Evaluation of the glycosaminoglycan content in healthy and degenerated menisci with gagCEST at 3T

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Introduction:

Human menisci are C-shaped fibrocartilaginous structures which are important in many ways for optimal knee function, including shock absorption, load bearing, joint stabilization, proprioception and joint lubrication[1]. Two main factors leading to meniscal degeneration are ageing and overloading[2].The pathology of degenerated menisci is characterized by mucinous degeneration, the appearance of acellular zones, and loss of normal collagen fiber organization[3]. Glycosaminoglycans are responsible for the viscoelastic properties of menisci[4]. Degeneration of the menisci is characterized by a significant decrease of glycosaminoglycans and by an increase of water content[5,6]. Glycosaminoglycan Chemical Exchange Saturation Transfer (gagCEST) imaging is a recently developed quantitative imaging method. The gagCEST effect (MTR_{asym}) is related to the glycosaminoglycan content and has been shown to be a useful noninvasive technique to investigate GAG content in various tissues such as joint cartilage[7] and intervertebral discs[8]. The aim of this study was to demonstrate the feasibility of gagCEST imaging for the detection of degenerated menisci and to compare it with mono and bi-exponential T_2* relaxation times.

Methods and Materials:

MRI data from 20 subjects (12 male, 8 female) with a mean age of 37 (σ=12) was used for this study. From the total number of subjects, on morphological images 9 suffered from degenerated menisci (degenerations and tears) in the posterior horn and 11 subjects were normal, with no known meniscal pathology. All MRI acquisition were performed on a 3T MRI whole-body system (Siemens Magnetom Trio). For both, ^{1}H imaging and gagCEST, a 8-channel Tx/Rx knee coil (Siemens Healthcare, Erlangen, Germany) was used. gagCEST was imaged using Gaussian RF pulses followed by signal readout with a 3D RF spoiled GRE sequence. The following saturation parameters were used: B_1-CWAE (continuous wave amplitude equivalent) = 0.6 μT, number of CEST pulses = 8, pulse duration PD = 99 ms, interpulse delay IPD = 100 ms. The GRE imaging parameters were: FOV =130 x 160 mm^2, spatial resolution = 1.6 x 1.6 mm^2, slice thickness = 3.3 mm, TR/TE = 927 ms/3.3 ms, flip angle = 11°, acquisition duration =10:23 min. The CEST curves were calculated for each pixel and were shifted for the water resonance to appear at 0 ppm of the z-spectrum. The magnetization transfer asymmetry rate (MTR_{asym} (δ) = MTR (+δ) – MTR(-δ)) was integrated over the offset range δ from 0.6 – 1.8 ppm, which corresponds to the resonance frequency range of GAG – hydroxyl protons, and was used as signal intensity for gagCEST images. Since all of the meniscal tears were detected in the posterior horn, we tested an age-matched control group consisted of 11 healthy subjects with no morphologically visible degeneration in the posterior horn of the menisci to rule out the possibility that posterior horns have natively lower GAG effect compared to the anterior horn.

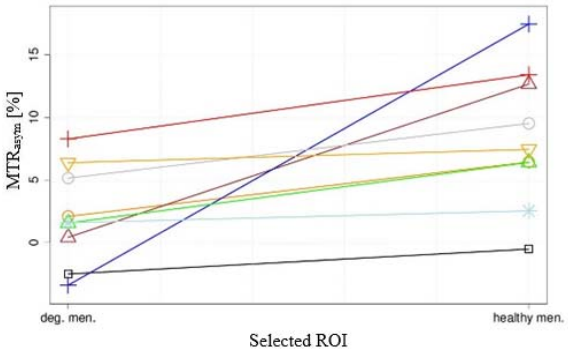

Fig.1: Magnetization transfer (MTR) asymmetry from ROIs selected in healthy and degenerated menisci.

