An automated approach for the quantification of brain oxygen metabolism

Peiying Liu[1], Yan Cao[2], Jinsoo Uh[1], and Hanzhang Lu[1]

[1]*Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [2]*Department of Mathematical Science, University of Texas at Dallas, Dallas, Texas, United States*

INTRODUCTION: Cerebral metabolic rate of oxygen ($CMRO_2$) is an important index of tissue viability and brain function, but traditionally the quantification of this parameter is a "niche market" of Positron Emission Tomography (PET). Xu et al. have recently proposed an MRI technique to estimate whole-brain $CMRO_2$ by combining non-invasive measures of CBF, arterial and venous oxygenation (1). The arterial oxygenation is measured by pulse oximetry, the venous oxygenation is measured by the newly developed TRUST MRI technique (2,3), and the whole brain CBF is measured by the phase-contrast (PC) MRI technique. While extensive technical testings have revealed that the method can provide a non-invasive (no exogenous agent), fast (<5 min in scan time), and reliable (coefficient of variation, CoV<3%) estimation of $CMRO_2$ (thus may have immediate clinical utilization), the only major obstacle before wider applications is that the slice positioning of the PC MRI scans requires considerable training and expertise. The PC scans need to be positioned perpendicular to feeding arteries at the entry point of skull. Given large variability in arterial trajectory across individuals, this task presents a major challenge to the operator and contributes significantly to measurement noise. In the present work, we developed an automatic positioning algorithm for the PC MRI based on image analysis of a time-of-flight angiogram. We tested the reproducibility of $CMRO_2$ measures using the proposed approach and compared the results to those obtained with manual positioning by an experienced operator.

METHODS: *Framework of the $CMRO_2$ measurement:* The proposed MRI procedure for a complete $CMRO_2$ dataset is illustrated in Fig. 1. First, a time-of-flight angiogram covering the foramen magnum is performed to visualize the feeding arteries for the PC MRI positioning. Then the operator exports the angiogram dataset to another computer where the automatic positioning algorithm is running. While the algorithm is calculating the PC slice coordinates, the TRUST MRI scan is performed to measure the venous oxygenation (Y_v). After that, the calculated positioning parameters (off-center distances and angulations in F-H, R-L and A-P directions) from the automatic positioning algorithm can be used to position the PC MRI scans, without any subjective inputs from the operator. Four PC scans will be performed, which correspond to the major feeding arteries of the brain, i.e. left and right internal carotid arteries (ICA), left and right vertebral arteries (VA). The sum of fluxes in these arteries gives the whole-brain CBF measure. Once Y_v and CBF are obtained, the whole-brain $CMRO_2$ can be calculated according to the Fick Principle: $CMRO_2=CBF\cdot(Y_a-Y_v)\cdot C_a$, where Y_a can be measured by pulse oximetry, and C_a is the amount of oxygen molecules that a unit volume of blood can carry and is well established in physiology literature (4). The total duration of the whole scanning procedure is less than 5 minutes.

The automatic positioning algorithm: The algorithm is consisted of the following steps (Fig 2):

1. The dataset of the 3D angiogram is loaded into memory;
2. The dataset is segmented into several objects based on a multi-level thresholding of the image intensity. The carotid arteries (including both internal and external carotid arteries) and the VA are detected based on the size and position of the objects, then the skeleton curve representations of these arteries are extracted;
3. The derivative in z (F-H) direction of the left VA is compared to a template (obtained from the averaging of 10 typical subjects) to identify the centers of PC imaging slice for left ICA and left VA, respectively, the matching of the template and VA derivative is based on cross-correlation;
4. The angulation of the PC imaging slice is determined so that the normal direction of the plane is along the tangent of the artery skeleton curve, where the tangent vector is determined by the best fitting line in a small neighborhood;

Steps 3 and 4 are repeated for the right ICA and right VA. The off-center distances and angulations in relative to the iso-center of the scanner are calculated for each of the determined plane. These values as the output of the algorithm are the positioning parameters of the PC MRI scan for the brain's feeding arteries.

