Structural and Anatomic Restoration of the Anterior Cruciate Ligament Is Associated With Less Cartilage Damage 1 Year After Surgery

Healing Ligament Properties Affect Cartilage Damage

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Background: Abnormal joint motion has been linked to joint arthrosis after anterior cruciate ligament (ACL) reconstruction. However, the relationships between the graft properties (ie, structural and anatomic) and extent of posttraumatic osteoarthritis are not well defined.

Hypotheses: (1) The structural (tensile) and anatomic (area and alignment) properties of the reconstructed graft or repaired ACL correlate with the total cartilage lesion area 1 year after ACL surgery, and (2) side-to-side differences in anterior-posterior (AP) knee laxity correlate with the total cartilage lesion area 1 year postoperatively.

Study Design: Controlled laboratory study.

Methods: Sixteen minipigs underwent unilateral ACL transection and were randomly treated with ACL reconstruction or bridge-enhanced ACL repair. The tensile properties, cross-sectional area, and multiplanar alignment of the healing ACL or graft, AP knee laxity, and cartilage lesion areas were assessed 1 year after surgery.

Results: In the reconstructed group, the normalized graft yield and maximum failure loads, cross-sectional area, sagittal and coronal elevation angles, and side-to-side differences in AP knee laxity at 60° of flexion were associated with the total cartilage lesion area 1 year after surgery ($R^2 > 0.5$, $P < .04$). In the repaired group, normalized ACL yield load, linear stiffness, cross-sectional area, and the sagittal and coronal elevation angles were associated with the total cartilage lesion area ($R^2 > 0.5$, $P < .05$). Smaller cartilage lesion areas were observed in the surgically treated knees when the structural and anatomic properties of the ligament or graft and AP laxity values were closer to those of the contralateral ACL-intact knee. Reconstructed grafts had a significantly larger normalized cross-sectional area and sagittal elevation angle (more vertical) when compared with repaired ACLs ($P < .02$).

Conclusion: The tensile properties, cross-sectional area, and multiplanar alignment of the healing ACLs or grafts and AP knee laxity in reconstructed knees were associated with the extent of tibiofemoral cartilage damage after ACL surgery.

Clinical Relevance: These data highlight the need for novel ACL injury treatments that can restore the structural and anatomic properties of the torn ACL to those of the native ACL in an effort to minimize the risk of early-onset posttraumatic osteoarthritis.

Keywords: ACL; reconstruction; healing; cartilage; osteoarthritis

Anterior cruciate ligament (ACL) tears are common and can lead to the early onset of posttraumatic osteoarthritis (OA), even after surgical reconstruction.[34,35,45,60] Given the high incidence of ACL injuries in younger patients, preventing the development of posttraumatic OA in these patients is an important clinical challenge. The precise mechanisms contributing to joint arthrosis after ACL reconstruction are not well understood. However, various factors have been suggested to contribute to the risk, ranging from the joint inflammatory response to altered biomechanics.[10] In particular, altered joint kinematics and kinetics are believed to play an important role

in the development of posttraumatic OA.[4,8,32,46] Abnormal joint motion and loading have been associated with non-anatomic ligament alignment, graft tissue degeneration, loss of tissue neurosensory function (proprioception), and neuromuscular deficit.[22,24,53]

Despite substantial research efforts to study the changes in joint biomechanics after ACL reconstruction, little is known about the links between the graft structural properties and the risk of posttraumatic OA. This may be due to various factors, including the challenges associated with the direct measurements of structural graft properties in humans and because posttraumatic OA may remain undetectable in a clinical cohort for a decade or more. Some of these limitations can be mitigated with animal models to study the outcomes of ACL surgery. Posttraumatic OA in animals often occurs within 1 month to 1 year after injury, with smaller animals developing macroscopic changes in cartilage structure sooner than larger animals.[39,49] Furthermore, animal joints can be opened to directly evaluate the integrity of the graft and articular cartilage. For these reasons, animal models have been long used to study ACL injuries, treatments, and associated complications.[6,11,14-17,20,43,44] Among animal models, the porcine knee has been shown to be closest to the human knee based on its size, anatomy, and functional dependency on the ACL.[9,29,42,48,63] Furthermore, it has been shown that pigs develop posttraumatic OA following ACL transection and reconstruction in a pattern similar to that reported in humans but at a faster rate, with the joint changes at 1 year reflective of those seen at 10 to 15 years after ACL reconstruction in humans.[39] This faster onset of posttraumatic OA allows for more rapid assessment of factors that may influence the development of posttraumatic OA after ACL injury and treatment.

Using the porcine model, we studied how the structural (tensile) and anatomic (cross-sectional area and orientation) properties of the graft, as well as knee laxity, affect the magnitude of cartilage damage following ACL reconstruction. We also studied these relationships for a novel surgical procedure—bridge-enhanced ACL repair, which has shown biomechanical outcomes and a lower risk of posttraumatic OA comparable to ACL reconstruction in preclinical models.[38,39,59] We hypothesized that the structural and anatomic properties of the reconstructed graft or repaired ACL were correlated to the tibiofemoral cartilage damage lesion area, as a surrogate for posttraumatic OA risk, 1 year after ACL surgery. We also hypothesized that the side-to-side differences in anterior-posterior (AP) knee laxity were related to the cartilage damage lesion area 1 year after ACL surgery.
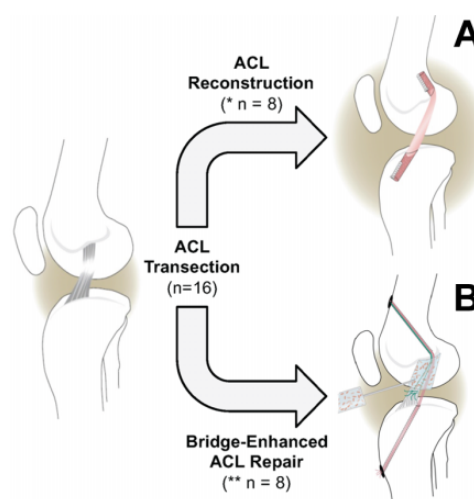

Figure 1. Diagram of the treatment groups evaluated in this study: (A) ACL reconstruction: *All 8 animals were included in analyses related to graft mechanical properties and side-to-side differences in knee laxity, while 7 animals were included for the analyses related to graft anatomic properties. (B) Bridge-enhanced ACL repair (adapted and modified from Murray and Fleming[39]): **Seven animals were included in analyses related to ACL mechanical properties and side-to-side differences in knee laxity, while 6 animals were included for the analyses related to ACL anatomic properties. ACL, anterior cruciate ligament.

