On the Use of DSC-MRI for Measuring Vascular Permeability

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TARGET AUDIENCE: Researchers interested in obtaining measures of vascular permeability from DSC-MRI data.

PURPOSE: Contrast agent (CA) extravasation has been shown to confound measurements of tissue perfusion extracted from dynamic susceptibility contrast (DSC)-MRI experiments. Leakage of CA can manifest as T_1 and/or T_2^* effects in the dynamic ΔR_2^* tissue time-course. Weisskoff [1] and Boxerman [2], and more recently Bjornerud [3] et al, have developed correction techniques for mitigating these effects in DSC-MRI measures of perfusion (e.g. CBV). Intrinsic to the correction methods themselves, parameters (K_2 and K_a) can be extracted that have been postulated to reflect vessel permeability. In addition, dual gradient-echo acquisitions have also been used to mitigate T_1 leakage effects [4]. A by-product of these measurements is the ability to extract dynamic T_1-weighted information from the DSC-MRI data [5,6]. This information can be used in conjunction with traditional DCE-MRI pharmacokinetic modeling to extract measures of the volume transfer constant K^{trans} [6,7]. With the ability to simultaneously compute the previously described parameters, the goal of this study was to investigate the use of DSC-MRI for estimating vascular permeability via *in vivo* voxel-wise comparisons of single- and multi-echo derived measures of K_2, K_a and K^{trans}. In addition, the availability of dual-echo data allows further exploration of potential echo time dependencies and competing T_1 and T_2^* leakage effects on measures of K_2 and K_a.

METHODS: Multiple gradient-echo data were acquired in high-grade glioma patients (n = 7) at 3T (Achieva, Philips Healthcare) using a 32 channel head coil for data reception. Either dual gradient-echo EPI (DE) or SAGE EPI data [7] were acquired with: TR = 1.5s (DE) or 1.8s (SAGE), TE_1/TE_2 = 7.0/31.0ms (DE) or 8.3/25ms (SAGE), SENSE = 2, FOV = 240 x 240mm^2, Voxel Size = 2.5 x 2.5 x 5.0mm^3, and slices = 15. Measurements were made before, during, and after administration of Gd-DTPA (0.1 mmol/kg, infusion rate = 4ml/s). The scan duration was 7.5 minutes. Dynamic estimates of ΔR_2^* were computed for each echo ($\Delta R^*_{2,TE1}$ and $\Delta R^*_{2,TE2}$). Additionally, an arterial input function (AIF) was extracted from the dual-echo data using an automated process [8]. K_2 was computed as previously described [1,2] using 80s of pre-bolus baseline data and 70s of post-bolus data (2.5 min total) in the model fit. Following the work of Bjornerud et al. [3], K_a was computed from the tail of the tissue residue function using 60s of data after a time equivalent to the mean transit time (MTT). To compute K^{trans}, T_1-weighted signal time-courses were extracted from the dual-echo data [5-7] and combined with a pre-contrast T_1 map to produce R_1 time-courses. Tofts' modeling [9] was then performed to estimate K^{trans} and v_e. In this study, a voxel exhibiting T_2^* effects ('T_2^* voxel') (T_1 effects ('T_1 voxel')) was defined by a positive (negative) mean $\Delta R_{2\ TE2}^*$ over a 20s period following the first pass of the CA.

Table 1. Correlation between leakage correction and DCE-MRI model parameters.

