QUANTITATIVE TISSUE OXYGEN MEASUREMENT IN MULTIPLE ORGANS USING ^{19}F MRI

S. Liu[1], L. J. Wilmes[1], V. Kodibagkar[2], M. F. Wendland[1], N. Hylton[1], H. W. Hopf[3], R. P. Mason[2], and M. D. Rollins[4]

[1]Radiology, University of California, San Francisco, San Francisco, CA, United States, [2]Radiology, University of Texas at Southwestern, Dallas, Tx, United States, [3]Anesthesiology, University of Utah, Salt Lake City, UT, United States, [4]Anesthesia & Perioperative Care, University of California, San Francisco, San Francisco, CA, United States

Introduction: Ensuring adequate perfusion and oxygenation of vital organs is the primary goal in management of critically ill patients. Tissue hypoxia correlates with organ failure and poor prognosis in severe disease states. Frequently used clinical surrogates for tissue oxygenation include global measures such as blood pressure, heart rate, cardiac filling pressures, cardiac output, hemoglobin saturation, systemic blood gas measurement, and lactate levels. Unfortunately, these central measures give no specific information about the oxygen status of individual organs. Tissue oxygenation is complex and depends not only on perfusion and hemoglobin (Hb) carrying capacity, but also arterial oxygen tension as a driving force, hemoglobin dissociation conditions, mass transfer resistances, and local oxygen consumption. The ability to measure organ tissue oxygen levels directly and accurately would help guide medical care by providing endpoints to titrate therapies and evaluate interventions in a variety of areas including resuscitation drugs and strategies, and cancer therapeutics. A quantitative method using fluorine-based MRI allows regional dynamic changes to be measured from sequential images of tissue oxygen, and has been previously used in oncologic research (1-2). ^{19}F MRI is minimally invasive, directly measures tissue partial pressure of oxygen (pO_2) and has been validated by comparison to electrode measurements. This ^{19}F MRI method uses the linear relationship between longitudinal relaxation rate (R_1) of fluorine compounds, in this case hexafluorobenzene (HFB), and tissue pO_2. The R_1 of HFB has minimal temperature dependence, and is not significantly influenced by pH or CO_2 The goal of our study was to evaluate the feasibility of the ^{19}F MRI method for organ measurement and examine the influence of hyperoxia on individual organs by quantitatively measuring the pO_2 in brain, kidney, liver, gut, muscle and skin during the inhalation of room air and 100% oxygen.

Methods: A male Sprague-Dawley rat was anesthetized with isoflurane and ventilated via a tracheostomy. An invasive arterial line was used for blood pressure monitoring and arterial blood gas sampling to confirm arterial oxygen concentrations and ensure eucapnia. Rats were kept euthermic. HFB (50-75 µl) was injected into each organ of interest using a 33 ga. needle. The initial inspired gas was room air. After a 30-minute equilibration time a 0.2 ml sample of arterial blood was taken for pO_2 and hemoglobin analysis. A Varian 7T small animal imaging system with a ^{19}F/^{1}H dually tunable birdcage volume coil was used. Abdominal images were acquired with respiratory gating. Data was acquired using the fluorocarbon relaxometry echo planar imaging for dynamic oxygen mapping (FREDOM) sequence. This combines pulse burst saturation recovery (PBSR) and echo planar imaging (EPI) to acquire longitudinal relaxation time (T_1=1/R_1) weighted ^{19}F images. The alternated relaxation delays with variable acquisitions (ARDVARC) scheme was used to acquire 14 delays in the order: 90 s, 200 ms, 60 s, 400 ms, 40 s, 600 ms, 20 s, 800 ms, 16 s, 1 s, 8 s, 1.5 s, 4 s, and 2 s, which were optimized to reduce clearance effects. The corresponding number of averages was set to 1 for all delays. T_1 was calculated voxel by voxel with a three-parameter fit. Voxels were 1x 1x 5 mm. in FREDOM images. A linear calibration curve of pO_2 vs. R_1 was previously determined using 1 ml HFB in water equilibrated with six premixed gases of O_2/N_2 ranging from 0% to 100% oxygen. Equilibrium and imaging of the calibration samples was done at 37°C. Following the initial organ scans, the inspired gas was changed to 100% oxygen, and the above procedure repeated. Spin echo multiple slices proton images of the corresponding organs were also acquired as a reference. These images and comparative results are displayed in Figure 1 and 2 below.

Results:

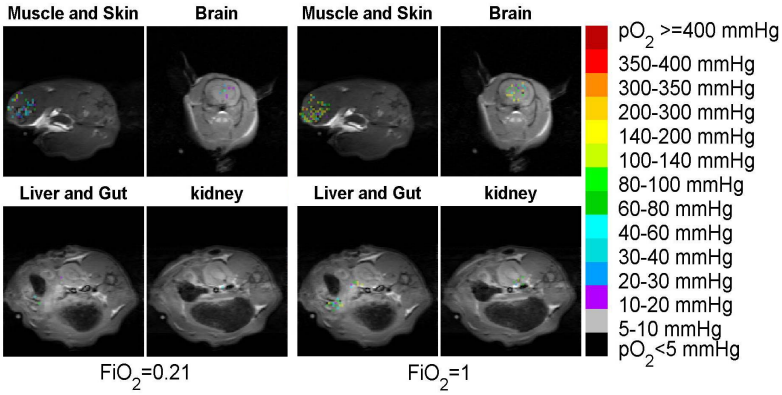

Figure 1. PO_2 mapping superimposed on the SEMS proton images on room air (FiO_2=0.21) on the left, and 100% oxygen (FiO_2=1.0) on the right.

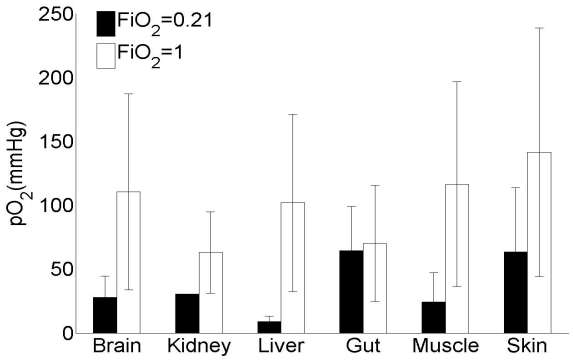

Figure 2. Mean values of pO_2 over the selected ROI ± standard deviation among voxels at FiO_2=0.21 and 1.0.

Discussion: Quantitative values of pO_2 in six different organs were successfully obtained using ^{19}F MRI. The pO_2 in all organs studied increased after changing from ventilation with room air to 100% oxygen. The marked variability and different absolute increases in the organ tissue pO_2 show the diversities of oxygenation in various organs and the potential benefit of regional vs. global measurements. This minimally invasive imaging technique has the potential to improve our understanding and optimize the effects of various resuscitation drugs and fluids used to stabilize critically ill patients, as well as guiding cancer therapeutics. Future experiments are underway to statistically quantify the organ differences using this model.

Acknowledgement: Funding for this research was provided by The Foundation for Anesthesia Education and Research.

References: 1 Mason RP, et al., (1996) *NMR Biomed*, 9(3): 125-34. **2** Zhao D, et al., (2004) *Methods Enzymol*, 386:378-418.