SODIUM MRI OF CARTILAGE REPAIR TISSUE IN THE ANKLE JOINT AT 7T

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TARGET AUDIENCE: Radiologists and orthopedic surgeons interested in biochemical MRI of cartilage and cartilage repair tissue.

PURPOSE: Different surgery techniques such as microfracture (MFX) or matrix-associated autologous chondrocyte transplantation (MACT), are available for the treatment of articular cartilage lesions in the ankle joint. Only repair tissue with sufficient glycosaminoglycan (GAG) content provide optimal long-lasting substitute for the native cartilage, thus a noninvasive evaluation of the GAG content is highly desirable. Since the GAG molecules are counterbalanced by sodium (23Na) ions, 23NaMRI can be used for the direct evaluation of GAG content in cartilage.[1] 23Na MRI recently showed a significantly lower GAG content in the repair tissue after MFX compared to MACT repair tissue in the femoral cartilage.[2] Thus, the aim of this 7T study was: i) to validate our ^{23}Na-MRI protocol by comparing 23Navalues with histochemical analyses of GAG content in cadaver ankle samples; ii) to evaluate the 23Na concentration, indicating GAG content, in tibial and talar cartilage of healthy volunteers; iii) and to compare 23Na values in repair tissue between the patients after MFX and MACT treatment.

METHODS: Institutional Review Board approval and informed consent from all study participants were obtained. For ^{23}Na-MRI protocol validation, five fresh human cadaver ankle joints (4 females, 1 male; mean age (±standard deviation), 47.2±7.5 years) were measured. Six asymptomatic volunteers (3 females, 3 males; mean age, 27.4±3.2 years) without any history of trauma or surgery in ankles were recruited. Eight patients after cartilage repair surgery on the trochlea of talus, 4 MFX patients (2 females, 2 males; mean age, 35.9±11.2 years; mean postoperative interval, 108.5±27.5 months) and 4 MACT patients (2 females, 2 males; mean age, 35.0±6.7 years; mean postoperative interval, 85.7±23.9 months) were included in this study. All MRI scans were acquired at 7T whole body system (Magnetom, Siemens Healthcare, Erlangen, Germany), and the same sequence with the identical measurement parameters were used in all in vivo and ex vivo measurements. A proton-density weighted 2D turbo spin echo images with fat suppression (**Figs.2,3**) were acquired in sagittal and coronal plane using a 28-channel knee array coil (Quality Electrodynamics, Mayfield Village, OH) and served for morphological evaluation of cartilage and for manual segmentation of tibial and talar cartilage as well as repair tissue.23Na images were acquired with a Cartesian spoiled gradient echo sequence optimized for 23Na MRI of cartilage (**Figs.2,3**) (measurement parameters: resolution= 1.79×1.79×3.0mm^3; TR = 17ms; TE = 8.3ms; flip angle= 50 degrees; bandwidth= 80Hz/pixel; 12 averages; measurement time = 31:53min) using a 15-channel 23Na-only knee array coil (Quality Electrodynamics, Mayfield Village, OH).

All region-of-interest (ROI) analyses were performed with the JiveX (VISUS GmbH, Bochum, Germany) software. For comparing 23Na MRI with histochemical analysis, mean 23Na signal intensity was evaluated in talar and in tibial cartilage situated in lateral, central and medial part of ankle, resulting in 6 values per ankle joint. For more accurate comparison, 23Na normalized signal intensities (NSI) were calculated by multiplying each mean signal intensity with a factor derived from the signal intensity of the reference sample, which was attached to knee coil and measured together with each ankle sample. Quantification of 23Naconcentration in the cartilage was achieved by simultaneous imaging of subjects and 10% w/w agarose phantoms with different concentrations of 23Na (100, 150, 200, 250 and 300 mmol/L), which provided a calibration curve. 23Na images were corrected for the inhomogeneous sensitivity of the knee coil using a correction matrix from phantom measurements and scripts written in IDL (Research Systems Inc, Boulder, CO) and Matlab (Mathworks, Natick, MA). Finally, mean 23Na signal intensities from ROI evaluations of corrected 23Na images were adjusted for differences between relaxation times of calibration phantoms and articular cartilage, and 23Na concentration was calculated using the calibration curve as previously described.[3] To compare the quality of repair tissue between MFX and MACT treatment, ROIs were selected in the repair tissue and in intact reference cartilage contralaterally to the repair tissue location.23Na NSI values were then calculated for repair tissue and reference cartilage of MFX and MACT patients. Pearson correlation coefficient (r) and Student's t-test were used for the statistical evaluations in the SPSS software (SPSS Institute, Chicago, IL).

