Conclusions: We revealed in this study that joint immobilization induced hypoxic condition in the capsule. The decreased number of blood vessels and the increased number of cells might indicate decreased blood flow and fibrosis in the capsule. Hypoxia is an important factor of deterioration of joint contracture after immobilization.

136 A NEW IMPACTION SYSTEM TO CREATE “CRITICAL” CARTILAGE INJURY IN LIVING RABBIT KNEES
Y. Tsuchi, M. Rudert, D.C. Fredericks, A.B. Al-Hilli, M. Arunakul, T.D. Brown, T.O. McKinley. Univ. of Iowa, Iowa City, IA, USA

Purpose: In post-traumatic OA, death and dysfunction of chondrocytes associated with acute cartilage injury presumably plays an important role in triggering the pathomechanical cascade that eventually leads to whole-joint degeneration. To study details of the disease mechanisms, or to pilot treatment to amend the disease process, a survival animal model in which OA predictably develops after mechanically-introduced acute cartilage injury is crucial. A novel impaction system has been developed to create such acute cartilage injury in living rabbit knees. The present study aimed to test if this surgical insult would predictably cause cartilage degeneration as “critical” in the sense of the cartilage injury created causing progressive cartilage degeneration.

Methods: With institutional approval, twelve New Zealand White rabbits received blunt impaction insult to the left knee. By approaching through a posterior arthrotomy, the posterior aspect of the medial femoral condyle was bluntly impacted using a custom drop-tower device. In this system, the rabbit was positioned prone, with the left thigh mounted on the leg holder. The distal femur was placed in a V-shaped groove, and was secured using a cannulated bone pusher, with guidance of a 1.25 mm K-wire embeded into the posterior femoral metaphysical cortex. A metal platen with a flat impaction face (5 mm diameter) was then placed on the medial femoral surface, and an impaction force was delivered by a 1.55 kg drop mass. The magnitude of energy delivery was controllable (up to 5.0 joules) by adjusting the drop height. The animals were impacted at 2.0, 3.0, or 4.0 joules, and were sacrificed 1 or 8 weeks post-impaction (n = 2 for each combination of impaction magnitude and test period). The experimental joints were subjected to histo-morphological evaluation of the femoral and tibial surfaces in both medial and lateral compartments. For evaluation of the medial femoral surface, histological sections were prepared at 0.5 mm intervals, and a section that included the most severe cartilage injury was identified.

Results: All of the six experimental joints harvested at 1 week post-impaction had full-thickness cartilage injury on the medial femoral condyle, at a region where cartilage was thickest (Figure). There was no recognizable relationship between injury severity and energy delivery magnitude. However, in the joints harvested at 8 weeks, the most severe injury (cartilage defect reaching the calcified zone) was identified only in the 4J-impaction joints. Findings in the rest of 8-week joints (2J- or 3J-impaction) were variable across specimens, from nearly no damage to full-thickness injury. On the medial tibial surface, all 8-week joints had surface roughness, with cracks reaching the transitional to radial zone.

Conclusions: Although not fully reproducible, critical-level acute cartilage injury was inducible in the primary weight-bearing region of the medial femoral joint surface. Secondary effect on the opposing tibial surface was also suggested. This new impaction system appears to permit modeling OA development following acute cartilage injury in living rabbit knees.

137 MEDIAL MENISCUS DESTABILIZATION FOR MODELING CUMULATIVE ABNORMAL CONTACT STRESS IN LIVING RABBIT KNEES
Y. Tsuchi, M. Arunakul, D.C. Fredericks, A.B. Al-Hilli, T.D. Brown, T.O. McKinley. Univ. of Iowa, Iowa City, IA, USA

Purpose: In post-traumatic OA, cumulative abnormal contact stress presumably plays an important role in the disease progression in the chronic phase. To study details of the disease mechanisms, or to pilot treatment(s) to alter the disease process, a survival animal model in which OA predictably develops purely due to cumulative abnormal contact stress is crucial. A novel surgical insult technique has been developed to model localized contact stress elevation in the rabbit knee, with minimal effects on the whole-joint mechanics. The present study aimed to test if this surgical insult would predictably cause cartilage degeneration in living rabbit knees.

