Validation of Oxygen Extraction Fraction Measurement by qBOLD Technique

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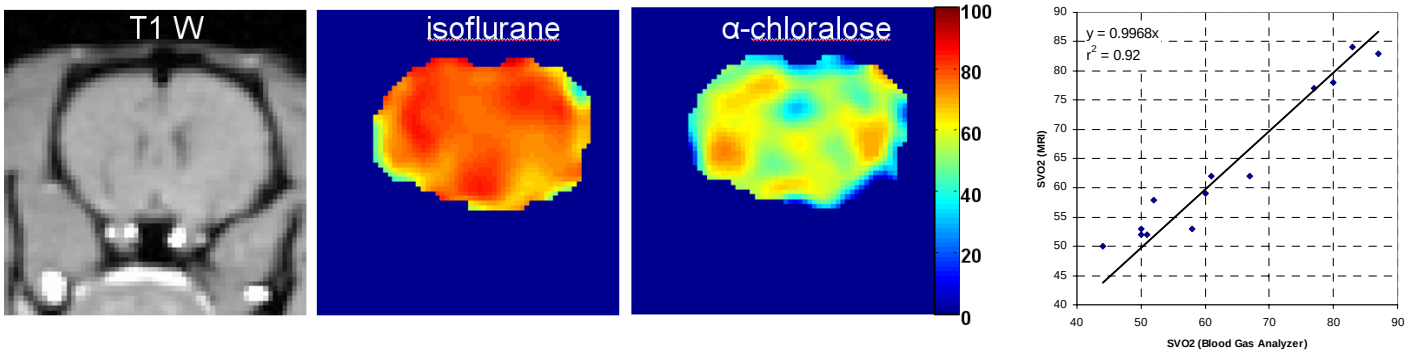
Introduction: Measurements of the brain tissue oxygen extraction fraction (OEF) in both baseline and functionally-activated states can provide important information on brain functioning in health and disease. The recently proposed quantitative BOLD (qBOLD) model [1] is based on a previously developed analytical BOLD model [2] and incorporates *prior* knowledge about the brain tissue composition including contributions from GM, WM, CSF and blood. In particular, the qBOLD approach allows separation of contributions to the BOLD signal from the OEF and the deoxygenated blood volume (DBV). The objective of this study is to validate OEF measurements provided by the qBOLD technique against direct OEF measurements in a rat model. Cerebral venous blood oxygen level of rat was manipulated by utilizing different anesthesia methods and different level of oxygen in inhaled air. The venous blood samples were drawn directly from the superior sagittal sinus. The averaged across the brain OEF results obtained from MRI-based qBOLD approach were compared with the venous blood oxygenation level measured with a blood gas analyzer. These results demonstrate a very good agreement between qBOLD and direct measurements.

Methods: All experiments were performed on 4.7 T Varian scanner using a birdcage transmit/receive RF coil. All surgical procedures were conducted under the guidelines of the Washington University Institutional Animal Care and Use Committee. Male Sprague-Dawley rats weighting 260-400 g were initially anesthetized with a ketamine/xylazine mixture. Rats were then intubated through tracheotomy and mechanically ventilated with 30% O2 balanced with either N2 or pure O2. A small incision was made along the interaural line on the top of the rat's head, and a 0.3 mm diameter burr-hole was drilled to expose the superior sagittal sinus. To manipulate the OEF values, two anesthesia methods were used. One method relies upon the injection of 40 mg/kg alpha chloralose 30 mins prior to the start of MR scanning followed by booster injections of 20 mg/kg every half hour using an i.p. line. Another method applies a continuous flow of 1.2% isoflurane into the breathing gas. Venous blood from superior sagittal sinus was sampled both before and immediately after the MR scan. Compared with the jugular venous oxygenation monitoring approach, this method eliminates contamination from extracranial sources [3, 4]. Blood oxygen saturation level was measured using an i-STAT Portable Clinical Analyzer.

A 3D gradient echo sampling of spin echo sequence (GESSE) was employed. Data acquisition was performed using the following acquisition parameters: FOV 36x36x18 mm^3, sampling matrix of 64x64x32, TR of 230 msec, NEX of 8. The spin echo occurs at the 11^{th} of 31 echoes (56 msec after excitation). All 3D MR data were filtered by a Hanning filter to improve SNR and to reduce the Fourier leakage.

The MR signal was then analyzed using the qBOLD model that includes signals from tissue, deoxygenated blood, and CSF [1]. In particular, the free induction decay of MR signal from the brain tissue was described in terms of the BOLD model [2] and the signal from the deoxygenated blood was modeled as originating from a network of randomly oriented cylindrical blood vessels [5].

Results: The figure below shows a representative T1 weighted image and maps of the estimated venous oxygen saturation level (color bar) from one slice in the same rat under isoflurane and alpha-chloralose anesthesia.



Isoflurane is known to slightly elevate cerebral blood flow (CBF) and significantly reduce brain metabolism [6]. Alpha-chloralose is known to suppress both CBF and metabolism [7]. Hence, we can expect that the venous blood oxygen level under isoflurane anesthesia should be much higher than in the alpha-chloralose case. This is consistent with the figure, which shows a fairly homogenous venous blood oxygen saturation level across the brain, with an estimated mean venous O_2 level of 77% under isoflurane anesthesia and 62% under alpha-chloralose anesthesia. Good correspondence is also seen with the venous blood oxygen saturation levels measured using the i-STAT analyzer (77% and 64%, respectively).

The plot on the right illustrates the results obtained from 13 experiments where the venous oxygen level was varied from 44% to 87% by manipulating the concentration of inhaled oxygen and the type of anesthesia.

Conclusion: Good agreement (R^2=0.92) was demonstrated between the MR qBOLD-derived and direct blood gas measured oxygen saturation levels in rat brain providing a direct validation of the qBOLD technique.

References: [**1**]. He and Yablonskiy, *MRM*, 2007. 57(11): p.115-126. [**2**]. Yablonskiy and Haacke, *MRM*, 1994. 32(6): p.749-763. [**3**]. Traystman and Rapela, *Circ. Res.*, 1975. 36(5): p.620-630. [**4**]. Raichle, *et al.*, *J. Appl Physiol*, 1976. 40(4): p.638-640. [**5**]. Sukstanskii and Yablonskiy, *JMR*, 2001. 151(1): p.107-117. [**6**]. Lenz, *et al.*, *Anesthesiology*, 1998. 89(6): p. 1480-1488. [**7**]. Nakao, *et al.*, *PNAS*, 2001. 98(13): p. 7593-7598.