Mouse Lumbar Spinal Cord Blood Flow Imaging using pseudo-continuous ASL (pCASL) at very High Field

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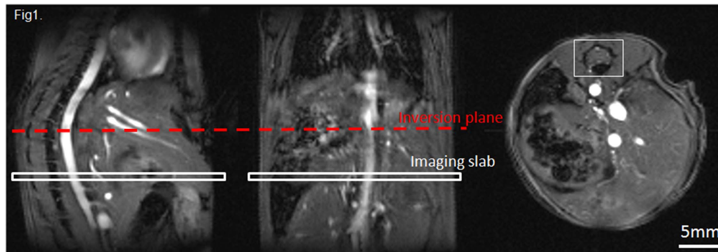
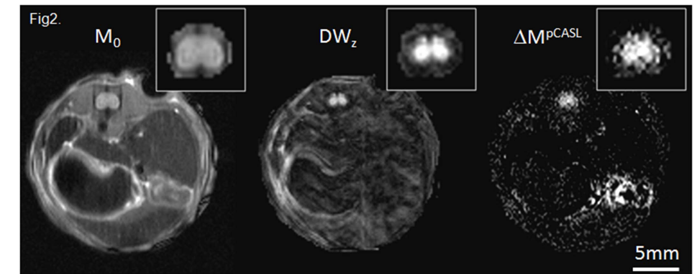
Target audience: people interested in a robust method able to non-invasively quantify spinal cord blood flow (SCBF).

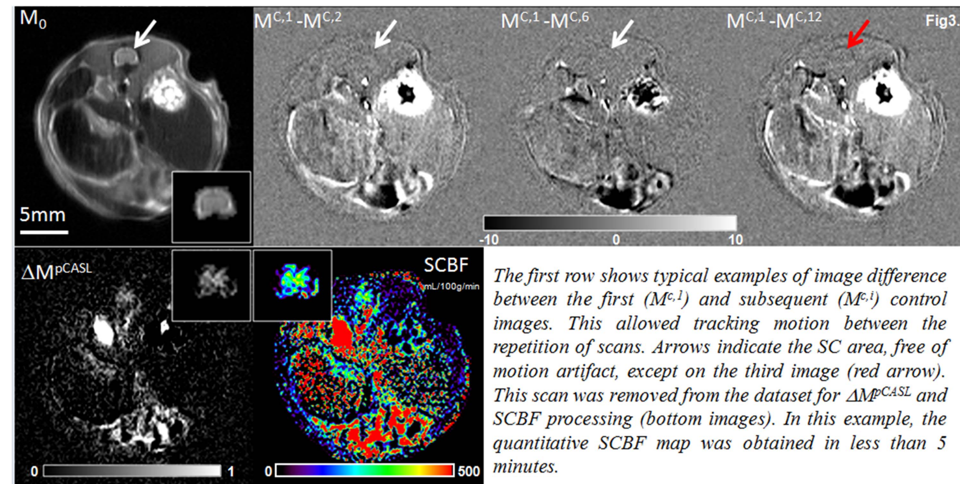
Introduction: Spinal cord ASL perfusion imaging, performed at the cervical level with a presat-FAIR EPI technique[1] has shown to provide valuable information relative to tissue alteration and recovery in a mouse model of spinal cord injury (SCI)[2]. Numerous rodent models of SCI are however developed at the thoracic or lumbar levels and, although FAIR EPI also appeared to be feasible at these levels[3], the technique suffered from several drawbacks. First, in order to enhance the sensitivity of the FAIR signal and to limit the inflowing fresh blood effects[4], a large blood volume was required to be submitted to the global inversion FAIR labeling pulse. This consequently implies constraints on the animal positioning in the RF coil. Moreover, when used in combination with respiratory gated acquisition, the FAIR strategy required full relaxation conditions, limiting then the sensitivity per unit of time. Additionally, in order to minimize distortion artifacts which are likely to occur at this level of the cord and at very high field, segmentation of the EPI readout module was required. This imaging strategy was thus very sensitive to motion. As an alternative to FAIR-EPI for lumbar spinal cord blood flow imaging, we investigated the feasibility of pseudo-continuous ASL[5] (pCASL) combined with single-shot RARE imaging, with the objective of benefiting from higher sensitivity[6], more flexibility and more robustness to motion.



