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## Bridge-Enhanced ACL Repair Leads to Greater Offloading of the Surgical Knee and Less Cartilage Damage in the Porcine ACL Transection Model

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### Abstract

**Background:** The extent of posttraumatic osteoarthritis (PTOA) in the porcine ACL transection model is dependent on the surgical treatment of that injury. In a previous study, animals treated with bridge-enhanced ACL repair using a tissue-engineered implant developed less PTOA than those treated with ACL reconstruction. Alterations in gait, including asymmetric weight bearing and shorter stance times, have been noted in clinical studies of subjects with osteoarthritis.

**Hypothesis:** Animals receiving a surgical treatment that results in less posttraumatic osteoarthritis (i.e., bridge-enhanced ACL repair) would exhibit fewer post-surgical gait asymmetries over a 1-year period when compared to treatments that result in greater PTOA (i.e., ACL reconstruction and ACL transection).

**Study Design:** Controlled laboratory study

**Methods:** 36 Yucatan minipigs underwent ACL transection and were randomized to: 1) no further treatment, 2) ACL reconstruction, or 3) bridge-enhanced ACL repair. Gait analyses were performed pre-operatively, and at 4, 12, 26 and 52 weeks post-operatively. Macroscopic cartilage assessments were performed following euthanasia at 52 weeks.

**Results:** Knees treated with bridge-enhanced ACL repair had less macroscopic damage in the medial tibial plateau than those treated with ACL reconstruction or ACL transection ( $P$ -adj=.03 for both comparisons). The knees treated with bridge-enhanced ACL repair had greater asymmetry in hindlimb maximum force and impulse loading than the knees treated with ACL transection at 52 weeks ( $P$ -adj<.05 for both comparisons). There was evidence to show that knees treated with bridge-enhanced ACL repair also had greater asymmetry in hindlimb maximum force and impulse loading ( $P$ -adj<.10 for both comparisons) compared to ACL reconstruction.

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The study was performed at Rhode Island Hospital & Brown University

**Conclusions:** Contrary to our hypothesis, the surgical treatment resulting in the lowest amount of macroscopic cartilage damage exhibited greater asymmetry in load-related gait parameters than the other surgical groups. This finding suggests that increased off-loading of the surgical knee may be associated with a slower rate of PTOA development.

**Clinical Relevance:** Less cartilage damage at 52 weeks was found in the surgical group that continued to protect the limb from full body weight during gait. This finding suggests that protection of the knee from maximum stresses may be important in minimizing the development of PTOA in the ACL-injured knee.

### Keywords

Anterior cruciate ligament; Gait; ACL reconstruction; bridge-enhanced ACL repair

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### Introduction

Anterior cruciate ligament (ACL) injured patients develop posttraumatic osteoarthritis (PTOA) even after ACL reconstruction.<sup>1</sup> New treatments that would minimize cartilage damage, while providing mechanical stability, would be of significant value. Bridge-enhanced ACL repair is an innovative approach for the treatment of ACL injuries.<sup>24–26</sup> In the porcine model, macroscopic cartilage damage of the tibiofemoral joint was shown to be less in knees receiving bridge-enhanced ACL repair at 1 year post-surgery compared to those treated with ACL reconstruction and those who had an untreated ACL transection.<sup>23</sup> The mechanism by which bridge-enhanced ACL repair confers chondroprotection has yet to be determined, and may be dependent on the degree of stability conferred by the healing ligament or graft, differences in joint loading during activities such as gait, and/or biological factors. In a previous porcine study, it was found that both bridge-enhanced ACL repair and traditional ACL reconstruction resulted in similar knee stability and ligament/graft biomechanics.<sup>23</sup> Likewise, the gene expression profiles between the two groups within the acute phase of healing have been shown to be similar.<sup>32,33</sup> To the best of our knowledge, longitudinal gait changes during PTOA development in animals that underwent bridge-enhanced ACL repair or ACL reconstruction have not been compared.

Patients with knee osteoarthritis (OA) reduce joint loading by decreasing the extensor knee moment,<sup>14</sup> which can be approximated in the porcine model as a change in maximum vertical ground reaction force normalized to body weight. Patient-reported outcomes in people with knee OA also correlate with gait asymmetries during the single limb support phases of gait.<sup>7,8</sup> However, longitudinal studies of gait changes in humans corresponding to direct measures of the cartilage damage have yet to be reported, likely due to the decades of time required to develop end-stage disease and the invasive procedure required to directly visualize the cartilage. Without longitudinal studies, the long-term effects of limb offloading on the injured knee in human patients remains unknown.

The pig provides a relevant model to longitudinally study alterations in gait during PTOA development. We have previously shown that the porcine knee reliably develops PTOA after an ACL transection or an ACL reconstruction within a 1-year period.<sup>23</sup> Furthermore, gait assessments, similar to those used in humans and small animal models of PTOA,<sup>6</sup> can also

be performed in pigs. As bridge-enhanced ACL repair has been shown to result in less PTOA in the porcine model,<sup>23</sup> a comparison of these three surgical groups (ACL transection, ACL reconstruction and bridge-enhanced ACL repair) would provide an opportunity to evaluate longitudinal gait changes between groups of animals undergoing varying degrees of disease progression.

