Mathematical Framework of Deconvolution Algorithms for Quantification of Perfusion Parameters

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Abstract

Purpose: MR perfusion weighted imaging (PWI) has been used as sensitive indicator of tissue at risk for infarction. Quantitative perfusion parameters such as cerebral blood flow (CBF), mean transit time (MTT) and cerebral blood volume (CBV) can be obtained from post processing of PWI data using standard singular value decomposition algorithm (SVD). Assumption regarding absence of arterial – tissue delay (ATD) used in SVD algorithm results in underestimation of perfusion parameters. To estimate accurate values for perfusion parameters it is important to understand the mathematical framework behind SVD and improved SVD algorithms (bSVD and rSVD).

Method: This study explains the mathematical framework of SVD and improved SVD algorithms and uses computational techniques that use bSVD algorithm to obtain perfusion parameters maps of CBF, CBV and MTT for acute stroke patient.

Result: Computational techniques based on mathematical deconvolution algorithms are used to post process CBV, CBF and MTT maps where decrease in CBF and CBV were seen in left hemisphere.

Conclusion: The bSVD algorithm is found to be sensitive to ATD and provides more accurate estimates of perfusion parameters than the SVD algorithm, however CBF estimates from bSVD and rSVD still remain influenced by other artifacts

Keywords: PWI = perfusion weighted imaging, CBF= cerebral blood flow, MTT = mean transit time, CBV= cerebral blood volume, SVD = singular value decomposition algorithm.

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INTRODUCTION

Perfusion MRI provides information on cerebral hemodynamic parameters such as cerebral blood flow (CBF), mean transit time (MTT) and cerebral blood volume (CBV). Measurement of signal loss in cerebral vessels after the injection of bolus of an MR paramagnetic contrast agent is used to generate perfusion maps of

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various hemodynamic parameters like CBF, CBV and MTT[1,2]. This approach has been used in clinical computed tomographic perfusion imaging (CTP) studies of cerebral ischemia and in evaluation of acute stroke patients[3-5]. Mathematical methods such as deconvolution method and Fourier transform methods have been purposed to determine CBF using concentration-time curves obtained from perfusion MRI [3,6,7].

The measurement of CBF from perfusion-MRI data requires the measurement of the arterial input function (AIF) and the deconvolution of the concentration time curve. AIF is estimated in a major artery such as the middle cerebral artery (MCA), and this single measurement has been usually used as the AIF for the whole brain in the past studies [3,8,9]. Past studies purpose deconvolution algorithm using model-independent approach of singular value decomposition (SVD) as reliable option [6,10]. Deconvolution algorithm itself can be a source of error as a past study found variations in CBF values obtained using different deconvolution methods [7].

One of the fundamental assumptions while measuring CBF from perfusion MRI data is the absence of delay and dispersion of the bolus between the site where the AIF is measured and the most distant tissue [6]. Single measurement has been usually used as the AIF for all the cerebral vessels [6]. However, past studies indicate that the CBF values determined using SVD approach depend on the arterial-tissue delay (ATD) between the first non-zero signal components of the arterial input and contrast agent concentrations [9,11]. Acquisition slice order and AIF determined from a vessel with abnormal flow may cause changes in ATD [8].

In order to provide accurate values for perfusion parameters such as CBF, CBV and MTT we need to consider the factors that may affect accuracy i.e. delay and dispersion effect. This study explains the mathematical framework of SVD and improved SVD algorithms. The assumption primarily used in SVD is that there is no delay between the first non-zero signal components of the arterial input and contrast agent concentrations. Mathematical frameworks of improved versions of SVD called as bSVD, rSVD are discussed to remove the artifacts associated with SVD and estimate accurate perfusion parameters. Perfusion parameters maps of CBF, CBV and MTT will be obtained using computational techniques that use block circulant single value decomposition (bSVD).

