IMPROVING AND VALIDATING A LOCAL AIF METHOD

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Introduction: Simulation and *in vivo* studies of DSC-MRI have shown that in stroke patients the contrast bolus can be delayed and/or dispersed (D/D) in time as it flows through abnormal vasculature [1,2]. When a global arterial input function (AIF) is used in the deconvolution analysis, these distortions can result in a significant overestimation of the tissue Mean Transit Time (MTT), and underestimation of Cerebral Blood Flow [3], thereby exaggerating any perfusion abnormality. One approach to reduce such perfusion errors is to try and remove D/D from the analysis by using local AIFs estimated closer to the actual tissue input and downstream of the abnormal vasculature. These cannot be measured directly because of partial volume effects, but may be estimated using various techniques eg. [4,5,6]. Although some studies have investigated the role of local AIFs in predicting stroke outcome [7,8], to date there have been no published studies validating the estimated local AIFs.

The method in [6] (referred to herein as method1) identifies the local AIFs as the bolus concentration time-course C(t) in the voxels located at the local minima in a map of the First Moment (FM) of C(t), FM[C]. Method1 however is biased towards identifying local AIF voxels in short MTT tissue. This may not be appropriate for defining local AIFs in transition regions between normally and abnormally perfused tissue. In this work we improve method1 by minimising its sensitivity to MTT. We assess the improvement by comparing the amount of D/D remaining in the deconvolved tissue response after each local AIF approach and compare both methods with the standard global AIF analysis. The D/D is measured using Maximum-Likelihood Expectation-Maximisation deconvolution regularised with an oscillation-index and wavelet-thresholding (owMLEM) [9], which has been shown to accurately characterise the tissue response and hence identify residual D/D [9,10].

Methods: Using simulated data as described in [9,11], the FMs of C(t), and of the oSVD [12] deconvolved tissue response oR(t), were calculated. Because of noise and large sampling intervals TR, it was necessary to fit C(t) to gamma-variate functions [11]. Similarly, the oR(t) were interpolated in the Fourier domain [13] prior to calculating their FM and time-to-maximum value (Tmax). It is common for DSC-MRI images to be aquired with TR>1.5s. At this temporal resolution, it is not possible to distinguish a bolus delay from bolus dispersion, even in the ideal case of no deconvolution errors [9]. We therefore consider it appropriate to use Tmax to indicate the presence of both bolus delay and/or disperion (D/D), since Tmax increases in the presence of either (see Results, Figure 1a/b).

The equation governing perfusion analysis is $C \propto AIF \otimes R \otimes VTF$, where R is tissue residue function and VTF is the Vascular Transport Function describing the D/D through the vasculature [3]. Since FMs are additive under convolution, the relationship becomes $FM[C]=FM[AIF]+FM[R]+FM[VTF]$. By definition, $localAIF=AIF \otimes VTF$, therefore $FM[localAIF]=FM[C]-FM[R]$. oSVD deconvolution using a global AIF provides an estimate of $R \otimes VTF$, therefore $FM[oR]=FM[R]+FM[VTF]+\varepsilon$, where ε contains the deconvolution errors. By making the approximation, $FM[VTF]=Tmax$, an approximation to FM[localAIF] may be obtained: "FM[localAIF]"=FM[C]-FM[oR]+Tmax. We sought to minimise the influence of the tissue MTT on the selection of local AIF voxels by identifying the local AIFs as the C(t) in voxels located at the local minima in a map of "FM[localAIF]" (referred to herein as method2).

Maps of FM[C] and "FM[localAIF]" were calculated in 8 sub acute stroke patients, selected to have a perfusion mismatch using global AIF analysis. For each FM map the local AIFs were found by screening the 3x3x3 voxel neighbourhood for lower FM values until a local minimum of FM was found [11]. oSVD MTT maps were calculated using the local AIFs obtained by method1 and method2, and compared with those obtained using a global AIF. The success of the methods in removing D/D was measured by calculating the owMLEM deconvolved response functions owR(t) [9], interpolating them in the Fourier domain [13] and measuring Tmax. In regions where the local AIFs have successfully removed D/D from the deconvolution, Tmax will be very small. In areas where Tmax>0, MTT may still be overestimated.

Results: Figure 1 shows some results from the simulations demonstrating the dependence of the FMs and Tmax on delay, dispersion and MTT. Although FM[C] has the desired dependence on delay and dispersion, it is also strongly dependent on the tissue MTT. "FM[localAIF]" also increases with delay and dispersion, but has much less dependence on MTT.

