MR Imaging of Pulmonary Perfusion and Gas Exchange by Intravenous Injection of Hyperpolarized ^{129}Xe

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Introduction: We present a new method to image pulmonary perfusion and gas exchange by intravenous injection of hyperpolarized (HP) ^{129}Xe dissolved in saline. Xenon is only moderately soluble in saline (~10%) and thus, upon passing through the pulmonary capillaries, is mostly released into the alveolar airspaces. Gaseous ^{129}Xe in the airspaces has a frequency ~200ppm lower than ^{129}Xe in blood or tissue, making it possible to image selectively. The resulting image reflects the product of perfusion and gas exchange across the blood-gas barrier. The method should be exquisitely sensitive to pulmonary pathology and consumes only a few ml of ^{129}Xe.

Methods: Five Fischer 344 rats (Charles River, Raleigh, NC) weighing 330-425g were prepared for imaging according to a Duke approved IACUC protocol. Animals were anesthetized using ketamine/diazepam injection, perorally intubated, and ventilated on a HP-gas compatible constant-volume ventilator at 60 breaths/min with 2.7ml tidal volume (1). Hyperpolarized ^{129}Xe, enriched to 83% (Spectra Gases, Alpha, NJ) was produced in batches of 120ml at P≈12% for perfusion imaging and 500 ml at P≈8% for ventilation imaging using a prototype commercial polarizer (model 9800, MITI, Durham, NC). ^{129}Xe imaging used a 23.6MHz linear birdcage coil (L=8cm, ϕ=7cm) in a 2T, horizontal, 15cm clear-bore magnet (Oxford Instruments, Oxford, UK) with 180mT/m shielded gradients and GE EXCITE console (GE Healthcare, Milwaukee, WI). For ventilation imaging HP ^{129}Xe and O_2 were delivered at a ratio of 75:25, and images were acquired using 400 radial projections (10 views/breath) without slice selection and a variable flip angle with a final flip of 90° (*TR* 20ms, bandwith 8kHz, matrix 128×128, FOV 4cm). For perfusion/gas-exchange imaging, HP ^{129}Xe was dissolved in 30-40ml of half-concentrated saline and shaken vigorously by hand for 20s (2). Then, 5ml of saturated saline was withdrawn and injected over a period of 15s into the rat's tail vein (Fig. 1A) while its respiration was suspended. Images of ^{129}Xe released into the alveolar airspaces were acquired over a 16s period starting 5s after injection, using a gradient-echo sequence (α 30°, *TR*= 250ms, bandwidth=4kHz, matrix=64×64, FOV=7.5cm, no slice). Alternatively, spectra were acquired, without post-injection delay, for 30s (α=10-60°, *TR*=125-250ms) to study the dynamics of the three ^{129}Xe resonances (0, 197, and 211ppm) in the thorax.

Results and Discussion: The rats tolerated the saline/Xe injections, allowing as many as 6 separate 5ml injections to be made in a 9-min period without obvious adverse effects. T_1 of ^{129}Xe in the shaker with saline was ~12min, allowing us to re-mix ^{129}Xe many times and signal average images over multiple injections. Figure 1B shows the signal evolution of ^{129}Xe in RBC, saline/plasma, and airspace compartments of the lung after injection. Figure 1C shows a ventilation image of the rat with 0.3×0.3mm^2 resolution. Figure 1D shows a perfusion/gas-exchange image obtained in the same rat by averaging 1.2×1.2mm^2 gas-phase images acquired from 3 injections.

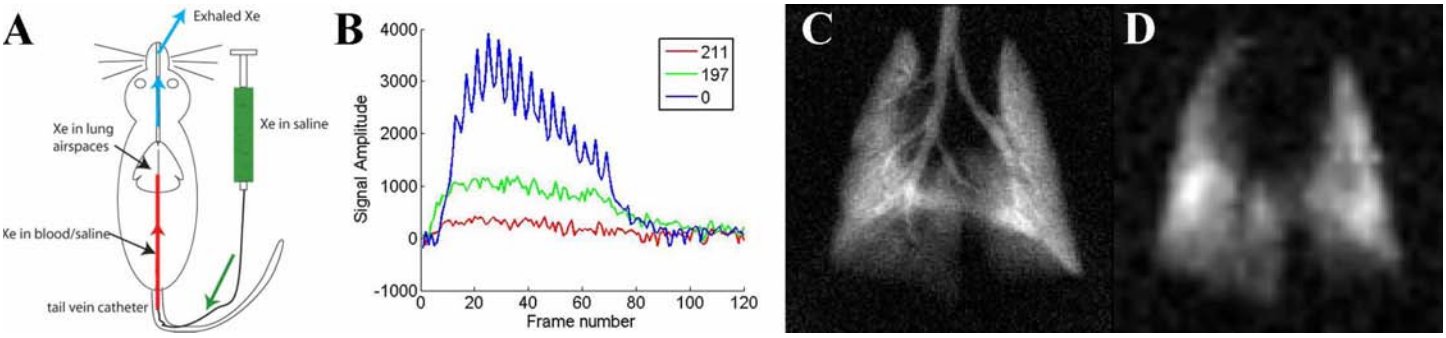

Figure 1 A. Schematic of tail-vein injection of hyperpolarized ^{129}Xe in saline. **B.** Plot showing the arrival of signal at 0, 197, and 211ppm frequencies in the thorax corresponding to ^{129}Xe in airspace, saline/plasma, and red blood cells. **C.** ^{129}Xe ventilation image of a rat **D.** ^{129}Xe perfusion image in the same rat acquired by imaging the gas phase ^{129}Xe released from the capillaries through gas exchange.

Conclusions: This method of imaging perfusion and gas exchange using injectable ^{129}Xe has several important advantages compared to most perfusion-imaging methods. By selectively imaging gas-phase ^{129}Xe, we detect only those atoms that have traversed the smallest capillary beds and crossed the blood-gas barrier. We thus image the end-result of pulmonary perfusion and gas exchange rather than an intermediate parameter. Gas-phase ^{129}Xe has a much longer T_2* (~20ms) than dissolved ^{129}Xe in lung (~2ms) or lung protons, allowing lower bandwidth to be used, resulting in higher SNR. Because the ^{129}Xe signal decays quickly, or can be deliberately destroyed by RF, injection can be repeated many times for signal averaging or repeat imaging. Since Xe is cleared through exhalation, continuous ^{129}Xe infusion could be implemented to generate high-resolution 3D perfusion maps or repeat scans. Adaptation of the Kety-Schmidt theory allows quantitative perfusion information to be determined.

References: 1. Chen BT, et al., Magn Reson Med 2003;49(1):78-88. 2. Moller HE, et al., Magn Reson Med 1999;41(5):1058-1064.

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