Practical Investigation of pseudo-Continuous Arterial Spin Labeling (pCASL) feasibility at very high field (11.75T)

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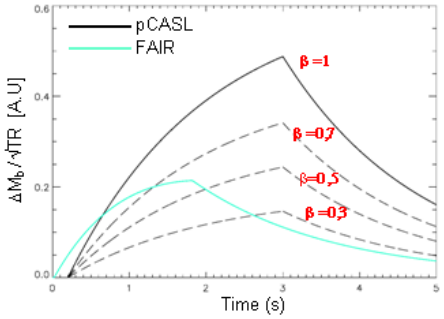
Introduction: A new strategy for continuous arterial spin labeling (CASL) using pulsed RF and gradient fields and referred as pseudo-continuous ASL (pCASL), has recently been developed and optimized for human studies at 3T[1,2]. Promising results demonstrated that pCASL combines advantages of pulsed ASL (PASL) and CASL by providing good labeling efficiency, high Signal to Noise (SNR) and multi-slice capability. ASL also plays an important role for small animal studies where numerous brain pathologies are investigated. Although ASL sensitivity already benefits from small animal high blood flow and long T_1 relaxation times relative to high field strengths, there is still a need to improve the technique so that higher SNR, temporal and spatial resolutions could be achieved. Moreover, multi-slice perfusion investigation, infrequently used in small animal studies, should also be considered. Thus, pCASL should be in principle a method of choice to reach these objectives. However, its feasibility as well as its SNR advantages over PASL techniques at very high field ($B_0 \geq 9.4$T, now commonly used for small animals studies) remain to be demonstrated. In particular, the labeling efficiency is expected to be challenged by the effects of short blood T_2 values and hardware constraints (e.g. limited RF amplitude). This work presents a practical investigation of pCASL implementation and feasibility at very high field (11.75T) for mouse brain perfusion studies. SNR and labeling efficiency (β) were considered by comparing absolute quantitative perfusion values obtained with pCASL and PASL (FAIR).

Methods: Experiments were performed on an 11.75T vertical MR system (Bruker, AV 500WB) with a transmitter/receiver volume coil (∅ 3cm, length 5cm). Single-shot SE-EPI sequence (matrix 128x64, FOV 2.5x2.5cm^2, slice thickness 0.75mm, TE 14ms) was used for image acquisition.

FAIR experiments were performed with adiabatic global/slice-selective inversion (4ms sech pulse), a single inversion time TI=1.7s and a recovery time TR^{FAIR}=10s, leading to a total repetition time of TR=(TR^{FAIR}+TI)=11.7s. Magnetization difference, ΔM_b^{FAIR}, was averaged during 12 minutes (32 NEX). An extra IR-slice selective scan was used with several TI values to determine M_b^0, α (inversion efficiency) and T_{1app} (apparent relaxation time) parameters by fitting the standard inversion recovery function $M=M_b^0(1-2\alpha.e^{-TI/T1app})$ to the data[3].

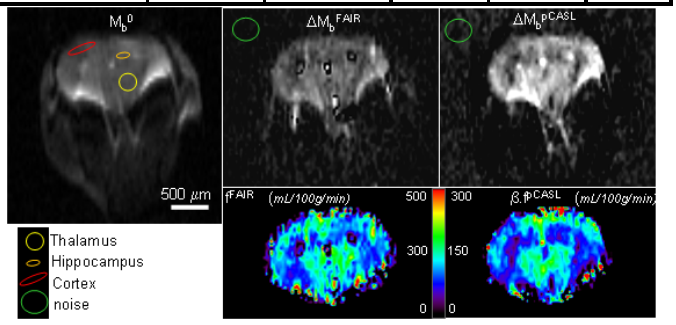
$$\begin{cases} \Delta M_b^{FAIR} = 2\dfrac{M_b^0}{\lambda} f^{FAIR} \cdot \alpha \cdot \dfrac{e^{-\frac{\delta^{FAIR}}{T_{1a}}}}{\frac{1}{T_{1app}} - \frac{1}{T_{1a}}} \cdot \left(e^{-\frac{TI-\delta^{FAIR}}{T_{1a}}} - e^{-\frac{TI-\delta^{FAIR}}{T_{1app}}} \right) \\ \Delta M_b^{pCASL} = 2\dfrac{M_b^0}{\lambda} f^{pCASL} \cdot \beta \cdot T_{1app} \cdot e^{-\frac{\delta^{pCASL}}{T_{1a}}} \cdot e^{-\frac{w-\delta^{pCASL}}{T_{1app}}} \cdot \left(1 - e^{-\frac{\tau}{T_{1app}}} \right) \end{cases}$$

