Imaging Pulmonary Gas Exchange Using Hyperpolarized ^{129}Xe

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Introduction: We present a method for imaging pulmonary gas exchange enabled by differentially imaging ^{129}Xe that is taken up in lung tissue versus capillary blood. The ^{129}Xe-blood image is sensitive to micron scale changes in the thickness of the blood gas barrier which will delay the appearance of the characteristic 211ppm blood resonance. We both validate and demonstrate the utility of the method by showing that ^{129}Xe uptake in blood is impaired in rats with unilateral fibrosis. Blood/tissue separation was achieved by using a 1-point variant of the Dixon technique [1] in combination with projection encoding.

Methods: Fischer 344 rats (Charles River, Raleigh, NC) weighing 170-200g were instilled with 2.5units/kg bleomycin (Mayne Pharma, Paramus, NJ) or saline sham in either the left or right lung in accordance with a Duke approved IACUC protocol. Animals were prepared for imaging 7-15 days post bleomycin instillation using ketamine/diazepam injection, peroral intubation and ventilation on a hyperpolarized gas compatible constant volume ventilator at 60 bpm with 2 ml tidal volume [2]. Hyperpolarized ^{129}Xe, enriched to 83% (Spectra Gases, Alpha, NJ) was produced in batches of 0.5 liter at 8% polarization using a prototype commercial polarizer (model 9800, MITI, Durham, NC). ^{129}Xe imaging used a 23.639MHz linear bird cage coil (L=8cm, ϕ=7cm) in a 2.0T, horizontal, 15cm clear bore magnet (Oxford Instruments, Oxford, UK) with shielded gradients (18G/cm), controlled by a GE Excite console (GE Healthcare, Milwaukee, WI). Ventilation images were acquired at 128×128 matrix, 4cm FOV, no slice, 8kHz bandwidth, filling k-space with 400 radial projections, 10 views per breath, TR=20ms and a variable flip angle with a final flip of 90°. Dissolved phase images were acquired using a 64×64 matrix, 8cm FOV, no slice selection, 15kHz bandwidth, 2400 radial trajectories without respiratory gating. The dissolved resonances were selectively excited (without gas-phase contamination) using a 90°, 1.2ms sinc pulse centered on the 211ppm line. Using a TR of 50ms with 90° flip, the dissolved images effectively probe a diffusion length scale of $z \leq 2\sqrt{D} \approx 15\mu$m. To separate the 197ppm "tissue" image and the 211ppm blood image we employed a 1-point variant of the Dixon technique for fat-water imaging. The frequency difference of the dissolved resonances creates a phase difference that is linear in echo time. By setting our "echo time" for a 90° phase difference, and creating phase-sensitive images, ^{129}Xe in blood and tissue could be separated. The echo time is calculated according to $TE = 1/4\Delta f$, where Δf=330Hz is the blood/tissue frequency difference.

Results and Discussion: Figure 1 shows images of ^{129}Xe ventilation, tissue uptake and blood uptake in a healthy rat and a rat with left lung fibrosis. Most notable, is the absence of ^{129}Xe blood uptake in the fibrotic lung (F), whereas tissue uptake perfectly matches the ventilation pattern. Absence of blood uptake on the 50ms time-scale we are probing is consistent with thickening of the blood gas membrane beyond its healthy thickness of 1µm to greater than 15µm (assuming $D=1\times10^{5}$cm^{2}s^{-1}), a scale estimate qualitatively confirmed by histology using H&E and Masson's Trichrome staining. Reduced ^{129}Xe blood uptake was observed in all 7 injured animals studied. Dynamic, whole-lung spectroscopy [3] did not reveal any delay in blood signal, but did yield an overall reduction in the ratio of blood to tissue signal.

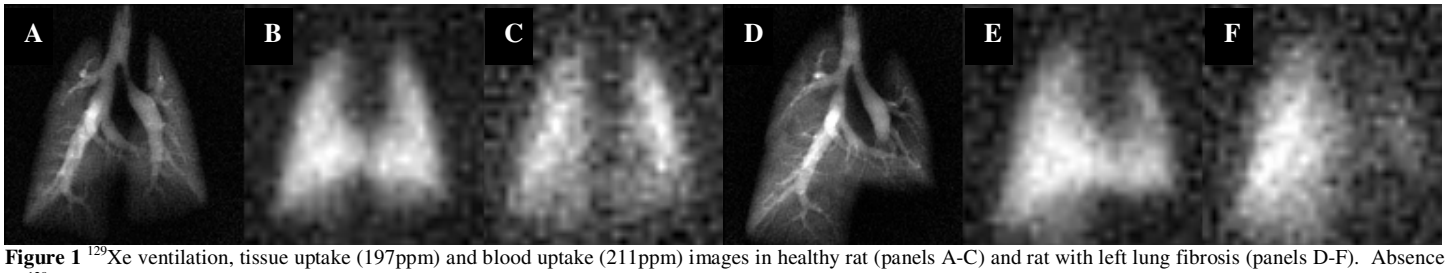

Figure 1 ^{129}Xe ventilation, tissue uptake (197ppm) and blood uptake (211ppm) images in healthy rat (panels A-C) and rat with left lung fibrosis (panels D-F). Absence of ^{129}Xe blood uptake in the fibrotic lung is evidence of thickening of the blood gas barrier beyond 15µm.

Conclusions: We have presented several novel results for ^{129}Xe imaging. First, is the ability to image ^{129}Xe dissolved in lung despite very short T_2* (1.72ms). Most importantly, by separating the ^{129}Xe image into tissue and blood components we enable imaging of alveolar-capillary gas exchange, the most fundamental role of the lung. Several improvements can be considered. First, larger volumes of gas and higher polarization levels will enable 3-D imaging. Second, phase distortions currently evident in the blood/tissue images can potentially be corrected using a phase map created from the ^{129}Xe ventilation image. Third, the much lower diffusion coefficient for the dissolved resonances may enable more efficient sequences such as RARE to be used.

References

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