Hemodynamic Segmentation of MR Brain Perfusion Images Using Independent Component Analysis, Thresholding, and Bayesian Estimation

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Dynamic-susceptibility-contrast MR perfusion imaging is a widely used imaging tool for in vivo study of cerebral blood perfusion. However, visualization of different hemodynamic compartments is less investigated. In this work, independent component analysis, thresholding, and Bayesian estimation were used to concurrently segment different tissues, i.e., artery, gray matter, white matter, vein and sinus, choroid plexus, and cerebral spinal fluid, with corresponding signal–time curves on perfusion images of five normal volunteers. Based on the spatiotemporal hemodynamics, sequential passages and microcirculation of contrast-agent particles in these tissues were decomposed and analyzed. Late and multiphasic perfusion, indicating the presence of contrast agents, was observed in the choroid plexus and the cerebral spinal fluid. An arterial input function was modeled using the concentration–time curve of the arterial area on the same slice, rather than remote slices, for the deconvolution calculation of relative cerebral blood flow. Magn Reson Med 49:885–894, 2003. © 2003 Wiley-Liss, Inc.

Key words: cerebral blood hemodynamics; brain perfusion MRI; magnetic resonance imaging; image segmentation; independent component analysis

Dynamic-susceptibility-contrast MR perfusion imaging is a widely used imaging tool for in vivo study of cerebral blood perfusion (1–7). In this technique, a bolus injection of contrast agent is administrated intravenously. The passage of contrast agent particles through the brain creates local susceptibility inhomogeneity, which in turn causes signal changes on the perfusion images. This signal-change process reveals blood supply patterns in different brain tissues and it can be recorded using an echo planar imaging technique at a temporal resolution of about 1 sec. Based on residue detection of the indicator dilution theory (8–9), cerebral hemodynamic parameters including relative cerebral blood volume (CBV), relative cerebral blood flow (CBF), and relative mean transit time (MTT) may be obtained from the perfusion images. These parametric images facilitate the diagnosis and staging of brain diseases such as infarct (1,7), occlusive cerebral-vascular disease (4), stroke (6,7), migraine aura (6), tumor (3,6,7), and radiation necrosis (3,7). However, the spatiotemporal information of the perfusion hemodynamics of various tissue components is not fully presented in these parametric images. Moreover, the concentration–time curve for a brain-feeding artery (e.g., the carotid or vertebral artery (2,4) or the middle cerebral artery (6)) at a remote slice location is needed for the deconvolution calculation of relative CBF.

Because it is difficult to visually incorporate all the information available on the perfusion and parametric images, segmentation of perfusion images is valuable in distinguishing tissues with different blood supply patterns and in modeling an arterial input function for the deconvolution calculation of relative CBF. Rogowska et al. (10) developed a similarity mapping technique to segment astrocytoma and cysts in a human brain on dynamic perfusion images. Correlation coefficients for all voxels were calculated using the measured signal–time curve within a region of interest (ROI) as a reference function. Wiart et al. (11) modified this technique for segmenting gray and white matter on perfusion images of six normal subjects. They used measured arterial input functions and an autoregressive moving average technique to reduce the random noise of the reference functions, which were measured at different tissue areas. However, these two techniques require manual selections of ROIs and they are limited to only one similarity map per ROI. These techniques may be subjective and cumbersome for the segmentation of brain perfusion images because there are many different blood supply patterns that require many user-defined ROIs.

Martel et al. (12) applied a factor analysis technique that combined principle component analysis (PCA) with statistical constraints to extract factor images and corresponding signal–time curves from perfusion images of 107 human subjects. Their results showed that arterial and venous structures dominated the first and second factor images, but the appearance of other output factor images...
varied considerably between cases and the tissue types were not consistently identified.

