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Surgical Reattachment of the Anterior Horn Slows OA Progression in a Large Animal Injury Model

Brendan D Stoeckl, MSE[1,2]
Kyle D. Meadows, BSE[3]
Edward D. Bonnevie, PhD[1,2]
John M. Peloquin, PhD[3]
Adriana Barba, DMV[4]
Klaus Hopster, DMV[4]
Sonia Bansal, PhD[1,2]
David R. Steinberg, MD[1,2]
Thomas P. Schaer, VMD[4]
Miltiadis H. Zgonis, MD[1,2]
Dawn M. Elliott, PhD[3]
Robert L. Mauck, PhD[1,2]

[1]University of Pennsylvania, Philadelphia, PA

[2]Corporal Michael J. Crescenz Veterans Affairs Medical Center, Philadelphia, PA

[3]University of Delaware, Newark, DE

[4]University of Pennsylvania, School of Veterinary Medicine, Philadelphia, PA

Introduction

The meniscus is a critical tissue for the mechanical function of the knee. Meniscal injuries are common, and when injured, the ability of the meniscus to distribute loads is impaired, leading to aberrant forces on the knee cartilage and progression to OA[1]. Our previous work developed an arthroscopic model of DMM, where the anterior horn of the meniscus was resected[2] This model resulted in deleterious changes in the knee cartilage, however many of these changes appeared to be transient, as the anterior horn attachment scarred back in place and began bearing load[2]. The aim of this study was thus two-fold: 1) to increase the severity of the initial DMM injury to induce a more degenerative cartilage pathology, and 2) to evaluate whether surgical repair via acute reattachment could prevent progression to an OA phenotype.

Methods

Eight skeletally mature (12-month-old) Yucatan minipigs underwent mini-arthrotomy of the right stifle. In all animals, the anterior attachment of the medial meniscus was transected. This attachment was either immediately repaired using a vertical mattress suture and suture anchor (Repair) or a 5mm section of the attachment was resected *en bloc* (Injury). Animals were sacrificed at ± weeks post-op, and intact contralateral limbs were used as controls. All animal procedures were performed with IACUC approval. After euthanasia, stifle joints were dissected, synovium tissue was identified and isolated, and the tibial plateaus were assessed for cartilage wear using India ink. Osteochondral segments of the medial tibial plateau were removed. These were potted using a low-melting temperature bismuth alloy with the cartilage surface exposed, submerged in a PBS solution containing protease inhibitors, and indented with a 2mm diameter spherical indenter at four locations—two each on cartilage regions previously covered by the meniscus or on more central uncovered regions. Fifteen-minute duration creep tests at a 0.1N load were fitted to a model of Hertzian biphasic creep[3], and values for compressive modulus, tensile modulus, and permeability were determined. Values for the covered and uncovered regions were averaged. Next, osteochondral tissues were scanned via uCT at 70kVp, 85μA, with a voxel size of 10.3μm. Trabecular thickness and bone volume fraction were calculated for 3mm diameter cylindrical regions of interest superficial (0-1mm) and deep (2-4mm) to areas previously covered or uncovered by the meniscus.These osteochondral units were then decalcified, paraffin processed, embedded, sectioned, and stained with Safranin O/Fast Green. Synovium sections were stained with Hematoxylin/Eosin. All quantitative data were compared with one-way ANOVA followed by Tukey's post hoc tests, with significance set at $p < 0.05$.