Methods: Experiments were performed at 11.75T on a vertical MR system (Bruker, AV 500WB, transmitter/receiver volume coil:∅ 2cm, length 3cm) on anaesthetized mice (C57BL/6j, 10 weeks, weight 25±1g, N=4). pCASL experiments were performed with the unbalanced (ubpCASL) scheme[6] (b_{1ave}= 4.7 µT, G_{max}/G_{ave}=90/10 mT/m, Hanning pulse duration δ=200µs and repetition rate Δt=450 µs, labeling duration τ=3s, post-labeling delay *w*=0.3s, recovery time 3s). The transverse labeling plane was located perpendicularly to the descending aorta, ~6 mm above the axial imaging slab placed at the lumbar level of the spinal cord (Fig1.). Single-shot RARE readout (TE=2.37ms, TE_{eff}=28.5ms, fat sat) was used with an in-plane resolution of 200x200µm^2 (FOV 2.5x2.5cm^2, slice thickness 0.75mm, matrix 128x128). The ASL signal ($\Delta M^{pCASL}=M^{Control}-M^{Label}$) was averaged during 5 minutes (16 NEX) and acquisitions were synchronized to the respiratory rate (90±10 bpm). For spinal cord structure delineation, diffusion weighted imaging (DWz) was additionally performed with a standard Stejskal-Tanner SE sequence (b=700s/mm^2, Z-direction, δ/Δ=2.3/6.8ms)[7]. Quantitative SCBF values were obtained by derivation of the classical CASL equation[8], with T_{1a}=2.1s and assuming blood transit time delays values of δ^{pCASL} = 200 ms: $SCBF^{pCASL} = \Delta M^{pCASL}/(2M_b^0.\beta.T_{1app}.e^{-\delta_{pCASL}/T1a}.e^{-(w-\delta pCASL)/T1app}.(1-e^{-\tau/T1app}))$. M_b^0 (equilibrium magnetization) and T_{1app} (apparent relaxation time) were determined with a slice-selective inversion recovery prescan[3] and the pCASL inversion efficiency (β) was estimated to 0.6.



Results: Typical M_b^0, DW_z and ΔM^{pCASL} images are shown on Fig 2. The long echo train length of the single-shot RARE sequence led to slight blurring visible on the M_b^0 image. The contrast of the *DWz* image highlights the spinal cord gray matter (GM) structure relative to the white matter (WM). The ASL image (ΔM^{pCASL}) shows very clean subtraction signal, highlighting good robustness to motion. Hypersignal can be seen in the highly perfused SC GM area (ventral and dorsal horns) whereas less-perfused WM showed low signal (see enlarged images, Fig2.). Motion evaluation and a typical quantitative SCBF map obtained in less than 5 minutes are reported on Fig3. Quantitative measurements performed in the total gray matter (ventral and dorsal horns) gave a mean percentage of signal change ($\Delta M^{pcASL}/M_0$) of 6% (n=4, SNR>6.5), which corresponded to SCBF of 240±50 mL/100g/min (fig3).



The first row shows typical examples of image difference between the first ($M^{c,1}$) and subsequent ($M^{c,i}$) control images. This allowed tracking motion between the repetition of scans. Arrows indicate the SC area, free of motion artifact, except on the third image (red arrow). This scan was removed from the dataset for ΔM^{pCASL} and SCBF processing (bottom images). In this example, the quantitative SCBF map was obtained in less than 5 minutes.

Discussion: pCASL combined with single-shot RARE imaging was used to obtain quantitative lumbar SCBF images. The pCASL labeling, performed in the descending aorta, allowed efficient upstream tagging of the blood nourishing the lumbar spinal cord. Unlike for the FAIR technique, the positioning of the animal inside the RF coil had no effect on the pCASL sensitivity and perfusion quantification. Absolute SCBF values obtained in this study were however slightly lower than those previously obtained with the FAIR technique (240±50 *vs* 285±27 mL/100g/min[3]), which is more likely due to a slight loss of the pCASL inversion efficiency (true-β <0.6). A careful study of β, which takes into account B_1 and B_0 inhomogeneities[9], should help in increasing the pCASL sensitivity. Moreover, the single-shot RARE sequence combined with respiratory synchronization appeared very robust despite the high motional area, and, compared to segmented-EPI imaging, very few images were altered by motion artifacts in the spinal cord area. Five minutes only were required to obtain 200x200 µm^2 spatial resolution quantitative SCBF maps. Further studies will investigate higher spatial resolution. Finally, since multislice imaging can be straightfully performed with pCASL, the proposed technique might be a method of choice for investigating perfusion alteration in mouse models of SC impairments.

***References*:** *[1] Duhamel et al., MRM (2008.) [2] Callot et al., ISMRM (2012). [3] Duhamel et al., MRM (2009). [4] Pell et al.,MRM (1999). [5] Dai et al, MRM (2008). [6] Duhamel et al., MRM (2012). [7] Callot et al, MRM (2010).). [8] Buxton et al, MRM (1998).). [9] Jahanian et al, NMR biomed (2011).*