The independent component analysis (ICA) technique was originally proposed to separate observed signals into statistically independent source signals (13,14). This process is also called “blind source separation.” It has been successfully applied to functional MRI data to identify spatially independent cortical activation areas (15,16), to perfusion images to remove arterial signals before calculating hemodynamic parameters (17), and to diffusion-weighted images to remove artifacts and random noise before calculating diffusion tensor coefficients (18). In this study, we use ICA, thresholding, and Bayesian estimation (ICA-TBE) techniques to segment perfusion images of five normal human volunteers. The specific aims are: 1) to develop an objective and systematic segmentation method, based on spatiotemporal hemodynamics, for tissue classification that can improve analysis and interpretation of perfusion images; and 2) to define an appropriate arterial input function on the same slice location for calculation of relative CBF.

THEORY
Partial Volume Mixing on Perfusion Images

Signal intensities on MR images are observed from voxels of finite size. Consequently, partial-volume mixing of different tissues on these voxels is inevitable. Suppose that q tissues are identified on a set of perfusion images composed of v voxels. Fractional volumes of the q tissues in the v voxels can be described by a q×v fractional-volume matrix:

$$\mathbf{V} = \begin{bmatrix} F_{1,1} & F_{1,2} & \cdots & F_{1,v} \\ F_{2,1} & F_{2,2} & \cdots & F_{2,v} \\ \vdots & \vdots & \ddots & \vdots \\ F_{q,1} & F_{q,2} & \cdots & F_{q,v} \end{bmatrix}$$  \[1\]

where $F_{i,k}$ is the fractional volume for $i^{th}$ tissue in the $k^{th}$ voxel, with a value between zero and one. Using this notation, $v$ voxels in a two dimensional image are reordered into a row vector. Each row represents a fractional-volume image for a tissue type.

For a dynamic study with $p$ temporal images, the signal intensities of voxels occupied by the $q$ tissues can be expressed using a $p×q$ mixing matrix:

$$\mathbf{M} = \begin{bmatrix} M_{1,1} & M_{1,2} & \cdots & M_{1,q} \\ M_{2,1} & M_{2,2} & \cdots & M_{2,q} \\ \vdots & \vdots & \ddots & \vdots \\ M_{p,1} & M_{p,2} & \cdots & M_{p,q} \end{bmatrix}$$  \[2\]

where $M_{i,j}$ is the signal intensity on the $i^{th}$ temporal image for the $j^{th}$ pure tissue. Each column represents a signal-time curve on the perfusion images for a voxel occupied by a pure tissue type. The observed signals on the $p$ temporal images for the $v$ voxels can be represented using a $p×v$ matrix:

$$\mathbf{X} = \mathbf{M} \mathbf{F}.$$  \[3\]

If an inversion matrix can be found, the fractional-volume images are calculated as follows:

$$\mathbf{F} = \mathbf{M}^{-1} \mathbf{X}.$$  \[4\]

However, usually only the observed signals are known, and it is not possible to calculate $\mathbf{M}^{-1}$ based on $\mathbf{X}$ alone. The present study applies ICA to decompose the $\mathbf{X}$ matrix into an independent-component matrix that is related to the $\mathbf{F}$ matrix.

Independent Component Analysis

Suppose that there are $q$ mutually independent random variables described by a vector variable:

$$\mathbf{f} = \begin{bmatrix} f_1 \\ f_2 \\ \vdots \\ f_q \end{bmatrix}$$  \[6\]

where $f_i$ is an independent random variable. Suppose another vector variable, $\mathbf{x}$, is a linear combination of these $q$ independent random variables described by a vector-matrix multiplication:

$$\mathbf{x} = \begin{bmatrix} x_1 \\ x_2 \\ \vdots \\ x_p \end{bmatrix} = \mathbf{M} \mathbf{f}$$  \[7\]

where $x_i$ is the sum of many independent random variables and $x_i$ approaches a Gaussian distribution as com-
pared to the latent variables $f$, according to the central limit theorem (19).

