A streamlined approach to mapping the oxygen extraction fraction (OEF) and deoxygenated blood volume (DBV) using the quantitative BOLD technique

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Target Audience: Researchers and clinicians interested in an easy to implement method for mapping OEF and DBV in the human brain using endogenous contrast

Purpose: Quantitative BOLD (qBOLD) is a non-invasive MR technique capable of producing quantitative measurements of the haemodynamic and metabolic properties of the brain[1]. This is achieved by modelling the transverse MR signal decay in the presence of a blood vessel network by exploiting the sensitivity of the reversible transverse relaxation rate ($R_2'=R_2^*-R_2$) to the Oxygen Extraction Fraction (OEF) and Deoxygenated Blood Volume (DBV)[2]. Here we propose a refinement of the qBOLD methodology in order to provide a clinically feasible method for the mapping of OEF and DBV. A novel acquisition protocol is used to remove confounding effects from the measurement of R_2' and improve the robustness of the resultant parametric maps.

Background: The qBOLD method is fundamentally reliant on the acquisition of R_2'-weighted data that is specifically sensitive to the effect of deoxygenated blood within the blood vessels. In practice there are several confounding effects which include (i) enhanced R_2' decay due to macroscopic field inhomogenities (MFIs), (ii) inaccurate removal of underlying R_2-weighting, and (iii) off-resonance effects of partial volumes of cerebral spinal fluid (CSF). In the original qBOLD implementation all of these effects were included in a comprehensive model of the MR signal[2]. However, this model is complex and may be over parameterised resulting in issues disentangling OEF and DBV[3]. Therefore, in this work we aim to remove these effects during data acquisition by; (i) using the Gradient Echo Slice Excitation Profile Imaging (GESEPI) method to correct for MFIs without the need to separately acquire magnetic field maps[4], (ii) using an Asymmetric Spin Echo (ASE)[5] acquisition to directly measure the R_2'-weighted signal with a constant R_2-weighted signal contribution, and (iii) nulling the CSF signal by using a FLuid Attenuated Inversion Recovery (FLAIR) preparation[6]. By combining GESEPI (inherent reduction in MFI's), ASE (direct measure of R_2') and FLAIR (removal of CSF contamination) we reduce confounding effects to offer a streamlined qBOLD approach. This is beneficial in terms of simplifying acquisition and modelling allowing parametric maps of OEF and DBV to be calculated in a refined implementation.

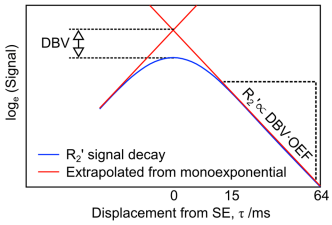

Fig1: Demonstration of the measurement of R_2' and DBV from ASE data sampled at multiple refocusing pulse offsets (τ). When R_2' and DBV have been estimated from the data in this manner Eq. 1 can be used to calculate OEF.

Eq1 $$OEF = \frac{R_2'}{DBV.\gamma.\frac{4}{3}.\pi.\Delta\chi_0.Hct.B_0}$$

Methods: 7 healthy participants (aged 24-32; mean age 28±3; 4f:3m) were scanned using a 3T TIM Verio system (Siemens Healthcare, Erlangen, Germany). For each subject a high-res anatomical and two GESEPI ASE scans were acquired with and without a FLAIR preparation for comparison (ASE scan time 6mins 18s each, TI_{FLAIR} = 1210 ms). Imaging parameters were FOV 240mm^2, 64×64 matrix, ten 5mm slices, TR/TE = 3s/74ms, BW 2004Hz/px. Raw data were Hanning filtered prior to reconstruction. ASE images were acquired with no R_2'-weighting (τ=0ms) and R_2'-weighting in the mono-exponential regime[7] ($\tau_{start}: \Delta\tau : \tau_{finish}$= 16:4:64ms). The GESEPI acquisition was implemented by phase encoding each 5mm slice in the z-direction. In effect each 5mm slice was split into four 1.25mm sub-slices and acquired with 100% partition oversampling to reduce aliasing (total 8 k-space partitions). The four reconstructed sub-slices were then summed to produce a single 5mm slice. For each ASE acquisition, R_2' was calculated using a linear fit to the mono-exponential regime (τ>15ms[7]) of the ASE data (**Fig1**). The intercept of this fit and the spin-echo signal (τ=0ms) were subtracted in order to provide a measure of DBV. OEF was then calculated using **Eq1** where DBV and R_2' were measured and other parameters are known or assumed constants[2] ($\Delta\chi_0$=0.264x10^{-6}, Hct=0.34). This parameter estimation was performed for datasets with FLAIR (ASE_{FLAIR}) and without ($ASE_{NoFLAIR}$). ROI analysis was performed for grey and white matter ROI's defined by an automated segmentation of the anatomical images (FAST, FSL) registered to the parameter maps.

