Quantification of the local dynamic of the cerebrovascular autoregulation

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Introduction: To quantify local cerebrovascular autoregulation in function of the arterial partial pressure of CO_2 (PaCO2), we combined quantitative cerebral blood flow (CBF) measurements using Arterial Spin Labeling (ASL) and Blood-oxygen-level-dependent (BOLD) cerebrovascular reactivity (CVR) measurements together with controlled prospective end tidal PaCO2 targeting. CVR is defined as % BOLD signal change per mmHg of PaCO2.

In neurovascular patients, CVR is a clinically well-established risk assessment metric. BOLD MRI can be used for CVR measurements, a derivative of cerebral blood flow changes under vasoactive stimuli. Previous studies found a good correlation between CBF and BOLD[1, 2], even if other parameters might play a subordinate role. On the other hand, ASL can quantify CBF, but the long acquisition time (TA) prohibits dynamic measurements. In our previous studies[3], breath holding induced PaCO2 changes in cerebral tumor patients, with great intra/inter-subject variability. Prospective end tidal targeting provides reliable and repeatable PaCO2 changes[4] and was therefore incorporated in our protocol. We acquired dynamic CVR with BOLD and quantitative CBF with ASL in healthy subjects and neurovascular patients and demonstrate how to combine these data and discuss their advantages relative to the actual clinical standard H2O-PET acquired on the same patients.

Methods: Eight healthy subjects (mean age 29.8±3.7) and one patient (age 51) with left internal carotid occlusion and left hemisphere infarction were scanned on a 3T Skyra with a 32 channels headcoil. Using a respiration mask, PaCO2 was manipulated using a prospective end tidal gas blender (RespirAct^{tm}) to describe a step and ramp protocol during the acquisition of BOLD fMRI GE singleshot EPI voxel:3×3×3 mm^3, slice gap 0.3 mm, acq. matrix 64x64x35, GRAPPA factor 2, TR/TE 2000/30 ms, ~280 volumes. Quantitative CBF was measured during hypocapnia and hypercapnia in two separate acquisitions of 2D PICORE Q2T singleshot EPI ASL, with fat sat, voxel:4×4×8 mm3, slice gap 2 mm, acq. matrix 64x64x9, TR/TE 2500/12 ms, 2x45+1 measurements. Flow limit 100.0 cm/s, Bolus Duration 700 ms, TA: 3:52. Automatic CBF calculation is provided on the scanner for the 2D ASL data.

Using statistical parameter mapping (SPM12), healthy subjects data were realigned, co-registered to the T1MPRage, normalized to MNI space, and smoothed. For the steno occlusive patient data were not normalized. PaCO2 was resampled and time shifted to account for the respiratory-vascular Impuls Response Function (≠ HRF) delay of the BOLD data. GLM included PaCO2, temporal high pass filter, and motion regressors.

Results: Mean± std CVR, CBF and PaCO2 are summarized in **Table 1**. The CVR as BOLD activation map relative to the PaCO2 is shown for the patient **(Figure 1)**, no activation can be seen in the area of the infarction and in surrounding tissue on the left side. The H2O-PET data **(Figure 2),** demonstrates impaired left sided CBF to a lesser extent after a Diamox challenge. Patient hypocapnia ASL **(Figure 3)** and hypercapnia ASL **(Figure 4)** also show a lower CBF increase on the left hemisphere.

The CBF autoregulation by the cerebrovasculature in function of the PaCO2 can be quantified locally (**Figure 5** healthy subject; **Figure 6** patient).

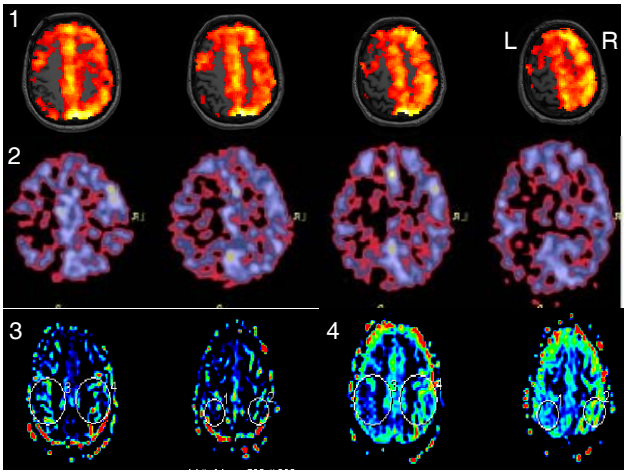

Table 1. CVR, CBF and PaCO2 values for healthy Subjects and Patient				
	Healthy Subjects (N = 8)		Patient (N = 1)	
Sex (male:female)	2:6		1:0	
Bold: Mean Baseline CO2	40.7 (±2.1)		40.6	
CVR whole brain (step)	0.211 (±0.045)		0.159	
Lowest point CO2 ramp	34.5 (±2.3)		31.6	
Highest point CO2 ramp	51.9 (±2.5)		51.7	
Mean CO2 hypocapnia ASL	33.6 mmHg (±3.0)		33.8 mmHG	
Mean CO2 hypercapnia ASL	47.4 mmHG (±2.6)		48.5 mmHg	
Hemisphere	Left	Right	Left	Right
Mean CBF hypocapnia	49 (±18)	50 (±21)	32	33
Mean CBF hypercapnia	72 (±21)	57 (±19)	59	79
Delta % CBF increase ASL	26% (±44)	13% (±31)	89%	139%
CO2 in mmHg, Mean CBF is calculated over a combined total of 242 voxels.				

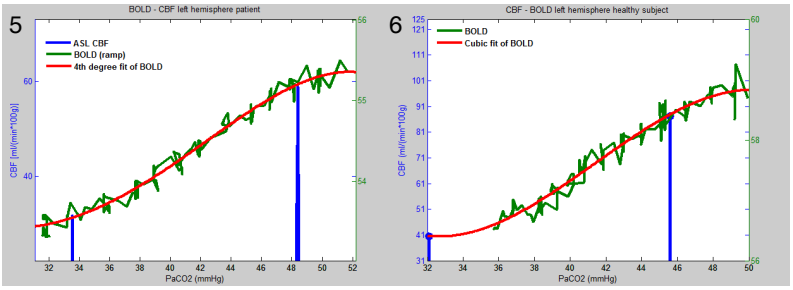

Figure 5: *Patient quantitative CVR on the ischemic left hemisphere. Using the quantitative CBF of the ASL, the CVR can be scaled.*

Figure 6: *On the healthy subjects, the CVR is delayed to higher PaCO2 and high CBF.*

Conclusion: Combining BOLD CVR during a CO2 challenge in healthy and neurovascular patients with quantitative cerebral blood flow changes allows the assessment of a quantitative CVR curve and to deliver a multi-parametric cerebrovascular autoregulation map. This mapping needs a precise control of the PaCO2 and do not suffer from the effect uncertainty of other vasoactive stimuli.

References:

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