The ICA techniques intend to find a $q \times p$ unmixing matrix, $\mathbf{W}$, which converts the vector variable $\mathbf{x}$ into another vector variable, $\mathbf{c}$, composed of $q$ mutually independent random variables described by:

$$\mathbf{c} = \begin{bmatrix} c_1 \\ c_2 \\ \vdots \\ c_q \end{bmatrix} = \mathbf{W} \mathbf{x}.$$  \[8\]

The mutual independence of $c_i$ means that if $P(c_i)$ represents the probability distribution of the $i^{th}$ component, the joint probability distribution for all components can be factorized as:

$$P(c_1, c_2, \ldots, c_q) = P(c_1)P(c_2) \cdots P(c_q).$$  \[9\]

The ICA techniques use this assumption of mutual independence and an iterative process to compute $\mathbf{W}$ matrix. Ideally, $\mathbf{c}$ and $\mathbf{f}$ should describe the same $q$ independent random variables, except that their order of components may be different and the means and variances of the corresponding components are rescaled.

To apply ICA to perfusion images, the meanings of the $\mathbf{F}$ and $\mathbf{X}$ matrices are modified as follows. The sample space for $\mathbf{f}$ is represented by the $\mathbf{F}$ matrix shown in Eq. [1]. Each row in the $\mathbf{F}$ matrix is treated as the $v$ measurements for an independent random variable, $f_i$. Here we assume a spatial independence for the sample space of $\mathbf{f}$. This implies that the fractional-volume images are statistically independent with respect to each other. The sample space of $\mathbf{x}$ is represented by the $\mathbf{X}$ matrix shown in Eq. [3]. There are $v$ measurements for each $x_i$ and the $\mathbf{X}$ matrix is the only known information in this study.

Similarly, the sample space for $\mathbf{c}$ is calculated as:

$$\mathbf{C} = \begin{bmatrix} C_{1,1} & C_{1,2} & \cdots & \cdots & C_{1,v} \\ C_{2,1} & C_{2,2} & \cdots & \cdots & C_{2,v} \\ \cdots & \cdots & C_{k,k} & \cdots & \cdots \\ \cdots & \cdots & \cdots & \cdots & \cdots \\ C_{q,1} & C_{q,2} & \cdots & \cdots & C_{q,v} \end{bmatrix} = \mathbf{W} \mathbf{X}$$  \[10\]

where the matrix element $C_{k,k}$, for $k = 1, 2, \ldots, v$, is the sample space for the independent variable $c_k$. The $i^{th}$ row in $\mathbf{C}$ is treated as the $i^{th}$ independent-component image, which is related to one of the fractional-volume images described by the rows of $\mathbf{F}$ matrix. Because the $\mathbf{C}$ matrix is the calculated sample space for the vector variable $\mathbf{c}$, it follows that the independent-component images are uncorrelated and their inner products are expected to be zero:

$$E[c_ic_j] = \frac{1}{v} \sum_{k=1}^{v} C_{ik}C_{jk} = 0, \text{ if } i \neq j$$  \[11\]

where $E(\cdot)$ is the expected value and $k$ is the location of a voxel in an image. The signal–time curves for the independent-component images can be obtained from the columns of the pseudo-inverse of $\mathbf{W}$.

In PCA, both the output images and the signal–time curves are required to be orthogonal. However, the orthogonal requirement on the signal–time curves is unrealistic in perfusion MRI experiments. While the ICA technique makes a more stringent statistical-independence requirement on the output independent-component images as described by Eq. [9], it imposes no restriction on the output signal–time curves (15,16).

**Bayesian Estimation**

Using Bayesian estimation (19), each voxel can be assigned to a tissue type according to its posterior probability with respect to each tissue type, denoted by $P(s_i|\mathbf{p}_u)P(\mathbf{p}_u)$ (20). Here $P(\mathbf{p}_u)$ is the probability density for tissue type $i$ on the perfusion images. The conditional probability density function is assumed to be a Gaussian distribution described by:

$$P(s_i|\mathbf{p}_u) = \frac{1}{(2\pi)^{p/2}|\Sigma|^1/2} \exp \left\{ \frac{1}{2} (s_i - \mathbf{p}_u)^\top \Sigma^{-1} (s_i - \mathbf{p}_u) \right\}$$  \[12\]

where $p$ is the number of perfusion images, $s_i$ is the signal–time curve for the $k^{th}$ voxel, $\mathbf{p}_u$ is the mean signal–time curve for tissue type $i$, and $\Sigma$ is the variance matrix of signal–time curves for voxels belonging to tissue type $i$.

