Imaging Impaired Gas Uptake in a Rat Model of Pulmonary Fibrosis with 3D Hyperpolarized 129Xe MRI

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Target Audience: Hyperpolarized Gas MRI, Preclinical imaging, Lung Imaging

Purpose: Imaging impaired gas uptake is challenging, because the distribution of CO_2 and O_2 in the lungs cannot be detected directly. However, hyperpolarized (HP) ^{129}Xe can serve as a surrogate for these metabolically active gases, because it is moderately soluble in tissues and possesses a large chemical shift range, allowing alveolar ^{129}Xe to be detected separately from ^{129}Xe dissolved in red blood cells (RBCs) or pulmonary barrier tissues (capillary plasma and interstitium)[1-3]. Further, because ^{129}Xe diffuses across the same barrier tissues as CO_2 and O_2, barrier thickening (e.g., due to interstitial lung disease), will delay ^{129}Xe transit and reduce the RBC-specific MR signal. Previously, these properties were exploited to generate 2D MR images depicting regions where gas exchange is impaired in rats with Bleomycin-induced pulmonary fibrosis[4]. Here we demonstrate that this approach can be extended to 3 dimensions, and that the resulting 3D images can be used to quantify regional gas-exchange impairment.

Methods: Fisher rats (treatment group: n=6, vehicle control: n=3, untreated control n=3) were prepared following IACUC-approved procedures. Treated and vehicle control animals were imaged 25±2 days after unilateral instillation of Bleomycin[5] (3 U/kg) or saline, respectively. HP ^{129}Xe was cryogenically accumulated using a prototype polarizer (MITI, Durham, NC). 3D MRI of gaseous ^{129}Xe and ^{129}Xe dissolved in barrier tissues and RBCs was performed using a 2-T, 30-cm clear-bore magnet (Oxford Instruments, Oxford, UK), a 23.6-MHz quadrature birdcage coil, and a GE EXCITE console (GE Healthcare, Milwaukee, WI), modified as described previously[6]. Gaseous images were obtained over multiple breaths using a 3D radial acquisition[7] (views=4291, B= 8 kHz, TR/T =10/1 ms, matrix=64×64×64, FOV=5 cm, views/breath=20) that employed a variable flip angle scheme[8]. Dissolved HP ^{129}Xe images were acquired with the same multi-breath radial sequence using a 1-Point [4] variant of the Dixon method (8 views=1073, BW=15.63 kHz, TR = 75 ms, matrix = 32×32×632, FOV=5 cm, views/breath, α=90°, NEX=4). The TE needed to achieve the 1-Point Dixon condition (i.e, 90° phase separation between the RBC and barrier resonances) was determined spectroscopically[4]. During experiments, rats were mechanically ventilated with a 25% O_2/75% N_2 or 25% O_2/75% Xe mixture during MR experiments[9]. Following experiments, lungs were excised and prepared for histology (H&E and Masson's trichrome).

Results: In Bleomycin-treated rats, dissolved ^{129}Xe signal was observed from barrier tissues, regardless of the tissue's fibrotic state (Fig. 1A&B, center). However, RBC-specific signal was dramatically reduced in fibrotic regions (Fig. 1A&B, white arrows, right). In contrast, control animals displayed homogeneously distributed barrier- and RBC-signal throughout the lungs (not shown).

Discussion and Conclusions: 3D MRI of ^{129}Xe uptake is feasible and sensitive to diffusion impairment induced by fibrotic interstitial thickening in rats. Moreover, ^{129}Xe displays similar spectral properties in human lungs, suggesting that ^{129}Xe MRI will provide a noninvasive method to longitudinally assess 3D gas-exchange impairment in human subjects with interstitial lung disease.

Acknowledgements: Duke Center for In Vivo Microscopy (NIBIB P41 EB015897), NHLBI 1R01 HL105643, and NHLBI 1K99 HL111217-01A1.

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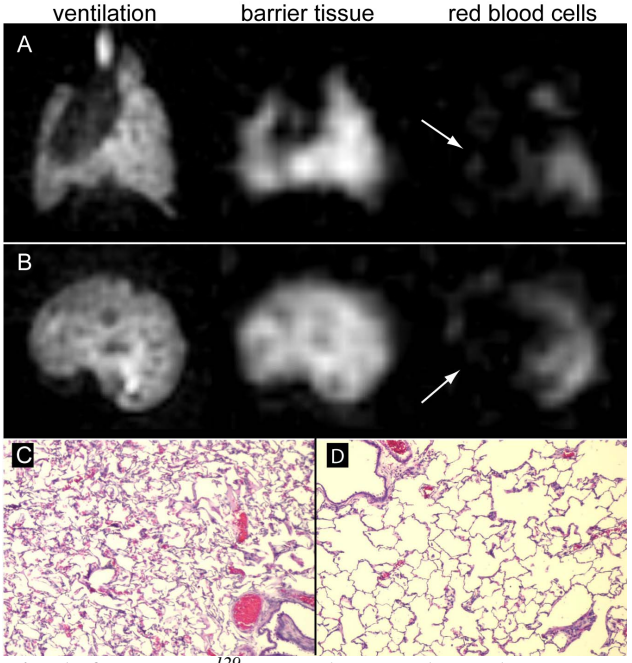

Fig. 1: *3D MRI of ^{129}Xe uptake in a fibrotic lung. Arrows denote regions of impaired gas exchange.* ***(A)*** *Coronal slices from 3D images of ventilation, barrier tissue, and RBCs.* ***(B)*** *Axial slices from the same 3D images.* ***(C)*** *Right lung H&E histology.* ***(D)*** *Left lung H&E histology.*