METHODS

Institutional animal care and use committee approval was obtained before initiating this study. A total of 16 adolescent Yucatan minipigs (age, 15 ± 1 months; weight, 61 ± 7 kg) underwent unilateral ACL transection and were randomly treated with either conventional ACL reconstruction (n = 8) or bridge-enhanced ACL repair (n = 8) under the direction of a board-certified and sports medicine fellowship–trained orthopaedic surgeon (Figure 1). ACL transection was performed through a medial arthrotomy, which allowed us to isolate and cut the ACL at midsubstance with a surgical blade.[39] A Lachman test was then performed to verify functional loss of the ACL. The surgical knee was randomly selected, and the contralateral ACL-intact knee served as a control. Note that these animals were part of a previously published study evaluating the long-term effects of the bridge-enhanced ACL repair and ACL reconstruction procedures.[39] In the current study, we performed additional image analyses to determine whether the biomechanical and anatomic properties of the reconstructed

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graft or repaired ACL influenced cartilage integrity 1 year after surgery. We included all the animals of the parent study that were observed for 1 year after ACL reconstruction or bridge-enhanced ACL repair.[39] However, 1 animal in the repair group was shipped to the external holding facility at 2 weeks rather than 4 weeks postoperatively, a deviation in the postoperative rehabilitation, and was euthanized before the follow-up point; thus, it was excluded from the analysis. One animal in the reconstruction group had metal artifact that precluded reliable magnetic resonance imaging (MRI) measurements on the treated knee. In the repair group, 1 animal had missing MRI of the contralateral knee. These 2 animals were not included in the analyses conducted on ACL anatomic properties.

Surgical Procedure

ACL reconstruction was performed with fresh-frozen bone–patellar tendon–bone allografts from age-, weight-, and sex-matched donors as previously described.[17] The entire patellar tendon (∼10 mm in width) was used for the soft tissue portion of the graft with trimmed bone plugs. Grafts were then washed in a 10% penicillin-streptomycin antibiotic solution. The 8-mm femoral and tibial tunnels were drilled to the insertion sites of the native ACL. Once the tunnels were completed, the graft was introduced intra-articularly through a mini-arthrotomy. Prior to insertion, the distal bone block was folded back onto the midsubstance of the graft to adjust its length to fit within the bone tunnels. One bone block was passed into the femoral tunnel and rigidly fixed with a 6-mm bioabsorbable interference screw (BioSure; Smith & Nephew). The graft was then passed retrograde into the tibial tunnel, firmly tensioned with the knee in maximal extension (30° in the pig), and secured in the tibia with another 6-mm interference screw. Graft pretension levels were not quantified; however, the same surgical technique and graft fixation approach were used in all the reconstructed knees to ensure consistency. The tibial screw was inserted into the tibial tunnel at the distal end of the tunnel, and the screw was countersunk 3 mm below the cortical surface of the tibia.[39]

The bridge-enhanced ACL repair was performed with an extracellular matrix–based scaffold following the technique previously described.[41] Briefly, a Kessler suture with No. 1 Vicryl (Ethicon) was placed in the tibial stump of the transected ACL. The 4.5-mm femoral and tibial tunnels were then drilled slightly anterior to the ACL footprint on the femoral attachment and slightly posterior to the tibial attachment to protect the native ACL insertion sites.[27,40] An Endobutton (Smith & Nephew) carrying 3 looped sutures was passed through the femoral tunnel and flipped to engage the cortex. Two sutures were threaded through the scaffold, and the scaffold was introduced into the notch until femoral contact was visually verified. Sutures were then passed through the tibial tunnel and fixed extracortically with a button while the knee was in maximum extension (30° in the pig). The remaining suture was tied to a Kessler suture of No. 1 Vicryl in the tibial ACL stump to position the remaining ACL tissue in its anatomic

orientation from femoral attachment to tibial attachment. Three milliliters of autologous blood, aspirated during surgery, was used to saturate and activate the scaffold in situ. The scaffold-blood composite was allowed to set for 60 minutes before the animal was moved from the operating table. After surgery, all animals were housed for 4 weeks in individualized pens and then shipped to a farm for long-term care (Coyote Consulting Corp Inc). The animals were then sacrificed after 1 year of healing, and the limbs were harvested, imaged, and immediately frozen at –20°C until mechanical testing.

Imaging and Anatomic Index Measurements

The intact and treated limbs of each pig were imaged at full extension (30°) with a 20-cm volume extremity coil and a 3-T MRI scanner (TIM Trio, Siemens; MRI Research Facility, Brown University) immediately after harvest. A high-resolution T1-weighted gradient echo 3-dimensional FLASH (fast low-angle shot) sequence (repetition time/echo times/flip angle, 25 ms/7.36 and 15.24 ms/12°; field of view, 140 mm; matrix, 512 × 512; slice length/gap, 0.85 mm/0 mm; mean, 3; bandwidth, 130) was selected to acquire the images. This sequence produced high contrast among the soft tissues, bony geometry, and joint fluid, which facilitated anatomic index measurements.[36] The ACL or the graft cross-sectional area, with the sagittal and coronal elevation angles, was measured following established techniques.[23,51,61] All the dimensions were measured with Osirix Viewer (Pixemo SARL) and reported in millimeters or degrees. The knees were then frozen at –20°C until mechanical testing.