METHODS

2.1 Mathematical framework of SVD

Mathematical framework of SVD is discussed in this section. The theoretical relationship between the arterial and tissue concentration curves is given by the convolution equation [1]. The objective is to get accurate values for CBF or F_t from Eq. [1]

$$C(t) = F_t.(C_a(t) \otimes R(t)) \quad [1]$$

Reducing Eq. [1] to convolution integrals

$$C_{VOI}(t) = CBF\int_{-\infty}^{+\infty} c_a(\tau)R(t-\tau)d\tau = \int_{-\infty}^{+\infty} c_a(\tau)R'(t-\tau)d\tau, \quad [2]$$

In Eq. [2] R (t) is the tissue residue function. Residue function is the fraction of injected tracer still present in vasculature at time 't'. C(t) is the tracer concentration, $C_a(t)$ is the AIF and CBF or Ft is the cerebral blood flow. $R'(t)$ represents the maximum of the scaled residue function.

$$R'(t) = CBF\ R(t) \quad [3]$$

Estimates of CBF can be obtained from the maximum of the scaled residue function $R'(t)$ by deconvolution of Eq. [1] for the known values of $C_a(t)$ and C(t). For deconvolution of Eq. [1] SVD is purposed to be the best method [6]. Algebraic reformulation of the convolution integrals in Eq. [2] has been used in past studies for the quantification of tracer transport functions[12-14]. For Algebraic reformulation assume that the arterial and cerebral concentrations are measured at a set of equally spaced time points $t_1, t_2, \ldots t_n$. Another assumption is that, the residue function and arterial input values are constant over small time intervals. The convolution in Eq. [2] can then be formulated as matrix Eq. [4]

$$R'_{sSVD} = \frac{1}{\Delta T_{EXPT}} C_a^{-1} C_{VOI} \quad [4]$$

In Eq. [4] Matrix C_a *is* constructed from the N sampled values of arterial functions, $c_a[t1 + n\Delta T_{EXPT}]$; $0 \leq n < N$, Where T_{EXPT} *is* the interval between samples and t_1 is the time point when first non-zero component of arterial input is measured.

$$C_a = \begin{bmatrix} c_a[t1] & 0 & 0 & \dots & 0 \\ c_a[t1 + \Delta T_{EXPT}] & c_a[t1] & 0 & \dots & 0 \\ \vdots & \vdots & \ddots & \ddots & \vdots \\ \vdots & \vdots & & \ddots & 0 \\ c_a[t1 + (N-1)\Delta T_{EXPT}] & c_a[t1 + (N-2)\Delta T_{EXPT}] & \dots & \dots & c_a[t1] \end{bmatrix} \quad [5]$$

Similarly N x 1 vectors C_{VOI} and R'_{sSVD} in Eq. [4] are -

$$C_{VOI} = (c_{VOI}[t1],\ c_{VOI}[t1 + \Delta T_{EXPT}],\ \dots\ c_{VOI}[t1 + (N-1)\Delta T_{EXPT}] \quad [6]$$

$$R'_{sSVD} = (R'_{sSVD}[t1],\ R'_{sSVD}[t1 + \Delta T_{EXPT}],\ \dots,\ R'_{sSVD}[t1 + (N-1)\Delta T_{EXPT}])^T. \quad [7]$$

Standard singular value decomposition (SVD) algorithm is used to solve matrix Eq. [4] for $R'(t)$. The SVD constructs matrices V, W, and U^T so that the inverse of C_a in Eq. [4], is written as

$$C_a^{-1} = \text{V.W.}U^T \quad [8]$$

Where W is a diagonal matrix (i.e., off-diagonal elements are zero). V and U^T are orthogonal and transpose orthogonal matrices (i.e., have orthogonal, unit length columns). Given this inverse matrix, $R'(t)$ is obtained as -

$$R' = \frac{1}{T_{EXPT}} \quad \text{V.W.}U^T \cdot C_{VOI} \quad [9]$$

CBV is calculated as

$$\text{CBV} = \frac{\int_{-\infty}^{\infty} C_{\text{VOI}}(\tau)d\tau}{\int_{-\infty}^{\infty} C_a(\tau)d\tau} \quad [10]$$

MTT is calculated according to the central value theorem [15,16]

$$MTT = CBV / CBF \quad [11]$$

2.2 Mathematical Framework of bSVD

One of the assumptions used while formulating the Eq. [4] is absence of delay between the first non-zero signal components of the arterial input and contrast agent concentrations. However, the AIF can lag C (t) by a time delay t_d in practice when the chosen AIF comes from a highly diseased vessel. Due to this R (t) cannot be properly estimated by deconvolution of Eq. [4].

