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 pO_2. 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_a, capillary hematocrit Hct, water diffusion coefficients D_{iv} 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 ($\Delta\chi$) and the induced field inhomogeneities (ΔB_Z), for spheres (to simulate red blood cells) and cylinders (blood vessels):

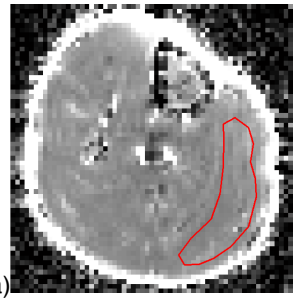
$$\Delta B_Z = B_0 \frac{\Delta\chi}{3}\left(\frac{r_c}{r}\right)^3 [3\cos^2(\theta)-1] \qquad \Delta B_Z = B_0 \frac{\Delta\chi}{2}\left(\frac{r_a}{r}\right)^2 \cos(2\varphi)\sin^2(\theta)$$

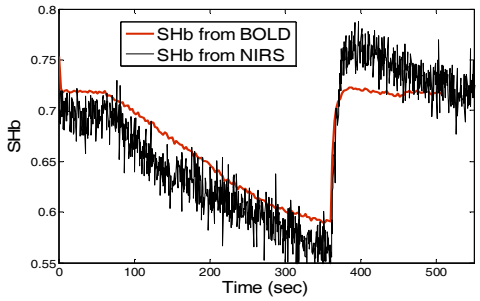
where r_c is the radius of a red blood cell, r_a is the radius of a blood vessel, θ and φ are angles defining the position of the cell or vessel relative to B_0. Summing the field inhomogeneity from all of the blood vessels gives the ΔB map for the extravascular space of a voxel. We then simulated the 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_{2P}, 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_{2P} 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_{2P}, we can get SHb value given R_{2P} 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).

Fig. 1. (a) Example of calf-muscle R_2* map (from acquisitions at baseline). Region of interest (ROI) was drawn at gastrocnemius medialis, the target of NIRS measurement. We averaged the R_2* values for the voxels within the ROI. (b) Using the proposed approach, the averaged R_2* values for all acquisitions were converted to SHb values (red line). SHb values measured with NIRS are shown as well (black noisy line).


(a)



(b)

Discussion: This preliminary study shows promising agreement between BOLD MR 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.

Reference: 1. Carlier et al NMR medicine 19:954-67. 2. Lebon et al ISMRM 1998 p1421. 3. 3. Martindale et al MRM 59:607-18. 4. Zuo et al ISMRM 2011 p3263