Ligament Cross-sectional Area. To measure the ligament cross-sectional area, sagittal- and coronal-oblique views that showed the complete ligament between the femoral and tibial attachments were used to define an axial slice corresponding to one-third the total ligament length from its tibial attachment (Figure 2, A and B). Then, the axial-oblique view of the same slice was used to measure the cross-sectional area by outlining the outer boundary of the ligament (Figure 2, C and D).[61] The area measurement was conducted at the distal third of the ACL or graft length, consistent with the known location of the minimum ACL cross-sectional area.[18]

Ligament Multiplanar Orientation. To measure the ligament elevation angle in the sagittal plane, a sagittal-oblique slice was selected that showed the entire ligament from the femoral attachment to the tibial attachment. The longitudinal axis of the tibia was established with the technique described by Hudek et al[19] (dashed red line in Figure 3A). Briefly, a central sagittal slice was selected in which the tibial attachment of the posterior cruciate ligament, the intercondylar eminence, and the anterior and posterior tibial cortices appeared in a concave shape. Then, 2 circles were fitted to the tibial head: a cranial circle touching the anterior, posterior, and cranial tibial cortex and a caudal circle touching the anterior and posterior tibial cortex (green circles in Figure 3A). The line connecting the center of the 2 circles was defined as longitudinal tibial axis. The perpendicular line to the longitudinal axis of the tibia was
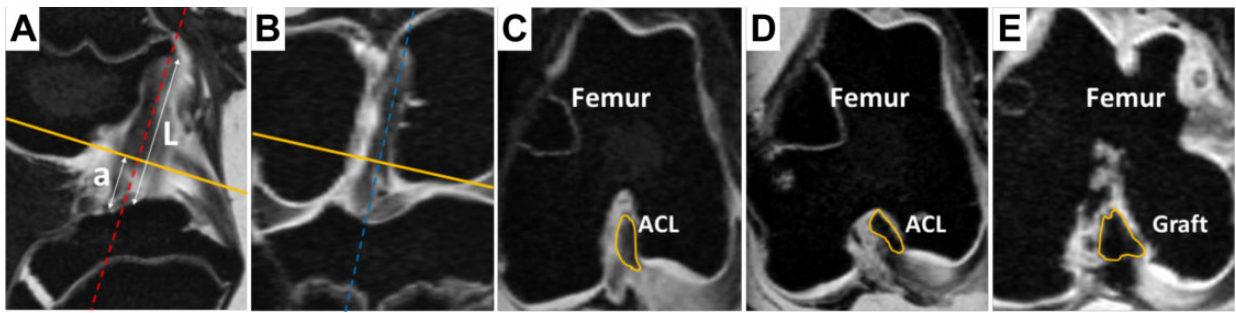
Figure 2. Measurement approach used to quantify ligament cross-sectional area. (A, B) Solid yellow line represents the location of the axial slice used to quantify the ligament cross-sectional area; dashed red and blue lines represent the longitudinal axis of the ACL in sagittal and coronal planes, respectively. Outlined (C) intact ACL, (D) repaired ACL, and (E) reconstructed graft. a, one-third of the ligament length from tibial attachment; ACL, anterior cruciate ligament; L, ligament length.
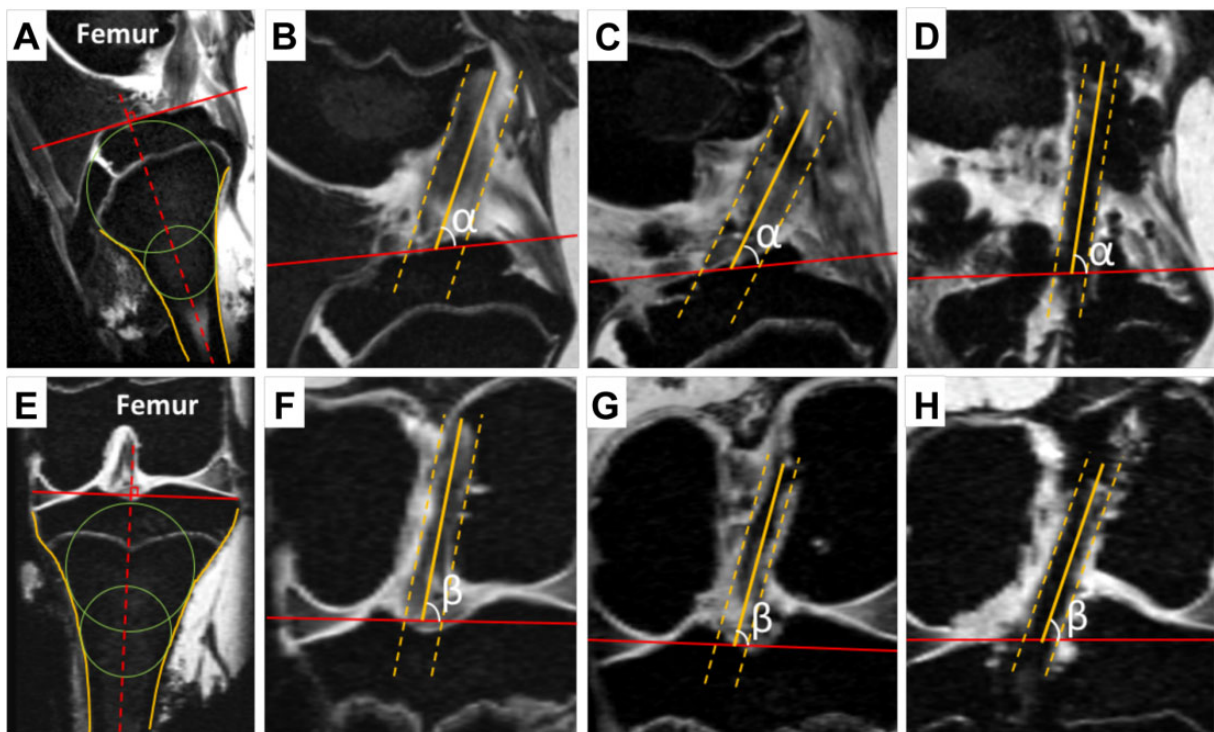

