Suppression of Free Fluid Perfusion Artefacts in Velocity Selective ASL using a BIR-4 T_2-FLAIR Preparation

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Introduction: Velocity selective arterial spin labeling (VSASL) is a pulsed ASL technique that is made insensitive to Bolus Arrival Time (BAT) by applying a pair of velocity selective filters to isolate signal from spins that have decelerated into the capillary bed [1]. VSASL is potentially useful when increased BAT prohibits reliable perfusion measurements with standard spatial ASL methods (eg. pseudo-continuous ASL (pCASL)), such as may be the case in stroke or in tumors of the body. For the VSASL tag condition VS gradients saturate spins from within vessels with laminar flow, whilst the VS gradients are off in the control condition. These large VS gradients have a small b value (≈1-5 mm^2/s). Although any diffusion-related signal difference is on the order of only 0.5% for $D = 2\times10^{-3}$ s/mm^2, this is the same order of magnitude as the VSASL perfusion signal. This results in spins with a high ADC contributing unwanted positive signal in the perfusion weighted subtraction. In the healthy brain the primary source of contamination is CSF, which can increase the apparent perfusion in grey matter through partial volume effects. Similarly, our initial experiments in glioma (n=2) show an overestimation of tumor perfusion with VSASL compared to pCASL even when accounting for increased BAT (Fig. 1). We hypothesise this is due to contamination from edema or other inflammatory responses with elevated T_1, T_2 and ADC, similar to CSF. Previous solutions to CSF contamination in VSASL include using a long-TE second echo (500 ms) and correcting for T_2 [2]. However, this limits the number of slice acquisitions per inflow time and so reduces the volume coverage of the sequence. Here, a T_2-FLAIR [3] method is used to null long T_1 & T_2 species at the time of the velocity selective tag/control pulse, so the acquired data is free from unrestricted fluid artefacts.

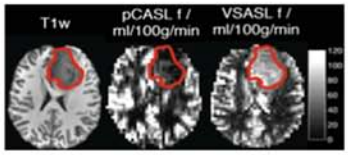

Fig 1: Structural, pCASL and VSASL in glioma (red outline) demonstrating apparent hyperperfusion with VSASL.

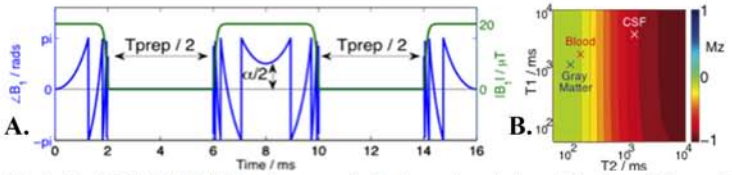

Fig 2: **A**: BIR-4 T_2-FLAIR pulse magnitude (green) and phase (blue) – adding $\alpha/2$ phase to segments 2 & 3 will result in an α degree, adiabatic pulse. **B**: Bloch equation simulation of the resulting M_z after the application of the pulse with $\alpha = \pi$, T_{prep} = 350 ms for T_1 & T_2 between 20 ms and 10 s.

Methods: Segmented BIR-4 pulses have previously been used as adiabatic, ΔB_0-insensitive, non-selective T_2 preparations, with resulting $M_z \approx \exp(-T_{prep}/T_2)$ [4]. In this work $\pi/2$ radians of phase is added to segments 2& 3, which produces an inversion rather than a 0^O pulse (Fig. 2a). For short T_2 species relative to T_{prep} (e.g., blood, gray matter) this acts as a saturation ($M_z \approx 0$), whereas for long T_2 species (eg., CSF) this acts as an inversion with $M_z \approx -\exp(-T_{prep}/T_2)$ (Fig. 2b). The BIR-4 T_2-FLAIR pulse is then used to null long-T2 species at the time of the VS preparation by choosing the appropriate T_1-nulled inversion time (Fig. 3b) given for CSF by:

$$T_{inv} = T_1^{CSF} \ln \left| \frac{\exp\left(\frac{-T_{prep}}{T_2^{CSF}}\right)+1}{\exp\left(\frac{(T_{prep}-T_{SAT})}{T_1^{CSF}} - \frac{T_{prep}}{T_2^{CSF}}\right)+1} \right| \quad \text{(Eq. 1)}$$

Where T_{SAT} is the time between the global pre-saturation and the subsequent VS preparation. The T2-FLAIR pulse will reduce the available $M_{0,blood}$ at the time of VS tag/control to:

$$M'_{0,blood} = M_{0,blood} \cdot \left(\exp\left(\frac{-T_{inv}}{T_1^{blood}}\right) \cdot \left\{\exp\left(\frac{-T_{prep}}{T_2^{blood}}\right) \cdot \left[\exp\left(\frac{T_{prep}+T_{inv}-T_{SAT}}{T_1^{blood}}\right) - 1\right] - 1\right\} + 1\right) \quad \text{(Eq. 2)}$$

