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DELAY OF 2 OR 6 WEEKS ADVERSELY AFFECTS THE FUNCTIONAL OUTCOME OF AUGMENTED PRIMARY REPAIR OF THE PORCINE ANTERIOR CRUCIATE LIGAMENT

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Abstract

BACKGROUND—Enhanced primary ACL repair, in which suture repair is performed in conjunction with a collagen-platelet composite to stimulate healing, is a potential new treatment option for ACL injuries. Previous studies have evaluated this approach at the time of ACL disruption.

HYPOTHESIS—In this study, we hypothesized that delaying surgery by 2 or 6 weeks would have a significant effect on the functional outcome of the repair.

STUDY DESIGN—Controlled Laboratory Study

METHODS—Sixteen female Yorkshire pigs underwent staged, bilateral surgical ACL transections. ACL transection was initially performed on one knee and the knee closed. Two or six weeks later, enhanced primary repair was performed in that knee while the contralateral knee had an ACL transection and immediate repair. Biomechanical parameters were measured after 15 weeks in vivo to determine the effect of delay time relative to immediate repair on the healing response.

RESULTS—Yield load of the repairs at 15 weeks was decreased by 40% and 60% in the groups where repair was delayed for 2 and 6 weeks respectively ($p=0.01$). Maximum load showed similar results (55% and 60% decrease in the 2 and 6 week delay groups respectively, $p=0.011$). Linear stiffness also was adversely affected by delay (50% decrease compared to immediate repair after either a 2 or 6 week delay, $p=0.011$). AP laxity after 15 weeks of healing was 40% higher in knees repaired after a 2 week delay, and 10% higher in those repaired after a six week delay ($p=0.012$) when tested at 30 degrees of flexion, but was not significantly affected by delay when tested at 60 or 90 degrees ($p=0.21$).

CONCLUSIONS—A delay between ACL injury and enhanced primary repair has a significant negative effect on the functional performance of the repair.

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What is known about the subject: The anterior cruciate ligament can be repaired in animals using an enhanced suture technique.

What this adds: The timing of the repair is critical to the functional outcome of the repair – a clinically relevant delay of even two weeks can diminish the effectiveness of the suture repair technique.

CLINICAL RELEVANCE—As future investigations assess new techniques of ACL repair, the timing of the repair should be considered in the design and the interpretation of experimental studies.

Keywords

ACL; Platelets; Suture repair; tissue engineering; knee; in vivo; porcine

INTRODUCTION

Anterior cruciate ligament (ACL) ruptures occur in over 175,000 patients a year, and can have devastating effects that last far beyond the time of injury, including a 78% risk of the development of radiographically evident osteoarthritis after only 14 years.²¹ Following injury, the ACL does not heal on its own. Therefore surgical reconstruction with a graft of tendon to replace the torn ACL is performed in most patients to improve knee stability and limit future meniscal injury.

While reconstruction has been shown to improve the gross stability of the joint, the procedure has limitations including its inability to restore the natural kinematics of the joint,^{1, 2, 20} which may explain, in part, the high rate of osteoarthritis seen after an ACL tear and reconstruction.²¹ Thus, new techniques for ACL treatment are of interest to the sports medicine community. Enhanced primary repair, where a suture repair of the ligament is supplemented with a cytokine-laden scaffold to stimulate healing biology, has recently been shown to enhance healing of the ACL,^{6, 16} and thus has generated renewed interest in repair and regeneration of the ACL after rupture.