Figure 3. Measurement approach used to quantify the sagittal (α) and coronal (β) elevation angles of an intact ACL (B and F), a repaired ACL (C and G), and a reconstructed graft (D and H). (A and E) Dashed red line represents the longitudinal axis of the tibia in sagittal and coronal planes; green circles indicate the 2 cranial and cadual circles used to establish the longitudinal axis of the tibia. Solid red line in all panels represents the reference line perpendicular to the tibial axis to calculate the ligament elevation angles. (B-D and F-H) Dashed orange lines show the edges of the ligament, and orange line represents the longitudinal axis of the ligament. ACL, anterior cruciate ligament.

then established as the reference for measuring the sagittal elevation angle of the ACL or graft (solid red line in Figure 3A). With the same sagittal-oblique slice, the ligament longitudinal axis was defined as the line passing through the center of the tissue parallel to the anterior and posterior edges of the ligament (solid orange line in Figure 3, B-D). To minimize measurement error and to improve reproducibility, the contrast, saturation, and brightness of the images were adjusted to improve the ACL visibility during the

measurement procedure. The parameters were optimized to achieve clear ACL boundaries (edges). The ligament sagittal elevation angle was measured as the angle between the longitudinal axis of the ligament and the reference line (Figure 3, B-D).

To measure the ligament elevation angle in the coronal plane, the coronal-oblique view of the ligament from the same MRI slice for measuring the sagittal elevation angle was used. The longitudinal axis of the tibia (dashed red line
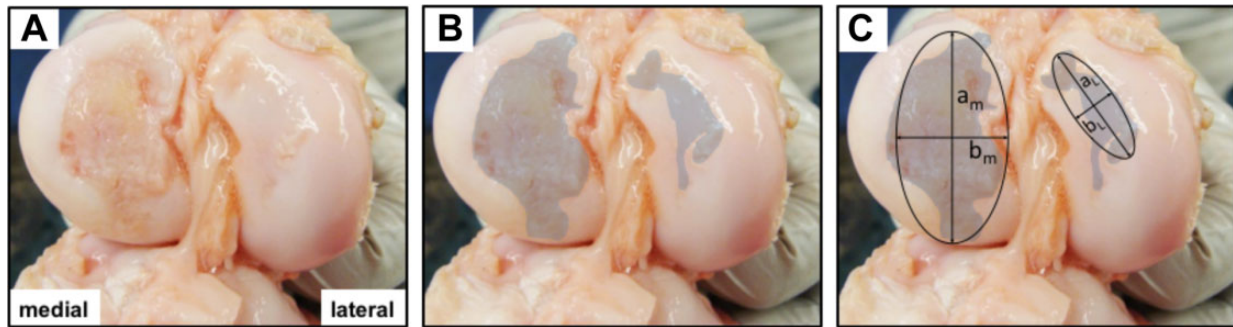
Figure 4. Measurement approach used to quantify macroscopic cartilage lesion area. (A) Macroscopic cartilage damage across the medial and lateral femoral condyles. (B) Staining the surface irregularities with india ink. (C) Measurement of the lesion area across each compartment by fitting an ellipse to each lesion. a_m and b_m, the length and width of the surface lesion across the medial femoral condyle, respectively; a_L and b_L, the length and width of the surface lesion across the lateral femoral condyle, respectively. Area across each compartment was calculated as $\Pi \times (a/2)^2 \times (b/2)^2$. Similar approach was used to quantify lesion areas across the medial and lateral tibial plateaus.

in Figure 3E) and the reference line perpendicular to the tibial axis (solid red line in Figure 3E) were established. With the same coronal-oblique view, the ligament longitudinal axis was defined as the line passing through the center of the tissue parallel to the medial and lateral edges of the ligament (solid orange line in Figure 3, F-H). The ligament coronal elevation angle was measured as the angle between the longitudinal axis of the ligament and the reference line (Figure 3, F-H). This method has been used by other investigators to measure the multiplanar orientation of human ACL graft.[2,7,51]

Biomechanical Testing

The knees (surgically treated and the contralateral intact) were thawed to room temperature prior to biomechanical testing. Specimens were sectioned at the proximal femur and distal tibia, with all soft tissues external to the joint capsule removed. The distal tibia and proximal femur were then potted for rigid attachment to a tensile testing frame (MTS 810; Material Testing Systems).[17] The joints were wrapped in towels saturated with physiologic saline to prevent dehydration. Investigators were blinded to the experimental group during preparation and testing.

Knee Laxity. AP knee laxity values were measured with a custom fixture at 30°, 60°, and 90° of knee flexion.[16,17] The knees were locked at each flexion angle with axial tibial rotation constrained in the neutral position while tibial translation and rotation were unconstrained in the coronal plane.[17] The knees were subjected to 12 cycles of ±40-N AP shear loads at each specific flexion angle while the AP displacements were measured. AP knee laxity was defined as the overall translational motion of the femur with respect to the tibia within the AP shear load limits of ±30 N.[16,17]

Ligament Structural Properties. After the laxity assessment, all remaining soft tissues were dissected from the joint, leaving the ACL or graft intact. The femur–ACL (or graft)–tibia constructs were then secured in a custom-designed tensile-testing fixture so that the mechanical axis of the ACL or graft was collinear with the load axis of the

test frame.[17] The femoral axial rotation was unconstrained, and the tibia was connected to the test frame through a sliding X-Y table to help the specimen to seek its own physiologic position under tensile loading. Specimens were then loaded in tension to failure at 20 mm/min.[16,20,25,62] The recorded load-displacement data were used to quantify ligament linear stiffness, yield, and maximum loads.[25]

Macroscopic Cartilage Assessment

After biomechanical testing, the articular cartilage across the medial and lateral femoral condyles and the medial and lateral tibial plateaus for the treated and contralateral intact knees was stained with india ink to highlight surface irregularities. The length and width of all visible lesions in the 4 regions of interest—the medial and lateral femoral condyles and the medial and lateral tibial plateaus—were measured with calipers as previously described (Figure 4).[39] Lesion areas were estimated per the assumption of elliptical fits. The lesion areas for each region were summed to give the total lesion area for each knee joint. Two independent examiners, who were blinded to the leg and treatment group, performed all measurements. The values for each examiner were averaged.