Past Study purposed bSVD algorithm to estimate accurate values for perfusion parameters where linear deconvolution is replaced by circular deconvolution [17]. By zero-padding the N point time series C_a (t) and C (t) to length L, where L ≥ 2N, time aliasing is avoided. The C_a matrix in Eq. [4] is replaced by block-circulant matrix D. The elements of matrix D are given by Eq. [12]

$$d_{ij} = \begin{cases} C_a(t_{i-j+1}) & j \leq i \\ C_a(t_{N+i-j+1}) & j > i \end{cases} \quad [12]$$

Eq. [4] can now be written as

$$\text{f} = \frac{1}{T_{EXPT}} D^{-1}.\,\text{g} \quad [13]$$

In Eq. [13] g matrix is zero padded matrix C (t) and matrix f represents residue function. The inverse of D is decomposed and written as

$$D^{-1} = V_C\ .\ W_c\ .\ U_c^T \quad [14]$$

SVD is employed on Eq. [13] to solve for f by using Eq. [14]

$$\text{f} = V_c\ .\ W_c\ .\ U_c^T\ .\ \text{g}.\frac{1}{T_{EXPT}} \quad [15]$$

Matrix f is obtained by solving Eq. [15]. Matrix f

represents residue function and CBF can be estimated from the obtained residue function.

2.3 bSVD algorithm computer simulation

The bSVD approach was implemented using in house developed software and Lupe toolbox (https://www.msf.lu.se/research/mr-physics-group/software/lupe/download). The AIF was determined by a user-assisted, semiautomatic, AIF-identification algorithm. All data were analyzed by using bSVD algorithm.

2.4 Acquisition method

Written informed consent was obtained from patient (age = 70 years) suffering from acute ischemic stroke. Contrast-enhanced T2*-weighted images were collected using a single-shot gradient-echo EPI sequence (TR/TE/flip/slices 1800 ms / 40 ms / 60° / 5) on a clinical 1.5 T MR scanner (Signa; General Electric) from Tri-service General Hospital, Taipei. During imaging, 20 ml of contrast agent (Magnevist; gadopentetate dimeglumine, Bayer Health Care pharmaceuticals Inc.) was injected at 5 ml s^{-1}. Regions in infarcted and contralateral tissues were manually defined.

3. RESULTS

3.1 Estimation for CBF, CBV and MTT

For bSVD, decrease in CBF and CBV were seen in left hemisphere (Fig 1 (a), Fig 1(b)). Left hemisphere has low MTT as compared to the right hemisphere (Fig 1 (c)). Decreased CBF indicates tissue at risk for infarction.

4. DISCUSSION

In this study we firstly explained the mathematical concept behind the deconvolution methods used in quantification of perfusion parameters. Secondly, we used the model-independent technique, i.e., bSVD, which is insensitive to ATD to post process perfusion maps for CBV, CBF and MTT. Past studies have reported that delay and dispersion result in significant underestimation of CBF and overestimation of MTT when SVD was used; however for bSVD the blood flow estimates were virtually insensitive to ATD [7,8,17].

Error introduced by the delay can be corrected by using the information of the arrival time of the bolus. Block circulant matrix was used in bSVD, however accurate values for perfusion parameters insensitive to ATD can also be done by alternate methods which do not use block circular matrices. Past Study offered an alternative replacement for SVD methods and purposed rSVD i.e. reformulated SVD which is insensitive to ATD effect [8]. The framework for rSVD is as follows-

Mathematical framework of rSVD

Matrix C_a and vectors C_{VOI} and R'_{sSVD} used in SVD algorithm does not provide the accurate values for perfusion parameters. SVD is reformulated and the mathematical framework for rSVD is as follows-

Assume that the first nonzero components of the residue function, arterial and tissue signals occur at $t_1 + T_R$, $t_1 + T_A$ *and* $t_1 + T_{VOI}$ times respectively. Using the convolution shift theorem, these arrival times are interdependent i.e. $t_1 + T_{VOI} = t_1 + T_R + t_1 + T_A$ giving an arterial tissue delay (ATD) of ATD = T_{VOI} -T_A = $t_1 + T_R$.

