Pseudocontinuous Arterial Spin Labeling (pCASL) at Very High Field (11.75T) for Mouse Brain Perfusion Imaging

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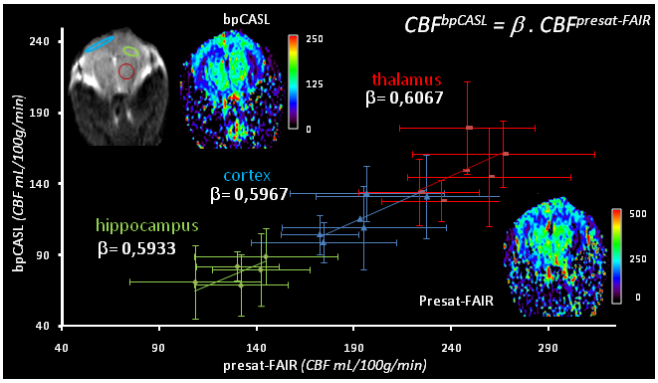
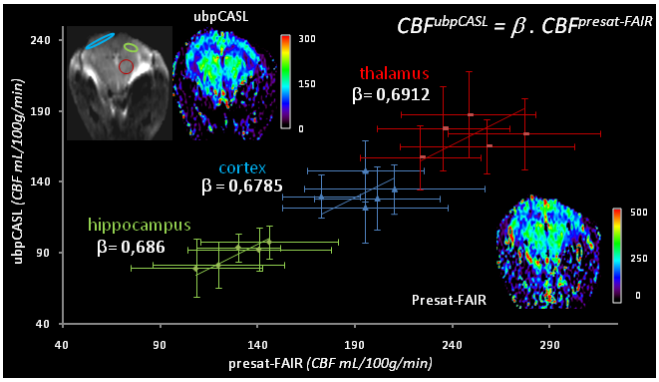
Introduction: Transgenic mouse models of human brain diseases (e.g. stroke, neuronal pathologies...) are increasingly developed and studied with MRI. Multimodal approaches, including structural, functional and anatomic imaging are usually used, leading to long acquisition times despite the gain in sensitivity obtained with the use of very high field strengths (B_0 > 7T). Therefore, improvements of the MR sequences are required to obtain high spatial resolution images (~200µm) in reasonable scan times. For brain perfusion studies with arterial spin labeling (ASL), the continuous method (CASL) should in principle give the best results in terms of sensitivity. However, its successful application in the mouse can be challenging for several reasons: RF power constraints, loss of inversion efficiency with the increasing field (short blood T_2 values) and when multislice labeling is considered... Pulsed ASL (PASL), and in particular FAIR sequences[1,2], appeared to be a good alternative, fully benefiting from the increased blood T_1 value measured at very high field. The recent pseudo-continuous (pCASL) technique[3,4], now largely applied for human studies at different magnetic fields, might be the best candidate for mouse brain perfusion since it overcomes the main limitations of CASL and gives, in principle, higher efficiency than PASL. However, at very high field, the performance of pCASL could be challenged by a loss of the inversion efficiency caused by increased B_1 and B_0 inhomogeneities, and gradients imperfections. This work presents the development of pCASL techniques at very high field (11.75T) and the evaluation of their performances (sensitivity, SNR, quantitative blood flow values) relatively to a presaturated FAIR (presat-FAIR) sequence fully optimized for mouse brain perfusion. pCASL inversion efficiencies (β) were estimated and multislice approaches were also investigated.





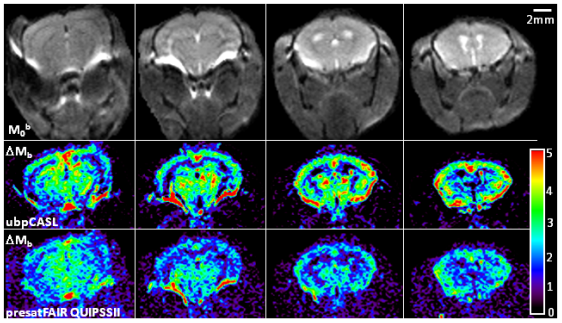
Methods: Experiments were performed on an 11.75T vertical MR system (Bruker, AV 500WB, transmitter/receiver volume coil:∅ 3cm, length 5cm) on anaesthetized mice (C57BL/6j, 10 weeks, weight 25±1g, N=5). Single-shot SE-EPI was used for image acquisition: FOV 2.5x2.5cm^2, slice thickness 0.75mm, matrix 128x64.

presat-FAIR experiments were performed with parameters described in [5]. A single inversion time (TI=1.7s) and a recovery time TR^{FAIR}=3.4s were used. M_b^0 (equilibrium magnetization), α (FAIR inversion efficiency) and T_{1app} (apparent relaxation time) were determined with a slice-selective inversion recovery prescan[5].

