

Novel Small Animal Model of Hip Osteoarthritis Secondary to an Induced Femoral Head-Neck Deformity: A Platform to Study Mechanism of Hip OA

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Disclosures: Kenichi Kikuchi (N), Tomoyuki Kamenaga (N), Robert H. Brophy (AAOS; AJSM; AOA; AOSSM), Regis J. O'Keefe (Fate Therapeutics; Journal of Orthopaedic Translation), John C. Clohisy (Microport; Microport Orthopedics, Inc.; Wolters Kluwer Health – Lippincott Williams & Wilkins; Zimmer; Department of Defense), Cecilia Pascual-Garrido (OREF; NIH)

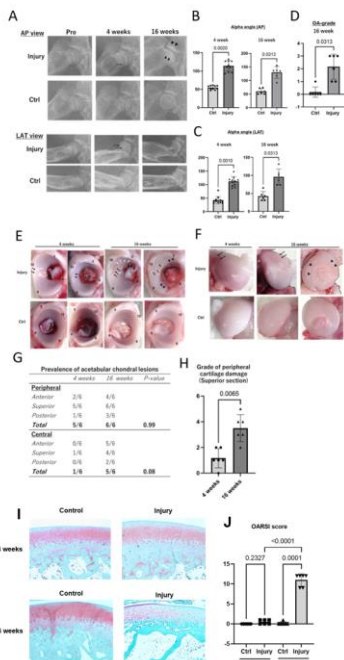
INTRODUCTION: Femoroacetabular impingement (FAI) is a leading cause of hip osteoarthritis (OA). We have previously established the novel rabbit model of head-neck cam type hip deformity [1]. We aim to investigate if the established head-neck deformity results in hip OA.

METHODS: 6-week-old immature New Zealand White rabbits (male n=10, female n=10) were used and subjected to right hip surgery. All surgeries were performed as previously reported [1]. We used a 1.6-mm drill bit to create a 3 × 2 × 6-mm defect in the epiphysis at the medial third of the epiphysis of the femoral head (FH). Groups were divided in early pre-OA group (4 weeks n=10) and late OA group (3 months n=10). Contralateral hips were served as control (n=20). Radiographically, the alpha angle was used to assess the head-neck deformity, and a semi-quantitative scoring system was used to evaluate the presence and severity of osteoarthritis (Tonnis Score). As a macroscopic evaluation, rabbits were sacrificed at the end of the assigned ambulatory period (pre-OA group 4 weeks or late OA group 16 weeks). Both hip joints were dislocated to expose the entire joint and further tissue processing. The acetabular and femoral head chondral lesions were classified using Beck's classification. Safranin-O staining was used for histological assessment (OARSI score). Osteoarthritis was confirmed using micro computed tomography (μCT). We assessed gene expression for cartilage degeneration including Col2, Col10, and MMP13 (RT-PCR). The comparison between groups was performed using Mann-Whitney U test. The level of significance was set as P value less than 0.05. Data is presented as mean ± standard deviation for parametric test.

RESULTS: Radiographs taken at 4 and 16 weeks after surgery demonstrated a FH deformity confirmed on AP and lateral hip views (black arrow, Fig 1-A). Femoral head-neck deformity was confirmed with higher alpha angles in both AP and lateral views at 4 weeks (control vs. injured hip, AP-view, 54.9 ± 5.4° vs. 114.3 ± 4.7° p=0.002, lateral-view, 42.7 ± 13.4° vs. 112.0 ± 17.8° p=0.001, Fig. 1-B and 1-C) and 16 weeks after surgery (control vs. injured hip, AP-view, 54.9 ± 5.4° vs. 114.3 ± 14.7° p=0.031, lateral-view, 60.3 ± 10.5° vs. 130.2 ± 21.8° p=0.031, Fig. 1-B and 1-C). Additionally, radiographs at 16 weeks after surgery clearly showed OA changes including bone sclerosis and joint space narrowing (black arrow, Fig 1-B), suggesting progression to hip OA with a Tonnis grade > 2 in injured hips (control vs. injured hips : 0.16 ± 0.41 vs. 2.17 ± 0.97, p=0.031, Fig 1-D (Tonnis grade equal or >2 is considered OA)). Macroscopic cartilage lesions were observed in the peripheral acetabular area of injured hips at 4 weeks (control vs. injured hip, 0% vs. 83.3%, p=0.015) and 16 weeks after surgery (control vs. injured hip, 0% vs. 100.0%, p=0.002), when compared to control hips (0%, Fig 1-E, F, G). Additionally, more severe cartilage lesions were observed during late stage of disease (16 weeks) (Fig 1-H). Injured hips showed loss of Safranin-O staining compared with control hips at 16 weeks (Fig 1-I) and OARSI score was higher in injured hips compared with control hips at 16 weeks (control vs. injured hips: 0.5 ± 0.37 vs. 11.0 ± 1.41, p<0.0001, Fig 1-J). Subchondral bone evaluation with μCT confirmed degenerative OA changes in the femoral head and acetabular at 16 weeks (Fig 2). μCT of FH showed higher bone volume fraction (BV/TV) and trabecular thickness (Tb.Th) than control-hips (control vs. injured-hip: BV/TV, 0.48±0.025 vs. 0.53±0.020, p=0.0001, Tb.Th, 0.15±0.012 vs. 0.16±0.01, p=0.0007) at 16 weeks (Fig 2-A, B). At 16 weeks, RT-PCR analysis confirmed increase expression of cartilage catabolism with decreased expression of Col2 and increased expression of Col10 (control vs. injured hip, Col2, p=0.043, Col10, p=0.021, Fig. 3) in both FH and acetabular cartilage. (control vs. injured hip, Col10, p=0.016, MMP13, p=0.0414, Fig. 3).

DISCUSSION: Today, there has only been published one large animal model of hip impingement and there are some limitations in this model, including the high cost and availability compared with small animals and that is not reproducing the natural etiology of hip FAI [2]. In the present study, the proposed induced FH deformity results in hip OA at 16 weeks. The injured joint progressed with microscopical and macroscopical intraarticular cartilage damage and osteoarthritis, similar to what we see in the human species. Therefore, this model has the potential to tremendously impact the field, as it will allow, for the first time, to have a low cost, small translational animal model of hip FAI and hip OA. This model could be used as a platform to understand in-depth the mechanisms of hip OA, test interventions and translate our discoveries to patient care.

Figure 1



SIGNIFICANCE: We propose small translational animal model of hip FAI and hip OA for the first time.

REFERENCES: 1. Kamenaga T. et al. *Am J Sports Med* 2022.

2. Schmaranzer F. et al. *Osteoarthritis Cartilage*. 2018.

Figure 1: Safranin-O staining of p21 +/- and p21 -/- chondrocytes at 1 week, day 10, and 2 weeks.

Figure 2: μCT parameters at acetabular and femoral head.

Figure 3: Relative gene expression of Col2, Col10 and Mmp13 at acetabular and femoral head.

Figure 2

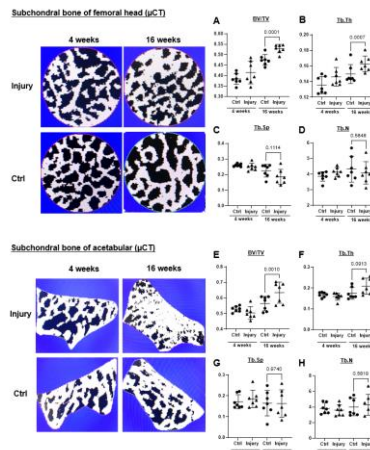


Figure 3

