Breath-hold CEST-MRI of Liver Cirrhosis: A Clinical Feasibility Study

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Target audience

The target audience includes basic scientists and clinicians who are interested in the chemical exchange saturation transfer (CEST) technique and the MR imaging of liver cirrhosis.

Introduction

CEST imaging is a specific magnetization transfer (MT) MRI technique that can indirectly detect low-concentration solutes with exchangeable protons, such as amide protons in protein backbones (resonance frequency offset = 3.5 ppm downfield from water) and hydroxyl protons (1.2 ppm downfield from water), through the bulk water signal [1, 2]. CEST-MRI has been exploited to non-invasively detect liver glycogen via hydroxyl protons [3]. Liver cirrhosis is one type of glycogen storage disease without an increased amount of glycogen. Instead, the glycogen that does build up in the liver has very long outer branches, which may have a significant contribution to the transfer ratio of hydroxyl protons in CEST-MRI measurements. The objective of this study was to assess whether an in vivo breath-hold CEST-MRI is capable of detecting the mobile protein level and the glycogen outer branches in liver cirrhosis.

Materials and methods

A total of six healthy volunteers (3M/3F, age: 27 yrs.) and three patients with liver cirrhosis (2M/1F, age: 60 yrs.) have been enrolled in this study. The CEST-MRI data acquisition was performed on a 3T scanner (Philips Healthcare), using an ultrafast 3D gradient echo (3D TFE) sequence with breath-hold. The imaging parameters were the following: TFE shot interval = 1888.8 ms, TR/TE = 2.8/1.4 ms, TFE factor = 60, slice thickness = 10 mm, voxel size = 2×2 mm^2, # slices = 12, acquisition time = 12 sec). The saturation pre-pulse was composed of a train of sixteen 1800º block pulses, each with a pulse length of 29 ms and a saturation amplitude of 172 Hz (4.1 μT). The MT-spectrum was acquired using four saturation pre-pulse frequency offsets (±3.5 and ±1.2 ppm). S_0 was acquired using the same 3D TFE sequence without any saturation pre-pulse. A B_0 field map was acquired using a dual-echo 3D TFE sequence (TE1/TE2 = 2.2/3.2 ms, acquisition time = 7.9 sec). All of the CEST-MRI data were analyzed with software that was developed in-house and written in IDL (Exelis Visual Information Solutions, Boulder, CO). The magnetization transfer ratios (MTRs) including MTR(±3.5ppm), MTR(±1.2ppm), MTR_{asym}(3.5ppm), and MTR_{asym}(1.2ppm) were calculated from a region of interest (ROI) drawn on liver tissues, excluding hepatic vessels and cysts. A student t-test was used to compare the MTR parameters in the healthy livers against those in the liver cirrhosis regions. Statistical significance was considered to be at $p < 0.05$.

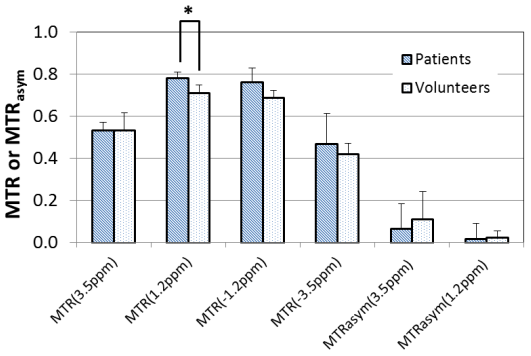

Figure 1. MTR results from the liver regions. The MTR(1.2ppm) was significantly higher in the patients with liver cirrhosis than in the healthy volunteers, revealing the longer glycogen outer branches in liver cirrhosis.

Results and Discussion

Amide protons: The MT spectra from the liver ROIs showed a large asymmetric ratio at 3.5ppm downfield from the water resonance, indicating CEST-MRI detectable mobile protein levels in the liver tissues (Figure 1), although there were no significant differences in liver MTR(3.5ppm) and MTR(-3.5ppm) between the patients with liver cirrhosis and the healthy volunteers. The patients with liver cirrhosis showed a lower but nonsignificant liver MTR_{asym}(3.5ppm) (6.5±11.6%) than healthy volunteers (11.1±13.0%, $p = 0.631$). A fatty liver can result in a higher MTR at -3.5 ppm in the patients with liver cirrhosis, which was related to various possible NOE or pseudo-NOE effects [4,5]. A water-only image, based upon the DIXON method, may be used in the CEST-MRI acquisition to eliminate the fatty tissue effect.

Hydroxyl protons: The patients with liver cirrhosis exhibited a significantly higher MTR(1.2ppm) (78.1±2.8%) than the healthy volunteers (71.1±3.4%, $p = 0.024$, Figure 1), with high-quality MTR(1.2ppm) and MTR_{asym}(1.2ppm) images (Figure. 2). Due to the over-saturation from a high B_1 power (4.1 μT), the liver MTR_{asym}(1.2ppm) was very small and close to zero. A lower B_1 power with optimization may provide the best capability for differentiating the patients with liver cirrhosis from the volunteers by using MTR(1.2ppm) and MTR_{asym}(1.2ppm).

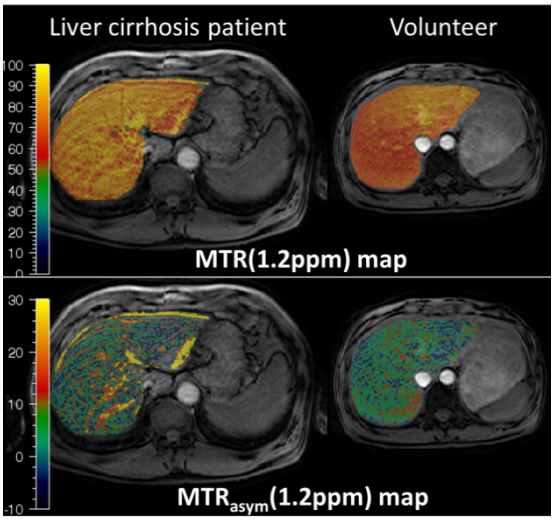

Figure 2. MTR(1.2ppm) and MTR_{asym}(1.2ppm) maps of a patient with liver cirrhosis and a healthy volunteer. The liver cirrhosis patient showed a higher MTR(1.2ppm) than the volunteer.

Conclusion

We have shown that it is clinically feasible to obtain CEST spectra in the liver with the breath-hold technique. Liver cirrhosis exhibited a significantly higher MTR at the resonance frequency of hydroxyl protons (1.2ppm), indicating a higher concentration of glycogen outer branches in liver cirrhosis. Further experiments are necessary to assess the stability and reproducibility of the results.

References

1. Zhou J, et al., Nat Med, 9(8):1085-90 (2003).
2. Sun PZ, et al., MRM, 58(6): 1207-15 (2007).
3. van Zijl PCM, et al., PNAS, 104(11): 4359-64 (2007).
4. Jones CK, et al. NeuroImage, 77:114-124 (2013).
5. Lu J, et al., MRM, (2014).