Bolus Tracking Perfusion Imaging in Humans Using Quantitative Arterial Input Function

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TARGET AUDIENCE: Developers of methodology for perfusion measurements, clinicians searching for advanced methods.

PURPOSE: We recently presented a method for the quantitative determination of the arterial input function[1]. The method is based on measuring the tracer concentration in the carotid arteries with measurement parameters optimised for blood and exploits the frequency shift induced by the contrast agent. Verification in the porcine model was successful. In this work, we present measurements in two patients. Based on the quantitative AIF, we present and discuss obtained CBV and CBF values. We further present a method for verification of the mean blood flow by measuring the total inflow to the brain using phase contrast MRI.

METHODS: The sequence[1] is based on standard perfusion EPI. In between each slice acquisition in the brain, a slice at the neck is excited. The arterial signal in this slice can be singled out using the following principles: One-dimensional projection of the slice, background suppression with inversion recovery and measuring with a very short echo time. In our previous work[1], the input function was determined using the frequency shift induced by the contrast agent. In this work, we used the corresponding phase shift at a finite TE=4.7ms, similar to the approach known as "phase AIF"[2], as it better suits the measurements with lower contrast agent dose applicable to humans as compared to animals. The tracer concentration in the brain was quantified using the model introduced by Yablonskiy and Haacke[3].

Two male patients with a one-sided carotid stenosis were measured in a 3T Siemens TIM TRIO scanner with the following parameters: 17 mL @ 3 mL/s of 0.5mol/L Gd-DTPA contrast agent (Multihance, Bracco). EPI: 13 slices, $TE_{GE}/TE_{SE}/TR$=20/86/1590 ms, resolution 2.62x2.62mm^3. Parameters for the neck slice: thickness: 13 mm, TE=4.7 ms. Cardiac Output (CO) was calculated from the AIF using the Stewart-Hamilton formula.

The total inflow to the brain was determined evaluating a phase contrast (PC) measurement (VENC 80 cm/s, resolution (0.7x0.7x5) mm^3) in a slice comprising both internal carotid and the basilar artery. The mean perfusion in the brain was then estimated dividing the time-averaged flow in all three arteries by the brain volume (sum of gray and white matter obtained with a segmentation using SPM).

RESULTS: The AIF could be unambiguously found from the neck slice with a much higher temporal resolution than for the time series in the brain. Perfusion parameters were calculated using Tikhonov regularization. Quantitative maps for one patient are shown in Fig. 1. Histograms of CBF and CBV for gray and white matter are shown in Fig. 2 for both patients.

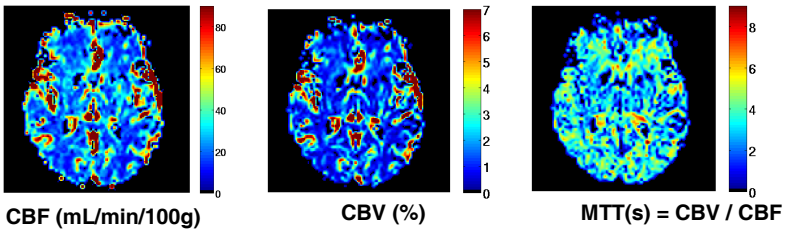

Fig 1: Quantitative perfusion maps for one patient

	CBF *GM*	CBF *WM*	CBV *GM*	CBV *WM*	PC brain	CO (L/min)
P1	33 , 26	21 , 18	2.21 , 1.74	1.44 , 1.15	47	6.9
P2	37 , 27	21 , 16	2.18 , 1.61	1.07 , 0.81	66	6.8

Table 1: Perfusion parameters (mean , median) for gray and white matter. CBF and PC flow are given in mL/(min 100g), CBV in %

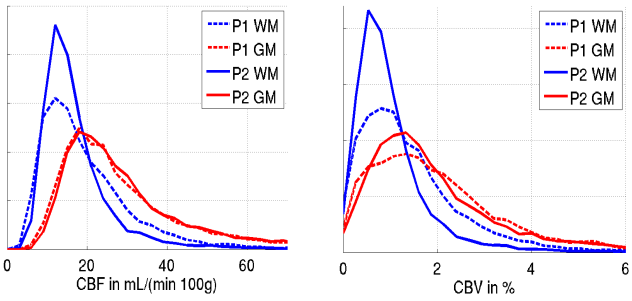

Fig. 2: Histograms of CBF and CBV in white matter (blue) and gray matter (red) for both patients.

DISCUSSION: The obtained cardiac output values are reasonable and suggest the correct AIF quantification. CBV and CBF values are about a factor of 2-3 smaller than usually reported in PET studies. This cannot be explained by an error in the AIF quantification, since the necessary correction would result in an unrealistically high CO. Note that the obtained CBV in gray matter is in a very good agreement with the volume fraction of the capillaries determined using confocal laser microscopy[3] and other direct methods. This can be discussed in terms of poor applicability of statistical relaxation theory[3] to large vessels. The discrepancy with PET CBV can arise from the indirect way of CBV evaluation in PET using diffusible tracers (typical values 3-6%). On the other hand, PET-determined CBF is rather reliable (typically 20 and 60mL/min/100g for WM and GM, respectively).

The mean flow in the whole brain derived from the phase contrast measurement is in the order on values reported in literature. A slight overestimation of our result might follow from neglecting perfusion of the dura mater. The 2.5–3 - fold lower CBF obtained with the perfusion evaluation can be explained by two aspects: It is known, that the necessary regularization in the perfusion calculation causes underestimation of flow. Another thing is the dispersion of the tracer bolus from the AIF measurement site to the tissue. To demonstrate this, we calculated the expected local AIF by convolving the measured one with a transport function derived theoretically from the laminar flow model in a 12-generations vascular tree. Although such local AIF had only a 1.4-fold lower peak concentration, the change in overall shape resulted in CBF values in the expected range. Note that this operation left the CBV values unchanged.

CONCLUSIONS: We demonstrate the feasibility of our recently proposed method for AIF quantification[1] in patient measurements performed in the standard clinical setting. The absence of any correction coefficients or adjustment parameters in the proposed method provides a framework for discussing the biophysical content of CBV and CBF measurements with DCS MRI, the long-standing issues of bolus dispersion, numerous correction schemes and a comparison with PET. Acquisition of further data from patients with carotid stenosis goes on.

References: 1. Kellner E et al. Arterial input function measurements for bolus tracking perfusion imaging in the brain. MRM 2012;DOI: 10.1002/mrm.24319 **2.** Van Osch M J et al. Measuring the arterial input function with gradient echo sequences. MRM 2003;49:1067 3**.** Yablonskiy D and Haacke M. Theory of NMR Signal Behavior in Magnetically Inhomogeneous Tissues: The Static Dephasing Regime. MRM 1994;32:749-763 4**.** Lauwers F e tal. Morphometry of the human cerebral cortex microcirculation: General characteristics and space-related profiles. NeuroImage 2008 39;936–948