Direct Human Adenoviral BMP-2 or BMP-6 Gene Therapy for Bone and Cartilage Regeneration in a Pony Osteochondral Model
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Objective:
To evaluate healing of surgically created large osteochondral defects in a weight bearing femoral condyle articular surface in response to direct injection of adenoviral (Ad) vectors containing coding regions for either human bone morphogenetic proteins 2 (BMP-2) or BMP-6.

Methods:
Four 13 mm diameter and 7 mm depth circular osteochondral defects were drilled, 1 per femoral condyle (n= 20). Direct injection of Ad-BMP-2, Ad-BMP-6 or green fluorescence protein (Ad-GFP) into the defect was performed 14 days after surgery. Quantitative magnetic resonance imaging and computed tomography were serially performed at 12, 24 and 52 weeks. At 52 weeks, histomorphometry and microtomographic analyses were performed to assess final subchondral bone and cartilage repair tissue quality. Outcome measurements included: T1relaxation time (Delayed gadolinium-enhanced MRI of cartilage (dGEMRIC)), Bone mineral density (BMD) within the lesion, drill and subchondral bone, surface irregularity, perimeter gap, frequency of central cavitation and chondrocyte clustering.

Repeate-measure analysis of variance (ANOVA) (SAS Institute Inc., Cary, NC) was used to evaluate the effects of Ad-BMPs gene therapy using Proc Mixed models for continuous outcomes (i.e., MRI, micro-CT) and Genmod models for categorical outcomes (i.e., histologic data).

Results:
Direct adenoviral delivery of BMP-6 into healing large femoral condyle lesions demonstrated evidence of greater GAG-positive repair tissue at 12 weeks. Direct adenoviral delivery of BMP-2 demonstrated greater subchondral bone density by 12 weeks that persisted to 24 weeks. Despite these observations of earlier cartilage repair (BMP-6) and greater bone regeneration (BMP-2), the tissue within the defect at 52 weeks was suboptimal in all groups due to lesser quality repair cartilage and central fibrocartilage repair and cavitation.

Conclusions:
Delivery of BMP-2 or BMP-6 to large weight-bearing osteochondral defects via adenoviral vector and direct injection provided evidence of early support to cartilage and subchondral bone regeneration but was insufficient to provide long-term quality cartilage repair in the model.

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