Pseudocontinuous ASL (pCASL) Combined with EPI, RARE and TrueFISP for High Resolution Multi-Orientation Mouse Brain Perfusion Imaging

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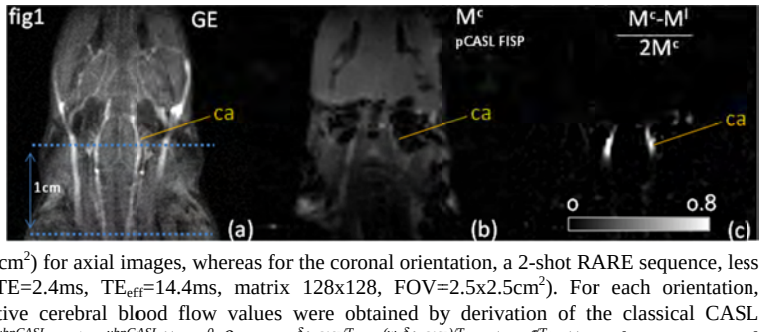
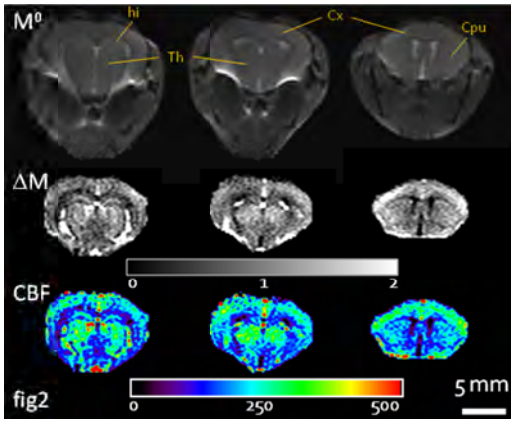
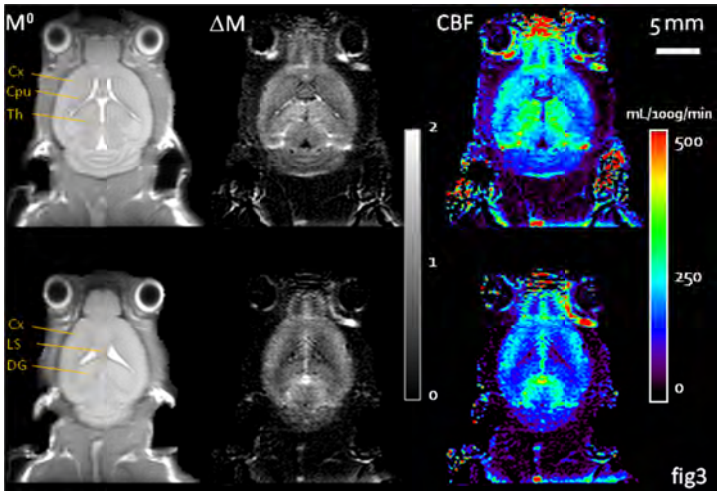
Introduction: Mouse models of human brain diseases (tumor, stroke, Alzheimer's disease …) are extensively studied with long scan time multimodal MR protocols that include functional, metabolic and structural approaches. To further describe the pathologies, there is then a real need for a high resolution, sensitive method which allows assessing quantitative whole brain perfusion within a reasonable scan time.
The pseudo-continuous ASL technique[1] recently applied at very high field for mouse brain perfusion measurement[2] has demonstrated a sensitivity gain of ~40% compared to pulsed ASL performed with an optimized presat-FAIR sequence and a high capability for multislice perfusion imaging. However, this previous work, performed with a large volume coil required thirty minutes of data averaging to obtain reliable CBF maps in the axial plane only. Moreover, the pCASL inversion efficiency was not calculated but estimated as a first approximation by comparison of the CBF values obtained with pCASL and FAIR. The proposed work presents a significant improvement of the previous study by allowing the calculation of the pCASL inversion efficiency and by the acquisition of multislice CBF maps in coronal and axial orientations within a reduced scan time.