pCASL experiments were performed with the unbalanced pCASL method[1]. Hanning window-shaped pulses (duration 300μs) were repeated every Δt=1.1ms during τ=2.8s. A G_{max} value of 90 mT/m was applied and a range of values for G_{ave} ([2-10]mT/m) and B_{1ave} ([2.2-4.7]μT) was investigated. An extra delay, w=0.3s, was added after the labeling. The control scan used a zero-averaged gradient (G_{ave}=0) and the sign of consecutives pulses was alternated insuring a zero-averaged B_1 (B_{1ave}=0). The inversion plane was located at the isocenter, in the neck region, 1.4cm from the brain imaging slice. A recovery time, TR^{pCASL} of 4s was allowed leading to a total repetition time, TR=(τ+w+TR^{pCASL})=7.1s. ΔM_b^{pCASL} signal was averaged during 12 minutes (54 NEX). Quantitative cerebral blood flow values (f^{FAIR} and f^{pCASL}) were obtained by derivation of the classical CASL and PASL equations[4], assuming transit time delays of δ^{FAIR}=10ms and δ^{pCASL} =100 ms.



Results: The graph hereinafter shows theoretical indexes of SNR (expressed as the timescale-independent quantify $\Delta M_b/\sqrt{TR}$) simulated for FAIR and pCASL as a function of time, using typical relaxation times measured at 11.75T (T_{1a}=2.1s, T_{1app}=1.8s)[3]. Labeling efficiencies were chosen equal to 1 for α and to 1, 0.7, 0.5 and 0.3 for β. Simulated curves show that the labeling efficiency can dramatically reduce the SNR benefit of pCASL with respect to FAIR. The figure shows M_b^0, ΔM_b^{FAIR} and ΔM_b^{pCASL} images obtained for 12 minutes of signal averaging (with G_{ave}=10mT/m and B_{1ave}=4.2μT for pCASL). SNR values were evaluated for both pCASL and FAIR in 3 different regions of the brain (thalamus, hippocampus and cortex) by dividing the mean ΔM_b values by the standard deviation of the noise (σ_N), measured outside the brain area. SNR values were found to be approximately 15% higher with pCASL (see table). Corresponding quantitative f^{FAIR} and $\beta.f^{pCASL}$ maps (in mL/100g/min) are also shown on the figure. Assuming in first approximation that FAIR and pCASL should give the same perfusion values ($f^{FAIR}=f^{pCASL}$) one can obtain an estimation of the pCASL labeling efficiency (β). Then, for regions of interest (ROI) taken into the cortex, hippocampus and thalamus areas, β was estimated to 0.58, 0.55 and 0.55. Interestingly, the perfusion map obtained for pCASL appeared to be more homogenous and the brain structures more sharply delineated. This is confirmed by the quantitative perfusion values which show in-ROI variations (expressed as in-ROI standard deviation/mean value) in the order of 15% for FAIR and 12% for pCASL.

	SNR^{FAIR}	SNR^{pCASL}	f^{FAIR}	$\beta.f^{pCASL}$	β
	$<\Delta M_b>/\sigma_N$		mL/100g/min		
Cortex	12	14 (+17%)	213±35	124±17	**0.58**
Hippocampus	10	11 *(+10%)*	142±21	78±10	**0.55**
Thalamus	15	18 *(+20%)*	266±38	145±13	**0.55**



Discussion: This work presents our initial experience with the implementation of pCASL at very high field for mouse brain perfusion measurement. Far from being fully optimized, the pCASL technique applied at 11.75T in this study highlighted promising advantages over PASL (FAIR) in terms of SNR and variability. The estimated value for pCASL labeling efficiency is quite low (β~0.56), but in the order of expecting values[1]. A careful and complete study would however be necessary to improve this efficiency. In particular, G_{ave} and B_{1ave} would require to be optimized with respect to blood T_2 and hardware constraints, so that the adiabatic inversion condition (expressed for velocity driven adiabatic fast passage as 1/T1, 1/T2 << $G_{ave}v/B_{1ave}$ << γB_{1ave}) can be fully satisfied. Moreover, according to simulated curves (graph), the SNR would also be increased by making the duration of labeling (τ) longer since for τ=2.8s only, ΔM_b^{pCASL} is far from having reached its steady state value (i.e $1-e^{-\tau/T1app}$ <1). Practical investigations of the labeling duration effect are currently being done. To fully benefit of the pCASL advantages, a multi-slice version of the sequence has been developed and is applied in mouse brain perfusion studies. Finally, recent works successfully demonstrated the feasibility of measuring spinal cord blood flow (SCBF) by FAIR techniques[3,5], but with long acquisition time. The capacity of pCASL in measuring SCBF with advantages over FAIR is currently under investigation.

References: *[1] Dai et al., MRM (2008). [2] Wu et al., MRM (2007). [3] Duhamel et al., MRM (2008).[4]Buxton et al., MRM (1998).[5] Duhamel et al., MRM (2009).*