Correction of Bolus Dispersion in the quantification of perfusion and haemodynamics using DSC-MRI

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Target Audience: Scientists and Clinicians with an interest in perfusion MRI

Introduction: DSC-MRI quantification requires the measurement of an arterial input function (AIF) for the voxel-wise deconvolution of the concentration time curve (CTC). Deconvolution allows estimation of both Cerebral Blood Flow (CBF) and the tissue residue function (R(t)); with R(t) encapsulating information about capillary haemodynamics [1]. It has been recently shown that the Control Point Interpolation (CPI) method is able to robustly evaluate variations in the shape of R(t) in pathology [2–4]. In practice a global AIF is often measured at a site distant from the tissue voxel; during transit the measured AIF is deformed by dispersion. If dispersion is not taken into account, it can lead to underestimation of CBF and distort R(t) preventing the evaluation of variations in shape [5]. The effects of dispersion can be separately modelled with the inclusion of a dispersion kernel (DK) [6] into the analysis; however the appropriate DK to model dispersion *in vivo* is not known. In this work, we correct for dispersion within the CPI technique using three DKs. We investigated the effects of dispersion both on quantification of CBF and accuracy in estimation of true residue function.

Table 1: Three DKs and the value of dispersion parameters used in simulations

Dispersion Kernel	Parameters	Dispersion values used for Simulations
$GDK(t) = \frac{s^{1+sp}}{\Gamma(1+sp)} \cdot t^{sp} \cdot e^{-st}$	p: time-to-peak s: sharpness DC = $1/s$	Low: p =1s, s =2 Medium: p =3s, s=1 High: p =5s, s=0.5
$EDK(t) = \frac{1}{\theta} e^{\frac{-t}{\theta}}$	θ: time constant DC = θ	Low: θ =1s Medium: θ =2s High: θ =4s
$LNDK(t) = \frac{1}{t\sigma\sqrt{2\pi}} e^{\frac{-(\ln(t)-\mu)^2}{2\sigma^2}}$	σ: shape parameter μ:location parameter DC = σ	Low: σ =1s; μ = -1 Medium: σ =0.75s, μ = -0.15 High: σ =0.78s, μ =0.59

Methods: Simulations were performed with Cerebral Blood Volume=4ml/100g, CBF in the range 10-60 ml/100g/min, exponential tissue R(t) and 3 DKs to model dispersion (table 1): 1) Gamma DK (GDK) [6], 2) Exponential DK (EDK) [7] and 3) Log-Normal DK (LNDK) [8]. A range of low to high level of dispersion were evaluated (shown in table 1). CTC were generated as in [2], converted to signal time course with an SNR = 50 (100 realisations). The simulated data were analysed using 5 methods: a) delay insensitive SVD (oSVD) [9], b) CPI [2], and c-e) CPI with DK, which introduced extra parameters of the DK to be estimated. Accuracy in residue function achieved by the methods was performed by calculating the sum of squared error (SSE) for estimated residue function against simulated, and accuracy in CBF estimation with the ratio of CBF (CBFratio) as estimated CBF against true CBF. For empirical evaluation, perfusion data were retrospectively analysed from a patient (65yrs, F) with atherosclerotic disease (ICA stenosis left 90%, right 40%). Under institutional review board approval, DSC data were acquired on a Siemens 3T Trio using single-shot gradient-echo EPI: *TR/TE*=1.5sec/30msec, 78 volumes, 128x128x22 matrix, 1.7x1.7x5 mm^3 voxels. A bolus injection of 0.1 mmol/kg Magnevist® was performed (injection rate = 10ml/s) followed by a 20 ml saline flush. In each case a single parameter from the estimated DK was used as measure of dispersion *in vivo,* referred to as the *dispersion co-efficient* (DC, table 1), chosen such that higher values of DC were associated with more dispersion.

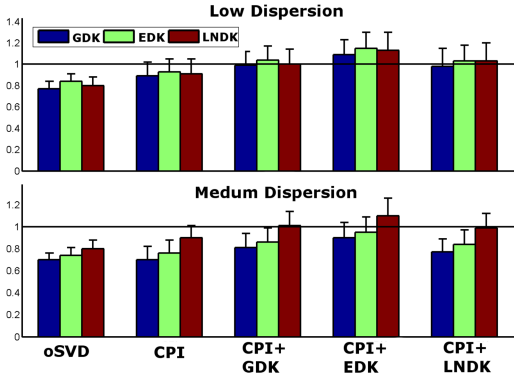

Figure 1: CBFratio at low and medium dispersion with GDK, EDK and LNDK.

