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## Persistent Underloading of Patellofemoral Joint following Hamstring Autograft ACL Reconstruction is Associated with Cartilage Health

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### Abstract

**Objective**—To determine the longitudinal changes of patellofemoral joint (PFJ) contact pressure following anterior cruciate ligament reconstruction (ACLR). To identify the associations between PFJ contact pressure and cartilage health.

**Design**—Forty-nine subjects with hamstring autograft ACLR (27 males; age 28.8 [SD 8.3] years) and 19 controls (12 males; 30.7 [4.6] years) participated. A sagittal plane musculoskeletal model was used to estimate PFJ contact pressure. A combined T<sub>1ρ</sub>/T<sub>2</sub> magnetic resonance sequence was obtained. Assessments were performed preoperatively, at 6 months, 1, 2, and 3 years postoperatively in ACLR subjects and once for controls. Repeated ANOVA was used to compare peak PFJ contact pressure between ACLR and contralateral knees, and t-tests to compare with control knees. Statistical parametric mapping was used to evaluate the associations between PFJ contact pressure and cartilage relaxation concurrently and longitudinally.

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Author contributions

TCL, RB, and VP provided conception and design of the manuscript as well as interpretation of the data. TCL, AB, and MS performed the analysis and assembly of data. Drafting of the article was mainly done by TCL. All authors contributed to critical revision and final approval of the article.

Conflict of interest

There are no conflicts of interest to disclose.

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**Results**—No changes in peak PFJ contact pressure were found within ACLR knees over 3 years (preoperative to 3 years, 0.36 [CI, -0.08, 0.81] MPa), but decreased over time in the contralateral knees (0.75 [0.32, 1.18] MPa). When compared to the controls, ACLR knees exhibited lower PFJ contact pressure at all time points (at baseline, -0.64 [-1.25, -0.03] MPa). Within ACLR knees, lower PFJ contact pressure at 6 months was associated with elevated  $T_2$  times ( $r=-0.47$  to  $-0.49$ ,  $p=0.021$  to  $0.025$ ).

**Conclusions**—Underloading of the PFJ following ACLR persists up to 3 years and has concurrent and future consequences in cartilage health. The non-surgical knees exhibited normal contact pressure initially but decreased over time achieving limb symmetry.

### Keywords

anterior cruciate ligament reconstruction; cartilage relaxation times; hamstring autograft; osteoarthritis; contact pressure

## Introduction

Anterior cruciate ligament (ACL) tear is a common sports-related injury, with an estimated 20,000 ACL injuries occurring annually in the United States,<sup>1</sup> and as many as 80% of patients opting for ACL reconstruction (ACLR).<sup>2</sup> Despite undergoing reconstruction surgery, there is growing evidence suggesting a link between post-traumatic osteoarthritis (OA) and ACL dysfunction. Radiographic patellofemoral joint (PFJ) OA has been reported in 11 to 90% (median 36%) of subjects 2 to 15 years after the surgery,<sup>3-6</sup> while worsening of cartilage defects as seen on magnetic resonance (MR) imaging in the patellofemoral compartment occurred in 44% of subjects 5 years following surgery.<sup>6</sup> The high prevalence of PFJ OA in this population stresses the importance of understanding its disease mechanisms, and the risk factors leading to development of disease.

Early stages of OA in the articular cartilage include a failure to synthesize the extracellular matrix components, loss of proteoglycans, collagen and thus elasticity and reduction in water content.<sup>7</sup> Quantitative MR imaging offers tools to probe the biochemical composition of articular cartilage.  $T_{1\rho}$  and  $T_2$  relaxation times are related to the proteoglycan content and collagen orientation of the cartilage, respectively, and can thus provide information on the state of cartilage health.<sup>8</sup> Elevated  $T_{1\rho}$  and  $T_2$  relaxation times have been associated with the development of knee OA<sup>9, 10</sup> and may present as biomarkers for early cartilage degeneration.<sup>11</sup> In particular, elevated  $T_2$  times in the trochlear cartilage has been found in ACLR knees when compared to the contralateral non-surgical knees 3 years following ACLR.<sup>12</sup> In addition, higher cartilage  $T_{1\rho}$  and  $T_2$  times have been found in ACLR knees when comparing to controls, and they remain elevated over time.<sup>13</sup>

When considering the factors contributing to the high PFJ OA prevalence post ACLR, several biomechanical factors come into play, one of which is the altered patellar kinematics following ACLR. Several studies have reported greater patella lateral displacement and lateral tilt in ACLR knees when compared to contralateral and control knees,<sup>14, 15</sup> all of which have been linked to common PFJ disorders such as patellofemoral pain and chondromalacia.<sup>16, 17</sup> With faulty patellar kinematics, it is likely that ACLR knees exhibit

altered PFJ loading behaviors that further influence cartilage integrity and joint health. Limited in vivo studies have found a lower PFJ peak contact forces and stress in ACLR knees<sup>18, 19</sup> while one study found the opposite,<sup>20</sup> with the assessment time ranging from at the time of return-to-sports and 12 to 24 months post ACLR. It is unclear if PFJ loading behaviors following ACLR change over time, resulting in the discrepancy between studies.

