Evaluation of the GAG content of articular cartilage in the knee joint using gagCEST: correlation to the gold-standard with multicompartmental biochemically analyzed GAG content

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Target audience

Musculoskeletal radiologists, OA scientists

Purpose

It was shown that gagCEST magnetic resonance imaging (MRI) has the potential to become a viable technique for non-invasive monitoring of cartilage GAG content [1, 2]. However, so far, no study has evaluated the dependency of gagCEST signal intensity on tissue GAG concentration in intact morphological structures. The purpose of this study was the comparison of biochemically determined GAG content in knee joints of human cadavers to gagCEST values.

Methods

The study comprised four knee samples from human cadavers, which were examined on a 7T MR System (Siemens, Erlangen, Germany) with a standard knee coil. PDw images were acquired with fat-saturated (FS) turbo spin-echo (TSE) imaging in the sagittal plane (TE=22ms, TR=4000ms, resolution=0.36×0.36×3mm^3). GagCEST imaging was performed using a segmented 3D RF-spoiled gradient-echo (GRE) sequence (TE=3.46ms, TR=7.9ms, resolution=0.7×0.7×3mm^3, scan time 11:17 min). Selective RF presaturation was achieved using a series of 5 Gaussian RF pulses with pulse duration T_p = 100ms, an interpulse delay T_d = 10ms and a B1 of 0.8μT. Z-spectra from images were corrected for B0 inhomogeneities on a pixel-by-pixel basis by a smoothing spline method. The asymmetry of the magnetization transfer rate (MTR) as determined by MTRasym (∂) = MTR(+∂)- MTR(-∂) was integrated over the offset range ∂ from 0.5 to 2ppm, which corresponds to the resonance frequency range of exchangeable GAG -OH protons, and used as signal intensity for gagCEST images. For quantitative biochemical analysis of absolut GAG content based on 1,9-dimethylmethylene blue binding in cartilage, BlyscanTM Sulfated Glycosaminoglycan Assay (Biocolor Ltd., IRL) was used. Each condyle was divided into two compartments (medial, lateral) and additionally from each compartment, 9 contiguous cartilage samples were taken to determine absolute GAG content (μg/mg). The water content of the probes was calculated comparing dry and wet weight samples. The calculated GAG concentrations were expressed as the relative weight per cartilage wet weight (% GAG/mg WWt). To compare MRI data to biochemical analysis, cartilage areas were segmented in MR images. Five continuous Regions of Interest (ROI) were drawn in regions corresponding to the specimens used for biochemical analysis (Fig.1). The mean MTRasym (gagCEST) values and absolute GAG content were calculated for the corresponding compartments. The correlation coefficient (r) between MTRasym values obtained from gagCEST experiments and the biochemical essays was determined using Pearson correlation analysis.

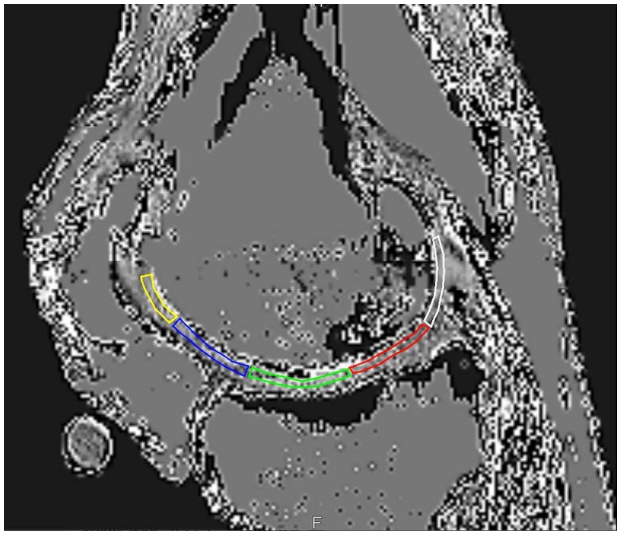

Figure 1: Five continuous ROI's were drawn in the compartments corresponding to the biopsies.

Results

All examined knees showed morphologically intact cartilage on PD_w MR images. Altogether, 144 biopsies (4 cadavers * 4 compartments * 9 biopsies) were taken and demonstrated an average GAG content of 2.59 ± 0.61% GAG/mg WWT as determined by the GAG assay. The average measured MTRasym was 5.86 ± 1.94. The correlation between the measured GAG content and MTRasym appeared to be linear with r = 0.863 ($p < 0.001$) (Fig.2).

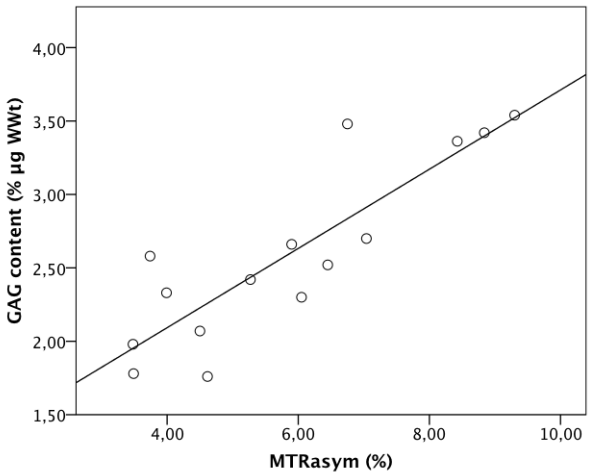

Figure 2: Biochemically determined cartilage GAG content plotted against MTRasym revealing a correlation coefficient of r = 0.863 ($p<0.001$)

Discussion:

The excellent correlation between the MTRasym and cartilage GAG content demonstrates the feasibility of the technique. The results are in agreement with CEST theory, which yields that CEST effect scales linearly with the concentration of exchanging protons in bulk water [3]. Our results indicate that gagCEST imaging at 7T is sensitive to cartilage GAG content in intact tissue samples. Further work will be the evaluation of the sensitivity in other parts of the knee joint and the evaluation at a clinical 3T system.

Conclusion:

Our results demonstrated a strong correlation between gagCEST values and the gold standard of biochemically measured GAG content.

References:

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