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 ($P_O_2$) are still lacking. The aim of this study is to detect changes in molecular oxygen concentrations in brain tissues using the relationship between $P_O_2$ 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 $r_{1,dHb} = 1.21 \times 10^{-3}$ s$^{-1}$kPa$^{-1}$ [1], and $r_{1,ox} = 1.46 \times 10^{-5}$ s$^{-1}$mM$^{-1}$[2] for deoxy-haemoglobin. $R_1$ can then be expressed as a function of $P_O_2$:

$$R_1(P_O_2) = R_1(0) + r_{1,ox} \cdot P_O_2 + r_{1,dHb} \cdot [dHb]$$

A saturation recovery (SR) sequence, as described by [3], can therefore be described by the signal equation:

$$S(P_O_2) = M_0 (1 - e^{-r_2 T_1(P_O_2)})$$

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 T1 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 $\Delta P_O_2$ of 4.2 kPa during hyperoxia assuming literature values for baseline $R_1$ and CBV [4] [5]. This corresponds well with literature values of $\Delta P_O_2$ of 4.9 +/- 4 kPa in the cortex of patients with normal CBF [6].

Discussion: TOLD detected changes in $P_O_2$ 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 $\Delta P_O_2$ 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 $P_O_2$ monitoring which may increase the efficiency of therapies and diagnostics in various neurologic diseases.