Dynamic Subtraction VASO with Second Image Acquisition Allows for Combined CBV and CBF Estimation In-vivo

Alexander Graeme Gardener[1], and Peter Jezzard[1]
[1]FMRIB Centre, University of Oxford, Oxford, United Kingdom

Introduction and Theory: In VASO [1] brain magnetization is non-selectively inverted and an image acquired after a time delay TI1, which is chosen to be at the null point of the blood (1190ms at 3T for long TR), to produce CBV-weighted contrast and relative signal change between rest and activation. The MR signal should be zero inside vessels and will be suppressed in tissue as it recovers from inversion (as blood T_1 > tissue T_1). Dynamic Subtraction VASO (DS-VASO) has been proposed as a method of measuring Cerebral Blood Volume (CBV) [2] and modifies the original approach to acquire two sets of images – the first (null) inverts globally, directly followed by a slice selective inversion ("flip-back"); the second (control) uses two back-to-back slice inversions only. In this way static tissue magnetization in-slice is returned to equilibrium. In post-processing, [control – null] subtraction will give a positive CBV signal as tissue subtracts away. This is similar to pulsed ASL, except CBV contrast is generated by acquiring at the blood null time, before perfusion into tissue occurs [3]. However, this method is time intensive with a single slice acquired per scan (as the null point is only crossed once). In this study we use the fact the tagging scheme is comparable to ASL in order to simultaneously obtain CBV and a second CBF-weighted image at a delay time TI2, when blood will have perfused into tissue. We need to retain a TI1 short enough such that the blood is still in the vascular space, whilst TI2 is long enough to provide a CBF signal. By using a shortened TR time and by maintaining a wide tag inversion region, we can achieve a steady-state inflowing blood condition and use this to reduce TI1, according to: $TI1 = 1 - 2*\exp(-TI1/T_1) + \exp(-TR/T_1)$, where blood T_1 is taken as 1627ms at 3T [3].

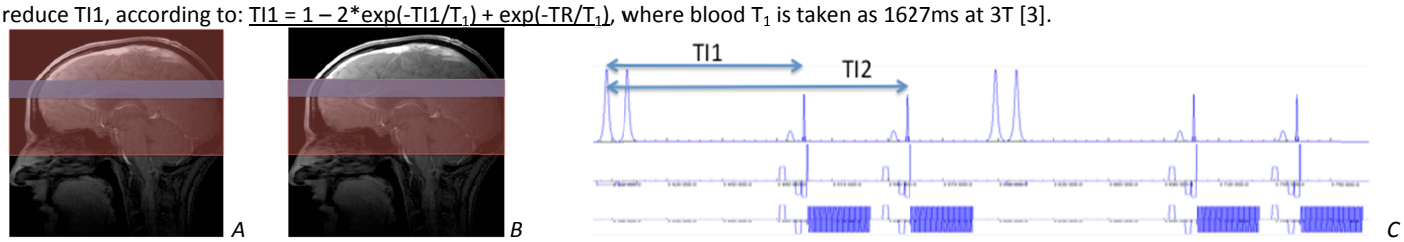


Figure 1: Two tagging schemes that invert: (A) all blood flowing into slice or (B) arterial inflow only. Red inversion is applied on the null scan, followed by the blue (flip-back); for control two back-to-back blue inversions are applied. (C) Schematic of the pulse sequence A for Control and Tag showing TI1,2 time delays.

Methods and Results: Studies were run on a 3T Siemens Verio system; subjects gave written, informed consent (4 healthy male adults, age 28 ± 2 years). Acquisitions used a 32-channel head coil, with gradient echo EPI sequences (parameters: 64^2 voxels at 3x3x5 mm^3; TE=18 ms; partial-Fourier phase 6/8). Two combined DS-VASO+ASL acquisition schemes were employed as shown in Fig. 1, with two sets of TR/TI1/TI2 [long 1.4/0.84/1.35 s; short 1.15/0.76/1.1 s]. Twenty image pairs were acquired as default, with sufficient preparation scans to achieve initial steady state (not included). From Scheme A tag images it was possible to see sagittal sinus venous blood signal nulled at TI1, confirming the times used were appropriate. A multi-TI (0.8, 1.1, 1.4, 1.7 s) QUIPSS2 pulsed-ASL sequence [4] was used to independently assess CBF (fitted to the Buxton kinetic model [5]), to compare to values found by our dual methods. To generate grey-matter masks a double inversion recovery sequence was acquired with TI1/2=3.2/3.7 s; TR=20 s; also unprepared (M_0) images were acquired (TR=20 s) for quantification. In addition, two subjects had scheme A scans performed where widths of control inversion pulses were systematically increased, which offset the slice from edge of the inflowing blood tag. Images were coil-bias and motion corrected in FSL [6], with individual difference images (ΔS) averaged together to improve CNR. To estimate CBV Eq. 2 of [3] was used, assuming the same blood delivery and transit times across the slice and subjects; this assumption is discussed more fully in the reference. To estimate CBF a version of the kinetic model was used for single TI [5].

