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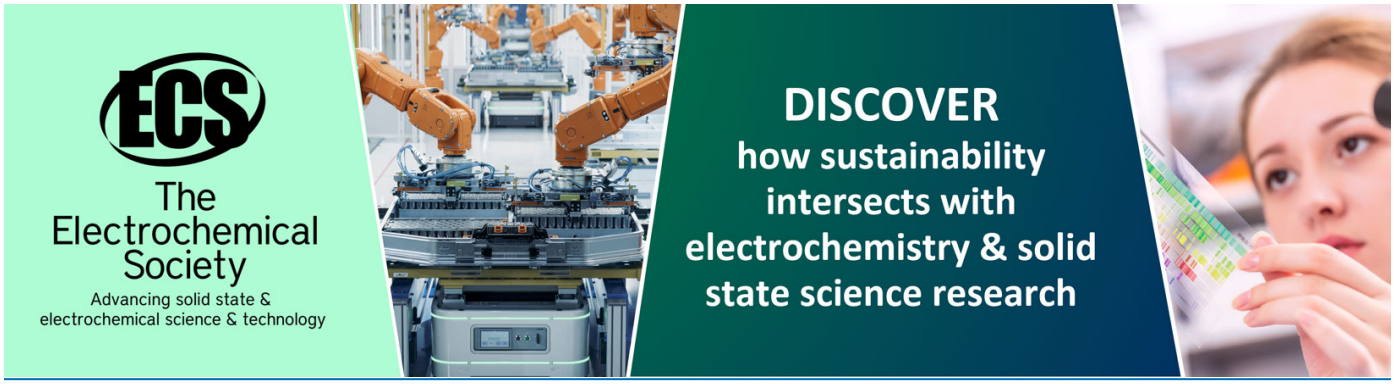

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Automated detection of arterial input function in DSC perfusion MRI in a stroke rat model

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ABSTRACT: Quantitative cerebral blood flow (CBF) estimation requires deconvolution of the tissue concentration time curves with an arterial input function (AIF). However, image-based determination of AIF in rodent is challenged due to limited spatial resolution. We evaluated the feasibility of quantitative analysis using automated AIF detection and compared the results with commonly applied semi-quantitative analysis. Permanent occlusion of bilateral or unilateral common carotid artery was used to induce cerebral ischemia in rats. The image using dynamic susceptibility contrast method was performed on a 3-T magnetic resonance scanner with a spin-echo echo-planar-image sequence (TR/TE= 700/80 ms, FOV= 41 mm, matrix= 64, 3 slices, SW= 2 mm), starting from 7 s prior to contrast injection (1.2ml/kg) at four different time points. For quantitative analysis, CBF was calculated by the AIF which was obtained from 10 voxels with greatest contrast enhancement after deconvolution. For semi-quantitative analysis, relative CBF was estimated by the integral divided by the first moment of the relaxivity time curves. We observed if the AIFs obtained in the three different ROIs (whole brain, hemisphere without lesion and hemisphere with lesion) were similar, the CBF ratios (lesion/normal) between quantitative and semi-quantitative analyses might have a similar trend at different operative time points. If the AIFs were different, the CBF ratios might be different. We concluded that using local maximum one can define proper AIF without knowing the anatomical location of arteries in a stroke rat model.

KEYWORDS: Data processing methods; MRI (whole body, cardiovascular, breast, others), MR-angiography (MRA)

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Contents

1 Introduction

Dynamic susceptibility contrast-enhanced magnetic resonance imaging (DSC-MRI) that uses a contrast medium provides brain perfusion images such as cerebral blood flow (CBF), cerebral blood volume (CBV), and vascularmean transit time (MTT) image. DSC-perfusion MRI has been widely applied to assess ischemia in small animal stroke models. Quantitative CBF estimation requires deconvolution of the tissue concentration time curves with an arterial input function (AIF). However, image-based determination of AIF in rodent is challenging due to limited spatial resolution.

Quantitative perfusion measurements may be derived by different postprocessing methods [1–3] and algorithms. Although the estimated AIF is used as a global AIF for the whole brain some literatures has been shown that the presence of bolus delay and dispersion between the artery and the tissue of interest can be a significant source of error in CBF quantification [5–7]. There is no conclusive proof that result. So our paper Remove recirculation from the calculated contrast agent concentration signal identify and select arterial input functions (AIFs) [8], perform deconvolution. The aim of our paper is to define the feasiblely AIFs automatically for the perfusion MRI.

