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Automatic measurements of arterial input and venous output functions on cerebral computed tomography perfusion images: A preliminary study

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ABSTRACT

Background: The current automatic techniques for measuring arterial input function (AIF) and venous output (VOF) on cerebral computed tomography perfusion images are prone to motion artifact and random noise, and their failure rates vary between 10% and 65%. We developed a new automatic technique to overcome these problems.

Methods: A principle axis transformation was applied to perfusion images to correct for translational and rotational motion artifacts. Bone voxels and neighboring voxels were removed from the perfusion images. Only brain voxels were included in the AIF and VOF measurement procedures. The selection criteria, such as large area under the concentration–time curve, early arrival of contrast agents, and narrow effective width, were used to select appropriate arterial and venous voxels for the AIF and VOF measurements. The proposed automatic technique was tested in 20 patients with unilateral cerebral arterial stenosis. The results of the proposed technique were compared to the results obtained by manual measurements and commercially available automatic selection software.

Results: The AIFs and VOFs were successfully measured using the proposed automatic technique in all 20 patients. The curve shapes, including the area under the concentration–time curve, peak concentration, time to peak, and effective width of the automatically measured AIFs or VOFs were comparable to that were measured manually.

Conclusion: The proposed automatic measurement technique successfully overcomes the motion artifact and random noise problems encountered in measuring AIF and VOF. It can be easily integrated into software for the automatic calculation of cerebral blood volume and flow.

1. Introduction

Cerebral computed tomography perfusion (CTP) images provide information on the local perfusion of brain tissue for patients with cerebral vascular diseases, such as acute ischemic stroke and proximal arterial stenosis [1–3]. Using this technique, the passage of contrast agents through the brain is recorded by acquiring dynamic images. According to the indicator dilution theory, the cerebral blood volume (CBV) for a tissue voxel is calculated as the ratio of the areas under the concentration–time curve (AUC) between a tissue voxel and a reference voxel containing 100% blood [2–5]. Typically, a voxel at the sinus confluence or an adjacent superior sagittal sinus, straight sinus, or transverse sinus is used as the reference voxel, and its concentration–time curve is called the venous output function (VOF).

For the deconvolution calculation of cerebral blood flow (CBF), an additional arterial input function (AIF) is needed [1–5]. The AIF is the concentration–time curve of an arterial voxel containing 100% blood. Because arterial vessels are smaller than the voxel size of CTP images, the measured concentration–time curve at an arterial voxel, $C_{artery}(t)$, is reduced by a factor equal to the partial volume (PV) of blood in the voxel. The AIF can be calculated from $C_{artery}(t)$ using the VOF as a correction reference 3–5. Typically, a

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voxel at either the anterior cerebral artery or the middle cerebral artery that is not affected by proximal arterial stenosis or occlusion is selected for measuring $C_{artery}(t)$.

Automatic techniques have been developed by vendors for the automatic measurements of AIF and VOF from CTP images. Sanelli et al. found the failure rate for correctly measuring both AIF and VOF is 65% in 20 patients, by using a vendor's automated post-processing software [6]. Soares et al. report that the failure rates are 16.7% and 10% in measuring AIF and VOF in 30 patients, respectively, by using another vendor's software [7]. They found that VOF voxels are selected on skull bone and AIF voxels are selected on superior sagittal sinus in the failed cases [7]. Motion artifact and random noise might be the causes of errors in these automatic techniques. Therefore, an experienced neuroradiologist is needed to manually identify the arteries and veins on CTP images for measuring AIF and VOF. As a result, postprocessing of the CTP images cannot be fully automatic in clinical practice.

In this study, we report an improved automatic measurement technique with the reduction of motion artifact and random noise. This technique was applied to CTP images in 20 patients with unilateral arterial stenosis for measuring AIF and VOF as a test (Table 1). The measurement results were compared to that obtained by manual measurements and commercially available automated postprocessing software.

2. Materials and methods

2.1. Theory

The concentration of contrast agents for a voxel on CTP images is related to the attenuation changes expressed as:

$$C(t)=k_1[S(t)-S_0] \quad (1)$$

where k_1 is a constant that converts the Hounsfield units to concentration, $S(t)$ is the attenuation at time t, and S_0 is the baseline attenuation before the arrival of the contrast agents. Because k_1 is a constant, and it is canceled out in the CBV and CBF calculation, we set $k_1=1$ and $C(t)$ is expressed in Hounsfield units to simplify the calculation.

Table 1
Patient demographics.