However, the studies that have been performed to date in large animal models have focused on enhanced suture repair at the time of ACL transection, whereas in clinical treatment of these injuries, there is routinely a delay between the time of injury and time of surgery. For most patients, it takes a minimum of two weeks to be evaluated by an orthopaedic surgeon and to be scheduled for surgery. In addition, many surgeons prefer to wait at least six weeks after injury to allow the initial inflammatory response of the joint to return to normal before performing ACL reconstruction surgery.¹⁹

The objective of this study was to determine whether clinically relevant delays between injury and repair would influence healing when using the enhanced primary repair technique. Our hypothesis was that a delay of 2 or 6 weeks would result in significant decreases in the yield load and linear stiffness of an ACL repair, and significant increases in AP knee laxity of the ACL repaired joint relative to the immediate repair condition. A porcine model was selected for this study because of its anatomical, physiological, biomechanical and hematological similarities to the human condition.^{9, 16, 22} The enhanced primary repair technique, which has been previously validated in the porcine model, was utilized.^{3, 4, 6, 12, 14} A collagen-platelet composite (CPC) was used to enhance the repair because it provides a mechanism to deliver growth factors to the ACL transection site.⁶

MATERIALS AND METHODS

Experimental Design

Approval from the Institutional Animal Care and Use Committee was obtained prior to the beginning of this study. Sixteen female 30 kg juvenile Yorkshire pigs underwent ACL transections and collagen-platelet enhanced primary repair. The animals were randomly assigned to one of two experimental conditions; 1) two week delayed repair, or 2) six week delayed repair. Each animal had an ACL transection procedure performed on one side, and

the knee was closed. Then at the designated delay time point (either 2 or 6 weeks), both knees were opened and the previously cut ACL underwent a delayed repair, while the contralateral ACL was severed and underwent an immediate repair using the same technique and identical scaffold (Figure 1). All animals were allowed to heal for 15 weeks following ACL repair. After euthanasia, the hindlimbs were disarticulated at the hip, wrapped in saline soaked towels, placed in a double layer of plastic bagging with air removed and frozen at -20 degrees C.

Scaffold Preparation

The collagen scaffold was made by solubilizing bovine fascia. Fresh bovine fascia was harvested and dissolved in an acidified pepsin solution at a pH of 2.0 to create an atelocollagen solution. The resulting solution was then frozen at -80 degrees C, lyophilized, and rehydrated with a specified amount of water to create a solution with a collagen content of 12 mg/ml. This concentrated collagen slurry was then neutralized using HEPES buffer (Mediatech Inc, Herndon, VA), sodium hydroxide (Fisher Scientific, Fair Lawn, NJ), PBS (HyClone, Logan UT), and calcium chloride (Sigma-Aldrich, St. Louis, MO). The neutralized solution was then transferred into cylindrical molds with an inner diameter of 16mm, frozen and lyophilized. The resulting scaffolds were measured individually using a ruler and found to be 14 mm in diameter and 40 mm in length. Scaffolds were stored frozen and under vacuum until use.

Platelet Concentrate Preparation

Autologous platelets were prepared by centrifugation of anti-coagulated blood from each animal at 100 g for 15 min. This resulted in an approximate increase in platelet concentration from $354,000 \pm 63,000$ per mm^3 (range of 246,000 to 504,000 per mm^3) to $1,634,000 \pm 310,000$ per mm^3 (range of 1,173,000 to 2,151,000 per mm^3), consistent with a 4 ± 1 -fold increase in platelet concentration.

Surgical Procedures

After the induction of general anesthesia, blood was drawn from the femoral vein of each animal into tubes containing Anticoagulant Sodium Citrate (Cytosol Laboratories, Inc., Braintree, MA). A total volume of 60cc was taken for platelet and leukocyte counting and to manufacture the platelet concentrate. Pre-operative measurements of the maximum flexion angle and minimum extension angle were obtained by stabilizing the femur with the hip in 90 degrees of flexion and neutral abduction and using a goniometer to measure the maximal extension and flexion at the knee. The clinical Lachman maneuver was performed by stabilizing the femur above the knee and manually shifting the tibia anterior. The resulting tibial shift (in mm) from resting baseline was estimated when a resistant endpoint was felt. The maneuver was performed by one orthopaedic surgeon to eliminated inter-examiner bias.

ACL Transection Procedure

A medial arthrotomy was made at the medial border of the patellar tendon and the ACL exposed. The ACL was then cut at the junction of the proximal and middle thirds using a knife. The Lachman was repeated to verify functional loss of the ACL (loss of endpoint). The knee was closed in layers. The animals were allowed ad lib activity for 2 or 6 weeks following surgery depending on their experimental condition.

