Measurement of White Matter Perfusion Using ASL-MRI at 4T

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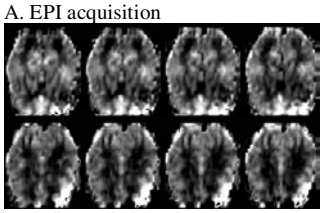
Introduction: Measurement of cerebral blood flow (CBF) in white matter (WM) has been a major challenge for radioactive tracer (i.e.PET), contrast MRI, and arterial spin labeling (ASL) MRI methods. This is because WM CBF yields a poor signal-to-noise ratio (SNR), primarily due to the fact that WM perfusion is 40% less than gray matter (GM) [1]. In addition, generally long arterial transit time in WM is an additional challenge for ASL-MRI, because of signal loss due to T1 relaxation. However, technical factors can play a significant role as well. For example, since R2* relaxation rates are higher for WM than for GM, echo-planar imaging (EPI) may loose a substantial fraction of the CBF signal in WM. In addition, magnetization transfer noise, which ASL usually induced, is more amplified in WM than GM due to higher WM myelination. Therefore, the overall goal of this study was to improve CBF measurements in WM by optimizing ASL MRI method to reduce dependence on R2* and magnetization transfer noise. Specifically, the objectives were 1) to develop a new labeling method and to determine an optimal post labeling delay for measuring WM CBF at a 4T and 2) to compare the ability of EPI and Turbo-FLASH (TFL) based ASL sequences to reliably measure CBF.

Methods and Materials: For pulsed ASL, a slab-selective double inversion scheme, termed IDOL, was developed to reduce background noise from stationary spins and to compensate for magnetization transfer effects This was accomplished by applying in the control scan two inversion pulses of equal amplitude and bandwidth in presence of a magnetic field gradient, effectively flipping spin magnetization back to equilibrium, similar to the UNFAIR [2] technique. In the labeling scan, the two inversion pulses of equal amplitude and bandwidth are applied again to balance magnetization transfer effects, but one of the pulses is transmitted in presence of lower magnetic field gradient, so that spins outside the imaging slab are inverted.

Labeling by IDOL was combined with gradient-echo EPI (EPI-IDOL) or TFL (TFL-IDOL) readouts for perfusion-weighted imaging. The sequences were implemented on a 4T MRI system (Bruker/Siemens, MedSpec) and tested on seven healthy volunteers (mean age=51, STD=5 years, range 44 to 57 years, 6 men and 1 woman). The acquisition parameters of EPI-IDOL were: TR=3500ms, TE=9ms, matrix=48x64, voxel size= 4x4x7.5 mm (6mm slice thickness with 1.5mm gap), number of slices = 9, number of measurements = 60. The acquisition parameters of TFL-IDOL were: TR=155ms (time from the first excitation pulse to the last acquisition), TE=2.28ms, flip angle=10 degree with centric reordering and RF spoiling, bandwidth=320 Hz/pixel. The rest of imaging parameters were the same as in EPI-IDOL. To account for variable arterial transit delays, a series of ASL images at different post-labeling delay times (TI2) varying from 1200ms to 3000ms in steps of 300ms were acquired. Measurement times for each TI2 were 3.34 min for EPI-IDOL and 4.30 min for TFL-IDOL. Using SPM2 software [3], both global and regions-of-interest (ROI) analyses were performed included in anterior (AC) and posterior (PC) cingulate cortex and central semiovale white matter. CBF maps for both sequences were computed for each ASL-MRI frame based on a single compartment and instant equilibrium model [4].

Fig. 1. A representative CBF maps from a volunteer acquired with EPI and TFL at TI2=2400 ms.
A. EPI acquisition



B. TFL acquisition

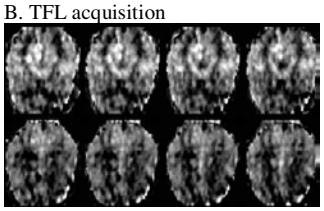


Fig. 2. Ratio CBF in GM to that in WM TI2 acquired with EPI (black) and TFL (pink).

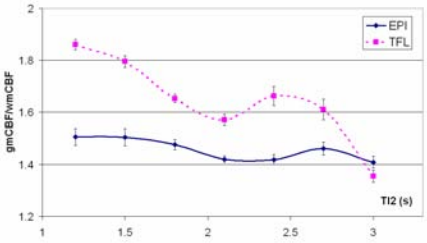
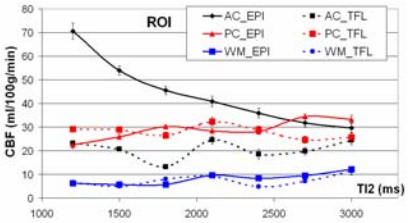


Fig. 3. CBF changes against TI2 acquired with EPI (solid) and TFL(dashed) for each ROI.



Results: Fig 1 shows a representative CBF maps from a volunteer obtained with EPI and TFL at TI2=2400ms. Fig.2 shows GM/WMCBF ratios as a function of post labeling delays (TI2), separately for EPI and TFL acquisitions. Overall, TFL yielded substantially higher GM/WM CBF ratios (on average 1.61) than EPI (on average 1.45) until T1 relaxation diminished the ASL signal. This means contrast between GM and WM is better with TFL than with EPI. CBF measurements in three regions in the brain are depicted in Figure 3, separately for EPI and TFL based acquisition. The regions included posterior (PC) and anterior (AC) cingulate cortex, representing gray matter regions and a region in centrum semiovale, representing white matter. CBF measurements using TFL showed stability in all brain regions, while EPI had the disadvantage of high variability in AC.

Discussion: The results show that WM CBF can be measured at 4T even at relatively long post labeling delays to compensate for long arterial transit times. At the same time, TFL provides better stability of CBF measurements than EPI acquisitions. A striking observation was that TFL accomplished stable CBF measurements in the anterior cingulate while measurements using EPI were unstable. The most likely explanation for this is that EPI – in contrast to TFL - could not compensate for signal loss due to large magnetic susceptibility effects in the frontal brain region. Another explanation is that intra-vascular signal contributed to EPI measurements while no intra-vascular contributions are expected from TFL due to saturation by the rapid RF pulse trains of TFL.

In conclusion these results demonstrate that perfusion of WM can be reliably obtained by optimizing post labeling delays. This improved method should facilitate investigation of white matter perfusion in aging, multiple sclerosis, and other brain diseases that affect white matter.

References: 1. Ye, et.al 7th ISMRM 1999, p 1847; 2. Helpern, J.A., et al., Magn Reson Imaging, 1997. 15(2): p. 135-9.
3. Ashburner and Friston, Hum Brain Mapp 1999, p254; 4. Buxton, et al, MRM 1998, p383.