Evaluation study: Seven young, healthy subjects (4 male, 26.4±3.7 years) were studied on a Philips 3T scanner. Each subject underwent two sessions. During each session, the PC MRI scans were performed twice, one with automatic positioning and the other with manual positioning. The operator performing the manual PC positioning was blinded from the automatic positioning outcome. Data processing of TRUST and PC MRI followed methods used previously (1,2). The resulted $CMRO_2$ calculated using CBF obtained from the manual and automatic positioning methods were compared. The reproducibility of the slice location of the two positioning methods was also assessed. Paired t-test was utilized for statistic analysis.

RESULTS and DISCUSSION: The mean $CMRO_2$ were 157.37±21.88 μmol/100g/min and 155.80±21.48μmol/100g/min from the automatic PC positioning and manual PC positioning, respectively. They are highly correlated (Fig. 3, p=0.0002), but without significant differences (p=0.41). Thus, the automatic positioning algorithm does not create systematic bias in the results, as compared to an experienced operator. Table 1 summarizes the reproducibility of the two positioning methods in terms of $CMRO_2$ values as well as slice coordinates. The inter-session difference of $CMRO_2$ measures using the automatic PC positioning and the manual PC positioning were not significantly different (p=0.81). The inter-session difference in slice location and angulation were also not significantly different between the two positioning methods (p=0.06 and 0.34, respectively). These findings suggest that the automatic PC positioning algorithm provides measures that are at least as accurate and precise as an experienced operator.

Our study provided a turn-key solution for the quantitative evaluation of the whole-brain $CMRO_2$, which has minimal operator-dependence. Although this method does not provide spatial information, the simplicity and reliability features of this technique are highly desirable for many researchers and may significantly enhance the clinical utility of the important parameter, $CMRO_2$, in understanding many brain diseases that are of diffused or neurodegenerative nature.

REFERENCES: 1) Xu et al. MRM 62 :141, 2009; 2) Lu and Ge, MRM 60:357, 2008 ; 3) Xu et al., MRM in press, 2011; 4)Guyton and Hall, Textbook of medical physiology, 2005.

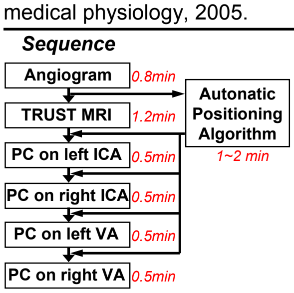

Fig 1 The MRI procedure for a complete $CMRO_2$ dataset.

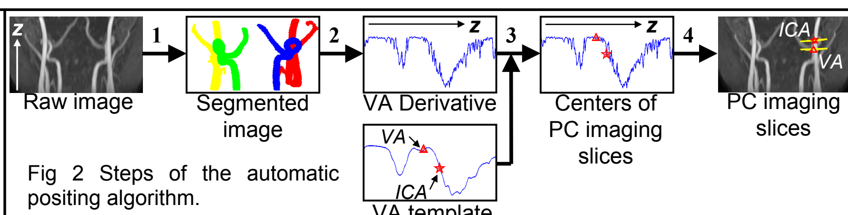

Fig 2 Steps of the automatic positing algorithm.

Table 1 Reproducibility analysis between session 1 (S1) and session 2 (S2).

	$CMRO_2$ Difference (%)	Location Difference (mm)	Angulation Difference (º)
Manual S1 vs. S2	7.62±5.59 (p=0.87)	1.42±0.97 (p=0.33)	2.88±1.74(p=0.20)
Auto. S1 vs. S2	7.07±7.80 (p=0.42)	0.95±1.00 (p=0.93)	2.11±2.30(p=0.87)

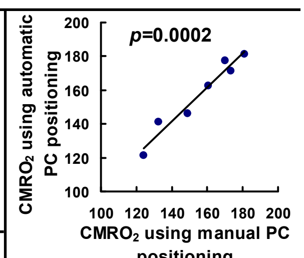

Fig 3 Scatter plot of the two $CMRO_2$ measures (μmol/100g/min) using manual and automatic PC positioning, respectively (N=7).