Methods: With institutional approval, five New Zealand White rabbits were subjected to medial meniscus destabilization (MMD) surgery. Approaching through a posterior arthrotomy, the posterior horn of the medial meniscus was sharply released from the tibial attachment. Major ligamentous and muscular structures surrounding the knee, particularly the quadriceps tendons, were left uninjured. Eight weeks later, the animals were sacrificed, and the A-P joint laxity was measured for both knees. Then, the experimental joints were prepared for histo-morphological evaluation. Femoral and tibial surfaces in both medial and lateral compartments (at the primary load bearing region for each surface) were rated individually using Mankin score (0–14 points). These results were compared with data archived from previous studies, in which rabbit knee cartilage histology was evaluated 8 weeks after total medial meniscectomy (MMtomy, n = 5), complete anterior cruciate ligament transection (ACLT, n = 10) or sham control surgery (n = 10).

Results: Difference in A-P laxity (neutral-zone length) between the experimental and contralateral knees was minimal (0.21 mm or less). In gross anatomical observation, all (5/5) MMD knees had the medial meniscus still released at the posterior attachment, with the body of meniscus moderately degenerated. Histologically, 4/5 of the MMD knees had distinct cartilage degeneration (Mankin score ≥ 4 points) in the medial compartment, on both the femoral and tibial surface (Figure). All MMD knees had a medial tibial score higher than the 75th-percentile value of the previous sham surgery data, and these scores were comparable with those of the previous ACLT and MMtomy data. The medial femoral score for 4/5 of the MMD knees was higher than the 75th-percentile values of the sham surgery dataset. These elevated scores were higher than most of those in the ACLT dataset, and comparable with those in the MMtomy dataset. Histological changes in the lateral compartment were minimal (≤ 2 points) in most cases.

Conclusions: MMD is a well-accepted surgical insult technique to model OA in the mouse knee. It has been experimentally evidenced that detachment of the posterior attachment of the medial meniscus from the tibia causes significant increase of contact stresses in the medial compartment in the human knee. Our technique allows MMD of the
Methods: Mouse joint injuries were induced in anesthetized mice using a custom tibial compression jig mounted in a Bone Enduratec instrument. Mouse tibiae were loaded to 10–12 N at a rate of 1 mm/sec, causing anterior translation of the tibia relative to the distal femur and injuring the soft tissues of the knee (Figure 1). Mice were euthanized at 1, 3, 7, 14, 28, and 56 days after knee injury, and compared to uninjured control mice (n = 6 per group). Injured and uninjured knees were imaged using micro-computed tomography (SCANCO μCT35), and the volume of the trabecular bone analyzed at several locations including the femoral epiphysis.

Results: Joints were consistently injured at approximately 10–12 N, with very little variation in the force required for injury. All mice survived the joint injury well, with no apparent change in activity levels or obvious signs of discomfort. Analysis of the trabecular bone volume at the femoral epiphysis and proximal tibial epiphysis showed a rapid and unexpectedly large loss of trabecular bone after injury, which was readily detectable at day 3 and reached a maximum loss of >40% BV/TV (bone volume/total volume) at day 7. This was followed by a period of partial recovery of bone volume. A more mild but still significant loss of trabecular bone volume was observed in the uninjured contralateral limbs, which indicates a systemic response to the injury (Figure 2). There was very little variation in the extent of injury between mice of the same group, indicating these observations are highly reproducible.

Conclusions: The immediate and significant loss of trabecular bone volume following a relatively mild non-invasive joint injury is a novel observation. Since OA is initiated at the molecular and cellular level shortly after injury occurs, the optimal timeframe for therapeutic intervention may also be shortly after the joint injury. A more thorough characterization of the early changes in an injured joint will enable the future design of more accurate OA biomarkers and more effective therapeutic intervention strategies.

Figure: Histological results. Note: solid squares and bars indicate the medians and upper/lower quartiles for the control and ACLT data sets.

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