Sodium Imaging of Patients after Matrix-Associated Chondrocyte Transplantation at 7 Tesla: Preliminary Results and Comparison with dGEMRIC at 3 Tesla

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Introduction: Glycosaminoglycans (GAG), one of the major components of articular cartilage have a negative fixed charge density, which is balanced by positively charged sodium in the cartilage [1]. Imaging of cartilage sodium is therefore a potential tool to evaluate spatial GAG content. Sodium MRI has been demonstrated as an imaging modality to detect GAG loss in cartilage [2, 3]. During the last decade, cell-based techniques for cartilage repair have been developed which should provide hyaline-like tissue formation in the repair tissue, developing a significant amount of GAG over time [4] nevertheless still less than the surrounding native cartilage. The aim of our study was to assess and quantify GAG content in repair tissue in patients after matrix-associated autologous chondrocyte transplantation (MACT) by the use of sodium MR imaging at 7T and compare with the results of delayed Gadolinium enhanced MRI of cartilage (dGEMRIC) at 3T.

Material and Methods: Ethical approval for this study was provided by the local ethics commission and written informed consent was obtained by all patients. Twelve patients (6 females, 6 males with the mean age of 32.6 years) with the mean time of 56 months after MACT (range 11 – 102 months) were examined on a 7 Tesla MR scanner (Magnetom, Siemens, Erlangen, Germany) whole body system. Sodium measurements were performed using a ^{23}Na-only (78.61 MHz) circularly polarized transmit/receive knee coil with the inner diameter of 19 cm (Stark Contrast, Erlangen, Germany). A reference sample containing 308 mM of NaCl was fixed to the inner surface of the sodium coil to enable normalization of the inter-scan signal variability. After the flip angle calibration and localizer, 3D-GRE sequence optimized for sodium imaging was employed with these parameters: TR/TE = 10.0/3.77 ms, flip angle = 56°, FOV = 199 mm, 48 slices, matrix size = 64x128, resolution = 3.11x1.55x3.0 mm^3, measurement time = 30:45 min.
Seven of the 12 patients were additionally examined at 3 Tesla MR scanner (TimTrio Siemens, Erlangen, Germany). The mean time between the 3T and 7T measurements was 11 days (range: 0-40 days). A variable 3D GRE flip angle technique was used for T1 mapping before and after contrast administration (dGEMRIC) with an eight-channel knee-coil at 3T [5]. The T1 maps were calculated with built-in software (Siemens Medical Solutions, Erlangen, Germany).
All regions-of-interest (ROI) analysis of T1 maps and sodium images were performed with an in-house written IDL (Interactive Data Language, Research Systems, Inc., Boulder, CO) evaluation tool. Sodium signal and T1 post-contrast values were measured from a region covering the cartilage repair tissue and an equally sized region in normal native cartilage. For the comparison between subjects, the mean cartilage sodium signal from all ROIs was normalized by the mean sodium signal from the ROI placed in the reference sample. To assure comparability between 3T dGEMRIC and 7T Sodium MRI similar sized ROIs were drawn in the cartilage repair tissue and the native cartilage, in the same positions on identical slices in a side-by-side evaluation.
Pearson correlation coefficient was calculated to evaluate associations between sodium normalized values and T1 post-contrast values.

Results: The mean normalized sodium values were 125.3 (range: 72.3 – 244.3) for the repair tissue within the cartilage transplant and 191.7 (range: 98.4 – 259.4) for healthy cartilage. The corresponding sodium values for healthy cartilage and repair tissue of transplant in each patient is shown in figure 1. Note that in one patient, the normalized sodium values were similar in the transplant area 16 months after surgery in comparison to healthy cartilage, corresponding to a comparable GAG content, which was confirmed by dGEMRIC evaluation in the same patient. A high Pearson correlation coefficient of 0.75 was found between normalized sodium values and T1 values on post-contrast T1 map (Fig. 2).

Figure 1 shows corresponding sodium values for healthy cartilage and repair tissue of transplant in each patient, after MACT of the medial femoral condyle.