Results

Injured joints showed more macroscopic signs of degeneration than intact controls, with a significantly greater proportion of the medial tibial plateau positive for India ink staining. Qualitatively, repair joints showed less wear than injured joints and were not significantly different from the Intact group (Figure 1**).** While tensile and compressive modulus were not significantly different between groups in covered and uncovered regions of the cartilage, the uncovered permeability trended higher

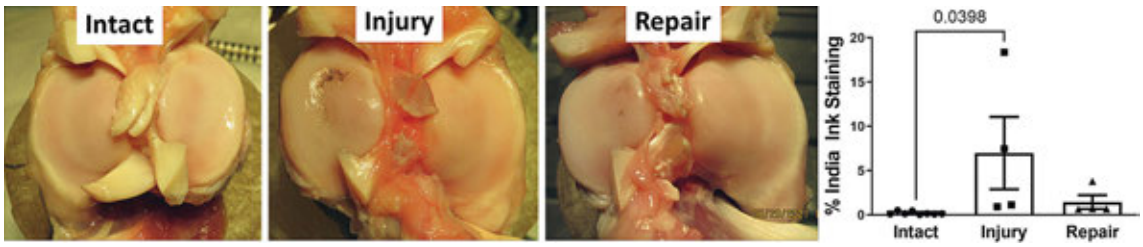

Figure 1. Group median images of tibial plateau with India ink staining and quantification of medial tibial plateau cartilage damage (% area positive, mean ± SD).

(p = 0.084) in the Injury vs. Intact groups (Figure 2). The bone volume fraction in the covered, superficial zone of the Injury group was significantly higher than that of the Intact group, and trended higher than that of the Repair group (p = 0.054). Intact and Repair were not significantly different. The trabecular thickness in the covered deep zone was significantly higher in the Repair group compared to Intact. Histologically, the Injury group showed more degeneration and greater proteoglycan loss compared to the Intact or Repair groups, and the synovium in the Injury group showed the greatest signs of inflammation.

Discussion

This study evaluated osteoarthritic changes in the porcine knee in a model of meniscus injury and repair. Macroscopic as well as histological evidence suggests that the repair of the transected anterior root of the medial meniscus was chondro-protective and slowed joint degeneration. This is further supported by analysis of the subchondral bone, which showed sclerotic changes immediately below the cartilage in the Injury group that were attenuated in the Repair group. Changes in deep zone trabecular thickness on the medial (covered) side of the joint may indicate bony remodeling in response to the suture anchor. Increases in cartilage permeability are an early indicator of OA[4], and permeability trended higher in the Injury group compared to Intact. These data are consistent with clinical evidence of the therapeutic impact of meniscal root repair[5]. However, this pilot study was limited in sample size; while showing promising trends, most mechanical indicators of cartilage health did not reach the level of statistical significance. Despite these limitations, this study indicated that anterior root repair in this large animal model of meniscus injury slowed the progression of OA. Ongoing work is evaluating changes to the femoral condyle, and the inflammatory profile of the synovial fluid, and future

