Global intravascular and local hyperoxia contrast phase-based blood oxygenation measurements

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Target: The measurement of venous blood oxygenation (Yv) is important in cases where oxygen extraction fraction (OEF) may be perturbed, e.g. multiple sclerosis, traumatic brain injury and carotid stenosis; and also for hyperoxia-based BOLD calibration[1,2]. **Purpose:** Phase-based measurements of Yv provide a simpler data acquisition to R_2'- and R_2-based methods[3,4,5]. Previous phase-based approaches measure the intravascular (IV) phase of a large draining vein[6,7], recently we have described a technique to compare the change in phase distribution local to a vein between normoxia (NO) and hyperoxia (HO)[2] that does not require knowledge of the vein's geometry. This approach assumes the phase distribution on NO is dominated by the effect of IV deoxyhaemoglobin and thus provides a template for the field change on HO (applying *Eq.1* over a limited range of r) due to a change in Yv.

$$\Delta\phi_{HO}(r) = \alpha \cdot \Delta\phi_{NO}(r) \quad \text{- Eq1}$$

$$(1 - Y_v) = \frac{\Delta\phi_{IV}}{\gamma \cdot TE \cdot B_0 \cdot \Delta\chi_{do} \cdot Hct \cdot \beta} \quad \text{- Eq2}$$

$$Y_v = \frac{\left[-\Delta Y_h \cdot \left(\Delta\chi_{oxy} - \Delta\chi_{do}\right)/(1-\alpha)\right] - \Delta\chi_{do}}{\left(\Delta\chi_{oxy} - \Delta\chi_{do}\right)} \quad \text{- Eq3}$$

Aim: To assess three approaches for measuring Yv, using: the IV phase in the superior sagittal sinus and an infinite cylinder model (*Method A*) or a forward field calculation (*Method B*) of the IV field shift; or the phase distribution change on hyperoxia to measure localised values of Yv (*Method C*).

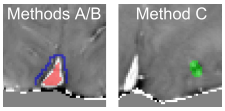

Figure 1: ROIs used. ($-1 \le \phi \le 1^{rad}$)

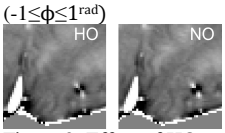

Figure 2: Effect of HO. ($-0.5 \le \phi \le 0.5^{rad}$)

Methods: 8 healthy volunteers (7M/1F, 22-32y.o.) were scanned, using a Philips Achieva 7T system with volume transmit/32-channel receive head coil. For 6 subjects, 3D whole-head FLASH data (0.65mm isotropic voxels, TR/TE=9.5/5ms; SENSE=2.25(AP); flow compensated; T_{AQ}=3.5 min) were acquired at NO and at HO, controlling end-tidal O_2 ($P_{ET}O_2$) and CO_2 ($P_{ET}CO_2$) partial pressures using a Respiract™ (Thornhill Research Inc., Toronto, Canada). $P_{ET}O_2$ was targeted between the subject's baseline (~110 mmHg; NO) and 500 mmHg (HO), whilst $P_{ET}CO_2$ was held constant. To assess the reproducibility of Methods A&B, two further subjects were scanned 6 times at 5.5 min intervals while breathing room air. For all subjects, a multi-echo FLASH scan was acquired at NO to identify veins (3 echoes, $TR/TE_1/\Delta TE$=21/5/5ms; SENSE=2.25/1.4(AP/FH)). Phase images were unwrapped, magnitude images were co-registered using FLIRT (FSL) and a homodyne filter (FWHM 8mm) was applied to phase images. *Method A & B:* In 5 slices in which the sagittal sinus was parallel to B_0, the phase difference ($\Delta\phi_{IV}$) between IV and extravascular (EV) ROIs (*Fig1*) was found. *Eq.2* was used to calculate Yv from $\Delta\phi_{IV}$, assuming a susceptibility difference between tissue and deoxygenated haemoglobin of $\Delta\chi_{do}$ =0.247 ppm(cgs)[8], and β*=1/3 (Method A)* or β calculated using a forward field calculation[9] for the sagittal sinus (*Method B*). *Method C:* A vein mask was formed by thresholding the R_2* map created from the multi-echo data (R_2*>100s^{-1}). For each vein, this mask was dilated by 1 voxel to include the EV field perturbations (*Fig1*). HO induced increases in Yv (ΔY_h) reduce the amplitude of the EV field perturbation (*Fig2*). The HO phase distribution ($\Delta\phi_{HO}(r)$) was fitted to the NO phase distribution ($\Delta\phi_{NO}(r)$) for α (*Eq1*) over all voxels in the dilated mask of each vein. The value of α was then used in *Eq. 3* (derived in[2]) to calculate Yv for each vein, where $\Delta\chi_{oxy}$ =-0.017 ppm(cgs)[8] is the susceptibility difference between tissue and oxygenated haemoglobin. ΔY_h was then estimated from $P_{ET}O_2$[1], assuming $P_{ET}O_2 \equiv$arterial PO_2 (validity discussed in[2]). Monte Carlo simulations were performed, to assess how noise propagates through *Eqs.1&3*.