The study objective was to compare longitudinal changes in gait, and how those differed between groups of animals developing PTOA at different rates. We hypothesized that animals receiving a surgical treatment (i.e., bridge-enhanced ACL repair) that produces less PTOA, as determined by macroscopic and microscopic assessments, would exhibit less post-surgical gait asymmetries over a 1-year period when compared to those treatments exhibiting more PTOA (i.e., ACL reconstruction or untreated ACL transection).

## Methods

### Study Design

Institutional Animal Care and Use Committee approvals were acquired prior to beginning the study. Thirty six Yucatan mini-pigs in late adolescence [age (mean±SD): 15.3±1.6 months; weight: 52.1±4.6 kg] underwent ACL transection and were block randomized (using a random number generator) to one of three experimental groups: 1) no treatment (ACLT group), 2) ACL reconstruction with bone-patellar tendon-bone allograft (ACLR group), and 3) bridge-enhanced ACL repair using a scaffold combined with autologous blood (BE-R group).<sup>23</sup> Randomization was blocked so that an equal number of male and female animals were represented in each group. Justification of the model and details of the surgical procedures have been previously reported,<sup>23</sup> and are summarized in an online supplement (see Supplemental Methods). Detailed information regarding animal husbandry and pain management are available in the online supplement (see Supplemental Methods). The sample size was established by an *a priori* power analysis based on gait parameters (see Supplemental Methods). Longitudinal gait analyses were performed pre-operatively, and at 4, 12, 26 and 52 weeks after surgery. Macroscopic and microscopic cartilage assessments of the articular cartilage, as well as microscopic evaluation of the synovium, were performed following euthanasia and limb harvest at 52 weeks. No animals were excluded from the assigned treatment or any of the analyses. All post-operative assessments were performed with the animals blinded to the group assignment.

### Gait measurement

Gait was evaluated using a pressure mat (HRV6 Walkway System; Tekscan Inc, Boston, MA) with an active sensing area of 292.6 x 44.7 cm.<sup>6</sup> Animals were trained to walk on the pressure mat in one direction using food for encouragement. Based on the pressures observed for this cohort, a step calibration was performed for each sensing tile using a 58 kg custom three-legged phantom as recommended by the manufacturer. Data were collected at 104 Hz using the first hoof contact as a trigger until the animal stepped off the mat. Commercial software (Walkway 7.0; Tekscan Inc, Boston, MA) was used for data collection and analysis. Five trials were obtained for each animal at each timepoint (preop, 4, 12, 26 and 52 weeks). For analysis, hoof strikes were automatically identified by the software, and

partial strikes were discarded. Gait data were generated using the force, spatial and temporal parameters of the identified foot strikes. Force parameters including maximum force (kg) as a percentage of body weight, impulse (kg-sec) as a percentage of body, and maximum peak pressure (KPa) were calculated for each limb. The spatiotemporal parameters included the stance time, stride time, stride length, and stride velocity. The average of five trials was reported for each outcome as a ratio of surgical and contralateral knees. The ratios at each time point were compared between treatment groups.

### **Macroscopic Articular Cartilage Analysis**

Knee joints were opened using aseptic technique immediately after euthanasia. Macroscopic damage of the articular cartilage surfaces was assessed according to OARSI guidelines for sheep and goat.<sup>19</sup> Damage to six articular surfaces, including the medial femoral condyle, medial tibial plateau, lateral femoral condyle, lateral tibial plateau, femoral trochlea, and the patella, was scored from 0 (i.e., normal) to 4 (i.e., large erosions down to subchondral bone). Scores from the four tibiofemoral surfaces were then added to make up the total macroscopic score of the tibiofemoral joint, which ranged from 0 to 16.

### **Microscopic Articular Cartilage Analysis**

Bilateral osteochondral samples were harvested from the medial femoral condyles for histopathological analysis. Central coronal slabs were fixed in 10% neutral buffered formalin and decalcified in 10% formic acid (EMD Millipore, Darmstadt, Germany)/5% formalin solution (Acros Organics, Belgium) before dehydrating and embedding in paraffin. Serial sections were stained with hematoxylin and eosin (H&E), Safranin-O and Fast green (Saf-O), and nuclear fast red (NFR). Microscopic scoring of the articular cartilage was performed according to OARSI guidelines<sup>19</sup> by three independent experienced readers (BCF, NPK, BLP), who were blinded to the experimental condition of the samples. Examiner scores were averaged for analysis.

### **Microscopic Synovium Analysis**

Central sections of medial meniscus and the adjacent synovium were fixed in formalin, dehydrated and embedded in paraffin. 6 µm sections were stained with H&E. Scoring was performed by an examiner blinded to treatment group using three individual features of the synovial membrane (synovial cell lining layer, cellular density of the synovial stroma, and inflammatory infiltrate).<sup>18</sup> Each feature was graded on a scale of 0-3. The sum of the three individual sub-scores was defined as the synovitis sum score. Knees with total scores of 0 or 1 were classified as having no synovitis, 2-4 as low-grade synovitis, and 5-9 as high-grade synovitis.