	K^{trans}		K^{trans}		v_e		v_e	
Patient	K_2 (TE_2)	K_a (TE_2)	K_2 (TE_1)	K_a (TE_1)	K_2 (TE_2)	K_a (TE_2)	K_2 (TE_1)	K_a (TE_1)
1	0.033	-0.025	0.260	-0.114	0.408	-0.362	0.755	-0.751
2	-0.142	-0.032	0.481	-0.495	0.057	-0.139	0.710	-0.601
3	0.286	-0.276	0.336	-0.321	0.827	-0.797	0.889	-0.865
4	0.013	-0.053	0.337	-0.238	0.393	-0.307	0.656	-0.474
5	0.332	-0.201	-0.523	-0.529	0.585	-0.516	0.715	-0.691
6	0.302	-0.280	0.400	-0.398	0.501	-0.451	0.617	-0.612
7	0.374	-0.418	0.621	-0.630	0.744	-0.739	0.919	-0.919

RESULTS AND DISCUSSION: Both K_2 and K_a were found to have a poor voxel-wise linear correlation with K^{trans} (Table 1). When computed at TE_1, only moderate increases in correlations were observed. A strong inverse relationship was observed, however, between K_2 and K_a [R = 0.689-0.994]. Contributing to these correlations, Fig. 1 shows the effect of T_1 and T_2^* leakage effects on the dynamic relaxation rate time-courses. Significantly different ($p < 0.05$) mean estimates were found between T_1 and T_2^* voxels across patients for K_2 (2.429 min^{-1} vs 0.359 min^{-1}) and K_a (-0.335 min^{-1} vs -0.118 min^{-1}). K^{trans}, however, was observed to be almost identical (0.214 min^{-1} vs 0.212 min^{-1}) between cohorts, displaying insensitivity to the type of CA leakage effect. Significant differences in v_e (0.457 vs 0.301) were also observed between cohorts, validating the observation of larger v_e with 'T_1 voxels'. Interestingly, both K_2 and K_a were found to have moderate to strong correlations with v_e (Table 1) at both echo times, suggesting a relationship between these parameters and the extravasation space of the CA.

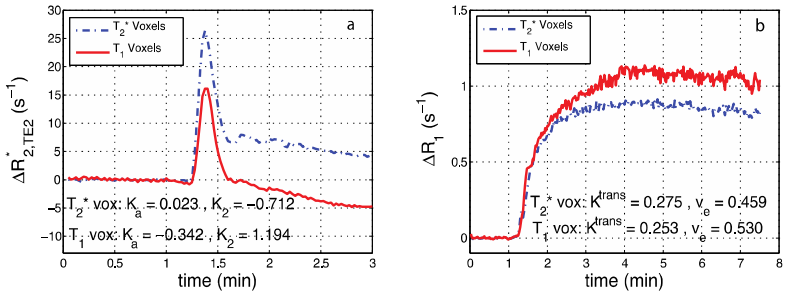

Figure 1. a) Mean ΔR_2^* curves from a tumor ROI for voxels with predominately T_2^* (blue dashed) or T_1 (red) leakage effects. b) ΔR_1 curves from the same cohorts.

CONCLUSION: Vascular permeability may be simultaneously estimated from multiple-echo DSC-MRI using the pharmacokinetic parameter K^{trans}. Model parameters extracted from single-echo DSC-MRI leakage correction techniques, K_2 and K_a, were found to poorly correlate with K^{trans}, due in part to the effect of competing T_1 and T_2^* leakage and the influence of pulse sequence parameters. A moderate correlation was found, however, between K_2 and K_a and the extracellular-extravascular tissue space. Therefore, caution should be used in assuming a direct relationship between these parameters and the actual vessel permeability.

REFERENCES: 1. Weisskoff RM et al. Proc Soc Magn Reson 1994; 279. 2. Boxerman JL et al. AJNR 2006; 27(4): 859. 3. Bjornerud A et al. J Cereb Blood Flow Metab 2011; 31(10): 2041. 4. Paulson E et al. Radiology 2008; 249(2): 601. 5. Vonken EP et al. Magn Reson Med 2000; 43(6): 820. 6. Quarles CC et al. Magn Reson Imag 2012;30(7):944. 7. Skinner JT et al. Magn Reson Imag 2014; Early View. 8. Newton AT et al. Proc Int Soc Magn Reson Med 2013; 3064. 9. Tofts PS et al. J Magn Reson Imaging 1999; 10(3): 223.