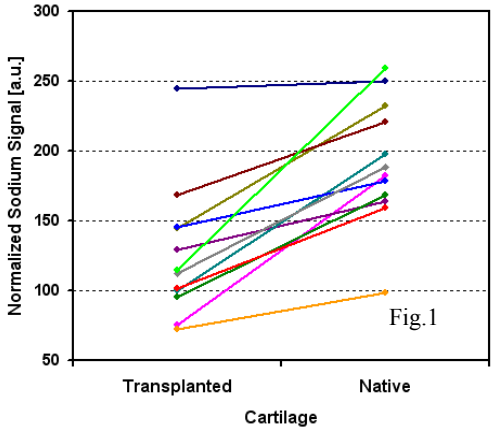
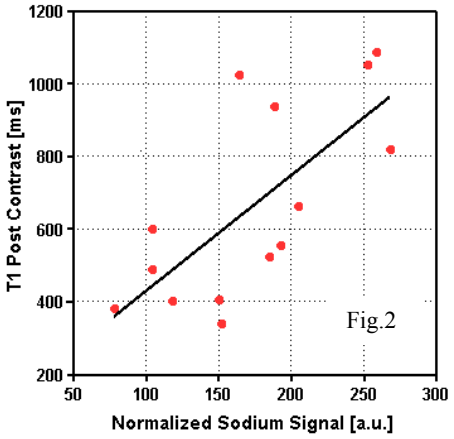


Figure 2 shows the correlation coefficients between normalized sodium values and T1 values on postcontrast T1 map.



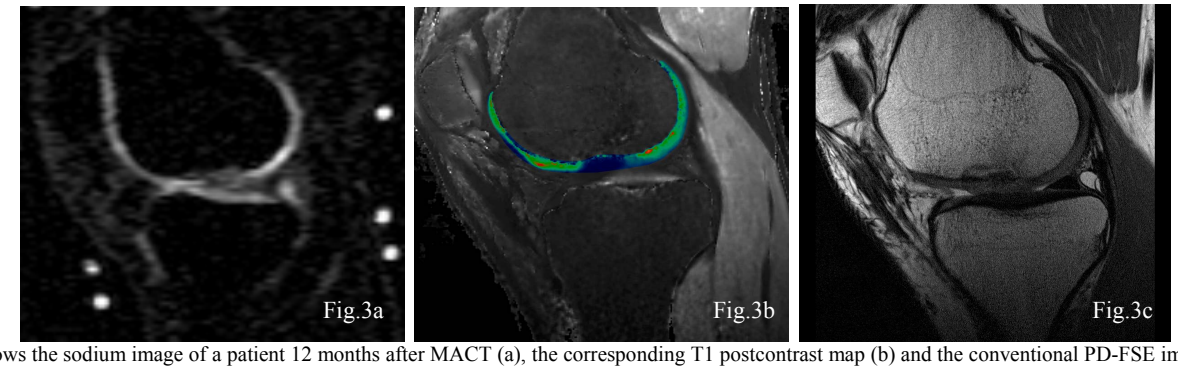


Figure 3 shows the sodium image of a patient 12 months after MACT (a), the corresponding T1 postcontrast map (b) and the conventional PD-FSE image (c). Note that on conventional MR an excellent filling of the defect and integration of the transplant is visible, while the sodium content and thus the GAG content are low.

Discussion: By employing an optimized 3D GRE sequence at 7 Tesla for sodium imaging, a sufficiently high signal to noise ratio was achieved. We have shown that these images are able to visualize cartilage transplants within the femoral condyle cartilage layer and can be used for quantifying different concentrations of sodium and hence GAG content within the cartilage transplants compared to healthy cartilage. A significantly high correlation between sodium imaging and dGEMRIC in the quantification of the GAG concentration in patients after MACT was found. Our methodological study shows that sodium imaging has the potential to monitor the development of GAG in cell-based cartilage repair techniques.

References: [1]. Mankin HJ. Orthop Clin North Am 1971. [2]. Shapiro EM Magn Reson Med 2002. [3]. Borthakur A. Osteoarthritis Cartilage 2000. [4]. Knutsen G J Bone Joint Surg Am, 2004. [5]. Trattnig S. JMRI 2007