Repair of a critical size defect in osteoporotic mice

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Osteoporosis is a major health issue for our aging society. Mostly women suffer from reduced bone stability due to menopausal changes in hormone levels. Bisphosphonates (BP) are a common treatment to prevent osteoporotic bone loss. Uptake of BP by osteoclasts leads to a block of cellular activity and bone resorption. Consequentially, BP therapy effectively reduces fracture risk in osteoporosis. But still, patients under BP medication suffer from bone fractures and large defects due to trauma or tumor resection. Currently, critical-size defects are filled with natural or synthetic bone grafts, often in combination with the osteoinductive bone morphogenetic protein-2 (BMP-2) to improve bone healing. It is still debated, whether prolonged therapy with BP interferes with biomaterial turnover during repair of defects fitted with β-tricalcium phosphate (βTCP) ceramics. To investigate the effect of BP on bone healing and turnover of biomaterials, a murine model for post-menopausal osteoporosis was used to study the healing process of a critical-size defect. Eight weeks after induction of osteoporosis by ovariectomy, and after detection of bone loss, treatment with alendronate (ALN), a commonly used BP, commenced. Five weeks later, a critical-size defect was applied in the left femur, filled with βTCP cylinders that were coated with BMP-2 and L51P. L51P has high binding affinity to BMP-2 antagonists, blocking their activity and thereby potentially reducing the required amounts of BMP-2 stimulating bone formation and repair. The implantation site was rigidly fixed, using an osteosynthesis system with an internal fixateur. Femora were collected six and twelve weeks post-surgery to assess implant turnover and bone healing processes by micro-computer tomography, histology and by transcriptome analysis. The performed pilot study demonstrated the suitability of our animal model to study bone repair and revealed sufficient induction of bone healing by high dosage of BMP-2 in comparison to the control group.