AN INDEPENDENT COMPONENT ANALYSIS APPROACH TO PERFUSION WEIGHTED IMAGING

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ABSTRACT

In dynamic susceptibility contrast perfusion weighted imaging, recirculation effect is normally removed by gamma-variate fitting from concentration curves before estimating hemodynamic parameters. At lower SNR, however, many fitting failures may be resulted. Moreover, when cerebral hemodynamics is compromised e.g., cerebral ischemia, a substantially broadened concentration curve is anticipated, resulting in the first passage overlapping with recirculation, which again causes a gamma-fit to fail to consistently discern recirculation contributions from the first passage. We propose to exploit independent component analysis to obviate recirculation effect. We demonstrate that such a technique can remove recirculation in normal and ischemic brain tissues while preserving the first passage. This in turn allows for accurate recirculation elimination and hence improved estimation of cerebral blood volume particularly when overlapping between first passage and recirculation is suspected as in the case of an ischemic lesion.

1. INTRODUCTION

Dynamic susceptibility contrast (DSC) approaches have been widely utilized in the study of tissue perfusion. In a DSC experiment, we inject a bolus of paramagnetic contrast agents (for example, Gd-DTPA) into the brain. The presence of intravascular contrast agents passing through brain capillaries induces a signal drop. By rapidly acquiring images prior to, during and after the injection of a contrast agent, the temporal signal changes induced by the presence of a contrast agent can be obtained. This typically consists of a baseline signal, a first passage and a recirculation of contrast agent.

In DSC perfusion weighted imaging (PWI) approaches, the temporal susceptibility signals are converted to concentration time curves and effects of recirculation need to be removed prior to the estimation of cerebral blood flow (CBF) and cerebral blood volume (CBV). The concentration curves are normally fitted to a gamma-variate function in an attempt to remove recirculation. However, this approach may be inaccurate at low *SNR* ([1]). In addition, important physiological information might be compromised by imposing a common analytic equation to all measured concentration curves.

Independent component analysis (ICA) is a widely used method for blind source separation, i.e., to determine underlying independent signal sources from observed data without any prior knowledge of the sources ([2]-[5]). In this investigation, we propose to use ICA to remove recirculation from the concentration curves assuming that the first passage and recirculation can be distinguished as different components regardless whether these two are overlapped. Our results demonstrate that the reconstructed concentration curves after removing the components contributed by recirculation are free of recirculation in both normal volunteers and stroke patients.

2. GAMMA-VARIATE FITTING

In DSC perfusion weighted imaging approaches, effects of recirculation need to be removed prior to estimating CBF and CBV. Concentration curves are normally fitted to a gamma-variate function $C_I(t)$ defined by Eq. (1) in an attempt to remove second bolus and residual signal decrease after the end of the first pass bolus ([6], [7]).

$$C_\Gamma(t) = \begin{cases} A(t-t_0)^B e^{-D(t-t_0)} & t \geq t_0 \\ 0 & otherwise \end{cases} \quad (1)$$

where A, B and D are shape parameters for the bolus, and t_0 is the time to arrival (TTA) for the contrast agents to arrive in the region of interest (ROI).

The parameters A, B, t_0, and D may be determined by a regression of $C_I(t)$ on samples of the concentration curve $C(t)$ up to the right turning point using Levenberg-Marquardt method. The right turning point of $C(t)$ is estimated to lie in the half maximum after the time to peak (TTP), whereas TTP is determined when $C(t)$ reaches the maximum. At convergence, the fitted curve are extrapolated from the right turning point to the end to get the full ranged fitted curve $C_f(t)$.

This approach has, however, several drawbacks. First, at lower SNR, the fit highly depends on the time resolution of the imaging sequence and the maximal

signal drop of the corresponding susceptibility signal yielding a higher number of fitting failures can be caused ([1]). The performance of gamma-variate fitting may thus, deteriorate for broadened and noisy concentration time curves in case of cerebral ischemia. Second, important physiological information might be compromised by imposing a common analytic equation to all measured concentration curves. Third, this approach will only work in cases where the first passage can be well separated from the recirculation. When cerebral hemodynamics is compromised such as cerebral ischemia, a substantially broadened concentration curve is anticipated, leading to an inevitable overlap of the first passage with recirculation. Under such a condition, a gamma-variate fit is unlikely to offer a consistent means of discerning contributions of recirculation from the first passage.

3. AN ICA METHOD TO REMOVE RECIRCULATION EFFECTS

Independent component analysis (ICA) is a widely popular approach to decompose observed data into unknown latent statistically independent signal sources without any prior knowledge of the sources.