Enhanced Suture Repair of the ACL

At 2 or 6 weeks following the index ACL transection, both knees were prepared for surgery. In the knee in which the ACL transection was previously performed, the enhanced repair procedure was performed as follows (Figure 1). After exposure of the intercondylar notch

through the prior incision, a variable depth suture was placed in the tibial stump. The knee was irrigated with 500 cc sterile saline using a bulb syringe. A resorbable suture bridge from the femoral ACL footprint to the tibial footprint was then created to hold the collagen-platelet implant. First, the femoral tunnel was drilled using an 4.5 mm Endobutton drill over a guidewire. An Endobutton with three sutures trailing from it was passed up the tunnel and engaged on the proximal femoral cortex. The collagen scaffold was then threaded onto two of the exiting Vicryl sutures, and placed in the intracondylar notch. These two sutures were then brought down through a 4.5 mm tunnel in the tibia and tied over a tibial button with the knee held in 30 degrees of flexion (maximum extension for the porcine knee). Thus, the suture bridge of resorbable Vicryl served as a temporary stabilization of both the collagen scaffold and the knee. The remaining Endobutton suture was then tied to the variable depth suture in the tibial stump (Figure 1). The platelet concentrate was allowed to saturate the scaffold to fill the defect and notch. For the contralateral knee undergoing immediate repair, the exposure, ACL transection, and repair procedures were performed as described above.

Knee Harvest

The animals were euthanized 15 weeks following ACL repair. Prior to euthanasia, the clinical measurements of maximum and minimum knee flexion angles and the Lachman maneuver were performed by an examiner blinded to the treatment group. The leukocyte and systemic platelet counts were also repeated using blood samples taken at time of euthanasia. The hindlimbs were disarticulated at the hip, wrapped in saline soaked towels, placed in a double layer of plastic bagging with air removed and frozen at -20 degrees C.

Biomechanical Testing

18 hours prior to testing, the hindlimbs were removed from the freezer and thawed at room temperature. All extraneous muscle and soft tissue were carefully removed from the joint leaving the knee capsule intact. Specimens were kept moist throughout the test protocol with a wrap of normal saline-soaked gauze. Two pairs of drywall screws were inserted bicortically and perpendicular to each other in the tibia and femur to ensure stable fixation when the bones were potted. Sections of 3.8 cm diameter, schedule 40 PVC pipe were cut to 14 cm lengths. These “cannons” had eight 1 cm holes drilled through the wall to allow the potting compound to interdigitate with the cannon. Each bone was rigidly embedded in a urethane potting compound (Smooth On, Easton, PA) leaving approximately 5 cm of exposed bone to the joint line. The bones were oriented such that the long axes of the bone and cannon were coaxial.

AP laxity testing was performed with the knee flexed at 30° , 60° and 90° as previously described.^{3, 14} Knees were supported on custom fixtures and rigidly attached to an MTS 810 servohydraulic load frame (MTS Systems Corporation, Eden Prairie MN) using a 1000 N load cell (Model 661.18, MTS Systems Corp). Fully-reversed, sinusoidal anterior-posterior directed shear loads of ± 40 N were applied to the joint at 0.0833 Hz for 12 cycles. Load and displacement data were acquired at 20 Hz and plotted using Excel to depict the load-displacement curve. During the AP laxity tests, axial rotation was locked in the neutral position, while the varus-valgus angulation and the coronal plane translations were left unconstrained.

