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 CO2 and O2 in the lungs cannot be detected directly. However, hyperpolarized (HP) 129Xe 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 129Xe to be detected separately from 129Xe dissolved in red blood cells (RBCs) or pulmonary barrier tissues (capillary plasma and interstitium)1-4. Further, because 129Xe diffuses across the same barrier tissues as CO2 and O2, barrier thickening (e.g., due to interstitial lung disease), will delay 129Xe 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 fibrosis5. 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 Bleomycin6 (3 U/kg) or saline, respectively. HP 129Xe was cryogenically accumulated using a prototype polarizer (MITI, Durham, NC). 3D MRI of gaseous 129Xe and 129Xe 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 previously6. Gaseous images were obtained over multiple breaths using a 3D radial acquisition7 (views=4291, B= 8 kHz, TR/T =10/1 ms, matrix=64x64x64, FOV=5 cm, views/breath=20) that employed a variable flip angle scheme8. Dissolved HP 129Xe 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 = 32x32x632, 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 spectroscopically9. During experiments, rats were mechanically ventilated with a 25% O2/75% N2 or 25% O2/75% Xe mixture during MR experiments6. Following experiments, lungs were excised and prepared for histology (H&E and Masson’s trichrome).

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

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Fig. 1: 3D MRI of 129Xe 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.