In vivo cross-validation study of contrast kinetic model analysis with simultaneous B_1/T_1 estimation

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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. Recently, we proposed active control encoding (ACE)-MRI [1, 2], which enables estimation of transmit RF field homogeneity (B_1) and pre-contrast longitudinal relaxation time (T_{10}), in addition to contrast kinetic parameters, by encoding the B_1 and T_{10}-related information in the slow washout portion of DCE-MRI time course using multiple flip angles (α) and repetition times (TR). We also proposed a novel approach of ACE-MRI, namely a model free approach [2], which separates estimation of T_{10}/B_1 from estimation of contrast kinetic parameters, and consequently improves parameter estimation accuracy and precision. The purpose of this study was to compare the contrast kinetic parameters estimated from ACE-MRI data with those estimated from conventional DCE-MRI experiments with separate measurements of T_{10} and B_1 for cross-validation.

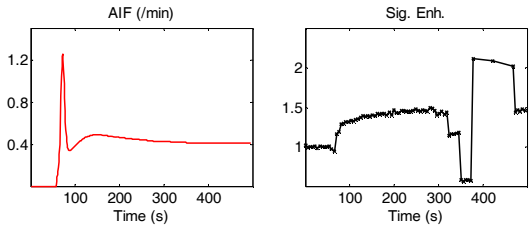

Figure 1: Representative ACE-MRI data for reference tissue arterial input function and a single voxel in a tumor.

Materials and Methods: In the ***model free approach of ACE-MRI***, T_{10} and B_1 are first estimated from the slow washout portion of ACE-MRI curve itself by assuming relaxation rate (R_1) changes linearly. Then the obtained T_{10}/B_1 can be used in the subsequent estimation of pharmacokinetic parameters, such as K^{trans}, v_e, and v_p. To validate the performance of ACE-MRI, in vivo studies were carried out using GL261 murine GBM model. ***MRI***: Three eight-wk-old C57BL/6 mice with GL261 brain tumors were 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 animals were mounted on a cradle with respiratory and temperature monitoring probes. A 3D FLASH sequence was used to minimize the flow effect (TR/TE=12 and 3.83ms, image matrix = 100x100x9, resolution = 0.15x0.15x1 mm^3). This sequence was run to acquire 78 3D images for about 10 min with multiple flip angles (10°, 12°, 8°, 5°, 2°, 90°(TR=100ms), 10°) and different number of repetitions (50, 5, 5, 5, 5, 3, 5). Temporal resolution was 5.4s for small flip angles and 45s 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. T_{10} and B_1 were separately measured using RareVTR sequence [3] and signal null method [4] with large flip angles (140, 150, and 160 degree) respectively for cross-validation. This study was approved by the institutional animal care and use committee. ***Data Processing***: For ACE-MRI, B_1 and T_{10} were estimated from the washout region of the ACE-MRI curve. Extended general kinetic model (GKM) was used to estimate K^{trans}, v_e and v_p with the estimated T_{10}/B_1. For conventional DCE-MRI analysis, independently measured T_{10}/B_1 was used for GKM model analysis. Arterial input function was generated with a reference tissue approach.

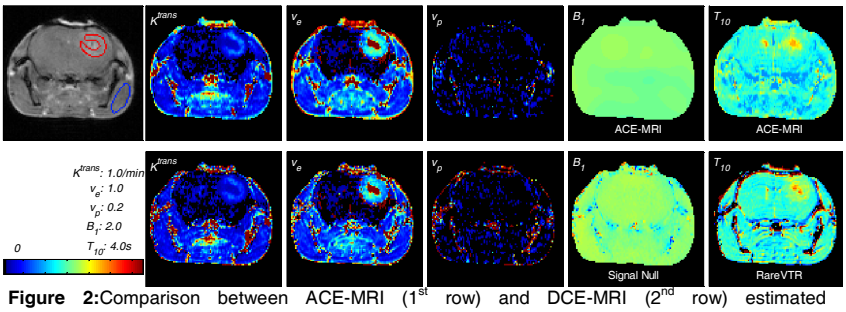

Figure 2: Comparison between ACE-MRI (1st row) and DCE-MRI (2nd row) estimated pharmacokinetic parameters, ACE-MRI estimated T_{10}/B_1 maps and T_{10}/B_1 maps from separate signal null method and RareVTR method measurements.