Taken together, the joint loading behaviors in PFJ following ACLR are unclear and may be subjected to changes over time. Additionally, to the best of our knowledge, there is no study that has examined the association between PFJ OA features and joint loading behaviors in individuals following ACLR. As such, the aims of this study are twofold. First, to determine the longitudinal changes in PFJ contact pressure in individuals following ACLR and to compare these variations, if present, with the non-surgical contralateral knees and control knees. Second, to identify associations between PFJ contact pressure and cartilage relaxation times at 6 months and 3 years following ACLR.

## Methods

This is an observational cohort study.

### Subjects

Subjects between the ages of 15 and 50 years who underwent unilateral hamstring autograft ACLR were recruited from the Sports Medicine clinics in the Department of Orthopaedic Surgery at the University of California, San Francisco (UCSF) between July 2011 and May 2017.<sup>13, 21–23</sup> The study was approved by the Committee of Human Research at UCSF and prior to data collection, all subjects signed a written informed consent. The exclusion criteria were (1) concomitant ligamentous injuries that needed surgical treatment, (2) a history of inflammatory or primary OA, (3) previous knee surgery, and (4) meniscal repair required at the time of ACLR, as meniscus tears have been shown to be a risk factor associated with the development of OA following ACLR.<sup>24</sup> ACLR subjects were invited for assessments preoperatively, and at 6 months, 1 year, 2 years, and 3 years postoperatively. Additionally, 19 controls with no history of knee injuries or surgeries were recruited and assessed at one time point. Of all 57 ACLR and 21 control subjects recruited, five and three subjects from each group dropped out, respectively. Three additional subjects were excluded in the ACLR group as they received a cadaver allograft instead of hamstring autograft. In total, forty-nine ACLR and 19 controls were included in the baseline analysis (Figure 1).

All ACLR subjects underwent anatomic single-bundle hamstring autograft by 1 of 3 board-certified, fellowship-trained orthopedic surgeons at a single institution. The femoral tunnels were drilled using anteromedial portal drilling. All ACLR subjects had the same fixation method with suspensory femoral fixation and interference screw tibial fixation. All ACLR subjects participated in standard post-operative ACL rehabilitation program. Immediately post-operative recovery emphasized control of pain and swelling, and regaining motor control. The operative knee was kept in a hinged knee brace at all times, which was locked in extension while walking (except during physical therapy sessions) until quadriceps control and normal gait were achieved. The primary focus for the first 6 weeks was on return of normal range of motion and quadriceps control. Return to running was allowed at

approximately 4 months, when core stability was appropriately achieved, and return to sport at 6 to 8 months, as long as the subject had achieved appropriate functional milestones.

### Patellofemoral Joint Contact Pressure

All biomechanical testing was performed in the Human Performance Center at UCSF. Three-dimensional lower extremity position data were collected at 250 Hz using a 10-camera motion analysis system (VICON, Oxford Metrics, Oxford, UK), while ground reaction forces were recorded at a rate of 1000 Hz using two in-ground force plates (AMTI, Watertown, MA, USA) simultaneously.

Nineteen reflective markers were placed on the following bony landmarks: first and fifth metatarsal heads, medial and lateral malleoli, medial and lateral femoral epicondyles, greater trochanters, iliac crests, anterior superior iliac spines, and the L5-S1 junction. In addition, segment tracking was performed using marker clusters mounted on semi-rigid plastic plates and were placed on the lateral surfaces of the subjects' thighs, shanks, and heel counters of the shoes. Following a one-second standing calibration trial, subjects were asked to perform over-ground walking at a fixed speed of 1.3 m/s as this is the average smooth surface walking speeds of men and women.<sup>25</sup> Practice trials were permitted to allow subjects to become familiar with the procedures. Three successful walking trials were obtained. A successful trial was defined as the foot of the tested limb falling within the borders of the force plate and the speed was within  $\pm 5\%$  of the target speed. Two timing gates were used to confirm the speed of each trial. Feedback on gait speed was given immediately after each trial with "too fast" or "too slow" in order for the subjects to achieve target speed.

Marker position and ground reaction force data were low-pass filtered using 4<sup>th</sup> order, zero lag, Butterworth filters with cut-off frequencies of 6Hz and 50Hz, respectively, using Visual3D (C-Motion, Germantown, MD). Knee flexion angles and internal knee extensor moments during the stance phase of gait were derived from the biomechanical testing through Cardan rotation sequence and inverse dynamics, respectively, and used as inputs to estimate PFJ contact pressure. The stance phase of gait was defined when the foot hit the ground and the vertical GRF was greater than 20N (initial contact) to the time point where the vertical GRF was less than 20N (toe-off).

PFJ contact pressure was computed using a previously described sagittal plane motion analysis-based model<sup>26, 27</sup> with subject-specific inputs (knee flexion angle and knee extensor moments) and data from literature (quadriceps effective moment arm,<sup>28</sup> ratio between quadriceps force and PFJ reaction force,<sup>29</sup> PFJ contact area<sup>30</sup>). First, quadriceps effective moment arm was estimated as a function of knee flexion angle by fitting a nonlinear equation.<sup>28</sup> Next, quadriceps muscle force was calculated dividing knee extensor moment by the effective moment arm. The next step was to multiply the quadriceps force to a coefficient that determines the relationship between quadriceps force and PFJ reaction force as a function of knee flexion angle.<sup>29</sup> Next, PFJ contact area was estimated as a function of knee flexion angle by fitting a second-order polynomial curve.<sup>30</sup> Last, joint reaction force was divided by contact area to estimate PFJ contact pressure. Peak PFJ contact pressure (MPa) during the first 50% of the stance, where the peak usually occurs,<sup>26</sup> was used for statistical analysis.

