.00 (-0.01 to 0.01)
2 years	0.00 (-0.01 to 0.01)	0.01 (-0.01 to 0.03)
	[1.37 mm (0.65 to 2.08)]	[0.01 mm (-0.59 to 0.61)]
	[0.93 mm (0.21 to 1.64)]	[0.44 mm (-0.03 to 0.91)]
	[0.20 mm (-0.43 to 0.82)]	[0.09 mm (-0.56 to 0.73)]
	[0.14 mm (-0.84 to 1.12)]	[0.29 mm (-0.59 to 1.18)]

\* Statistically significant  $p < 0.05$ . Note: Values are reported as normalized average difference (95% confidence interval) followed by (absolute average difference [95% confidence interval]).

**Table 7.****Significant Longitudinal Changes in Lateral CP of Non-Injured Knee**

	<b>6 Months</b>	<b>1 Year</b>	<b>2 Years</b>
Baseline	0.00 (-0.02 to 0.03)	0.01 (-0.02 to 0.04)	0.02 (0.01 to 0.04)*
6 months	[0.03 mm (-1.31 to 1.37)]	[0.41 mm (-1.02 to 1.84)] (0.00 to 0.02)	[1.1.6 (0.38 to 1.93)] 0.01 (-0.01 to 0.03)
1 year		[0.38 mm (-0.20 to 0.96)]	[0.58 mm (-0.30 to 1.45)] 0.00 (-0.02 to 0.02) [0.20 mm (-0.67 to 1.07)]

\* Statistically significant  $p < 0.05$ . Note: Values are reported as normalized average difference (95% confidence interval) followed by (absolute average difference [95% confidence interval]).

**Table 8.**Six Month Medial CP Compared to 1 Year T<sub>1p</sub> and T<sub>2</sub> in the Posteromedial Tibial Compartment

	Standard Error	B	p-Value
T <sub>1p</sub>	21.85	-47.07*	0.044
T <sub>2</sub>	12.15	-21.10	0.098

\* Statistically significant ( $p < 0.05$ ). Note: Analysis performed with linear regression models.

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