Simutaneous 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^{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 simulations 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 (15°) and TR (10 ms), (b) a second part for T_1 encoding by changing flip angles (25°, 20°, 10°, and 5°), and (c) a third part for B_1 encoding by using a large flip angle (90°) 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^{trans}=0.2505(/min), v_e=0.45, v_p=0.06 [3], T_1 =2.3s, 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 (α=15°) with TR=10ms and temporal resolution T=5s/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.

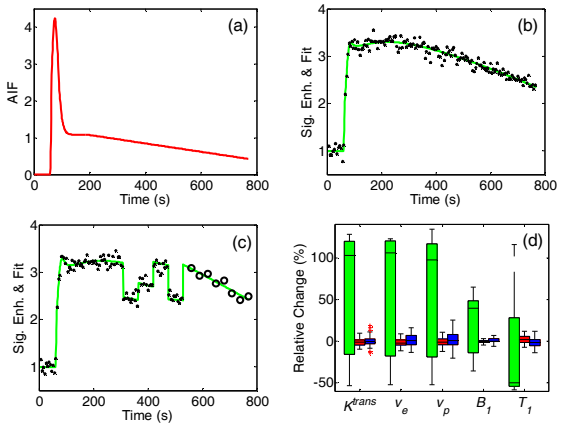

Figure 1: Simulation: (a) AIF. (b) Simulated lesion enhancement curve using one flip angle (15°) with SNR=10 (black dots) and fitting (green solid). (c) Simulated lesion ACE-MRI enhancement curve with SNR=10 (black dots: small flip angle with TR=10ms and T=5s; black circles: 90° large flip angle with TR=60ms and T=30s) and fitting (green solid). (d) Relative parameter estimation error using multiple noises. (green: one flip angle curve fitting with SNR=20; red and blue: ACE-MRI curve fitting with SNR=20 and SNR=10.

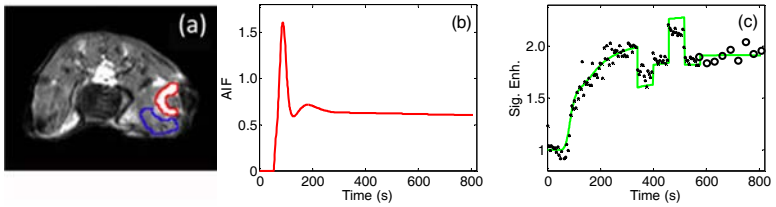

Figure 2: In vivo: (a) Axial slice with muscle ROI (blue) and lesion ROI (red). (b) AIF. (c) Lesion enhancement curve (black dots and circles) from one pixel in tumor ROI with fitting (green solid).

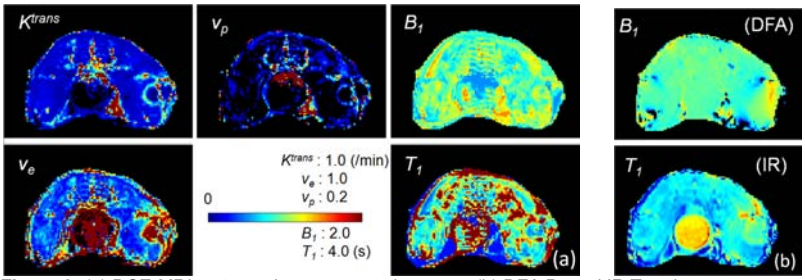

Figure 3: (a) DCE-MRI estimated parameter color maps. (b) DFA B_1 and IR T_1 color maps.

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 minimize the flow effect (TR/TE=7.5 and 45ms/2.638ms, image matrix = 128x128x9, resolution = 0.25x0.33x2 mm). This sequence was run to acquire 127 3D images for about 13.5 min with multiple flip angles (15°, 25°, 20°, 10°, 5°, 90°) and different number of repetitions (60, 12, 12, 12, 12, 9). Temporal resolution was 4.86s for small flip angles and 29.16s for 90° 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°/120° 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 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 1b 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.

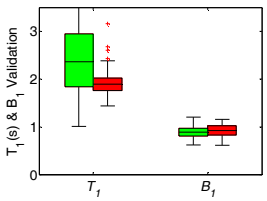

Figure 4: Tumor ROI (Fig 2a) T_1 and B_1 from DCE-MRI measurement (green) compare with IR measured T_1 and DFA measured B_1 (red).

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 is used. Future study is warranted to further optimize the ACE-MRI protocol.

Reference:[1] Sung K. et al, *JMRI* 38:454–459 (2013). [2] Zhang and Kim, *Proc. Intl. Soc. Mag. Reson. Med.*(2011). [3] Buckley DL, *MRM* 47:601–606(2002).

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