Introduction: Alendronate, a second generation bisphosphonate, is known to increase bone density by inhibiting osteoclastic bone resorption. It is clinically used to treat osteoporosis, Paget’s disease and hypercalcemia associated with malignancy [1]. In clinical trials and animal studies, the effects are typically quantified by measuring bone mineral density. In this study, we sought to determine whether healthy canine bones exhibit increased structural or mechanical properties following alendronate treatment. We tested both whole long bones and trabecular bone samples, because a prior study with pamidronate had different findings with these two sample types [2]. We hypothesized that alendronate treatment would increase the structural properties of bones and mechanical properties of bone tissue in healthy dogs.

Methods and Materials: The treatment group consisted of 8 healthy, male, mongrel dogs given 5 mg/day of oral alendronate sodium (Fosamax, Merck, Rahway, NJ) for 23 weeks. Eleven untreated male dogs served as a control group. All dogs were subjected to hip arthroplasty as part of a related study [3]. After 23 weeks of therapy the dogs were sacrificed and the second, third, and fourth metacarpals of both forepaws and lumbar vertebrae were dissected, stripped of all soft tissue and fresh-frozen until testing. Retrieved metacarpals were tested in bending and torsion, and trabecular bone samples from lumbar vertebral bodies were tested in compression.

The metacarpals from each paw were structurally tested in four-point bending, using a displacement-controlled load-to-failure test with a crosshead speed of 20 mm/min. The epiphyses of the bones from the contralateral paw were resected, leaving a standard specimen length of 6 cm. A crosspin was placed in each of the bones and the bone ends were embedded in a block of bone cement. The constructs were tested in torsion using a biaxial testing machine (Instron 8521). Each specimen was twisted at a rate of 5 deg/s, while a 2 N preload was applied. The bone ends were allowed to thaw for 3 hours and the constructs were tested in torsion. The data from each set of three bones from each dog were averaged to produce cylinders nominally 14 mm long and 7 mm in diameter.

The trabecular bone samples were allowed to thaw for 3 hours and the length and width were measured using dial calipers. A 2 N preload was applied to each specimen, followed by a displacement-controlled load-to-failure test with a crosshead speed of 5 mm/min. The specimens were tested to produce cylinders nominally 14 mm long and 7 mm in diameter.

The trabecular bone samples were tested in compression using a uniaxial testing machine (Instron Model 4502, Canton, MA). A 2 N preload was applied to each specimen, followed by a displacement-controlled load-to-failure test with a crosshead speed of 1000 mm/min. The constructs were tested in torsion using a biaxial testing machine (Instron 8521). Each specimen was twisted at a rate of 5 deg/s, while a 2 N preload was applied. The bone ends were allowed to thaw for 3 hours and the constructs were tested in torsion. The data from each set of three bones from each dog were averaged to produce cylinders nominally 14 mm long and 7 mm in diameter.

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Results: For the metacarpal tests, the data from each set of three bones from the same dog were pooled, to minimize variation due to differences in bone size and shape, and comparisons were made between dogs. The stiffness under the bending load, maximum four-point bending moment, the torsional stiffness, and the maximum torque for the treated and control groups are shown in Table 1. No significant differences in any of the metacarpal properties were found between treated versus control groups.

For trabecular bone compression tests, data from three specimens were lost due to errors in the Instron software. The average Young’s modulus for the treated dogs was 868 ± 220 MPa and was not significantly different from the control dogs, 851 ± 209 MPa (Figure 1). We observed a significant increase in the ultimate compressive strength in the treated specimens (p=0.038). The ultimate strength of treated specimens was 12.9 ± 3.2 MPa versus 11.2 ± 2.9 MPa for the control specimens (Figure 2).

Discussion: In accordance with our hypothesis, this study demonstrates significantly higher compressive strength in trabecular bone of healthy animals treated with alendronate. Contrary to our hypothesis, however, no significant differences were found for the elastic modulus of trabecular bone or for structural properties of the metacarpals. A previous study by Acito et al. examined the effects of treatment with pamidronate on canine bone properties [2]. Similar to our study, they did not demonstrate significant differences in the structural properties of whole tibia. They did find trabecular bone from treated animals to have significantly higher compressive strength and elastic modulus. Though neither study showed differences in whole bone structural properties, the trend toward higher average properties in treated animals was consistent for all measures. The effects of alendronate are likely more pronounced in trabecular bone due to the greater surface area available for remodeling. Also, cortical bone density is likely already near its maximum density, so large changes in bone mass and strength may only be attained through external remodeling of bone geometry.

In conclusion, this study indicates that alendronate can increase the ultimate strength of trabecular bone even in normal, healthy animals. We plan to correlate our current strength data with the ash densities of our specimens, to provide a link between biomechanical studies and clinical (density) measures of the effectiveness of alendronate.

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References:

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