2 Materials and methods

2.1 Animals

This experimental study was performed in two operation methods accordance with the guidelines of Chang Gung Memorial for the care and use of laboratory animals. SHR rats (weight 200-250g), which were housed under diurnal lighting conditions and were allowed free access to food and water, were anesthetized with Ketamina/Xylazine (2% xylazine and 10% ketamine : 1:2, administration of 1 μl/g of body weight, therefore, equivalent to a dosage of 68.75mg of ketamine/kg and 6.25 mg of xylazine/kg.) One method is the left common carotid artery (CCA) and the external carotid artery (ECA), and the external jugular vein (EJV) were meticulously exposed under an operative microscope while the cerevical sympathetic trunk was preserved. The left ECA was ligated and resected at its origin. The ipsilateral CCA and EJV were ligated and divided above the ligature.

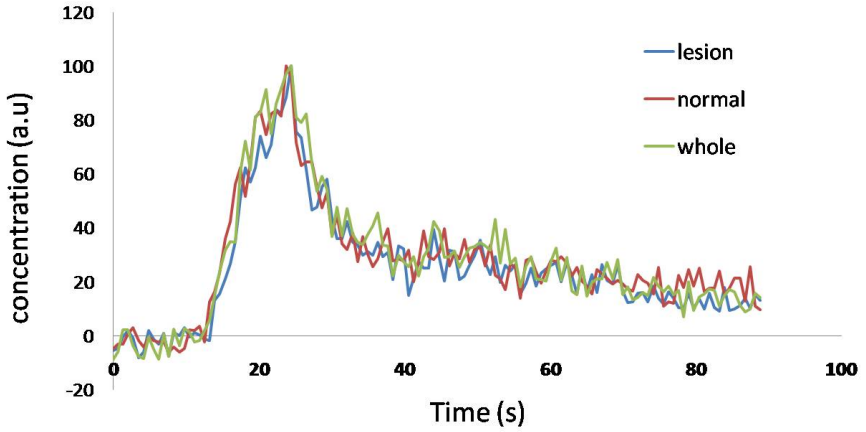

Figure 1. Automatically determined arterial input function (AIF) based on pixels with maximal contrast enhancement in different regions of interest (e.g. whole brain, hemisphere without lesion and hemisphere with lesion). The AIFs were in similar shape with literatures. In this stroke model (occlusion of bilateral common carotid artery), no significant difference was observed between the AIFs obtained in these three regions.

According to the method reported by Morgan et al., an end-to-end anastomosis of the rostral ends of both vessels was completed, as illustrated in figure 1. The internal jugular vein was hypoplastic, and the cerebral venous blood drains mainly to the external jugular veins throught the transverse sinus and the retroglenoid veins in rats. Another method is bilateral common carotid artery occlusion (BICCAO) were carefully exposed and dissected out. The mid-portion of both common carotid arteries were permanently ligated with silk sutures (No.1.5) The animals were allowed to liver at ambient temperatures (25-30 $^{\circ}$ C) after recovery from anesthesia. Reperfusion time points were 1 day, 1 week, 2 weeks, and 4 weeks. Sham-control animals were prepared in the same way except for the ligation of both common carotid arteries. All the rats received tail pressure measurement immediately before the anesthesia. Rats with tail mean blood pressure lesser than 160 mmHg in SHR. Before MRI examination, the rats were anaesthetized with intraperitoneal injection of 2.5 mg ketamine hyhrochloride and 1.16 mg xylazine (2-(2.6-xylidino-)-5.6-dihydro-4H-1.3 thiazine hydrochloride) per 100 grams body weights plus intramuscular injection of the foregoing mixing anesthetics (ketamine hyhrochloride and xylazine mixed solution) when the condition required. Then, left inguinal area was carefully exposed, and the left femoral vein was dissected out. For contrast (0.15 mmol Dimeglumine gadopentetate contrast, Magnevist, Germany) injection, biomedical silicone catheter with 0.64mm in external diameter was inserted into the femoral vein and was well fixed. The skin was closed temporarily with two sutures.

2.2 fMRI acquisition

For MRI examination, the rats were placed prone in a 3.0-T scanner system (Trio A Tim System, Siemens, Germany) with wrist coils. Scout multi-slice T2-weighted spin-echo MR images (TR/TE = 4000/102 ms, slice thickness 2 mm, 7 slices) were acquired in xz planes to control rat head positioning. The field of view was 3.5 $\times$4 cm2 and the matrix size was 112 $\times$128 mm^2. Axial multi-slice perfusion-weighted images (PWI) were acquired by using a T2*- echo-planar imaging

