Vascular Space Occupancy (VASO) MRI Demonstrates Changes in Cerebral Blood Volume in Internal Carotid Artery Stenosis Patients After Carotid Revascularization

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Introduction. In patients with steno-occlusive internal carotid artery (ICA) disease, cerebral hemodynamic impairment at the brain tissue level is an important indicator of stroke risk (1). Previous studies have demonstrated that patients with ICA stenosis either maintain cerebral blood flow (CBF) through adequate compensatory collateral flow (no hemodynamic impairment), or exhibit a more serious stage I hemodynamic impairment (1), in which CBF is maintained by autoregulatory increases in cerebral blood volume (CBV). Therefore, CBV determination may aid in identifying patients who will benefit most from carotid revascularization. We noninvasively measured CBV in a series of ICA stenosis patients using vascular space occupancy (VASO)-MRI, a recently developed blood-nulling technique sensitive to CBV (2). VASO-fMRI reactivity measurements to breath hold were made in healthy volunteers and symptomatic ICA stenosis patients before and after carotid revascularization.

Methods. *Experiment.* Gradient-echo VASO-fMRI was performed at 3T on symptomatic ICA stenosis patients (n=7) before and one month after revascularization (stent placement or carotid endarterectomy). Healthy volunteers (n=7) were scanned for comparison. VASO images were acquired at both short TR (TR/TI=2/0.711s) and long TR (TR/TI=5/1.054s). Subjects were instructed to perform a task consisting of 60s normal breathing, 4s exhalation and 14s breath hold, repeated three times; mean signal changes ($\Delta S/S$) in voxels meeting activation criteria (cc<-0.15, cluster size≥3) were calculated separately for right and left hemispheres for each TR. Duplex ultrasound was used to determine degree of ICA stenosis pre- and post-intervention; patients with bilateral stenoses (n=4) received intervention on the symptomatic side only and were grouped separately. Other MR parameters: FOV=240mm, matrix=80x80, slice thickness=3mm, TE=15ms. *Qualitative Interpretation.* Long TR $\Delta S/S$ ($\Delta S/S_{TR=5s}$) is more negative when baseline CBV is increased, whereas short TR $\Delta S/S$ ($\Delta S/S_{TR=2s}$) is sensitive to both CBF and CBV (3). Therefore, qualitative CBV changes are apparent in $\Delta S/S_{TR=5s}$, which were the focus of this study. *Quantitative Interpretation.* The model of Donahue et al. (3) was fit to mean voxel $\Delta S/S_{TR=2s}$ and $\Delta S/S_{TR=5s}$ in each brain hemisphere. Specifically, assuming only gray matter (GM) signal changes between rest and activation, $\Delta S/S$, in terms of MR signal S and volume fractions X, may be written,

$$\frac{\Delta S_{Total}}{S_{Total}^{rest}} = \frac{\left(X_{CSF}S_{CSF} + X_{GM}S_{GM}^{act}\right) - \left(X_{CSF}S_{CSF} + X_{GM}S_{GM}^{rest}\right)}{\left(X_{CSF}S_{CSF} + X_{GM}S_{GM}^{rest}\right)} \quad [1]$$

for $S_{CSF} \sim C_{CSF} \cdot M_{CSF}(TR,TI) \cdot e^{-TE/T_{2,CSF}^{*}}$ [2] and $S_{GM} \sim (C_{GM} - CBV_{GM} \cdot C_b) \cdot M_{GM}(TR,TI,CBF) \cdot e^{-TE/T_{2,GM}^{*}}$ [3]

where C is water density (4), $M_{CSF}(TR,TI)$ is steady-state CSF water magnetization and $M_{GM}(TR,TI,CBF)$ is the CBF-dependent steady-state GM magnetization (3). A mean X_{CSF}=0.15 based on FAST segmentation was used for all patients. It has been shown that in stage I hemodynamic impairment, resting CBF (CBFres) is maintained (1); therefore, healthy CBFres=55 ml/100g/min was assumed and breath hold CBF (CBFact) and CBV (CBFact), as well as resting CBV (CBVres) were determined by fitting. The Grubb relationship (5) with α=0.5 (6) was applied between CBF and CBV to ensure unique fit solutions (3,7).

