Original Article

Evaluation of Glycosaminoglycan in the Lumbar Disc Using Chemical Exchange Saturation Transfer MR at 3.0 Tesla: Reproducibility and Correlation with Disc Degeneration*

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Abstract

Objective This study aims to explore the clinical applicability and relevance of glycosaminoglycan Chemical Exchange Saturation Transfer (gagCEST) for intervertebral disc.

Methods 25 subjects ranging in age from 24 yrs to 74 yrs were enrolled. gagCEST was acquired using a single-slice TSE sequence on a 3T. Saturation used a continuous rectangular RF pulse with B_1=0.8 μT and a fixed duration time =1100 ms. Sagittal image was obtained firstly without saturation pulse, and then saturated images were acquired at 52 offsets ranging from ±0.125 to ±7 parts per million (ppm). MR T2 relaxivity map was acquired at the identical location. Six subjects were scanned twice to assess scan-rescan reproducibility.

Results GagCEST intraclass correlation coefficient (ICC) of six subjects was 0.759 for nucleus pulposus (NP) and 0.508 for annulus fibrosus (AF). Bland-Altman plots showed NP had a mean difference of 0.10% (95% limits of agreement: -3.02% to 3.22%); while that of AF was 0.34% (95% limits of agreement: -2.28% to 2.95%). For the 25 subjects, gag CEST in NP decreased as disc degeneration increased, with a similar trend to T2 relaxivity. Gag CEST of AF showed a better correlation with disc degeneration than T2 relaxivity.

Conclusion GagCEST in NP and AF decreased as disc degeneration increased, while gagCEST in AF showed a better correlation than T2 relaxivity.

Key words: Glycosaminoglycan; Chemical Exchange Saturation Transfer (CEST); Reproducibility; Disc degeneration

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INTRODUCTION

Intervertebral disc degeneration is a process that begins early in life and is the consequence of a variety of genetic, mechanical, traumatic and nutritional factors, as well as normal ageing[1]. Early signs of disc degeneration are manifested by biochemical changes, including a loss of proteoglycans, a loss of osmotic pressure and hydration. In the later stages of disc degeneration,

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morphological changes occur, including a loss of disc height, disc herniation, annular tears and radial bulging. On T2-weighted MR images, disc degeneration is seen as a reduction in signal of the nucleus pulposus (NP) and inner fibres of the annulus fibrosus (AF). With more severe disc degeneration, disc height decreases. Pfirrmann et al.[2] devised a 5-level grading system for disc degeneration based on MR signal intensity, disc structure, distinction between nucleus and annulus, and disc height. Recently, an 8-level grading system has been proposed and successfully applied in a number of clinical studies[3-4] .

Quantitative MR techniques that reflect the intrinsic material properties of disc tissues are being explored to facilitate early disc degeneration detection and assessment, such as *in vivo* sodium (Na) MRI, quantitative high-resolution magic angle spinning NMR spectroscopy, proton T2 imaging, T1rho imaging, and diffusion weighted imaging[5-13]. Ideally, these measurements may have the potential to detect subtle differences in the composition and organization of the degenerative disc from the normal one that may not be apparent with morphologic MRI assessment. However, till now the underlying relationship between these MRI parameters, i.e. T2 and T1rho relaxation time, apparent diffusion coefficient, and disc composition have not yet been well understood yet.

Chemical exchange saturation transfer (CEST) has been proposed as a novel MRI contrast mechanism in recent years and been actively explored for a variety of clinical applications[14-26]. CEST MRI shares similar theoretical principle as T1rho MRI, while shows the advantages of specificity to certain biochemistry components such as amide, glycosaminoglycan (GAG), glycogen glutamate and glucose. In disc degeneration studies, glycosaminoglycan CEST (gagCEST) has been proposed to specifically assess the GAG concentration loss associated with degeneration procedure. With phantom study, Kim et al.[18] reported high correlation between gagCEST and GAG concentrations. In addition, they also demonstrated proof-of-principle the technical feasibility of gagCEST *in vivo* imaging at 3 Tesla on a cohort of healthy volunteers in axial plane of lumbar discs. Haneder et al.[19] applied the gagCEST in sagittal plane at 3T in a small number of patients with low-back pain and investigated the correlation of gagCEST and Pfirrmann grading as well as T2 relaxation time. However, their gagCEST map demonstrated low signal-to-noise ratio[19].

To facilitate the use of gagCEST MRI for routine clinical use, the aim of the current study was to evaluate the *in vivo* reproducibility of measuring glycosaminoglycan of the lumbar disc using CEST imaging at a 3.0-T system and to determine the feasibility of correlating the MR measurement with the degree of disc degeneration with reference to the 5-level and 8-level semi-quantitative disc degeneration grading systems[3-4], and compare the relative performance of gagCEST *vs.* MR T2 relaxivity.

MATERIALS AND METHODS

Subjects

A total of 25 subjects were enrolled in this prospective study, including 12 healthy volunteers (10 males and 2 females; mean age: 30.3 years, age range: 24-47 years), and 13 consecutively patients with unspecific low-back pain (5 males and 8 females; mean age: 59.1 years; age range: 29-74 years). Except for intervertebral disc degeneration, there was no other spine disease in 13 patients, as confirmed by medical history and diagnostic MRI. Six of the healthy volunteers underwent gagCEST MRI scan twice time with two days' time interval to assess scan-rescan reproducibility. Patient scans were performed during Saturday morning, while volunteers were performed during working day evenings. The study was approved by the human research ethics committee of the local university, and all subjects provided written informed consent.

MR Data Acquisition

All subjects were scanned using a Philips Achieva 3T scanner (Philips Healthcare, Best, the Netherlands) with a body coil for transmission and a 12-channel spine coil array for reception. Standard diagnostic MRI sequences were completed including sagittal T1 weighted and T2 weighted images covering whole lumbar spine with the following parameters: T1 weighted sagittal imaging Turbo Spin Echo (TSE) sequence, TSE factor=5, TR=407 ms, TE=8 ms, FOV=(160 × 270) mm^2, voxel size=0.9 mm × 2.1 mm, slice thickness= 4 mm, slice gap=0.4 mm, NSA=4, Flip angle=80°; T2 weighted sagittal imaging TSE sequence, TSE factor=30, TR=3700 ms, TE=110 ms, FOV=(160×273) mm^2, voxel size=0.8 mm × 1.72 mm, slice thickness=4 mm, slice gap=0.4 mm, NSA=2, Flip angle=90°.

GagCEST imaging data were acquired using a