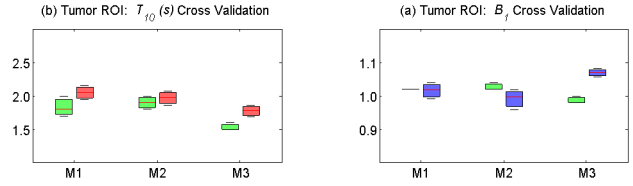

Figure 3: B_1/T_{10} multiple animals (n=3) cross validation. (a) B_1 cross validation between model free approach (green) and signal null method (blue) for tumor ROI. (b) T_{10} cross validation between model free approach (green) and RareVTR method (red) for tumor ROI.

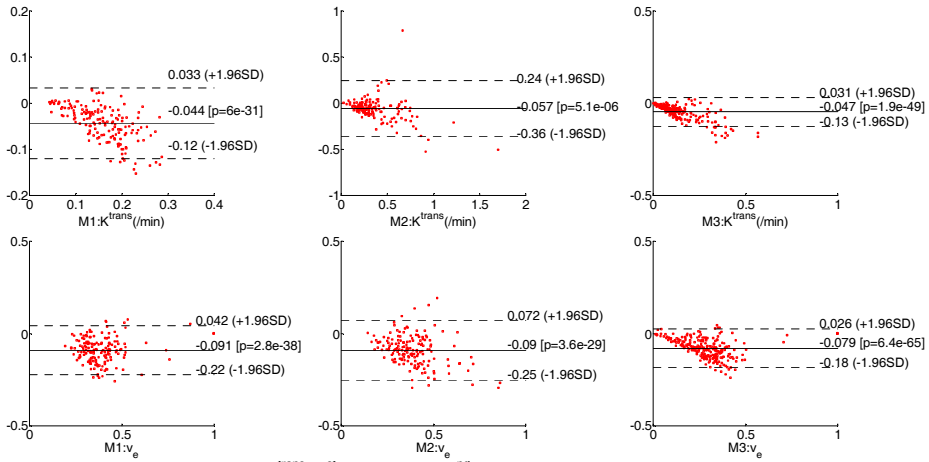

Figure 4: Bland Altman plots for K^{trans} (1st row) and v_e (2nd row) validation for the three animals, one in each

Results: Figure 1 shows sample AIF function and ACE-MRI time-intensity curve which shows step changes of the curves in the washout phase for active encoding of T_{10} and B_1. Figure 2 shows one example of comparison between ACE-MRI and DCE-MRI of GL261 tumor, in terms of GKM model parameters. The T_{10} and B_1 estimated from the model free approach of ACE-MRI in the 1st row appear to match well with the independently measured T_{10}/B_1 in the 2nd row. The GKM model parameters, K^{trans}, v_e and v_p, in both cases appear to be well in agreement as well. Figure 3 shows comparison of the B_1 and T_{10} estimated by ACE-MRI and independent measurement in 3 animals. The Bland-Altman plots [5] shown in Figure 4 demonstrates that the contrast kinetic parameters estimated by the two methods are in good agreement, although there is a weak trend of the difference within the boundaries of agreement.

Discussion: Our preliminary results demonstrate that model free approach of ACE-MRI can combine estimation of pre-contrast T_{10}, RF-coil transmit field sensitivity B_1 and kinetic model parameters together. This technique may reduce the scan time by eliminating the need for separate T_{10} and B_1 measurement in traditional DCE-MRI and also eliminate the need to co-register different modality images for post-processing. Future study is warranted to test the method with a large cohort of animals.

Reference:[1] Zhang and Kim, *Proc. Intl. Soc. Mag. Reson. Med.*(2014). [2] Zhang and Kim, *ISMRM Cancer Workshop.*(2014). [3] Bruker Biospin 7T manual. [4] Dowell N. G, et al, MRM 58:622-630.[5] R. Klein, *Matlab Central File Exchange.*

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