Variability of CBF calibration using venous output function in DSC-MRI of rat brains

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Introduction Dynamic susceptibility contrast (DSC) MRI is a promising technique for the assessment of cerebral blood flow (CBF). Absolute quantification of CBF is desirable for stroke management, longitudinal tumor therapy monitoring and diagnoses of dementia. One of the challenges for quantifying CBF with DSC-MRI is to obtain an accurate estimation of arterial input function (AIF). In particular, identifying the AIF from MR images in small animals may be more problematic due to the inevitable partial-volume effects. Previous researchers had proposed a method of using venous output function (VOF) for calibrating the AIF in DSC-MRI of human subjects (1,2). The VOF was obtained from the sagittal sinus and had to be carefully corrected for signal saturation. This study aimed to investigate the feasibility and variability of using this method for estimating absolute CBF in rat brains.

Materials and methods The experiment was performed on six normal Sprague-Dawley female rats. The rats were initially anaesthetized with 5% Isoflurane at 1L/min air flow and then maintained with 1.5~2% Isoflurane throughout the experiment. For injection of contrast medium (0.5 mmol Dimeglumine gadopentetate contrast, Magnevist, Bayer Schering Pharma, Berlin, Germany), biomedical silicone catheter with 0.64 mm in external diameter was inserted into the femoral vein and well fixed. When performing MRI examination, the rats were placed prone in a 7T animal MRI system (BRUKER ClinScan 70/30 USR, Germany) with the brain covered by a phased array coil optimized for rat brain imaging. A single-shot gradient-echo EPI sequence was used for DSC-MRI with TR/TE/FA = 600 ms/ 10 ms/ 50°, GRAPPA with iPAT factor = 2, in-plane matrix = 128 x 128, slice thickness = 2 mm without gap, in-plane resolution= 0.3 mm x 0.3 mm, dynamics = 160, total scan time of 96s. The contrast agent was injected into the femoral vein, started at the 10th dynamic measurement. Signal-time curves were first converted into changes of delta-R2* time curves on a voxel-by-voxel bases. An AIF were obtained from a voxel close to the middle cerebral artery. Relative CBF was calculated by a deconvolution method with the singular value decomposition algorithm using the Nordic ICE software (ver. 2.2). To calibrate the relative CBF into an absolute estimate, a VOF with minimal partial volume averaging was obtained. In brief, a saturated time curve was first obtained from a voxel within the sagittal sinus. To correct for the signal saturation, another time curve was obtained from an adjacent small vein (sVOF), with the similar temporal profile but without signal saturation. The VOF was then obtained by time shifting and magnifying the sVOF to match the increasing and decreasing slopes of the original saturated curve. A calibration factor (CF) was calculated as the ratio of areas under the curves (AUC) from VOF versus that from the AIF. Three methods for integrating the AUC were compared: (1) integration of the whole time curve, (2) integration of the time period of the first-pass, (3) integration of the whole first-pass time curve, obtained by fitting with a gamma-variate function. The absolute CBF maps were then obtained by dividing the relative maps with the CF. To evaluate the variability of the calibration, four voxels within the sagittal sinus were selected as the VOFs, from which four CFs were calculated. The range of the calibrated CBF values from these four CFs was then determined for each rat.

Table 1 CBF values (ml/100g/min) obtainedfrom the three methods.

Method	Mean CBF (SD)
Method 1	63.5 (241.4)
Method 2	135.9 (53.3)
Method 3	123.9 (34.2)

Table 2 CBF values (ml/100g/min) obtained from varied VOF locations

Rat no.	Mean (SD)	Maximum	Minimum	(Max-Min)/Mean
1	102.7 (8.7)	114.7	94.7	19.5%
2	103.4 (3.4)	108.3	100.5	7.6%
3	101.3 (11.9)	111.8	84.3	27.1%
4	101.3 (1.5)	105.6	92.5	8.6%
5	134.7 (16.8)	149.0	116.3	24.3%
6	199.9 (10.8)	211.9	185.6	13.2%

Results and Discussion Table 1 listed CBF values of the cortical region after the calibration using the CFs from the three integration methods. In general, methods for determining AUC from AIF and VOF curves affected the calibration results significantly. In particular, Method 1 resulted in a large standard deviation in CBF. This may be due to the variation in baseline concentration after the first-pass, which can be affected by recirculation and/or vessel permeability. Method 2 is problematic because the overlapping regions of the first- and the second pass are not separated. Method 3 is more time consuming during image processing, but should be more accurate and the results exhibited less variations among rats. Original VOFs obtained by different voxels in the sagittal sinus in one of the rats are showed in figure 1(a). These curves (VOFs) are corrected by an adjacent small vein and then obtained the corrected concentration time curves (cVOFs) in figure 1(b), which appear consistent to each other. Table 2 lists the CBFs obtained from different voxels within the sagittal sinus and the ranges are between 7.6% and 27.1%. The amount of variation is generally smaller than the CBF change due to diseases such as stroke(3,4). Figure 2 shows the brain maps of coefficient of variance (CV) between rats. It demonstrates that the variance in CBF values is reduced after the calibration. In summary, we have demonstrated that the VOF-based calibration for CBF quantification is feasible in DSC-MRI of rats. Variability of CBF caused by the selection of VOF was determined, which could serve as a reference for studies of diseased models.

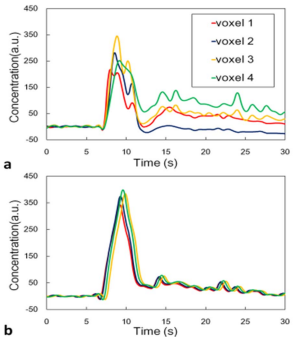

Figure 1(a) Original concentration time curves (VOFs) and (b) the correspondingly corrected time curves (cVOFs)

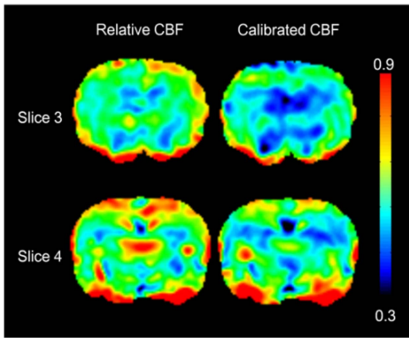

Figure 2 Brain maps of coefficient of variance (CV) of all rats. Left side is CV maps of relative CBF, and right side is CV maps of calibrated CBF.

References

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