Measuring changes in brain oxygenation using dynamic T1 weighted imaging

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Introduction: Despite the crucial role of hypoxia in several disorders and treatments, reliable clinical methods to quantify tissue oxygenation ($P_{bt}O_2$) are still lacking. The aim of this study is to detect changes in molecular oxygen concentrations in brain tissues using the relationship between PO_2 and R_1, which has not previously been demonstrated successfully to our knowledge.

Methods: Previous studies have determined the relaxivity of dissolved oxygen in fluids as $r_{1,ox} = 1.21\text{x}10^{-3}$ $s^{-1}kPa^{-1}$ [1], and $r_{1,dHb} = 1.46\text{x}10^{-2}$ $s^{-1}mM^{-1}$[2] for deoxy-haemoglobin. R_1 can then be expressed as a function of PO_2: $R_1(PO_2) = R_1(0) + r_{1,ox} \cdot PO_2 + r_{1,dHb} \cdot [dHb]$

A saturation recovery (SR) sequence, as described by [3], can therefore be described by the signal equation: $S(PO_2) = M_0(1 - e^{-T_d \cdot R_1(PO_2)})$ TOLD and BOLD data were collected for 11 subjects during two breathing paradigms using hyperoxia(100% O_2). The first was three 2 min intervals of normoxia interleaved with two 2 min intervals of hyperoxia ('repeated hyperoxia') and the second breathing paradigm was 2min normoxia, 7 min hyperoxia and 7 min normoxia ('prolonged hyperoxia'). TOLD was a dynamic saturation recovery gradient recalled sequence with a Td of 612 ms acquiring 8 slices with a spatial resolution of 3x3x6 mm^3 using flip angles/ TR/ TE = 30°/ 3.8 msec/ 2.1 msec and a SENSE factor of 2. Temporal resolution was 6s. BOLD data was acquired with a gradient echo EPI sequence with 32 slices of 4 mm thickness, resolution= 2.9x2.9 mm, temporal resolution=3.0s, flip angles= 90°, TE= 35 ms, and flip angle=90°. A high resolution structural scan for segmentation was obtained using a 3D T_1 weighted gradient echo sequence with TR=10 ms, TE = 5 ms, flip angle=8°, voxel size =1x1x1 mm and SENSE factor = 2.

Results: A significant TOLD signal increase was found in grey matter, white matter and CSF. TOLD imaging had a higher contrast to noise (higher z values on especially group level analysis), fewer artefacts and a rise to peak time approximately twice as long compared to BOLD. The magnitude of the TOLD response corresponds to a $\Delta P_{bt}O_2$ of 4.2 kPa during hyperoxia assuming literature values for baseline R_1 and CBV [4] [5]. This corresponds well with literature values of $\Delta P_{bt}O_2$ of 4.9 +/- 4 kPa in the cortex of patients with normal CBF [6].

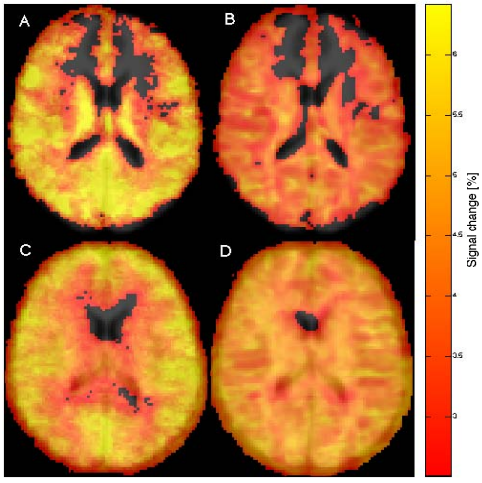

Figure 1. Average z-score maps from statistical analysis (FEAT from FSL software) of repeated hyperoxia. First level analysis used each subject's $P_{ET}O_2$ trace as a covariate The average z-score map across N subjects for BOLD data are shown in panel A, while the z-score corresponding to the group level are shown in B. Similarly, average subject-level and group level z-scores for TOLD are shown in panel C and D.

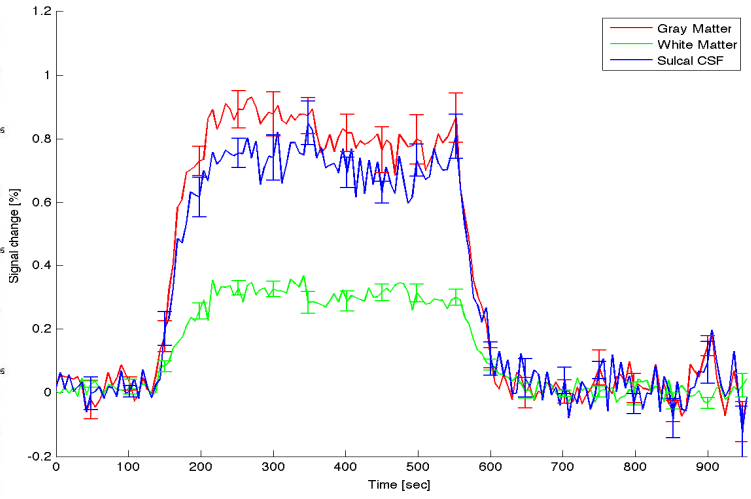

Figure 2. Signal increase from TOLD segmented into sulcal CSF, grey and white matter. Prolonged hyperoxic period was interval 120-600s

Discussion: TOLD detected changes in PO_2 in all brain tissues, was regionally and temporally unique from BOLD and had better contrast to noise. The magnitude of the TOLD signal response indicates an increase in extravascular tissue oxygenation. Calculated $\Delta P_{bt}O_2$ using baseline R_1 and CBV values gave results close to literature values.

Conclusion: This study provides evidence that T_1 and T_2*-weighted imaging during hyperoxic challenge offers unique complementary biomarkers of brain oxygenation. These findings may be useful in improved understanding of oxygen transport and allow whole brain PO_2 monitoring which may increase the efficiency of therapies and diagnostics in various neurologic diseases.

References [1] Pilkinton et al. 2012 *Magn Reson Med.* Jun.;67(6):1556–65.[2]Blockley et al. 2008 *Magn Reson Med* 60:1313–1320.[3] Larsson HBW et al. 2008 *J Magn Reson Imaging* Apr.;27(4):754–62. [4] Rostrup et al. 2005 *NeuroImage* Jan.1;24(1):1–11. [5] Rooney et al. *Magn Reson Med* 57:308–318. [6]Hlatky et al. *J Neurosurg.* 2008;108(1):53–8.