

Calibrated MRI in patients with occlusive cerebrovascular disease.

J. B. De Vis¹, E. T. Petersen¹, N. S. Hartkamp¹, A. Bhogal¹, C. J.M. Klijn², L. J. Kappelle², and J. Hendrikse¹

¹Radiology, University Medical Center Utrecht, Utrecht, Netherlands, ²Neurology, University Medical Center Utrecht, Utrecht, Netherlands

Introduction and purpose: Calibrated MRI has increasingly been used to measure brain metabolism in healthy volunteers. Hemodynamic parameters, evaluated with calibrated MRI, related well to literature values obtained with gold standard oxygen-15 positron emission tomography (O15-PET)¹. Therefore, non-invasive calibrated MRI has the potential to replace invasive O15-PET. In clinical practice, O15-PET is of value when investigating hemodynamic impairment in patients with cerebrovascular disease². The purpose of this study was to investigate whether calibrated MRI could be used, in a similar way as O15-PET, to detect hemodynamic impairment in patients with cerebrovascular disease.

Methods: This study was approved by our institutional ethical review committee. The MRI protocol (3T, Philips) consisted of an MP-RAGE and dual-echo pseudocontinuous arterial spin labeling (pCASL: TR/TE₁/TE₂: 4000/13.8/36.3 ms, label duration 1650 ms, postlabel delay 1550 ms, voxel 3x3x7 mm and 135 dynamics). A prospective end-tidal gas targeting system (RespiractTM, Thornhill Research Inc., Toronto, Canada) was used to deliver two 105s hypercapnia challenges during the pCASL acquisition. First echo data were used to quantify cerebral blood flow (CBF) using a general linear model³, while second echo data provided BOLD signal changes. A general BOLD signal model^{4,5} was applied to calculate oxygen extraction fraction (OEF) and cerebral metabolic rate of oxygen (CMRO₂). Fifteen patients with occlusion of one or both of the internal carotid arteries (ICA) were included. Four patients were excluded due to claustrophobia (2 subjects) or anxiety during hypercapnic breathing. Of the remaining 11 patients, 4 patients had right ICA occlusion, 4 left ICA occlusion and 3 double-sided occlusion. Patients were age-and gender matched to one or two (in case of double-sided occlusion) healthy control subject(s). For all subjects CBF maps, ASL-and BOLD CVR maps, OEF maps, and CMRO₂ maps were co-registered to the Montreal Neurological Institute standard brain template (MNI152) using flirt linear registration⁶ and fnirt nonlinear registration (fsl fmrib software). An in house developed perfusion territory template was then applied to obtain ROIs of each perfusion territory. These ROIs were combined with a gray matter mask to obtain gray matter values. Values obtained in the ipsilateral medial cerebral artery (MCA) territory as well as whole brain values of patients were compared to the controls using student's t-tests.

Results: Delayed bolus arrival which propagated from the ASL maps to the OEF and CMRO₂ maps (Figure 1) was visualized in 3 of the 11 patients. Therefore, data were analyzed with and without these subjects. Results are shown in Table 1. Significant differences were found in BOLD reactivity, with lower BOLD reactivity in the ipsilateral MCA perfusion territory and the whole brain gray matter of patients compared to controls ($p < 0.01$ and $p < 0.05$, respectively). ASL reactivity in the ipsilateral MCA perfusion territory trended towards reduced reactivity in patients compared to healthy controls ($p = 0.053$ for all patients, and $p = 0.096$ in the patients without delayed arrival). None of the other hemodynamic parameters showed significant differences.