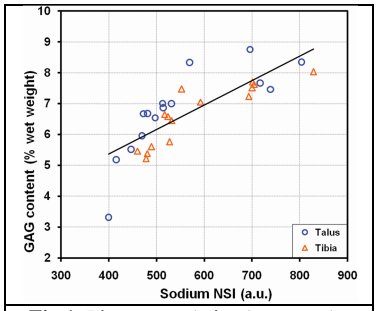

Fig.1: Linear correlation between the 23Na NSI and the GAG content.

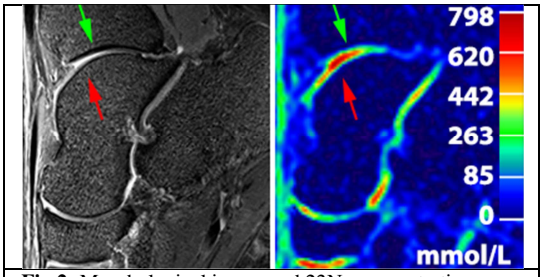

Fig.2: Morphological image and 23Na concentration map. Arrows denote tibial (green) and talar (red) cartilage.

RESULTS: Measurements of cadaver knee samples revealed a strong linear correlation between the 23Na NSI values and GAG content obtained from histochemical analyses (r=0.80; p<0.001; R^2=0.64) (**Fig.1**). The mean 23Na concentrations in the volunteers were 399±26 mmol/L for tibial cartilage and 376±20 mmol/L for talar cartilage (**Fig.2**). There was no significant difference in 23Na concentration between tibial and talar cartilage (p=0.32). The patients after MFX treatment showed the mean 23Na NSI values of 661±104 in reference cartilage and 532±182 in repair tissue. The mean 23Na NSI values in the MACT patients were 649±127 in reference cartilage and 578±157 in repair tissue (**Fig.3**). We did not observe any statistically significant differences; neither between repair tissue and native cartilage in both groups, nor between MFX and MACT patients in both repair tissue and reference cartilage.

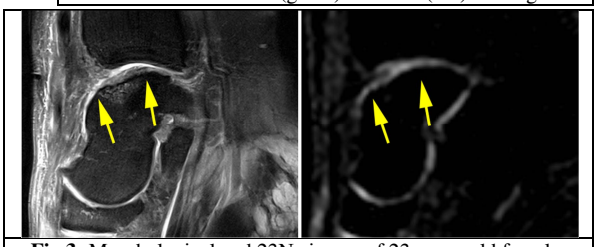

Fig.3: Morphological and 23Na image of 23-years-old female, 46 months after MACT. Arrows denote repair tissue area.

DISCUSSION: Kuettner et al. reported that the GAG content in talar cartilage of ankle joint is about 57% higher than the GAG content in femoral cartilage of knee.[4] Since the 23Na concentration in femoral cartilage is about 260 mmol/L[1], the expected 23Na concentration in talar cartilage is about 400 mmol/L. Thus, our 23Na concentrations in tibial and talar cartilage are in good agreement with the previous findings. The lack of any significant differences between repair tissue and reference cartilage, as well as between MFX and MACT patients, is probably due to a low number of patients included in this study so far. The measurements on patients are therefore still in progress.

CONCLUSION: To our best knowledge, this is the first report on employing 23Na MRI for the evaluation of native cartilage and cartilage repair tissue in the ankle joint. Data from cadaver ankle samples demonstrate that 23Na MRI is sensitive to changes in the GAG content of thin tibial and talar cartilage in the ankle joint. This study also demonstrates that the quantification of 23Na concentration in cartilage of the ankle joint is feasible at 7T. 23Na MRI may be useful for the noninvasive evaluation of the repair tissue in the ankle joint.

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