Following AP laxity testing, the joint capsule, menisci, collateral ligaments and the PCL were dissected from the joint leaving the femur-ACL scar mass-tibia complex intact to prepare them for tensile testing.^{4, 14} The tibia and femur were positioned on the MTS platform so that the mechanical axis of the ACL was collinear with the load axis of the material test system. The knee flexion angle was initially set at 30° . The tibia was mounted to the base of the MTS via a sliding X-Y platform. The femur was unconstrained to internal-

external rotation and varus-valgus angulation. This enabled the specimen to seek its own position so that the load was distributed more uniformly over the cross section of the healing ligament once the tensile load was applied. The crosshead was lowered until the load across the joint surface was 5N of compression to provide a reproducible starting point for displacement at which the tensile load ramp was then initiated. The tensile load was measured using a 25k N load cell (Model 661.19, MTS Systems Corp). A ramp at 20 mm/min was performed, and the load-displacement data were recorded at 25Hz.¹⁴ From the MTS load-displacement tracing, the displacement to 5 N of tensile load (low-load displacement), displacement to yield, displacement to failure, yield load, maximum failure load, and linear stiffness were determined^{4, 6}.

Statistical Analyses

Mixed model analyses of variance were used to evaluate the study hypotheses for each outcome measure. The fixed factor within the model was the delay condition (2 vs. 6 weeks), which was randomized across animals. The within-subject factor corresponded to the leg (immediate vs. delayed repair), which was also assigned by chance within each animal. The dependent variables included the yield load, maximum load, linear stiffness, yield displacement, maximum displacement, and AP laxity at 30, 60, and 90 degrees. Pair-wise comparisons were performed between experimental conditions using Fisher's LSD procedure. Similarly, analyses of variance with an additional within-subject factor (time) were used to make comparisons between experimental conditions, leg, and time for those measures obtained at baseline (before the first surgery), before the second surgery, and 15 weeks following the second surgery (i.e. minimum extension angle, maximum flexion angle, and manual Lachman tests). Two-way repeated measures analyses of variance were used to compare systemic leukocyte counts and systemic platelet counts between the 2 and 6 week delay conditions and time. All statistical analyses were performed using SAS statistical software Version 9 (PROC MIXED; SAS Institute Cary, NC).

RESULTS

Physical Examination

There were no significant differences in either the maximum knee flexion or minimum knee extension angles between the immediate and delay repaired knees at 15 weeks in the 2-week delay (Flexion, 135 ± 4.6 degrees vs. 135 ± 5.4 degrees respectively, $p=.43$; and Extension, 33.1 ± 2.6 vs. 33.8 ± 3.5 respectively, $p=.78$) or in the 6-week delay (Flexion, 137.5 ± 2.7 degrees vs. 135 ± 4.6 degrees respectively, $p=.35$; and Extension, 33.8 ± 3.5 vs. 34.3 ± 5.0 respectively, $p=.42$) conditions at the final time point. There were also no significant differences in the clinical Lachman exam results between the immediate and delay repaired knees (2-week $p=.19$; 6 week $p=.54$) after fifteen weeks of healing. As would be expected, the Lachman sign was significantly higher in the ACL transected knee at the time of the second surgery when compared to the contralateral intact knee before it was cut (Table 1, 2-week $p=.008$, 6-week $p=.005$).

No significant differences were seen in the change from baseline systemic leukocyte count across time points for both the 2 and 6 week delay conditions ($p=0.25$). There was a significant decrease in the systemic platelet count over the course of the experiment for the both the 2 and 6 week delay conditions ($p<0.01$) with no evidence of the change in the 2 and 6 week conditions being different ($p=0.56$). Mean platelet counts at the 15 week time point were significantly lower than baseline for both delay conditions ($p<0.01$).

Biomechanical Outcomes

The yield load of the repaired ligaments decreased by 40% with a 2 week delay and by 60% with a 6-week delay when compared to the immediate repair condition (Table 3, $p=0.01$). However, the yield load was not significantly different between the 2 and 6-week delay time ($p=0.26$).

The maximum load of the repaired ligaments decreased by 55% with a 2 week delay and by 60% with a 6 week delay when compared to the immediate repair condition (Table 3, $p=0.008$). However, the maximum load was not significantly different between the 2 and 6-week time delay times ($p=0.68$).