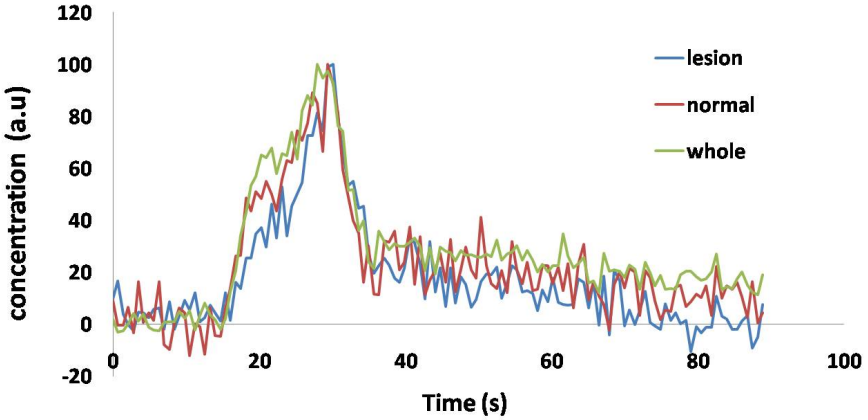

Figure 2. Automatically determined arterial input function (AIF) based on pixels with maximal contrast enhancement in different regions of interest (e.g. whole brain, hemisphere without lesion and hemisphere with lesion). The AIFs were in similar shape with literatures. But the AIF obtain from lesion side in this stroke model (ipsilateral CCA and EJV were ligated and divided above the ligature to induce ischemia), was found significant delay compared with the AIFs obtained in others ROIs.

weighted sequence (TR/TE =700/80 ms, slice thickness =2 mm, 3 slices). During the dynamic image series of 128 measurements production, the contrast material was injected into femoral vein started at 7th second when dynamic image series of 11th measurement was produced. The field of view was 4.1 $\times$ 4.1 cm2 and the matrix size was 64 $\times$64 mm^2.

2.3 fMRI data analysis

Perfusion data were using nordicICE v2.2 software (NordicImagingLab AS, Norway.) to obtain AIF (arterial input function) and perfusion maps. For quantitative analysis, AIF was obtained from three different ROIs (region of interest) , whole brain, pick up 20 pixels with greatest contrast enhancement, hemisphere without lesion and hemisphere with lesion pick up 10 pixel with greatest contrast enhancement and used for deconvolution. For the semi-quantitative analysis ,relative CBF and CBV was estimated by the integral divided by the first moment of the relaxivity time curves. Images were analyzed with the Alice program (PAREXEL International Corporation, USA). In all animals, perfusion values including cerebral blood volume (CBV), cerebral blood flow (CBF), were calculated in the brain regions shown in figure 2. Comparing the CBF and CBV ratios (lesion/normal) between quantitative and semi-quantitative analyses.

3 Results and discussion

Automatically determined arterial input function (AIF) based on pixels with maximal contrast enhancement in different regions of interest (e.g. whole brain, hemisphere without lesion and hemisphere with lesion), show in figure 1. The AIFs were in similar shape with literatures. There are two different kinds of the stroke model (occlusion of bilateral and ipsilateral common carotid artery). As the diagrams indicate no significant difference was observed between the AIFs obtained in these three regions (figure 1a) (occlusion of bilateral and common carotid artery). It

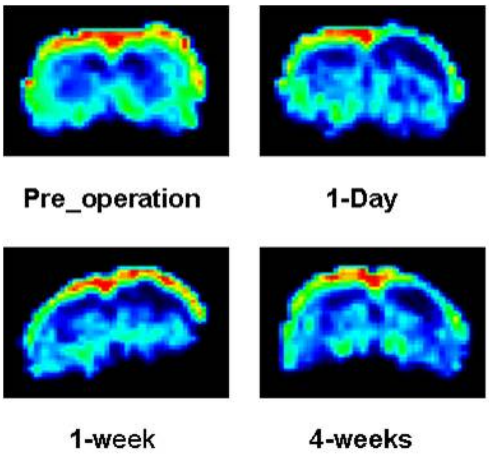

Figure 3. The rat with first operation method. Quantitative CBF maps obtained at four different time points pre- and post-operation. The ischemic lesion was observed at one side of the brain one day after operation.