Based on the assumption that the temporal concentration signals are linear superposition of hemodynamic changes resulting from contributions such as arterial, venous, tissue, recirculation and noise (including cardiac, respiratory and white noise), we proceed in this work to isolate recirculation contribution from other sources blindly. These underlying sources are temporally statistically independent in the sense that the first pass bolus and primary concentration increase resulting from the arterial component has the earliest TTA, followed by venous contribution, tissue contribution, and secondary bolus and residual concentration increasing due to recirculation contribution.

Infomax ([3]) is one of the most widespread ICA algorithms and based on higher order statistics. It aims to minimize the redundancy between the unknown sources. Temporal Infomax algorithm using a maximum likelihood formulation (ICAML) analysis was applied to concentration time curves for each 5×5 ROI as Eq. (2).

$$C_i(t_j) = \sum_{k=1}^{M} a_{ik} s_k(t_j) \quad (i = 1, \cdots, 25; j = 1, \cdots, N) \tag{2}$$

where $C_i(t_j)$ is the concentration curve of voxel i at t_j, a_{ik} is the mixing coefficient which suggests the expression level of the kth latent source at voxel i, while $s_k(t_j)$ is the kth temporal independent component (IC) at t_j, N is the number of measurement, and M is the number of sources.

Since the number of latent components, M, is unknown, a Bayesian Information Criterion (BIC) method was employed to estimate the number of sources ([8]). The model order is determined by estimating the posterior probability of the model containing N components given the observed data. The Matlab code for ICAML with BIC is available through the website ([9]). Our BIC results indicate that M varies at different SNR values. However, by applying BIC to both normal volunteers and stroke patients with different SNRs and inspecting the component outcomes, we found that between 5 and 7 components account for most signal variance hence agreeing with our original assumption that the temporal signal is a linear combination of arterial, venous, tissue, recirculation and noise contributions. In our approach, M was first set to 5. ICs were ranked according to the relative energy P_k (k = 1, ..., M) in a descending order as Eq. (3).

$$P_k = \frac{\sum_{i=1}^{25} a_{ik}^2 \sum_{j=1}^{N} s_k^2(t_j)}{\sum_{k=1}^{M} \sum_{i=1}^{25} a_{ik}^2 \sum_{j=1}^{N} s_k^2(t_j)} \quad (k = 1, \cdots, M) \tag{3}$$

ICs with a low relative energy and a late broad dip were identified as the recirculation components. If no recirculation associated IC was identified, M was increased up to 7 and ICA was repeated. After identifying the recirculation components, such components were excluded (Eq. (4)) and concentration curves were reconstructed using the remaining ICs as Eq. (5).

$$\tilde{s}_k(t_j) = \begin{cases} 0 & \text{if } s_k(t) \text{ is a recirculation IC} \\ s_k(t_j) & \text{otherwise} \end{cases} \tag{4}$$

$$\tilde{C}_i(t_j) = \sum_{k=1}^{M} a_{ik} \tilde{s}_k(t_j) \quad (i = 1, \cdots, 25; j = 1, \cdots, N) \tag{5}$$

4. RESULTS

Perfusion-weighted images were acquired from three healthy volunteers (one male, two females, age 24-33) at a 3T scanner (Allegra, Siemens) and five acute stroke patients (three males, two females, age 63-83) within 3-6 hrs from symptom onset at a 1.5T scanner (Vision, Siemens) using a single shot T_2^*-weighted EPI sequence. The imaging parameters were similar for both patients and volunteers with the exception of the repetition time (TR) and echo time (TE) (1.5s and 28 msec at 3T and 2s and 54 msec at 1.5T). Cerebral spinal fluid (CSF) regions were removed and susceptibility signals were converted to concentration curves. Then ICAML analysis was applied.

To evaluate the performance of ICA for removing recirculation effects, the concentration curves were also fitted by Gamma-variate functions as a comparison. The fitting was implemented in Matlab using the curve fitting toolbox.

