Simultaneous measurement of pharmacokinetic model parameters and $T_1/B_1$ using Active Contrast Encoding MRI

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Introduction: $T_1$-weighted dynamic contrast enhanced magnetic resonance imaging (DCE-MRI) has been widely used to probe tumor microenvironment using kinetic model parameters, such as transfer constant $K^\text{trans}$, extra cellular space volume fraction $v_e$, and vascular space volume fraction $v_p$. Accurate estimation of these kinetic parameters requires $B_1$-corrected $T_1$ values [1]. However, it is not trivial to measure $B_1$ and $T_1$ accurately. In addition, the measurement of $B_1$ and $T_1$ could take a long scan time, often longer than DCE-MRI scan itself. This is one of major challenges that limit the use of kinetic model analysis of DCE-MRI for clinical applications. In this study, we propose a novel approach, namely Active Contrast Encoding (ACE) MRI, to measure both $B_1$ and $T_1$ values along with kinetic parameters from a single DCE-MRI data. A proof-of-concept study was conducted to demonstrate the proposed method using numerical simulation and an in vivo mouse study.

Materials and Methods: ACE-MRI

The main idea of ACE-MRI is to use the second half of the DCE-MRI curve, which is typically slow-varying, to actively encode the signal intensity to have various $T_1$ and $B_1$ weighting using different flip angles and TRs. TE is kept constant to avoid changes in $T_2$ weighting. In the subsequent kinetic model analysis, both $T_1$ and $B_1$ are included as free parameters to be estimated. In this study, we divided a DCE-MRI scan into three parts: (a) injection phase with a conventional protocol with fixed flip angle $\alpha=90^\circ$ and TR [10 ms], (b) a second part for $T_1$ encoding by changing flip angles ($25^\circ$, $20^\circ$, $10^\circ$, and $5^\circ$), and (c) a third part for $B_1$ encoding by using a large flip angle ($90^\circ$) and a long TR (60 ms).

Simulation: A numerical simulation study was conducted using an arterial input function (AIF) obtained from a previous 7T mouse study [2] (Figure 1a). Tissue contrast enhancement curve was generated using the AIF with $K^\text{trans}=0.2505$/min, $v_e=0.45$, $v_p=0.06$ [3], $T_1=2.3$s, and $B_1$ scaling factor=1. Figure 1b shows a simulated tissue signal enhancement ratio curve using a conventional DCE-MRI protocol with one flip angle ($\alpha=15^\circ$) with TR=10ms and temporal resolution $T=5$s/frame. Figure 1c shows an example of ACE-MRI curve with the active encoding described above. The temporal resolution was assumed to be 5s/frame for the first two parts and 30s for the last part with flip angle of 90°. Rician noise with signal to noise ratio (SNR) 20 or 10 was added. Fifty different noises with 60 initial guesses for each noise were used to fit the extended general kinetic model using the simplex method.

In vivo mouse study: One eight-wk-old BALB/c mouse with 4T1 breast cancer xenograft was scanned using a 7T horizontal bore magnet with a volume transmit and receive coil. General anesthesia was induced by 1.5% isoflurane in air. The animal was mounted on a cradle with respiratory and temperature monitoring probes. A 3D FLASH sequence was used to acquire the baseline case (Figure 1d) and for active encoding with TR=12 s and T=5s. This sequence was run to acquire 127 3D images for about 13.5 min with multiple flip angles ($15^\circ$, $25^\circ$, $20^\circ$, $10^\circ$, $5^\circ$, $90^\circ$) and different number of repetitions (60, 12, 12, 12, 9). Temporal resolution was 4.86s for small flip angles and 29.16s for $90^\circ$ flip angle. A bolus of 10 mM Gd-DTPA in saline, corresponding to dose 0.1 mmol/kg, was injected through a tail vein catheter, starting 1 min after the acquisition of pre-contrast images. Double flip angle (DFA) method (TR=12 s, 20min scan) with flip angles $60^\circ$/$120^\circ$ and the inversion recovery (IR) method (TR=12 s, 20min scan) with inversion time 50ms/2.5s were implemented to obtain $B_1$ and $T_1$ maps, maps for cross validation. This study was approved by the institutional animal care and use committee.

Results: Simulation: Figure 1d shows relative errors from the true values for a conventional DCE-MRI case shown in Figure 1a and an ACE-MRI case shown in Figure 1c. In the conventional DCE-MRI case, it was impossible to achieve accurate estimation of all five parameters including $B_1$ and $T_1$. However, in ACE-MRI, the accuracy and precision for all parameters were dramatically improved to have relative median errors less than 3% for all parameters. Please note that the relative errors did not increase noticeably when the SNR decreased from 20 to 10. In vivo mouse study: Figure 2a shows axial slice of interest with muscle and tumor ROIs. The AIF derived from the muscle ROI is shown in Figure 2b. Figure 2c shows a representative tissue curve and a kinetic model fit. Figure 3 shows color maps for the estimated parameters. Please note that the kinetic model parameter maps appear very well regularized, indicating that the model fit was robust. The estimated $B_1$ and $T_1$ maps were compared with separately measured $B_1$ and $T_1$ maps, respectively. Figure 4 shows that the tumor $T_1$ and $B_1$ values from ACE-MRI are compatible with those from dedicated scans.

Discussion: In this proof-of-concept study, both simulation and in vivo results suggest that the proposed ACE-MRI method can be used to estimate $T_1$ and $B_1$ along with kinetic model parameters. It should be also noted that estimation of kinetic parameter was remarkably robust as the good quality of parametric maps were obtained. This study successfully demonstrated that ACE-MRI can be used to shorten the scan time by eliminating the need to have separate $B_1$ and $T_1$ mapping procedures. In addition, it is also noted that there is no need to co-register $B_1$ and $T_1$ maps to DCE-MRI data, when ACE-MRI protocol is used.


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