A Non-Weight Bearing Model of Osteoporosis for Histomorphometric and Mechanical Evaluation of Bone Repair Using Bone Graft Substitutes

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Introduction: A true animal model of human estrogen depletion osteoporosis is not known. However, a relevant local osteoporotic state can be obtained through prolonged, decreased weight bearing of a specific limb. The purpose of this study was to develop a canine non-weight bearing model to replicate the bone loss occurring in osteoporosis and to evaluate the ability of a synthetic bone graft substitute, compared to autogenous bone graft, to enhance bone volume and restore bone strength in critical-size defects in this bone deficient environment.

Materials and Methods: Under an IACUC-approved protocol, 9 skeletally mature, male dogs (25-34 kgs) had their left front limb placed in a shoulder sling with the limb in flexion, to affect complete non-weight bearing, and were placed into one of three groups: no bone defects, autograft-treated defects, bone graft substitute-treated defects (Table 1). Cortical and medullary changes in the humerus and radius of the immobilized limb were followed by radiographs at 0, 16, and 26 weeks. After 26 weeks of immobilization, 6 animals had a critical-size, axial medullary defect (13mm dia. X 50mm) created in the proximal left humerus [1] and a large cylindrical defect (7 x 25 mm) was also created transversely in the left distal radius. Both defects were filled with the same graft material, either cancellous autogenous bone or a calcium sulfate/calcium phosphate composite bone graft substitute (PRO-DENSE®, Wright Medical Technology). Following the surgery, the animals were followed for an additional 13 weeks of non-weight bearing. Radiographs were obtained at 0, 2, 6, and 13 weeks post-operative.

Table 1. Study Design

Group	N	Initial Non-Weight Bearing Period	Critical-Size Defects	Continued Non-Weight Bearing
No Defect	3	**26-30 weeks**	**No**	**No**
Autograft	3	**26 weeks**	**Yes**	**13 weeks**
Bone Graft Substitute	3	**26 weeks**	**Yes**	**13 weeks**

Transverse, undecalcified stained sections of the bones were prepared. The area fractions of new bone and residual implanted materials in the defects were quantified using standard point-counting techniques. Total area of bone was quantified by digitizing high resolution contact x-rays of specimen cross sections selecting for cortical and trabecular bone. The yield strength and modulus of an 8mm dia X 20mm test cylinder cored from the midlevel of each humeral defect was determined in unconfined, uniaxial compression tests.

Results: Global bone loss was achieved in the entire non-weight bearing front limb of the animals in all three groups. The mean area fraction of trabecular bone in the no-defect group was 10.4% and was less than the weight bearing humeri (15.0%, p=0.083) (Figure 1). Notably, the area fraction of bone in these weight bearing humeri was comparable to that previously reported for normal humeri in healthy canines (p=0.584) [2], indicating that there was no hypertrophy of the bone in the contralateral weight bearing limb. The strength of bone (0.51 MPa) was less in the non-weight bearing no-defect group compared to the contralateral humerus (0.81MPa).

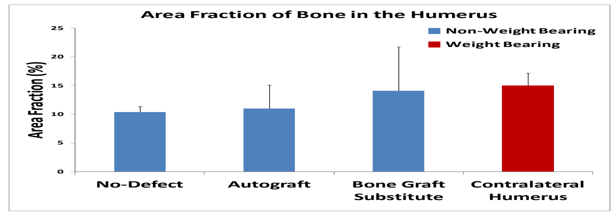

Figure 1. Area fraction of new bone in non-weight bearing bones (blue bars) compared to the weight bearing contralateral bone (red bar).

Total bone area was also decreased in the non-weight bearing humerus and radius. Changes in total area were most notable in the radii and ranged from 21.3% proximal to 36.3% distal. For the humerus, the decrease ranged from 9.1% proximal to 18.7% distal. In the non-weight bearing humerus and radius, cortical bone loss was seen at both the periosteal and endosteal surfaces (Figure 2).

Figure 2. Reduced cortical width and trabecular thinning in a non-weight bearing radius **(right)** compared to the contralateral weight bearing bone **(left)**. Basic Fuchsin/Toluidine Blue, X10.

New bone formation was present in all of the defects in the radius and humerus. The amount (14.1%) and strength (0.81MPa) of new bone in the bone graft substitute group was equivalent to that of the weight bearing non-treated contralateral humeri (p=0.564). In contrast, the amount (11.0%) and strength (0.58MPa) of new bone in the autografted group was similar to the non-weight bearing humeri (p=0.827) (Figure 1).

Conclusions: Substantial loss of bone was achieved in a gradient along the entire non-weight bearing limb, by placing the front limb of a canine in a non-weight bearing sling for at least 26 weeks. This was reflected most dramatically distally in the radius and was also seen in the humerus, while hypertrophy of the weight bearing contralateral bones was not observed. In this bone deficient environment, the use of a calcium sulfate/calcium phosphate bone graft substitute in critical sized defects restored bone volume and strength to values similar to that of the weight bearing limb.

References: [1] Turner TM JBJS 2001; 83A (Supp.2-1):8-18; [2] Urban RM CORR 2007; 459:110-17.

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