## MR Imaging Assessment

All subjects underwent bilateral knee MR imaging using a 3.0T GE MR scanner (General Electric, Milwaukee, WI, USA) with a quadrature transmit and 8-channel receive knee coil (Invivo, Inc., Gainesville, FL) at each assessment. The subject was instructed to lay fully supine with knee extended in a resting position. MR sequences included a sagittal high-resolution 3D intermediate-weighted FSE CUBE sequence for cartilage segmentation (TR/TE = 1500/25 ms, FOV = 16 cm, matrix = 384 × 384, slice thickness = 1 mm) and a sagittal combined 3D T<sub>1ρ</sub>/T<sub>2</sub> mapping sequence<sup>31</sup> (T<sub>1ρ</sub> TR/TE = 9 ms/min, 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 ms, spin-lock frequency = 500 Hz; T<sub>2</sub> preparation TE = 0/12.87/25.69/51.39 ms).

Image post-processing for obtaining VBR was performed in MATLAB integrated with Elastix registration toolbox for non-rigid image registration,<sup>32, 33</sup> using a previously described methodology.<sup>22</sup> A single reference image was identified through an iterative process aimed to minimize the global image deformation. All images were then non-rigidly registered and aligned to the single reference image. Relaxation maps were computed on a voxel-by-voxel basis by fitting the morphed images from different TSLs or TEs, for T<sub>1ρ</sub> or T<sub>2</sub> respectively, employing Levenberg-Marquardt mono-exponentials applied to each voxel ( $S(\text{TSL}) \propto \exp(-\text{TSL}/T_{1\rho})$ ) for T<sub>1ρ</sub> and ( $S(\text{TE}) \propto \exp(-\text{TE}/T_2)$ ) for T<sub>2</sub>.

## Statistical Analysis

To examine the longitudinal changes within the ACLR group, two-way repeated ANOVA (limb × time) was used to examine peak PFJ contact pressure between the ACLR and contralateral knees over time (preoperatively, and at 6 months, 1 year, 2 years, and 3 years postoperatively). If significant interaction existed, one-way repeated ANOVA would be used to examine peak PFJ contact pressure over time in the ACLR and contralateral knees. Paired t-tests were used to examine pressure between ACLR and contralateral knees at various time points. Last, independent t-tests were used to examine pressure between ACLR and control, as well as contralateral and control knees, individually.

Within the ACLR knee, statistical parametric mapping was used to evaluate the associations between peak PFJ contact pressure at 6 months and cartilage relaxation times at 6 months and 3 years using Pearson partial correlations on a voxel-by-voxel basis. Percentage of voxels showing significant correlation (PSV), average correlation coefficient ( $r$ ) of voxels showing significant correlation, and average p values of voxels showing significant correlation were reported from the statistical parametric mapping. Only results with PSV more than 8% of the voxels were considered to provide more clinically significant patterns.<sup>34</sup> Random Field Theory correction was used to take into account possible false positives due to multiple comparisons.<sup>35</sup> Thresholds for both cluster-defining and cluster-inference were set at 0.05. In addition, a 3×3 spatial smoothing filter was used. Statistical parametric mapping was performed using in-house developed MATLAB scripts with the covariates of sex, age, and body mass index. The statistical analyses were performed through SPSS 28.0.0.0. The alpha value was set at 0.05.

## Results

Forty-nine subjects with ACLR (27 males, 28.8 [95% CI 26.5, 31.1] years) and 19 controls (12 males, 30.7 [28.6, 32.9] years) participated in the study. Number of subjects at each follow-up were reported in Figure 1. Demographics of the ACLR subjects and controls are presented in Table 1. Time since ACL injury to preoperative assessment was reported an average of 70.5 [56.0, 86.9] days. When comparing peak PFJ contact pressure within the ACLR group, a significant limb and time interaction was found ( $p < 0.001$ , partial  $\eta^2 = 0.190$ ) (Figure 2). Post-hoc one-way repeated ANOVA revealed that no changes in peak PFJ contact pressure was observed in ACLR knees ( $p = 0.173$ ), whereas PFJ contact pressure decreased over time in the contralateral non-surgical knees ( $p < 0.001$ , partial  $\eta^2 = 0.191$ ). Specifically in the contralateral knees, peak PFJ contact pressure was significantly lower at 2 years and 3 years postoperatively when compared to preoperatively and at 6 months ( $p = 0.009$  to  $0.027$ , Cohen's  $d = 0.586$  to  $0.639$ ). When compared between ACLR and contralateral knees, peak pressure was significantly lower in the ACLR knees at preoperatively, at 6 months and 1 year postoperatively ( $p = <0.001$  to  $0.015$ , Cohen's  $d = 0.979$  to  $1.128$ ). When compared to the controls, ACLR knees exhibited lower PFJ contact pressure at all time points ( $p = 0.001$  to  $0.023$ , Cohen's  $d = 0.646$  to  $0.920$ ). In contrast, contralateral knees exhibited lower PFJ contact pressure at 2 years and 3 years when compared to the controls ( $p = 0.011$  and  $0.007$ , Cohen's  $d = 0.676$  and  $0.751$ , respectively). Table 2 shows the peak PFJ contact pressure in all groups over time, as well as the between-group and within-group means.

