Improved Deconvolution of Residue Function in MR Perfusion in the Presence of Bolus Delay and Dispersion Using Least-Absolute-Deviation Regularization

K. Wong[1], C-P. Tam[2], M. Ng[2], S. T. Wong[1], and G. Young[3]

[1]Department of Radiology, The Methodist Hospital Research Institute, Houston, Texas, United States, [2]Department of Mathematics, Hong Kong Baptist University, Hong Kong, China, People's Republic of, [3]Department of Radiology, Brigham and Women's Hospital, Harvard Medical School, Boston, MA, United States

Introduction MR perfusion imaging is becoming increasingly widely used for evaluation of a number of neuropathologies including acute stroke, vasospasm, chronic cerebrovascular disease and diagnosis, grading and therapeutic follow-up of primary and metastatic brain tumor. Dynamic susceptibility contrast (DSC) perfusion weighted imaging (PWI) is the most widely used clinical MR perfusion method because it is fast, robust and technically straightforward to perform on current 1.5T or 3.0T MRI. The most popular deconvolution method for CBF estimation is singular value decomposition (SVD) [1] which does not require a prior model of the vasculature. The standard SVD method (sSVD) has been shown to overestimate CBF by 2-4 fold in voxels where the bolus arrives more than 2 seconds earlier than the measured arterial bolus [2, 3]. Such negative apparent time delays (ATD) could conceivably be encountered in a number of situations including posterior circulation territories, tissue contralateral to a cervical or intracranial stenosis, selection of a distally located AIF region of interest (ROI) and tumors with arterial shunting or extra and intracranial arterial supply among others. Several delay insensitive SVD methods have been proposed to reduce the dependence of CBF estimation on ATD [2, 3]. All these proposed SVD methods underestimate CBF by 20% to 40% for MTT less than or equals to 4.8 seconds [2, 3],which unfortunately include most of the normal tissue. This leads in turn to an equivalent overestimation of MTT. Second, in all these methods, the estimated residue function oscillates around the underlying true residue function, making interpretation of the true residue function very difficult. When CBF is low, the residue function baseline oscillation leads to underestimation of MTT. Thus these methods underestimate CBF at low MTT and overestimate CBF at high MTT.

Methods To eliminate the effect of delay dependence in the estimation of $R(t)$, we used the same formulation as rSVD by offset the contrast concentration curve by 10 seconds for both simulation and patient data. Regularization is accomplished by substituting the least-absolute-deviation (LAD) method for rSVD, resulting in the following decomposition solution [4]: $r_\lambda = \min_r\{\|Ar-c\|_1 + \lambda\|Lr\|_1\}$

l1 norms were used in the data fitting term $\|Ar\text{-}c\|$ and regularization term $\|Lr\|$. L is a regularization function which is chosen as a first order difference operator in our model and λ is a regularization parameter. The minimization problem is formulated as linear programming problem and is solved iteratively by the interior point method [4]. During iteration, the interior point method solves a linear system using the preconditioned conjugate gradient method. A total of 8 iterations were required to produce sufficiently accurate results. In order to allow for possible sharp changes in the initial portion of the residue function, as in linear, monoexponential, or multiexponential models, we modified the regularization terms during the iterative approximation process by identifying the peak solution and releasing the regularization function around the peak by setting $L(r_{\text{peak-2}}, r_{\text{peak-1}})=0$ and $L(r_{\text{peak-1}}, r_{\text{peak}})=0$). We then identify and re-estimate the boxcar function using unmodified LAD method.

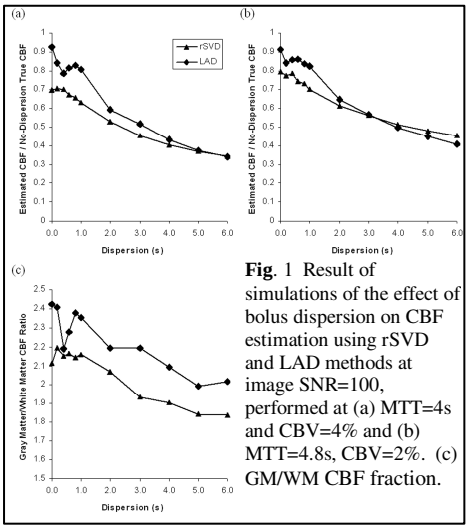

Fig. 1 Result of simulations of the effect of bolus dispersion on CBF estimation using rSVD and LAD methods at image SNR=100, performed at (a) MTT=4s and CBV=4% and (b) MTT=4.8s, CBV=2%. (c) GM/WM CBF fraction.

