Introduction. Several studies have reported on the effect of synthetic estrogens (tamoxifen, raloxifene, droloxifene, etc.), on bone mass in small mammals, but few (1) have reported on their effect in old large animals: 1) have Haversian (intracortical) remodeling and, 2) demonstrate bone loss following ovariectomy (OVX). We conducted a dose-response study in aged OVX ewes and found improved bone mineral density (BMD), vertebral trabecular bone density, and compressive strength with the selective estrogen receptor agonist, raloxifene.

Methods. The project was approved by the IACUC (protocol 96-093A-01). Forty-two aged ewes (7-8 years old); same breed/housing, were randomly divided into five groups: Sham-operated (Sham; n = 7), Ovariectomized (OVX; n = 10), OVX + estradiol implant (OVXE; n = 8), raloxifene (Ral 0.02mg/kg/day; n = 10) and a higher dose of raloxifene (Ral 0.1 mg/kg/day; n = 13).

Dual-energy X-ray absorptiometry (DEXA): Under general anesthesia, following OVX or Sham procedure, BMD (g/cm2) of the last four lumbar vertebrae was measured using DEXA with the Hologic 1000W (Hologic, Inc., Waltham, MA) densitometer using software version V6.10.1. The BMD of L3-L6 was measured in a standard dorsoventral view and the mean of all four vertebrae was used for analysis. To determine intra-assay variations, short term precision was evaluated by measuring BMD of L3-L6, in an anesthetized sheep repostioned between 10 scans.

Results. The in vivo precision of BMD for L3-L6 was 1.4%. The change in spine BMD was influenced by the treatment group (p = 0.031, Figure 1). For example, at six months, the spine BMD in the high-dose raloxifene group had increased 9.49 ± 7.69%, whereas the spine BMD in the OVX group decreased 5.40 ± 7.69%.

Discussion. This study confirmed findings of others that the aged OVX ewe, like humans, loses bone after OVX and is a suitable large animal model for evaluation of therapeutic agents for osteoporosis. Results were similar to those in rats where the effects of raloxifene on bone mass was comparable to treatment with estradiol. We showed an even greater response than estradiol, of bone mass and compressive strength to the synthetic antiestrogen. This is the first report of improved mechanical properties of bone in a large animal, in response to a synthetic estrogen receptor modulator.


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