The differences between immediate and delayed repaired ligaments were similar for both the 2 and 6 week delayed conditions for both linear stiffness and low load displacement to 5N (Table 3). In the case of linear stiffness, a decrease of 50% was observed for both the 2 week and 6 week delayed repair conditions ($p=0.011$). There were no significant differences between the delayed and immediate repair (Table 3) with respect to the displacement to yield (Table 3, $p=0.21$) or displacement to maximum load ($p=0.14$). Load-displacement data from each of the four groups was averaged at 1mm increments from no displacement to 5mm of displacement and the data plotted in Figure 2. Note the decrease in load-displacement curves in the groups undergoing delayed repair. Standard errors of the mean (SEM) were also calculated for each group at each displacement value.

The AP laxity of the knees which underwent delayed repair had increased laxity relative to their contralateral immediate repaired knees (Table 3, $p=0.012$). The increase in laxity relative to the immediate repaired knee was 40% at 30 degrees for the 2 week delay and 10% for the 6 week delay. There was no evidence of any differences between delay and immediate repaired knees in AP laxity at 60 degrees ($p=0.21$). However, there was evidence of an interaction ($p=0.06$) indicating that the difference between the two limbs was dependent on the delay time. The AP laxity of the immediate limb was 20% better than that of the 2 week delay limb ($p=0.051$), while there was no difference between the immediate and 6 week delay limbs ($p=0.46$) at 60 degrees of flexion. There were no significant effects of repair delay on the laxity of knees when tested at 90 degrees of flexion ($p=0.10$).

DISCUSSION

A delay of two or six weeks between ACL injury and enhanced suture repair reduced the structural properties of the ligament repair and increased AP laxity of the joint. This suggests that the enhanced ACL suture repair, which was found to be effective for the immediate injury, may need to be significantly modified to function in the current clinical environment.

The mechanisms behind the functional loss of healing with delay of repair remain unknown. One possibility is that the retraction of the stump noted to occur after an ACL tear in humans¹³ may also occur in the porcine model. When the knees were reopened after two weeks, there was significant synovitis around the distal ligament stump, which prevented good suture “bite” in the tissue. Thus, only minimal tension could be applied when these sutures were tied to the sutures exiting the femur in the two week animals. Similarly, while there was less synovitis noted in the 6 week animals, the stump had retracted and was smaller than that seen at time of transection. In the 6 week case, while sutures could be placed with tension in the tibial stump similar to that in the immediate repairs, the gap between the tibial stump and the femur was larger in the delayed repair knees than in the immediately repaired knees. Whether these observed differences contributed to the differences in the biomechanical outcome measures studied here requires further study.

The effect of delayed repair on AP knee laxity was depended on the angle at which the AP laxity was measured. At 30 degrees (full extension in the pig), where capsular restraints are likely to have the greatest contribution, there was a significant difference with the knees repaired immediately having less laxity than those repaired after a delay. However, when measured at 60 degrees, where the ACL itself has a greater contributory role, the AP laxity was worse in knees where repair was delayed by 2 weeks, but not in knees where the repair was delayed by 6 weeks. One possible explanation for this may be a detrimental effect on the ACL repair tissue itself which occurs when the knee is operated on during a relatively acute inflammatory phase (2 weeks) which may not be present when the inflammation is allowed to subside prior to a second surgery. Additional work is required to further develop and test this hypothesis.

The AP laxity at 60 degrees in the repaired knees ranged from 13 to 16 mm at the 15 week euthanasia time point. This is a large increase from the baseline value of 4.3 ± 0.6 mm previously reported for Yorkshire pig knees in similar age animals, but remains below that of a porcine knee with the ACL transected, where the AP laxity is greater than that permitted by the testing system (32 mm).³ In other studies of ACL reconstruction in the pig model, standard ACL reconstruction with bone-tendon-bone allograft resulted in an increase of 10.6 mm over the intact knee laxity at 60 degrees,⁵ which would lead to a range similar to that seen in this study.

