T2 and T2* relaxation as a means to evaluate cartilage repair tissue - initial results

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Introduction: The capability of magnetic resonance imaging (MRI) to visualize morphological and biochemical changes of articular cartilage give it the potential to follow-up different therapy procedures. Since pathological changes of articular cartilage and following osteoarthritis can significantly reduce the quality of life and are an enormous economic burden, the therapy is of great importance. Two of the most common surgical treatment options of full thickness cartilage defects are microfracture therapy (MFX), a relatively simple one-step arthroscopic procedure (1) and matrix associated autologous cartilage transplantation (MACT), a more complex two-step surgical method based on the implantation of chondrocyte cells on a membrane (2). A possible non-invasive statement about the produced cartilage repair tissue remains challenging and founded the need for modern evaluation techniques. Reported techniques to directly visualize cartilage structure and molecular composition are, among others, delayed Gadolinium enhanced MRI of cartilage (dGEMRIC) and quantitative T2 mapping (3,4). As those techniques should preferably be able to be added during a routine MRI follow-up examination, both methods have limitations in their clinical practicability. While dGEMRIC is based on i.v. contrast agent administration, a time delay of about 90 minutes from contrast agent administration to the MR examination limits its clinical use, T2 mapping with sufficient signal to noise and high resolution needs a relatively long scan time. Underlying reliable results, T2* mapping with its possible short scan time seems to offer a potential alternative (5). Taking the promising results of cartilage studies using T2 mapping into consideration, it would be attractive to achieve comparable results by means of T2* mapping in a shorter scan time. In a recent study the accuracy and efficiency of the used T2* fitting algorithm was validated and the use of T2* maps, created in clinically acceptable time frames and with resolutions that allow a detailed analysis of the cartilage, was shown (6).
The goal of the presented feasibility study was to use T2* mapping in the follow-up of two different cartilage repair procedures and to compare it to the established T2 mapping by a multi-echo spin-echo (SE) technique. Special interest was given to zonal variation of T2 and T2* values, introduced in recent animal studies as a possible marker for hyaline or hyaline like cartilage composition of cartilage repair tissue(7).

Material and Methods: 15 patients with a follow-up period of 32.3±18.3 months after MFX (4 female, 11 male; 10 right knees, 5 left; 12 medial femoral condyle(MFC), 3 lateral(LFC); Mean age 39.6±13.7 years) and 15 patients with a follow-up period of 33.9±13.9 months after MACT (4 female, 11 male; 8 right, 7 left; 11 MFC, 4 LFC; Mean age 39.2±8.1 years) were enrolled. For MACT, Hyalograft®C, a hyaluronan based scaffold (Fidia Advanced Biopolymers, Abano Terme, Italy) was used. MRI was performed on a 3 Tesla MR scanner (Siemens, Erlangen, Germany) using a dedicated 8-channel knee coil. The protocol consisted of a multi-echo spin-echo (SE) sequence using 6 echoes (TE 13.8 ms, 27.6 ms, 41.4 ms, 55.2 ms, 69 ms and 82.8 ms) for the standard T2 mapping (TR 600 ms FoV 160x160mm, pixel matrix 384x384, voxel size 0.6x0.6x3.0mm, bandwidth 230 Hz/pixel; 3 slices; acquisition time 3:50 min) and a GRE sequence using 6 echoes (TE 5.7 ms, 9.8 ms, 14 ms, 18.1 ms, 22.2 ms and 26.4 ms) for assessment of the T2* maps (TR 602ms; FoV, matrix and voxel size were kept identically for better comparability; bandwidth 260 Hz/pixel, 3 slices; acquisition time 1:50 min). A 3D-Double Echo Steady State (DESS) sequence (TR 15.1ms, TE 5.11 ms; flip angle 25°; FoV 160x160mm, pixel matrix 250x250; voxel size 0.6x0.6x0.6mm; scan time 6 min 32 sec) was added for morphological evaluation. The isotropic 3D-DESS data was used for planning the sagittal 2D T2 and T2* acquisitions on the affected femoral condyle covering the cartilage repair area. T2 and T2* maps were obtained using a pixel wise, mono-exponential non negative least squares (NNLS) fit analysis. In combination with the morphological images provided by the DESS sequence and the surgical reports, the cartilage repair tissue as well as healthy seen cartilage sites were identified on the T2 and T2* map images. Regions of interest were manually drawn by an experienced senior musculoskeletal radiologist in consensus with an orthopedic surgeon and divided into deep and superficial aspects. Quantitative evaluation was done by analyses of variance using a three way ANOVA with random factor using SPSS version 15.0 (SPSS Institute, Chicago, IL, USA), a P value less than 0.05 considered a statistically significance. For correlation between T2 and T2* values, a correlation using the Pearson coefficient was achieved.