### **Statistical analyses**

Data were imported into commercial software (SAS version 9.4; SAS Institute Inc., Cary, NC) for analysis. Generalized estimating equations (GEEs) were used (1) to model the gait parameters as a function of animal within time and experimental group, and (2) to model the macroscopic articular cartilage measures, the microscopic articular cartilage measures, and the synovitis histology measures as a function of knee within animal and experimental

group. A linear distribution was assumed for all gait parameters, while a binomial distribution was assumed for all remaining macroscopic, microscopic, and synovitis measures. Classical sandwich estimation was used to adjust for any possible model misspecification. Pairwise comparisons between groups were conducted via orthogonal contrasts. The Holm-test was used to adjust for multiple comparisons to maintain a two-tailed familywise alpha at 0.05. All modeling was completed using *PROC GLIMMIX* and all orthogonal contrasts were completed using the *lsmeans* statement. A p-value of 0.05 was used to determine statistical significance.

## Results

There was a significant effect of surgical group on the post-operative gait changes (Table 1, Supplemental Table S1). Pre-operatively, no significant differences ( $P\text{-adj}>.05$ ) were observed between treatment groups for any of the gait parameters. Four weeks after surgery, the surgical limb of the BE-R group had a 20% lower mean ratio of maximum force (%BW) of the surgical to the contralateral limb (Table 1,  $P\text{-adj}=.003$ ), a 20% lower mean impulse ratio ( $P\text{-adj}=.003$ ), a 16% lower maximum peak pressure ( $P\text{-adj}=.03$ ) and some evidence for a lower stance time ratio ( $P\text{-adj} = 0.05$ ) than the ACLT group. There were no differences between the BE-R and ACLR groups for gait at 4, 12 or 26 weeks after surgery. The ACLR group at four weeks had a 13% lower mean impulse ratio ( $P\text{-adj}=.03$ ) and 7% lower mean stance time ratio ( $P\text{-adj}=.03$ ), compared to the ACLT group at the same time point.

Fifty-two weeks after surgery, the BE-R group had a lower mean maximum force ratio ( $P\text{-adj}=.02$ ) and mean impulse ratio ( $P\text{-adj}=.01$ ) compared to ACLT and there was some evidence for a lower mean maximum force ratio ( $P\text{-adj}=.07$ ), mean impulse ratio ( $P\text{-adj}=.09$ ), and higher stride velocity ( $P\text{-adj}=.07$ ) compared to ACLR. No significant differences in mean stride time and stride length ratios were observed between groups at any time point ( $P>.05$  for all comparisons).

### Macroscopic Articular Cartilage Score

There was a significant effect of surgical treatment on the mean tibiofemoral macroscopic damage scores in the articular cartilage of the surgical knees at 52 weeks (Figure 1; Table 2; Supplemental Table S2). Compared to ACLT and ACLR, the knees treated with BE-R had significantly lower scores in the medial tibial plateau (Table 2;  $P\text{-adj}<.03$  for both comparisons). The medial tibial plateau had erosions of cartilage down to the subchondral bone in 3 of the ACL transected knees, 4 of the ACL reconstructed knees and 0 of the BE-R knees. Compared with ACLT, the knees treated with BE-R and ACLR had significantly lower scores in the lateral femoral condyle (Table 2;  $P\text{-adj}<.01$  for both comparisons). For the lateral femoral condyle, 5 of the ACL transected knees had erosions down to subchondral bone, 1 of the ACL reconstructed knees had large erosions to bone and 1 of the bridge-enhanced ACL repair knees had a small area of erosion down to bone. There were no significant differences between groups for damage to the medial femoral condyle or lateral tibial plateau, trochlea or patella (Table 2). There were also no significant differences in the contralateral macroscopic damage scores between the groups (Table 2, Supplemental Table S2;  $P\text{-adj}>.05$  for all comparisons).

### Microscopic Articular Cartilage Score

There were no significant differences in the microscopic OARSI scores between the surgical groups for either the surgical knee or the contralateral knee at 52 weeks (P-adj>.09 for all comparisons, Figure 2, Supplemental Table S3). The mean OARSI microscopic score in the surgical knee was twice as high as the score of the contralateral knee in the BE-R group (P-adj=.04) and four times as high for the ACLR group (P-adj<.001), while no difference between the surgical and contralateral knees was noted for the ACLT group (P-adj=.28).

### Synovitis Assessment

There were significantly higher mean synovitis sum scores in the surgical knees compared to contralateral knees in all groups at 52 weeks (P-adj<.01 for the ACLT and ACLR groups, P-adj=.06 for the BE-R group; Figure 3, Supplemental Table 4), and the mean synovial cell densities were higher in the surgical knees compared to the contralateral knees in the ACLR and ACLT groups (P-adj<.05 for both comparisons). There was no difference in the surgical or contralateral knee scores between groups (P-adj>.05 for all comparisons; Figure 2, Supplemental Table 4). There was no evidence of a higher inflammatory infiltrate in the surgical knee compared to the contralateral knee in any of the groups (P-adj=.15 for ACLT and P-adj=1.0 for ACLR and BE-R groups).