Discussion: Our results show decreased BOLD reactivity in response to hypercapnia in patients compared to healthy controls. We did not find differences in the OEF between these groups, suggesting that the reduced BOLD signal change may be due to decreased vascular reactivity. This notion, however, was not supported by our ASL reactivity measurements possibly due to the lower SNR in ASL compared to BOLD images. In cases where cerebral perfusion pressure is reduced due to vascular disease, the initial cerebro-autoregulatory response generally involves vascular dilatation restoring adequate perfusion at the cost of vascular reserve capacity. If this mechanism is insufficient OEF must increase to counteract tissue hypoxia⁷. The fact that we observed decreased reactivity without a concomitant increase in OEF may be due to our patient selection; all patients were asymptomatic for at least one year. Important to note is that we found some limitations of calibrated MRI in vascular diseased patients; hypercapnic breathing induced anxiety in 13% and delayed arrival artifacts were present in 27%. Future studies should explore the additional value of OEF-and CMRO₂ measurements over BOLD reactivity.

	N		CBF (ml/100g/min)		ASL CVR (%)		ΔBOLD		OEF (%)		CMRO ₂ (μmol/100g/min)	
	MCA	wb	MCA	wb	MCA	wb	MCA	wb	MCA	wb	MCA	wb
Patients												
All	14	11	40 ± 4	42 ± 6	11 ± 11	15 ± 13	1.3 ± 0.7	1.7 ± 0.6	28 ± 9	34 ± 10	109 ± 37	129 ± 45
No DA	11	8	40 ± 3	41 ± 5	10 ± 12	12 ± 14	1.4 ± 0.7	1.6 ± 0.6	30 ± 8	36 ± 10	114 ± 41	135 ± 51
Controls												
All	14	11	39 ± 10	38 ± 9	19 ± 11	20 ± 10	2.2 ± 0.4	2.3 ± 0.3	30 ± 10	31 ± 4	115 ± 33	111 ± 33
No DA	11	8	38 ± 10	36 ± 8	19 ± 11	20 ± 12	2.2 ± 0.3	2.3 ± 0.3	31 ± 7	30 ± 4	108 ± 32	100 ± 24

Table 1: Hemodynamic parameters were calculated both in the gray matter of the ipsilateral MCA perfusion territory (MCA) and in whole brain gray matter (wb); ASL CVR and ΔBOLD are given for a 10 mmHg increase in end-tidal CO₂. Patients data are compared to healthy age-matched controls. Analysis is performed on all datasets (all) and in the patients without delayed arrival of flow (No DA).

References: [1] Wise RG et al. Neuroimage 2013. [2] Powers WJ et al. JCBFM 1985. [3] Buxton RB et al. MRM 1998. [4] Davis TL et al. Proc Natl Acad Sci USA 1998. [5] Hoge RD et al. MRM 1999. [6] Jenkinson M et al. Neuroimage 2001.

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Figure 1.

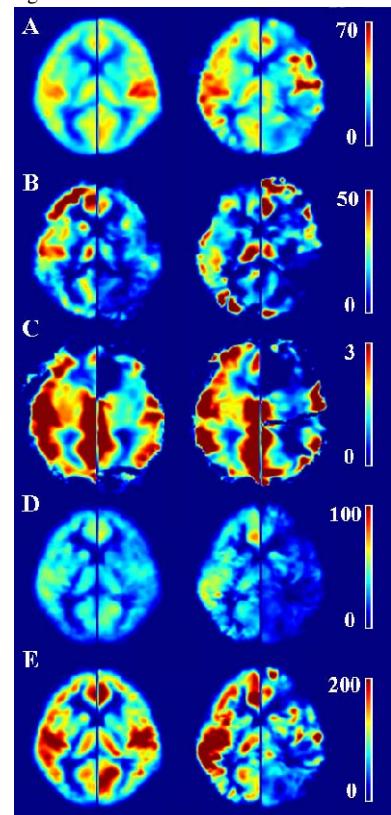


Figure 1: In all images, the right hemisphere represents data of the healthy controls, the left hemisphere shows the data of the occlusion patients. The images in the left column show the patients without delayed arrival artefacts and their control subjects. The right column shows the data of the subjects with delayed arrival and their controls. (A) ASL CBF map. (B) ASL CVR map. (C) BOLD CVR map. (D) OEF map. (E) CMRO₂ map.