The maximum loads of the immediate repairs in this study were approximately 210 to 240 N after 15 weeks of healing. This is similar to other studies of ACL repair in pigs, where the maximum load at 15 weeks has been reported to average 270 N with this repair technique,¹² and is in contrast to ACL reconstructions in the same animal model, where the maximum loads of the ACL grafts averaged 311 N.⁵ Stiffness values for ACL reconstruction with a patellar tendon allograft in this pig model averaged 48 N/mm,⁵ where the values here in the immediate repairs averaged 44 N/mm for the 2 week group. These data would suggest that primary repair is still inferior to ACL reconstruction, and is not ready for clinical adoption. However, in the comparison ACL reconstruction studies, the entire patellar tendon was used as the ACL graft, as opposed to the central third as would be done in the clinical setting. Whether the results reported here for primary repair would compare more favorably to ACL reconstruction if only the central third of the tendon had been used as a graft remains to be seen.

The displacement to 5 N was almost twice as high in the delayed repair group as it was in the immediate repair group (Table 3). These low-load displacements may be clinically relevant, as they may represent how much slack in the ACL that must be taken up before the ACL bears load.⁴ Because the compressive load that is applied to the joint for this low-load displacement measure is very small (-5 N), we feel that variations due to differences in cartilage stiffness and joint curvature would be minimal and that the resulting measure would show differences between the ligaments themselves. If the ACL is more slack in one group than in another, but the laxity of the knee is unchanged, this may be due to the secondary restraints around the knee. However, relying on these secondary restraints may alter the more subtle rotational biomechanics and predispose the knees to increased shear load across the articular surface. Further study of these measures and long-term in vivo studies of these treatment techniques are needed to assess these potential long-term outcomes.

The anatomic and kinematic differences between quadrupeds and bipeds can be perceived as a limitation of all large animal models of ACL injury and treatment. However, these translational models fill an important need to show both the safety and efficacy of new treatment strategies before they should be moved into humans. With that said, we realize

that the range of flexion-extension motion is different between quadrupeds and humans and that this may affect the loads on the ACL. However, the mechanisms that limit hyper-extension in the human are responsible for limiting extension to 30 degrees of flexion in the pig. These mechanisms include the relative position and interaction of the cruciates and the intercondylar notch, and condyle geometry. Therefore the porcine model may be a good translational model for the ACL.

The porcine model has a few limitations that are common to large animal studies in quadrupeds in that they weight bear on four limbs. While the pig model was selected due to its anatomical and biomechanical similarities to the human knee, there may be differences in gait and rehabilitation which cannot be reliably accounted for. For example, maximum extension of the pig knee is limited to 30 degrees short of full extension. In this study, we measured AP laxity at that angle, and at 60 and 90 degrees of flexion, where the posterior joint capsule was more relaxed and the joint was more likely dependent on the ACL to resist tibial translation (as in the exam in humans conducted at 30 degrees of flexion). How this difference in normal range of motion could affect ACL healing is as yet undefined. Furthermore, there may be subtle differences in the wound healing cascade between pigs and humans that are not yet appreciated.

In our gradual translation of enhanced ACL repair from the “bench” to the “bedside”, we have used various models starting from 2-D cell culture,^{7, 8, 10} moving to 3-D hydrogels in vitro,^{8, 11, 15} then to the in vivo central defect model,^{17, 18} and now advanced using the complete transection model in the pig.^{4, 6, 12, 14, 16} These models are all stepping stones with gradations of cost, complexity and animal lives. In this paper, we used ACL transection as a simplified model for ACL injury. In a true ACL injury, the ligament tissue likely has a broader zone of injury than that in the model used here. In addition, subchondral bone, articular cartilage, meniscus and capsular injury are also present. Future studies which add these degrees of complexity to the model will be warranted if we can demonstrate treatment efficacy in this simpler model.

In our previous large animal studies, a relatively large variability between animals has been observed and reported.^{4, 6, 12, 14, 16} In order to increase the power of the current study to detect significant differences between the delayed and immediate repair knees, we utilized a paired comparison. This design enabled us to control the variability inherent to ligament and knee size, as well as growth rate of each animal. However, the effects of bilateral surgery (i.e. immediate weight bearing on the repaired joints and the potential for a higher spike in inflammatory response due to bilateral trauma) must be acknowledged. Although the study was adequately powered to detect differences between the immediate and delayed repair conditions within animals, it was under powered to detect differences between the two delayed conditions (2 vs. 6 weeks) across animals. A much larger study would be required to find a difference between the two delay conditions. Nonetheless, the study clearly shows that a delay between injury and surgical repair degrades healing.

