Quantitative assessment of muscle oxygen saturation with BOLD MRI: validated by near-infrared spectroscopy (NIRS)

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Target audience: Clinicians and researchers interested in measuring physiologic parameters of skeletal muscle with MRI.

Purpose: To test the feasibility of a Monte Carlo model in estimating oxygen saturation (SHb) from calf-muscle BOLD MRI. Utilizing the paramagnetic property of deoxyhemoglobin, BOLD MRI provides a non-invasive way for estimating skeletal muscle oxygenation. Compared with more established tools such as near infrared spectroscopy (NIRS), not only is BOLD MRI similarly non-invasive, but it also is able to evaluate deep tissue and allows a combination of functional data with high-resolution anatomic images [1]. BOLD signals are usually analyzed by fitting to an exponential function to obtain transverse relaxation rate $R_2^*$. Higher $R_2^*$ values typically correspond to lower muscle tissue oxygenation. However, $R_2^*$ may be confounded by many factors that are not related to tissue pO2. For example, Lebon et al [2] found that $R_2^*$ values from calf muscle were strongly affected by the angle between the leg and magnetic field $B_0$. In this study, we take into account multiple confounding factors by simulating muscle BOLD with a realistic Monte Carlo model, and quantify blood oxygen saturation (SHb) from BOLD data based on the model.

Monte Carlo simulation: We developed Monte Carlo simulations for muscle BOLD signals using parameters (vascular fraction $v_v$, capillary hematocrit Hct, water diffusion coefficients $D_w$ and $D_{ev}$, and SHb) specific to the muscle. Similar to its application in the brain [3], the simulation was based on the physical relationships between the magnetic susceptibility difference ($\Delta B$) and the induced field inhomogeneities ($\Delta B_2$), for spheres (to simulate red blood cells) and cylinders (blood vessels):

$$\Delta B_2 = B_0 \frac{3}{2} \left( \frac{\rho}{r} \right) \left[ \cos^2(\theta) - 1 \right]$$

$$\Delta B_2 = B_0 \frac{3}{2} \left( \frac{\rho}{r} \right) \cos(2\phi) \sin^2(\theta)$$

where $r$ is the radius of a red blood cell, $r$ is the radius of a blood vessel, $\theta$ and $\phi$ are angles defining the position of the cell or vessel relative to $B_0$. Summing the field inhomogeneity from all of the blood vessels gives the $\Delta B$ map for the extravascular space of a voxel.

We then simulated the random diffusion of water protons within the voxel of inhomogeneous magnetic field, and recorded the signal decay produced by the dephasing effect of the protons. Exponential fitting of the signal vs. time curve resulted in $R_2^*$, the component of $R_2^*$ that is induced by the BOLD effect. Varying the SHb values within its typical range, we repeated the simulation, and thus obtain a look-up table between $R_2^*$ and SHb.

Experiment of cuff ischemia: One healthy subject (39 year old male; 73kg) was included. Two separate sessions, -4 weeks apart, were performed to evaluate the medial gastrocnemius muscle oxygenation, one with BOLD MRI and another with NIRS. During each session, the same cuff ischemia paradigm was utilized. A cuff was placed below the knee and inflated to 250 mmHg for 5 minutes, followed by release of the cuff. BOLD or NIRS was performed for 1 min prior to, 5 min during, and 2 min after cuffing. With a 3T scanner (Siemens Tim Trio), BOLD was performed using gradient multi-echo sequence and a 4 channel flexible coil around the calf with the following parameters: TR 53 ms, slice thickness 20 mm, 15 TE 2-37 ms, averages 1, flip angle 25, FOV 256x128 mm, matrix 128x64. In post processing, for BOLD images of the same acquisition (15 echoes) we fitted exponential function to the 15 signals of every voxel to obtain a $R_2^*$ map. Without measuring $R_2$ for this subject, we assumed calf-muscle $R_2$ as 25 s$^{-1}$ [4]. Based on the look-up table between SHb and $R_2^*$, we can get SHb value given $R_2^*$ value. For NIRS measurement, tissue oxygenation was monitored at 2 Hz with a NIRS oximeter (OxiplexTS oximeter, Champaign, Illinois) equipped with 8 infrared light sources (four emitting a 690 nm and four emitting at 830 nm) and one detection channel. This oximeter uses intensity modulated light beam and frequency-resolved spectroscopy thus providing absolute measurements of tissue hemoglobin SHb.

Results: Fig.1 shows SHb values estimated from BOLD and from NIRS, which correlate with each other significantly ($r = 0.911$).

Discussion: This preliminary study shows promising agreement between BOLD MRI and NIRS measurements of muscle hemoglobin saturation. The difference between our estimates and NIRS data (particularly in the release period) could be due to their measurement on different days, or the possible deviation of BOLD ROI from NIRS's targeted region, or the assumptions in our model.


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