

# Progressive Degenerative Cartilage Changes with Persistence of Dysplastic Deformity in Rabbit Hips

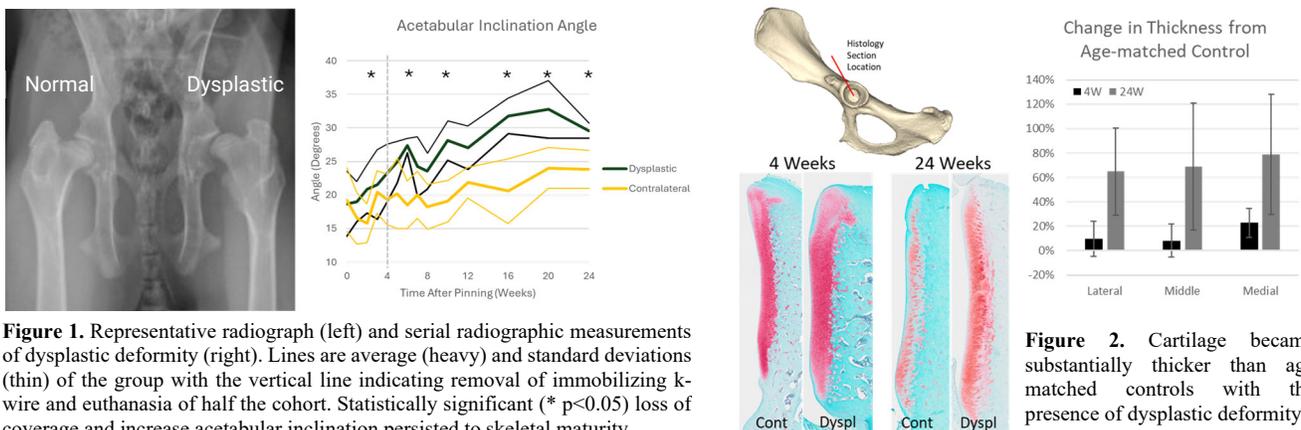
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**Disclosures:** D.C. Fredericks: 5; Lightning Bio, OrthoRebirth, Bone Solutions, Vivorte, SurGenTech. D.J. Rivas: None. D.C. Cruse: None. E.B. Petersen: None. J.B. Holt: None. M.C. Willey: 5; Mend, Naitive, Excere, Medacta, PDI. 8; JBJS CME Committee. 9; OTA Research Committee, MAOA Membership Committee, AAOS OITE Committee. J.E. Goetz: 5; Medacta. 8; Foot & Ankle International.

**INTRODUCTION:** Hip dysplasia is a musculoskeletal deformity affecting both pediatric and adult patients in which the acetabulum insufficiently covers the femoral head. Pediatric presentations of hip dysplasia can be quite severe with the femoral head completely dislocated from the acetabulum, whereas presentation of hip dysplasia in young adults typically involves bone deformity with subluxation. Systematic study of hip dysplasia can be performed in a rabbit model in which the hip deformity is created via growth alterations induced by prolonged extension of the knee.[1-3] However, most uses of the rabbit model are towards pediatric applications, and it is less clear if the presence of dysplastic deformity induced when the rabbit is still growing rapidly will persist into adulthood if the rabbit resumes normal ambulation with a flexible knee. Thus, the goal of this work was to determine to if dysplastic deformity persists to skeletal maturity in a rabbit hip that is reloaded normally by a knee that is rehabilitated to flex after immobilization, and to determine if degenerative cartilage changes develop/persist in skeletally mature rabbit hips in which the deforming stimulus was removed.