In order to determine the effectiveness of the proposed ICA approach in removing effects of recirculation, relative cerebral blood volume (*rrCBV*) was computed for each voxel as the area underlying each

concentration curve ([6]) with recirculation removal using ICA ($rrCBV^{(i)}$), gamma-variate fitting ($rrCBV^{(f)}$) and without recirculation removal ($rrCBV^{(wo)}$). Also, percentage *rrCBV* difference maps were computed as:

$$\Delta rrCBV^{wo,i} = (rrCBV^{(wo)} - rrCBV^{(i)}) / rrCBV^{(wo)} \quad (6)$$

$$\Delta rrCBV^{wo,f} = (rrCBV^{(wo)} - rrCBV^{(f)}) / rrCBV^{(wo)} \quad (7)$$

$$\Delta rrCBV^{f,i} = (rrCBV^{(f)} - rrCBV^{(i)}) / rrCBV^{(f)} \quad (8)$$

The proposed approach is highly effective and consistent for removing recirculation in normal volunteers as illustrated in Fig. 1. A PWI image is shown in (a), whereas the red square indicates the 5×5 ROI used for fitting and ICA analysis. Five ICs are observed and IC4 (marked by the black arrow) is identified as the recirculation component with a low relative energy of 1.09% and a late broad dip. The averaged unfitted $C(t)$ (solid line), gamma-variate fitted $C_f(t)$ (dashed line), and ICA result $\widetilde{C}(t)$ (plus line) after the removal of the recirculation component are shown in (c). The percentage *rrCBV* difference between gamma-variate fit and ICA analysis ($\Delta rrCBV^{f,i}$) is shown in (d). In addition, the percentage *rrCBV* differences demonstrate that the difference between unfitted vs. ICA analysis, unfitted vs. fitted, and fitted vs. ICA analysis is 0.331 ± 0.114, 0.338 ± 0.131, and -0.024 ± 0.121 respectively. These findings suggest that gamma-variate fitting and ICA have similar performance in recirculation removal when the first passage and the recirculation are well separated.

In addition, a representative example from an acute stroke patient is shown in Fig. 2. A T_2-weighted image is shown in (a), delineating the presence and extent of the ischemic lesions. The red square indicates the 5×5 ROI used for ICA in the ipsilateral hemisphere with respect to the lesion. Seven ICs are identified (b) and IC5 (marked by the black arrow) is identified as the recirculation component with a low relative energy of 9.06% and a late broad dip. It is immediately evident that in comparison to the gamma-variate fitting, the proposed approach substantially minimizes the contribution of recirculation while preserving the effects of first passage (c). The percentage *rrCBV* difference map $\Delta rrCBV^{f,i}$ is shown in (d). In addition, to compare ICA analysis with gamma-variate fitting among brain regions, T_2 image was employed to define two ROIs, namely, T_2-defined final lesions (i.e. infarct regions) and noninfarct regions in the ipsilateral hemisphere, while a normal ROI was defined in the contralateral hemisphere. The means and standard deviations of the percentage *rrCBV* differences are given in Table 1. As anticipated, the largest differences between fitting and ICA are located within the ischemic final lesion where the first passage and recirculation heavily overlap (Fig.2 (d) and Table 1).

5. CONCUSION

We have demonstrated that ICA is capable of removing effects of recirculation in both normal and, more importantly, the ischemic brain tissues while preserving the contributions of first passage. This approach is likely to have profound implications for the calculation of CBF and CBV, particularly in regions where a substantial overlap between first passage and recirculation is suspected as in ischemic lesion. In the future, more PWI images acquired from acute stroke patients will be studied to assess the effectiveness of ICA in removing recirculation effects while preserving the first passage.

In conclusion, the ability to accurately remove effects of recirculation should further improve the accuracy of DSC for obtaining CBV and CBF.

6. ACKNOWLEDGMENTS

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7. REFERENCES

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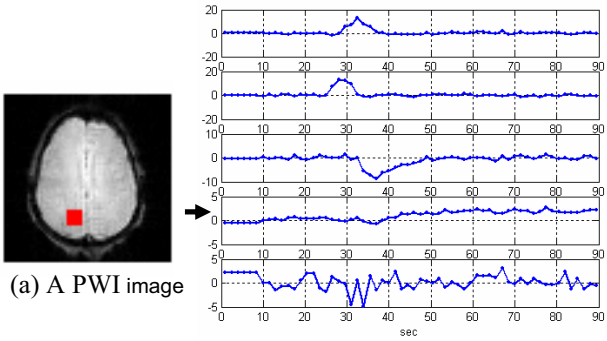
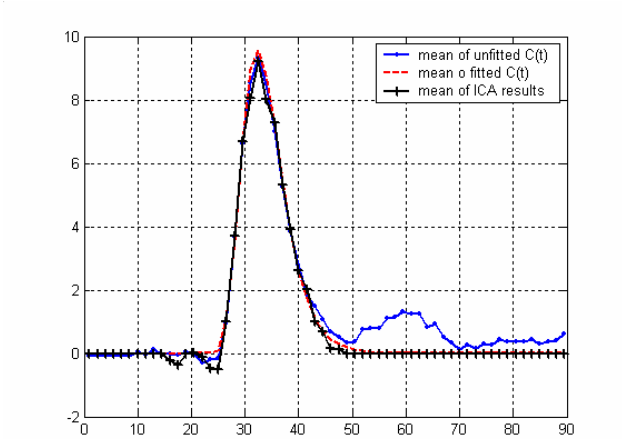
	$\Delta rrCBV^{wo,i}$	$\Delta rrCBV^{wo,f}$	$\Delta rrCBV^{f,i}$
Contralateral Normal ROI	0.445 ± 0.150	0.361 ± 0.191	0.103 ± 0.218
Ipsilateral noninfarct ROI	0.471 ± 0.163	0.352 ± 0.236	0.143 ± 0.255
T_2 lesion (infarct) ROI	0.484 ± 0.153	0.281 ± 0.340	0.157 ± 0.424

