Concurrent Nulling of Blood and CSF Signal (VASO-FLAIR) Allows for Simultaneous Measurement of CBV and CSF Volume Fractions

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Introduction. The ability of fMRI to quantify hemodynamic parameters has considerably illuminated the mechanisms underlying the brain's response to neuronal activation. However, quantification of these parameters in gray matter (GM) can be heavily affected by the fraction of CSF in the voxel (1), which may vary between subjects as well as with voxel location. We present an expansion of the fluid-attenuated inversion recovery (FLAIR) sequence (2) which nulls blood and CSF signal simultaneously, allowing for fast and reliable measurement of CSF fractions when used in succession with the vascular space occupancy (VASO) blood-nulling sequence, a new fMRI technique (3). Here, using VASO-FLAIR at high fMRI resolution at 3T, we show that GM voxels may have CSF fractions as high as 30%, thereby significantly affecting the quantification of hemodynamic parameters from corresponding fMRI data. In addition, we demonstrate that GM cerebral blood volume (CBV) maps can be generated quickly and noninvasively from combined VASO and VASO-FLAIR experiments.

Methods. *Theory.* The VASO-FLAIR sequence consists of two non-spatially-selective adiabatic inversion pulses, spaced such that the longitudinal components of CSF and blood water magnetization equal zero when an image is acquired (Fig. 1). Appropriate spacing was found by numerically minimizing the blood and CSF magnetization (Eqn. 1), for this two pulse experiment.

$$M_i(TI) = 1 - [\,2 - (2 - e^{-TR-TI1-TI2}) \cdot e^{-TI1/T_{1,i}}\,] \cdot e^{-TI2/T_{1,i}} \qquad i\text{=CSF or blood.} \tag{1}$$

TR, *TI*, *TI1*, and *TI2* are shown in Fig. 1. At 3T, $T_{1,CSF}$=3817 ms, $T_{1,blood}$ =1627 ms, and $T_{1,GM}$ =1200 ms. When neglecting possible white matter voxel contributions, VASO signal (M_{blood} = 0) is given by Eqn. 2, VASO-FLAIR signal (M_{CSF} = 0; M_{blood} = 0) by Eqn. 3, and *A*, a constant giving the MRI signal per unit volume of water protons at equilibrium that can be obtained from a reference ROI in the ventricles, by Eqn. 4.

$$S_{VASO} = A \cdot [(1 - X_{CSF}) \cdot (C_{par} - CBV \cdot C_{blood}) \cdot M_{GM}^{VASO}(TI) \cdot e^{-TE/T_{2,GM}} + X_{CSF} \cdot C_{CSF} \cdot M_{CSF}^{VASO}(TI) \cdot e^{-TE/T_{2,CSF}}] \tag{2}$$

$$S_{VASO\text{-}FLAIR} = A \cdot (1 - X_{CSF}) \cdot (C_{par} - CBV \cdot C_{blood}) \cdot M_{GM}^{VASO\text{-}FLAIR}(TI) \cdot e^{-TE/T_{2,GM}}) \tag{3}$$

$$A = S_{CSF}^{VASO} / \left(C_{CSF} \left| M_{CSF}^{VASO}(TI) \right| e^{-TE/T_{2,CSF}} \right) \tag{4}$$

where *TE*=echo time, water densities C_{par}=0.89, C_{blood}=0.87, and C_{CSF}=1; $T_{2,GM}$=70.8 ms (1), $T_{2,CSF}$=1442 ms, and S_{CSF}^{VASO} is VASO signal in a pure CSF voxel (ventricle). Optimal null times for *TR*=25s are *TI1/TI2*=4.299/1.008s (VASO-FLAIR) and *TI*=1.127 ms (VASO). Resultant *M(TI)* values are $M_{GM}^{VASO}(TI) = 0.22$, $M_{GM}^{FLAIR}(TI) = 0.16$, $M_{CSF}^{VASO}(TI) = -0.54$. *Experiment.* VASO (*TR/TI*=25/1.127s) and VASO-FLAIR (*TR/TI1/TI2* =25/4.299/1.008s) experiments were performed (n=3). Voxel volume = 1.89x1.89x3 mm^3, SENSE=2.5, single-shot EPI, *TE*=22 ms, 5 dynamics/scan. To test nulling efficiency and SNR, 9 VASO-FLAIR experiments were performed for *TI1*: 3899-4699 ms (100 ms increments).

