INTRODUCTION
Bone marrow cells are well known for improving healing. Recent studies report that stromal cell-derived factor-1 (SDF-1) and its receptor CXC chemokine receptor 4 (CXCR4) play roles in stem cell homing and are related to short-term and long-term engraftment. SDF-1 secreted from an injured organ can pass the endothelium barrier in a CXCR4-dependent manner into the bone marrow and recruit hematopoietic progenitors to the circulation. There is evidence to show that SDF-1 also has chemoattractive effects and is able to recruit mesenchymal stem cells and osteoprogenitors. Our previous study also showed that SDF-1 has an enhanced effect on osteoblastic differentiation of human mesenchymal stem cells. The purpose of this study is to investigate the effects of genetically modified bone marrow cells that overexpress SDF-1 on bone fracture healing in rat model. The hypothesis is that genetically modified rat bone marrow cells (rBMCs) that over expresses SDF-1 will enhance the fracture healing process compared to non-treated groups or to groups treated with only rBMCs.

MATERIALS AND METHODS
rBMCs were harvested from femora of young male Wistar rats. rBMCs were expanded ex vivo, and cells of passage 3 were used in the experiment. SDF-1 over-expressing rBMCs (rBMC-SDF-1) were engineered by infection of adenovirus carrying human SDF-1 gene at the multiplicity of infection (MOI) 500. Eighteen adult female Wistar rats were divided into three groups with 6 rats in each group: (1) rBMC-SDF-1, (2) rBMC and (3) control. A 3mm gap in the middle of femur was created during surgery and stabilized by an external fixator. In two groups three hundred thousand rBMCs or rBMCs-SDF-1 were seeded into a collagen sponge and transplanted into the gap. For the control group, sponges without cells were used. Rats were sacrificed 3 weeks after operation and the femora were harvested. Bone mineral content within the gap was measured immediately after operation and compared with the bone mineral content within the same gap at the third week by dual energy X-ray absorbptiometry (DEXA) scanning. The area of new bone formation was measured using histomorphometry on H&E stained sections and quantified by imaging analysis system. Results were analyzed by Mann-Whitney U Test and significance was assigned at the 95% level.

RESULTS
Figure 1 shows that there was new bone formation in all three groups. However, in the control group a less dense bone structure was seen when compared to the other two groups. rBMC-SDF-1 group showed an increased new bone formation in the fracture site. Our previous study also showed that SDF-1 could enhance the osteoblastic differentiation of human mesenchymal stem cells which may contribute to the strongest effects in this study as well. The control group showed an increased new bone formation in the histological analysis but a reduced bone mineral content after 3 weeks whereas in comparison the rBMC group showed a similar new bone area to the control group but a significantly higher bone mineral content. This may indicate a faster bone repairing ability with the BMCs. Both rBMC and rBMC-SDF-1 groups have a higher bone mineral content and a more compact new bone structure that may indicate an accelerated effect of rBMC in the bone mineralization. In this study, we show that SDF-1 induces improved bone formation in early fracture healing. The long-term effect of rBMC-SDF-1 on fracture healing in this model is continuing.

REFERENCES