**Indicator Dilution Theory**

Based on residue detection in indicator dilution theory, relative CBV for a voxel is equal to the integration of the concentration–time curve for a voxel of tissue, divided by the integration of the concentration–time curve for the arterial input, during the first pass of a contrast agent, which can be expressed as:

$$\text{relative CBV} = \int_{\text{first pass}} c_i(t) \, dt / \int_{\text{first pass}} c_a(t) \, dt$$  \[13\]

where $c_i(t)$ is the contrast-agent concentration–time curve for a voxel of tissue and $c_a(t)$ is the arterial input function for this voxel (1,2,5).

The concentration–time curve for a voxel of tissue also can be expressed as:

$$c_i(t) = (\text{relative CBF}) \cdot c_a(t) \odot R(t)$$  \[14\]

where $\odot$ denotes convolution and $R(t)$ is the residue function for the voxel (1,2,5,6). If $c_i(t)$ is known, the (relative CBF) $\cdot$ $R(t)$ curve for a voxel can be calculated using the singular value deconvolution technique (5,6). Because $R(t=0)=1$, as the indicator dilution theory assumes, the initial value of the deconvolved curve is equal to relative CBF. However, Ostergaard et al. (6) demonstrated that there are temporal delays observed on the curves for dif-
different tissues. Instead of the initial value, the maximum value should be used. Using the central volume principle, the relative MTT for contrast-agent particles to pass through a voxel can be calculated as (1,2,5):

\[
\text{relative MTT} = \frac{\text{relative CBV}}{\text{relative CBF}}.
\]

MATERIALS AND METHODS

Perfusion brain images of five healthy volunteers (three males, two females, ages 18–47) were acquired on a 1.5 T clinical scanner (Signa CV/i, GE Medical Systems, Milwaukee, WI). Written informed consent was obtained from all five volunteers. A birdcage head coil and a single-shot, gradient-echo, echo-planar-imaging pulse sequence were used. Scan parameters were: TE/TR = 60/1000 ms, flip angle = 90°, FOV = 24 cm × 24 cm, image matrix = 128 × 128, slice thickness = 5 mm, gap = 5 mm, three slices, one average, and 100 images per slice location. The body weights of the five volunteers were between 49 and 70 kg. Twenty ml of Gd-DTPA-BMA (Omniscan®, 0.5 mmol/ml, Nycomed Imaging, Oslo, Norway) followed by 20 ml of normal saline were administered through an antecubital vein at a flow rate of 3 ml/sec using a power injector (Spectris®, Medrad, Indianola, PA). The first three perfusion images were discarded because the steady state for baseline images was not reached. The last 27 perfusion images were also discarded because there was not much temporal signal variation on these images. Seventy perfusion images with a temporal resolution of 1 sec were used for analysis. Postprocessing was performed on a 450-MHz Pentium-based personal computer. Programs were written in MATLAB (MathWorks, Natick, MA).

Figure 1 illustrates the first (Fig. 1a) and the 29th (Fig. 1b) perfusion images at an upper slice location for the first volunteer (39-year-old male), showing the baseline image and the image with maximum signal drop, respectively. The difference image in Fig. 1c illustrates susceptibility contrast caused by the passage of the contrast agent. Figure 1d shows a proton density-weighted image displaying the anatomy for verification purposes. Note that the choroid plexus (CP) and the cerebral spinal fluid (CSF) are well observed in Fig. 1b,d.

