Enhanced perfusion measurement accuracy in DCE-MRI via improved baseline signal estimation

Y. Xue[1], J. Yu[1], M. A. Rosen[1], R. Rengan[2], H. S. Kang[1], S. Englander[1], R. Mick[3], and H. K. Song[1]

[1]Department of Radiology, University of Pennsylvania, Philadelphia, PA, United States, [2]Department of Radiation Oncology, University of Pennsylvania, Philadelphia, PA, United States, [3]Department of Biostatistics and Epidemiology, University of Pennsylvania, Philadelphia, PA, United States

Introduction: Dynamic contrast-enhanced (DCE-) MRI plays an increasingly important role in evaluating tumor perfusion and permeability of the microvascular wall. A spoiled gradient echo sequence is used to measure T_1 changes in tumor tissue and its arterial blood supply induced by the contrast agent. However, since TR is typically much shorter than T_1 of blood (~1200ms) and tumor tissues (~500-1000ms), the pre-contrast tissue signal can be very low, particularly at higher spatial resolutions. Under these low SNR conditions, the measured baseline signal can become biased due to noise which lead to significant errors in the perfusion measurement. In this work, we describe a method to compensate for errors in the baseline signal intensity of DCE-MRI series. The method involves utilization of a separate low flip angle pre-contrast image with substantially higher signal to estimate the true baseline signal of the dynamic series. The proposed methodology was first investigated in simulation experiments, and in vivo studies were carried out in DCE-MRI examinations of patients with lung tumors.

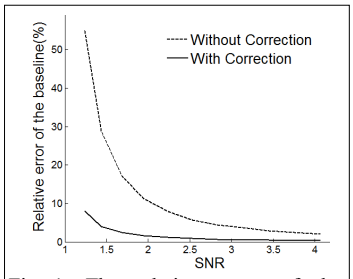


Fig 1. The relative errors of the baseline signal to the true value.

Methods: Blood and tissue signals prior to contrast arrival are often low due to short TRs and relatively large flip angles typically used (>25°). To get a better estimate of the baseline signal, one can use a low flip image (~3°), which has substantially higher signal intensities and which is often already available if the protocol includes measurement of baseline T_1 values (required for the perfusion measurements) using the variable flip angle technique [1]. Simulation experiments were first performed to evaluate the performance of this methodology. Signal for the arterial input function was simulated using an experimentally-derived model described previously [2]. Tumor concentration curves were subsequently generated using Tofts' model with K^{trans} of 0.4 and v_e of 0.5. Dynamic blood and tumor signals were then derived using the following parameters: $T_{10\ blood}$=1200ms, $T_{10\ tumor}$ = 850ms, relaxivity r_1 = 7.9 mM^{-1} sec^{-1} (Multihance), α=25° and TR=3.2ms. Normally distributed zero-mean complex noise with different standard deviations were added to both blood and tumor signals to examine the performance of this method at different SNRs. To test our low-angle baseline substitution methodology, blood and tumor baseline signals at low flip angle ($\alpha=3^0$) were also created and the same levels of noise were added to these data. The measured signals from these low-angle data were subsequently converted to the baseline DCE-MRI signals ("high" flip angle) according to the following equation:

$$Signal_{highFA} = Signal_{lowFA} \cdot \frac{\sin\alpha_{highFA}}{\sin\alpha_{lowFA}} \cdot \frac{1 - E_1 \cdot \cos\alpha_{lowFA}}{1 - E_1 \cdot \cos\alpha_{highFA}} \quad (1)$$

where $E_1=\exp(-TR/T_1)$. The entire baseline blood and tumor DCE-MRI signals were then replaced with the estimated signals. The Gd concentration curves were subsequently converted according to the corrected blood and tumor signal curves and K^{trans} calculated and compared with the true value. The proposed methodology was evaluated in DCE-MRI data acquired in subjects with lung tumors. Each patient had a pair of repeat scans on average two days apart.

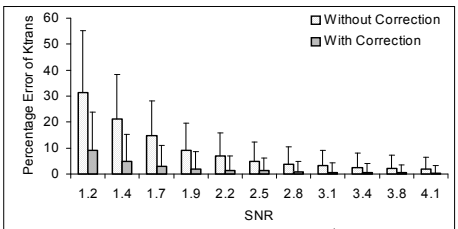
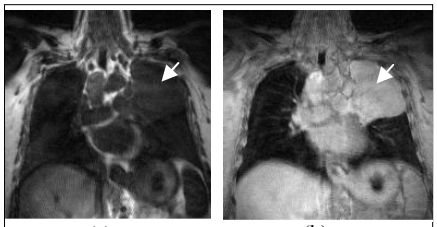


Fig 2. The relative errors of K^{trans} with and without baseline correction.

All scans were performed on a 1.5T Siemens Sonata MRI scanner. 3D DCE-MRI with hybrid radial acquisition scheme with dynamic KWIC reconstruction was utilized [3]. The scan parameters were as follows: coronal plane with FOV= 300 mm, slice thickness = 8 mm, 192 readout points, for 192x192 square pixel images, TR=3.2 ms, TE=1.6 ms, flip angle 25^0 and 32 slices with 80% partial Fourier encoding. Bolus injection of 0.07 mmol/kg Gd contrast (Multihance) at 1cc/sec, followed by a 20 cc saline flush, began two minutes after scanning began. Prior to the dynamic scan, subjects first underwent a native T_1 mapping series using the three-point variable flip angle method [1]. The scan parameters were identical to the DCE-MRI scan, except that the scan time was 2 minutes at each flip angle (3^0, 10^0 and 15^0).

Results and Discussion: Figure 1 shows the relative errors in the pre-contrast baseline signal intensities of the blood to the true value at various simulated SNR levels. SNR is defined as the mean signal measured in blood divided by the mean background signal (where signal is absent) in the pre-contrast magnitude images of the DCE-MRI data. As expected, at higher SNRs (above 3 or so) the baseline signals measured from the DCE-MRI data ($\alpha=25^0$) are close to the true value (< 5% error). However, when the SNR falls below 2, which is typically what we observe in our in vivo data using the above imaging protocols, significant errors occur in the baseline intensity of the DCE-MRI data. In contrast, the low-angle image can provide accurate estimation of the true baseline signal at much lower SNR levels. The signal from the 3^0 flip angle image is roughly a factor of 2.5~3 higher than that of the 25^0 image of the dynamic data set for a T_1 of 1200ms. Figure 2 shows the resulting errors in the computed tumor K^{trans} values (median ± std) at different noise levels. The figure shows that the accuracy of K^{trans} values is improved following correction of the baseline, particularly at lower SNRs. Figure 3 shows the pre-contrast ($\alpha=25^0$) image and pre-contrast low flip angle ($\alpha=3^0$) image, demonstrating the SNR advantage in using the lower flip angle image to estimate the baseline signal. A comparison of K^{trans} values for the two repeat scans with and without baseline correction are shown in Fig. 4. For scan-rescan reliability, the within-patient coefficient of variation (CV) was derived from the within-patient variance of log transformed K^{trans} from a mixed effects model; a model-based approach to estimate variability is preferable when data consist of only 2 scans per patient. The within-patient CV was 11.1% with baseline correction and 28.4% without correction.



(a) (b)

Fig 3. (a) DCE-MRI pre-contrast ($\alpha=25^0$) and (b) low flip angle ($\alpha=3^0$) images of a lung tumor patient. The tumor is indicated by the arrow.

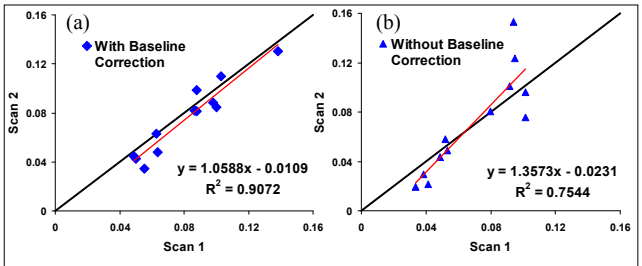


Fig 4. K^{trans} values for the two repeat scans with (a) and without (b) baseline correction.

Conclusion: We have presented a baseline correction method for DCE-MRI by which the low SNR baseline AIF and tumor signals can be more accurately estimated using higher SNR low flip angle data. The resulting perfusion parameter values were significantly improved with this technique. Although we have evaluated radial acquisition methods, same corrections could be applied for standard Cartesian techniques.

Acknowledgments: American Cancer Society RSG-08-118-01-CCE; NIH P41-RR02305; NIH R01-CA125226; NIH R21-CA144190; ASTRO Junior Faculty Career Research Training Award, NIH 1R21CA144190-01A1.

Reference: 1. Cheng et al. MRM 2006; 55: 566-574. ***2.*** Parker et al. MRM 2006; 56: 993-1000. ***3.*** Lin W et al. MRM, 2008. 60:1135-1146.