A variable echo time (vTE) sequence[9] was used for T_2* analysis. This sequence is based on 3D Cartesian spoiled gradient echo sequence, but was modified to use asymmetric readout and a variable echo time technique in the phase and slice encoding direction, which enables the use of sub-millisecond effective echo time. The sequence parameters are: TR = 35 ms, TE = 0.97, 2.81, 4.92, 7.38, 9.84, 12.3, 14.76, 17.22, 19.68, 22.14, 27.06, 29.52 ms, FOV = 148 x 179 mm^2, spatial resolution = 224 x 272, flip angle = 15°. Mono and bi-exponential T_2* analysis was performed by using a three- and five-parametric, respectively, non-linear Levenberg Marquart algorithm curve fitting method. Mono- and Bi-exponential T_2* as well as gagCEST images were analyzed by using a manual region-of-interest (ROI) based evaluation. The ROI position over the whole menisci was selected based on morphological images, which were acquired with a fat-saturated turbo spin-echo (TSE) sequence in the sagittal plane. The ROIs were placed on the degenerated menisci horn and the morphological normal meniscal horn for comparison.

Results:

The mean of asymmetries in gagCEST z-spectra summed over all offsets from 0.6 to 1.8 ppm was significantly lower ($p < 0.02$, two sample t-test) in degenerated meniscal horns (2.2 ± 5.5 %) compared to healthy meniscal horns (8.4 ± 3.9%), which indicates a decrease in GAG in the degenerated menisci (Fig.1, 2). In healthy subjects, the difference of gagCEST effect between the posterior (2.5 ± 3.7 %) and anterior horn (3.5 ± 3.4%) was not statistically significant ($p > 0.05$), which supports the assumption that the lower gagCEST values in degenerated menisci is in fact due to the GAG content loss.

Bi-exponential analysis showed that the short component of T_2* is significantly higher ($p < 0.02$) in the degenerated menisci (2.8 ± 0.37 ms) compared to the healthy menisci (2.4 ± 0.29ms). This has been assumed as a result from compositional alteration of the collagen matrix[10].The monoexponential T_2* showed no significant difference between healthy (4.9 ± 1.6) and degenerated menisci (4.2 ± 1.3), which supports our previous results showing that bi-exponential fitting in menisci provides more relevant information than monoexponential fitting.

Discussion and Conclusion:

The results show that in healthy subjects the difference of the gagCEST effect of the anterior and posterior horn of the menisci is not statistically significant, whereas the degenerated menisci show a significant loss in gagCEST which indicates GAG content loss. However it is not possible to perfectly assign the gagCEST signal of a tissue to the respective GAG content, because similar chemical structures have protons with similar exchange properties and the chemical structure of the polysaccharide GAG is similar to other polysaccharides in the human body[7]. In menisci the GAG content in dry weight is around ~0.9 to 4 % [4] (outer to inner menisci, respectively) which is higher than the content of saccharides with similar chemical structure. Therefore, we believe that changes in gagCEST effect in menisci can be predominantly attributed to the GAG content. Moreover it was shown that the GAG content is not equally distributed over the menisci[4] and that the inner menisci contains higher GAG content compared with the outer parts. The ROI we selected contained all menisci regions, therefore we hypothesize comparable GAG values of both anterior and posterior menisci horn. Further study with larger patient groups are necessary to confirm our hypothesis. This study demonstrates that gagCEST imaging holds great potential as a biomarker to differentiate between healthy and degenerated menisci.

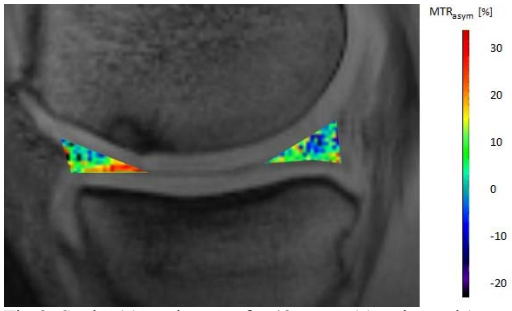

Fig.2: Sagittal knee image of a 42-year-old patient with degeneration in the posterior horn. The overlayed gagCEST map demonstrates the sensitivity of gagCEST in detecting meniscal degeneration.

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