Rapid CEST Detection Using EPI

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Introduction: PARAmagnetic Chemical Exchange Saturation Transfer (PARACEST) contrast agents provide unique advantages over standard MRI contrast agents that modulate relaxation time constants[1]. The use of PARACEST agents to report physiological conditions such as temperature and pH requires the acquisition of multiple images with various saturation frequencies[2]. Therefore minimization of image acquisition time is of paramount importance for in-vivo studies. Until recently, PARACEST image acquisition times have typically required minutes to effectively detect CEST in-vivo. However, recently a method called FISPCEST, which applies a CEST saturation pulse prior to a Fast Imaging with Steady-State Free Precession (FISP) pulse sequence was introduced. FISPCEST reduced image acquisition time to less than 3 seconds with only a 15% decrease in the CEST sensitivity compared to the standard spin echo technique[3]. The purpose of this study was to evaluate echo-planar imaging (EPI) CEST, to determine whether the method maintains CEST sensitivity while minimizing acquisition time.

Methods: An Echo-Planar Imaging (EPI) pulse sequence (TR = 3000ms, TE = 17.4ms, echo-train length ~ 26 ms) with sinusoidal gradient readout lobes was utilized on a 9.4T Varian small animal MRI scanner. A CEST saturation pulse was added prior to the excitation (α) pulse. Comparisons were made to CEST acquisitions made using a fast low-angle shot (FLASH) sequence (TR/TE = 25/3.5ms) and a fast spin-echo (FSE) sequence (TR/TE = 3000/40ms, echo train length = 48ms). All images (EPI, FLASH and FSE), were preceded by a 2.5s, 15 μT continuous wave saturation pulse. Images were acquired (FOV = 25.6mm x 25.6 mm, single shot, 1 average, 0 dummy scans) of a 5 mm NMR tube containing 10 mM Eu^{3+}-DOTAM-glycine(Gly)–phenylalanine(Phe) in aqueous solution (pH = 7.5) at 35°C. CEST spectra were collected for all three methods, by varying the CEST saturation pulse frequency from -60 ppm to 60 ppm in 1 ppm increments. CEST spectra were also acquired using incrementally smaller EPI readout frequency bandwidths to determine the bandwidth that maximized signal to noise ratio (SNR) while maintaining CEST effect[4]. Images were acquired as described above (at 20°C), with the readout bandwidth set to 225, 200, 175, and 100 kHz. The CEST spectra were directly compared to identify changes in CEST effect. The SNR was also measured in each image acquired at -60ppm for each bandwidth by dividing the mean signal intensity of the sample by the standard deviation of the background noise.

Results: CEST spectra acquired using the three different pulse sequences are shown in Figure 1. Representative images rapidly acquired using the EPI sequence are shown in Figure 2 at several different saturation frequencies. Image characteristics are summarized in Table 1. CEST efficiency was calculated as defined by Liu et. al.[2]. EPI provides a means to detect CEST with high temporal resolution, without a loss in the CEST sensitivity. Reducing receiver bandwidth from 225 kHz to 100 kHz nearly doubles the SNR for EPICEST without decreasing the CEST effect (Figure 3).

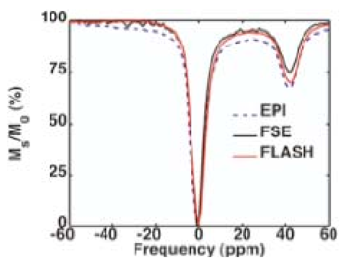

Figure 1: CEST spectra of 10mM Eu^{3+}-DOTAM-Gly-Phe using EPI, FSE and FLASH.

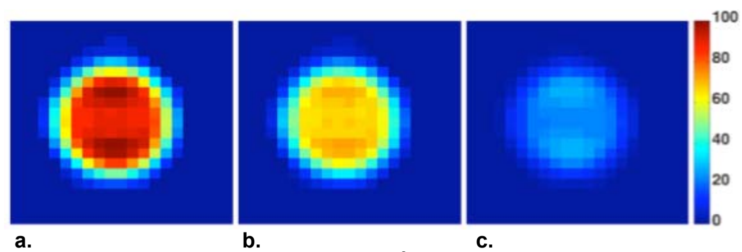

Figure 2: EPICEST images of 10 mM E Eu^{3+}-DOTAM-Gly-Phe. a. Image acquired with CEST saturation frequency of -41 ppm. b. Image acquired with CEST saturation frequency of 41 ppm. c. The difference (CEST EFFECT) between image intensities in a. and b..

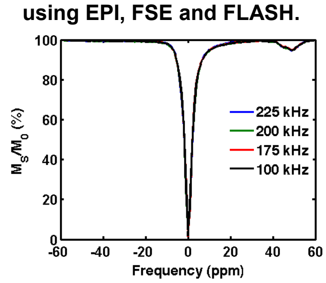

Figure 3: CEST spectra of 10 mM Eu^{3+}-DOTAM-Gly-Phe using different receiver bandwidths.

	FSE	FLASH	EPI
SNR	715	315	1050
CNR	190	110	250
CEST Effect (%)	25	25	25
CEST Efficiency ($s^{-1/2}$)	12	14	89
Total Acquisition Time (s)	120	30	4

Table 1: SNR, CEST effect, CEST efficiency and total acquisition time measured using FSECEST, FLASHCEST, and EPICEST in 10 mM Eu^{3+}-DOTAM-Gly-Phe

Discussion: These results demonstrate that EPI is an efficient and practical pulse sequence for in-vivo CEST detection. Decreasing readout bandwidth had no significant impact on acquisition time or CEST contrast but significantly increase image SNR. The strong CEST effect and rapid acquisition time will allow for the extension to multi-slice acquisitions by incorporating short saturation pulses prior to each slice acquisition to ensure the spin system remains fully saturated. EPI, provides high temporal resolution and SNR while fully maintaining CEST effect due to the short readout acquisition times.

References:

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4. Sun et. al., Magn Reson Med, 2005, 54, 222-225