### Discussion

Our hypothesis was that animals receiving a surgical treatment that results in less macroscopic cartilage damage (BE-R) would have smaller alterations in gait during the initial period of osteoarthritis development. To the contrary, we found that the BE-R animals offloaded the surgical limb post-operatively to a greater degree than the other groups, a difference that was statistically significant at 52 weeks, even with a relatively small number of animals in each group. This finding was despite the result that the BE-R knees had significantly less macroscopic cartilage damage than the ACLT or ACLR knees at that same time point. Interestingly, despite having less macroscopic damage, the microscopic cartilage changes were greater in the BE-R group than in the ACLT group, differences that were driven largely by increases in structure and cloning sub-scores in those groups. Finally, there was no difference in microscopic synovitis scores between the groups, suggesting that there was no ongoing synovial reaction to the implanted scaffold in the BE-R group.

The findings of lower maximum force and shorter stance time on the operated knee at the 4-week time point in all groups are consistent with those previously reported in rodent models of PTOA over 6 weeks, where prolonged swing phase, slower swing velocity, and loading asymmetry were observed.<sup>11,13,21</sup> An ovine model of bilateral medial meniscectomy also documented decreased ground reaction forces at 6 weeks post-surgery persisting over a duration of 20 weeks.<sup>5</sup> Using a longitudinal experimental design to evaluate knee joint kinematics, we were able to longitudinally assess gait asymmetries in the porcine model of PTOA over a 1 year period post-injury. We found that while the ACLT group had largely resolved loading asymmetries by the 12-week time point, and the ACLR group resolved them by the 26-week time point, asymmetry in maximum force and impulse loading persisted in the BE-R group at the 52-week time point. Interestingly, while the BE-R group

had slower resolution of loading asymmetries, that group also had significantly less macroscopic cartilage damage and a faster stride velocity than the ACLR and ACLT groups at 52 weeks.

Humans with osteoarthritis develop similar gait compensations to those seen in the BE-R group, including lower peak vertical forces.<sup>14,22</sup> Recently, less activity, and hence less knee loading, following ACL reconstruction in humans was associated with greater Kellgren-Lawrence scores at 5 years,<sup>15,35</sup> and higher T1rho values with MRI at 6 months,<sup>27,28</sup> both of which are imaging biomarkers suggesting more joint arthrosis. It is possible, however, that a joint treated with ACL reconstruction (where the ligament is removed and replaced with a tendon graft) responds differently than a joint that is treated with repair of the ligament. From previous studies in the porcine model, it was determined that the biomechanics of the joint following ACL reconstruction or bridge-enhanced ACL repair are similar,<sup>23</sup> and that the inflammation of the joint in the acute phase following injury/surgery is also similar for both treatments.<sup>32,33</sup> Therefore, other factors may be involved. One could speculate that the mechanoreceptors within the ACL remain intact following ACL repair, which would, in turn, preserve the neuromuscular control required to protect the joint long-term, while evidence suggests that the mechanoreceptors within the graft and the neuromuscular control of the reconstructed joint do not return to normal.<sup>17,38</sup> Future studies are required to test this hypothesis. Nonetheless, the current results suggest that limb offloading may be a protective mechanism for the joint, as the group which continued to put less force and impulse through the ACL transected knee also developed less cartilage damage.

Bridge-enhanced ACL repair resulted in less macroscopic cartilage damage than was seen in the ACLT and ACLR groups at 52 weeks, a difference that was most significant in the medial tibial plateau where 3 of the ACLT knees and 4 of the ACLR knees had erosions down to bone, while none of the knees in the BE-R group did. The medial compartment is the primary site of cartilage loss in ACL injured patients presenting with post-surgical osteoarthritis.<sup>3,34</sup> A porcine study evaluating the macroscopic cartilage damage of these three treatment groups was previously performed, and the results of the current study independently confirm the macroscopic findings of the previous study.<sup>23</sup> The current study was performed to determine if changes in gait were responsible, in part, for the development of the observed damage. The results indicate that this is true macroscopically.

Despite a difference in macroscopic cartilage damage, there were no significant differences noted between the surgical groups for the microscopic scores.<sup>19</sup> This may have been due to greater macroscopic damage occurring in locations other than the central coronal section of the knee where the microscopic scores were evaluated. In addition to the microscopic analysis of the cartilage, all treatment groups had low degrees of synovitis in their joints at 1 year, with no significant differences noted between groups. This finding suggests that there was not an additional synovial reaction to the implanted bridge material for the bridge-enhanced ACL repair procedure.<sup>30,31</sup> Since none of the surgical knees for the three treatment groups were free of synovitis, the mild, yet persistent, synovial changes suggest that the metabolic activity may be increased in an effort to repair the joint.<sup>2,32</sup> Future research is required to determine the long-term effects of these observed synovial changes.

