Detection of Pulmonary Ischemia using the Oxygen Sensitivity of Hyperpolarized Helium MRI in a Rodent Model of Pulmonary Embolism

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Introduction: The time course of the partial pressure of oxygen during a breath hold can be characterized by monitoring the longitudinal relaxation time of hyperpolarized helium (HP-^{3}He). This technique has been shown to be sensitive to pulmonary ischemia in humans and in varying animal models of pulmonary embolism. The utility of this methodology in detecting ischemia in rodent models of pulmonary embolism has not been previously established. In this work, we demonstrate the sensitivity of this technique in monitoring pulmonary ischemia in a novel rodent model of pulmonary embolism.

Methods: Twelve Sprague Dawley rats were anesthetized with isoflurane and given tracheotomies. We separated animals into control (n=6) and experimental (n=6) groups. Animals in the experimental group were transported to an angiosurgical suite (Philips Allura FD20) that was adjacent to the MRI suite. Under fluoroscopic guidance, a microcatheter was advanced over the wire via a transjugular approach to the selected pulmonary artery branch. We embolized the branch with a mixture of n-butyl-2-cyanoacrylate and Lipiodol (Codman Neurovascular). Perfusion deficit was confirmed with both radiographic visualization of the embolic material and Digital Subtraction Angiography (DSA)(Fig. 1). Once the pulmonary artery branch was embolized, we transferred animals to a 3.0T MRI (Philips Acheiva). Animals in the control group were transferred to the MRI without further surgical intervention.

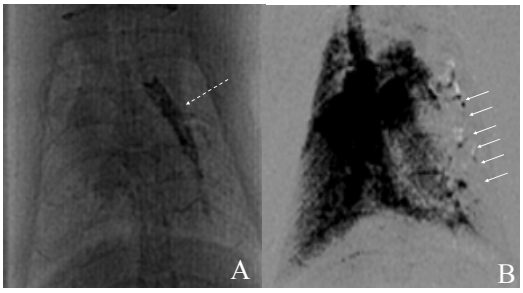

Figure 1. Radiographs visualizing the results of the pulmonary embolic surgery. (A) A radiograph of an experimental animal post pulmonary embolism placement. The dashed arrow points to the embolic material situated in a division of the left pulmonary artery. (B) Visualization by DSA of the opacification of the lung during iodinated contrast bolus transit. The solid arrows indicate areas of low perfusion as determined by minimal opacification.

We performed MRI imaging using a custom-made single-turn solenoid coil tunable to both ^{1}H and ^{3}He. Twelve hours prior to imaging, we polarized helium to 10–20% on a custom-made spin-exchange optical-pumping helium polarizer. Following proton localizer scans, animals were administered a volume of 6ml HP-^{3}He and 2ml of O_2. Then we imposed a 24-second breath hold on the animals, during which we measured the signal decay of the helium gas and serial images were acquired. The imaging sequence consisted of two consecutive images acquired with no delay, to allow for RF power calibration, followed by an image every 2 seconds. Details of the imaging sequence were as follows: FOV = 50 mm, TR=4 ms, TE=980 μs, FA =~10°, MTX = 64x32 (zero-filled to 64x64), and slice thickness = ∞ (i.e., projection image). We calculated the initial partial pressure of oxygen (p_o), the rate of oxygen uptake (R), and the excitation flip angle (α) using the analysis of Fisher et al., based on the HP-^{3}He signal decay[1]. The values of p_o and R were extracted for ROIs selected in areas of ischemia as indicated by DSA, as well as in the contralateral side.

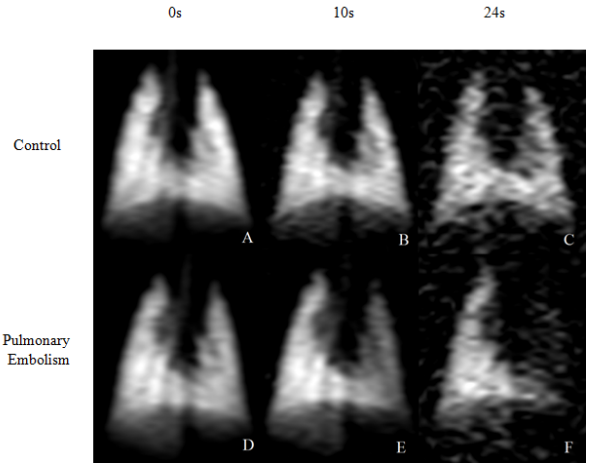

Figure 2. Representative images of the decay of the HP-He signal in the lungs in normal (A-C) and embolized (D-F) animals 0 (A,D), 10 (B,E) and 24 (C,F) seconds after helium administration.

Results: Figure 1 shows an example of a successful occlusion of a branch of the pulmonary artery as visualized by radiography and digital substraction angiography. HP-^{3}He MRI reveals uniform signal distribution in both groups early during the breath-hold with a faster decay of the helium signal in the embolized lung of the experimental animal. In control animals, left lung values for p_o and R were 162.13 ± 33.28 mbar and 6.40 ± 1.05 mbar/s, respectively, and right lung values were 167.55 ± 43.35 mbar and 6.35 ± 1.00 mbar/s, respectively. In the experimental animals, the values of p_o and R in the ischemic lung were 244.85 ± 19.28 mbar and .017 ± 0.40 mbar/s, respectively. In the contralateral normal lung, results show values for p_o and R of 149.10 ± 15.54 mbar and 4.42 ± 1.07mbar/s, respectively. Statistical analysis revealed significantly different values of p_o between the ischemic lung and the contralateral normal side, as well as between the ischemic lung and both sides of the control lungs. Statistical analysis of R reveals there were statistically different values between the ischemic lung and both the contralateral lung in the experimental animals as well as between the contralateral lung and both control lungs. We found no statistically significant differences in excitation flip angle between groups.

Discussion: In this study, we showed that pulmonary embolism in rats is detectable using the oxygen sensitivity of HP-^{3}He through the monitoring of HP-^{3}He signal decay. Further, we showed that both the p_o and R show large changes in areas of ischemia versus the contralateral side. These finding can be useful in understanding the effects of pulmonary ischemia on lung function in rodents, and may eventually be used to assess the effect of treatment on the recovery of lung function.

References: [1]**Fischer et al. MRM 2004 52(4):766–73.**