Scan-Rescan Variability in DCE-MRI Comparing Signal Difference and Concentration-Based Methods

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Target Audience: This abstract should be of interest to anyone with an interest in the use of DCE-MRI for the assessment of change over time in blood flow and vascular permeability in either tumors or normal tissues.

Purpose: This experiment was designed to assess the scan-rescan reproducibility in the measurement of vascular parameters obtainable from DCE-MRI scans in patients with solid tumors, and in particular to compare results obtained by converting image pixel values to millimolar concentration of gadolinium to those obtained by making use of simple signal differences in terms of both variability and bias. This experiment addresses the question of whether T1 mapping and conversion of data to gadolinium concentration values are necessary or desirable components of a DCE-MRI study.

Methods: IRB approval was obtained for this experiment, and all patients provided informed consent. Dual baseline DCE-MRI scans were acquired for a total of 43 patients with solid tumors in the chest, abdomen, or pelvis, with temporal separation between scans ranging from 1 – 6 days. Patients were drawn from three different Phase 1 clinical trials across 8 sites. DCE-MRI data were acquired using a 3D fSPGR sequence with an 8cm slab and 42cm FOV. TE/TR/FA were 0.9/2.8/20. Data were reconstructed into 16 5mm slices with a 128x128 acquisition matrix. Temporal resolution was ~4.0s/phase. T1 mapping was carried out using a three sequence multiple flip angle approach, with flip angles of 30, 10, and 3 degrees. Data were analyzed by VirtualScopics (Rochester, NY, USA) using internally developed software. Tumor boundaries were identified by a radiologist, and an arterial input function (AIF) was estimated for each DCE scan[1]. Parameters were estimated first by using signal intensity differences, then by converting signal intensity values directly to millimolar concentration of gadolinium[2]. Vascular parameters were estimated using the standard Tofts[3] model. The model-free parameter $AUCBN_{90}$ ($IAUC_{90}$ normalized by the area under the AIF over the same period) was also estimated.

Coefficients of variability (CoV) were estimated for each calculated parameter for both signal difference images and gadolinium concentration images using the following process: 1. For each pair of measurements, calculate both mean and standard deviation. 2. For each pair, produce an adjusted SD by multiplying the SD by 1.25331 (this adjusts for the bias resulting from estimation using n=2). 3. For each pair, produce a local CoV by dividing the adjusted SD by the mean. 4. Produce a global CoV by averaging the local CoV across all pairs. Bias between parameters estimated using signal difference relative to those estimated using gadolinium concentration values was also calculated.

Results: CoV and relative bias were calculated using 43 distinct tumors, drawn from 34 patients. Of the 43 original patients, scan-rescan data for 9 were not viable due to acquisition errors or poor quality. CoV for the measured parameters are given in Table 1:

Table 1: Coefficients of variability for each measured parameter.

Data Type	Parameter	CoV	95% CI
Signal difference	K^{Trans}	15.5%	10.4% thru 20.6%
Gadolinium concentration	K^{Trans}	20.2%	15.1% thru 25.4%
Signal Difference	$AUCBN_{90}$	14.8%	11.0% thru 18.7%
Gadolinium concentration	$AUCBN_{90}$	20.0%	16.1% thru 23.8%

Discussion and Conclusions: Variability results for K^{Trans} and $AUCBN_{90}$ were generally in line with those that have been reported previously[1]. Variability was lower for both parameters using signal differences. However, this difference was not statistically significant for either K^{Trans} ($p=0.20$) or $AUCBN_{90}$ ($p=0.06$). The explanation for this is that the observed differences were driven by a minority of cases in which the gadolinium concentration data showed very high variability, while for the balance of cases variability between the two methods was similar. In particular, gadolinium concentration estimation showed significantly higher vulnerability to patient motion and other acquisition artifacts, while the signal difference method appeared to be more robust to lower-quality data.

Parameter values calculated using the signal difference method were consistently higher (K^{Trans}: 24% ± 8%, $AUCBN_{90}$: 34% ± 8%) than those calculated using gadolinium concentration values. This is as expected, since the peak AIF concentration will be under-estimated in the signal difference method due to the non-linear relationship between signal change and gadolinium concentration at values exceeding 1mM.

References: 1. Ashton E, Raunig D, Ng C, Kelcz F, McShane T, Evelhoch J: J Magn Reson Imag 2008; 28:791. 2. Ashton E, Shah V: Medical Imaging Principles and Practices, CRC Press, 2013. 3. Tofts P: J Magn Reson Imag 1997; 7:91.