Tissues with different blood supply patterns were assumed to be distributed in a spatially independent manner on the perfusion images, so that they could be distinguished by ICA. We used the FastICA technique (13,14) to process perfusion images. The FastICA technique uses a fixed-point algorithm and the approximative Newton iteration process to maximize negentropy, which is a measure of nongaussianity. It is a more efficient method for estimating independent components than the conventional gradient descent techniques. In the FastICA calculation, PCA was used as a preprocessing step for the iterative ICA calculation. Because the number of tissue types, \(q\), is unknown, we tried to determine the number of output independent-component images, \(N_{ic}\), based on either the eigenvalues or the Akaike information index (21,22) of perfusion images. However, these quantitative measures revealed smoothly decreasing curves plotted against \(N_{ic}\) and it was difficult to make a decision. After visually examining the computed independent-component images

![Figure 1](https://example.com/figure1.png)

**FIG. 1.** Perfusion and proton-density-weighted images at an upper slice location for the first volunteer (39-year-old male). The first perfusion image (a) showing baseline signals; the 29th perfusion image (b) showing the maximum signal drops; the difference image (c) of a and b, displaying the signal changes; an anatomical proton-density-weighted image (d) used for verifying the segmentation results.
for various \( N_c \) values, we concluded that \( N_c = 5 \) was a good choice, based on our knowledge of anatomy. We found the output independent-component images provided only a coarse segmentation of the perfusion images. Furthermore, the corresponding signal–time curves were rescaled during the FastICA optimization process and these curves cannot be used for the calculation of hemodynamic parameters. To refine segmentation results, we utilized thresholding and Bayesian estimation on the perfusion and independent-component images. We applied a threshold on the 29th perfusion image, as shown in Fig. 1b, to generate a mask image for CSF. Similar to functional MRI studies where the task-related areas were identified by suitable thresholding on independent component images (15,16), we applied different thresholds to the five output independent-component images to generate mask images for CP, artery, vein and sinus (VS), gray matter, and white matter. These six mask images were taken as an initial guess in the Bayesian estimation for assigning each voxel to a tissue type. The probability density function for each tissue type, \( P(\mu_i) \), was determined by the voxel numbers in the six mask images. Sample means and sample variance matrices for the signal–time curves were computed for voxels in the mask images as an estimate for \( \mu_i \) and \( \Sigma_i \). In the Bayesian estimation, each voxel was assigned to the tissue type with the largest posterior probability and a color-coded composite image was generated to illustrate the assignments. These assignments were used as new ROIs to compute the averaged signals across time, which were taken as the true signal–time curves.

For the hemodynamic parameter calculations, a linear relationship was assumed between \( c_i(t) \) and the change of relaxation rate, \( \Delta R_2^*(t) \), described by:

\[
c_i(t) = \Delta R_2^*(t) \times -\frac{1}{TE} \ln \left( \frac{S(t)}{S_0} \right)
\]

where \( TE \) is echo time, \( S(t) \) is the signal at time \( t \), and \( S_0 \) is the baseline signal for a voxel (1,2,6,23,24). The concentration–time curve for the artery region on the same slice was used as an arterial input function in the subsequent relative CBF calculation. Using Eqs. [13]–[15], relative CBV, relative CBF, and relative MTT values were calculated for the color-coded regions of different tissues. The relative CBV value was calculated as the area under the concentration–time curve for data from the 20th to the 42nd image. In the deconvolution calculation of relative CBF, all 70 images were used and a cut-off value was set at 20% of the maximum eigenvalue in the singular value decomposition calculation to reduce random noise (6). Parametric images for relative CBV, relative CBF, and relative MTT were also calculated on a voxel-by-voxel basis.