Methods: Experiments were carried out on an 11.75T vertical MR system (Bruker, AV 500WB, transmitter/receiver volume coil: ∅ 2cm, length 3cm) on anaesthetized mice (C57BL/6j, 10 weeks, weight 25±1g, N=5).
ASL perfusion imaging was performed with the ubpCASL method optimized for mouse brain perfusion imaging[2] (b_{1ave}= 4.7 µT (fa 33°), G_{max}/G_{ave}=90/10 mT/m, Hanning pulse duration δ=200µs and repetition rate Δt=450 µs, labeling duration τ=3s and post-labeling delay, *w*=0.3s). The axial labeling plane, perpendicular to the carotid arteries was located in the neck area, ~1.5 cm below the imaging slab. A global first order shimming was performed. The ubpCASL module was combined with a 2-shot SE-EPI sequence (3 slices, thickness 0.75mm, TE= 9ms, matrix 128x128, FOV 2.5x2.5cm^2) for axial images, whereas for the coronal orientation, a 2-shot RARE sequence, less prone to susceptibility artifacts was preferred (2 slices, thickness 1mm, TE=2.4ms, TE_{eff}=14.4ms, matrix 128x128, FOV=2.5x2.5cm^2). For each orientation, magnetization differences, $\Delta M_b^{ubpCASL}$, were averaged 10 minutes. Quantitative cerebral blood flow values were obtained by derivation of the classical CASL equation[3]: $CBF^{ubpCASL} = \Delta M_b^{ubpCASL}/(2M_b^0.\beta.T_{1app}.e^{-\delta_{ubpCASL}/T_{1a}}.e^{-(w-\delta_{ubpCASL})/T_{1app}}.(1-e^{-\tau/T_{1app}}))$, with T_{1a} =2.1s and the blood transit time, $\delta^{ubpCASL}$, assumed equal to 150 ms. The M_b^0 (equilibrium magnetization) and T_{1app} (apparent relaxation time) values were determined with a slice-selective inversion recovery prescan[4], whereas the pCASL inversion efficiency, β, was measured in the carotid arteries according to the protocol described on Fig1. A low resolution angiographic scan (Fig 1a, scan time <1 min) was run in order to determine the carotid arteries location. Then, ubpCASL (τ=2s, *w*=0.01s) combined with a single shot FISP sequence (matrix 72x72, TE=0.730ms, TR=1.46ms, FA=70°, image acquisition time=67ms, 4 NEX, total scan time <1min) was run to acquire label/control images of a slice containing the carotids arteries (Fig1b) where the values of β= abs(M^C-M^L)/2M^c were evaluated (Fig1c).





Results: Mean inversion efficiency values measured in the carotids ranged from 0.63 to 0.72. These values might be slightly underestimated (3-5%) due to the blood relaxation effect (T_{1a}=2.1s) which ocurred during the transit time (estimated to ~70-100ms for a mean blood velocity of ~10-15cm/s in the carotids[5] and a distance between the inversion plane and the imaging slab of 1cm, fig1a). For each orientation, no slice effect or inversion efficiency loss was observed across the slices, resulting on a uniform sensitivity of the $\Delta M_b^{ubpCASL}$ maps (fig 2, ubpCASL-EPI and fig3, ubpCASL-RARE). Typical axial and coronal CBF maps show classical heterogenous blood flow distribution within different brain structures. Quantitative analyses (*mean value (in-ROI variations) ± group standard deviation*) were performed in ROIs selected in highly perfused areas (thalamus (*th*), *CBF=230 (33)±27 mL/100g/min*, septal nucleus (*Ls*), *CBF=224 (36)±30 mL/100g/min*, cortex (*cx*) *CBF=197(24)±21 mL/100g/min*) and moderately perfused areas (caudate putamen (*Cpu*), *CBF=166(21)±21 mL/100g/min*, hippocampus (*hi*) *CBF=148(25)±23 mL/100g/min*, dendate gyrus (*DG*) *CBF=140 (18)±12 mL/100g/min*). The mean in-ROI variations and group standard deviations represented ~15% and ~12% respectively, highlighting the good accuracy of the ubpCASL method.



Discussion: This work presents the use of the ubpCASL module in combination with fast imaging sequences for the acquisition of high resolution quantitative mouse CBF maps within a short scan time protocol. The measurement of the ubpCASL inversion efficiency required less than 1 minute and the image acquisition time of the FISP sequence (67ms), shorter than the blood transit time (70-100ms), insured minimal underestimation of β. The 2-shot EPI sequence produced high SNR, good quality images in the axial direction. RARE imaging, although less sensitive, was a good alternative to EPI for the acquisition of coronal images, free of susceptibility artifacts. For both ubpCASL-EPI and ubpCASL-RARE, 10-min of $\Delta M^{ubpCASL}$ averaging was sufficient to obtain accurate quantitative CBF maps (~15% of in-ROI variations) with 200x200µm^2/pixel of resolution. On the overall, 25 min were required for the whole protocol, which was performed with a standard volume coil (Ø 2cm, L=3cm) well-suited for mouse brain multimodal studies.

***References*: [1] Dai et al., MRM (2008) [2] Duhamel et al., MRM (2011). [3] Buxton et al., MRM (1998) [4] Duhamel et al., MRM (2008) [5] Parzy et al., NMR in biomed (2009)**