Arterial cerebral blood volume (aCBV)-weighted inflow vascular-space-occupancy (iVASO) provides complementary hemodynamic information to dynamic susceptibility contrast in patients with stenotic artery disease.

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Introduction. Active and passive mechanisms for controlling cerebral blood volume (CBV) at the arterial, capillary and venous levels are incompletely understood, yet central to cerebral blood flow (CBF) regulation. Furthermore, knowledge of CBV changes in different vascular compartments would be important for investigations of fMRI contrast and in clinical scenarios where flow-volume coupling may be impaired. Recently, inflow vascular-space-occupancy (iVASO) was proposed as a non-invasive approach for isolating arterial CBV (aCBV) reactivity [1] and absolute aCBV [2,3]. Specifically, by acquiring an image with and without inflowing blood water signal, a difference image ($\Delta M/M_0$) can be obtained which is proportional to aCBV. This iVASO with dynamic subtraction (iVASO-DS) principle has been proposed [2,3], however it has not been validated against MR-standard dynamic susceptibility contrast (DSC) measurements, nor has it been compared against other hemodynamic measures such as CBF, total CBV and mean transit time (MTT=CBV/CBF). Here, we compare iVASO-DS contrast with DSC-measured CBF, CBV, and MTT in patients with varying degrees of steno-occlusive disease of the internal carotid artery (ICA).

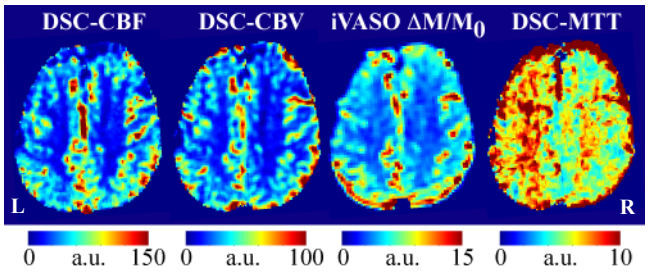

Fig. 1. Maps for 75 yr male with L / R stenotic burden = 80 / 100 %.

Methods. All patients (n=17; age=72.6±7.9 yrs) provided informed, written consent and were scanned at 3.0T (Siemens) using a protocol consisting of DWI, T1-weighted (T1w), DSC, and iVASO-DS. Patient preparation. Stenosis degree in left and right ICAs were measured by duplex ultrasound; patients were grouped as mild stenosis (stenosis<60%) (n=8) and moderate-to-severe stenosis (stenosis≥60%) (n=9). Experiment. Scan parameters were optimized for each modality: *DWI*: TR/TE=4400/93, 1.6x1.6x3.0 mm^3, b-value=1000 s/mm^2. *3D T1w MPRAGE*: TR/TI/TE=1800/900/4.4 ms, 1.7x1.7x2.0 mm^3. *DSC with intravenous Gd-DTPA injection* [4]: TR/TE=1481/30 ms, 1.7x1.7x5.0 mm^3. *iVASO-DS* [2]: TR/TE/TI=1778/18/989 ms, 2.4x2.4x5.0 mm^3. Processing. All data were corrected for motion and baseline drift [5], spatial smoothing (FWHM=5 mm) was applied to DSC and iVASO-DS images, and gray matter (GM) masks were generated. GM quantification was performed separately in affected (aff) and unaffected (unaff) brain hemispheres, defined as contralateral or ipsilateral to maximum ICA stenosis burden, respectively. For DSC, PErfusioN Graphical User Interface (Penguin) software with a singular value decomposition was applied to calculate CBF, CBV and MTT [6]. Quantification is sensitive to arterial input function (AIF) choice; we used automated AIF detection available in the software and conservatively characterize all maps in arbitrary units (a.u.). iVASO $\Delta M/M_0$=(control-null)/M_0 was calculated, with white matter signal in the absence of preparation pulses being used for M_0 calibration. $\Delta M/M_0$ scales linearly with aCBV when TI= capillary arrival time (CAT; time for nulled blood to reach capillaries) [2,3], which at TI=989 ms has been assumed to be approximately correct. Additionally, we attempt to account for CAT asymmetries using the DSC-measured MTT, which in the absence of collateral flow would be expected to be proportional to flow velocity and hence to CAT. This yields a new, corrected (’), $\Delta M/M_0$ ratio:

$$\left[\left(\frac{\Delta M}{M_0}\right)_{aff} \Big/ \left(\frac{\Delta M}{M_0}\right)_{unaff}\right]' = \left[\left(\frac{\Delta M}{M_0}\right)_{aff} \Big/ \left(\frac{\Delta M}{M_0}\right)_{unaff}\right] \cdot \left(\frac{MTT_{aff}}{MTT_{unaff}}\right) \qquad [1].$$

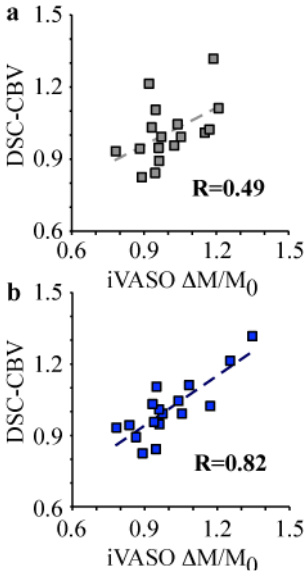

Fig. 2. DSC vs. iVASO left:right uncorrected (a) and MTT-corrected (b) ratios.

