IN VIVO MRI ASSESSMENT OF SUBCHONDRAL BONE IN AN EQUINE MODEL

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Objective: Using MRI as a serial non-invasive technique to detect and evaluate condylar subchondral bone changes of surgically created large osteochondral defects in a weight-bearing femoral condyle that underwent gene therapy treatment.

Methods: Four osteochondral defects were created for each pony (n=20) and treated with gene therapy (Bone Morphogenetic Proteins, BMPs) under general anesthesia, qMRI,3T (Achieva, Philips, Cleveland, Ohio, USA) was performed serially at 12, 24 and 56 weeks using a transmit quadrature body coil in combination with a four-channel array of 10 cm loop coils/knee. qMRI Included: T2 mapping; a multi-echo TSE sequence (TR/TE ¼3000/10, 20, 30, 40, 50, 60, 70, 80 ms; FOV ¼ 165 _165 mm2; matrix ¼164 _165; slice thickness ¼3 mm) was performed on each defect. T2 values were calculated via linear least-squares fit. For dGEMRIC, a sagittal slice through each defect was imaged via a multiinversion recovery turbo spin echo (IReTSE) sequence (TR/TE¼3740/28 ms; TSE factor¼ 10; FOV¼ 165_165 mm2; matrix¼ 332_ 328; slice thickness¼ 3mm). Six acquisitions were taken of each slice with varied inversion times (0, 60,150, 350, 1100, 1680 ms). Post-Gd-DTPA imaging was taken after 30min of passive exercise following injection. This protocol was adapted from human clinical patients [1]. T1 values were calculated by performing LevenbergeMarquardt least-squares fit. DCE-MRI was performed by administering a bolus injection of double dose (0.2mmol/kg) post-gadopentate dimeglumine (Gd-DTPA; Magnevist_, Wayne, NJ, USA) while acquiring a three dimensional (3D) T1 weighted turbo field echo (T1-TFE) sequence (TR/TE ¼3.15/1.60 ms; flip angle¼ 12^0; TFE factor¼ 50; FOV ¼ 64_180_180 mm3; matrix¼ 32_120_120; slice thickness¼ 4mm; 30 dynamic scans,15.14 s/scan). Dynamic parameters were calculated by fitting to a pharmacokinetic modified Brix model with arterial input function sampled from the popliteal artery using LevenbergeMarquardt[2].

Computed Tomography (Lightspeed 3, GE Healthcare, Wisconsin, USA) was performed, under anesthesia, serially at 12, 24 and 56 weeks. The images were acquired in bone algorithm and reconstructed in detail (soft tissue) algorithm (170 mA, 140 kVp, 40 cm FOV) using a transverse scan; 0.625 mm contiguous images were scanned. The image was comprised from tissue just proximal to the patella to 2 cm distal to the tibial plateau.

At 52 weeks, hitomorphometry was performed to assess final subchondral bone quality.