This study has several strengths. The porcine model enabled us to evaluate gait changes at discrete time points following treatment. Gait asymmetries were assessed using a pressure mat system that reliably measures peak pressures and maximum forces in humans<sup>39</sup> and other large animal models.<sup>10,20</sup> Given that the Yucatan minipig is of similar size and weight to a human, the pressure mat was appropriate to measure the same parameters used in human studies. The porcine model was also well suited for this project given the anatomic and biomechanical similarities between the pig and human.<sup>4,29,37</sup> Furthermore, the articular cartilage thickness of the porcine knee is closer to that of humans compared to other animal models of osteoarthritis.<sup>16</sup> Furthermore, disease progression is accelerated in the porcine model which limits the time required to complete the study, as it takes years for significant PTOA to develop in humans.<sup>23</sup> Finally, the pre-clinical model also allowed us to harvest the joints to directly assess articular cartilage damage, which would not be possible in human patients. Macroscopic examination of the cartilage surface, which was performed using the OARSI guidelines for common large animal models,<sup>19</sup> allowed for comparisons to be made of the damage over the entire articulating surfaces of the tibiofemoral joint instead of at discrete locations as was done with the microscopic assessment.

There are several study limitations to consider. The pig is a quadruped and therefore does not fully represent the human condition. However, the model advantages described above may at least in part alleviate this limitation. Although gait asymmetries at the hoof were assessed using a pressure mat, no kinematic measurements of the hindlimb were performed, which could have provided additional insight into functional gait changes inducing PTOA.<sup>12,27,36</sup> The number of animals in each group was relatively small. However, significant changes were detected in several of the gait and macroscopic assessment variables. It is possible that additional differences in some of the other outcome measures could have been found with a larger sample size. Finally, microscopic OARSI scoring for the goat and sheep<sup>19</sup> was performed using a central coronal section from the medial compartment. Chondral damage existing in other locations of the articulating surfaces between groups would have been missed, as the location of maximum cartilage damage was not always at the center of the articular cartilage surface with ACL disruption, unlike the pattern seen with meniscal destabilization.<sup>9</sup> However, the macroscopic scoring system allowed us to consider the entire articulating surfaces of the tibiofemoral joints to assess the extent of cartilage damage.

In conclusion, contrary to our initial hypothesis, the surgical treatment resulting in the lowest amount of cartilage damage (bridge-enhanced ACL repair) exhibited greater asymmetry in load-related gait parameters (i.e., more offloading of the surgical limb) than ACL reconstruction or untreated ACL transection 1-year post-operatively. This finding suggests that increased off-loading of the surgical knee may be associated with a slower rate of development of PTOA after ACL injury and surgery.

## Supplementary Material

Refer to Web version on PubMed Central for supplementary material.



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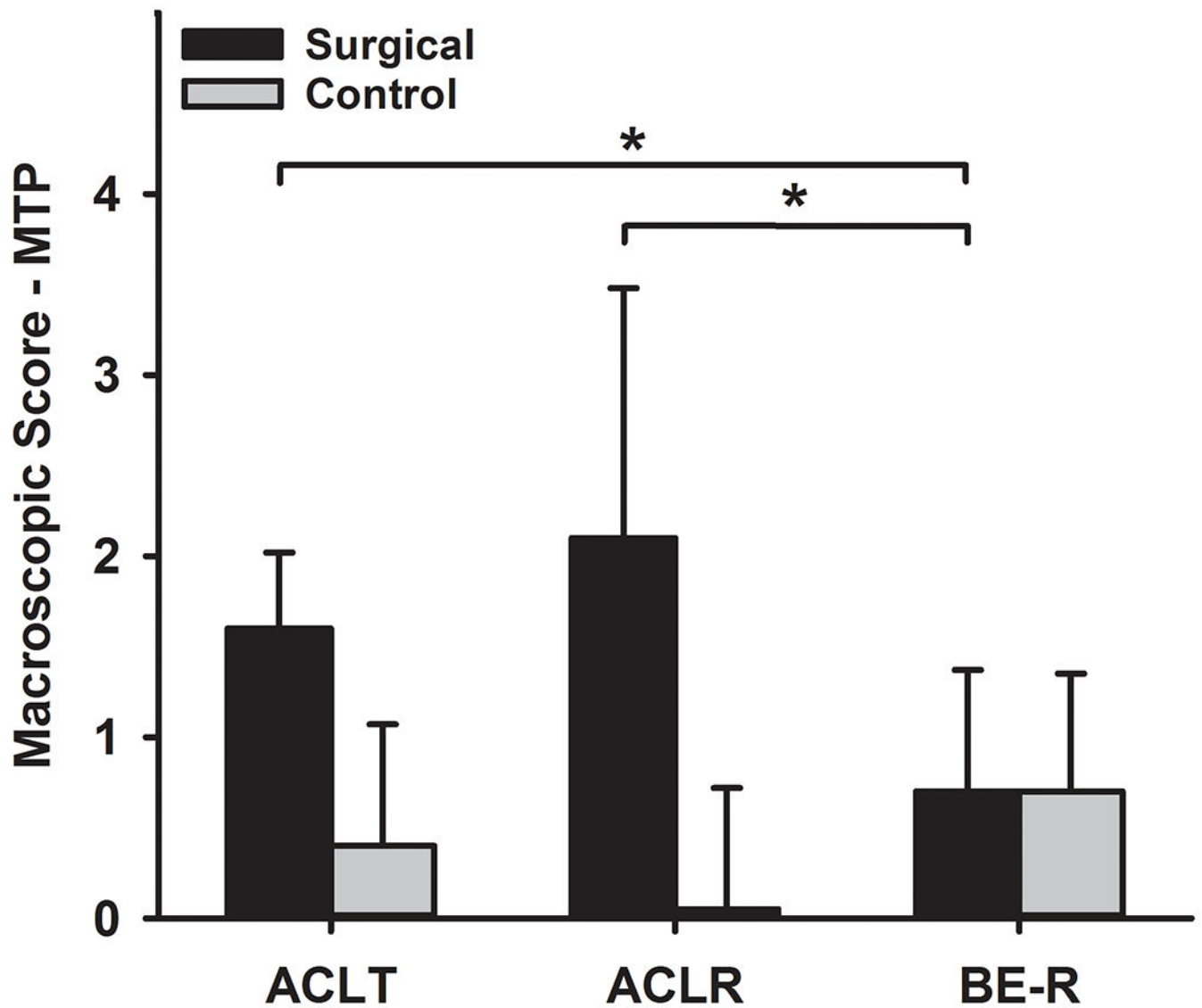
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**What is known about the subject:**