Table 2: SSE in estimation of R(t) by five analysis methods under conditions of simulated no and low to high levels of dispersion with multiple DKs.

	Analysis Models				
Dispersion Simulation	**oSVD**	**CPI**	**CPI + GDK**	**CPI + EDK**	**CPI + LNDK**
No	0.92±0.28	0.17±0.25	0.16±0.16	0.23±0.20	0.20±0.24
GDK					
Low	1.92±0.35	0.23±0.33	0.16±0.17	0.19±0.17	0.23±0.29
Medium	4.31±0.52	1.42±1.55	0.47±0.62	0.33±0.43	0.81±0.74
High	7.26±1.00	6.2±3.84	3.18±2.39	1.92±1.30	2.85±1.44
EDK					
Low	1.41±0.33	0.27±0.45	0.14±0.16	0.20±0.21	0.23±0.34
Medium	2.20±0.38	0.77±0.88	0.35±0.49	0.23±0.27	0.57±0.58
High	3.89±0.61	2.76±2.18	1.53±1.35	0.99±0.86	1.96±1.37
LNDK					
Low	1.22±0.34	0.25±0.52	0.15±0.19	0.21±0.19	0.19±0.29
Medium	1.60±0.36	0.23±0.28	0.15±0.15	0.21±0.21	0.22±0.25
High	2.53±0.39	0.78±0.96	0.34±0.45	0.21±0.24	0.54±0.54

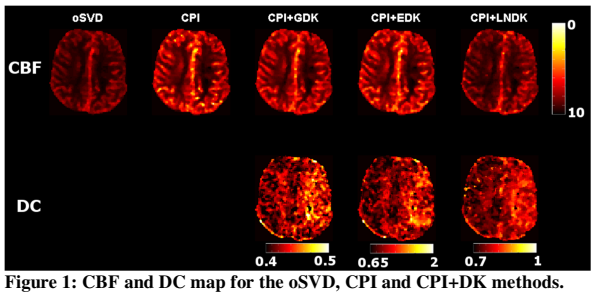

Figure 1: CBF and DC map for the oSVD, CPI and CPI+DK methods.

Results: oSVD underestimated CBF by 15% to ~45% in cases where there was no or high level of dispersion, respectively. Figure 1 shows the CBFratio for the five analysis methods under conditions of Low-Medium dispersion. CPI was found to be most accurate in CBF estimation in the case of no dispersion however in combination with DK (CPI+DK) it tended to overestimate CBF by 10-18% (data not shown). CPI+DK performed consistently better than oSVD and CPI in case of dispersion. Table 2 shows the SSE in estimation of R(t) for all the methods. CPI and CPI+DK showed smallest error in estimation of R(t) with no significant difference in case of no dispersion. CPI+DK showed significant benefit over CPI for estimation of R(t) in case of simulated dispersion. The error in the estimation of residue function increased from low to high level of dispersion with all the methods. Figure 2 shows the CBF and DC map for a patient; CPI+LNDK had lower estimates of CBF than CPI+GDK and CPI+EDK. All the CPI+DK methods had similar performance in estimation of spatial variations in dispersion.

Discussion: CPI+DK tended to overestimate CBF (by 10-18%) in simulations with no dispersion which suggests that *in vivo* overestimated CBF might be observed in healthy tissue. Although, a single global AIF is commonly used for analysis *in vivo* and some dispersion (probably low) might be expected even in the contralateral tissue. Thus this error is likely to be reduced *in vivo*. It was found that addition of a DK to correct for effects of bolus dispersion in perfusion analysis was useful both in simulations and *in vivo*. However, selection of appropriate DK model remains uncertain, as no consistent benefit of one DK over others was observed neither in simulations nor in *in vivo* analysis. An analysis of dispersion in Arterial Spin Labelling angiography [6] has advocated the use of a GDK to model dispersion *in vivo* and similar arguments could be used for DSC perfusion.

Conclusion: A Dispersion kernel within the CPI method provides a robust measure of CBF and accurate estimation of shape of residue function in the presence of dispersion. No DK had significant benefit over others both in simulation or *in vivo*, however, their use in combination with CPI is recommended for the analysis of patient data where dispersion is suspected.

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