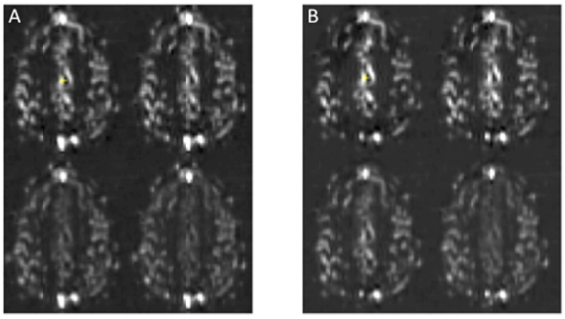
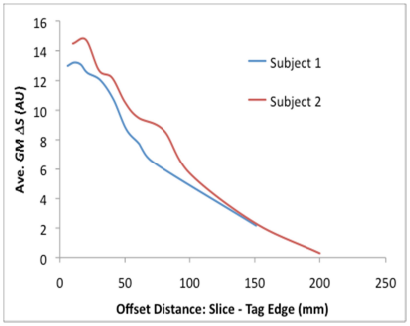


Figure 2 (A) and (B) – averaged ΔS images (a.u.) for Scheme A/B at TI1 and TI2 (top/bottom) for short (l) and long (r) TR/TI1/TI2.



(C) GM averaged ΔS (scheme A) as spatial extent of flip-back pulse increased.

Scheme A CBV (mL / 100mL)	
CBV (TI1 = 0.76)	4.2 ± 0.9
CBV (TI1 = 0.84)	3.2 ± 0.9
Scheme A CBF (mL / 100g / min)	
CBF (TI2 = 1.1)	63 ± 8
CBF (TI2 = 1.35)	67 ± 7
Scheme B CBV (mL / 100mL)	
CBV (TI1 = 0.76)	3.9 ± 1.0
CBV (TI1 = 0.84)	3.5 ± 1.1
Scheme B CBF (mL / 100g / min)	
CBF (TI2 = 1.1)	53 ± 5
CBF (TI2 = 1.35)	61 ± 7
pASL CBF (ml/100g/min)	***67 ± 6***

(D) Table 1: CBV and CBF values averaged across subjects for grey matter.

Fig. 2A and B show higher signal difference across the CBV images (upper), with more even, widespread, signal difference across CBF images (lower). Fig. 2B shows reduced venous contribution in the sagittal sinus, as the label is applied only to below-slice (arterial) blood. Fig. 2C shows the result of increasing the flip-back width, and of offsetting the inflow label edge from the slice; showing lowered signal for a gap of 40+ mm.

Discussion: The DS-VASO approach is extended to provide both CBV- and CBF- weighted images during a single acquisition, improving the time efficiency of the measurements. CBV estimates (Table 1) were slightly higher than expected; but these are dependent on the parameters in Eq. 2 of [3]. CBF estimates matched the order of literature values (GM voxels ~1-2% signal change) and were comparable to QUIPSS2 PASL values. The interaction of the tag/control inversion pulses on various blood components is complex, which complicates fitting. Both CBV/F may benefit from acquiring additional TR/TI combinations to perform combined fitting, and extract better parameter estimations for model terms, as well as using flow crushing and/or saturation pulses around image acquisition. Future work will incorporate double-echo acquisition to obtain additional BOLD-weighted images, to generate concurrent CBV, CBF and BOLD data at rest and activation. Ultra-high field may allow higher voxel resolution to better separate CBV and CBF signal - this study used a relatively coarse voxel size.

References: 1 - Lu, MRM, 2003; 2 - Donahue, JCBFM, 2010; 3 - Hua, NMR BioMed, 2011; 4 – Wong, MRM, 1998; 5 - Buxton, MRM, 1998; 6 – Smith, NeuroImage, 2004. Funded by the UK MRC.