Introduction: Spinal arthrodesis is a common standard surgical procedure for spinal fusion. However, it can be associated with substantial morbidity and high pseudoarthrosis rates. Recombinant bone morphogenetic proteins (BMPs) have also been used successfully in clinical trials. However, large doses of BMPs are required to induce adequate bone repair. Hence, regional gene therapy may be a more efficient method to deliver proteins to a specific anatomic site. Adenoviruses have been the most commonly tested viral delivery vehicles in gene therapy for bone healing. However, the potential disadvantages associated with the use of adenoviral vectors in clinical situations include the lack of persistent target gene expression and pronounced host immune response to adenoviral envelope proteins in immune competent animals and humans. Recently, lentiviral vectors based on human immunodeficiency virus have been developed for gene therapy. Our previous studies demonstrated that lentiviral gene therapy allowed high levels of expression of target protein and prolonged protein production. However, lentiviral gene therapy for spinal fusion has not been compared with adenoviral gene therapy and recombinant protein therapy.

Materials and Methods: Primary rat bone marrow cells (RBMCs) were harvested from the femurs and tibias of young Lewis rats and cultured. Complimentary DNA (cDNA) from BMP-2 was ligated into a lentiviral vector carrying the murine leukemia virus (MLV) promoter; the vector was constructed and adenoviral vectors were also constructed. Then transductions were carried out. Prior to implantation in animals, an ELISA was performed using the cells transfected with adenoviral vectors were also constructed. Then transduction of target protein and prolonged protein production. However, lentiviral gene therapy for spinal fusion has not been compared with adenoviral gene therapy and recombinant protein therapy.

Results: Spinal fusion was observed in all animals in Group I, II, and V rats at 8 weeks. None of the rats in Groups III, IV, VI and VII showed spinal fusion. Analysis of the microCT images revealed that the volumes of new bone in the area between the top of the L4 transverse process and the bottom of the L5 transverse process were greater in Group I rats than in Group II, and V rats with a statistically significant difference (Figure 1). Histological analysis of the spines in Group I rats demonstrated abundant trabeculae bridging the transverse processes. The spines in Group II rats showed fusion; however, the fusion masses were composed of thin trabecular bone, unlike those of Group I rats. The spines of Group V rats also showed fusion and were composed of thin trabecular bone. The transverse processes of Group VI rats showed minimal evidence of new bone originating from the decorticated transverse processes, (Group III and IV appeared similar to this group); however, this bone did not bridge the gap between the 2 transverse processes to cause fusion. Minimal to no new bone formation was observed in Group VII rats.

Discussion: Spine surgeons continue to seek different strategies to enhance spinal fusion. No single strategy may be used to successfully treat all cases. The recombinant BMP proteins that are used to clinically induce spinal fusion appear to be promising. However, high doses of protein are required in humans. Therefore, a single administration dose strategy may have a very limited duration of action and may not be ideal in certain spine fusion applications such as multilevel spine fusions and revision site is not optimal. The short-term protein production associated with adenoviral gene therapy may be better suited for these situations. In our study, RBMCs transfected with Adeno-BMP-2-induced spinal fusion and the volumes of new bone in Group II (Adeno-BMP-2) rats were greater than in Group III (rhBMP-2) rats. However, the bone masses were not abundant. Adenoviral vectors retain their ability to synthesize adenoviral proteins, which stimulate the host immune response. Host immunity destroys the transduced cells and reduces the effect of transgene expression. Interestingly, RBMCs transfected with Lentivirus vector, and do more animal studies to ensure the safety of lentivirus gene therapy.