Table 3 and 4 show the cartilage relaxation times in all group over time. Results of the statistical parametric mapping that evaluated the correlations between peak PFJ contact pressure with cartilage relaxation times concurrently at 6 months revealed that lower contact pressure was associated with elevated  $T_2$  times at the patellar cartilage (PSV = 14.1%,  $R = -0.45$ ,  $p = 0.020$ ) (Table S1). Longitudinal assessment revealed that lower PFJ contact pressure at 6 months was associated with elevated  $T_2$  times at the patellar (PSV = 9.0%,  $R = -0.49$ ,  $p = 0.021$ ) and trochlear cartilage (PSV = 11.2%,  $R = -0.47$ ,  $p = 0.025$ ) at 3 years, where the associations were mostly found in the lower portion of the patellofemoral compartment (Figure 3). No associations were found between peak PFJ contact pressure and  $T_{1\rho}$  times at any time points.

## Discussion

The purpose of this study was to evaluate the longitudinal changes in PFJ contact pressure preceding and following ACLR and its association with cartilage health. The results indicated that underloading of the PFJ following ACLR persists up to 3 years and has concurrent and future consequences in cartilage health. More specifically, peak PFJ contact pressure during walking in ACLR knees did not change over time, however the contact pressure was lower when compared to controls at all time points. On the contrary, peak PFJ contact pressure in the nonsurgical contralateral knees were comparable to controls at initial assessments, but decreased over time and reached limb symmetry. The association analysis revealed that lower peak PFJ contact pressure at 6 months postoperatively was associated



with elevated  $T_2$  times at 6 months and 3 years. No associations were found for  $T_{1\rho}$  times with PFJ contact pressure.

Our results that ACLR knees exhibit lower PFJ contact pressure were consistent with previous findings,<sup>18, 19</sup> suggesting that the integrity of ACL not only affects tibiofemoral joint function but also the PFJ. The current study reported averages of 2.5 to 2.8 MPa peak PFJ contact pressure during walking in ACLR knees throughout all time points assessed. The pressure magnitude was less than the average 4.6 MPa reported in individuals at 3 months following ACLR.<sup>18</sup> However, it should be noted that PFJ contact pressure was estimated during walking in the current study while the previous study estimated pressure during a single leg squat, which requires higher knee joint demands.

The results indicated that PFJ contact pressure in ACLR knees remained stable over time and showed approximately 35.7% less pressure than controls. The persistent lower PFJ contact pressure preceding and following ACLR suggests that altered PFJ loading behaviors occur at the time of the ACL injury, and while reconstruction may restore the stability of the knee, it does not restore the altered kinetics during walking in the PFJ. While altered PFJ loading is multifactorial, some of the factors attributing to lower PFJ loading are altered patellar and knee kinematics, patellar contact area, and quadriceps forces.<sup>36, 37</sup> In our simplified sagittal model, PFJ contact pressure is the product of knee flexion angle and knee extensor moments. In our post-hoc analysis, we indeed found both knee flexion angle and knee extensor moments at the time of peak PFJ contact pressure to be lower at all time points in ACLR knees ( $p$  ranged from  $<0.001$  to  $0.016$ ), except knee flexion angle preoperatively ( $p = 0.437$ ) when compared to the controls (Table 5). These altered tibiofemoral biomechanics have previously been reported in individuals following ACLR and are possibly due to pain avoidance<sup>38</sup> and become a learned behavior when the pain subsides.

It is not surprising to observe a higher PFJ contact pressure in the non-surgical knees as compared to ACLR knees preoperatively and at initial follow-ups, which is consistent with previous studies.<sup>18, 19</sup> However, to our surprise, peak PFJ contact pressure in the non-surgical limbs decreased over time following the surgery, and ultimately became comparable to ACLR knees at 2 and 3 years postoperatively. The biomechanical behaviors of the non-surgical limb have not been as commonly studied as the ACLR limb itself although it has sometimes been used as a “good knee” to compare against ACLR knees. Limb asymmetry is a common behavior that has been observed immediate after ACL injury and persists several months to years following the surgery.<sup>38, 39</sup> Normally we observe a restoration of the faulty mechanics in the ACLR limb over time and ultimately the limb mechanics become comparable to the non-surgical limb over a period of 2 to 3 years.<sup>14, 40</sup> In the current study, rather than restoring the ACLR limb, we observed a reduction in pressure of the non-surgical limb to reach symmetry. Although limb symmetry may appear to be advantageous, it may indicate a negative effect on the intact limbs instead of an advantageous adaptation. The altered loading behaviors, in both limbs, can lead to detrimental effects on the PFJ.

We examined the associations between PFJ contact pressure and cartilage health at different time points as we presumed that cartilage relaxation times fluctuate over time following



ACLR. In one study, the authors reported the greatest change in  $T_{1\rho}$  relaxation times was observed from preoperatively to 6 months following ACLR, while  $T_{1\rho}$  values fluctuated less over 6 months to 3 years. Nevertheless, 20% of the subjects exhibited cartilage degeneration in the patellofemoral compartment over 3 years, defined as an increase in  $T_{1\rho}$  values by 14.3%.<sup>41</sup> Our goal was to determine if abnormal PFJ loading is predictive of patellar and trochlear cartilage health at various time points, which the results indicated that the associations occurred concurrently and longitudinally.

