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Original contribution

Gender, BMI and T2 dependencies of glycosaminoglycan chemical exchange saturation transfer in intervertebral discs

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ABSTRACT

Purpose: The purpose was to investigate the dependence of glycosaminoglycan chemical exchange saturation transfer (gagCEST) effect of lumbar intervertebral discs (IVD) on gender, body mass index and T2 value.

Methods: T2 imaging and gagCEST imaging was performed in 34 healthy volunteers (17 males, 17 females) without low back pain at a 3 T MRI system (Magnetom Trio, A Tim System, Siemens Healthcare, Erlangen, Germany). The body mass index was determined for each volunteer. The mean and standard deviation of MTR_{asym} and T2 values were calculated for nucleus pulposus (NP) and annulus fibrosus (AF) as descriptive statistics for females and males. An unpaired student's t-test was applied in order to validate obtained differences. Pearson correlation was determined in order to reveal, if gagCEST effect and T2 values decrease with increasing body mass index (BMI). Pearson correlation analysis was additionally performed between gagCEST and T2 values.

Results: GagCEST effect and T2 values were significantly higher in females compared to males [gagCEST effect (nucleus pulposus, females) = 3.58 ± 1.49 %; gagCEST effect (nucleus pulosus, males) = 3.01 ± 1.63 %, p-value (gagCEST effect, nucleus pulposus) = 0.02); T2 (nucleus pulposus, females) = 134.56 ± 30.27 ms, T2 (nucleus pulposus, males) = 122.35 ± 27.64 ms, p-value (T2, nucleus pulposus) = 0.01)]. Pearson correlation analysis showed a significant negative relation between BMI and gagCEST effect (nucleus pulposus: $\rho = -0.16$, $p = 0.03$) and between BMI and T2 values (nucleus pulposus: $\rho = -0.30$, $p < 0.01$). The correlation between gagCEST effect and T2-values was highly significant (nucleus pulposus: $\rho = 0.59$, $p < 0.01$).

Conclusions: Significantly lower gagCEST effects were found in males compared to females and with increased body mass index. The gagCEST effect was highly correlated with quantitative T2 imaging.

1. Introduction

Glycosaminoglycan loss is an early step in the degeneration process of intervertebral discs (IVDs) and is associated with low back pain (LBP) [1–4]. Glycosaminoglycan chemical exchange saturation transfer (gagCEST) imaging is a non-invasive magnetic resonance (MR) method to assess glycosaminoglycan concentration and which does not need contrast agent or specific hardware [5].

CEST imaging is based on the exchange between solute protons and water protons [6]. If a radiofrequency pulse is applied at the Larmor frequency of the solute proton pool, protons in this pool are excited. The magnetization of solute protons is transferred to the water pool due to chemical exchange. If a long radiofrequency pulse is applied, this exchange process is repeated resulting in a reduction of magnetization of the water pool. During CEST imaging, a so-called Z-spectrum is acquired by applying radiofrequency pulses at different frequency offsets in relation to the Larmor frequency of the water pool. The CEST effect is then determined by an asymmetry analysis of the Z-spectrum.

gagCEST imaging in lumbar intervertebral discs was applied previously in patients with low back pain (LBP) showing a reduced gagCEST effect in discs with morphological degeneration [2]. In addition, a reduced gagCEST effect was reported in patients with spondyloarthritis compared to healthy volunteers [7]. Recently, age-dependency of the gagCEST effect was reported in healthy volunteers of different age [8]. To the best of our knowledge, the

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Table 1
Detailed sequence parameters.

		T2-weighted imaging (sagittal)	T2-weighted imaging (transversal)	T2 mapping	CEST	WASSR
TE	[ms]	105.0	113.0	9.1, 18.2, 27.3, 36.4, 45.5, 54.6, 63.7, 72.8, 81.9, 91.0	3.9	3.9
TR	[ms]	3100.0	4510.0	800.0	1760	442.0
Field of view	[mm^2]	300 × 300	300 × 240	300 × 300	300 × 300	300 × 300
Voxel size	[mm^2]	1.2 × 1.2	0.8 × 0.6	1.6 × 1.6	1.6 × 1.6	1.6 × 1.6
Slice thickness	[mm]	3.0	3.0	5.0	5.0	5.0
Flip angle	[°]	160	140	180	12	12
Duration	[min:sec]	3:39	5:13	4:23	9:09	3:43
Averages		2	1	3	2	2
Basic resolution		256 × 256	384 × 307	192 × 192	192 × 192	192 × 192
Number of slices		15	27	1	1	1

dependence of gagCEST effect on other patient properties like gender and body mass index has not been investigated yet.