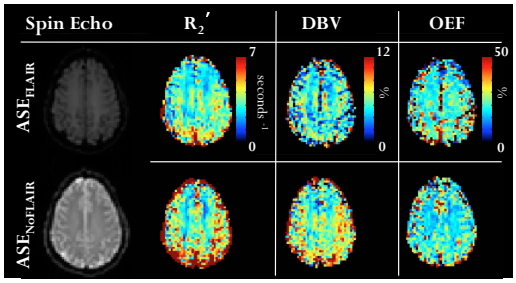

Fig2: Example parametric maps (R_2', DBV and OEF) from a single subject calculated using ASE_{FLAIR} (top row) and $ASE_{NoFLAIR}$ (bottom row).

Results & Discussion: Fig2 shows parameter maps calculated in a single slice for an example subject. Maps of R_2', DBV and OEF were calculated for ASE_{FLAIR} and $ASE_{NoFLAIR}$. Reduced R_2' values were observed in cortical regions for ASE_{FLAIR} compared with $ASE_{NoFLAIR}$, consistent with an increased CSF fraction as observed previously[6]. **Table1** shows group average parameter values from grey and white matter ROIs. Despite the expected reduction in SNR due to the FLAIR preparation, grey matter R_2' estimates from ASE_{FLAIR} have reduced variance compared with $ASE_{NoFLAIR}$. Grey matter DBV is reduced in ASE_{FLAIR} compared with $ASE_{NoFLAIR}$, which may be associated with the reduction in mean R_2' for ASE_{FLAIR}. However, ASE_{FLAIR} does not appear to affect the grey matter mean OEF. When compared with literature values[8] (OEF~0.36, DBV~0.035) grey matter DBV estimates are high and OEF values are low. Further investigation is required to compare these measurements with more established techniques for global OEF estimation. White matter R_2', DBV and OEF values are relatively unchanged by ASE_{FLAIR}, presumably due to a smaller CSF partial volume effect. White matter DBV estimates are similar to grey matter values despite an expected 50% lower DBV in white matter[9]. White matter OEF values are lower than grey matter values. Both of these effects are likely to be due to the presence of paramagnetic myelin, which is not accounted for in the qBOLD model, meaning that quantitative estimates in white matter may be unreliable[10]. However, for applications where the main aim is to visualise regions of white matter where the OEF is altered with respect to normal appearing tissue, this method may still provide useful diagnostic information.

N=7	R_2' (s^{-1})	DBV	OEF
ROI Grey Matter			
ASE_{FLAIR}	3.2 ± 0.3	0.057 ± 0.007	0.24 ± 0.02
$ASE_{NoFLAIR}$	4.3 ± 0.6	0.068 ± 0.008	0.24 ± 0.02
ROI White Matter			
ASE_{FLAIR}	3.3 ± 0.2	0.056 ± 0.003	0.21 ± 0.01
$ASE_{NoFLAIR}$	3.2 ± 0.2	0.060 ± 0.004	0.19 ± 0.01

Table 1: Group averaged (mean ± stdev) measures of R_2', DBV and OEF calculated in GM & WM for ASE_{FLAIR} & $ASE_{NoFLAIR}$. (N=7)

Conclusion: FLAIR GESEPI ASE has the potential to provide parametric maps of R_2', OEF and DBV with good brain coverage, in clinically feasible times (<7 mins) and in a non-invasive, patient friendly manner without the need for external contrast. However, further investigation is required to assess the sensitivity and reproducibility of these parametric measures.

References: [1] Yablonskiy et al. NMR Biomed. 2012,26(8):963; **[2] He & Yablonskiy** Magn Reson Med. 2007,57:115; **[3] Christen et al.** Magn Reson Med. 2011,67(5):1458; **[4] Blockley** Proc ISMRM 2014, #2997; **[5] Wismer et al**. J Comp Assist Tomo. 1988,12(2):259; **[6] Dickson et al.** Proc ISMRM 2009 #1640; **[7] Yablonskiy & Haacke,** Magn Reson Med. 1994,32:749; **[8] Perlmutter et al.** J Cereb Blood Flow Metab. 1987,7:64; **[9] Rempp et al.** Radiology.1994,193:637; **[10]** Bouvier et al. Proc. ISMRM 2013, #2492