Several studies have drawn a connection between abnormal joint stress and cartilage health,<sup>42, 43</sup> this also holds true in the patellofemoral compartment.<sup>44</sup> One of the mechanisms towards joint degeneration is elevated joint stress directly causing wear and tear of the cartilage, eventually progressing to the subchondral bone and resulting in pain. It may be intuitive to consider that offloading the joint, on the other hand, has a protective effect on joint health. However, our results suggested that persistent lower PFJ contact pressure following ACLR has a negative impact on cartilage health. A lower peak PFJ contact pressure during walking in ACLR knees was associated with elevated  $T_2$  relaxation times over time. This is consistent with the earlier findings that unloading of the knees due to lower extremity injuries exhibited elevated  $T_{1\rho}$  and  $T_2$  relaxation times in the tibial cartilage immediately after non-weight bearing. Additionally,  $T_2$  relaxation times remained elevated after 4 weeks of full weight bearing.<sup>45</sup>

The behavior coincides with previous theory that a curvilinear (inverse U-shaped) relationship exists between joint loading behavior and cartilage health, with the optimal joint stress occurring at the intermediate level. This concept is well-known in bone remodeling in which the detrimental effects in the absence of gravity and how optimal stress is needed for bone growth according to Wolff's law. Given that cartilage has similar mechanobiology, Seedhom<sup>46</sup> brought up that too little and too much stress initiate the deconditioning of cartilage leading to osteoarthritic process. As stated above, overloading and underloading of the knee have negative effects on cartilage health.<sup>42, 43, 45</sup> Van Ginckel<sup>47</sup> further confirmed that cartilage health appears to positively respond to moderate running when compared to a sedentary lifestyle. More interesting, one can speculate that cartilage mechanobiology in response to stress following trauma may have shifted and/or narrowed the U-shaped relationship. Indeed, it has been shown that cartilage material property during impact loading is significantly stiffer following mechanical injury.<sup>48</sup> More studies are warranted to examine cartilage response to stress after post-traumatic events.

Caution should be taken when taking the results of the current study. The use of the 2D sagittal plane biomechanical model that was first put forward by Brechter and Powers<sup>27</sup> has its substantial limitations. The PFJ contact pressure is solely based on subject-specific inputs of knee flexion angle and knee extensor moments, the algorithm then relied on data from literature such as quadriceps lever arm and PFJ contact area to calculate quadriceps muscle forces and contact area dependent on those inputs. In addition, the sagittal plane model does not account for frontal plane and transverse plane motions which are known to have an impact on PFJ loading behavior.<sup>36</sup> Other more sophisticated 3D modeling approaches such as finite element analysis and static optimization, may provide more robust and reliable results. To address this issue, we performed additional analysis to validate our 2D

biomechanical model. Static optimization was used to further estimate quadriceps muscle forces in a subset of the subjects (3 ACLR and 2 controls, 10 knees total). Only quadriceps muscle forces were compared instead of PFJ contact pressure as muscle force is the only modifying variable based on the two approaches. The results revealed that muscle forces estimated from the two approaches differed in magnitude but showed a strong correlation and followed similar curve pattern over stance ( $r = 0.78$ ), suggesting that the overall findings of this work would not have necessarily change if a more sophisticated modeling approach was used to estimate PFJ contact pressure. Nevertheless, it should be noted that when comparing PFJ contact pressure between different studies, the approach that is used to estimate pressure should be taken in consideration.

In light of the findings in the current study, there are several other limitations that need to be addressed. First, our study attempted to minimize the confounding factors such as surgical procedures and post-surgical rehabilitation by recruiting subjects from a single site. All subjects underwent hamstring autograft; therefore, we were not able to examine the effects of graft type on patellar alignment and generalize our results to other graft types. Our study used statistical parametric mapping to examine the associations between pressure and cartilage relaxation times on a voxel-by-voxel basis which is subjected to family-wise error.<sup>49, 50</sup> Even though Eklund et al.<sup>49</sup> has earlier suggested a smaller cluster-defining threshold of 0.01 in their sensitivity analysis, their study was performed with fMRI data which exhibit distinct characteristics as compared to cartilage relaxation times; therefore not generalizable to our application. Nevertheless, caution should be taken when interpreting the results. Last, walking task was selected in the current study which has low joint demand in nature. Future study should focus on higher intensity tasks or sports related activities such as running, cutting, and deceleration which are more relevant to individuals following ACLR.

In conclusion, underloading of the PFJ following ACLR was found pre- and postoperatively when compared to control subjects. Moreover, the altered loading behavior persisted up to 3 years. On the other hand, the contralateral knees exhibit normal PFJ contact pressure regardless of the ACL status, but decreased over 2 years postoperatively and eventually reached limb symmetry. Underloading of the PFJ has concurrent and future consequences in patellar and trochlear cartilage health while previous studies have suggested otherwise (overloading). Taken together, a curvilinear (inverse U-shaped) relationship may exist between joint loading and cartilage health, with the optimal joint loading occurring at the intermediate level.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.

