Perfusion-based high-resolution fMRI in the primate brain using a novel vertical large-bore 7 Tesla setup

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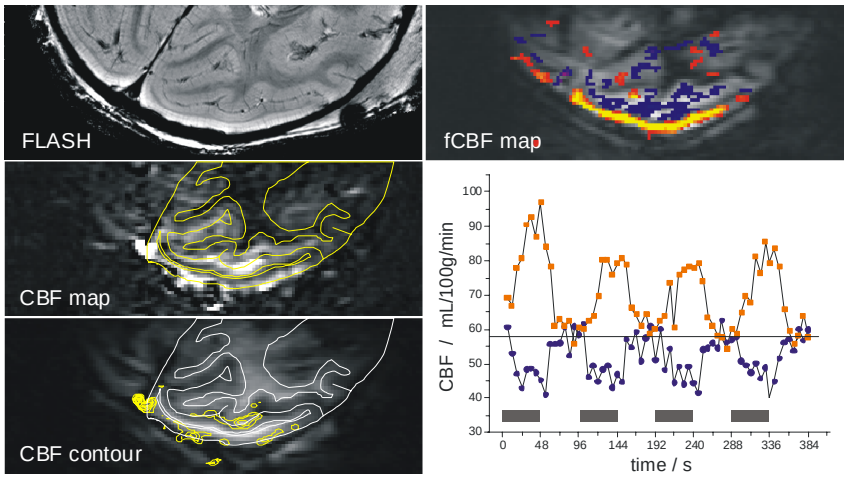
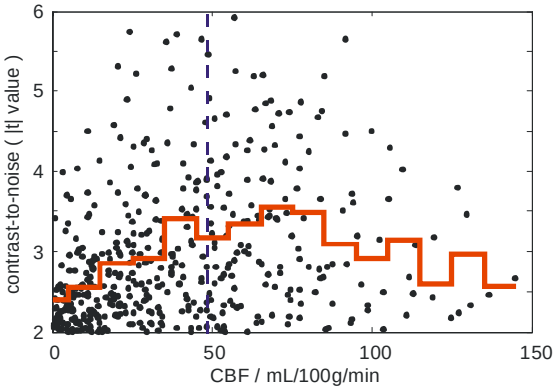
Introduction Functional MR imaging in monkeys promises a bridge between brain research in humans and the large body of systems neuroscience work in animals. Prerequisite for successful interspecies-comparisons, however, is a profound understanding of the neural events underlying the hemodynamic responses. Combined physiology and neuroimaging experiments made the first step in this direction by examining directly the relationship of cell activity to the BOLD signal [1]. The tight coupling between regional neural activity and blood flow, however, suggests that perfusion-based MRI may improve even further the electrophysiological investigations of the neurovascular coupling, as perfusion imaging measures cerebral blood flow (CBF) directly at the capillary level. Moreover, CBF changes and interleaved-acquired BOLD data can be combined to compute changes in oxygen consumption rate.

Obtaining functional CBF maps with high spatial resolution is challenging, because the CBF signal is intrinsically low and the signal-to-noise is critical. Here we report the first high-resolution CBF maps in the *Macaca mulatta* that were obtained with voxel sizes as small as 0.5 x 0.5 x 3 mm^3. High sensitivity was achieved by using a 7 T system and custom-made RF coils in TORO mode. fCBF data were acquired and compared with BOLD data in the macaque primary visual cortex. The fCBF signal was entirely localized within cortex, providing unequivocal evidence for its high spatial specificity. This specificity is of paramount importance for studies seeking to understand the physiological basis of functional neuroimaging.

Methods A novel large-bore *vertical* MR system (7 T/ 60 cm, Bruker) was set up for MRI in the anaesthetized or the awake, behaving monkey [2]. An actively-decoupled RF saddle coil was used for transmission and a 30-mm surface coil for reception. A full-field visual stimulus (8-Hz flickering LED array) was used in a block design with 4 repetitions of on- and off-stimulation-periods (48 s, 8/8 images). *Single-shot* zoomed GE-EPI was acquired at 500-µm in-plane resolution (128x48, FOV 6.4x2.4 cm^2) using outer-volume suppression [3]. The FAIR module used adiabatic slice-selective/ non-slice-selective inversion (TR = 3 s x 2, TIR = 700–1500 s, inversion slice thickness 8 mm). Functional CBF and BOLD scans (FAIR off) were acquired interleaved with TE = 12 and 20 ms, respectively. For semi-quantitative analysis, a M_0 image was measured at TR = 10 s and CBF was calculated according $CBF = (S_{SS} - S_{NS}) / M_0 \cdot \lambda / (TI \cdot (2 \cdot \exp(-TI/T_1) - \exp(-TR/T_1))$, λ=0.9mL/g. T_1 was measured for gray matter in V1 to be 1.9 s.





Results and Discussion Anatomical FLASH and CBF maps at 500-µm in-plane resolution are shown in Fig. 1 (left). Excellent single-shot EPI image quality was achieved by the use of OVS-aided FOV reduction in phase-encode [3]. T2* blurring was still negligible at a readout duration of 31 ms, which is similar to T2* of (29±10) ms at 7 T. Upon visual stimulation, CBF increased in average by 38% from 58.6 (3.8 *sd*) mL/100g/min at rest to 80.9 (5.6 *sd*) mL/100g/min during activation (Fig. 1, right). CBF decreased by –21% in medial areas. A *t*-test revealed activated voxels along the whole visual cortex V1 (t = 2 - 8, red…yellow). Robust functional CBF changes were observed, excellently localized within gray matter only. In contrast, the BOLD signal was spatially more spread. This observation is consistent with the fact that functional CBF maps are more localized to gray matter microcapillaries than BOLD maps, which suffer from contributions of proximal draining veins.

Investigating the baseline CBF values of the voxels (t > 2) in the activated area V1, we found that CBF revealed much higher values and variance (large flow pial vessels) compared to corresponding t values. Concretely, while CBF varied from 30 to 150 mL/100g/min, the mean of corresponding t values was largely constant (t ~ 3, see histogram of mean t values in Fig. 2). Our hypothesis is that functional activity was determined by mainly capillary contributions and that large vessel CBF contributions superposed to the capillary CBF do not significantly affect functional contrast-to-noise ratio. This observation can be utilized to optimize protocols and SNR in functional CBF with the goal of more specific and localized mapping of brain function.

References: [1] Logothetis et al. *Phil.Trans.R.Soc Lond. B* 357:1003 (2002); *Nature Neurosci* 2(6):555-62 (1999); *Nature* 412:150-57 (2001). [2] Pfeuffer et al. *Proc. ISMRM Toronto* 1877, 2089 (2003). [3] Pfeuffer et al. *Magn. Reson. Med.* 47:903-11 (2002).