

ated with cartilage volume loss ( $p=0.284$ ,  $\rho=-0.60$ ). Similarly, the increase in GCA correlated significantly with less severe cartilage defect ( $p=0.001$ ,  $\rho=-0.99$ ), joint effusion ( $p=0.041$ ,  $\rho=-0.89$ ) and BML ( $p=0.004$ ,  $\rho=-0.97$ ). At week 26, higher PVF significantly ( $p=0.013$ ,  $\rho=0.95$ ) correlated with more severe meniscal tears while higher CGA correlated ( $p=0.037$ ,  $\rho=-0.90$ ) with cartilage volume loss. In line with these findings, the evolution of meniscal tears significantly correlated with less osteophytosis ( $p=0.013$ ,  $\rho=-0.95$ ) and joint effusion ( $p=0.028$ ,  $\rho=-0.92$ ).

**Conclusions:** This exploratory study reveals multiple binary associations between a number of joint structural defects and the extent of OA-induced functional disability. Data revealed that PVF and GCA are mainly affected by BML and cartilage defects, whereas meniscal integrity is more affected by gait biomechanics. These results highlight the need for a physiopathologically-based statistical analysis strategy to better understand the structure-activity relationships of the injured joint.

## 078

### EARLY SYNOVIAL RESPONSES TO ANTERIOR CRUCIATE LIGAMENT AUTOGRAFTING IN THE OVINE STIFLE JOINT

**B.J. Heard, Y. Achari, M. Chung, N.G. Shrive, C.B. Frank**  
*Univ. of Calgary, Calgary, AB, Canada*

**Purpose:** Anterior cruciate ligament (ACL) reconstruction using tendon autografts aims to restore the function of a completely damaged ACL. However, evidence suggests that such grafts may be less than ideal due, in part, to abnormal graft tensioning and perhaps-related post-surgical inflammation. We have developed a biomechanically idealized ACL autograft model (using the native ACL itself as an immediate replacement with and without excessive 'graft' tensioning) to study the biological responses to such surgery. The present study focussed on identifying the alterations to early markers of synovial inflammation and tissue remodelling proteinases. The hypothesis for this study was that all grafts would induce inflammation but overtensioning of ACL grafts would further increase the expression of inflammatory and tissue remodelling bio-markers.

**Methods:** All surgeries were performed using protocols approved by the animal care committee of the University of Calgary. Fifteen skeletally mature 3-4 year old female Suffolk-cross sheep were allocated equally into 5 groups: anatomical ACL-core, twist tight ACL-core, twist loose ACL-core, sham, and non-operated controls. The ACL core surgeries were accomplished via arthrotomy to the right stifle joint. The patella was dislocated medially to expose the ACL. The proximal head of the lateral femoral condyle was the entry point for a guide pin that was inserted to mark the femoral insertion of the ACL. A dry nitrogen drill was used to core down to the marked insertion. After the ACL insertion was freed, the core was either a) immediately fixed in place (anatomical), b) pulled 1mm away from the joint while being twisted 90 degrees and then fixed (twist tight), or c) pushed 1mm into the joint while being untwisted 90 degrees and then fixed (twist loose). For shams, the core was stopped at the halfway mark between the surfaces of the proximal femoral condyle to the femoral ACL insertion, a distance of roughly 1.5cm. The non-operated controls were age matched and housed for the same duration of time as the experimental subjects. All animals were sacrificed 2 weeks post-injury. At dissection, synovium from both left and right stifle joints were isolated and examined for different matrix metalloproteinases, interleukins and lubricin using real-time RT-PCR.

**Results:** Synovial tissue from the treated joint of the anatomical, twist tight and twist loose core groups all exhibited significant increases in the mRNA levels of the matrix metalloproteinases examined. MMP-1 and MMP-3 mRNA levels exhibited maximum elevation in the twist-tight core groups, followed by anatomically

placed ACL and twist-loose core group. However MMP-13 mRNA levels exhibited maximum elevations in the anatomical core group followed by twist tight and twist loose groups. The matrix metalloproteinases mRNA levels did not change in either the contralateral limbs of the treated groups or the limbs of the non-operated controls. Investigation of IL-1 $\beta$  mRNA levels revealed an 8-10 fold increase in the three treated groups respectively with not much variation between the groups. Interestingly the IL-6 did not exhibit any change in the mRNA levels in any of the groups. Lubricin mRNA levels followed the same pattern as MMP-1 and MMP-3.

**Conclusions:** The tension of an ACL graft can influence the mRNA levels of certain MMPs, interleukins and lubricin in the synovium, which in turn may influence the structure and biomechanical properties of the graft.

