CBF quantification in the face of dispersion and separation of its effects from normal cerebral haemodynamics: a comparison of deconvolution methods in DSC-MRI

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

Introduction: Bolus dispersion is a recognised effect in perfusion techniques that involve a global arterial input function (AIF) from a site distant that is used to characterize tissue signals, typically via a deconvolution operation; the problem is likely to be amplified in cases of cerebral ischemia. Dispersion introduces errors in the Cerebral Blood Flow (CBF) estimates [1] and it is generally not possible to separate the effects of dispersion from the true residue function when using the common singular value decomposition methods [2]. In this work we investigated dispersion on two levels: 1) in terms of CBF accuracy, and 2) the ability to isolate dispersion effects in the residue function. Our study assessed a range of deconvolution approaches, including those specifically designed to handle bolus dispersion. Specifically, we have extended our recently proposed control point interpolation (CPI) method [3] to address the issues of dispersion.

Methods: Simulations were performed with Cerebral Blood Volume=4ml/100g, CBF in the range 10-60 ml/100g/min, exponential tissue residue function (TRF), and two vascular transport functions (VTF) to model dispersion: 1) Gamma and 2) Exponential kernels [1]. The Gamma kernel was parameterised by the following: time-to-peak (ttp) and sharpness (s) [4]; a range of low to high dispersion were evaluated using ttp = 1-5sec; s = 2-0.5sec^{-1}. The Exponential kernel was parameterised by one parameter time-constant (tconst) that was varied from 1-5sec. Concentration time curves were generated as in [2], converted to signal time course, to which Gaussian noise was added to achieve an SNR = 50 (100 simulations). The simulated data were analysed using 6 deconvolution methods: a) delay insensitive SVD (oSVD) [2], b) vascular model (VM) [5], c) VM with a VTF, which introduces extra parameters of the VTF to be estimated, d) CPI [3], and e-f) two extended variants of CPI (see below). Quantification of residue function fitting achieved by the methods was performed by calculating the coefficient-of-determination, R^2 for estimated residue function against simulated, and accuracy of CBF estimation with the regression coefficient (*Y*) for estimated CBF against simulated CBFs.

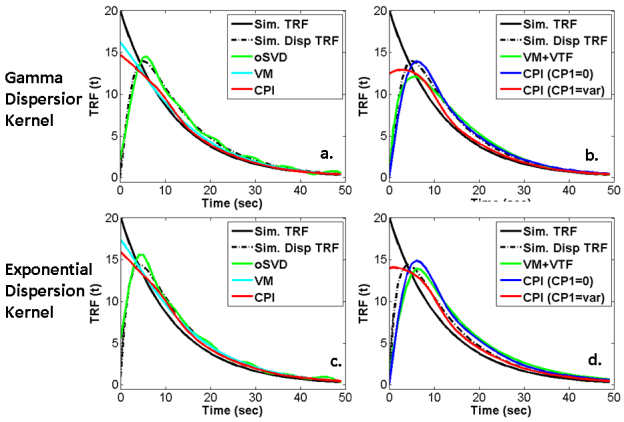

Figure 1: Simulated TRF, dispersed TRF, mean fit achieved with oSVD, VM, CPI (a,c); VM+VTF, CPI (CP_1=0), CPI (CP_1=var.) (b,d). Gamma Dispersion Kernel (a,b) and Exponential Dispersion Kernel (c,d).

In CPI the residue function is estimated from a set of control points (CP) that form the basis of a smooth piecewise cubic spline interpolation [3]. Each CP is allowed to vary in both amplitude and time, except for the first CP that is set to 1 (CP_1=1). This CP_1 restriction could lead to errors when applied to dispersed data, where the initial value of the residue function subject to dispersion may no longer be unity [1]. Two possible solutions were considered: i) CPI (CP_1=0): CP_1 fixed at 0, ii) CPI (CP_1=var.): CP_1 has a variable amplitude (range 0-1) that is an additional parameter of the method.