Number	Sex	Age	Arterial condition
1	F	55	Occlusion, right M1
2	M	80	95% stenosis, right ICA
3	M	84	Occlusion, left CCA
4	M	45	Occlusion, left M1
5	M	78	Occlusion, right ICA
6	M	71	Occlusion, right ICA
7	F	38	Occlusion, left ICA
8	M	78	Occlusion, left ICA
9	M	53	95% stenosis, right ICA
10	F	40	Occlusion, right ICA
11	M	78	Occlusion, left ICA
12	M	68	95% stenosis, left ICA
13	M	75	90% stenosis, right ICA
14	F	46	Occlusion, left distal ICA
15	M	74	Occlusion, right ICA
16	M	61	Occlusion, right ICA and M1
17	F	83	Occlusion, right M1
18	F	80	Occlusion, right M1 and A2
19	M	62	90% stenosis, right ICA
20	F	64	Occlusion, right ICA and M1

The abbreviations used are: M: male, F: female, M1: horizontal segment of the middle cerebral artery, ICA: internal carotid artery, CCA: common carotid artery, A2: the second segment of the anterior cerebral artery.

According to the indicator dilution theory [2–5], the CBV for a voxel is the ratio of the AUC's between a tissue voxel, $C_{tissue}(t)$, and a voxel containing 100% blood, $C_{blood}(t)$, during the first pass of the contrast agent as described by:

$$\mathrm{CBV}=\frac{k_H}{\rho}\frac{\int_{first\ pass}C_{tissue}(t)dt}{\int_{first\ pass}C_{blood}(t)dt} \quad (2)$$

where k_H is a correction factor that accounts for the difference in hematocrit between the vessel and the capillaries, and ρ is the density of the brain tissue [2,5,8,9]. The concentration–time curve, $C(t)$, can be fitted to a gamma-variate function to extract the first pass of contrast agents [10]. The mathematical form for a gamma-variate function is described by:

$$C_{gamma}(t)=k_2(t-t_g)^{\alpha}e^{-(t-t_g)/\beta} \quad (3)$$

where k_2 is a constant, t_g is the contrast agent arrival time of the fitted gamma-variate function, and α and β are related to the wash-in and wash-out of contrast agents, respectively. The AUC for the fitted curve is described by:

$$\mathrm{AUC}_{fit}=\int_{first\ pass}C_{gamma}(t)dt=k_2\beta^{\alpha+1}\Gamma(\alpha+1) \quad (4)$$

The fitted peak concentration is:

$$\mathrm{Peak}_{fit}=k_2(\alpha\beta)e^{-\alpha} \quad (5)$$

The effective width (EW) of the curve is the AUC_{fit} divided by the peak concentration described by:

$$\mathrm{EW}_{fit}=\alpha^{-1}\beta^{\alpha}e^{\alpha}\Gamma(\alpha+1), \quad (6)$$

and time to peak (TTP) of the fitted curve is:

$$\mathrm{TTP}_{fit}=t_g+\alpha\beta \quad (7)$$

Because AIF and VOF are both assumed to be measured from voxels containing 100% blood, their CBV are the same, and this relationship is expressed as:

$$\int_{first\ pass}\mathrm{AIF}(t)dt=\int_{first\ pass}\mathrm{VOF}(t)dt \quad (8)$$

however, arterial vessels are smaller than the voxel size on CTP images, and the concentration–time curve measured at an arterial voxel, $C_{artery}(t)$, is affected by the PV of the blood in the arterial voxel, described by:

$$C_{artery}(t)=\mathrm{PV}\cdot\mathrm{AIF}(t)+(1-\mathrm{PV})C_{tissue}(t) \quad (9)$$

Because AIF(t) is much larger than $C_{tissue}(t)$, assuming that PV is between 20% and 100% for arterial voxels, $C_{artery}(t)$ can be approximated as:

$$C_{artery}(t)=\mathrm{PV}\cdot\mathrm{AIF}(t) \quad (10)$$

As a result, the PV value for an arterial voxel can be calculated as:

$$\mathrm{PV}=\frac{C_{artery}(t)}{\mathrm{AIF}(t)}=\frac{\int_{first\ pass}C_{artery}(t)dt}{\int_{first\ pass}\mathrm{AIF}(t)dt}=\frac{\int_{first\ pass}C_{artery}(t)dt}{\int_{first\ pass}\mathrm{VOF}(t)dt} \quad (11)$$

and the AIF(t) can be calculated as:

$$\mathrm{AIF}(t)=\frac{C_{artery}(t)}{\mathrm{PV}}=C_{artery}(t)\frac{\int_{first\ pass}\mathrm{VOF}(t)dt}{\int_{first\ pass}C_{artery}(t)dt} \quad (12)$$