Modelling the Bolus Dispersion from DSC-MRI data

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Introduction

Perfusion maps calculated from the deconvolution of a dynamic susceptibility contrast (DSC)-MRI data are commonly used to make predictions of tissue that may infarct after acute stroke (1). However, since the arterial input function (AIF) used in the deconvolution is often measured in a major artery, there may be dispersion of the bolus of contrast during its passage from the artery to the tissue where the perfusion is to be measured. Bolus delay and dispersion are expected in patients with vascular abnormalities, such as stenosis, occlusion or collateral flow. It has been shown that dispersion introduces an underestimation of cerebral blood flow (CBF) and overestimation of mean transit time (MTT) measurements (2). This bias has important implications for the classification of ischemic tissue, and hence the selection of patients for treatment. An assessment of the bias is difficult since the function describing the transport of the bolus through the vasculature (the vascular transport function, VTF) is unknown. In a previous study the VTFs in a group of patients with vascular abnormalities were empirically determined (3). In this present work, a function is presented that is flexible enough to accurately describe the large range of dispersion observed. A realistic model for the VTF will facilitate the simulation of DSC-MRI data to describe a variety of cerebrovascular situations. Testing on simulated data sets (where the true perfusion values are known) has now become a crucial stage in the development of any DSC-MRI analysis technique. A model for the VTF is therefore an important step in the assessment of perfusion measurement errors.

Theory

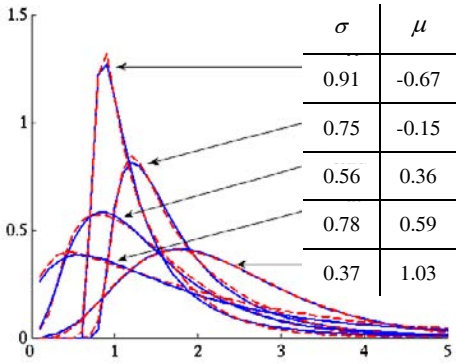
The VTF is the probability distribution of transit times between the major artery used to estimate the AIF, $C^{est}{}_a(t)$, and the tissue input where the true local AIF, $C^{true}{}_a(t)$, is defined, such that (3):

$$C^{true}{}_a(t) = C^{est}{}_a(t) \otimes VTF(t) \qquad [1]$$

Theoretical fractal modelling has shown that the flow distribution through a vascular network can be described by a lognormal distribution (4). One might expect there to be a corresponding lognormal distribution of transit times. Formally, a lognormal distribution of transit time t is written as (5):

$$VTF(t) = \frac{1}{(t-t_0)\sigma\sqrt{2\pi}} \exp\left(-\frac{1}{2\sigma^2}(\ln(t-t_0)-\mu)^2\right) \qquad [2]$$

The skewness of the VTF shape is determined by σ, the scale by μ and the location by t_0. These parameters will depend on the arterial network structure as well as possible stenosed or occluded arteries. Thus, a unique VTF describes dispersion to each voxel in each patient.



σ	μ	t_0 /s	MVT T /s	VVT T /s^2
0.91	-0.67	0.54	0.78	0.80
0.75	-0.15	0.63	1.14	1.00
0.56	0.36	-0.30	1.67	1.22
0.78	0.59	-0.51	2.45	5.01
0.37	1.03	-0.78	3.00	1.32

Figure 1: Experimental VTF (dashed) (3) and lognormal fit (solid)

Methods

In a previous study, 20 characteristic examples of the VTF from in vivo data in 15 patients with various cerebrovascular abnormalities were measured (3). This was achieved by deconvolving Eq. [1] for a global AIF (measured in the middle cerebral artery), and calculated local AIFs (using independent component analysis (6)); the VTFs were subsampled at 0.1s over 20s.