Statistical Analysis

All quantified ligament structural and anatomic properties were normalized to the contralateral ACL-intact knee (percentage intact). Measured knee laxity values for the treated knees were also normalized to the contralateral ACL-intact knee (*treated knee – contralateral ACL-intact knee*) and reported as side-to-side differences in AP knee laxity. ACL structural and anatomic properties with AP knee laxity for the ACL-intact knees were compared between the treatment groups with the independent-samples *t* test. This comparison was done to ensure that the animals allocated to each group had similar baseline properties. To test our hypotheses, bivariate linear regression analyses assessed the associations between the macroscopic lesion area

TABLE 1
Differences in ACL Structural and Anatomic Properties
and AP Laxity of the Contralateral ACL-Intact Knees
Between the Treatment Groups[a]

Measured Outcome[b]	ACLR (n = 8)	Repair[c] (n = 7)	P Value
ACL			
Yield load, N	1523 ± 333	1346 ± 259	.277
Maximum load, N	1777 ± 189	1793 ± 301	.902
Linear stiffness, N/mm	260.1 ± 42.2	247.8 ± 28.6	.526
Cross-sectional area,[d] mm^2	22.1 ± 4.9	23.7 ± 4.1	.556
Sagittal elevation angle[d]	51.3 ± 6.8	49.1 ± 7.6	.581
Coronal elevation angle[d]	83.2 ± 11.3	77.7 ± 5.3	.298
AP knee laxity, mm			
At 30° of flexion	2.4 ± 0.4	3.1 ± 1.1	.119
At 60° of flexion	3.1 ± 0.4	3.3 ± 0.8	.546
At 90° of flexion	2.4 ± 0.4	2.3 ± 0.4	.550

[a]Values are presented as mean ± SD. ACL, anterior cruciate ligament; ACLR, ACL reconstruction; AP, anterior-posterior.
[b]Obtained from the contralateral ACL-intact knee.
[c]Bridge-enhanced ACL repair.
[d]ACLR, n = 7; repair, n = 6.

(dependent variable) and each of the ligament structural and anatomic properties and AP laxity parameters (independent variables) for each treatment group. As a secondary analysis, the normalized anatomic properties of the reconstructed grafts and repaired ACLs were compared between the 2 surgical groups with the independent samples t test. The comparisons and correlations were considered statistically significant at $P \leq .05$. For this study, no a priori power analysis was performed to estimate the sample size, as the data were obtained from a previously reported study comparing cartilage damage between treatment groups in which the sample size was fixed.[39] Instead, we included all the eligible samples and data points available from the original study.[39] Post hoc power analyses, based on fixed-effects F tests, indicated that the study was adequately powered (>0.85) to test the associations between ACL (or graft) mechanical and anatomic properties and total cartilage lesion area. However, the study was underpowered to assess the links between side-to-side difference in knee laxity and extent of cartilage damage.

RESULTS

The mean values for the ACL structural and anatomic properties and the AP knee laxity obtained from the contralateral ACL-intact knees for each experimental group are presented in Table 1. No significant differences in the measured outcomes of the contralateral knee were observed between the animals assigned to the ACL reconstruction group and those assigned to the bridge-enhanced ACL repair group ($P > .1$ for all comparisons).

Macroscopic cartilage damage was observed in the treated knees, primarily across the medial femoral condyle, with substantially bigger lesions in reconstructed knees versus repaired knees.[39] Moreover, both groups showed
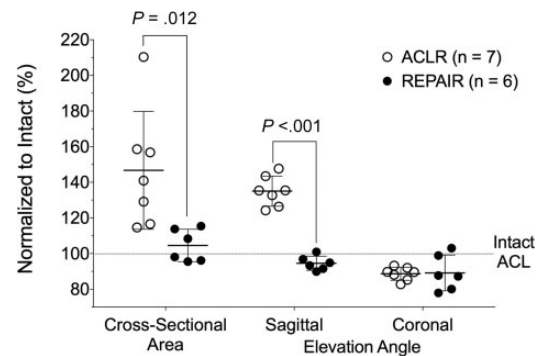

Figure 5. Differences in normalized ligament cross-sectional area and elevation angles in the sagittal and coronal planes at 1 year after surgery. ACL, anterior cruciate ligament; ACLR, ACL reconstruction; REPAIR, bridge-enhanced ACL repair.

similar normalized ligament structural properties and side-to-side differences in AP knee laxity at 1 year after ACL surgery ($P > .1$).[39] However, the reconstructed grafts had a significantly higher normalized cross-sectional area and sagittal elevation angle (more vertical) than the repaired ACLs (Figure 5). There were no differences in normalized coronal elevation angles between reconstructed grafts and repaired ACLs ($P = .548$) (Figure 5).

In animals treated with conventional ACL reconstruction, normalized graft yield and maximum loads, cross-sectional area, sagittal and coronal elevation angles, and side-to-side difference in AP knee laxity at 60° all were significantly correlated with total cartilage lesion area developed 1 year after surgery ($R^2 > 0.5$, $P < .04$) (Figure 6). Increased normalized graft yield and maximum loads and normalized graft elevation angle in the coronal plane were associated with decreased cartilage lesion area (Figure 6, A, B, and F). Also, decreased normalized graft cross-sectional area and graft elevation angle in the sagittal plane, as well as decreased side-to-side difference in AP knee laxity at 60°, were associated with decreased cartilage lesion area (Figure 6, D, E, and H). No notable associations were observed between normalized graft linear stiffness and side-to-side differences in AP knee laxity at 30° and 90° and total cartilage lesion area at 1 year after ACL reconstruction ($R^2 < 0.4$, $P > .1$) (Figure 6, C, G, and I).