Results and Discussion. Fig. 2 shows typical VASO (a) and VASO-FLAIR (b) images. By calculating *A* (Eqn. 4) and then simultaneously solving for X_{CSF} and *CBV* (Eqns. 2-3), it is possible to generate CSF (Fig. 3a) and CBV (Fig. 3b) maps. CSF fractions in GM vary with voxel location, but are largest in anterior (X_{CSF}=0.33±0.17) and posterior (X_{CSF}=0.12±0.14) regions. The large standard deviation in X_{CSF} across subjects suggests that CSF fractions vary greatly, and should be calculated on a subject-by-subject as well as voxel-by-voxel basis in fMRI paradigms. GM CBV is found to be 4.9±1.9 ml blood/100 ml brain in a GM ROI, in good agreement with recent literature (4). GM SNR for two averaged VASO-FLAIR images (SNR=33.7±5.8) was not substantially below VASO (41.2±7.6), thus sufficient SNR is achievable in just two dynamic scans (time<1 min). Therefore, VASO-FLAIR can be performed along with other fMRI experiments (e.g. BOLD and ASL) without elaborate time compromises. Varying *TI1* allows for tissue contrast enhancements; measured signal (Fig. 4b) is generally in good agreement with model prediction (Fig. 4a; Eqn. 1). The ability to quickly calculate CSF fractions on a voxel-by-voxel basis, when used with other fMRI modalities, will improve quantification of physiological parameters. Likewise, the ability to generate CBV maps noninvasively should extend VASO-FLAIR to the clinic with obvious applications (e.g. stroke, tumor grading, etc.).

References. 1. Donahue et al., this meeting**; 2.**De Coene, *AJNR* 1992.13:1555-64**; 3**.Lu et al. *MRM* 2003.50:263-74; **4**.Lu et al. *MRM* 2005.In press

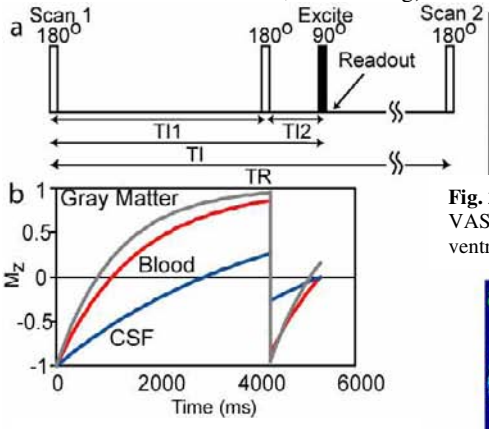

Fig. 1. The VASO-FLAIR pulse sequence (a) with corresponding gray matter, blood and CSF recovery curves (b).

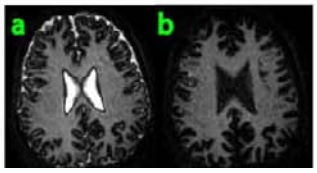

Fig. 2. VASO (a); VASO-FLAIR (b). The ability of VASO-FLAIR to null CSF can clearly be seen in the ventricles of (b).

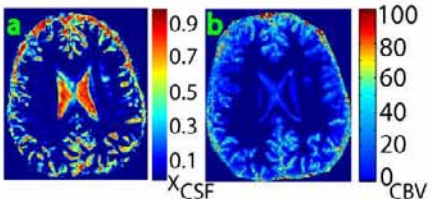

Fig. 3. CSF fraction map (a) and GM CBV map (b; ml blood/100 ml par) created from VASO + VASO-FLAIR data.

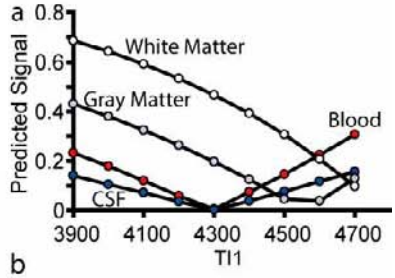

Fig. 4. Predicted (a) and measured (b) signal changes for varying *TI1*. Error bars represent STD over a ROI.