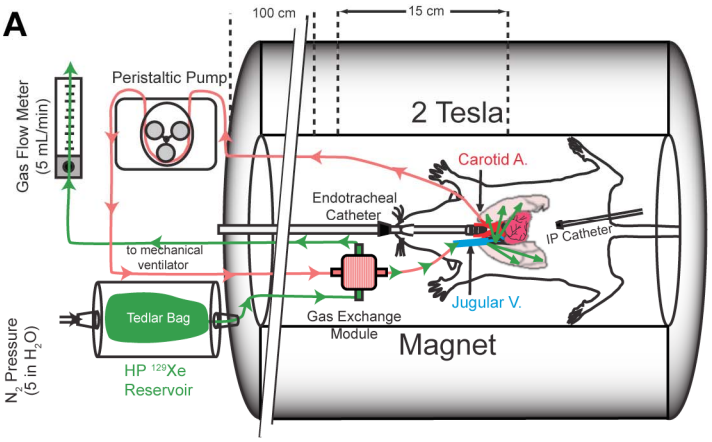
3D Imaging of Pulmonary Ventilation and Perfusion in Rats using Hyperpolarized 129Xe

Z. I. Cleveland[1], H. E. Moller[1,2], L. W. Hedlund[1], J. Nouls[1], M. Freeman[1,3], Y. Qi[1], and B. Driehuys[1]
[1]Center for In Vivo Microscopy, Duke University Medical Center, Durham, NC, United States, [2]Max Planck Institute for Human Cognitive and Brain Sciences, Leipzig, Germany, [3]Graduate Program in Medical Physics, Duke University, Durham, United States

Introduction: Proper matching of ventilation (V) and pulmonary perfusion (Q) is essential for efficient gas exchange. Moreover, mismatches between V and Q and spatial heterogeneity in the V/Q ratio are hallmarks of virtually all pulmonary diseases. Unfortunately, currently available methods of imaging V and Q in small animals: 1) lack 3D resolution, which is needed to measure V/Q heterogeneity; 2) employ multiple modalities or contrast agents, which complicates data quantification; or 3) require hour-long image acquisitions, which prevent monitoring acute changes in V/Q. Potentially, these problems can be avoided using hyperpolarized (HP) ^{129}Xe, which can generate lung images that reflect either ventilation or perfusion if delivered via the vasculature [1]. To exploit these unique properties, we previously introduced a method of continuously infusing ^{129}Xe to the blood using an extracorporeal (EC) circuit [2]. Here we demonstrate that EC infusion can be used to generate 3D images of pulmonary perfusion.

Methods: 5 male Sprague Dawley rats (290-420 g; Charles River, Wilmington, MA) were prepared according to a protocol approved by our IACUC. Animals were anesthetized with IP injections of pentobarbital/butorphanol, heparinized, and ventilated on a HP-gas compatible, constant-volume ventilator [3]. Vital signs were monitored by a MR-compatible, small-animal pulse oximeter (MouseOx, STARR Life Sciences, Oakmont, PA). Perfusion images were acquired by infusing HP ^{129}Xe into blood using an EC circuit (Fig. 1A), in which blood was drawn from the left carotid artery, passed through a gas-exchange module (MicroModule, Membrana, Charlotte, NC), where it was saturated with ^{129}Xe [4], and returned to the right jugular vein. Isotopically enriched Xe (83% ^{129}Xe; Spectra Gases, Alpha, NJ) was hyperpolarized to P≈10% and cryogenically accumulated in 300 mL batches using a prototype commercial polarizer (model 9800, MITI, Durham, NC).^{129}Xe imaging used a 23.6-MHz quadrature birdcage coil in a horizontal, 2-T, 30-cm clear-bore magnet (Oxford Instruments, Oxford, UK) operated with a GE EXCITE console (GE Healthcare, Milwaukee, WI). HP ^{129}Xe ventilation images were acquired using a variable flip angle 3D radial sequence (40 views/breath, views=6435, BW=15.6 kHz, TR/TE=10/0.8 ms, FOV=64 mm, matrix=64×64×32). Infusion images were acquired with a constant flip angle radial sequence (4 views/breath, views=2801, BW=8.0 kHz, TR/TE=180/0.8 ms, FOV=64 mm, matrix=32×32×32, α=30°).



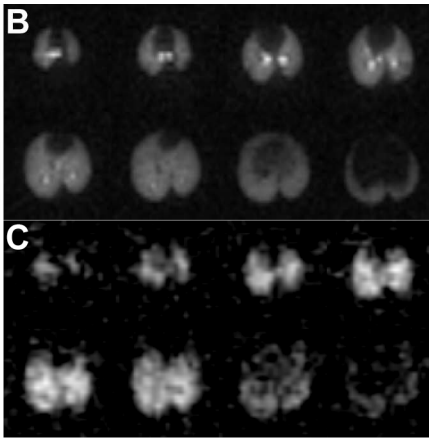


Fig. 1: A Schematic of HP ^{129}Xe EC infusion using a gas-exchange module. **B** Representative sections from a 3D, axial ventilation image. **C** Corresponding perfusion image acquired from gas-phase ^{129}Xe that had been delivered to the blood by EC infusion and that then diffused into the alveolar airspaces from the capillary bed. The images in B and C were obtained from the same supine rat.

Results and Discussion: HP ^{129}Xe perfusion images can be acquired with spatial resolution (2×2×2 mm^3) comparable to that achieved in small animals with conventional modalities such as SPECT [5] and PET [6]. However, HP ^{129}Xe images of perfusion can be acquired within 12 min, representing a five-fold advantage in temporal resolution over nuclear imaging. Moreover, ^{129}Xe magnetization can be completely destroyed with RF, enabling repeated scanning. In comparison, the contrast agents used to assess perfusion in nuclear imaging require days of clearance time between scans. Finally, 3D HP ^{129}Xe ventilation images can be acquired with 1×1×2 mm^3 resolution within 3 min. Thus, HP ^{129}Xe MRI allows the rapid assessment the V/Q distribution with a single contrast agent and may be useful in studying small animal models of acute lung diseases.

Conclusions: 3D pulmonary perfusion imaging in rats by EC infusion of HP ^{129}Xe is feasible. When coupled with 3D ventilation imaging, EC infusion will be sensitive to early pathological changes in ventilation, perfusion, and the V/Q ratio.

References: [1] B Driehuys et al. *Radiology* **2009** *252*, 386-393. [2] HE Möller, et al. *Proc. 17th Annual ISMRM* **2009** [3] J Nouls et al. **2010**, submitted [4] ZI Cleveland, et al. *J Phys Chem B* **2009** *113*, 12489-12499. [5] C Wietholt, et al. *Proc. SPIE* **2003** [6] T Richter, et al. *J Appl Physiol* **2010**, 108, 422-429.
Acknowledgements: Center for In Vivo Microscopy (NIH/NCRR P41 RR005959)