Automatic Analysis of Quantitative Cerebral Perfusion in Rodents

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Introduction: Dynamic susceptibility contrast (DSC) MRI is widely used clinically for evaluating cerebral perfusion. However, its application to rodents is limited because of many technical challenges. This study will focus on the two major challenges: automatic calculation of arterial input function (AIF) and the effect of different deconvolution methods on the calculation of various hemodynamic parameters that include cerebral blood volume (CBV), cerebral blood flow (CBF) and mean transit time (MTT). Calculating the AIF in rats is particularly difficult because of the small size of the vessels. We developed an algorithm that automatically and accurately calculates the AIF. We have also developed a deconvolution method based on singular value decomposition that automatically determines the threshold (Autoth SVD). The results of perfusion values obtained with our algorithm are compared with those obtained with different deconvolution methods, such as Inverse Fourier Transform (IFT), and SVD [1] and also with the published values.

Theory and Methods: Estimation of the contrast agent concentration, $C_t(t)$, in the tissue is necessary for calculating the hemodynamic parameters. It is calculated from the convolution of $AIF(C_a(t))$ with a residue function ($R(t)$), where $C_a(t)$ is the arterial concentration of the contrast agent. It is critical to select proper deconvolution algorithm to estimate $R(t)$. In the SVD method, the n x n matrix, A, is constructed from $C_a(t)$[1], and is computed as the product of a n x m orthogonal array U, a n x n diagonal array W, composed of the singular values, and the transpose of a n x n orthogonal array V[1]: $A=UWV^T$. A threshold must be set to identify and remove elements in matrix A that cause the solution to oscillate or lead to meaningless in biomedical modeling. Existing SVD methods require prior knowledge of SNR or prior simulation to manually determine the truncated threshold. These methods are time consuming and produce unreliable results. For example, manually set threshold introduces errors, since a global threshold is applied to all the pixels in the image without consideration to the specific data of individual pixels. As an improvement to the existing SVD method and eliminate manual intervention, we propose a method in which the error e between the original $C_t(t)$ and the reconstructed tissue concentration curve $A \bullet R(t)$ is minimized for each pixel, where $e=|C_t(t)-A \bullet R(t)|$. By decomposing A, we can get n singular values. For each pixel, we calculate $R(t)$ and e by iteratively setting a singular value from the 2nd to the (n-1)th singular values as threshold. The singular value which gives the minimum e is chosen as threshold for that pixel.

The AIFs needed for calculating the absolute values of CBV and CBF are selected automatically. Compared to $C_t(t)$, AIFs have higher peak (Peak(A)), narrower width at half maximum (FWHM(A)), shorter arrival time T0(A), shorter time to peak TTP(A), and larger area under the curve(AUC(A)). In our implementation, the AIFs are automatically searched within the whole brain after Gamma-variant fitting according to the following criteria: mean peak <Peak(A)<max peak, Δt<FWHM(A)<mean FWHM, mean AUC<AUC(A)<max AUC, T0(A)< mean T0, and TTP(A), < mean TTP. Then the selected AIFs in this group are shifted to minimum T0 and averaged to generate the representative AIF.

The above procedure was verified on DCE MRI acquired on Sprague-Dawley rats. All images were acquired on a 7T Bruker scanner with a horizontal bore. Following the tri-pilot scan, shimming, and optimization of EPI, GdDTPA was administered via a catheter attached to the jugular vein. Single-shot gradient echo EPI images were acquired with TR/TE = 400msec/28.8msec, acquisition matrix of 64x64, slice thickness = 0.5 mm, 8 slices, and 150 dynamics. The total scan time for acquiring the perfusion data was 60 s.

Results and Discussion: Figure 1 shows a few representative AIFs from one rat. The average AIF generated from this group of AIF's is shown in Fig. 2. Table 1 shows the results of CBV, CBF and MTT by three different methods with the same selected AIF. Our proposed Autoth SVD method yielded result which is in good agreement with published CBF value measured by microsphere method [2]. In contrast, IFT method underestimated CBF. SVD method with three thresholds 0.25, 0.45, 0.75 was also investigated. The threshold values of 0.25 and 0.45 overestimated CBF, while a threshold of 0.75, which is approximately the same as the optimal threshold obtained by Autoth SVD, yielded values close to Autoth SVD method. The important point is that is IFT is sensitive to noise and SVD depends on the truncated threshold, both of which would introduce errors. As can be seen from the results in Table 1, the optimized threshold that is automatically determined by Autoth SVD minimized these errors. The AIF selection is also important for calculating the absolute value CBV, CBF and MTT. With our method, AIF can be automatically be selected by setting proper criteria.

Our software is developed under IDL (IDL6.3, ITT Visual Solution Boulder CO) and implemented on a PC. The computational time for automatic determination of AIF is less than one minute and calculation of CBV, CBF and MTT maps by Autoth SVD method took less than 4 minutes. The automatic methods described above minimize human bias and yields consistent results.

References: (1) Ostergaard L, et al., MRM, 1996, 36:715 – 735 - general (2) Yamakami I, et al, J Cereb Blood Flow Metab, 1991, 11:655-660

Table1. Results of different deconvolution methods on perfusion measurements
In grey matter (GM) and white matter (WM)

	Methods	CBV (mL/100g)	CBF (mL/100g/min)	MTT (second)	Total Brain CBF (mL/100g/min)
WM	Autoth SVD	14.2±1.0	84.7±11.0	10.3±0.6	137.3±58.9
	IFT	13.6±1.1	40.6±5.0	20.8±0.2	74.2±35.0
	SVD(th=0.75)	14.2±1.0	94.0±7.3	9.4±0.2	174.8±52.0
	SVD(th=0.45)	14.1±0.9	125.8±8.7	7.6±1.3	228.2±79.0
	SVD(th=0.25)	14.1±0.9	152.4±12.0	5.9±0.4	261.6±102.8
GM	Autoth SVD	27.4±1.0	177.5±20.4	9.0±1.4	
	IFT	25.2±1.1	86.1±8.1	19.2±3.0	
	SVD(th=0.75)	27.5±1.0	195.6±17.6	8.3±0.3	
	SVD(th=0.45)	27.5±1.6	239.4±20.5	6.7±0.5	
	SVD(th=0.25)	27.5±2.1	322.2±31.5	5.6±0.0	
	Publish Value	-	-	-	127±27

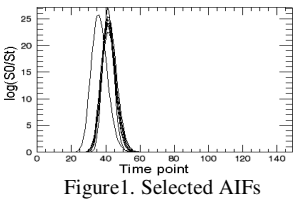

Figure1. Selected AIFs

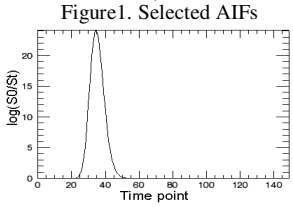

Figure2. Representative average AIF