In the patient data, the extent and severity of the MTT abnormalities and the regions of Tmax>0 were reduced in all 8 patients using both method1 and method2 compared with the global AIF analysis. In 4 of the 8 patients, method1 and method2 gave equivalent results. In the remaining 4 patients, method2 reduced the regions of Tmax>0 more than method1, suggesting a corresponding reduction in perfusion errors. Figure 2 illustrates this for a single patient with an MTT abnormality in the right frontal lobe. The top row shows the location of the local AIF voxels [11] using (a) method1 and (b) method2. Some voxels that feed tissue in this slice will be located in the adjacent slices. The lines show the linkage between the source and receiving voxels and are coloured according to the FM of the source voxel. The middle row shows MTT calculated using (c) a global AIF measured in a branch of the left MCA, (d) method1 and (e) method2. The bottom row shows Tmax maps for oSVD deconvolution using (f) the global AIF, (g) method1 and (h) method2. It can be seen that method2 identifies local AIF voxels within the abnormal MTT region (b), reduces the extent and severity of the MTT abnormality (e), and minimises D/D (h).

Discussion: The presented results demonstrate: 1.) "FM[localAIF]" is insensitive to variations in tissue MTT (Figure 1c), so the local AIFs identified using method2 may be located within abnormal MTT tissue, suggesting more improved local AIF identification at the boundaries between normal and abnormal MTT tissue (Figure 2a/b). 2.) The accuracy of local AIF methods may be assessed using owMLEM to measure residual D/D in the deconvolved owR(t) via the Tmax parameter. 3.) The local AIFs identified using method2 are more effective in removing D/D (Figure 2f/g/h), suggesting more accurate MTT measurement compared with both the global AIF and method1 (Figure 2c/d/e). Perfusion estimates free from D/D errors can potentially improve the characterisation and prediction of tissue at risk of infarction in stroke.

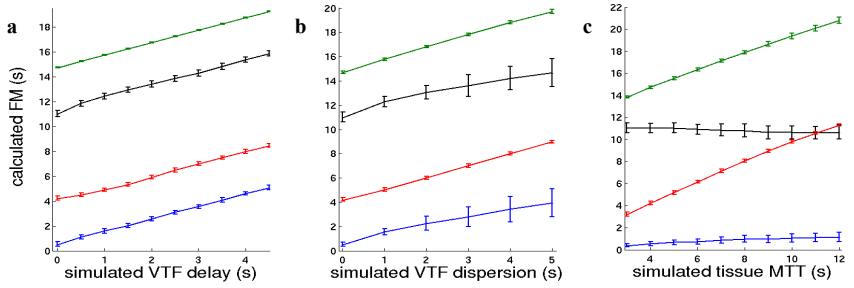

Figure 1: Simulation results: TR=1.5s, SNR(baseline signal)=50, baseline length 5s, CBV=4%. *Green*=FM[C], *Black*="FM[localAIF]", *Red*=FM[oR], *Blue*=Tmax[oR]. a) FM vs VTF-delay (MTT=4s, dispersion=0s), b) FM vs VTF-dispersion (MTT=4s, delay=0s), c) FM vs tissue MTT (delay=0s, dispersion=0s).

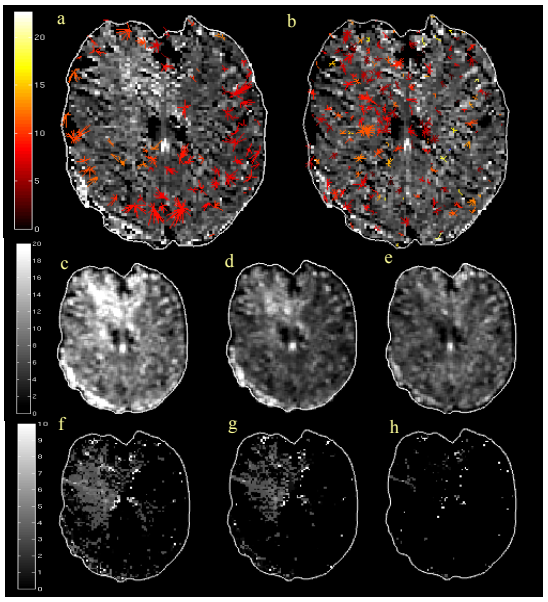

Figure 2: *In vivo* results from a single patient: Top row: local AIF source voxels. a) method1, b) method2. Middle row: MTT maps. c) global AIF, d) method1, e) method2. Bottom row: Tmax maps. f) global AIF, g) method1, h) method2.

References: [1] Calamante et al. 2003 Neuroimage. 19:341. [2] Willats et al. 2007 ISMRM Proc. p1445. [3] Calamante et al. 2000 MRM. 44:466. [4] Alsop et al, 2002 ISMRM Proc. p659. [5] Calamante et al. 2004 MRM 52:789 . [6] Christensen et al. 2007 ISMRM Proc. p591. [7] Lorenz et al. 2006 JMRI. 24:57. [8] Christensen et al. 2009 Stroke 40:2055. [9] Willats et al. 2008 NMR Biomed. 21:1126. [10] Willats et al. 2008 ISMRM Proc. p1956. [11] Christensen et al 2008 JMRI 27:1371. [12] Wu et al. 2003 MRM 50:164. [13] Salluzzi et al. 2006 Phys.Med.Biol 51:407.