**METHODS:** Eight female New Zealand White rabbits, 6-weeks of age were used for this IACUC-approved study. Given the substantially higher incidence of symptomatic hip dysplasia in females, this study used only female animals. Six rabbits were anesthetized and a trans-articular, 1.6-mm-diameter, stainless steel K-wire spanning from the greater trochanter, across the knee, to the distal tibial growth plate was inserted to immobilize the knee in extension. Immobilized rabbits underwent weekly radiographs and CT scans. 4 weeks after K-wire insertion, three immobilized rabbits and one age-matched control rabbit were randomly selected for euthanasia. The remaining three immobilized rabbits had the K-wire removed and underwent supervised knee rehabilitation. 24 weeks after initial immobilization, after confirming skeletal maturity, these animals and the age matched control underwent final CT scans, radiographs, and were euthanized. The femoral head and acetabulum for both hips was harvested, fixed in formalin, embedded in paraffin, sectioned, and stained with safranin-O and fast green. Radiographs were analyzed for progression/resolution of dysplastic deformity [4] using the Norberg angle (lateral center edge angle equivalent), acetabular inclination angle, and the Orthopedic Foundation for Animals (OFA) score. Differences in acetabular rim geometry and acetabular curvature were evaluated from 3D models generated from CT scans, and differences in cartilage thickness and chondrocyte health were evaluated on digitized safranin-O-stained histology sections.

**RESULTS:** All rabbits that underwent knee immobilization developed morphological changes of the hip on radiographs that indicated a decrease in lateral coverage and lateral subluxation of the femoral head, as well as statistically significant increased inclination of the acetabulum (Figure 1) that persisted to skeletal maturity even after removal of the knee immobilizing K-wire. The medial-to-lateral length of the acetabular weightbearing surface averaged 8% to 13% shorter after 4 weeks of knee immobilization to induce dysplastic deformity. By 24 weeks, the weightbearing surface length varied substantially by animal with major increases or decreases relative to age-matched control. Cartilage thickness increased in the dysplastic hips relative to in age-matched contralateral hips (Figure 2), with decreased chondrocyte organization, increased chondrocyte cloning, and irregular proteoglycan distribution.



**Figure 1.** Representative radiograph (left) and serial radiographic measurements of dysplastic deformity (right). Lines are average (heavy) and standard deviations (thin) of the group with the vertical line indicating removal of immobilizing k-wire and euthanasia of half the cohort. Statistically significant (\* p<0.05) loss of coverage and increase acetabular inclination persisted to skeletal maturity.

**Figure 2.** Cartilage became substantially thicker than age matched controls with the presence of dysplastic deformity.

**DISCUSSION:** This study confirmed the findings of other research groups that have described the rabbit hip dysplasia model which included reliable development of dysplastic deformity after immobilization of the knee in extension [1-3] and increased cartilage thickness in dysplastic hips [5]. Most studies have focused on the attainment of dysplastic deformity on radiographs or development of histological changes without consideration of the joint shape. This work confirmed that induced dysplastic deformity was still present in the hips upon reaching skeletal maturity, concurrent with persistent cartilage degenerative changes. The limited studies that have involved skeletally mature animals have not described the use of the limb, in which knee flexion is severely impeded. This work specifically describes findings when the animal has been rehabilitated to normalize knee function and dysplastic limb loading.

**SIGNIFICANCE:** The rabbit provides an appropriate model for systematic study of young adult human hip dysplasia in which patients ambulate relatively normally on a deformed and unstable, but not dislocated, hip joint.

**REFERENCES:** [1] Greenhill BJ, et al. 1995. *J Pediatr Orthop* 15:789-793. [2] Shimogaki K, Yasunaga Y, Ochi M. 2005. *J Bone Joint Surg Br* 87:1019-1023. [3] Michelsson JE, Langenskiold A. 1972. *J Bone Joint Surg Am* 54:1177-1186. [4] Pascual-Garrido C, et al. 2018. *J Orthop Res* 36:1807-1817. [5] Ding R, et al. 2021. *J Orthop Surg Res* 16:512.

**ACKNOWLEDGEMENTS:** The authors would like to thank the staff and students and the University of Iowa Animal Research Surgicenter for assisting with this work. This work was funded by Tyrone D. Artz Chair in Orthopedics at the University of Iowa.