Results: Figure 1 shows the simulated and dispersed tissue response function and mean fitting achieved with oSVD, VM, CPI (a,c) and with dispersion corrected methods (b,d), for gamma and exponential dispersion kernels used. Table 1 show the results with a moderate degree of dispersion (ttp=1.5, s=0.7, tconst=2). oSVD showed poorest performance at CBF estimation; VM+VTF with dispersion correction was found to be superior to VM alone in residue function shape estimation but CBF estimates were still not accurate. Both dispersion corrected variants of CPI method performed better than other methods used. CPI (CP_1=0) was found to be more precise at residue function shape estimation (R^2=0.93-0.97) (fig.1 b,d) whereas CPI (CP_1=var.) was found to be more accurate in CBF estimates (*Y*=0.93-0.99) in comparison to all other deconvolution methods used. Similar findings were obtained for the other simulated dispersion conditions.

Table 1: Regression coefficient (*Y*) for CBF estimate and coefficient-of-determination (R^2) for residue function shape estimate by six deconvolution methods using gamma and exponential dispersion.

	Coefficients	oSVD (a)	VM (b)	VM + VTF (c)	CPI (d)	CPI (CP_1=0) (e)	CPI (CP_1=var.) (f)
Gamma Dispersion	***Y***	0.60	0.62	0.75	0.63	1.13	0.93
	R^2	0.85	0.67	0.93	0.67	0.97	0.74
Exponential Dispersion	***Y***	0.65	0.67	1.11	0.70	1.23	0.99
	R^2	0.83	0.75	0.90	0.73	0.93	0.77

Discussion: Bolus dispersion is a practical problem in perfusion analysis, which is often ignored because of its unknown characteristics. It was hypothesised in the past that the true residue function and dispersion could be separated if a model-based approach is used (parameterising both the true residue function and dispersion). However, these simulations suggest that even a complete model-based deconvolution (VM+VTF) cannot clearly distinguish the two, leading to underestimation of CBF. Models with a more constrained relation between bolus arrival delay and dispersion have been proposed [6], but the existence of such a relationship still needs to be validated. Additionally, *in vivo* the actual residue function shape and VTF are both not known *a priori*, particularly in pathology. The CPI approach provides a method to avoid the strict model-based assumptions for the residue function and VTF, whilst still offering a smooth interpretable residue function estimate. Here a variant on the original CPI method was found to offer reasonable CBF estimation in the face of dispersion. However, CPI does not directly permit the separation of true residue function from the effects of bolus dispersion. Ultimately a further deconvolution of estimated dispersed residue function with an appropriate model of VTF might be required to separate these effects, where again some assumption has to be made for VTF. However, this may remain difficult given that there appears to be insufficient information in the MR signal to separate the two, even when both are reasonably well constrained as in the VM+VTF example. In practice, therefore, methods that derive more local AIFs might be favourable, assuming that these can be extracted with sufficient accuracy. Even though the ambiguity between the true residue function and dispersion cannot be resolved with any of the six deconvolution methods used, accurate estimates of cerebral perfusion can still be achieved with an effectively non-parametric CPI approach.

Conclusion: Accuracy of perfusion estimation even in the presence of dispersion can be improved using the CPI method, but separation of tissue haemodynamics and bolus dispersion could not be achieved because of their complex interaction.

References: [1] F. Calamante, *JMRI*, vol. 22, no. 6, pp. 718–22, 2005. [2] O. Wu et al; *MRM*, vol. 50, no. 1, pp. 164–74, 2003. [3] A. Mehndiratta et al; NeuroImage, 2012. [4] M. a Chappell et al; *MRM* 2012. [5] K. Mouridsen et al; *NeuroImage*, vol. 33, no. 2, pp. 570–9, 2006. [6] J. J. Mouannes-Srour et al; *MRM* 2011.