Spinal Cord Blood Flow (SCBF) measurement by Arterial Spin Labeling (ASL)

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Introduction:

The assessment of spinal cord (SC) perfusion plays a key-role in the physio-pathological description and understanding of diseases such as SC injury, ischemia or spinal tumor. While Dynamic Susceptibility Contrast (DSC) MRI methods are successfully used for human and small animal brain studies, they are still technically challenged by the small size of the spinal cord, the need of adequate spatial resolution and eventually by the susceptibility artifacts arising from the bony structure combined with single-shot EPI read-out. The application of such technique for mouse model imaging remains difficult due to the high capillary and arterial blood flow. An alternative method for perfusion measurement is the use of Arterial Spin Labeling (ASL). In the case of small animals, high fields usually used and high blood-flow values are advantageous for the sensitivity of such a technique. Because no contrast agents are used, ASL also permits repeated measurements and thus the use of segmented EPI, which would consequently contribute to greatly decrease image distortions. The purpose of this work was to demonstrate the feasibility of mice spinal-cord blood flow (SCBF) measurements using a Flow-sensitive Alternating Inversion Recovery (FAIR)-EPI ASL technique.

Methods:

Theory: In the FAIR labeling experiment, the difference between control (global inversion) and labeled (slice selective inversion) magnetization is directly related to blood flow by [1]: $\Delta M(TI) = M^{label} - M^{control} = 2M_0.\alpha_0.(SCBF/\lambda).[(e^{-TI.RIapp} - e^{-TI.RIa}) / (R1^a - R1^{app})]$ (eq.1), where M_0 is the equilibrium magnetization, α_0 the inversion efficiency, λ the blood tissue partition coefficient for water (0.9 ml/g), $R1^{app}$ the apparent longitudinal relaxation rate of the SC tissue and $R1^a$ the longitudinal relaxation rate of arterial blood.

Experiments: Experiments were performed on a 11.75T vertical MR system (Bruker, AV 500WB) with a 30-mm volumic transmitter/receiver coil. C57Bl/6J healthy male mice (n=5, age 14 weeks, body weight 25 g) were maintained anaesthetized with a mixture of air + isoflurane (~1.7%). Perfusion measurements were carried out in a transversal slice placed at the C3/C4 (cervical) level using a gradient-echo localizer pre-scan as reference. FAIR parameters were as follow: adiabatic inversion pulse, single and fixed inversion time TI, 4-segments Spin-Echo-EPI readout (matrix 128x128, FOV 1.7x1.7mm^2, slice thickness 0.8mm, TR/TE=8000/11ms) and 32 signal averages. Using the same imaging parameters, a slice-selective inversion recovery (IR)-EPI (8 TI values) scan and a diffusion-weighted (DW)-EPI (x-direction, 4 b) scans were ran. Finally, a similar FAIR experiment was performed in the brain, for comparison between Cerebral Blood Flow (CBF) and SCBF. Absolute perfusion values were calculated by solving (eq.1). The IR-EPI scan was used to determine M_0, α_0, and $R1^{app}$ by fitting the standard IR function $M=M_0.(1-2\alpha_0.e^{-TI.R1app})$ to the image data. The x-direction ADC map computed from the DW-EPI scan was used for clear delineation between gray (GM) and white (WM) matter ensuring correct localization of the regions-of-interest (ROIs).

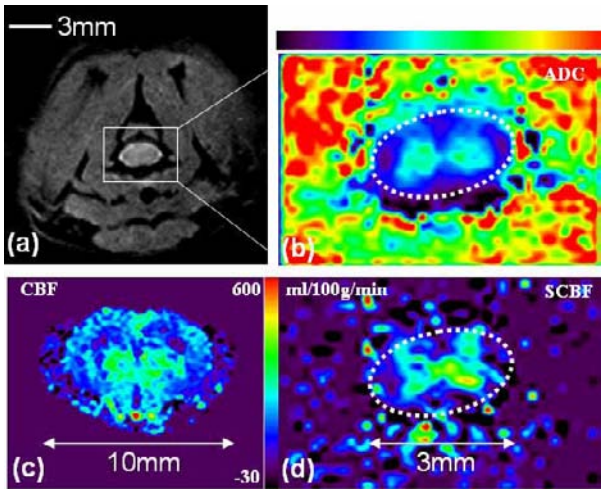

Fig.1 – native EPI-image (a), ADC map used for ROI delineation (b), absolute cerebral (c) and spinal cord (d) blood flow maps

Results:

A raw-EPI image acquired at the C3/C4 level is illustrated on figure 1a. Enlarged ADC and absolute-SCBF maps as well as a CBF map acquired on the same animal at mid-brain are shown on figure 1b, 1d and 1c, respectively.

The dotted ellipses drawn on the ADC and SCBF maps show that gray matter (dorsal and ventral horns) is significantly higher perfused than the surrounding white matter. Table 1 reports the individual (mean±std) SCBF values measured in ROIs selected in the dorsal (DH) and ventral horn (VH), in the whole gray matter, and in the lateral white matter (WM). Typical brain values measured in the thalamus and cortex of the same animals were equal to 290±60 and 200±50 ml/100g/min, respectively.

Subject	DH	VH	GM	WM
1	222±65	271±100	236±110	86±140
2	277±90	358±90	342±113	120±120
3	287±80	267±120	258±140	120±130
4	286±73	296±87	263±105	93±92
5	284±92	305±110	278±110	78±79
Mean±std	**271±25**	**305±40**	**276±40**	**98±18**

Table 1 – Individual and group mean±std SCBF values (ml/100g/min).

Discussion:

Absolute SCBF values measured with the FAIR-EPI technique were found to be in the range of those measured in the brain. Between the GM areas, no significant regional variations could be shown. Good inter-animal reproducibility was obtained, although standard deviations in the ROIs were comparatively high. SCBF values measured in the WM were, however, at the level of noise. To our knowledge, there are no literature reports of SCBF values measured by MRI in the spinal cord. The majority of reports on SC pathology models use Laser Doppler methods for relative SCBF measurements [2]. However, quantitative SCBF measurements have already been performed in rats using older techniques like the hydrogen clearance method. Comparable blood flow values in the spinal cord [3] and brain [4] were obtained, as observed in our study. In humans, blood volume values measured in the cervical spinal cord were recently shown to be in a similar range than those measured in the brain [5]. Although further technical improvements will be required to achieve better sensitivity, temporal and spatial resolutions, SCBF measurement with ASL in mice appears to be feasible and accurate. Potential contributions of respiration, CSF motion and partial volume effects are under consideration.

References

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