Feasibility of Chemical Exchange Saturation Transfer (CEST) MRI for Prostate Cancer Detection at 3T

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Introduction

CEST MRI has recently emerged as a new molecular-MRI technique, in which the magnetization transfer ratio (MTR) between the exchangeable solute protons (amide protons or hydroxyl protons) and the bulk water protons. It is able to detect various endogenous low-concentration molecules in tissue and has been developed to for evaluating the protein and peptide content in brain tumors (Amide-Proton-Transfer MRI) [1], liver glycogen level (glycoCEST) [2], and cartilage glycosaminoglycan concentration (gagCEST) [3]. This study is to evaluate whether CEST MRI is feasible to image prostate cancer patients for tumor detection.

Material and methods

<u>Subjects</u> In an ongoing 20 subject pilot study, four patients with biopsy-proven prostate cancer (age, 60 ± 7 years) and four healthy volunteers (age, 34 ± 3 years) are currently enrolled. This pilot study will be concluded Feb. 2009.

<u>CEST MRI</u> All subjects were imaged in a 3 Tesla MR system (Achieva, Philips) using an 8-channel SENSE Torso coil or 32-channel SENSE Torso/Cardiac coil. Whole prostate CEST MRI was acquired using an axial TSE sequence with the following parameters: TR/TE = 5625/21 ms; TSE factor = 15; FOV = 220×220 mm²; Matrix = 128×100 ; Slice thickness = 4 mm; Number of slices = 8; Spacing between slices = 0.4 mm; NSA=2. Saturation TSE images were acquired without and with pre-saturation pulse at two frequency offsets (3.5 and -3.5 ppm), which was composed of a train of sixteen 1400° block pulses with pulse length of 30 ms and saturation amplitude of 130Hz ($\sim3.0~\mu$ T). The scan time was 7 min. To obtain MT-spectrum, single slice CEST MRI was acquired using single-shot TSE sequence with the following parameters: TR/TE = 5240/84 ms; TSE factor = 74; FOV = 220×220 mm²; Matrix = 128×101 ; Slice thickness = 3 mm; NSA=1. The single slice image was acquired with pre-saturation pulse at 33 different frequencies (8 to -8 ppm with an interval of 0.5 ppm) and the scan time was 3 min. T2-w, DCE-MRI, pre- and post-contrast T1-w images were also acquired during patient scan.

Image Processing All CEST MRI data were analyzed with an-inhouse-developed software written in IDL (ITT, Boulder, CO). MTR_{asym}(3.5ppm) without B_0 correction was calculated from whole prostate CEST MRI by directly subtracting TSE images at 3.5 ppm from the images at -3.5 ppm. MTR_{asym}(3.5ppm) with B_0 correction was calculated from single slice CEST MRI with 33 frequency offsets, in which the MT-spectrum was fitted by a least-square polynomial to determine B_0 due to magnetic field inhomogeneities. Regions of interest (ROIs) were drawn on specific regions including tumor regions, non-cancerous peripheral zone (PZ), central gland (CG), fat, and muscle regions.

<u>Statistical Analysis</u> Student t-test was used in SPSS 15.0 (SPSS Inc.) to compare $MTR_{asym}(3.5ppm)$ in the histology identified tumor region and non-cancerous regions. Statistical significance was considered at p <0.05.

Results

High quality CEST MR images and MT-spectrum were achieved in healthy volunteers (Fig. 1) and prostate cancer patients (Fig. 2). MT-spectrum shows symmetric water saturation profile in both normal PZ, CG, and muscle regions. In peri-prostatic fat regions, MT-spectrum shows fat saturation with minor water saturation (Fig. 2).

MT-spectrum of the prostate cancer regions revealed asymmetric water saturation profile with higher MTR at negative frequency offsets, which gave larger MTR_{asym}(3.5ppm) in tumor regions than normal PZ and CG (Fig. 2). MTR_{asym}(3.5ppm) was $14.5 \pm 6.6\%$ in tumor regions, significantly higher than that in non-cancerous tissues, such as patient PZ ($-0.3 \pm 4.7\%$, p<-0.006), patient CG ($2.3 \pm 4.4\%$, p<-0.02), volunteer PZ ($2.0 \pm 5.5\%$, p=-0.03), and volunteer CG ($3.0 \pm 4.7\%$, p=-0.03) (Fig. 3).

Discussion and Conclusion

Unlike MT-spectrum in non-cancerous prostate tissues, MT-spectrum in prostate cancer showed dramatic asymmetric water saturation profile. This caused higher MTR $_{asym}$ (3.5ppm) in tumor regions. MTR $_{asym}$ was still large at high frequency offsets, which cannot be attributed to the effects of amide and hydroxyl proton transfer. The underlying mechanism of the asymmetric MT-spectrum in prostate cancer needs further investigation and will be evaluated.

The 32-channel SENSE torso/cardiac coil and single-shot TSE sequence were used to acquire MT-spectrum of the prostate with excellent quality. The initial applications may enable higher SENSE factor and faster imaging for acquiring MT-spectrum of the prostate. In conclusion, CEST MRI was found feasible in prostate cancer patients. This feasibility study provides a diagnostic potential of CEST MRI for tissue characterization in prostate cancer screening and lesion detection.

References

1. Zhou J, et al. Magn Reson Med. 2004 May;51(5):945-52. **2.** van Zijl PC, et al. PNAS. 2007 Mar 13;104(11):4359-64. **3.** Ling W, et al. PNAS. 2008 Feb 19;105(7):2266-70.

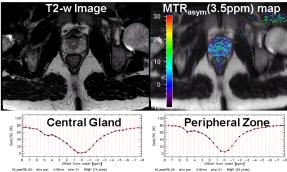


Figure 1. T2-w and CEST MRI from a healthy volunteer using 32-channel SENSE torso/cardiac coil at 3T. $MTR_{asym}(3.5ppm)$ with B_0 correction were relative low in prostate PZ and CG regions.

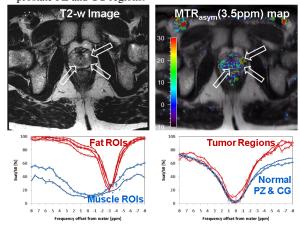


Figure 2. T2-w and single slice CEST MRI from a prostate cancer patient using 32-channel SENSE torso/cardiac coil at 3T. Three tumor areas were shown significantly higher MTR_{asym}(3.5ppm) than noncancerous PZ and CG tissues.

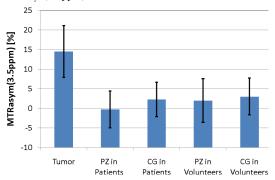


Figure 3. $MTR_{asym}(3.5ppm)$ in tumor regions was significantly higher than that in PZ and CG regions from prostate cancer patients and healthy volunteers.