In the present study, the same experimental VTF data were modelled with a three-parameter lognormal distribution (Eq. [2]). The mean and variance of the vascular transit time (MVTT and VVTT respectively) were also calculated from the fitted distributions (4):

$$MVTT = \exp\left(\mu + \frac{\sigma^2}{2}\right) \qquad [3] \qquad VVTT = \left(\exp(\sigma^2)-1\right)\exp(\sigma^2 + 2\mu) \qquad [4]$$

Note that the *MVTT* definition given here does not take into account the shift parameter t_0.The parameter ranges for μ, σ and t_0 found to describe the real data (see Results) were used define parameter ranges for a simulated set of lognormal VTFs. 528 VTF were simulated for each combination of parameter values: σ ranging 0.2 to 1.2s in steps of 0.2s, for μ ranging -1.5 to 2.0s in steps of 0.5s, and t_0 ranging -1.0 to +1.0 in steps of 0.2s. Corresponding MVTT and VVTT values were calculated and compared with experimental values.

Results

Real data: Figure 1 illustrates five experimental VTFs (dashed lines) and their lognormal fit (solid lines). Across the 20 VTFs, σ was found to vary between 0.30 and 1.05s, (larger σ gives a more skewed VTF), μ between -0.83 and 1.5s, (larger μ gives a broader VTF), t_0 between -1.37 and 1.82s, the MVTT between 0.66 and 5.50s, and the VVTT between 0.22 and 9.29s^2.

Simulated data: For each simulated value of μ, the simulated values of σ found to give an experimentally consistent MVTT and VVTT are given in Table 1. VTF defined with the largest σ appear approximately exponential, becoming more bell-shaped as σ is decreased. For each σ, VTFs defined with the smallest μ appear sharpest, becoming broader as μ is increased. Figure 2 exemplifies two simulated VTFs: The dashed line represents a mild stenosis (σ =1.0s, μ =-1.0s and t_0=0.2s, MVTT=0.607s and VVTT=0.632s^2). The solid represents a more severe stenosis (σ =0.2, μ =1.5 and t_0=-1.1s, MVTT=4.572s and VVTT=0.853s^2) (3).

μ	σ
-1.5	1.0-1.2
-1.0	0.8-1.2
-0.5	0.6-1.2
0.0	0.4-1.2
0.5	0.2-1.0
1.0	0.2-0.8
1.5	0.2-0.6
2.0	0.2-0.4

Table 1: Lognormal parameter ranges for realistic VTFs

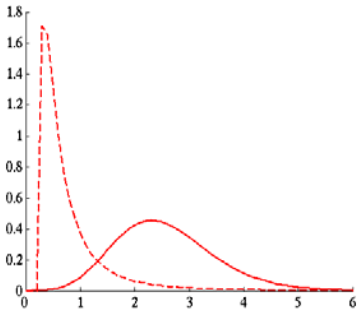


Figure 2: Simulated VTFs: dashed =mild dispersion, solid = severe dispersion

Discussion

The experimental VTFs show that a mild stenosis may be modelled with exponentially decaying VTF (3). This model has been assumed in many DSC-MRI simulation studies (e.g. (2)). However, an exponential model is incorrect for flow through a more severe stenosis (3). The lognormal was found to characterise the VTF for both mild and severe stenosis within a fairly narrow range of lognormal parameter values (Table 1). The experimentally informed VTF model for dispersion presented here could be used to simulate more realistic and flexible DSC-MRI data sets. These would be valuable for testing DSC-MRI analysis techniques across a broad range of cerebrovascular situations, and for the estimation of dispersion related perfusion measurement errors. Ultimately, this could have important implications for predictor models that utilise DSC-MRI perfusion maps to predict tissue infarction.

References

(1) Wu et al. (2001) Stroke 32:933. (2) Calamante et al. (2000) MRM 44:466. (3) Calamante at al. (2006) MRM 55:1185. (4) Qian et al. (2000) J theor Biol. 205:261. (5) Limpert et al. (2001) BioScience 51:341. (6) Calamante et al. (2004) MRM 52:789.