THE VASCULAR STRUCTURE OF BONE IS COMPROMISED WITH IMMOBILIZATION AND IS NOT RECOVERED WITH ANTI-RESORPTIVE TREATMENT AND REMOBILIZATION

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INTRODUCTION

Bisphosphonates are anti-resorptive drugs that suppress the bone loss of osteoporosis [1]. However, their use has been associated with atypical fracture of cortical bone in humans and lower cortical tissue toughness in animal models [2]. The bone loss associated with bed rest, spinal cord injury or space travel is more aggressive and we have been investigating the effects of bisphosphonates in these situations. Thus far we have demonstrated that cortical bone loss in an immobilized forelimb dog model is suppressed and allows for enhanced structural (endosteal and periosteal envelopes) recovery with remobilization [3,4]. However, mechanical fatigue life is adversely affected. In this study we have investigated the vascular structure of the intra-cortical envelope to gain a better understanding of how the largest pores of cortical bone may influence the mechanical properties of this tissue.

METHODS

Animal Model. In an IACUC-approved study adult female beagles were divided into 4 groups, plus age-matched control (n=6 /group, Figure 1a). The right forelimbs in the 4 groups were immobilized (IM) for 6 months (m) using thermoplastic splints (AquaPlast, Smith and Nephew) [5]. 2 groups were treated with daily doses of risedronate (RIS, 0.5 mg/kg/day) and 2 with sterile water vehicle (VEH). After 6 m IM, splints were removed in one RIS and one VEH-treated group, drug treatment was stopped, and dogs were allowed unrestricted weight-bearing and remobilization (RM) for 12 m. All groups (6m, 18m and age-matched control) were euthanized by pentobarbital overdose.

Cortical Beam Preparation. Beams (n=1/dog) with rectangular cross-sectional geometry (0.5x1.5x14 mm length) were sliced from the cortex of radii using a precision saw (Isomet 5000, Buehler). The osteon long axis was parallel to the long axis of each beam (Fig 1).

Micro-computed tomography. 3D micro-computed tomography (μCT) images of the beams were generated with a Skyscan 1172 system (Bruker, Belgium; 100kV; 100µA). The beams were immersed in PBS and individually scanned with a voxel resolution of 4.7µm. The measured porosity traits included total pore volume, degree of anisotropy and connectivity density (Conn).

Statistical Analysis. Results are shown as mean ± standard deviation (SD). Differences between groups were calculated by one way ANOVA with post-hoc Fisher's Least Significant Difference test for at p<0.05.

RESULTS AND DISCUSSION

With IM the total pore volume increased versus age-matched control and was not improved by either drug treatment or RM (Figure 2). The degree of anisotropy among all groups did not vary.
significantly (Fig. 2), remaining within 2% of control. Connectivity increased for all groups compared to control. The drug-treated remobilized (RM RIS) group was increased (p < 0.05) by 132% versus control (Fig. 3).

CONCLUSIONS

RIS is effective in slowing endosteal and periosteal bone loss. However, the intra-cortical envelope consisting mainly of the pores of the vascular supply appears not to be protected. In addition, very little recovery of this envelope occurs upon remobilization, regardless of whether previous drug treatment was attempted. This may partially explain some of our previous mechanical results for these beams, although not all, since drug treatment was beneficial to preventing the loss in toughness and fatigue life during immobilization. Regardless, a complete recovery of all the bone on all envelopes should be the goal of future work to optimize post-

IM recovery, restore mechanical properties and prevent fractures after the extended disuse that occurs with bed rest, spinal cord injury and space flight.

REFERENCES


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Figure 2. μCT images of the vascular pores of beams.

Figure 3. Comparison of connectivity. (* significance, p < 0.05, compared to control, in green)