In a previous study, the gagCEST technique was compared with T2 mapping in the knee of sixty-nine subjects [9]. The authors showed that high gagCEST values were accompanied by high T2-values [9]. T2 mapping and gagCEST imaging has also been applied by Haneder et al. in LBP patients resulting in a weak correlation between gagCEST effect and T2 relaxation time [2].

Several studies have reported an association between body mass index (BMI) and intervertebral disc (IVD) degeneration [10–15]. Further, changes in gagCEST values and T2 values have been reported with IVD degeneration [2,16]. Therefore, we hypothesized a reduced gagCEST effect and T2 values with increased BMI.

In the current study we used gagCEST imaging in young healthy volunteers to investigate the dependence of gagCEST effect on gender. Furthermore, we tested for a correlation between the gagCEST effect and the body mass index. Finally, we aim to validate if gagCEST effect is correlated with T2-value in lumbar intervertebral discs of healthy volunteers.

2. Materials and methods

2.1. Study population

Imaging was performed in 34 volunteers without low back pain (17 females (mean age 26 ± 5 years; minimum age: 21 years; maximum age: 39 years) and 17 males (mean age 26 ± 4 years; minimum age: 20 years; maximum age: 35 years)). Before MR examination, weight and body height were recorded. The study was approved by the local ethics committee and written informed consent was received from all volunteers before enrolment.

2.2. MR measurements

MR experiments were performed on a whole-body 3 T MR system (Magnetom Trio, A Tim System, Siemens Healthcare, Erlangen, Germany) using a spine matrix coil. Our MR protocol included a localizer, T2-weighted imaging in sagittal and transversal direction, a sequence for quantitative T2-mapping, prototype gagCEST and WASSR (Water Saturation Shift Referencing [17]) sequences. Sequence details of T2-weighted imaging, quantitative T2 imaging, CEST, and WASSR are listed in Table 1.

Biochemical imaging was performed using the gagCEST and WASSR sequences. These were composed of a saturation module and a segmented 2D RF-spoiled gradient echo module.

The parameters of the CEST and WASSR saturation module are described elsewhere in detail [7,8,18]. For both gagCEST and WASSR measurements a saturation band was applied anterior to the spine in order to suppress bowel movement artifacts and artifacts due to abdominal wall motion [7,8,18].

2.3. Data analysis

T2-weighted images were analysed to reveal the presence or absence of herniation. The body mass index was calculated for each volunteer following the standard approach: mass/$height^2$.

WASSR and CEST data were analysed as follows: After motion correction using a diffeomorphic registration approach [19] and field inhomogeneity correction [8,17], Z-spectra and corresponding MTR_{asym}

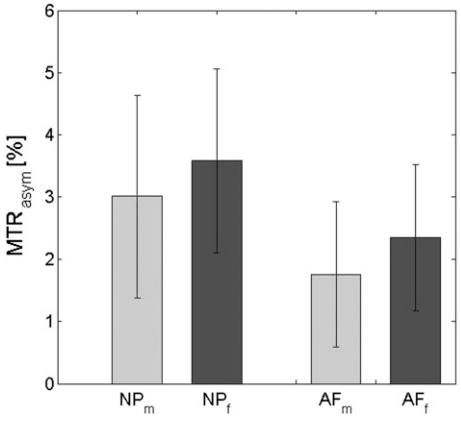

Fig. 1. Magnetization transfer ratio asymmetry (MTR_{asym}) as descriptive parameter for the CEST effect in nucleus pulposus (NP) and annulus fibrosus (AF) in males (m) and females (f).

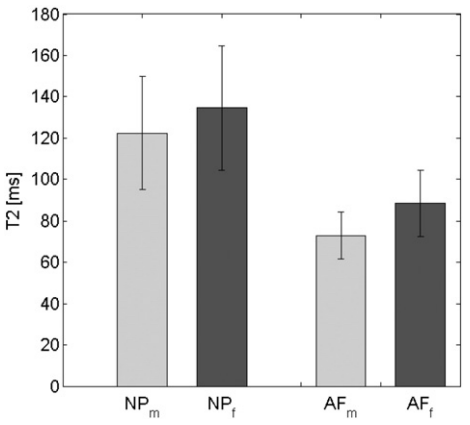

Fig. 2. Transverse relaxation time T2 in nucleus pulposus (NP) and annulus fibrosus (AF) in males (m) and females (f).