Results: T2 and T2* values given in ms. Healthy cartilage (as internal control) showed significant increase of T2 (MFX: $T2_{deep}$ 47.6±9.5, $T2_{sup}$ 55.7±7.5; MACT: $T2_{deep}$ 45.9±8.4, $T2_{sup}$ 54.3±5.7) as well as T2* (MFX: $T2^*_{deep}$ 19.0±4.8, $T2^*_{sup}$ 25.0±3.5; MACT: $T2^*_{deep}$ 16.8±4.6, $T2^*_{sup}$ 25.2±5.2) values from deep to superficial ($p<0.005$). Cartilage repair tissue after MFX showed decreased T2 ($T2_{deep}$ 46.1±10.2, $T2_{sup}$ 46.7±8.1) and T2* ($T2^*_{deep}$ 18.4±5.7, $T2^*_{sup}$ 18.5±3.1) values without a significant increase from deep to superficial (T2 p=0.60; T2* p=0.54). Cartilage repair tissue after MACT showed higher T2 ($T2_{deep}$ 46.8±8.5, $T2_{sup}$ 51.6±9.0) and T2* ($T2^*_{deep}$ 18.8±3.7, $T2^*_{sup}$ 22.9±5.5) values compared to MFX with a visible, but not significant increase from deep to superficial (T2 p=0.09; T2* p=0.07). Correlation of T2 and T2* showed a significant correlation, however higher values within healthy cartilage sites (0.764-0.828) compared to cartilage repair tissue (0.552-0.600).

Discussion: T2 and T2* relaxation in the evaluation of cartilage repair tissue and its zonal variation is showing promising results. Both techniques seem to be capable to differentiate between cartilage repair tissue and healthy cartilage as well as in between different cartilage repair tissues. However correlation analysis show higher values within healthy cartilage compared to cartilage repair tissue, indicating that both techniques are not measuring the same. Hence T2* could get an important additional technique in the assessment of cartilage ultrastructure but has to be histological evaluated in future studies to especially clarify its impact in the evaluation of cartilage repair.

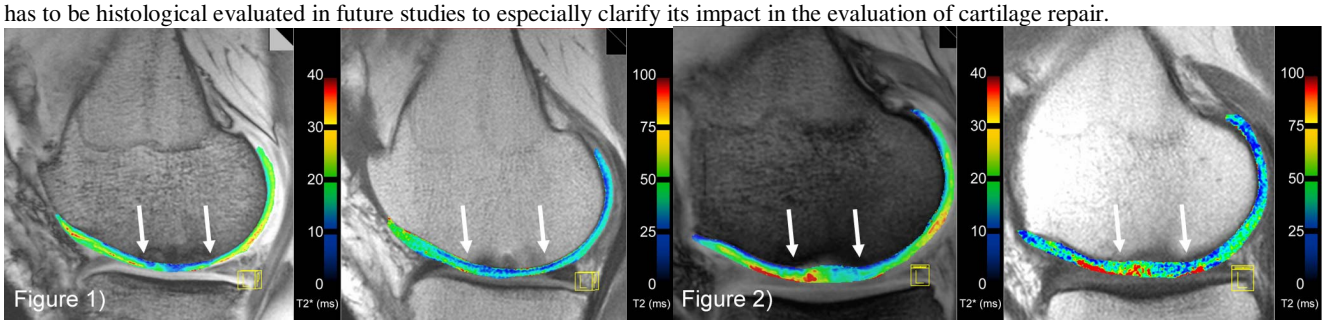

Figure 1) shows an exemplary T2* (left) and T2 (right) image of a patient after MFX (arrows) with visible deeper values within the area of cartilage repair. Figure 2) shows an exemplary T2* (left) and T2 (right) image of a patient after MACT (arrows) with beginning zonal variation within the area of cartilage repair.

References: 1. Steadman R. et al. J Knee Surg 2002;15(3):170-176. 2. Brittberg M. et al. Clin Orthop Relat Res 1999(367 Suppl):S147-155. 3. Mosher et al. Semin Musculoskelet Radiol 2004;8(4):355-368. 4. Burstein et al. Magnet Reson Med 2001;45(1):36-41. 5. Murphy et al. Skeletal Radiol 2001;30(6):305-311. 6. Hughes T et al. ISMRM, Berlin 2007. 7. White LM et al. Radiology 2006;241(2):407-414.