

# Morphological Assessment of Basic Multicellular Unit Resorption Parameters in Dogs Shows Additional Mechanisms of Bisphosphonate Effects on Bone

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# Morphological Assessment of Basic Multicellular Unit Resorption Parameters in Dogs Shows Additional Mechanisms of Bisphosphonate Effects on Bone

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## Abstract:

Bisphosphonates (BPs) slow bone loss by reducing initiation of new basic multicellular units (BMUs). Whether or not BPs simply prevent osteoclasts from initiating new BMUs that resorb bone or also reduce the amount of bone they resorb at the BMU level is not clear. The goal of this study was to determine the effects of BPs on three morphological parameters of individual BMUs, resorption depth (Rs.De), area (Rs.Ar), and width (Rs.Wi). After 1 year of treatment with vehicle (VEH), alendronate (ALN; 0.10, 0.20, or 1.00 mg/kg/day), or risedronate (RIS; 0.05, 0.10, or 0.50 mg/kg/day), resorption cavity

morphology was assessed in vertebral trabecular bone of beagle dogs by histology. Animals treated with ALN or RIS at the doses representing those used to treat postmenopausal osteoporosis (0.20 and 0.10 mg/kg/day, respectively) had significantly lower Rs.Ar (-27%) and Rs.Wi (-17%), with no difference in Rs.De, compared to VEH-treated controls. Low doses of ALN and RIS did not affect any parameters, whereas higher doses resulted in similar changes to those of the clinical dose. There were no significant differences in the resorption cavity measures between RIS and ALN at any of the dose equivalents. These results highlight the importance of examining parameters beyond erosion depth for assessment of resorption parameters. Furthermore, these results suggest that in addition to the well-known effects of BPs on reducing the number of active BMUs, these drugs also reduce the activity of osteoclasts at the individual BMU level at doses at and above those used clinically for the treatment of postmenopausal osteoporosis.

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