INTRODUCTION: Preservation or repair of damaged menisci is not always possible, and meniscal transplantation into knees of patients with previous meniscectomies or irreparable damage has become a means to protect the knee from progressive joint degeneration. The long-term surgical results of this operative intervention have not been well established, nor has the optimal timing for surgical transplantation been defined. It has become evident, however, that meniscal transplantation must be performed prior to the development of advanced joint degeneration. The results of this procedure are sub-optimal if transplantation is delayed until advanced radiographic changes are present. Thus, it is imperative to develop a tool to allow early identification of articular degeneration, in order to recommend reconstructive procedures in a timely fashion. The purposes of this project were to: 1. implement and evaluate the accuracy and reliability of various molecular markers for the quantification of early articular cartilage damage in an ovine post-meniscectomy degenerative knee model; and 2. correlate the molecular marker data with traditional outcome measures including biomechanical testing, gross inspection with india ink stain, histology, plain radiographs, and magnetic resonance (MR) imaging. The primary hypothesis was that changes in biochemical markers of cartilage destruction and joint homeostasis occur after total lateral meniscectomy in the sheep knee, and that these changes correlate with degeneration assessed by biomechanical testing, histologic criteria, and imaging studies.

METHODS: After IACUC approval was obtained, total lateral meniscectomies were performed on twelve skeletally mature Columbia X Rambouillet ewes. Four control animals underwent a sham operation consisting of takedown and repair of the lateral collateral ligament. Serum was collected prior to the initial surgical procedure, every three days for the first two weeks post-surgery, and every two weeks until sacrifice. Synovial fluid was collected prior to the initial surgical procedure and every two weeks until sacrifice. Six meniscectomy animals and two sham operation animals were sacrificed at two and four month time points. The markers that were studied included: synovial fluid and serum levels of keratan sulfate (KS)-5D4, COL2-3/4C, COL2-3/4C, and SOCS-3 marker were significantly greater on the operated side compared to the non-operated side at both two months and four months post-meniscectomy. Sixty meniscectomy knees were performed. Joint space narrowing, osteophyte formation, and subchondral sclerosis were seen at both two months and four months post-meniscectomy. MRI: MR imaging quantitatively evaluated cartilage wear, bone sclerosis, sub-chondral edema, and osteophyte formation. Spin echo T2 relaxation maps of the tibia were processed. MRI imaging demonstrated severe joint degeneration four months post-meniscectomy. At two months joint degeneration was present, but significantly less than at four months (p < 0.05). MR data correlated with biomechanical data (r = 0.7). Both MR and biomechanical findings correlated with gross inspection.

DISCUSSION: An increasing body of evidence has begun to demonstrate the utility of molecular biomarkers as predictors of joint degeneration. This study begins to elucidate early patterns of change for cartilage and bone biomarkers in the sheep post-meniscectomy OA model. As hypothesized, the changes in marker levels correlated with traditional outcome measures of cartilage destruction as all modalities indicated changes by two months and demonstrated differences between operated and non-operated limbs. It is imperative for the clinician to determine the onset and progression of joint deterioration in an early and timely fashion, as there is a critical time period after which surgical procedures such as meniscal transplantation will not provide the beneficial effects for which it is intended. This study helps to validate, by biomechanical testing, histology, and imaging, selective markers that monitor joint metabolism and disease load. By increasing the sensitivity and sophistication of our testing parameters through the identification of specific molecular markers for early articular cartilage breakdown, and integrating these tools with noninvasive imaging, surgical planning and timing, we hope to improve the outcome of future surgical interventions.