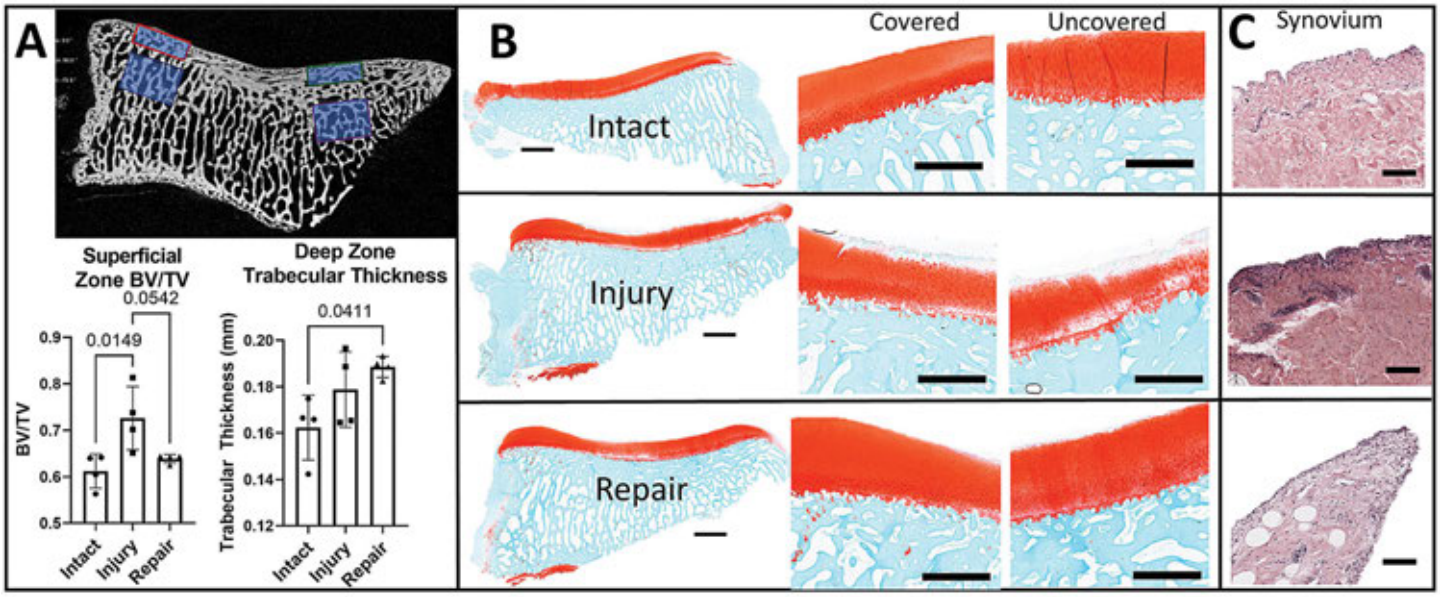

Figure 2. Compressive and tensile moduli and permeability of uncovered tibial plateau cartilage (mean ± SD).

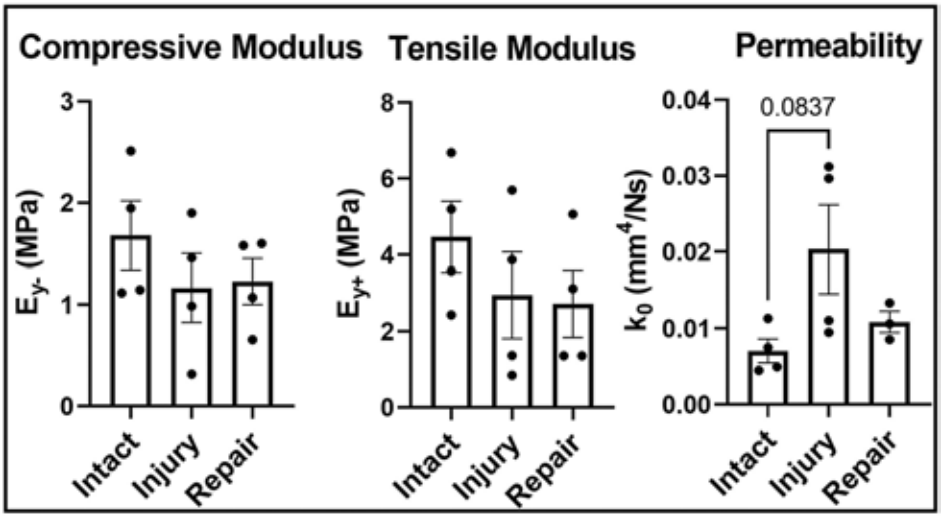

Figure 3. (A) Subchondral bone analysis showing ROIs within medial tibial plateau. Superficial zone BV/TV and deep zone trabecular thickness in covered region (mean ± SD); **(B)** Representative Safranin O /Fast green stained medial tibial plateaus. Scale = 2mm, 1mm insets; **(C)** Hematoxylin/Eosin-stained synovium from each group. Scale = 0.1mm.

studies will address limitations in sample size and extend the post-surgical time point to assess the durability of repair.

Significance/Clinical Relevance

This study demonstrated that meniscal root repair slows the progression of OA in large animal DMM model. Not only is this data relevant from a clinical perspective but establishes a test bed for the evaluation of therapies for OA.

Acknowledgement

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