A one-stop-shop for hemodynamic imaging in Moyamoya disease

Peiying Liu[1], Babu G Welch[2], Darlene King[2], Yang Li[1], Marco Pinho[1,3], and Hanzhang Lu[1]

[1]*Advanced Imaging Research Center, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [2]*Neurological Surgery Clinic, University of Texas Southwestern Medical Center, Dallas, Texas, United States,* [3]*Department of Radiology, University of Texas Southwestern Medical Center, Texas, United States*

TARGETED AUDIENCE: Physicians and researchers interested in cerebrovascular diseases.

PURPOSE: Brain stenotic diseases such as Moyamoya disease (MMD) are characterized by diminished cerebrovascular reserve, such that blood vessels lose their ability to direct more blood supply to tissues when needed, potentially resulting in transient ischemia. In recent years, there has been growing interest to estimate cerebrovascular reserve by mapping cerebrovascular reactivity (CVR), which denotes the vessel's response to a vasodilatory stimulus such as CO2 inhalation (1-3). Compared to single-point measures of resting perfusion, CVR may have added value on the diagnosis and treatment planning for these patients, especially in guiding surgical intervention and assessing the efficacy of surgical revascularization (1). Recently, a novel, time-efficient breathing paradigm was developed that is capable of mapping CVR in about 9 min (4). Furthermore, *concomitantly*, the same data can generate two other hemodynamic parameters, a venous CBV (vCBV) and a response time map. Therefore, this new technique may represent a "one-stop-shop" for mapping vascular properties in patients with cerebrovascular conditions, without using Gd contrast agent. In this study, we aim to demonstrate the utility of this technique in MMD patients. Our results showed that MMD patients have reduced CVR, although their vCBV seems to be intact. The response time (RT) map was able to depict vascular deficit regions, the contrast of which is qualitatively similar to the CT-derived time-to-peak (TTP) map.

METHODS: *Subjects:* 10 patients with MMD (2 males, age range 24-60 y) were recruited. 4 patients had right supraclinoid ICA stenosis, 2 had left supraclinoid ICA or MCA stenosis, and 4 had bilateral supraclinoid ICA stenosis. 8 of the 10 subjects have had surgical treatment (angioplasty or bypass) prior to this study, and 2 were untreated. Data from healthy volunteers were used for comparison purposes.

MRI Experiment with concomitant CO2/O2 breathing: All subjects were studied on a 3T (Philips). CVR, vCBV, and RT maps were computed from a single scan using a concomitant CO2/O2 challenge while continuously collecting BOLD images. The timing of the CO2 and O2 paradigms were carefully designed so that they are orthogonal to each other in the time domain and they have different frequencies in the frequency domain (Fig. 1) (4). BOLD signal change to CO2 is used as CVR; BOLD signal change to O2 reflects vCBV; and response time-shift relative to the stimulus onset is the RT. During the 9.3min breathing challenge, end-tidal CO2 (EtCO2) and O2 (EtO2) were recorded and BOLD images were continuously acquired with the following parameters: TR/TE=1510/21ms, 3.2mm isotropic voxels, whole brain coverage using 36 slices with 1mm gap. Time-of-flight MR angiogram (TOF-MRA) was also acquired in MMD patients, to assess the severity of the arterial stenosis.

Data analysis: Using frequency analysis described previously (5), CVR, vCBV, and RT maps were obtained for each subject. Qualitative assessment was conducted by visual inspection (e.g. Fig. 2). Quantitative assessment was conducted by ROI analysis in which average values in the perfusion territories of left and right anterior cerebral arteries (ACAs), middle cerebral arteries (MCAs) and posterior cerebral arteries (PCAs) (6) were determined.

Patient categorization: Based on the TOF-angiogram, an experienced radiologist (blinded to CVR maps) divided the MMD patients into two groups, the MMD^- group (N=6) with successful revascularization and good distal branches developed, and the MMD^+ group (N=4) with suboptimal revascularization and poor distal branches developed.

Correction of CVR with vCBV: BOLD-derived CVR index (like the one reported here as well as those in the literature) is unfortunately not a "pure" vascular reserve measure. It is also affected by vCBV, simply because of "more veins, more BOLD signal". Therefore, the vCBV measure is also important for proper interpretation/correction of the CVR data. We corrected the CVR value by computing a "Normalized CVR" as CVR divided by vCBV.