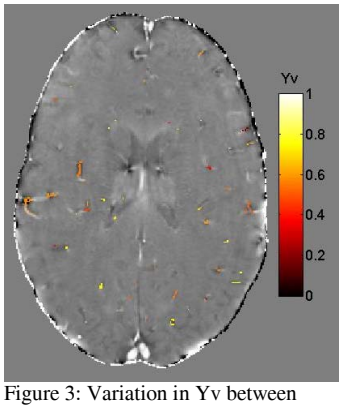

Figure 3: Variation in Yv between veins for a single subject, overlaid on the NO phase image. ($-1 \le \phi \le 1^{rad}$)

Results: *Method A*: Yv =0.70±0.01 (mean±SEM, 8 subjects). *Method B:* Yv =0.60±0.02, since β = 0.257±0.005 (<1/3 in all subjects), with reproducibility <1.5% for both subjects. *Method C:* $P_{ET}O_2$ increased by 320±20 mmHg (mean±SEM, 6 subjects) giving[1] ΔY_h =0.066±0.003 and Yv =0.60±0.01 averaged across veins. *Fig3* shows a map of Yv for veins identified on the R_2* map; visual inspection of these maps showed no apparent bias due to vessel orientation. *Fig4* shows the distribution of Yv measured across veins of all subjects.

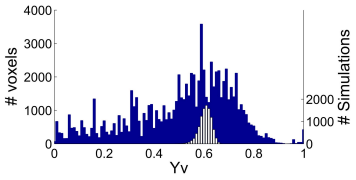

Figure 4: Histogram of venous Yv values (weighted by # voxels in each vein) including all 6 subjects. Monte Carlo simulation results (white) indicate the expected noise distribution.

Discussion: Methods A&B use large vessels and so provide high SNR, but require knowledge of the vein's size, shape and orientation, restricting the application to larger vessels to avoid partial voluming effects. Furthermore, Method A is limited to long, straight vessels. The HO phase contrast method (Method C) does not require knowledge of the vein's size, shape or orientation and can be used on smaller veins, but does require an estimate of ΔY_h[1]. The distribution in *Fig4* is centred on Yv~0.6, but skewed to lower Yv. Monte Carlo simulations produced a much narrower (but also skewed) distribution of Yv (*Fig4*-white histogram), suggesting that real Yv heterogeneity was detected *in vivo*, although there was no obvious change in Yv between brain regions. An 8 mm spatial filter width was used to preserve the phase contrast in the sagittal sinus, whilst removing large scale differences between NO and HO phase images. However, the systematically higher Yv values produced by Method A suggest that the filter attenuated the sagittal sinus phase, whilst Method B is less sensitive to this effect. Decreased tissue-vein $\Delta\chi$ due to increased tissue PO_2 on HO[10], will have a negligible effect here (tissue PO_2 increase of 50 mmHg, giving $\Delta\chi \approx 10^{-4}$ ppm).

Conclusion: Yv measured from phase in the superior sagittal sinus gave repeatable results, but this approach is limited in utility since it can only be applied to large veins. Method C measures Yv from the reduced field perturbation around a vein on HO, and is not limited to large veins, allowing the variation in Yv across the brain to be examined which will be important clinically.

References:1. Chiarelli et al. NeuroImage 37:808-820 (2007); 2. Driver et al. NeuroImage 63:1178-1187 (2012); 3. He and Yablonskiy MRM 57:115-126 (2007); 4. Lu and Ge MRM 60:357-363 (2008); 5. Bolar et al. MRM 66:1550-1562 (2011); 6. Haacke et al. HBM 5:341-346 (1997); 7. Jain et al. JCBFM 30:1598-1607 (2010); 8. Spees et al. MRM 45:533-542 (2001); 9. Marques, J.P., Bowtell, R. Concepts Magn Reson 25B, 65-78 (2005); 10. Schwarzbauer and Deichmann NeuroImage 59:2401-2412 (2012). **Acknowledgement:** Funded by the UK MRC.