Estimating Cerebral Blood Volume with Expanded VASO Slice Coverage

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INTRODUCTION

Recently, several research efforts have focused on complementing blood oxygenation level dependent (BOLD) contrast with measures that are more quantitative and have better specificity to neuronal activation. These efforts utilize arterial spin labeling (ASL) to measure cerebral blood flow (CBF) [1] and vascular space occupancy (VASO) to reflect cerebral blood volume (CBV) [2]. While ASL can quantify CBF, VASO reflects CBV-weighted images that are not easily quantifiable without assuming CBV_{REST}. Furthermore, the inflow of fresh unsaturated blood can alter the recovery of the longitudinal magnetization of the blood, causing error in VASO-related changes [3]. This confound is exacerbated in the simultaneous acquisition of VASO and CBF because CBF's slab-selective inversion requires a thinner slab for labeled images [4]. A recent noninvasive method to measure absolute CBV in a single slice based on VASO utilized a biophysical model with multiple acquisitions to vary the extent of BOLD/VASO weighting [5]. The present work extends this approach by (1) expanding it to multiple slices, (2) applying this model to data acquired with a multi-echo sequence simultaneously acquiring VASO, CBF and BOLD images and (3) incorporating the effect of inflow to both improve CBV estimation for singular VASO acquisition and enable this approach for a simultaneous sequence.

METHODS

Image Acquisition: Data were acquired for 2 subjects with a multi-echo sequence on a Siemens 3T TIM system utilizing an inversion recovery sequence with two excitations (5 slices, TR=2 sec) [4]. As shown in Fig. 1, following EPI acquisition of the VASO-weighted image a second excitation pulse prepares for two additional gradient echo images, CBF (TE=11 msec) and BOLD (TE=33 msec). The interleaved slab-selective/non-selective gradient is used for labeled/control perfusion images, respectively. An inversion slab thickness of 125 mm was empirically determined to balance VASO (thick slab) and CBF (thin slab) contrasts. Labeled and control images are subtracted to yield CBF-weighted images and added for VASO and BOLD-weighted images. For traditional VASO acquisition, the inversion time between the inversion pulse and the first excitation pulse (TI_1) is selected at the blood nulling point to yield a minimized signal from voxels containing blood. However, the present study collects 14 scans with different TI_1 values to vary the extent of blood nulling [5]. This enables expanded VASO coverage for the first time using this modelling approach with a different set of TI_1 values for each slice, each sufficiently covering the range of blood nulling required to apply the biophysical model (Fig. 2). For each TI_1, visual stimulus consisted of 24 seconds of rest, followed by 48 seconds of a flashing checkerboard with reversing contrast at 8 Hz and ending with 20 seconds of rest.

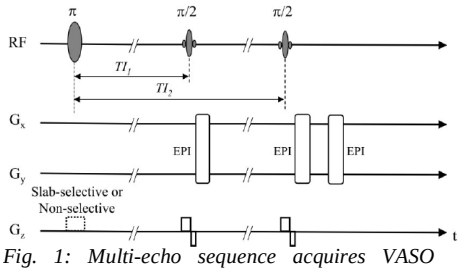

Fig. 1: Multi-echo sequence acquires VASO image from first excitation and ASL and BOLD images from second excitation. (Image and sequence from [4])

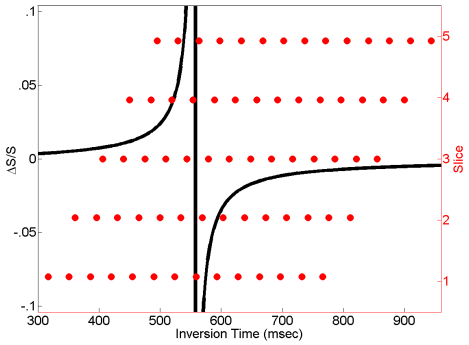

Fig. 2: Simulated ΔS/S for range of TI_1 (black) and TI_1 coverage for slices 1-5 (red).

