The Effect of Hormone Replacement Therapy on Elongation of the Macaque IGHL

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INTRODUCTION:
The effect of hormone treatment on the material properties of ligaments has been extensively studied for the anterior cruciate ligament. However, there have been few studies on the effects of hormones on the material properties of the shoulder. Shoulder ligaments contribute to overall shoulder stability, and an elongation of these ligaments could contribute to a change in overall shoulder laxity. This study used adult female cynomolgus macaque (Macaca fascicularis) monkeys to determine if estrogen had an effect on the elongation of the inferior glenohumeral ligament (IGHL) undergoing repetitive loading.

METHODS:
Twenty female cynomolgus monkeys underwent bilateral ovarioectomy at Wake Forest University after adulthood was reached. Drug therapy was initiated 4 months post-ovariectomy to allow time for the native hormonal effects to subside. Twelve of the animals received oral doses of estradiol (HRT) equivalent to doses taken by an average woman and eight of the animals received no treatment (OVX). The animals were allowed normal unrestricted cage activity for eight months of drug therapy and were then humanely euthanized. The study was approved by the Institutional Animal Care and Use Committees of both Wake Forest University and Columbia University. The shoulders were dissected free of the animal and immediately frozen. The inferior glenohumeral ligament (IGHL) was carefully dissected out and IGHL bone-ligament-bone (BLB) specimens were created [1]. The IGHL was separated into three anatomical regions: the superior band (SB), anterior portion of the axillary pouch (AP), and posterior portion of the pouch (PP). Failure loading was performed on a different set of monkeys to determine the sub-maximal (SM) failure strains for each anatomic region. The sub-failure strain was defined as the mean failure strain for a region less 1.5 times the standard deviation for that region. The bone-ligament-bone complexes were cyclically preconditioned to 25% of sub-failure strain, and then subjected, at a constant strain rate, to a series of cyclic strain loadings of 50% (50SM), 75% (75SM) and 100% (100SM) of SM failure strain. After cyclic loading, the specimens were allowed to recover first for 15 minutes (15RC) and then for 45 minutes (45RC). A tare load of 1.0 N was applied and any residual elongation was measured after each recovery period. Specimens were bathed in a phosphate buffered saline solution with protease inhibitors throughout testing. A three-way ANOVA, with treatment (OVX, HRT), ligament region (AP, PP, SB) and strain level (50SM, 75SM, 100SM, 15RC, 45RC) as repeated factors were run. Student-Newman-Kuels multiple comparisons tests were run for ligament region and strain level. Statistical significance was taken as p=0.05.

RESULTS:
HRT was found to have no effect on elongation of the IGHL at any of the strain levels (p=0.540), nor did it have an effect by ligament region (p=0.809). The post-hoc power of the study for a difference in elongation of 7% or greater was 80%. Elongation did differ by ligament region (p=0.009), with the AP showing significantly greater elongation than the SB and PP (Figure 2). This difference became more pronounced with increasing strain levels (p=0.0001). Elongations statistically increased with increasing strain level, with a small but not statistically significant recovery (1-4%) with rest (Figure 3).

DISCUSSION:
HRT was not found to increase elongation with repetitive loading in the macaque IGHL. This study does not address if elongation and subsequent acquired shoulder laxity and instability due to repetitive loading in the adult female shoulder is greater than in the male since no male macaques were available. Clinically, HRT may not increase elongation in the adult female shoulder following repetitive microtrauma. The differences observed between ligament regions suggest variability in collagen fiber microorganization between regions. The lack of significant recovery of ligament length after both 15 minute and 45 minute rest periods supports the premise that progressive collagen fiber microdamage and induced laxity occur with repetitive motion syndromes and is consistent with findings for the human IGHL. Variations in elongation were found between IGHL regions and were also consistent with similar observations in the human IGHL [2], supporting the use of macaque as a primate model of the shoulder.

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REFERENCES: