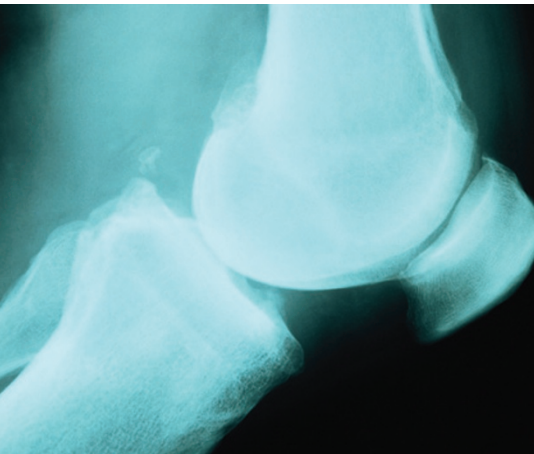


## OSTEOARTHRITIS

# Alendronate treatment improves pathology in animal model of OA by blocking osteoclastic bone resorption

Bone remodeling is thought to be central to the pathogenesis of osteoarthritis (OA). In a study published in *Bone*, Siebelt and colleagues show that pre-emptive treatment with the bisphosphonate alendronate—an inhibitor of osteoclastic bone resorption—slowed disease progression in a rat model of OA.



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To investigate the effect of alendronate in OA, animals were assigned to an untreated control group (OA induction only, consisting of moderate exercise on a motorized treadmill over 6 weeks plus weekly intra-articular injections of papain in the left knee for the first 3 weeks of the exercise protocol) or an alendronate-treated group (OA induction protocol plus 3 subcutaneous injections of alendronate [2.4 µg/kg] per week).

Severe OA developed within 6 weeks, with decreased trabecular bone volume fraction (BV/TV), development of subchondral sclerosis of the tibia and progressive loss of cartilage observed in joints that had undergone OA induction compared with contralateral control joints. Even though alendronate had no effect on the development of subchondral sclerosis during OA progression, a smaller increase in trabecular thickness ( $P < 0.001$ ) and improved preservation of both BV/TV and the cartilage extracellular matrix was

observed in the alendronate-treated group compared to the control group 12 weeks after the beginning of OA induction. Furthermore, consistent with preserved joint integrity, macrophage activation (inferred from local detection of a folate-based radiotracer) in affected joints was decreased in alendronate-treated animals when compared to controls.

Despite discouraging results from previous trials of bisphosphonates in OA, this study suggests that pre-emptive alendronate therapy might dampen disease progression. However, the therapeutic value of alendronate in OA requires validation in patients before translation to a clinical setting can occur.

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**Original article** Siebelt, M. et al. Inhibited osteoclastic bone resorption through alendronate treatment in rats reduces severe osteoarthritis progression. *Bone* doi:10.1016/j.bone.2014.06.009