RESULTS

Figures 2–5 demonstrate the postprocessing procedure of our technique applied to the same set of perfusion images as shown in Fig. 1. Figure 2 illustrates the application of FastICA on perfusion images with \( N_c = 5 \). The postprocessing time was 20 sec. The calculated signal–time curves plotted in Fig. 2a were all normalized to unit variance and the amplitudes of the curves were shifted so that the average values of the baseline signals for the first 20 sec were equal to 5.0, so that the curves may be compared with those in Fig. 4c. Each independent-component image consisted of two or three tissue types. The major tissue types of the five independent-component images were CP (Fig. 2b), artery (2c), VS (2d), gray matter (2e), and white matter (2f). A few VS voxels were assigned to CP and artery, as illustrated in Fig. 2b,c, respectively. Figure 2d demonstrates that VS was partially mixed with CP. Similarly, gray matter was slightly mixed with artery, VS, and CSF, as shown in Fig. 2e; white matter was mixed with CSF, as shown in Fig. 2f. The corresponding signal–time curves plotted in Fig. 2a reflected contributions from multiple tissues. One example was the signal–time curve for CP in which the signals increased above baseline between 28–35 sec, while other signal–time curves dropped below baseline. Examining the independent-component image for CP, some voxels with dark intensities (which indicates negative values) were identified in the VS area. The contamination on the signal–time curve of CP from that of VS was clearly demonstrated.

Figure 3 shows five binary images that were produced by applying different thresholds to the independent-component images. According to the anatomical proton-density-weighted image displayed in Fig. 1d, it is clear that most of the CP and artery are individually separated, as shown in Fig. 3a,b, respectively. In Fig. 3c, most of the bright voxels are VS, while the remaining voxels belong to CP. In Fig. 3d, most bright voxels are gray matter and some voxels are artery. In Fig. 3e, the major tissue type is white matter that is mixed with CSF. To generate mask images that were exclusive to each other, subtractions between binary images were performed. For example, the mask image for VS was produced by subtracting Fig. 3a from 3c, that for gray matter was produced by subtracting 3b from 3d, and that for white matter was produced by subtracting the binary image of CSF from 3e. Whenever a voxel was assigned to a tissue type it was excluded from the remaining assignment process. The mask images were generated sequentially in the following order: artery, CP, CSF, VS, gray matter, and white matter. Six final mask images were used to estimate \( \mu_i, \Sigma_i, \) and \( P(\mu_i) \) for the application of Bayesian estimation. Figure 4a displays the final segmentation result in a color-coded composite image generated using the Bayesian estimation. The overestimates of artery and VS areas were caused by the magnetic susceptibility effect. In order to analyze the hemodynamics, different colored areas were used as ROIs to compute the true signal–time curves on the perfusion images. Figure 4b,c displays the measured and normalized signal–time curves, respectively. The normalized signal–time curve for CP shown in Fig. 4c was greatly improved as compared to that in Fig. 2a. Figure 4d plots the concentration–time curves for these segmented areas calculated using Eq. [16]. The concentration–time curve of the artery region was modeled as an arterial input function for subsequent relative CBF deconvolution calculations. To illustrate the sequential passages of contrast agents, these curves were rescaled to their maximum values as illustrated Fig. 4e. The rescaled curves demonstrate that the bolus of contrast agent arrived at the artery first, followed by gray matter, white matter, and VS. Good reci-
calculation in these tissues was observed, indicating that their blood–brain barriers were all well intact. However, CP and CSF have different curve patterns because of their different microcirculations. The \((\text{relative CBF}) \cdot R(t)\) curves for these areas are shown in Fig. 4f. Note that the late arrival of contrast agent in CP, VS, and CSF, although clearly demonstrated, is not as dramatic as in Fig. 4e. Figure 5 shows parametric images for relative CBV (Fig. 5a), relative CBF (5b), and relative MTT (5c) for this slice. These parametric images display good contrast between tissues.