pCASL experiments were performed with both the unbalanced (ubpCASL) and balanced (bpCASL) control methods[3,4]. Although conventional pCASL schemes were used (RF pulses increment of 0°/180° for the labeling/control experiments and no phase compensation[6]), special care was taken in order to limit the B_0 inhomogeneities and frequency offsets effects. First, the labeling plane, located in the mouse neck area (~1.2 cm below the imaging slab) was placed at both the magnet isocenter and the RF coil center. Second, the frequency adjustment as well as a first order shimming was performed at the level of the tagging plane. Finally the high performance of the gradients system (G_{max}=1T/m, slew rate 900kT/m/s) was exploited to repeat Hanning window-shaped pulses (duration δ=200µs) at the high rate of Δt=400 µs. The highest sensitivity was obtained for G_{max}/G_{ave}=90/7 mT/m (resp. 90/10 mT/m) for bpCASL (resp. ubpCASL), b_{1ave}= 4 µT (flip angle 25°), τ=3s (labeling duration) and w=0.3s (postlabeling delay). Magnetization differences, $\Delta M_b^{ubpCASL}$, ΔM_b^{bpCASL} and $\Delta M^{presat\text{-}FAIR}$ were averaged for 15 minutes. Quantitative cerebral blood flow values were obtained by derivation of the classical CASL and PASL equations[7], with T_{1a}=2.1s and assuming blood transit time delays of δ^{FAIR}=10ms and δ^{pCASL} = 200 ms:

$$CBF^{pCASL} = \Delta M_b^{pCASL}/(2M_b^0.\beta.T_{1app}.e^{-\delta_{pCASL}/T1a}.e^{-(w-\delta pCASL)/T1app}.(1-e^{-\tau/T1app}))$$

$$CBF^{presatFAIR} = \Delta M_b^{presatFAIR}/(2M_b^0.\alpha.e^{-\delta_{FAIR}/T1a}.(e^{-(TI-\delta FAIR)/T1a}-e^{-(TI-\delta FAIR)/T1app})/(1/T_{1a}-1/T_{1app}).(1-e^{-TR_{FAIR}/T1a}))$$



Results: Figure above shows CBF^{bpCASL} and $CBF^{ubpCASL}$ values as a function of $CBF^{presat\text{-}FAIR}$ values for measurements performed in ROIs taken into the cortex (blue), hippocampus (green) and thalamus (red) for the 5 animals. Error bars represent the standard deviation of the mean values within the ROIs. Linear relations were obtained for each brain structure. Assuming to first approximation that presat-FAIR and pCASL give the same perfusion values (CBF^{pCASL}=$CBF^{presat\text{-}FAIR}$), the linearity coefficients correspond to the inversion efficiencies, β (cf equations) which were found pretty constant across the brain structures for both bpCASL and ubpCASL. Higher β was obtained for ubpCASL (mean value ~0.68) compared to bpCASL (mean value ~0.6). pCASL CBF maps appeared more homogenous and the brain structures more sharply delineated comparatively to presat-FAIR CBF maps, especially in the areas of lowest perfusion (hippocampus and cortex). SNR, defined as ΔM_b mean values divided by the standard deviation of the noise measured outside the brain area, was clearly higher for pCASL methods comparatively to presat-FAIR. Average SNR gains of 25% (in cortex), 24% (in thalamus) and 31% (in hippocampus) were found for ubpCASL, and 18%, 7% and 9% for bpCASL. As shown on the left figure (multislice ΔM_b images obtained with ubpCASL and with presat-FAIR combined with QUIPPSSII[8] (TI2/TI1=1.7/1.5s), 4 slices, 128x128, SE-EPI 2 shots, 30 min. averaging), the advantage of ubpCASL is clearly more pronounced for multislice perfusion imaging. Average ubpCASL SNR was more than 40% higher than average presat-FAIR-QUIPSSII SNR. Unlike FAIR techniques, which lost sensitivity due to the increase of the slice width in the control session (slice selective inversion), ubpCASL efficiency was not affected by the imaging slab width increase in multislice experiments.

Discussion: This work presents the development of pCASL at very high field for mouse brain perfusion measurement. ubpCASL, for which an inversion efficiency of β~0.68 was estimated (within the range of reported values found with CASL[8]), was clearly advantageous compared to presat-FAIR for sensitivity, SNR, CBF map quality and multislice concerns. Highly sensitive and high spatial resolution multislice CBF maps with sharp delineation of brain structures could then be obtained in 30 minutes with ubpCASL. bpCASL was less efficient (β~0.6) probably due to its sensitivity to B_0 inhomogeneities, potentially high at 11.75T.

References*: [1] Pell et al., MRM (1999) [2] Kober et al., NMR Biomed (2008) [3] Dai et al., MRM (2008). [4] Wu et al., MRM (2007). [5] Duhamel et al., MRM (2008) [6] Jung et al., MRM (2010) [7]Buxton et al., MRM (1998) [8] Foley et al., MRM (2006)