Morphological and Biochemical Assessment of Repair Tissue after Chondrosphere-Based Autologous Chondrocyte Transplantation

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Target audience: Musculoskeletal radiologists, orthopaedic surgeons as well as researchers with focus on cartilage evaluation techniques or CEST imaging.

Introduction:
Glycosaminoglycans (GAG) are elementary components of cartilage, responsible for their biomechanical properties. Focal loss of GAG represents the earliest stages of cartilage degeneration. MR techniques suggested for non-invasive assessment of cartilage quality via determinations of GAG content are delayed gadolinium-enhanced MRI of cartilage (dGEMRIC) [1], sodium imaging [2] and GAG-dependent chemical exchange saturation transfer (gagCEST). T2 mapping and assessment of the T1 relaxation time in the rotating frame (T1rot) have also been shown to be sensitive to GAG content although other, unspecific factors may have more dominant effects on these relaxation times [3]. Recent advances in research on gagCEST imaging demonstrated feasibility of the technique in intervertebral discs at 3 T [4,5]. The aim of our study was to compare gagCEST imaging and T2 mapping in a population of 30 patients after autologous chondrocyte transplantation in the knee at 3 Tesla.

Materials & Methods:
The study comprised patients after a novel chondrosphere-based autologous chondrocyte transplantation technique in the knee. The defects included retropatellar (RP) and trochlear (TRO) lesions as well as lesions in the lateral and medial femoral condyles (LFC/MFC). All patients gave written informed consent to participate in this institutional review board approved study. As a reference, the contralateral knee was examined in addition to the surgically assessed knee in 28 out of 30 patients. Experiments were performed on a clinical 3 T MR system (Siemens Healthcare, Germany) using a standard knee coil (InVivo, USA), and a routine morphological knee imaging protocol. For gagCEST imaging, a 3D RF-spoiled gradient-echo (GRE) sequence was employed (TE=4.94 ms, T1p=7.7 ms, resolution=0.6x0.6x3.3 mm³, matrix=256x248x30, scan time: 12:48 min). Selective RF presaturation was achieved using a series of 3 Gaussian RF pulses with pulse duration Tr=100 ms, an interpulse delay Tpr=10 ms, and a continuous-wave amplitude equivalent Br,CWAE of 2.6μT. Mapping of the T2 relaxation time was performed using a standard multi-echo spin-echo approach with 7 echo times from 11.9 to 71.4 ms (T1p=1200ms, resolution=0.4x0.4x3 mm³, matrix=320x320x13). For comparison of the ratio of the cartilage to reference signal intensity for exchangeable GAG –OH protons, and used as signal intensity for gagCEST images. In the datasets, the datasets were categorized in TRO, LFC/MFC and RP lesions. Differences between lesion and reference were assessed using Two-way ANOVA with Bonferroni correction for multiple testing. In addition to the functional techniques, a measure of the transplant morphology was determined using the MOCART score (maximum of 85 points because T1p weighted TrueFISP was not used).

Results:
Morphological imaging showed a total failure of transplants in only 3 cases (MOCART=0). The remaining cases, however, largely presented with morphologically intact transplants, which is also supported by a high median MOCART score of 65 points (interquartile range 15 points). Regarding the entire population, neither gagCEST nor T2 mapping revealed any significant differences between cartilage transplants and reference cartilage in the contralateral knee. Nevertheless, few individual cases showed clear differences between transplant and reference. Analysis of relationships between T2 values and gagCEST signal intensities showed no significant correlation (P=0.536).

Discussion and Conclusion:
The high morphologic integrity of the transplants together with no significant differences between transplants and reference cartilage in the biochemical imaging techniques suggests a high quality of the transplants. This is emphasized by results previous imaging studies on quality of repair tissue from alternative techniques such as microfracture, matrix-associated chondrocyte therapy or autologous osteochondral transplantation, which consistently revealed significant differences to reference cartilage in biochemical imaging. One reason may be the fact that our study used cartilage from the same anatomical region of the contralateral knee as reference. It is reasonable to assume that this tissue was subject to similar biomechanical burden as the repaired cartilage. In contrast, using reference tissue from the same knee but a different anatomical region may bear the risk of already including a systematic bias due to biochemical and structural differences between anatomical regions. In conclusion, this study indicated the superior quality of a novel cartilage transplant therapy compared to alternative techniques with respect to morphology (MOCART), GAG content (gagCEST) and ultrastructure (T2 mapping).

References: