Correction of Contrast Agent Extravasation Effects in DSC-MRI using Dual-Echo SPIRAL Provides a Better Reference for Evaluating PASL CBF Estimates in Brain Tumors

E. S. Paulson[1], D. E. Prah[1], and K. M. Schmainda[1,2]

[1]Department of Biophysics, Medical College of Wisconsin, Milwaukee, WI, United States, [2]Department of Radiology, Medical College of Wisconsin, Milwaukee, WI, United States

Introduction. Dynamic susceptibility contrast (DSC) and arterial spin labeling (ASL) are two MR perfusion imaging techniques that have the potential of providing absolute quantification of cerebral blood flow (CBF). Recently, several studies have begun to investigate how CBF estimates in normal brain and tumor obtained with ASL techniques compare to those obtained with DSC-MRI [1-3]. These studies have held DSC-derived CBF estimates as a reference or "standard" for evaluating ASL perfusion estimates. However, first-pass DSC time courses resulting from a bolus injection of gadolinium are strongly dependent on the status of the local microenvironment. Specifically, a disrupted blood brain barrier allows some fraction of the bolus to extravasate into the extravascular extracellular space (EES), where dipole/dipole interactions between gadolinium's unpaired electrons and local tissue water protons will cause T1 and T2 shortening. T1 shortening results in signal enhancement that competes with the susceptibility-induced signal decrease whereas T2 shortening results in signal attenuation beyond the susceptibility-induced signal decrease. Both of these effects can confound perfusion estimates obtained with DSC-MRI. We demonstrate here the utility of a combined dual-echo single-shot SPIRAL acquisition and post-processing algorithm to correct DSC-MRI time courses for contrast agent extravasation effects to provide a more accurate reference for evaluating ASL perfusion estimates in normal brain and brain tumors.

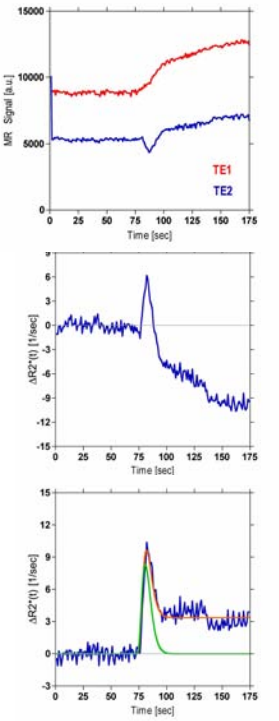
Methods. A prospective study was performed on eight patients with intracranial tumors who underwent perfusion analysis. Acquisition was performed on a 1.5T GE CV scanner (GE Healthcare, Milwaukee, Wisconsin) equipped with 4 G/cm gradients. Pre-contrast CBF images were obtained using a PICORE/QUIPSS II tagging scheme with a single-shot SE-SPIRAL-out sequence used for excitation and readout. The body coil was used for RF transmission and a commercial 8-channel phased array coil was used for reception. Tagging parameters consisted of: inversion time (TI, or TI2): 1400 msec, QUIPSS saturation time (tau or TI1): 700 msec, tag thickness: 20 cm, and tag/imaging slab gap: 1 cm. Acquisition parameters consisted of: field of view (FOV): 24 cm^2, matrix: 64x64, slice thickness: 5 mm, skip: 1.5 mm, number of slices: 12, echo time (TE): 11 msec, repetition time (TR): 2500 msec, repetitions: 84 (83 averages), total scan time: 210 seconds. Immediately following ASL acquisition, DSC images were acquired over the same slice geometry using a dual-echo, single-shot, GRE-SPIRAL-out sequence with the following parameters: TE1=3.3 msec, TE2=30 msec, TR=1000 msec, number of samples (reps)=180. A standard dose of Gadodiamide (0.1 mmol/kg, Omniscan) was injected at the 60th time point. Post-contrast T1W images were then acquired over the same slice geometry, TE/TR/Matrix/NEX/: 10/450/256^2/2.

Data analysis was performed offline using AFNI and additional programs developed at our Institution. The average of difference images obtained using a nearest-neighbor subtraction scheme was used to construct ΔM images from the ASL time series. DSC signal time courses from the second (more strongly T2*-weighted) echo were converted into concentration-time curves (i.e., $\Delta R2^*(t)$) via Equation 1. Note that these concentration-time curves can be contaminated by residual susceptibility and/or dipolar T1 and T2 effects. Correction of T1 leakage effects is achieved by taking the ratio of the second to first echo images at each time point as shown in Equation 2 [4-8]. Note that these concentration-time curves can still be confounded by residual susceptibility and/or dipolar T2 effects. Estimation of the magnitude of the dipolar T2 or residual susceptibility effects is accomplished by fitting a model to the concentration-time curves that accounts for the first pass and residual susceptibility or dipolar T2 effects as shown in Equation 3, where k, t0, alpha, and beta are the fit parameters for a gamma-variate function, and h is used to scale the cumulative integral of the gamma-variate function to the residual post-bolus baseline value [9]. As shown in Equation 4, concentration-time curves corrected for dipolar T1 and T2 and residual susceptibility effects are then generated by constructing a gamma-variate with the model parameters obtained from Equation 3. For CBF estimation, three voxels dominated by arteries were manually-selected from the uncorrected $\Delta R2^*(t)$ in Equation 1 and were averaged together to produce an arterial input function (AIF). Relative CBF was then estimated by deconvolving the AIF from the R2*(t) obtained in Equation 4 using singular value decomposition [10]. For comparison, the ASL ΔM images and DSC Relative CBF images were normalized to contralateral normal brain.

$$[1]\quad \Delta R_2^*(t)_{+T_1,T_2} = -\frac{1}{TE}\ln\left(\frac{S(t)}{S_0}\right) \qquad [2]\quad \Delta R_2^*(t)_{+T2} = \frac{1}{(TE_1 - TE_2)}\ln\left(\frac{S_{TE_2}(t)}{S_{TE_1}(t)}\cdot\frac{S_{TE_{10}}}{S_{TE_{20}}}\right)$$

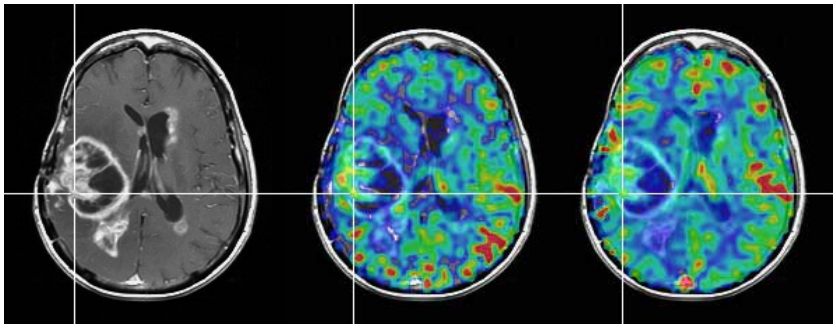
$$[3]\quad \Delta R_2^*(t)' = k(t-t_0)^\alpha e^{-\frac{(t-t_0)}{\beta}} + h\int_0^t k(t'-t_0)^\alpha e^{-\frac{(t'-t_0)}{\beta}}dt' \qquad [4]\quad \Delta R_2^*(t) = k(t-t_0)^\alpha e^{-\frac{(t-t_0)}{\beta}}$$

Figure 1: (top-to-bottom) Dual-echo time series', $\Delta R2^*(t)_{+T1T2}$ from Eqn 1., Correction of $\Delta R2^*(t)$ using Eqns 3 and 4.



Results and Discussion. Figure 1 displays a representative DSC-MRI voxel time course selected from a region of tumor. Note that significant contrast agent extravasation effects are apparent in the top and middle windows of Figure 1, but have been corrected for in the green curve depicted in the bottom window of Figure 1, which is used to determine CBF. Figure 2 displays post contrast T1W anatomical, and rCBF maps obtained from PASL and DSC, respectively. It is evident that ASL CBF estimates correlate well with DSC CBF estimates in both normal brain and tumor regions. In addition, both methods appeared to have similar rCBF contrast between normal gray and white matter. Similar results were obtained among all 8 patients studied.

Figure 2: (left-to-right) Post-contrast T1W image, PASL rCBF map, DSC rCBF map.



These results suggest that correction of DSC-MRI time courses using a dual-echo acquisition method, which compensates for T1 leakage effects, combined with a post-processing algorithm for correcting dipolar T2 and residual susceptibility effects may result in a superior reference for evaluating perfusion estimates in normal brain and brain tumor obtained with ASL techniques. Future work will include sequence parameter optimization, the collection of pre-contrast T1 maps to facilitate calculation of absolute CBF, and an independent validation of the newly described method with the goal of defining the most accurate method for estimating brain tumor perfusion.

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