Results and Discussion. $\Delta S/S_{TR=5s}$ in both age-matched controls (n=2; age:73±2; $\Delta S/S_{left}$=-0.021±0.006, $\Delta S/S_{right}$=-0.021±0.009) and non-age-matched controls (n=5; age:27±2; $\Delta S/S_{left}$=-0.014±0.002, $\Delta S/S_{right}$=-0.014±0.001) showed little variation between hemispheres. As expected, an age-dependence in $\Delta S/S$ was observed due to increased CSF in older volunteers. By contrast, slightly increased $\Delta S/S_{TR=5s}$ was observed ipsilateral to stenosis in all unilateral ICA stenosis patients (n=3; $\Delta S/S_{ipsilateral}$=-0.034±0.007; $\Delta S/S_{contralateral}$=-0.028±0.007) consistent with mild stage I hemodynamic impairment. This was not observed in bilateral ICA stenosis patients (n=3; $\Delta S/S_{ipsilateral}$=-0.042±0.01; $\Delta S/S_{contralateral}$=-0.042±0.01). One bilateral ICA stenosis patient had difficulty performing the breath hold and was excluded. Fig. 1a shows an example pre-intervention time course for a patient with right ICA stenosis. Increased $\Delta S/S_{TR=5s}$ and a large "post-stimulus overshoot," consistent with compensatory hyperventilation, are observed in the hemisphere ispsilateral to stenosis. This post-stimulus overshoot was observed to some degree in 4/6 patients, but not in controls. Upon fitting and extraction of CBFact, CBVres and CBVact, an increase in CBVres was found ipsilateral to the stenosis (Fig. 1b). In all unilateral ICA stenosis patients, a small decrease in $\Delta S/S_{TR=5s}$ was found post-intervention, consistent with the expected lower CBVres (Fig. 2). Patients with bilateral ICA stenosis did not show consistent decreases in $\Delta S/S_{TR=5s}$ or CBVres, likely due to residual hemodynamic impairment from the enduring stenosis, which was only removed on the symptomatic side. Fig. 3 shows the quantitative CBVres, CBVact and CBFact fitting results for unilateral ICA stenosis patients. Caution should be exercised upon interpretation, as absolute values will vary with X_{CSF} and CBFres, which were assumed to be the same in all voxels. Based on the promising results of this ongoing preliminary study, we believe that VASO-MRI may provide valuable information to complement conventional imaging protocols for ICA stenosis. Additional studies are needed to confirm the postulated relationship between VASO-MRI evidence of hemodynamic impairment and stroke risk, and to determine whether VASO-MRI might help in selecting candidates for carotid revascularization.

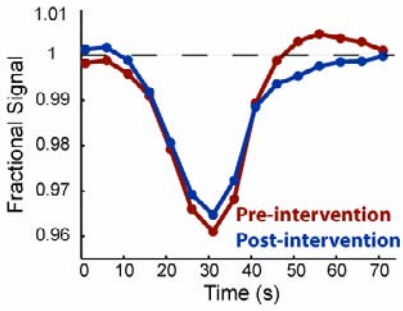

Fig. 2. Averaged TR=5s time course for all unilateral ICA stenosis cases (n=3) pre- and post-intervention. Note the decrease in $\Delta S/S$ post-intervention and the pre-intervention compensatory post-stimulus overshoot.

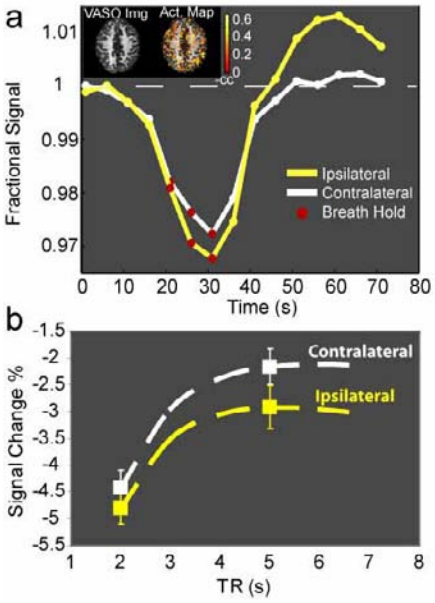

Fig. 1. Averaged TR=5s time course for patient with unilateral right ICA stenosis (a). Notice the larger ipsililateral $\Delta S/S$, consistent with increased CBVres, and ipsilateral post-stimulus overshoot, consistent with compensatory hyperventilation. VASO image and breath hold activation map shown in insert. When fitting the signal changes (b), CBVres ipsilateral is found to be higher contralateral to stenosis (see Fig. 3).

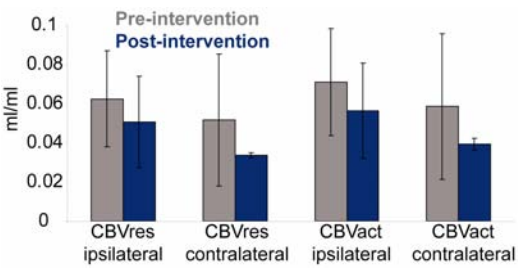

Fig. 3. CBVres and CBVact for patients with unilateral ICA stenosis (n = 3). Large error bars (SEM) reflect a large variation in CBVres and CBVact between patients.

References. 1. Derdeyn, C.P et al. *AJNR* 19,1463-9(1998). **2.** Lu et al. *MRM*. 2003Aug;50(2):263-74. **3.** Donahue et al. *MRM*. 2006 Oct 30; [Epub]. **4.** Lu et al. *JMRI*. 2005Jul;22(1):13-22. **5.** Grubb et al. *Stroke* 1974;5:630-639. **6.** van Zijl et al. Nat Med. 1998Feb;4(2):159-67. **7.** ISMRM 2007 Abs#228; Funding: NCRR RR15241, NIBIB EB004130, Philips Medical Systems.