In animals treated with the bridge-enhanced ACL repair, normalized ACL yield load, linear stiffness, cross-sectional area, and sagittal and coronal elevation angles were significantly associated with total cartilage lesion area developed 1 year after surgery ($R^2 > 0.5$, $P < .05$) (Figure 7). A borderline significant correlation was observed between the normalized ACL maximum load and total cartilage lesion area at 1 year ($R^2 = 0.56$, $P = .053$) (Figure 7B). Increased normalized ACL yield and maximum loads, linear stiffness, cross-sectional area, and ACL elevation angles in the sagittal and coronal planes were associated with decreased cartilage lesion area (Figure 7, A-F). No notable associations were observed between side-to-side differences in AP knee laxity and total cartilage lesion area at 1 year after bridge-enhanced ACL repair ($R^2 < 0.3$, $P > .25$) (Figure 7, G-I).
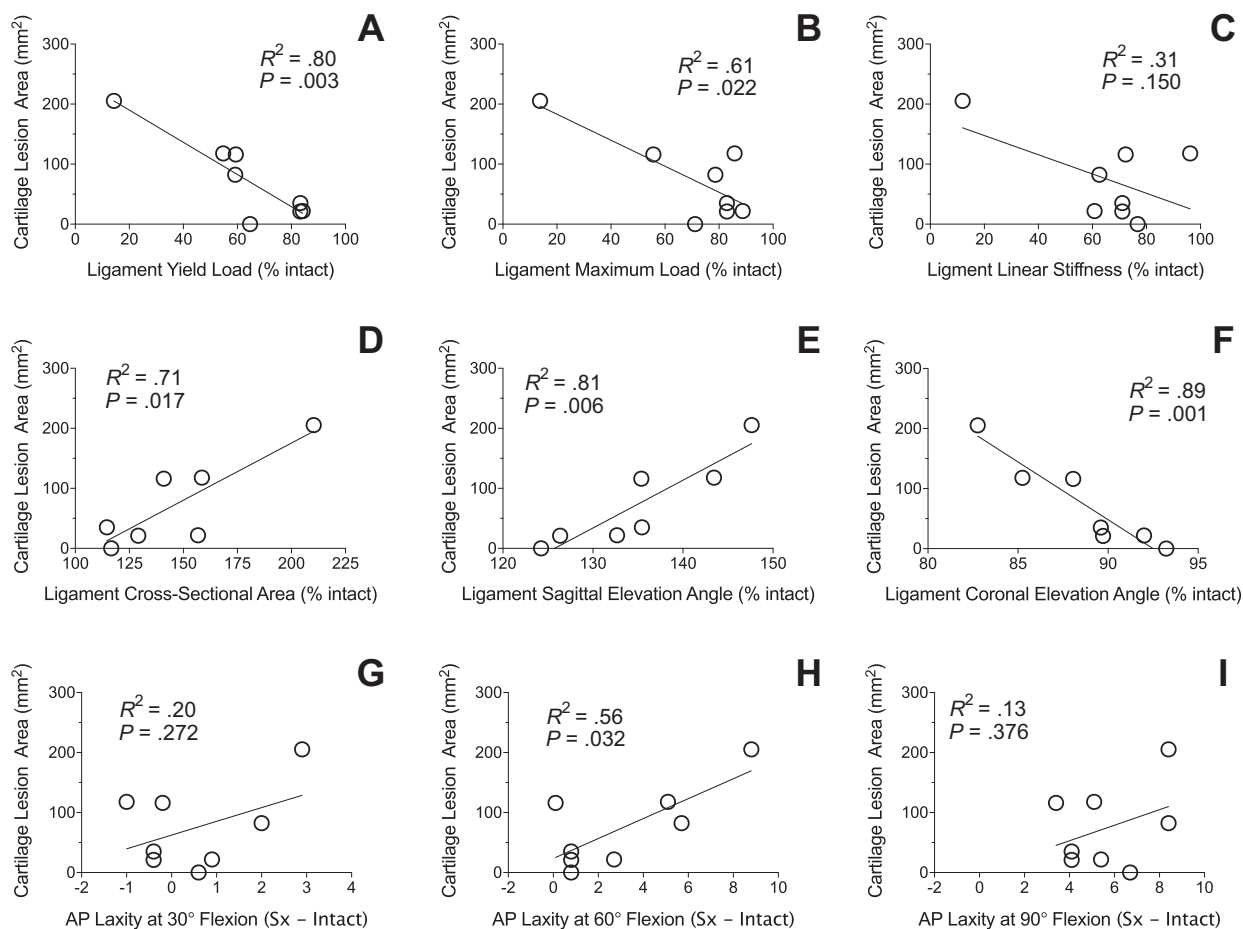
Figure 6. Linear associations between total cartilage lesion area and graft structural properties (A-C; n = 8), graft anatomic properties (D-F; n = 7), and side-to-side differences in AP knee laxity (G-I; n = 8) 1 year after anterior cruciate ligament reconstruction surgery. AP, anterior-posterior.

