Cross-Species Comparison of Naturally Occurring Osteoarthritis in Equine and Human Cartilage

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INTRODUCTION: Osteoarthritis (OA) is a chronic joint disease arising from untreated cartilage lesions and is characterized by a deterioration of cartilage's mechanical properties and the biochemical composition [1]. Progress in developing disease-modifying therapies has been limited by the lack of reliable preclinical models that faithfully replicate human OA. Large animal osteochondral plugs provide a reproducible ex vivo platform, yet validation against human disease remains necessary. Equine stifle joints are particularly relevant given their human-like cartilage thickness and preserved bone-cartilage interface [2]. This study compares equine and human cartilage across OA stages to evaluate the suitability of equine tissue as a translational in vitro model and to establish a quantitative reference database of OA-associated degeneration.

METHODS: Equine medial condyles (MC, N=5) were harvested post-mortem, frozen, and thawed prior to extracting 25 osteochondral plugs (Ø=4.8 mm). Human knees were obtained from 14 asymptomatic donors (12 patellas, 16 distal femurs (DF)) and 4 OA patients undergoing total knee replacement (TKR, patellar cartilage). In total, 106 plugs were extracted (Ø=3.5 mm). Cartilage integrity was evaluated using the QP measuring probe (Arthro-BST, Biomomentum Inc.) and the qualitative ICRS grading before extraction. The percentage of cartilage surface defects was computed as the proportion of articular surface area graded above ICRS 0. Mechanical testing provided fibril modulus, matrix modulus, and hydraulic permeability. All plugs were processed for histology, and group comparisons were performed with the Kruskal-Wallis test.

RESULTS: QP values consistently correlated with ICRS grading in both species (Fig. 1A). Mechanical properties deteriorated progressively with OA severity, with significant reductions in fibril modulus ($p<10^{-4}$) and matrix modulus ($p<10^{-4}$) and increased hydraulic permeability ($p<10^{-4}$). Defect prevalence reflected tissue origin: distal femurs showed minimal defects (avg. 5.9%, range 0–20.5%), patellae displayed higher defects (avg. 35.4%, range 0–75%), and all TKR patellae were affected (100%). Equine MC demonstrated a defect burden (avg. 38.6%, range 17–62%) that places it between largely intact distal femurs and fully diseased TKR patellae. Histology confirmed similar patterns of degeneration in both species, including progressive surface irregularities and glycosaminoglycans (GAG) depletion with advancing OA (Fig. 1B).

DISCUSSION: Equine cartilage exhibited mechanical, electromechanical, and histological responses aligned with human tissue across OA stages, supporting its potential use as an in vitro OA model. Donor baseline quality was a critical determinant, with less affected surfaces (DF) maintaining superior mechanics compared to more compromised ones (patellae, TKR, or equine MC), even at equivalent ICRS scores. QP measurements captured these differences, providing an objective and continuous readout aligned with mechanics and ICRS [3]. Its reproducibility supports consistent grading across studies, reducing variability that can limit visual scoring. Equine MC offered mid- to advanced-stage degeneration, bridging the gap between asymptomatic DF and late-stage TKR. To strengthen cross-species comparisons and expand tissue availability in accordance with the 3R principle, future work will include additional equine joint surfaces (patella, fetlock). This has the potential to facilitate broader in vitro screening of disease-modifying OA therapies, thereby supporting translational research.

SIGNIFICANCE/CLINICAL RELEVANCE: This study indicates that naturally occurring equine OA mimics human cartilage degeneration, highlighting its potential as a translational in vitro model. By addressing the scarcity of human tissue, the subjectivity of grading, and the limitations of current preclinical models, the dataset generated here offers also a robust reference for benchmarking induced OA models and for accelerating therapeutic development.

REFERENCES: [1] Wang, Y., Grodzinsky, A.J., et al (2015) Post-traumatic Arthritis; [2] Chevrier et al (2014) Journal of Orthopedic research, 33, 63-70. [3] S. Sim et al. (2014) Osteoarthritis and Cartilage

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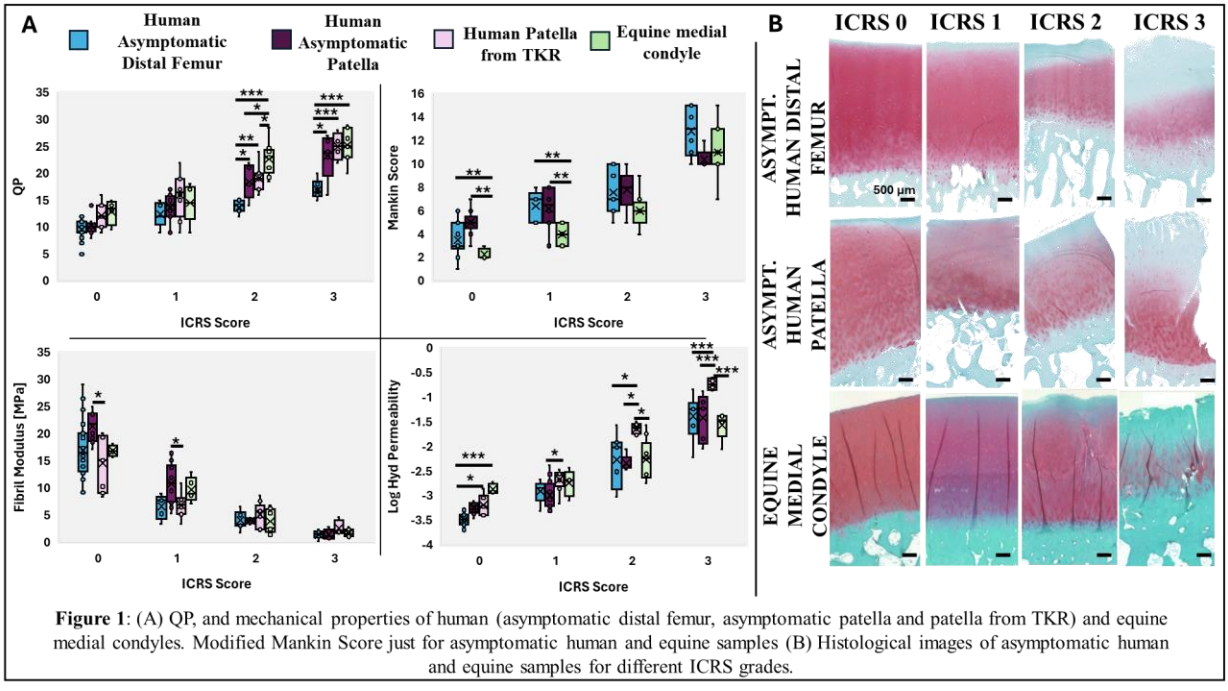

Figure 1: (A) QP, and mechanical properties of human (asymptomatic distal femur, asymptomatic patella and patella from TKR) and equine medial condyles. Modified Mankin Score just for asymptomatic human and equine samples (B) Histological images of asymptomatic human and equine samples for different ICRS grades.