STEROID VERSUS CRYO-INSULT INDUCTION OF FEMORAL HEAD OSTEOONECROSIS
IN A BIPEDAL LABORATORY ANIMAL MODEL

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INTRODUCTION: Osteonecrosis of the femoral head results from a wide variety of etiologic factors, leading to the final pathway of mechanical collapse of the femoral head. Steroid therapy, alcoholism, physical insult, and systemic disease are among the established risk factors. This wide variety of pre-disposing factors bears on the choice of methods to induce osteonecrotic lesions in a laboratory setting.

The head-collapsing emu bipedal animal model of osteonecrosis requires an external event to develop osteonecrotic changes. Due to the correlation between steroid use and osteonecrosis, a model with a steroid induced osteonecrotic lesion potentially holds attraction. However, for practical purposes, induction of osteonecrosis in an animal model needs to be an expeditious process, so an acute insult to cause osteonecrosis also holds attraction. Toward determining the most appropriate method to use for inducing osteonecrosis in the emu model, a steroid regimen was tested, as well as an acute cryo-insult procedure, both separately and in combination. Ease of the procedure and homology to naturally occurring necrosis are also factors deserving consideration.

METHODS: After obtaining IACUC approval, nine emus received a cryo-insult to the right femoral head. Nine additional emus received a cryo-insult, 5 mg/kg of methylprednisolone acetate, and permanent ligation of the medial and lateral circumflex arteries in the right hip. To minimize the number of animals used, the left, non-operated femurs of the group receiving steroids comprised the steroid-only group. One year post-op, all operated emus and two control animals were sacrificed. Femurs were harvested, fixed in formalin, decalcified, embedded in paraffin, and sections stained with Weigert’s hematoxylin and eosin.

Representative sections were taken from the central portion of the femoral head and scanned on a stepper-motor driven microscope stage. Each scan resulted in approximately 2000 sub-images of tissue physically 637x485 µm in size (1392x1040 pixels). Utilizing an in-house grading program written in Matlab to facilitate rapid data processing, each sub-image was given a grade of histologic osteonecrosis damage based on the scale described by Ficat (Table 1). All histologic evaluations were made by a single grader blinded both to the study group assignment and to the spatial location of the sub-image within the femoral head section.

RESULTS AND DISCUSSION: As expected, the normal femoral head sections (N) showed very small amounts of high-grade damage (Figure 2). The presence of a cryo-insult (C) increased the higher-grade damage from normal. The group receiving only steroids (S) had an increase in low-grade damage to the entire head. The group with steroids, vessel ligation, and cryo-insult (SLC) showed the highest amount of high-grade damage, as well as considerable global, low-grade damage.

Normal femoral heads showed no significant clustering of damage. Nine out of nine heads from the SLC group showed statistically significant clustering. Four out of nine heads from the C group, and two out of seven heads in the S group, showed significant clustering. The average z scores indicated little to no clustering in either the normal or the isolated steroid group (z=0.18 and z=0.80, respectively), and significant clustering in both the isolated cryoin insult group (z=3.17) and the steroid/ligation/cryo-insult group (z=5.62).

CONCLUSIONS: Use of a cryoin insult alone appears to be the best alternative for creating necrotic lesions in emus that mimic the human condition of focal lesions. Administration of steroids creates whole-head damage that could be a confounding factor when trying to develop focal necrotic lesions in the femoral head.

REFERENCES:

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