Morphological and Biochemical Assessment of Repair Tissue after Chondrosphere-Based Autologous Chondrozyte 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). T_2 mapping and assessment of the T_1 relaxation time in the rotating frame (T_{1rho}) 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 T_2 mapping in a population of 30 patients after autologous chondrocyte transplantation in the knee at 3 Tesla.

Materials & Methods:

The study comprised 30 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 (T_E=3.49 ms, T_R=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 τ_p=100 ms, an interpulse delay τ_d=10 ms, and a continuous-wave amplitude equivalent $B_{1\text{-}CWAE}$ of 2.6µT. Mapping of the T_2 relaxation time was performed using a standard multi-echo spin-echo approach with 7 echo times from 11.9 to 71.4 ms (T_R=1200ms, resolution=0.4x0.4x3 mm³, matrix=320x320x13). To compensate for movement of the knee during the course of a measurement, gagCEST datasets were registered using a non-rigid approach. Z-spectra were corrected for B_0 inhomogeneities by referencing the gagCEST datasets to dual-echo GRE phase maps. The asymmetry of the magnetization transfer rate (MTR) as determined by MTR_{asym} (δ) = MTR(+δ)-MTR(–δ) was averaged over the offset range from 0.6 to 1.8 ppm, which corresponds to the resonance signal distribution from exchangeable GAG –OH protons, and used as signal intensity for gagCEST images. GagCEST and T_2 mapping results were compared between the transplants and native cartilage in the contralateral knee or next to the lesion in the same knee. As biochemical composition of cartilage is known to vary between anatomical regions, 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 T_1 weighted TrueFISP was not used).

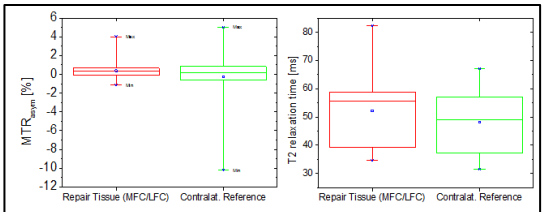

Fig. 1: Box-Whisker plots of MTR_{asym} values and T2 relaxation times from lesions in the LFC/MFC region. The transplants exhibit a very narrow distribution of MTRasym values compared to reference tissue. Mean values do not show significant differences in both parameters.

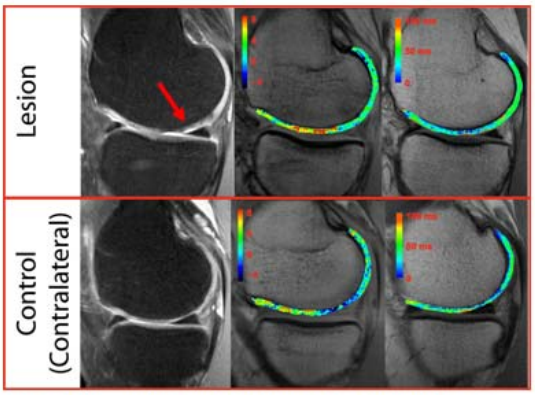

Fig. 2: Comparison of morphological PD fs image (left) with gagCEST (middle) and T2 overlay (right) on grayscale source data images. The transplant (upper row) is morphologically intact and well integrated in surrounding cartilage. The biochemical quality also seems high with no signal loss in gagCEST or increases in T2 mapping compared to adjacent cartilage. The contralateral reference, however, shows clear signal loss in the gagCEST image indicating early GAG loss while morphologically intact. This early loss is not visible in T2 mapping.

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 T_2 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 T_2 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 biochmecanical 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 (T_2 mapping).

References:

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