INTRODUCTION: If bone remodeling repairs microdamage, suppression of bone turnover should allow the accumulation of microdamage that could lead to increased bone fragility. Two years of risedronate treatment does not increase microdamage in the canine femoral neck in spite of the suppression of bone turnover (1). Those results were obtained from only one skeletal site and no biomechanical properties were evaluated. The purpose of this study is to evaluate the effects of reduced bone turnover caused by two different bisphosphonates, risedronate and alendronate, on microdamage accumulation and biomechanical properties of cortical bone in the rib of dogs.

MATERIALS AND METHODS: Twenty-three female beagles, 1-2 years old were divided into three groups. Control dogs were given daily subcutaneous injection of saline vehicle (CNT, n=8). The remaining two groups of dogs were treated daily with risedronate orally at a dose of 0.5mg/kg/day (RIS, n=8), or alendronate orally at 1.0 mg/kg/day (ALN, n=7). All dogs were treated for 12 months. Lateral thoracic X-rays were taken of all dogs at baseline and each month from 7-12 months to evaluate the occurrence of spontaneous rib fractures. After sacrifice, the 9th ribs were dissected bilaterally. The middle portion of the right 9th rib was divided into two parts. One part was bulk stained with basic fuchsin and 80 μm thick transverse sections were cut for microdamage evaluation of cortical bone. The other part was stained with Villanueva bone stain and conventional histomorphometric measurements of cortical bone were performed. The left 9th rib was tested to failure in 3 point bending using an MTS servohydraulic testing machine. Ultimate force, stiffness and energy absorption were measured. The data were analyzed by one-way ANOVA, using Fisher’s PLSD tests for post hoc analysis.

RESULTS: Microcrack mean length (Cr.Le) and density (Cr.Dn) were significantly greater in RIS compared to CNT (Fig.1). There was a clear tendency for RIS to have greater microcrack surface density (Cr.S.Dn) than CNT but this did not reach statistical significance. Cr.Le of ALN was significantly greater than CNT. There was a clear tendency for ALN to have greater Cr.Dn and Cr.S.Dn than CNT but this did not reach statistical significance. There were no significant differences among groups in cortical area (Cr.Ar) (Fig.2). Activation frequency (Ac.F) in ALN was significantly lower than CNT, but there was no significant difference between RIS and CNT, although RIS was reduced by about 40%. Osteoid thickness (O.Th) was significantly greater in RIS compared to CNT (Fig.1). There was a clear tendency for RIS to have greater microcrack surface density (Cr.S.Dn) than CNT but this did not reach statistical significance. There were no significant differences between RIS and ALN in any parameter. No fractures were observed in any group.

DISCUSSION: It has been hypothesized that inhibition of bone turnover can lead to increased bone fragility. Flora et al. reported that fractures of rib, vertebral spinous process and pelvis were observed after 9 to 12 months treatment with high dose etidronate in beagles (2) but whether this was caused by microdamage accumulation or the effects of increased osteoid caused by the suppression of mineralization is not resolved. In this study we used risedronate and alendronate, bisphosphonates that are potent inhibitors of bone resorption, to investigate the effect of suppression of bone turnover on skeletal fragility without suppression of mineralization. One year treatment with risedronate or alendronate suppressed intracortical remodeling by 40% or 75%, respectively, and allowed microdamage accumulation. However, this was not associated with a significant reduction in mechanical properties, nor did fractures occur. This indicates that suppression of bone turnover allows microdamage to accumulate but microdamage accumulation of these dose levels is not necessarily associated with increased skeletal fragility.

![Figure 1. Microdamage measurement of the right 9th rib](image1)

![Figure 2. Intracortical bone histomorphometry of the right rib](image2)

![Figure 3. Biomechanical test of the left 9th rib](image3)


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