Monte Carlo Simulation

The AIF was simulated as a gamma-variate function: $C_a(t) = \begin{cases} 0 & t \le t_0 \\ C_0 (t-t_0)^a e^{-(t-t_0)/b} & t > t_0 \end{cases}$

Based on the published literature, typical AIF in adults can be modeled by the parameters a = 3.0 and b = 1.5 s [2]. In the simulations, the bolus arrival time t_0 = 20 s and C_0 = 1 were used. . Three different models of $R(t)$ were simulated, including exponential, boxcar, and linear. Concentration time curves $C(t)$ were generated by numerical integration of the convolution integral of $C_a(t)$ and $R(t)$ at 0.1 s temporal resolution to avoid numerical error in simulation. Function values of $C(t)$ and $C_a(t)$ were sampled at TR = 1 s. As in previously published studies, the signal intensity-time curves were generated by the formula $S(t) = S_0 e^{-k \cdot CBV \cdot C(t) \cdot TE}$ with S_0 = 100, TE = 65 ms and the scalar k was chosen such that a signal drop of approximately 40% was observed at CBV=4% [1]. Later Gaussian signal intensity noise was added to $S(t)$ to simulate the desired SNR. Similarly, the AIF signal curve was generated by choosing a different scalar k_a to obtain 60% signal drop in the major artery using the formula $S_a(t) = S_0 e^{-k_a \cdot C_a(t) \cdot TE}$. Because AIF curves obtained in clinical data processing usually have very high SNR and are typically fit with a gamma-variate function, no noise was added during generation of the simulated AIF signal curve.

In order to determine the degree to which CBF estimates from LAD, rSVD and sSVD methods depend on ATD estimation, simulations were performed with ATD ranging from -2 s to 6s. For gray matter, CBV = 4% and MTT = 4 s. For white matter, CBV = 2% and MTT = 4.8 s. Zero ATD was used for all other simulations.

The accuracy of CBF estimation was estimated for exponential, boxcar, and linear models, including a monoexponential model with bolus dispersion [5] SNR levels of 20 and 100 were used in these simulations unless otherwise specified. Simulation conditions include CBV range from 1% to 10%, MTT from range 3.4 s to 24 s, and CBF range from 2.5 mL/100g/min to 175 mL/100g/min. CBF was calculated from the central volume theorem as CBF=CBV/MTT [6]. All simulations were repeated 100 times. During each simulation run, CBF was obtained by taking the maximum of $R(t)$, the identical procedure used to extract CBF in clinical data processing. Simulation results were generated in the form of mean ± SD for accuracy and stability analysis. The mean and SD of the solution of $R(t)$ over 100 runs were used for curve shape analysis.

Results Monte Carlo simulation of CBF estimation at SNR=100 using LAD, rSVD, and sSVD methods (PSVD=0.04 and PLAD=0.2) for different residue function model over a range of MTT, CBV and dispersion are summarized below. The results are shown as a ratio of estimated CBF to true CBF in the form of mean ± SD.

Simulated condition	SNR=100, CBV=4%, MTT=3.4s to 24s			SNR=100, CBV=2%, MTT=3.4s to 24s		
	LAD	rSVD	sSVD	LAD	rSVD	sSVD
Monoexponential R(t)	0.90 ± 0.06 to 1.17 ± 0.20	0.68 ± 0.04 to 1.16 ± 0.15	0.65 ± 0.04 to 1.17 ± 0.17	0.85 ± 0.10 to 1.22 ± 0.22	0.69 ± 0.09 to 1.54 ± 0.26	0.68 ± 0.07 to 1.53 ± 0.31
Linear R(t)	0.97 ± 0.14 to 1.21 ± 0.16	0.80 ± 0.05 to 1.29 ± 0.18	0.76 ± 0.06 to 1.28 ± 0.20	0.92 ± 0.16 to 1.34 ± 0.26	0.81 ± 0.08 to 1.79 ± 0.34	0.80 ± 0.08 to 1.75 ± 0.33
Boxcar R(t)	0.95 ± 0.08 to 1.13 ± 0.13	1.05 ± 0.06 to 1.52 ± 0.18	1.07 ± 0.08 to 1.53 ± 0.18	0.95 ± 0.10 to 1.25 ± 0.21	1.06 ± 0.08 to 2..00 ± 0.32	1.08 ± 0.11 to 2.05 ± 0.33
Monoexponential R(t) with Dispersion ≤ 1s	0.81 ± 0.08 to 0.92 ± 0.07	0.63 ± 0.04 to 0.70 ± 0.05	0.65 ± 0.05 to 0.68 ± 0.05	0.82 ± 0.12 to 0.91 ± 0.14	0.70 ± 0.08 to 0.79 ± 0.10	0.73 ± 0.09 to 0.78 ± 0.11

The effects of bolus dispersion in CBF estimation is shown in Fig. 1. All methods underestimate CBF. The CBF estimated using LAD method is significantly closer to the real value for mild degrees of dispersion (less than 1 second).

Discussion and Conclusion Simulation results demonstrate that the LAD provides a delay-insensitive estimate of CBF that is significantly more accurate than that produced by standard rSVD and sSVD methods throughout the range of clinically encountered parameters. In addition, the shape of the tissue residue function curve produced by the LAD method is significantly more accurate than that produced by either rSVD or sSVD methods.

References 1) Ostergaard L. et al. MRM 1996;36:715-25. 2) Wu O. MRM 2003;50:164-174. 3) Smith MR. et al. MRM 2004;51:631-4. 4) Fu H. et al. SIAM J Sci Comput 2006;27:1881-1902. 5) Willats L. et al. MRM 2006;56:146-56. 6) Steward GN. J Physiol 1893;15:1-89.