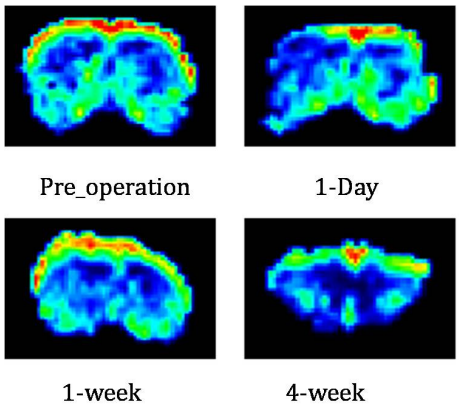

Figure 4. The rat with second operation method. Quantitative CBF maps obtained at four different time points pre- and post-operation. The ischemic lesion was observed at one side of the brain one week after operation.

was found obvious delay compared with the AIFs obtained in others ROIs in figure 1b, another diagrams with second Rat model. (ipsilateral CCA and EJV were ligated and divided above the ligature to induce ischemia.) We can say with fair certainty that we can detect the legitimate AIFs. The rat with first operation method. Quantitative CBF maps obtained at four different time points pre- and post-operation. The ischemic lesion was observed at one side of the brain one day after operation. The figure 2 display the rat with second operation method. Quantitative CBF maps obtained at four different time points pre- and post-operation. The ischemic lesion was observed at one side of the brain one week after operation. In figure 3a the CBF ratio(lesion/normal) between quantitative and semi-quantitative analyses showed the similar trend along different operative time points. The normal CBF values were obtained from ROIs with similar sizes as the lesion side but covering normal brain tissues in the contralateral side of the brain. The CBF ratio (lesion/normal) between quantitative and semi-quantitative analyses showed the semi-quantitative and AIF obtain

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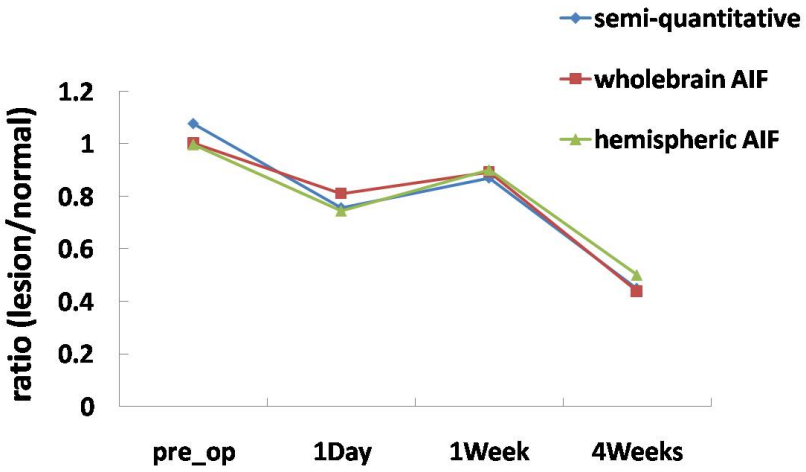

Figure 5. The CBF ratio (lesion/normal) between quantitative and semi-quantitative analyses showed the similar trend along different operative time points. The normal CBF values were obtained from ROIs with similar sizes as the lesion side but covering normal brain tissues in the contralateral side of the brain.

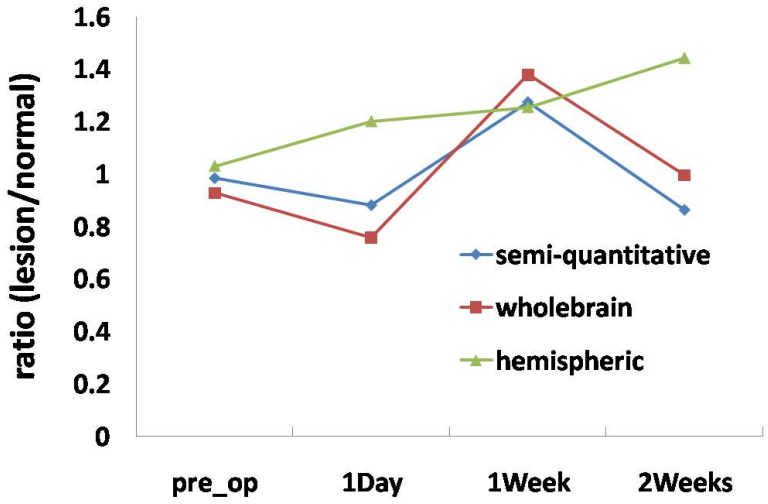

Figure 6. The CBF ratio (lesion/normal) between quantitative and semi-quantitative analyses showed the semi-quantitative and AIF obtain from wholebrain were in similar trend. And AIF obtain from hemispheric with and without lesion were underestimation along one day and two weeks operative time points. The normal CBF values were obtained from ROIs with similar sizes as the lesion side but covering normal brain tissues in the contralateral side of the brain.

from wholebrain were in similar trend. And AIF obtain from hemispheric with and without lesion were underestimation along one day and two weeks operative time points. The normal CBF values were obtained from ROIs with similar sizes as the lesion side but covering normal brain tissues in the contralateral side of the brain.

In conclusion, we evaluated the feasibility of automated AIF detection and compared the results with those obtained from commonly applied semi-quantitative analysis

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