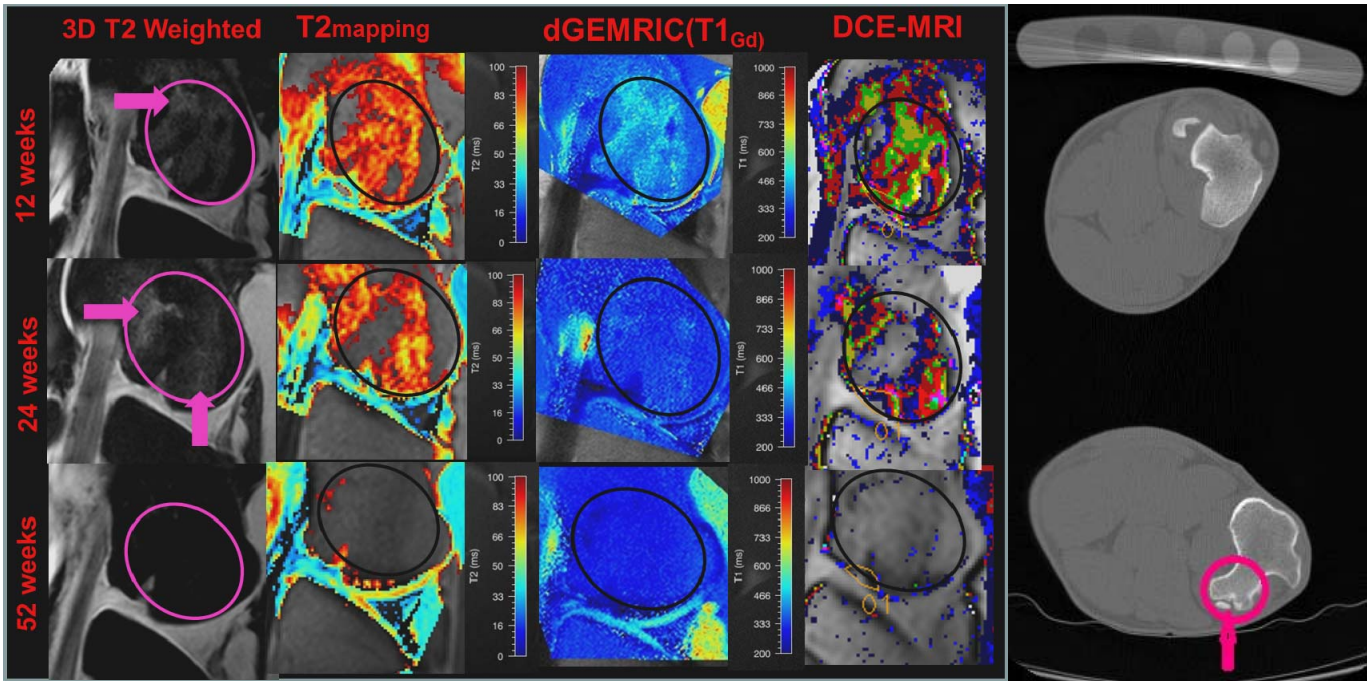

Figure 1: Left: Representative qMRI maps of sagittal sections through the femoral condyle subchondral bone (circles), showing the subchondral bone heterogeneity (arrows) across time using T2 mapping, dGEMRIC and DCE-MRI. Right: Representative 12 weeks CT axial view of the same femoral condyle showed in the figured on the left. Circle shows the femoral condyle and arrow points at the osteochondral lesion.

Results:

MRI detected changes in subchondral bone at 12, 24 and 52 weeks.

T2 mapping: The 3D T2 weighted detected subchondral bone lesions at 12, 24 and 52 weeks. At weeks 12 and 52, T2 relaxation time was significantly lower ($P<0.05$) for BMP-6 treated subchondral bone condyle than Saline, Green Fluorescent Protein (GFP) and BMP-2 treatments.

dGEMRIC: $T1_{Gd}$ at 12 weeks was significantly higher ($P<0.05$) for BMP-6 than BMP-2 and control. $T1_{Gd}$ was greater at 12weeks than 24 and 52 weeks ($P<0.05$), regardless of the treatment. (Figure1)

DCE-MRI: Amplitude in the subchondral bone was significantly greater at 12 weeks than 24 and 52 weeks. Being negligible by 52 weeks ($P<0.05$). (Figure 1)

CT was not able to detect condylar subchondral bone heterogeneity at the early stages of the healing process. (Figure 1)

Conclusions: Serial *in vivo* qMRI of condylar subchondral bone after surgically created osteochondral lesions provided evidence of support of subchondral bone changes that could not be visualized by CT. Furthermore, qMRI showed differences among different gene therapy treatments. Overall, MRI permitted an early detection of subchondral bone changes and follow up across time.

References:1. Domayer SE et al. Delayed gadolinium-enhanced MRI of cartilage in the ankle at 3 T: feasibility and preliminary results after matrix-associated autologous chondrocyte implantation. J Magn Reson Imaging 2010; **2.** Lee JH et al; Subchondral fluid dynamics in a model of osteoarthritis: use of dynamic contrast-enhanced magnetic resonance imaging. Osteoarthritis Cartilage 2009.