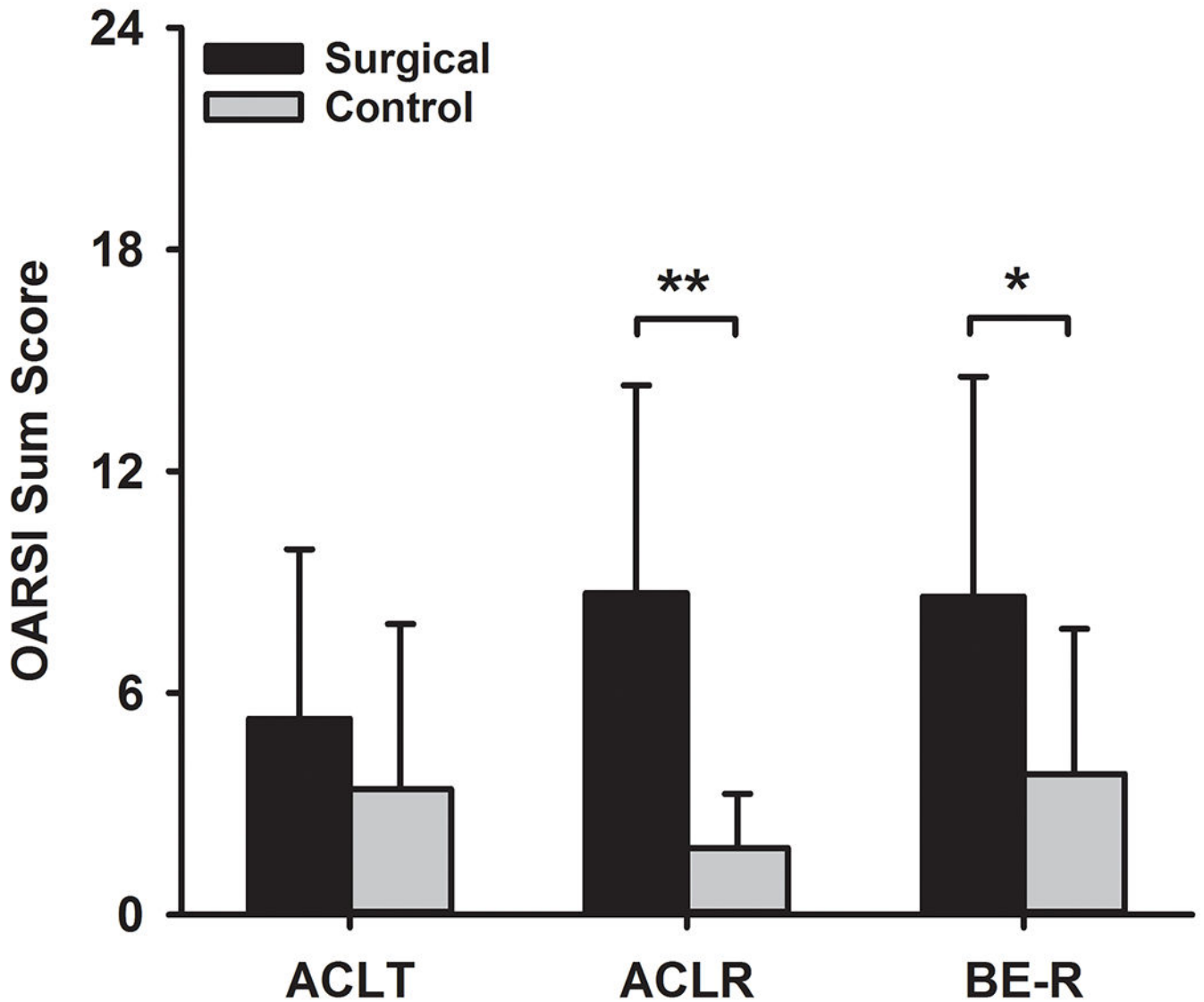
ACL injury has been reported to increase the risk for PTOA by 5X. The mechanisms behind PTOA development following ACL injury remains a topic of debate and are likely due to a combination of biomechanical, neuromuscular and biochemical factors. In order to understand these mechanisms, long-term, longitudinal clinical studies are required. However, these are difficult to perform due to confounding factors, time required for PTOA development, and the lack of direct methods to quantify PTOA. Thus, a clinically relevant large animal model provides an efficient method to better evaluate factors contributing to PTOA onset and progression.