RESULTS and DISCUSSION: Figure 1 shows the EtCO2 and EtO2 time courses and the resulted BOLD time course during the concomitant CO2/O2 breathing. Reliable CVR and vCBV maps were obtained in all MMD patients. Figure 2 shows CVR, vCBV, and normalized CVR maps in a MMD patient and a healthy subject. From the CVR maps, pronounced deficit was found in arterial territories consistent with the TOF-MRA abnormalities (red arrows in Fig. 2). Because of the vCBV effect, CVR maps showed strong contrast among large veins, gray matter and white matter, complicating the identification of parenchymal deficits. On the other hand, in the normalized CVR map, the extent of CVR deficit regions could be more easily delineated (green arrows in Fig. 2). No vCBV deficit was apparent.

Quantitative analysis showed that CVR of the control, MMD^- and MMD^+ groups are 0.23±0.04, 0.22±0.08 and 0.13±0.02 %/mmHg, respectively. MMD^+ group had significantly lower CVR than control (p=0.03) and MMD^- group (p=0.04), while MMD^- group was not different from control (p=0.86). vCBV of the three groups are 0.0050±0.0008, 0.0059±0.0011 and 0.0060±0.0008 %/mmHg, respectively, with no difference between the groups. When plotting the normalized CVR and vCBV in a scatter plot (Fig.3), it can be seen that normalized CVR was tightly distributed in healthy volunteers, while MMD patients had lower values. Within the MMD subgroups, MMD^+ had the most severe reduction but MMD^- also showed certain degree of reduction. For vCBV, the three groups were largely overlapped and, if any, the patient groups had slightly higher vCBV, possibly due to rich collateral vessels in this disease. This indicates that MMD patients have normal vCBV, but their vasodilatory function was aberrant in the disease-affected territories.

Figure 4 shows the RT maps in two MMD patients, along with their CT-derived time-to-peak (TTP) maps. We found that the RT maps were qualitatively similar to the TTP maps. Since TTP is an important index in clinical diagnosis of cerebrovascular diseases such as stroke, it is plausible that RT map using the gas-inhalation approach could also provide useful information in cerebrovascular diseases.

CONCLUSION: We proposed a "one-stop-shop" method for hemodynamic imaging in cerebrovascular diseases, in which resting-state and challenged-state vascular properties as well as kinetic properties are obtained in a single scan of about 9 minutes without need for radiation exposure of administration of exogenous contrast agents. We showed that MMD patients have diminished vasodilatory function while their baseline vCBV was intact. This method may be a practical and valuable method in cerebrovascular diseases.

REFERENCES: 1) Mikulis et al, J Neurosurg 103:347, 2005; 2) Heyn et al, AJNR 31:862, 2010; 3) Donahue et al, JMRI 38:1129, 2013; 4) Liu et al, ISMRM 2014, p753; 5) Blockley et al, MRM. 65:1278, 2011; 6) Tatu et al, Neurology 50:1699, 1998.

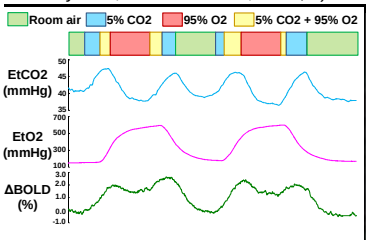

Fig. 1: Simultaneous CO2/O2 challenge. (a) Paradigm design. (b) Corresponding EtCO2 and EtO2 time courses.

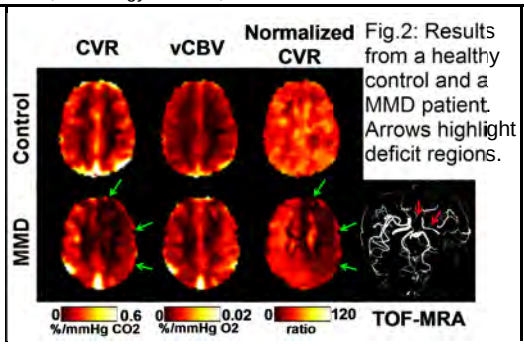

Fig.2: Results from a healthy control and a MMD patient. Arrows highlight deficit regions.

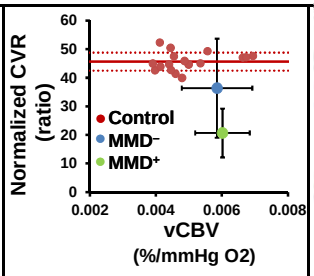

Fig. 3: Scatter plot of normalized CVR and vCBV.

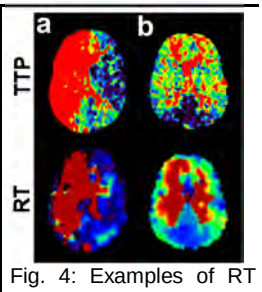

Fig. 4: Examples of RT map and CT-TTP map from two MMD patients.