Abstract:
Fractures in osteoporotic bones or segment defects are problematic bone lesions with a reduced biological capability of regeneration. We tested the hypothesis that cell-mediated ex vivo gene therapy to deliver BMP4 can heal critically sized defects and improve bone healing in osteoporotic rats. Primary muscle-derived cells were isolated from the hindlimb muscle of rats and retrovirally transduced to express bone morphogenic protein 4 (BMP4). The bone formation was evaluated following local application of these cells in critically sized defects and in fractures of osteoporotic bones. Radiographic analysis revealed bridging callus formation in a critically sized defect in all specimens using muscle-derived cells expressing BMP4 at 12 weeks. These findings were confirmed by histological evaluation, which revealed callus bone formation with good integration to the distal and proximal bone. Following treatment with muscle-derived cells expressing BMP4, the bone healing process in the osteoporotic bone was improved to the level similar to that of normal bone. The ex vivo gene therapy could be a promising tool for the treatment of osteoporotic fractures and critically sized defects. The reduced number of complications (nonunions, loss of reduction, and fragment dislocation), shortening of hospitalization period, and improvement of bone strength are decisive advocates for this treatment.