In summary, it appears that there are detrimental effects on the ACL repair tissue when delaying primary repair by two or six weeks in this large animal model. Additional work to determine the mechanisms behind these observed functional changes, and to develop methods to overcome these detrimental changes, is needed to allow for this new technique to become optimal for clinical application.

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Figure 1.

Schematic diagram depicting the primary suture repair with the collagen scaffold (green cylinder) in place. Sutures were fixed proximally with an Endobutton. The scaffold was threaded onto four of the trailing suture ends (RED) which were then passed through the tibial tunnel and tied over a button to provide initial knee stability. This suture bridge of resorbable Vicryl served as a temporary stabilization of both the collagen scaffold and the knee. The remaining two suture ends (GREEN) were tied to the sutures in the tibial stump of the ACL. All sutures were resorbable, and there was no sign of suture material remaining at the time of post-mortem testing (Reprinted with permission of John Wiley & Sons, Inc.⁴)

Figure 2. LOAD-DISPLACEMENT CURVES FOR IMMEDIATE AND DELAYED REPAIRS OF THE ACL

Low load-displacement curves for four groups of ligaments tested: the immediately repaired ligaments from the two-week and six-week groups and the two-week delayed repair group as well as the six-week delayed repair group. Note the decrease in load-displacement curves in the groups undergoing delayed repair. Bars represent the standard error of the mean (SEM) for each group at each displacement value.

Table 1

Lachman scores at Baseline, Time of Repair and 15 Week Endpoint

	Baseline		Time of Repair		15 Weeks after Repair	
	Immediate	Delay	Immediate	Delay	Immediate	Delay
2 Week Delay	1.6±0.5	1.8±0.5	2.9±0.83	8.5±1.4	5.1±3.4	3.4±1.4
6 Week Delay	3.3±0.9	3.5±0.8	1.8±0.5	12.1±2.0	1.9±0.7	2.6±2.4

Table 2
Change in Systemic Leukocyte and Platelet Counts from Baseline to the Time of Repair and 15 Week Endpoint

	Systemic Leukocyte Count			Systemic Platelet Count		
	Baseline	Time of Repair	Endpoint	Baseline	Time of Repair	Endpoint
2 Week Delay	15±3	15±3	12±3	402±115	346±76	305±56
6 Week Delay	14±4	14±2	12±5	391±91	369±50	247±135

Table 3

Biomechanical Data for Immediate and Delayed Repair Knees

	2 Week Delay		6 Week Delay		P-value
	Immediate	Delay	Immediate	Delay	
Displacement to 5N (mm)	4.1 ± 1.1	7.5 ± 1.1	4.9 ± 1.1	8.8 ± 1.1	0.009*
Yield Displacement (mm)	11.3±1.4	13.6±1.4	15.4±1.5	16.2±1.5	0.211
Max. Displacement (mm)	12.1±1.5	14.1±1.5	15.6±1.6	17.8±1.6	0.14
Yield Load (N)	150 ± 33	85 ± 33	239 ± 33	87 ± 33	0.011*
Max Load (N)	207 ± 34	92 ± 35	240 ± 37	97 ± 37	0.008*
Linear Stiffness (N/mm)	44 ± 6	19 ± 6	35 ± 7	18 ± 7	0.011*
AP Laxity 30 (mm)	9.4±1.0	13.1±1.0	10.6±1.1	11.6±1.1	0.012*
AP Laxity 60 (mm)	12.8±0.9	15.9±0.9	14.6±0.9	13.5±0.9	0.211
AP Laxity 90 (mm)	12.8±0.85	15.9±0.85	14.6±0.91	13.5±0.91	0.105

* Indicates a significant difference between immediate and delayed knees.