**What this study adds to existing knowledge:**

Using the minipig model, we previously demonstrated that different surgical interventions for an ACL injury produce different degrees of PTOA. Thus, the model provides us with an opportunity to evaluate different mechanisms of disease progression. Using this model, we established the relationships between biomechanical gait changes and cartilage damage between animals receiving no treatment, ACL reconstruction, and bridge-enhanced ACL repair following ACL transection.



**Figure 1.** Mean Macroscopic Damage Scores for the medial tibial plateau (MTP) for all groups at 52 weeks. ACLT=ACL Transection, ACLR=ACL reconstruction, and BE-R=Bridge-enhanced ACL Repair. Error bars represent the standard deviation. \* Significant differences P-adj=.03. The complete data related to the macroscopic cartilage damage set can be found in Supplemental Table S2.



**Figure 2.**

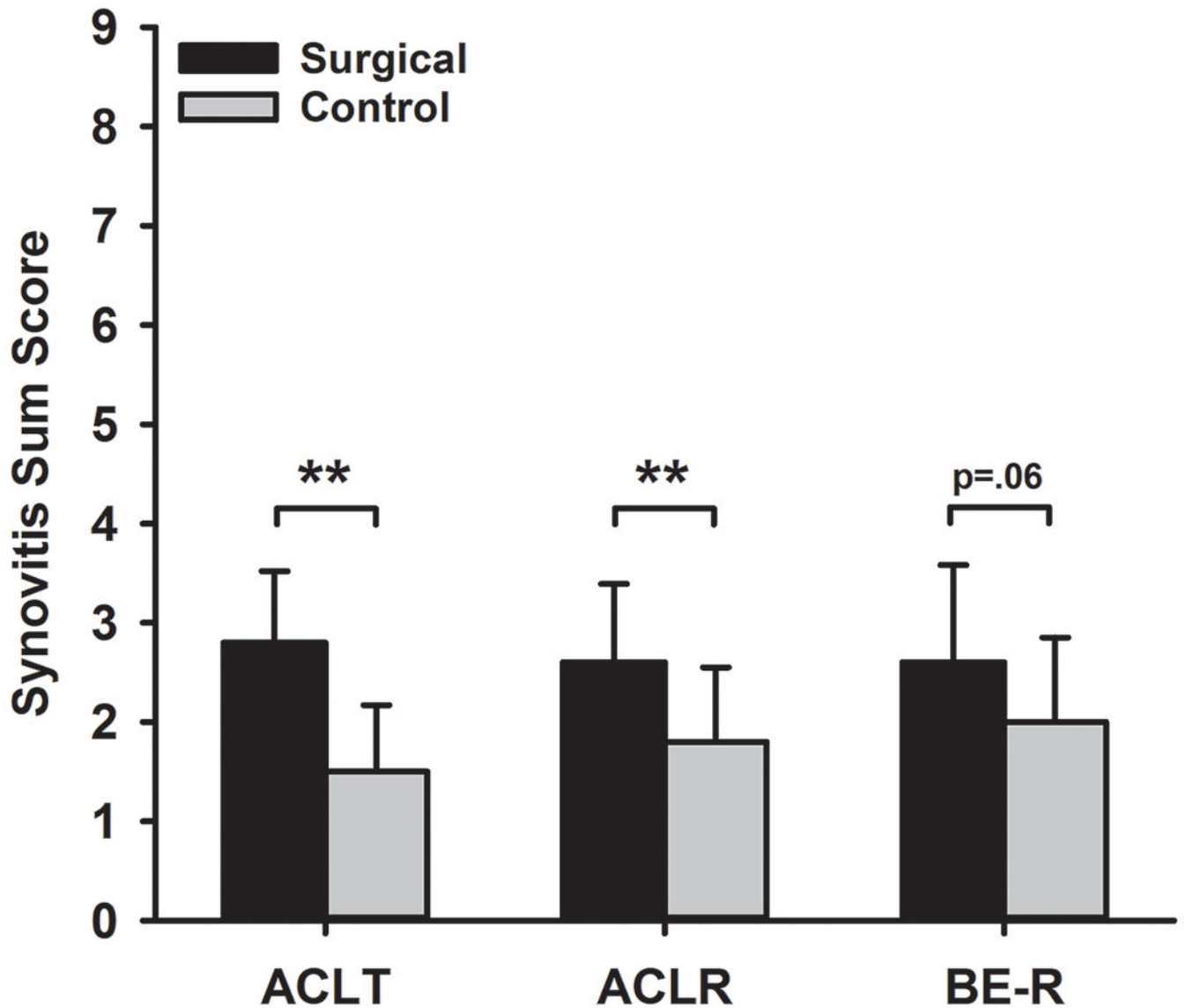
Microscopic OARSI Sum Scores (mean±standard deviations) for all groups at 52 weeks.

There were no significant differences between groups in the surgical or contralateral knees.

ACLT=ACL Transection, ACLR=ACL reconstruction, and BE-R=Bridge-enhanced ACL

Repair. \*\*Significant difference between surgical and contralateral,  $P\text{-adj}<.001$ . \*Significant

difference between surgical and contralateral,  $P\text{-adj}<.05$ . The complete data set related to the microscopic assessment can be found in Supplemental Table S3.