Segmentation results of the 15 slices (five subjects, three slices for each subject) of perfusion images can be summarized as follows: 1) artery areas were reliably segmented using \(N_{ic} = 5\); 2) the contrast agent was consistently observed to arrive first at the artery, followed by gray matter, white matter, and VS; 3) the late arrival and slow washout of contrast agent at the CP were also consistently observed; 4) the arrival of contrast agent at the CSF was delayed for another 1–3 sec as compared with the arrival at the CP; 5) cortical and subcortical gray matter could not be distinguished; and 6) the averaged ratios for relative CBV, rela-
multiple tissues were more statistically independent than our
that some linear combinations of the distributions of mutantated. Apparently, the FastICA algorithm determined
component images and the signal mixings of multiple tissues in the output independent-
gray matter, white matter, and VS. However, there were lium reaching the arterial component
of contrast agent through different tissues, with the gadolinium
al contrast medium, either iodinated or gadolinium,
The observation that intravenously administrated radiological contrast medium, either iodinated or gadolinium,
through the blood–CSF barrier on the surface of the CP.
The observation that intravenously administrated radio-
corticulation of contrast agent through cerebral vascular
channels. For example, sequential passage of the contrast
to the artery, gray matter, white matter, and VS were
clearly demonstrated and their curves consisted of the first
and recirculation of contrast agent, which indicated
the blood–brain barrier at these tissue regions were all
well intact.

However, the CP is one of the intracranial tissues in
which the blood–brain barrier interface is not found
(29,30) and a different curve was revealed in Fig. 4e. The
histological difference of a lack of a blood–brain barrier for
CP may explain the late arrival and slow washout of con-
trast agent. We postulate that the CP obtains its blood
supply from terminal branches of the internal carotid ar-
teries and that the arrival of contrast agent at the CP is
accordingly later than at the arteries, gray matter, and
white matter. Gadolinium may propagate from arteries to
capillaries and veins, while some of the particles penetrate
into the intercellular or interstitial spaces, causing slow
washout.

We also found that the arrival of contrast agent at the
CSF in the lateral ventricles was delayed for about 1–3 sec
as compared to that of the CP for all five normal volun-
teers. Because this phenomenon cannot be explained by
partial-volume mixing or other artifacts, we postulate that
gadolinium enters the CSF space in the lateral ventricle
through the blood–CSF barrier on the surface of the CP.
The observation that intravenously administrated radio-
logical contrast medium, either iodinated or gadolinium,
may enter the CSF is not novel. In 1979, Coin et al. (31)
observed enhancement of CSF on computed tomography
images in animal experiments and in patients following
intravenous injection of iodinated contrast medium. In
1991, Knutzon et al. (32) quantitatively determined the
visible shortening of the T1 value of CSF after intrave-
nously administering gadolinium to 12 dogs, obtaining

DISCUSSION

In applying ICA on perfusion images, voxels of the same
tissue type are grouped together according to their signal-
time curves, partial-volume mixing effect, and the assump-
tion of spatial independence of tissues. The FastICA tech-
nique uses the criteria of negentropy maximization to
maximize the spatial independence of output independent-
component images. The resultant independent-component
images shown in Fig. 2 provided an initial segmenta-
tion of brain tissues. Meanwhile, the corresponding sig-
nal–time curves in Fig. 2a illustrate the sequential passage
of contrast agent through different tissues, with the gado-
linium reaching the arterial component first, followed by
gray matter, white matter, and VS. However, there were
mixings of multiple tissues in the output independent-
component images and the signal–time curves were con-
taminated. Apparently, the FastICA algorithm determined
that some linear combinations of the distributions of mul-
tiple tissues were more statistically independent than our
assumption that each tissue had a spatially independent
distribution. Nevertheless, the FastICA technique did pro-
vide a good initial guess on the segmentation of perfusion
images, under the condition that we could recognize the
anatomical structure on the output independent-component
images.

Thresholding and Bayesian estimation were further ap-
lplied to the output independent-component images to
classify voxels by tissue type. In generating mask images,
we applied higher thresholds on independent-component images to select voxels belonging to one tissue type. In this
manner a number of voxels might be excluded in the six
mask images. However, all voxels were reassigned to a
tissue type in the Bayesian estimation. In an additional to
Bayesian estimation, other segmentation techniques such
as k nearest neighbors (20), fuzzy C-means (20), or Markov
random field (28) can also be used to refine tissue classi-
fications.