## 079

### A NEW INSULT TECHNIQUE FOR A LARGE ANIMAL SURVIVAL MODEL OF HUMAN INTRA-ARTICULAR FRACTURE

**Y. Tochigi, T.E. Baer, P. Zhang, J.A. Martin, T.D. Brown**  
*Univ. of Iowa, Iowa City, IA*

**Purpose:** To model human intraarticular fractures (IAFs) in the porcine hock joint (human ankle analogue) *in vivo*, a new fracture insult technique/system has been developed. In this technique, a joint is subjected to an injurious transarticular compressive force pulse, so as to replicate the most typical mechanism of human distal tibial "plafond" fracture. Figure 1 shows the custom interface device developed for this technique. The "tripod" of pins connects the distal impact face to the talus without soft tissue intervention, while the proximal fixator holds the tibial shaft tilted posteriorly. In this "offset" condition, a force pulse applied to a joint causes sudden elevation of vertical shear stresses in the anterior tibial juxtaarticular bone. With guidance from a stress-rising sawcut placed at the anterior cortex, well-controlled, reproducible anterior malleolar fractures are created (Figure 2). For an animal model of IAF to be scientifically meaningful, pathophysiological realism of fracture-associated cartilage injury is essential. The purpose of this study was to document the cell-level cartilage pathology introduced using this "offset" fracture impact technique.

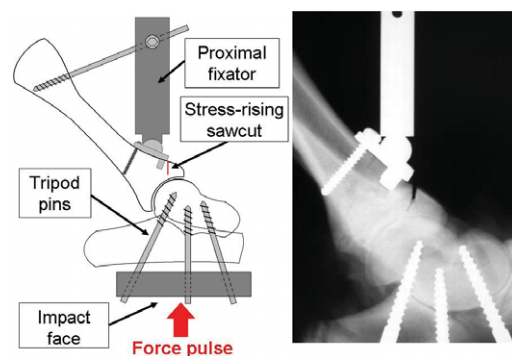


Figure 1. The "tripod" device-to-bone interface system.

**Methods:** Four fresh porcine hock specimens, in which chondrocytes were fully viable, were utilized. Of these, two were subjected to fracture insult using the offset impact technique, with a force pulse (30 joules) delivered by a drop-tower device. In the other two, morphologically similar distal tibial simulated fractures were created using a sharp osteotome (non-impact osteotomy control). Macroscopic fracture morphology was recorded by means of digital photography. The fractured distal tibial surface, harvested as osteoarticular fragments, was then incubated in culture medium.

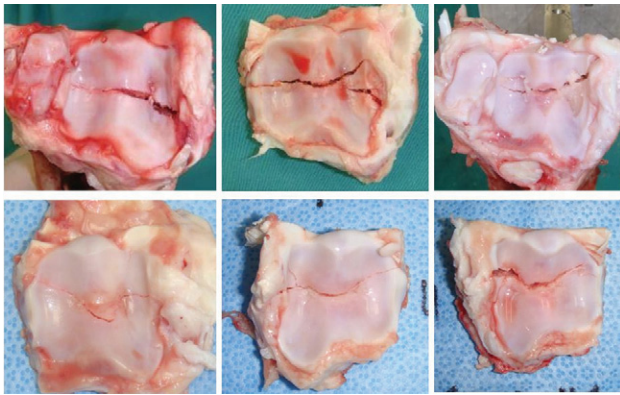


Figure 2. Reproducibility of fracture patterns in the pilot work.

Two days later, those fragments were subjected to chondrocyte viability analysis using the fluorescence live/dead assay, using a confocal laser-scanning microscope system. For each joint, scans were executed at several sites near fracture edges, as well as centrally in non-fracture areas. Chondrocytes in the superficial zone (within 100-150 microns from the surface) were scanned, and site-specific cell death rates were computed.

**Results:** In both fracture-impacted joints, appreciable chondrocyte death (cell death rate  $>25\%$ ) was identified only near fracture edges (Figure 3A). The cell death rate at near-edge sites ( $21.9 \pm 14.1\%$ ), although variable across specimens/locations (range 0.6 to 45.2%), was significantly higher than at central non-fracture sites ( $3.4 \pm 5.7\%$ ,  $p=0.001$ ). In the non-impact osteotomy joints, by contrast, very little chondrocyte death was identified at either near-edge (Figure 3B) or central sites ( $1.0 \pm 1.2\%$  and  $1.8 \pm 2.9\%$ , respectively).

