Computational modeling and optimized detection of PARACEST contrast agents with Echo Planar Imaging

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Introduction: In magnetic resonance imaging (MRI), contrast agents are often used to highlight abnormal tissue. This study focuses on the development of acquisition methods of a novel contrast agent that produces MRI signal variations via a mechanism called chemical exchange saturation transfer (CEST). PARAmagnetic CEST (PARACEST) contrast agents provide unique advantages over standard MRI contrast agents that modulate relaxation time constants[1]. In the presence of a CEST agent, a specific RF pulse (CEST pulse) is applied and chemical exchange between protons bound to the agent and bulk water protons efficiently reduces the measured net magnetization. Therefore, a low signal intensity is produced in regions containing PARACEST agent, generating image contrast. The use of PARACEST agents to report physiological conditions such as temperature and pH requires the acquisition of multiple images with various saturation frequencies [1]. Therefore minimization of image acquisition time is of paramount importance for in-vivo studies. Recently, reduced PARACEST image acquisition time had been demonstrated using Echo-Planar imaging (EPI) pulse sequences [2]. EPI is an efficient and practical pulse sequence for in-vivo CEST detection. The purpose of this study was to develop a computational model of imaging CEST contrast agents using MRI.The model will allow specific contrast agent and EPI imaging parameters to be strategically varied in order to determine parameter values that provide optimal CEST detection efficiency.

Methods: Using MATLAB, a computational model was developed to simulate the effects of an EPI pulse sequence with sinusoidal gradient readout lobes implemented on a 9.4T Varian small animal MRI scanner. The model simulated the imaging of a theoretical square (5 mm x 5 mm) NMR tube containing 10 mM Eu^{3+}-DOTAM-glycine(Gly)–phenylalanine(Phe) in aqueous solution (pH = 7.5). The model incorporated agent specific CEST radiofrequency (RF) pulses using a previously published mathematical model [3]. The theoretical magnetization was manipulated as if experiencing magnetic field gradients and RF α-pulses in the order of a specified EPI sequence. The model was then used to optimize the EPI acquisition. A detailed analysis of the effect of varying several imaging parameters on CEST detection was performed. The investigated parameters were 1) The *k*-space sampling order (linear or centric), 2) the number *k*-space segments or 'shots' (1,2,4, and 8), each preceded by a 15 μT continuous wave CEST pulse, 3) the CEST pulse duration (1, 2, 3, 4, 5 and 6 s), and 4) the α-pulse flip angle (2° to 20° in increments of 2°). EPI PARACEST imaging experiments were simulated with all possible combinations of the above parameters with a set of fixed acquisition parameters (FOV=30 mm x 30 mm, 1 average, matrix size = 32 x 32, readout bandwidth = 225 kHz). Normally distributed Gaussian noise (μ=0, σ = 0.01) was added to each simulation. Following the simulations, contrast to noise efficiency was measured and compared to identify the set of investigated parameters that provided optimal CNR efficiency. The CNR efficiency was measured in each simulation according to Liu et al [4].

Results: Figure 1 displays the CNR efficiency achieved with 1, 2, 4 and 8 shots and a fixed CEST pulse duration of 5 seconds. Figure 2 displays the optimal CNR efficiency attained for a single-shot EPI acquisition with a CEST pulse duration of 2 seconds and a flip angle of 90° (left most bar). Figure 2 also shows the optimal CNR efficiencies achieved by varying the CEST pulse durations and α-pulse flip angle. In all cases, the optimal CEST duration was 1 second and the optimal α flip angle was 20°.

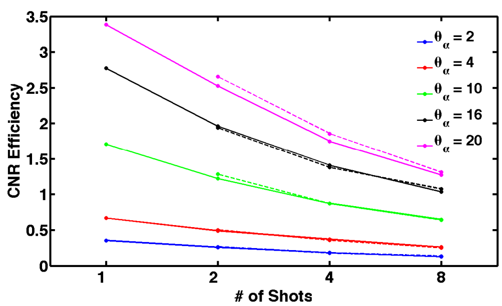

Figure 1: CNR efficiency vs. # of shots for different flip angles. CEST saturation length = 5s.
Solid line – Linear **Dashed line** - Centric

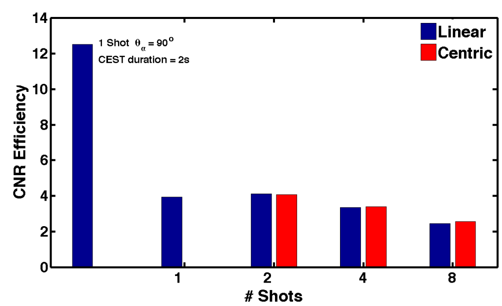

Figure 2: Optimal CNR efficiencies attained for each number of shots. CEST pulse durations were varied from 1 to 6s and flip angle was varied from 2 to 20°. Far left bar is CNR attained with flip angle = 90°.

Discussion: The results suggest that a single-shot 90° EPI sequence may be the optimal acquisition method for CEST detection in terms of CNR efficiency. Interestingly, the two shot approach appears to be optimal for low α-pulse flip angles. Figure 2 demonstrates that centric *k*-space sampling generally provides a slightly greater CNR efficiency compared to linear *k*-space sampling as expected. Also, the simulated results demonstrate an increase in CNR efficiency with increasing α-pulse flip angles. These trends were observed for all experiments with fixed CEST pulse durations. However, future work will determine whether an optimal α-pulse flip angle exists between 20° and 90°.

References:

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