Scanning was performed on a Siemens 3T Verio. VSASL used a BIR-8 VS tagging pulse [5] with V_{cut} = 2 cm/s in z, spin echo EPI readout with flow crushers, 4×4×8 mm^3 voxels, 13 slices, TE = 37 ms, inflow time = 1 s, 40 tag-control pairs. TR = 5 s and T_{prep} = 350 ms were optimised for SNR per unit time by maximising $\Delta M/\sqrt{(TR)}$, given $M_{0,blood}$ from Eq. 2 and assuming blood T_1/T_2 = 1.664 s/0.15 s, CSF T_1/T_2 = 3.7 s/1.3 s. Comparison pCASL-EPI data were acquired with the same slice prescription, bolus length = 1.4 s, 6 post label delays (250 ms to 1500 ms in 250 ms steps), TE = 14 ms, TR = 4 s and 48 tag-control pairs. Perfusion was quantified voxelwise using the general kinetic model [6]. Segmentations of CSF and grey matter were generated from the subject's structural using FAST and registered to the perfusion data using FLIRT (FSL, Oxford). The registered segmentations were then thresholded at >80% probability of a single tissue type.

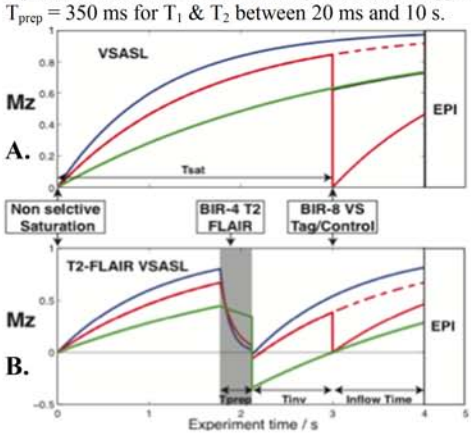

Fig 3: M_z of Grey Matter (Blue), Blood (Red, dashed = control, solid = tag) and CSF (Green) for **A**: VSASL, where the large M_z of CSF at the time of the VS pulse creates hyperperfused artefacts. **B**: T_2-FLAIR VSASL with the addition of the BIR-4 pulse T_{inv} before the VS tag, which nulls CSF at this time.

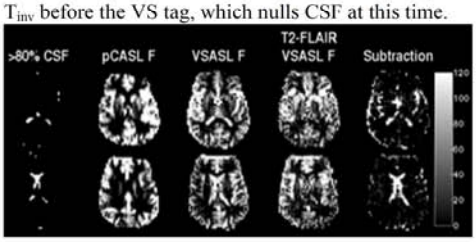

Fig 4: Representative images from two slices containing CSF in a healthy volunteer. From left to right: Voxels with 80% probability of being CSF from FAST. pCASL *f*, VSASL *f*, T_2-FLAIR VSASL *f* and the subtraction of the T_2-FLAIR VSASL *f* map from the VSASL *f* map are shown in ml/100g/min.

Sequence	GM *f*	CSF *f*
pCASL	76.2 ± 2.7	47.8 ± 4.5
VSASL	86.3 ± 2.1	180.0 ± 19.7
T2-FLAIR VSASL	75.2 ± 2.3	27.1 ± 6.2

Table 1: Mean ± SE *f* in each mask in ml/100g/min

Results: Fig 4 shows pCASL, VSASL and T_2-FLAIR VSASL data from two representative slices (of 13) containing CSF. The subtraction of T_2-FLAIR VSASL from VSASL on the same greyscale demonstrates the artifactual hyperperfusion arising from CSF. The addition of the BIR-4 T_2-FLAIR pulse to the VSASL sequence significantly reduced the apparent grey matter and CSF perfusion values ($P < 0.01$), comparable to pCASL levels (Table 1).

Discussion: In healthy volunteers T_2-FLAIR VSASL reduces perfusion contamination from CSF whilst maintaining the spatial coverage of the VSASL sequence, albeit at a cost of reduced SNR. Future work will include applying this method in tumors where VSASL overestimated *f* by optimising the null time for T_1 & T_2 of the inflammation response.

Conclusions: The BIR-4 T_2-FLAIR preparation reduces the contamination from long T_1 & T_2, high-ADC spins in the VSASL perfusion weighted subtraction, increasing the accuracy of VSASL perfusion measurements.

Acknowledgements: Funding from Cancer Research UK and EPSRC. **References**: [1] Wong et al. MRM 55:1334 (2006) [2] Guo et al. in proc. ISMRM p.2116 (2011) [3] Wong et al. MRM 45:529 (2001) [4] Nezafat et al. MRM 61:1326 (2009) [5] Meakin et al. MRM, in press (2012) [6] Buxton et al. MRM 40:383 (1998)