**Figure 3.**

Mean synovitis sum score between three treatment groups at 52 weeks. Sx and Ctrl indicate surgical and contralateral limbs respectively. ACLT=ACL Transection, ACLR=ACL reconstruction, and BE-R=Bridge-enhanced ACL Repair. Error bars represent the standard deviations. \*\*Significant difference between surgical and contralateral, P-adj<.01. The complete data set including the subscores related to the synovitis can be found in Supplemental Table S4.

**Table 1.**

Mean±standard deviations of the gait parameter ratios (surgical/contralateral) for the three treatment groups over time. ACLT=ACL Transection, ACLR=ACL reconstruction, and BE-R=Bridge-enhanced ACL Repair. Values in bold highlight significant findings. The complete data set related to the gait parameters can be found in Supplemental Table S1.

Gait Parameter	Time	ACLT	ACLR	BE-R
<b>Max force (%BW)</b>	Pre-op	1.01±0.08	1.01±0.06	1.03±0.08
	4 weeks	0.73±0.12	0.65±0.14	<b>0.55±0.15</b> *
	12 weeks	0.97±0.13	0.88±0.14	0.89±0.1
	26 weeks	0.98±0.07	0.97±0.11	0.91±0.09**
	52 weeks	1.01±0.09	1.00±0.12	<b>0.89±0.12</b> *,##
<b>Impulse (%BW)</b>	Pre-op	1.03±0.09	1.03±0.11	1.03±0.11
	4 weeks	0.72±0.11	<b>0.59±0.15</b> *	<b>0.52±0.19</b> *
	12 weeks	0.95±0.13	0.90±0.13	0.93±0.12
	26 weeks	1.00±0.07	0.96±0.10	0.93±0.10
	52 weeks	1.03±0.09	0.98±0.08	<b>0.91±0.10</b> *,##
<b>Max Peak Pressure</b>	Pre-op	1.02±0.12	1.00±0.12	1.03±0.07
	4 weeks	1.05±0.21	0.95±0.12	<b>0.88±0.11</b> *
	12 weeks	0.97±0.06	0.95±0.12	1.00±0.12
	26 weeks	1.03±0.14	0.97±0.08	1.00±0.1
	52 weeks	0.99±0.12	1.01±0.11	1.01±0.09
<b>Stance time</b>	Pre-op	1.01±0.06	0.98±0.06	1.02±0.10
	4 weeks	0.96±0.06	<b>0.89±0.06</b> *	0.87±0.11**
	12 weeks	0.98±0.05	0.99±0.08	1.00±0.08
	26 weeks	1.02±0.06	0.98±0.08	1.01±0.04
	52 weeks	1.03±0.05	1.00±0.09	1.01±0.04
<b>Stride velocity</b>	Pre-op	1.01±0.06	1.00±0.04	1.01±0.04
	4 weeks	0.98±0.05	1.00±0.04	1.00±0.05
	12 weeks	1.00±0.02	0.99±0.02	1.01±0.03
	26 weeks	1.01±0.03	0.99±0.03	1.00±0.03
	52 weeks	1.00±0.04	0.98±0.04	1.01±0.04##

\* different from ACLT, P-adj<.05 for all comparisons.

\*\* different from ACLT, .05< P-adj<.10 for all comparisons.

## different from ACLR, .05< P-adj<.10 for all comparisons.



**Table 2.**

Macroscopic Damage Scores (mean±standard deviations) for each region for all groups at 52 weeks. ACLT=ACL Transection, ACLR=ACL reconstruction, and BE-R=Bridge-enhanced ACL Repair, TF=tibiofemoral

	ACLT		ACLR		BE-R	
	Surgical	Contralateral	Surgical	Contralateral	Surgical	Contralateral
Medial Tibial Plateau	1.6±0.42	0.4±0.67	2.1±1.38	0.5±0.67	<b>0.7±0.67<sup>*,#</sup></b>	0.7±0.65
Medial Femoral Condyle	1.5±1.31	1.2±0.83	2.0±1.53	0.7±0.98	1.7±1.44	1.0±0.60
Lateral Femoral Condyle	2.2±1.03	0.3±0.45	<b>1.1±1.16<sup>*</sup></b>	0.1±0.29	<b>0.7±0.99<sup>*</sup></b>	0.2±0.39
Lateral Tibial Plateau	1.8±0.94	0.3±0.45	2.1±0.79	0.2±0.79	1.6±1.08	0.1±0.29
Trochlea	3.2±1.19	0 ±0	3.0±1.35	0.3±0.89	2.6±1.68	0.6±1.19
Patella	0.1±0.29	0±0	0.1±0.28	0±0	0.4±1.00	0.3±0.88
Total TF Macroscopic Score	7.8±2.79	1.8±1.27	7.5±2.68	1.4±2.68	<b>4.8±3.04<sup>*,##</sup></b>	1.9±1.24

\* P-adj<.05 compared to ACLT

\*\* P-adj=.06 compared to ACLT

# P-adj<.05 compared to ACLR

## P-adj =.06 compared to ACLR