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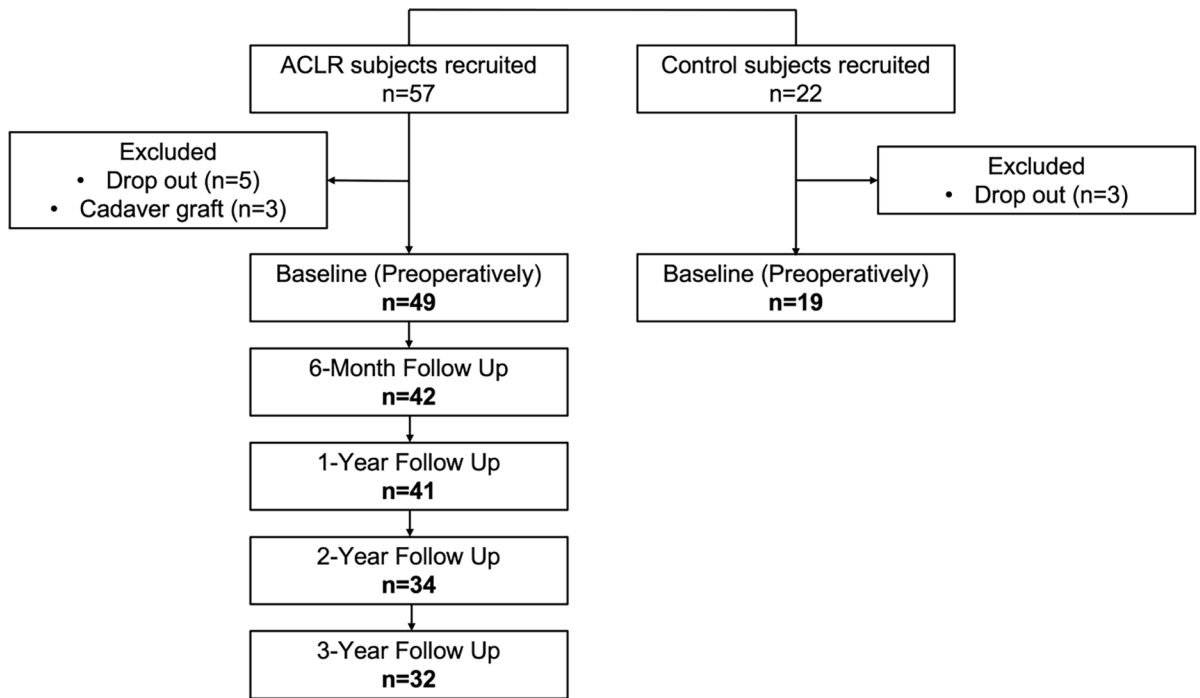
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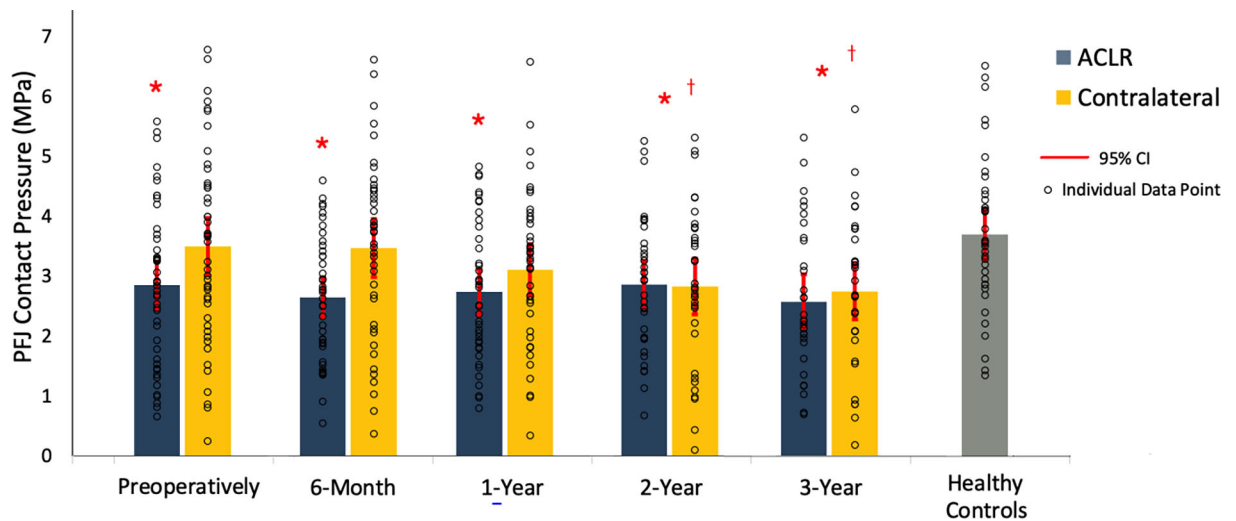
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**Figure 1.** Flowchart of subject enrollment and at each stage of study.