The results shown in Fig. 4 demonstrate the spati-
temporal scenario of the hemodynamics for various tissue
types in the human brain. The color-coded composite im-
age in Fig. 4a illustrates that voxels of different perfusion
dynamics were grouped together and the segmentation
result was in good agreement with the proton-density-
weighted image shown in Fig. 1d. The normalized concen-
tration–time curves in Fig. 4e reveal the passage and mi-
crocirculation of contrast agent through cerebral vascular
channels. For example, sequential passage of the contrast
agent to the artery, gray matter, white matter, and VS were
clearly demonstrated and their curves consisted of the first
pass and recirculation of contrast agent, which indicated
that the blood–brain barrier at these tissue regions were all
well intact.
average $T_1$ decreases of 23% at 60 min. They concluded that their observation should be regarded as a normal appearance, not a sign of pathology. In 2000, Mamourian et al. (33) demonstrated that the entrance of gadolinium in the CSF was intravenously dose-dependent in animal experiments. In human beings, the appearance of gadolinium in CSF on MR images has been reported in many patient studies at minutes to hours after i.v. administration of gadolinium, including: a patient with a primitive neuroectodermal tumor (34), a patient with a meningeal fibrosis and cryptococcal infection (35), four patients with meningeal carcinomatosis (36), six patients with pineal cysts (37), and a patient with renal failure (38). We observed the appearance of i.v.-administered gadolinium in CSF in all five normal volunteers. Our study suggests that the bolus of injected gadolinium agent penetrated into the CSF via the CP in the lateral ventricle. To our knowledge, it is the first in vivo demonstration of the first-pass of this phenomenon.

FIG. 4. ICA-TBE segmentation results for the same set of perfusion images as shown in Fig. 1. a: The Bayesian segmentation result displayed in a composite color-coded image. The six tissue types are: CP (magenta), artery (red), CSF (green), VS (blue), gray matter (yellow), and white matter (gray). b,c: The measured and normalized signal–time curves for the six segmented tissue types. The standard deviation of random noise measured in air on the perfusion images was 22.5 arbitrary units (25). d: The concentration–time curves for these tissues calculated using Eq. [16]. e: The rescaled concentration–time curves expressing their percentage changes, in which the curves were rescaled to their maximum values. f: The (relative CBF) · $R(t)$ curves for these tissues obtained using the singular value decomposition technique. The maximum value on each curve is the relative CBF value of the tissue.
In the deconvolution calculation of relative CBF, the concentration–time curve of a middle cerebral artery or an internal carotid artery at a remote slice location is a typical choice for the arterial input function (2,4,6). Our ICA-TBE method provides an artery area and corresponding concentration–time curve on the same slice. Either the initial guess mask image shown in Fig. 3b or the final assignment after the Bayesian estimation shown in Fig. 4a can be used as an ROI for measuring the concentration–time curve. It is an easy and obvious choice for the arterial input function. In all 15 slices of perfusion images, the artery regions were consistently segmented using the FastICA algorithm with \( N_v \geq 5 \). This observation indicates that the spatial-temporal distribution of artery is unique compared to other tissues and that the FastICA algorithm is robust in segmenting arterial voxels.

In conclusion, the ICA-TBE method for analyzing perfusion images has several advantages: 1) the concurrent and systematic segmentation of tissues with different hemodynamic patterns; 2) the delineation of sequential passage and microcirculation of contrast agent to these tissues; and 3) the effective modeling of an arterial input function on the same slice location for relative CBF calculations. The resultant information on tissue characteristics and hemodynamics will further expand our knowledge of cerebral blood circulation in human brains.

**ACKNOWLEDGMENTS**

The authors thank the Laboratory of Information and Computer Science in the Helsinki University of Technology, Finland, for providing the FastICA program as freeware.

**REFERENCES**


