

### Δ The Effect of Timing of Aminobisphosphonate Therapy on Fracture Healing: A Rabbit Osteoporosis Model

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**Purpose:** Aminobisphosphonates reduce the rate of fragility fractures, but little is known about the effect of aminobisphosphonates on fracture healing in osteoporotic patients.

**Methods:** Female New Zealand white rabbits underwent ovariectomy and IV methylprednisolone treatment to induce osteoporosis. Rabbits were divided into 4 groups on the basis of timing of zoledronic acid (ZA) treatment around radius osteotomy. The pretreatment group received 0.1 mg/kg IV ZA 2 weeks prior to osteotomy. The early treatment group began ZA treatment the day of osteotomy. The delayed treatment group received ZA therapy 2 weeks after osteotomy. The control group received no ZA. Bones were analyzed at 5 weeks biomechanically, histologically, and with micro-CT.

PAPER ABSTRACTS

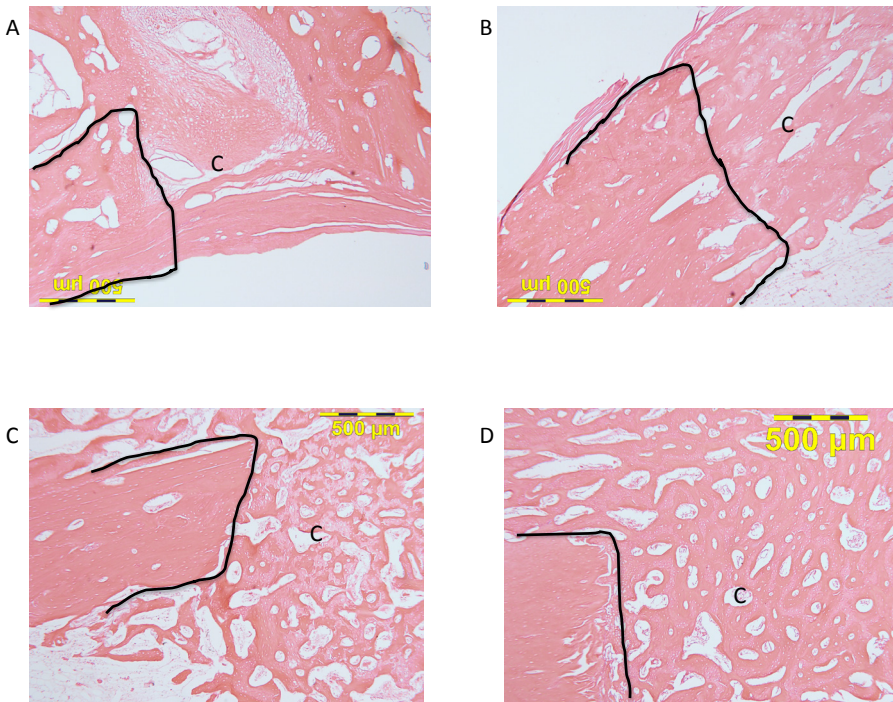


Figure 1. Histology of Fracture Callus. (A) Radius osteotomy callus stained with hematoxylin and eosin at 5 weeks post-osteotomy in rabbits treated with no zoledronic acid (control), and treated with zoledronic acid in (B) delayed, (C) early, and (D) pre-treatment periods. Line contour denotes osteotomized cortex; C denotes bridging fracture callus.

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See pages 49 - 106 for financial disclosure information.

**Results:** Fracture callus volume was greater with ZA pretreatment compared with early treatment ( $P = 0.02$ ) and control conditions ( $P = 0.04$ ). There was a trend in increasing cross-sectional area of fracture callus with longer exposure to ZA. Fracture callus mineral density increased with longer exposure to ZA, which achieved statistical significance in pretreatment ( $P = 0.04$ ) and early treatment ( $P = 0.008$ ) compared with the control group. Peak torque to failure was higher with ZA pretreatment compared with delayed ( $P = 0.003$ ) and control ( $P = 0.04$ ) conditions. Histologically, fracture callus showed an increase in woven bone formation with longer bisphosphonate exposure.

**Conclusion:** In our osteoporotic rabbit fracture model, aminobisphosphonate treatment allowed a robust fracture healing response, even when administered acutely. Longer exposure resulted in increased strength of fracture callus.