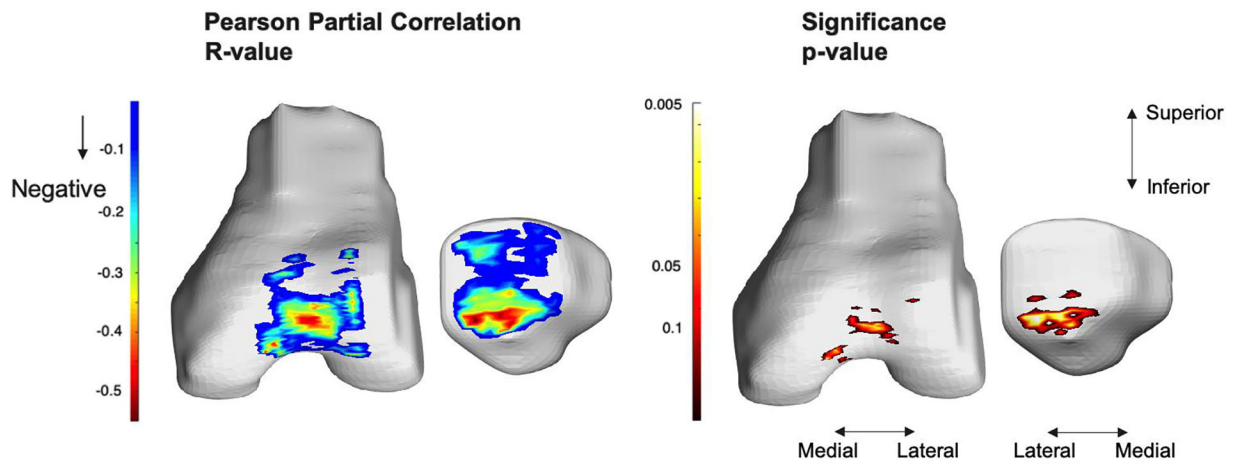


**Figure 2.**

Patellofemoral joint (PFJ) contact pressure in the anterior cruciate ligament reconstruction (ACLR), contralateral, and control knees over time. ACLR subjects were assessed preoperatively, and at 6 months, 1, 2, and 3 years postoperatively, and once for control subjects. Values are presented as mean with 95% CI including individual data points. † Indicates significant lower stress at 2 years and 3 years postoperatively when compared to preoperatively and at 6 months in the contralateral knees.

\* Indicates significant differences when compared to healthy controls.





**Figure 3.**

Representative of the statistical parametric mapping results. A lower peak patellofemoral joint contact pressure at 6 months postoperatively was associated with elevated  $T_2$  times in the patellar and trochlear cartilage at 3 years (percentage of voxels showing significant correlation = 9.0 to 11.2%; mean  $r = -0.47$  to  $-0.49$ ; mean  $p$  value = 0.021 to 0.025).

**Table 1.**

Demographics of the ACLR and control subjects.

	ACLR (n=49)	Control (n=19)
<b>Demographics</b>		
Sex, n	27 males, 22 females	12 males, 7 females
Age, y	28.8 (8.3)	30.7 (4.6)
Body mass index, kg/m <sup>2</sup>	24.4 (3.5)	24.1 (2.6)
Time since injury to preoperative assessment (days)	70.5 (52.3)	-

Data presented as mean (standard deviation) unless otherwise noted. Abbreviation: ACLR, anterior cruciate ligament reconstruction

Table 2.

Peak PFJ contact pressure during walking for ACLR, contralateral, and control knees over time.

	Group Means			Between-Group Means		
	ACLR knees	Contralateral Knees	Control Knees	ACLR – Contralateral (paired)	ACLR – Control (independent)	Contralateral – Control (independent)
<i>Preoperatively/Baseline</i>	2.87 (2.48, 3.27)	3.52 (3.04, 3.99)	3.72 (3.30, 4.14)	-0.64* (-0.93, -0.35)	-0.84* (-1.41, -0.27)	-0.20 (-0.84, 0.43)
<i>Postoperatively</i>						
6 months	2.65 (2.32, 2.98)	3.47 (2.99, 3.96)	-	-0.82* (-1.17, -0.46)	-1.06* (-1.59, -0.54)	-0.24 (-0.88, 0.38)
1 year	2.75 (2.37, 3.13)	3.12 (2.70, 3.55)	-	-0.37* (-0.68, -0.03)	-0.96* (-1.52, -0.41)	-0.59* (-1.18, -0.01)
2 years	2.86 (2.47, 3.26)	2.83 (2.36, 3.30)	-	0.03 (-0.28, 0.34)	-0.85* (-1.42, -0.28)	-0.88* (-1.50, -0.26)
3 years	2.57 (2.12, 3.03)	2.75 (2.29, 3.22)	-	-0.17 (-0.39, 0.04)	-1.14* (-1.75, -0.53)	-0.96* (-1.58, -0.35)
<b>Within-Group Means (Between-Time)</b>						
	<b>ACLR knees (paired)</b>			<b>Contralateral Knees (paired)</b>		
<b>Preoperatively – 6 months</b>	0.32 (<-0.01, 0.64)	0.09 (-0.23, 0.42)				
<b>Preoperatively – 1 year</b>	0.16 (-0.19, 0.52)	0.39 (-0.02, 0.82)				
<b>Preoperatively – 2 years</b>	0.08 (-0.33, 0.50)	0.71* (0.30, 1.11)				
<b>Preoperatively – 3 years</b>	0.36 (-0.08, 0.81)	0.75* (0.32, 1.18)				
<b>6 months – 1 year</b>	-0.14 (-0.47, 0.17)	0.29 (-0.06, 0.65)				
<b>6 months – 2 years</b>	-0.27 (-0.58, 0.03)	0.59* (0.22, 0.96)				
<b>6 months – 3 years</b>	0.01 (-0.41, 0.44)	0.70* (0.27, 1.12)				
<b>1 year – 2 years</b>	-0.11 (-0.41, 0.19)	0.32* (0.05, 0.60)				
<b>1 year – 3 years</b>	0.16 (-0.19, 0.51)	0.44* (0.09, 0.79)				
<b>2 year – 3 years</b>	0.29 (-0.02, 0.61)	0.07 (-0.23, 0.37)				

Data presented as mean (95% confidence interval). Abbreviation: ACLR, anterior cruciate ligament reconstruction; PFJ, patellofemoral joint.