DISCUSSION

The results of this study support our first hypothesis that multiple biomechanical and anatomic properties of the reconstructed graft or repaired ACL are related to the damaged cartilage lesion area following ACL surgery. The results partially support our second hypothesis that the side-to-side differences in AP knee laxity (at 60° of knee flexion) were associated with damaged cartilage lesion area 1 year after ACL reconstruction. In general, smaller lesion areas were observed in the knees with graft or repaired ACL structural and anatomic properties closer to those of the contralateral intact ACL. Also, smaller lesion areas were seen in the reconstructed knees with AP knee laxity values at 60° of flexion closer to those of the contralateral ACL-intact knee. Observed changes in AP knee laxity at 60° corresponded with clinical observations of side-to-side differences in AP knee laxity at 30° in patients with an injured ACL, given that the minimum flexion angle (full extension) for porcine knees is ~30°. Among all the biomechanical and anatomic factors, normalized ligament cross-sectional area and sagittal elevation angle, both of

which are strong indicators of cartilage damage, were significantly different between the treatment groups. The grafts were consistently >20% larger in cross-sectional area than the contralateral intact ACL, while the repaired ACL cross-sectional areas ranged from 95% to 115% of the contralateral intact ACL. In addition, when compared with the native contralateral ACL, the reconstructed knees had a substantially higher sagittal angle (a more vertical graft), while the repaired knees had a slightly lower sagittal angle (more horizontal ligament). Although we strived to consistently place the tunnels through the ACL footprint, small deviations in tunnel position during ACL reconstruction may have contributed to increased graft sagittal elevation angle.

In this study, we found that the reconstructed grafts or repaired ACLs that more closely resembled the structural and anatomic properties of a native ACL led to less damage to the tibiofemoral articular cartilage, regardless of the treatment group. Altered knee biomechanics following ACL surgery has been suggested as one of the primary causes of posttraumatic OA.[4,8,32,46] Given the critical role that the ACL plays in stabilizing tibiofemoral motion,[26,28,30,50] it is
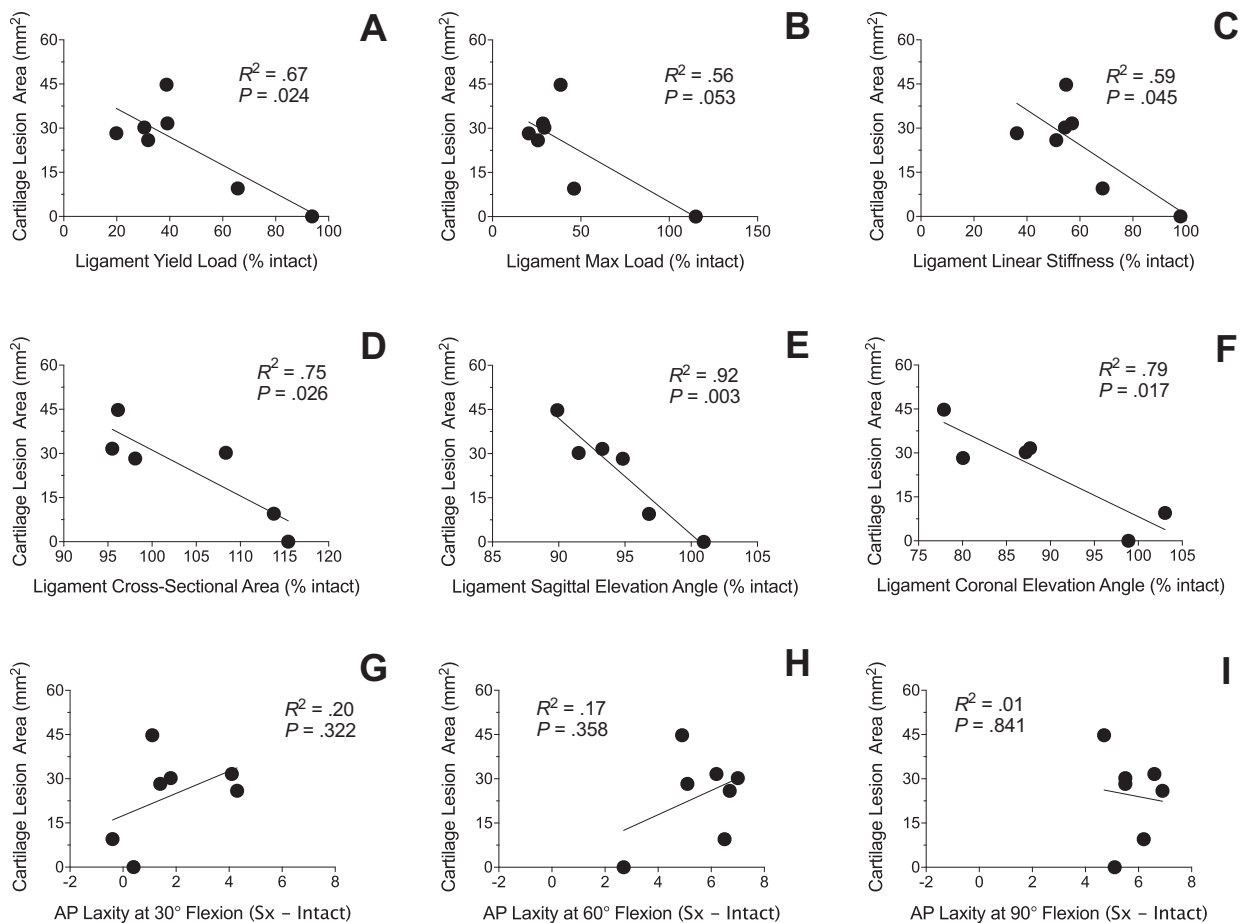
Figure 7. Linear associations between total cartilage lesion area and ACL structural properties (A-C; n = 7), ACL anatomic properties (D-F; n = 6), and side-to-side differences in AP knee laxity (G-I; n = 7) 1 year after bridge-enhanced ACL repair. ACL, anterior cruciate ligament; AP, anterior-posterior.

expected that any deviations in the structural and anatomic properties of a reconstructed graft or a repaired ACL may lead to abnormal joint motion. Abnormal rotations and translations across the tibiofemoral joint exert nonphysiologic compressive and shear forces on the articular cartilage, which may lead to cartilage breakdown over time, in particular within the hostile inflammatory synovial environment of the injured joint.[3,5,12,32,55,57] Previous in vivo studies have shown significant increases in anterior and medial tibial translations as well as increased axial tibial rotation (internally and externally) during daily activities (ie, walking, stair climbing) in patients with deficient ACLs.[3,32,58] Moreover, increases in these translations and rotations have been linked to decreased cartilage thickness within 6 to 36 months after ACL reconstruction.[46] These assertions are in agreement with our observations of greater cartilage damage in reconstructed knees with higher side-to-side differences in AP knee laxity. However, the fact that all except 1 of the observed associations were not statistically significant and not replicated across all tested flexion angles and surgical treatments indicates that AP instability alone may not be the only factor capable of

contributing to posttraumatic OA. It may be that multiplanar joint instability, which may include a combination of AP and medial-lateral translations as well as axial rotation, results in substantial cartilage wear after ACL surgery. As the current work was limited to the residual laxity in AP direction, further studies would be required to investigate the isolated and combined (eg, pivot shift) roles of these motions on cartilage loading and OA risk.