Use of Eq. [4] implies a non-physiologically relevant ATD that changes with the experimental start time t_1 Reformulated SVD (rSVD) deconvolution solution is purposed as - .

$$R'_{rSVD}|_{t\geq T_{OFFSET}} = \frac{1}{\Delta T_{EXPT}} C_a|_{t\geq t1}{}^{-1} C_{VOI}|_{t\geq t1+T_{OFFSET}}. \qquad [16]$$

In this solution the first nonzero estimate of the scaled residue function is obtained at time t = T_{OFFSET} . The N x N matrix $Ca|t > t_1$ is calculated from the experimental arterial signal as for the standard SVD algorithm, i.e. $Ca|t = C_a$. The N x 1 vector

$C_{VOI}|_{t\geq t1+T_{OFFSET}}$ is

$$C_{VOI}|_{t\geq t1+T_{OFFSET}} = (C_{VOI}[t1 + T_{OFFSET}],\ C_{VOI}[t1 + T_{OFFSET} + \Delta T_{EXPT}],\ \ldots,\ C_{VOI}[t1 + T_{OFFSET} + (N-1)\Delta T_{EXPT}])^T. \qquad [17]$$

The N x 1 vector representing the residue function

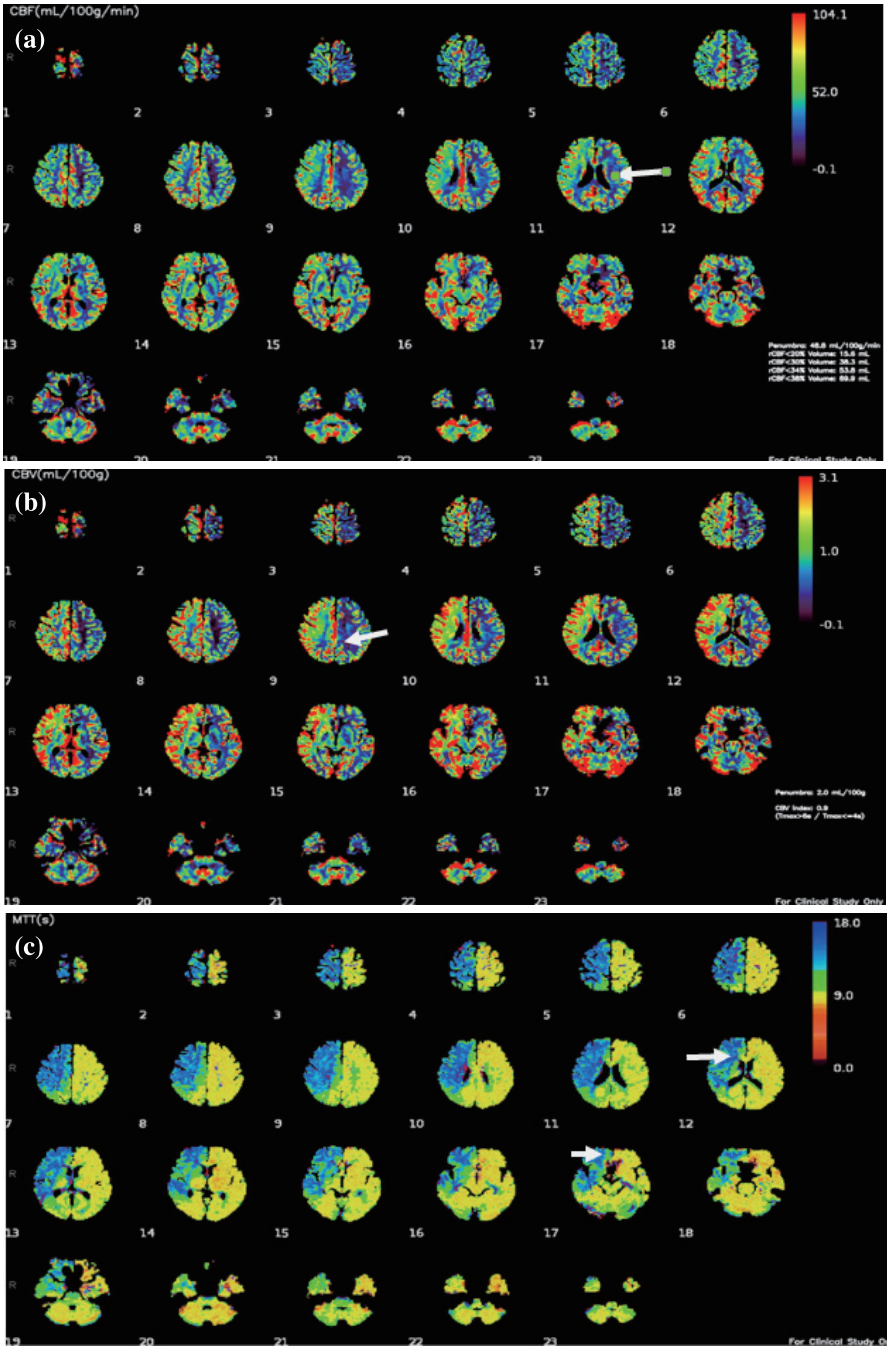

Figure 1: Perfusion Parameter maps. (a) CBF map (b) CBV map (c) MTT map. Different color coded brain maps display the values of CBF, CBV and MTT mentioned in color bars. (A) The arrow indicates the region with decreased CBF. Regions with lower CBF values in the figure indicate the regions which could be salvageable after appropriate therapies (B) Arrow indicates region with decreased CBV (C) Arrow indicates region with increased MTT.

estimates is given by:

$$R'_{rSVD}|_{t\geq T_{OFFSET}} = (R'_{rSVD}[T_{OFFSET}], R'_{rSVD}[T_{OFFSET} + \Delta T_{EXPT}], \ldots, R'_{rSVD}[T_{OFFSET} + (N-1)\Delta T_{EXPT}])^T \quad [18]$$

Deconvolution algorithms have been used to evaluate perfusion parameters other than CBV,CBF and MTT as several studies evaluated the performance of CBV, CBF, MTT parameters to predict the final infarct volume, with contradictory outcomes [18]. The TTP of a given tissue concentration curve, is defined as the time point at which the curve achieves its signal peak. The Tmax parameter is defined as the time point at which the residue function *R (t)*

