Evidence of Injury-Specific Mechanical Mechanisms of Articular Cartilage Degeneration in Ovine Models of Secondary Osteoarthritis

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Introduction: Following injury to one or more of the primary joint stabilizers, altered joint mechanics are thought to be important factors in the development of secondary osteoarthritis [1]. Using an ovine model of joint injury, we examined differences in in vivo tibiofemoral regions of close proximity and the location and extent of subsequent articular cartilage (AC) lesions at 20 weeks post-injury. **Hypothesis:** Differences in location of articular cartilage focal degeneration between lateral-meniscotomized (Mx) and combined anterior cruciate ligament/medial collateral ligament-transected (ACL/MCLx) stifles coincide with changes in tibiofemoral regions of close proximity (ROCP).

Materials and Methods: Data were collected for 13 skeletally mature Suffolk-cross sheep which were randomly assigned to one of three groups: combined ACL/MCLx (n=6), Mx (n=3), or sham-operated control (Sham) (n=4). All surgical procedures were reviewed and approved by our Institutional Animal Care Committee. ROCP: Kinematic data were collected prior to injury, and again at 2, 4, and 20w (weeks) post-injury using the methods described by Tapper et al. [2]. Briefly, removable rigid markers were affixed to previously implanted fracture plates on the hind right femur and tibia. The 3-dimensional spatial positions of the markers were collected using a high-resolution four-camera video-based system (Motion Analysis, CA, ± 0.4mm accuracy). Following sacrifice, anatomical landmarks were digitized (FaroArm, FL, ± 0.05mm accuracy) and used to construct femoral and tibial anatomical coordinate systems. Bone surfaces of the tibial plateaus and femoral condyles were also digitized and reconstructed using a thin-plate-spline (Matlab v.7.0, MA). Tibiofemoral ROCPs were calculated at hoof strike, early weight-bearing, full weight-bearing, hoof-off, early swing, and late swing. The points of maximum proximity between the tibial plateaus and the femoral condyles at each selected point in the gait cycle were used to quantify changes in cartilage-cartilage contact before and after the assigned surgery. Statistically significant differences in ROCP between groups at each post-injury time point were assessed using a repeated-measures 2-way ANOVA with a Tukey’s correction for group and time. **Cartilage Degeneration:** Following sacrifice, AC appearance and osteophyte formation were scored using modified Drez and Cummings scores, respectively. Articular cartilage samples were then harvested from the stifle at standardized locations so that a histological analysis could be performed using a modified Mankin score. Scores from each of the tests were summed for each experimental group, and the magnitude of overall joint degeneration was evaluated using a Kruskal-Wallis test. A Mann-Whitney test was then used to determine differences in extent of cartilage degeneration between groups of interest. A similar procedure was used to determine differences in site-specific cartilage lesions. Differences for all tests were considered significant when $p$ was ≤0.05.

Results: ROCP of the Mx group were statistically different from those of the ACL/MCLx and Sham groups ($p$<0.01). Total joint degeneration scores from the Mx group were greater than either the Sham or ACL/MCLx scores. When site-specific degenerative changes were examined, the Mx group exhibited moderately severe degenerative changes in the central region of the medial tibial plateau, the anterior aspect of the lateral tibial plateau, and posterior aspect of the lateral femoral condyle (Figure 1). These regions were significantly more degenerated than those same regions in the ACL/MCLx group ($p$<0.02), and correspond to the anterior-lateral shift of the tibial ROCP, and the posterior shift of the lateral femoral condyle ROCP. Interestingly, despite a predominantly posterior shift of the tibial ROCP in the ACL/MCLx group, the regions of most severe AC degeneration were the anterior aspect of the medial tibial plateau, the femoral groove, and retropatellar surface. To determine if the severity of joint degeneration might be predicted by the overall magnitude of change in ROCP, the absolute difference between ROCP during normal kinematics to 2w, 2w to 4w, and 4w to 20w post-injury were summed and compared to the total score of hind right degeneration using a Spearman’s rho correlation. Pooled data from the ACL/MCLx and Sham groups (both groups combined) showed a significant positive correlation (0.64, $p$=0.05), while the pooled Mx and Sham data did not (0.46, $p$=0.3).

Discussion: These findings suggest that the locations of focal AC degeneration in the ovine Mx model may be more closely associated with the changes in location of cartilage-cartilage contact than in the ovine ACL/MCLx model. In vitro, resection of the ovine medial meniscus leads to increased contact stress on the load-bearing regions of the medial stifle [3]. In our in vivo Mx model, an increase in joint contact stress coupled with a shift in ROCPs to areas that are normally protected by the meniscus would expectedly lead to focal AC lesions and supports our hypothesis. Conversely, the findings of the ACL/MCLx model suggest that different mechanical mechanisms of AC degeneration may be at play. Firstly, the increased patellofemoral degeneration may be the outcome of altered patellofemoral loading due to changes in neuromuscular activation patterns of the quadriceps and hamstrings. Secondly, while changes in the location of ROCPs are still an important consideration in the pathogenesis of secondary OA, the correlation between the magnitude of change in ROCP and severity of joint degeneration likely reflects that the changes in location of cartilage-cartilage contact occur over a relatively larger region of the ACL/MCLx and Sham joint surfaces leading to more generalized joint degeneration. Additionally, the menisci in these models remain intact, which also likely reduces the occurrence of focal AC lesions.