The current results also show that the reconstructed grafts or repaired ACLs with the largest deviations from the native ACL alignment resulted in higher degrees of cartilage damage under both surgical procedures. The effect of graft alignment on knee biomechanics and cartilage damage following ACL reconstruction has been the focus of several recent research efforts.[1,46,51] It has been shown that a more vertically aligned graft in the sagittal plane is less effective in resisting the anterior and medial tibial translations following ACL reconstruction.[1] These motions can exert excessive shear loads across the tibiofemoral articular cartilage and result in cartilage degeneration over time.[33,47,52,54] Despite nonanatomic positions of the femoral and tibial tunnels used in the bridge-enhanced

repair procedure (tunnels drilled slightly anterior to the ACL footprint), repaired ACLs more closely replicated the vertical alignment of the contralateral intact ACL in the sagittal plane (mean, 92%; range, 86%-101%). In contrast, the reconstructed grafts were substantially more vertical than their contralateral intact ACLs (mean, 135%; range, 124%-148%), even with anatomic tunnel positions. These observations indicate that the bridge-enhanced ACL repair technique is less sensitive to the tunnel positions and that repaired ACLs heal insertion to insertion.

Previous studies have also reported abnormal internal tibial rotation and knee flexion moment in patients with a vertically oriented graft in the coronal plane.[1,51] Although almost all the reconstructed grafts and repaired ACLs in this study had smaller coronal elevation angles than the contralateral intact ACLs, the results show that even a horizontally oriented ligament, below normal levels, can lead to increased cartilage damage. Future studies in human subjects are required to confirm these associations and to elucidate the underlying mechanisms responsible for such observations.

Similar to previously reported clinical observations,[31,56] the reconstructed grafts in pigs had a substantially bigger cross-sectional area at the midsubstance of the ligament (mean, 147%) when compared with intact ACLs of the contralateral knee. Our regression analysis showed that the grafts with bigger deviations from the cross-sectional area of the native ACL resulted in greater cartilage damage across the tibiofemoral joint. Unlike reconstructed grafts, the cross-sectional area of the repaired ACLs was almost identical to the area of the intact ACLs of the contralateral side (mean, 105%). Additionally, in the repaired knees, the higher normalized ACL cross-sectional area was associated with lower cartilage damage, which is in contrast to the trends seen in the reconstructed knees. A possible explanation for this paradox is the significant differences in normalized cross-sectional area of the reconstructed grafts (mean, 147%; range, 115%-210%) versus repaired ACLs (mean, 105%; range, 95%-115%). It is conceivable that increases in the cross-sectional area of the treated ligament up to a certain level result in improved structural properties of the tissue, which may contribute to improved joint stability and less cartilage damage. However, dramatic increases in the cross-sectional area of the treated ligament may be indicative of poor healing and remodeling, which may lead to inferior graft properties. It is also possible that a substantially bigger graft may cause mechanical impingement against the walls of the femoral notch. The repetitive contact between the healing graft and notch can negatively affect the graft structural properties. Improper graft healing can ultimately result in increased joint instability and cartilage damage. This is supported by a strong positive association between normalized cross-sectional area and normalized linear stiffness of repaired ACLs ($r = 0.74$, $P = .092$) and a negative association between normalized cross-sectional area and normalized linear stiffness of reconstructed grafts ($r = -0.72$, $P = .065$) in this study. Further studies are needed to confirm these findings and to better understand other potential contributing factors to observed associations.

There are limitations to consider when interpreting the study results. The porcine model does not fully represent the human condition. The pig is a quadruped, and postoperative rehabilitation is difficult to control, as with any animal model. Nonetheless, the porcine model has specific advantages for this study, given that many anatomic, biomechanical, and wound-healing similarities between the pig and human knee have been noted.[9,37,48,63] Another limitation is that the ACL injury was created with a scalpel to transect the ligament within its midsubstance. It is possible that a more frayed ligament would heal differently with the bridge-enhanced ACL repair. Moreover, for the ACL-reconstructed treatment groups, fresh-frozen allografts were used instead of autografts. In the porcine model, harvesting the patellar tendon autograft would compromise the extensor mechanism, while the hamstring autograft is not of sufficient length. It is possible that autografts would have provided different results. Nonetheless, the structural properties of the allografts in this study were similar to those reported for autografts in other quadruped models.[13,21] Finally, a small sample size of 6 to 8 per group may have hampered our ability to detect the relationships between some of the investigated outcomes and cartilage damage.

In summary, this study investigated the effects of several clinically relevant structural and anatomic properties of the reconstructed graft or repaired ACL as well as AP knee laxity on cartilage damage lesion areas within 1 year after 2 surgical procedures: ACL reconstruction, the current standard of care, and bridge-enhanced ACL repair, an emerging treatment currently under United States Food and Drug Administration–approved clinical trials.[40] The structural and anatomic properties of the reconstructed graft or repaired ACL were strongly related to the extent of damage across the tibiofemoral articular cartilage. Residual AP knee laxity, only at 60° of knee flexion, was also associated with cartilage damage 1 year after ACL reconstruction. In general, less cartilage damage was observed in the knees with structural and anatomic ACL properties closer to those of the native ACL. It was also shown that the bridge-enhanced ACL repair procedure was able to restore the sagittal elevation angle and cross-sectional area of a torn ACL.

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