Analysis: Data were motion corrected, spatially smoothed (6 mm FWHM kernel for VASO and CBF data only) and statistically analyzed using SPM2 (Wellcome Department, University College of London, London, UK) generating fourteen *t*-maps with varied BOLD/VASO weighting (positive/negative correlation to task). These individual maps were combined using multiple dataset analysis [5,6] by utilizing the inverse normal cumulative distribution function (Φ) and p-values corresponding to test statistics from each scan. Voxels with a combined test statistic > 5 were considered to be active with the VASO contrast at multiple TI_1 values and used for modelling the change in signal normalized to baseline ($\Delta S/S$). The previously described biophysical model by Gu *et al.* was modified in three ways. First, with two excitations in the sequence used in this study, one must consider TI_2 when calculating signal dependence. Second, the confounding inflow of blood which increases effective $R_{1,BLOOD}$ is modelled when fitting the empirical $\Delta S/S$ data to the biophysical model at different values of TI_1. Finally, this model is applied to multiple slice acquisitions, leveraging the TI_1 variability between scans to expand slice coverage. As with the previous model [5], the two points surrounding the tissue nulling point were excluded to avoid large error contributions and the remaining 12 points were fit to the model. In this work, we utilized an exhaustive search of parameter ranges for CBV_{REST}, CBV_{ACT}, CSF fraction (F_{CSF}), blood oxygenation during activation ($Y_{b,ACT}$) and $R_{1,BLOOD}$.

RESULTS AND DISCUSSION

The biophysical model was separately applied to each slice and utilized an average weighted with each slice's ROI size to yield estimates for each subject's active 3-dimensional ROI. As predicted, $R_{1,BLOOD}$ was higher (.67 and .68) than the expected value (.62) [7] for both subjects (Table 1). For both subjects, all parameters were within expected ranges based on published values [5]. As shown in Fig. 3, empirical $\Delta S/S$ is consistent with curve fitting. These results demonstrate the feasibility of this model for multiple slices and the ability to estimate effective $R_{1,BLOOD}$ through biophysical modelling.

Subject	CBV_{REST} (mL blood / 100 mL brain)	CBV_{ACT} (mL blood / 100 mL brain)	CBV Change (%)	$Y_{b,ACT}$	$R_{1,BLOOD}$
1	5.7	7.1	25.2	0.71	0.67
2	5.0	7.4	46.2	0.79	0.68

Table 1: Curve fitting results for both subjects using average over slices (weighted by each slice's ROI size).

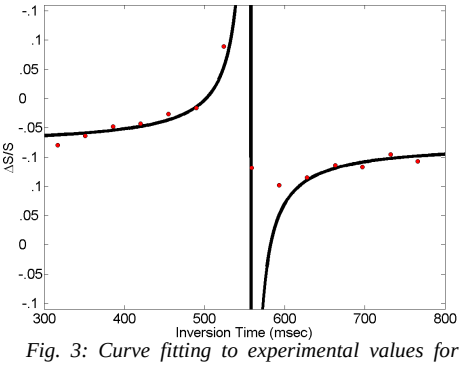

Fig. 3: Curve fitting to experimental values for subject 2 (CBV_{REST}=5.0 ml blood/100 ml brain, CBV_{ACT}=7.4 ml blood/100 ml brain, $Y_{b,ACT}$=.79, $R_{1,BLOOD}$=.68).

CONCLUSION

This work expands previous work for measuring absolute CBV to multiple slices, simultaneous acquisition of VASO, CBF and BOLD, and accounts for inflow of blood by allowing $R_{1,BLOOD}$ to be estimated. The estimation longitudinal relaxation can improve accuracy of CBV quantification for the singular VASO sequence, and even more so for simultaneous acquisition with CBF. Our results provide a foundation for expanded exploration of this method and potential estimation of oxygen metabolism using empirically-derived CBV quantification.

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