

Age-related assessment of intervertebral disc degeneration in the lumbar spine using gagCEST

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Introduction Degeneration of intervertebral discs (IVDs) is studied due to its link with back pain, but current protocols are based on gross morphological change (i.e. Pfirrmann grading [1]). Information regarding the molecular composition, in particular loss of glycosaminoglycan (GAG) content, is useful as an early sign of disc degeneration, and one that increases with degree of degeneration [2]. Recently Kim *et al.* showed that the contrast from chemical exchange saturation transfer associated with GAGs, i.e. gagCEST, could be used to provide information on its distribution [3]. The GAG content of IVDs decreases with degeneration, in particular from the nucleus pulposus (NP). This work looks at the change in the gagCEST contrast with age from IVDs at different levels within the lumbar spine.

Methods MR data was acquired from the lumbar spine of 8 female volunteers of varying age, in a 3T GE scanner using a spine coil for signal reception. Sagittal T₂-weighted images for Pfirrmann grading were acquired with a forced recovery fast-spin-echo sequence (FOV=26x26cm²; matrix=288x192; TE/TR=0.1/4s). CEST data were acquired using Gaussian pulses to saturate at specific offsets prior to a single-shot fast-spin-echo sequence (SSFSE), with FOV=30x30cm³; matrix=128x128; TE/TR≈33/6000ms, and corrected using the WASSR technique [4]. Data were acquired at offsets of -600+600Hz/-180+180Hz at 50Hz/15Hz intervals using five/one 50ms pulse(s) (B₁≈1.5/0.1μT) for CEST/WASSR respectively. The total scan time for acquisition of CEST and WASSR data was ~6mins per IVD. Maps were calculated based on the MTR_{asym}, the saturated signals at a positive offset subtracted from that at the negative offset divided by the unsaturated signal, averaged between 0.6 and 1.4ppm. The sequence was applied to an *in vitro* setup, which included chondroitin sulfate solutions of different concentrations (w/w) to represent GAG. *In vivo*, a region of interest (ROI) was selected based on the unsaturated image and used to quantify the CEST contrast. The ROI was chosen to encapsulate the NP for discs of grade II-III (n=28) since the NP is still distinct from the annulus, for grade IV (n=3) discs the contrast within the entire IVD was considered, and collapsed discs, i.e. grade V (n=1), were excluded.

Results & Discussion Figure 1 shows the results from use of the SSFSE based sequence, which gives a linear correlation between GAG concentration and the CEST contrast. Separation of the CEST data from different IVDs based on the level in the lumbar spine shows a decrease in the contrast with increasing degree of degeneration (Fig.2), which is expected from the decrease in GAG content [2]. There is a general trend of a decreasing CEST contrast from those IVDs at lower levels in the spine, in particular the L4/L5 IVDs. Figure 3 shows analysis of the CEST contrast separated based on the age of the volunteers. A significant decrease with age coincides with an increase in the average Pfirrmann grade. Conversely the increase at the L4/L5 level in going from the 21-30 to 31-40 group is matched by a decrease in the average grade from 3 to 2.6. This suggests that the Pfirrmann grade holds greater bearing than age, which is illustrated by the difference in CEST contrast between IVDs of different grade from an aged volunteer (Figs.4a-b) compared with the similarity between discs at the same level and grade from different volunteers (Figs.4a,c).

Conclusions A decrease in gagCEST contrast is observed to coincide with an increase in the degree of degeneration. This strengthens the potential of gagCEST as an imaging biomarker for disc degeneration.

References [1] Pfirrmann *et al.* Spine 26:1873-8 [2] Urban *et al.* JMRI 25:419-32 [3] Kim *et al.* NMR Biomed 24:1137-44 [4] Kim *et al.* MRM 61:1441-50

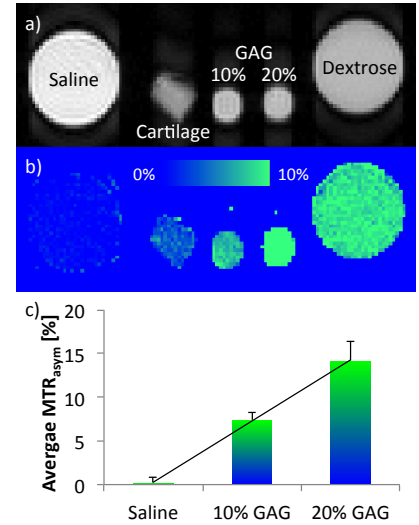


Figure 1 Illustration of phantom setup with a) unsaturated image, b) CEST map, and c) chart of contrast against GAG concentration.

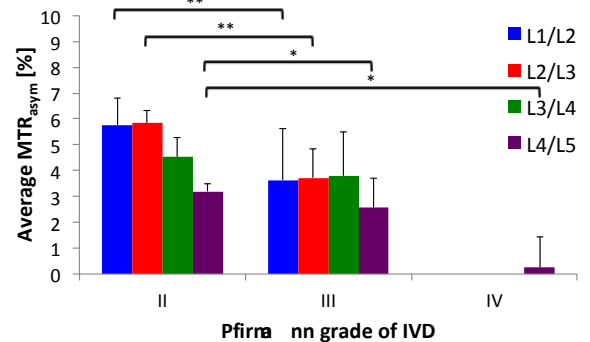


Figure 2 Chart of CEST contrast from IVDs of volunteers separated by Pfirrmann grade. One-tail Student t-tests applied between grades at the same level of significance * p < 0.1 and ** p < 0.05 are shown.

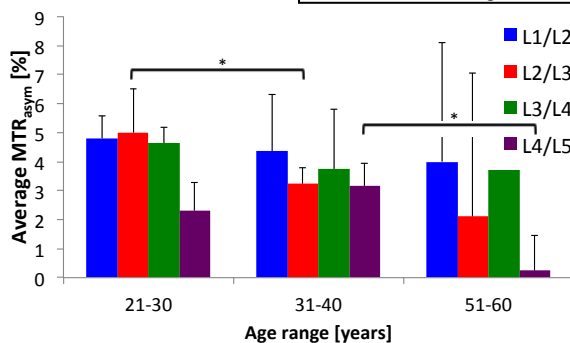


Figure 3 Chart of CEST contrast from IVDs of volunteers separated by age. One-tail Student t-tests applied between age groups at the same level of significance of * p < 0.1 are shown.

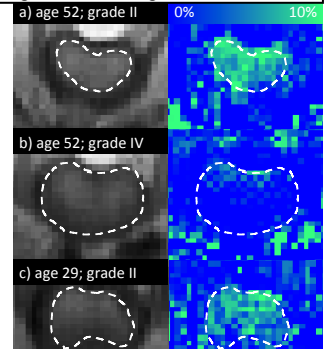


Figure 4 Unsaturated images (left) used to form ROIs for analysis of CEST maps (right).