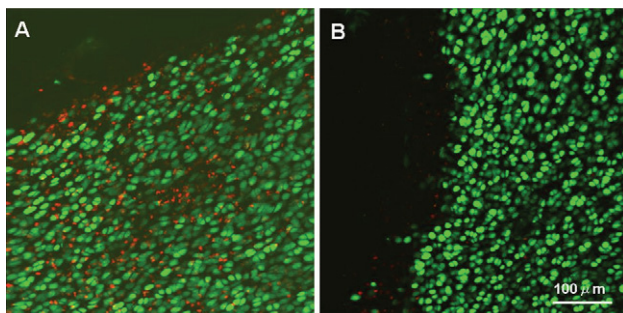


Figure 3. Confocal scanning images at an impactation fracture edge (A) and at an osteotomy edge (B). Cells stained green are alive, while those stained red are dead.

**Conclusions:** The cell death spatial distribution patterns in the impacted fracture fragments, concentrated near fracture edges, were analogous to those in human clinical IAFs (Kim et al., *OA & Cartilage* 2002; Hembree et al., *JBJS-Br* 2007). The striking difference in chondrocyte viability with respect to non-impact osteotomy fragments suggests that the acute mechanical damage to cartilage associated with the impactation fracture insult was very different from that with non-impact "fracture" simulation by osteotomy. This new fracture insult technique appears to have the potential to replicate the cell-level pathology of human IAFs in a large animal survival model.

## 080

### EVALUATION OF A NOVEL SURGICAL TECHNIQUE IN AN IN VIVO OVINE MODEL TO ACCESS THE POSTERIOR HORN OF THE MEDIAL MENISCUS

R.B. Modesto<sup>1</sup>, R.L. Mauck<sup>2</sup>, B.M. Baker<sup>2</sup>, C. Underwood<sup>1</sup>, T.P. Schaer<sup>1</sup>

<sup>1</sup>Univ. of Pennsylvania Sch. of Vet. Med. Dept. of Clinical Studies New Bolton Ctr., Kennett Square, PA; <sup>2</sup>Univ. of Pennsylvania Sch. of Med. Dept. of Orthopaedic Surgery, Philadelphia, PA

**Purpose:** Despite advances in surgical technique and fixation devices, a pressing clinical demand exists for new strategies for repairing the knee meniscus. Appropriate animal models are required to test engineered construct safety and efficacy in the context of the demanding loadbearing environment of native tissue. Ovine models are particularly useful, as their menisci are closer in size to that of human beings and show similar loading patterns. However, current open surgical approaches to ovine menisci do not provide full access and visualization of the red-white and white zone in the posterior horn, the most clinically relevant portion of the medial meniscus. The purpose of this in vivo pilot study was to evaluate a new surgical approach allowing for improved access to the posterior horn of the medial meniscus.

**Methods:** Under general anesthesia, the medial compartment was accessed via a lateral parapatellar arthrotomy subluxating the patella medially. A medial femoral condyle osteotomy was planned as a vertical cut starting directly medial to the femoral origin of the caudal cruciate ligament aiming to the medial transition of the femoral diaphysis and metaphysis. The osteotomized femoral condyle was then reflected to reveal the medial meniscus in its entirety. The osteotomy was anatomically reduced and repaired with two 4.5mm cortical bone screws placed in lag fashion. A tenotomy of the common calcaneal tendon was performed about 3 cm proximal to the calcaneus to obtain temporary non-weight bearing in the operated limb. Animals were confined until weight bearing. During that period they obtained three times daily physiotherapy of passive range of motion. Pre-, postoperative and endterm radiographs were obtained. Animals were euthanized at 6 months and both stifles were grossly examined, followed by histological, biochemical and mechanical analyses of medial tibial plateau and histological analysis of the medial meniscus. Contralateral limbs were used as controls.

**Results:** The medial femoral condyle osteotomy consistently offered full access to the medial meniscus and allowed for excellent visualization of the pars intermedia and pars posterior. Animals had uneventful recoveries and did not bear weight on the operated limb for 5-6 weeks postoperative while tolerating physiotherapy well. Gross visualization of the articular surfaces showed no marked change in cartilage appearance in operated or contralateral limbs. Histopathology of the medial menisci demonstrated mild decrease in proteoglycan content, but this was not significant. Histological analysis of the articular cartilage of the tibial plateau revealed no adverse changes in cartilage structure or differences in intensity of collagen or proteoglycan staining between groups. Biochemical analysis of proteoglycan content showed no significant changes between operated limbs and contralateral controls.

**Conclusions:** Although preclinical models replicate some of the features of the disease process modeled, they invariably fail to reproduce the complexity of the degenerative disorder. The current study is an attempt to create a relevant animal model to study regenerative repair in the posterior horn of the medial meniscus for the human patient. Using a medial femoral condylotomy greatly improves surgical access to the meniscus without injuring associated soft tissue structures. Our findings and observations thus far suggest that this model could greatly enhance regenerative research of the knee meniscus in large animal models when macroscopic devices need to be placed and evaluated in vivo.