\* indicates significant differences (p&lt;0.05).

**Table 3.**

Average T<sub>1ρ</sub> cartilage relaxation times within region of interest for ACLR, contralateral, and control knees over time.

Average T <sub>1ρ</sub> times (ms)	ACLR knees	Contralateral Knees	Control Knees
<b>Patellar Cartilage</b>			
<i>Preoperatively/Baseline</i>	38.6 (37.7, 39.5)	39.0 (38.1, 40.0)	39.6 (38.7, 40.6)
<i>Postoperatively</i>			
6 months	39.3 (38.3, 40.4)	40.0 (39.0, 41.0)	-
1 year	39.2 (38.1, 40.3)	40.2 (38.9, 41.6)	-
2 years	39.6 (38.7, 40.5)	40.0 (38.9, 41.1)	-
3 years	39.7 (38.5, 40.8)	40.0 (38.65, 41.5)	-
<b>Trochlear Cartilage</b>			
<i>Preoperatively/Baseline</i>	40.3 (39.6, 41.1)	39.8 (39.0, 40.6)	40.7 (39.8, 41.6)
<i>Postoperatively</i>			
6 months	42.2 (41.3, 43.1)	41.3 (40.4, 42.2)	-
1 year	42.2 (41.1, 43.2)	40.4 (39.6, 41.3)	-
2 years	42.5 (41.4, 43.5)	39.7 (38.8, 40.6)	-
3 years	42.7 (41.5, 44.0)	39.9 (38.8, 41.0)	-

Data presented as mean (95% confidence interval). Abbreviation: ACLR, anterior cruciate ligament reconstruction.

**Table 4.**

Average T<sub>2</sub> cartilage relaxation times within region of interest for ACLR, contralateral, and control knees over time.

Average T <sub>2</sub> times (ms)	ACLR knees	Contralateral Knees	Control Knees
<b>Patellar Cartilage</b>			
<i>Preoperatively/Baseline</i>	28.3 (27.5, 29.0)	28.3 (27.6, 29.0)	29.8 (28.7, 30.8)
<i>Postoperatively</i>			
6 months	28.6 (27.9, 29.4)	29.3 (28.4, 30.1)	-
1 year	28.9 (27.9, 29.8)	29.4 (28.4, 30.4)	-
2 years	29.3 (28.4, 30.3)	29.9 (29.0, 30.8)	-
3 years	29.2 (28.1, 30.4)	29.8 (28.7, 30.8)	-
<b>Trochlear Cartilage</b>			
<i>Preoperatively/Baseline</i>	31.3 (30.6, 32.0)	29.7 (29.1, 30.3)	31.4 (30.0, 32.7)
<i>Postoperatively</i>			
6 months	32.9 (32.0, 33.7)	31.7 (30.9, 32.4)	-
1 year	33.2 (32.3, 34.1)	31.1 (30.3, 32.0)	-
2 years	33.7 (32.8, 34.7)	31.7 (31.0, 32.5)	-
3 years	34.1 (33.2, 35.0)	31.6 (30.7, 32.4)	-

Data presented as mean (95% confidence interval). Abbreviation: ACLR, anterior cruciate ligament reconstruction.

**Table 5.**

Knee flexion angle and knee extensor moments at peak PFJ contact pressure for ACLR, contralateral, and control knees over time.

	ACLR knees	Contralateral Knees	Control Knees
<b>Knee Flexion Angle (°)</b>			
<i>Preoperatively/Baseline</i>	18.7 (16.9, 20.6)	18.0 (16.0, 20.1)	19.0 (17.0, 20.9)
<i>Postoperatively</i>			
6 months	15.7 (14.0, 17.5)	17.0 (15.1, 18.9)	-
1 year	15.1 (13.1, 17.1)	17.1 (13.1, 21.2)	-
2 years	14.6 (12.8, 16.3)	13.5 (11.4, 15.6)	-
3 years	14.2 (12.2, 16.2)	13.8 (11.9, 15.6)	-
<b>Knee Extensor Moments (Nm/kg)</b>			
<i>Preoperatively/Baseline</i>	0.48 (0.41, 0.55)	0.59 (0.51, 0.67)	0.64 (0.56, 0.72)
<i>Postoperatively</i>			
6 months	0.42 (0.37, 0.48)	0.57 (0.50, 0.65)	-
1 year	0.48 (0.41, 0.55)	0.55 (0.44, 0.65)	-
2 years	0.48 (0.41, 0.55)	0.47 (0.40, 0.55)	-
3 years	0.41 (0.33, 0.48)	0.44 (0.36, 0.51)	-