Results. No DWI or T1w lesions were observed in analyzed GM regions. Fig. 1 shows representative maps for a patient with a hemispheric MTT discrepancy. Qualitative contrast agreement between DSC-CBV and iVASO is generally apparent even in the presence of MTT discrepancies. Fig. 2a shows left:right DSC-CBV vs. left:right iVASO $\Delta M/M_0$ for all volunteers. In (a), iVASO ratios are uncorrected for MTT and show a detectable, albeit weak (R=0.49) correlation. When ratios are MTT-corrected (Eq. 1) (b), the correlation improves significantly (R=0.82). In Fig. 3, CBF (a), MTT (b) and aCBV (MTT-corrected) (c) values are shown for all subjects. Red shapes depict mild stenosis patients and blue shapes moderate-to-severe stenosis patients. The black line is a linear trend line for all data; the blue trend line is for moderate-to-severe patient data. DSC-measured CBF is largely symmetric irrespective of patient subgroup, whereas the largest discrepancy is found for iVASO. Some of this effect is due to one patient (Fig. 3c, black arrow), however when this patient is excluded, the correlation is still reduced in moderate-to-severe patients (R=0.69) compared to all patients (R=0.76). The reduced slope of the iVASO-aCBV trend line indicates elevated aCBV in the affected hemisphere and is consistent with regional autoregulation.

Discussion. First, iVASO contrast appears complementary to DSC-measurements, however small regional differences were observed (Fig. 1). These differences are frequently in regions of large vessels and may be due to differences in partial volume effects or differences between total CBV vs. aCBV weighting. Second, iVASO shows a detectable correlation with DSC-CBV between hemispheres (Fig. 2a); the correlation is significantly improved when regional MTTs are taken into account (Fig. 2b). iVASO is sensitive to CAT, which is different from MTT (mean time for bolus to pass through tissue given instantaneous AIF). While these transit times are likely related, additional improvements to iVASO aCBV quantification will require incorporating explicit information on CATs. Third, while a highly symmetric (R=0.85-0.89) DSC-measured CBF in patients was observed, MTT and iVASO $\Delta M/M_0$ in moderate-to-severe stenosis patients were more asymmetric. iVASO $\Delta M/M_0$ was the most asymmetric between hemispheres (R=0.69), even after MTT correction; therefore, aCBV may be a more sensitive indicator of early stage hemodynamic impairment than CBF in patients with stenotic artery disease. Future studies with additional patients, tracked over a longer period of time, will be necessary to validate this possibility. For iVASO, bipolar gradients to dephase large vessel signal will likely be useful for quantitatively understanding microvascular aCBV as well, and comparisons with other emerging aCBV-weighted approaches will be useful [7]. In conclusion, we assess the correlation between the non-invasive aCBV-weighted iVASO-DS and DSC in patients with stenotic artery disease; iVASO provides comparable contrast to DSC CBV, especially when CAT variations are taken into account and may provide an indicator of hemodynamic impairment in steno-occlusive disease.

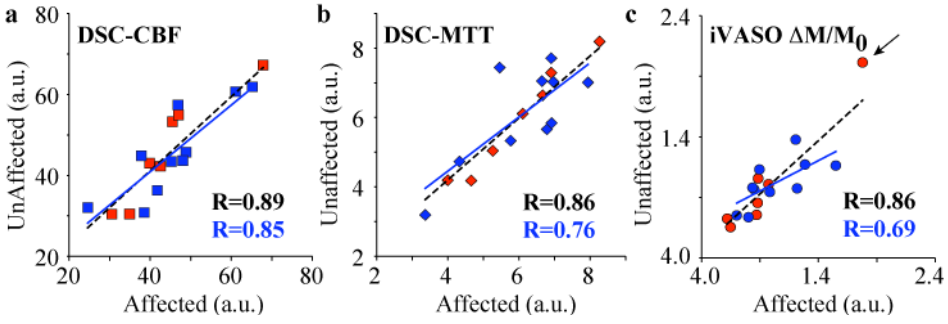

Fig. 3. CBF (a), MTT (b) and iVASO unaffected vs. affected hemisphere contrast.

References. [1] Hua J et al. ISMRM 2009. Abs.12. [2] Donahue MJ et al. ISMRM 2009. Abs. 627. [3] Hua J. et al. ISMRM 2009. Abs. 1533. [4] Wintermark M et al. AJNR 2008;29. [5] Jenkinson M and Smith S. Med Im Anal. 2001;5. [6] Ostergaard L. et al. www.cfin.au.dk/software/penguin. [7] Petersen ET et al. MRM 2006;55.

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