Pulmonary Blood Volume Mapping using a Modified T_1 Weighted, Steady State MRI Technique in a Rodent Model of Hypoxic Pulmonary Vasoconstriction

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Introduction: Microcapillary pulmonary blood volume (PBV) is a sensitive measurement of pulmonary vascular physiology. Whereas nuclear medicine based exams offer spatially localized measurements of pulmonary blood volume, MRI may have the ability to measure PBV without the use of ionizing radiation. In steady state MRI based blood volume measurement techniques, the change in the relaxation properties of tissue is characterized before and after injection of an intravascular contrast agent. Typically, a T_1 weighted inversion recovery or spoiled gradient echo imaging sequence is used for the measurement[1]. In this study, we modified the standard steady state blood volume inversion recovery measurement to include a spin echo readout to optimize the signal from the lung parenchyma for the measurement of PBV. We further implemented cardiac and respiratory gating to allow for image acquisition at similar points during the cardiac and respiratory cycle. We applied the technique to a rodent model of hypoxic pulmonary vasoconstriction (HPV).

Methods: Ten Sprague Dawley rats were injected IP with 5uL/g B.W. of a mixture of 100mg/ml Ketamine and 20mg/ml Xylazine. Animals were transferred to a 3.0T Philips Acheiva Clinical MR scanner for imaging. Physiological monitoring was conducted using an MR-compatible small animal monitoring device (SAI, Stonybrook, NY). Animals were exposed to breathing gas of either F_iO_2 = 60% O_2 (n=5) or 14% O_2 (n=5) during imaging.

Animals were placed in the center of a single turn solenoid RF coil tuned to the ^{1}H frequency. A solution of 20% Magnevist was placed next to the animal as a signal standard. For measurement of blood volume, an inversion recovery, spin echo sequence was used with the following parameters: TI = 100, 200, or 300ms, TR = 6s, TE= 4.95ms, NSA =2, matrix Size = 128x64, slice thickness = 3mm, and Field of View = 50mm. Images were interpolated to a matrix size of 128x128. In order to minimize physiological imaging artifacts, a simultaneous cardiac and respiratory gating scheme was implemented. To achieve image read out during mid cardiac cycle and end expiration, a trigger was administered to the scanner at a time equal to TI before image readout using the most recent measurement of the heart and respiratory rate. Images were acquired prior to and following the injection of an intravascular contrast agent, gadolinium-labeled protected graft copolymer (PGC-Gd)[2] at a dose of 30umole Gd/kg. The PBV was calculated as $(S_{lung,pre} - S_{lung,post})/(S_{blood,pre} - S_{blood,post})$ where $S_{lung, pre}$ and $S_{lung, post}$ are the signal intensities of the lung parenchyma prior to and following PGC-Gd injection, respectively and $S_{lung, pre}$ and $S_{lung, post}$ are the signal intensities of the blood prior to and following PGC-Gd injection, respectively[1]. This equation is valid assuming fast exchange of water between the intravascular and extravascular spaces[1].

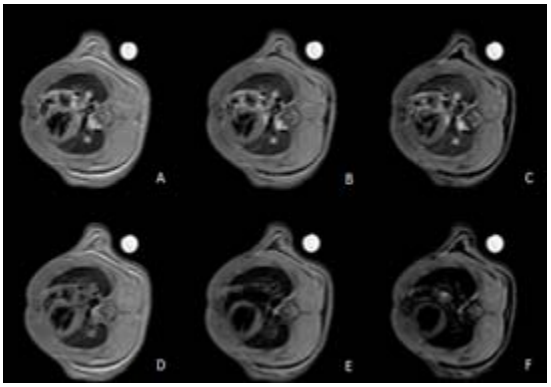

Figure 1. Images of rat lung parenchyma at TI=100ms (A, D), 200ms (B, E) and 300ms (C, F) at pre (A-C) and post (D-F) PGC-Gd administration in an animal breathing 60% O_2

Results: All animals tolerated anesthesia and hypoxia without adverse events. Figure 1 shows typical images of an animal breathing 60% O_2 before and after contrast injection at different inversion times. Lung parenchyma was clearly visible in these images and motion artifacts were minimized. Figure 2 shows the result of subtraction of images acquired prior to and following PGC-Gd injection using TI=300ms. In this example, high signal difference is evident in the lungs due to PGC-Gd injection. The average PBV as a function of hypoxia and inversion time is given in Table 1. Analysis of PBV revealed a statistically significant reduction with hypoxia and increase with inversion time ($p < .05$).

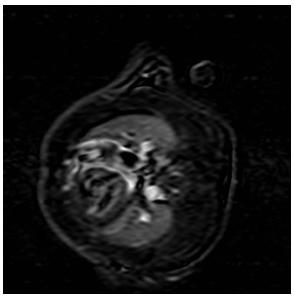
Figure 2. Subtraction of images acquired at TI=300ms prior to and following PGC-Gd injection. High signal difference in the lung parenchyma is clearly visible.

	Pulmonary Blood Volume		
F_iO_2	TI=100ms	TI=200ms	TI=300ms
14%	.08±.12	.16±.07	.27±.09
60%	.28±.08	.33±.08	.38±.07

Table 1 Effect of inversion time and inspired O_2 on PBV. Data is expressed as ml of blood/ml of tissue.

Discussion: In this report, we present results that show the feasibility of measuring PBV using a T_1 weighted, inversion recovery sequence with cardiac and respiratory gating and a spin echo readout. Our results show that PBV as indicated by our measurement is restricted as a response to alveolar hypoxia. The result of reduced PBV during alveolar hypoxia in the animal experiments confirms the results of other investigations of PBV during hypoxia[3]. Due to water exchange, increased TI times result in an overestimation of the PBV. In counter balance to this, the precision of the measurement is reduced with shorter inversion times due to a smaller SNR of the difference images. The data presented here reflects the suggested trend. In conclusion, we have demonstrated the sensitivity of a steady T_1 weighted PBV measurement in the lungs to changes in pulmonary vascular physiology. The measurement of PBV using this technique may have utility in investigations of lung vascular physiology and disease.

References: [1]Donahue et al. MRM 1996 36: 858-867 [2]Bogdanov et al. Radiology 1992187: 701-706, [3]Mistry et al. MRM 2010 63: 728-735