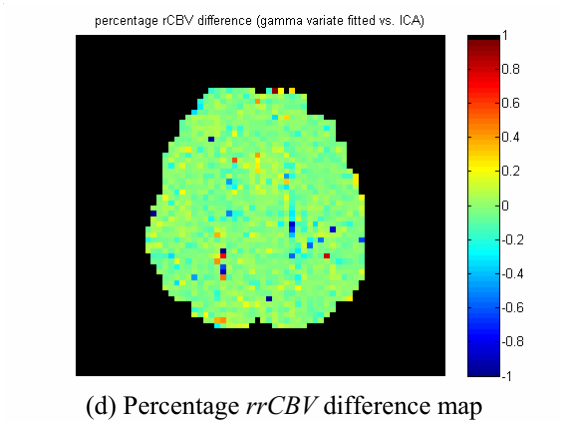
Table 1



(a) A PWI image (b) Five ICs

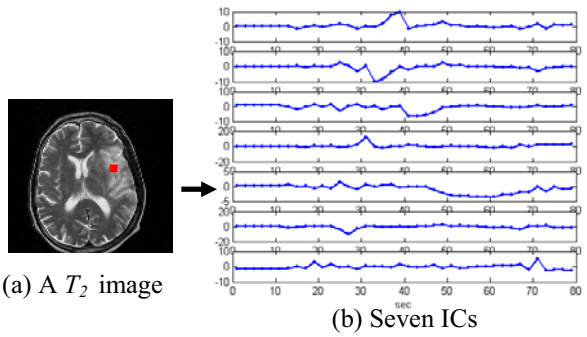


(c) Averaged concentration curves

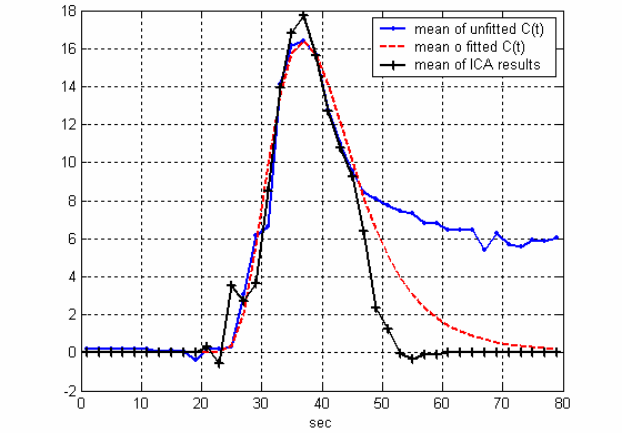


(d) Percentage *rrCBV* difference map

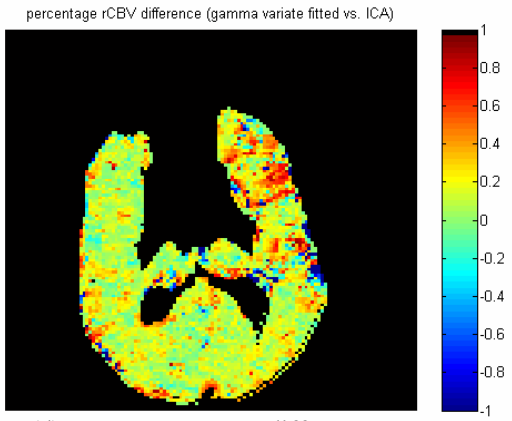
Fig. 1 A normal volunteer example



(a) A T_2 image (b) Seven ICs



(c) Averaged concentration curves



(d) Percentage *rrCBV* difference map

Fig. 2 An acute stroke patient example