attains maximum Recent studies focus on using Tmax and Tpeak (TTP) parameters to quantify mismatch between lesions identified in PWI-DWI MR imaging to identify tissue at risk of infarction in acute stroke [19].

An improved deconvolution algorithm to solve Eq. [4] can predict perfusion parameters more accurately. To obtain Tmax, TTP prior knowledge about behavior of R (t) obtained from deconvolution of Eq. [4] is to be known. CBF estimates from improved deconvolution algorithms i.e. bSVD and rSVD remain influenced by other artifacts as past study reports that ratio of measured CBF and true CBF does not equals unity [8]. It could be interesting for future studies to evaluate more sophisticated deconvolution techniques in combination with varying global or even local arterial input functions which are sensitive to artifacts and estimate correct values for Perfusion parameters.

CONCLUSION

Quantification of perfusion parameters such as CBV, CBF, and MTT depends on the deconvolution algorithm and correct deconvolution algorithm can predict perfusion parameters more accurately. In conclusion, detailed description of mathematical algorithms explains insensitivity of SVD algorithm towards ATD which could results in inaccurate estimates of perfusion parameters. bSVD algorithm formulated by mathematical improvements in SVD algorithm is sensitive to arterial-tissue delay and provide more accurate estimates for perfusion parameters than the SVD algorithm, however CBF estimates from bSVD and rSVD still remain influenced by other artifacts such as partial volume effects and dispersion of bolus or tracer particles.

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ETHICS STATEMENT

The local institutional review boards from participating institutions approved the study. All subjects or legal representatives gave their informed consent.

Data availability

The data that support the findings of this study are available from the corresponding author upon reasonable request.

Competing interests

The authors report no competing interests.

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