Hyperpolarized 129Xe MR Imaging of Alveolar-Capillary Gas Transfer in Human Volunteers

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Introduction: Hyperpolarized (HP) ^{129}Xe is a promising contrast agent for pulmonary MRI because of this isotope's reasonably high solubility (~10%) in blood and tissues and its unusually large, environment-dependent chemical shift. However, using these unique MR properties to image pulmonary gas exchange has proven challenging because of the lung's low tissue density and the unfavorable T_{2*} of ^{129}Xe dissolved in pulmonary tissues (1.5-2.4 ms at 1.5 T). As a result, Xe exchange is usually probed using indirect techniques such as Xenon polarization Transfer Contrast (XTC)[1]. Recently we demonstrated in rats that it is possible, despite the inherent difficulties, to directly image ^{129}Xe dissolved in pulmonary tissues[2] by using a 2D radial MR imaging. Here, we extend this method to humans and show that direct 3D imaging of ^{129}Xe uptake by the pulmonary tissues can be performed within a single, 16 s breath-hold. Additionally, we present strategies for optimizing dissolved ^{129}Xe MRI and discuss the physiological insights provided by directly imaging Xe gas exchange in the lungs. Finally, we present data from chronic obstructive pulmonary disease (COPD) patients, which suggest that dissolved ^{129}Xe MRI can detect the redistribution of capillary blood volume associated with pathology.

Methods: Dissolved ^{129}Xe MRI was developed while scanning 24 healthy volunteers during the technical run-in portion of a GE Healthcare sponsored, Phase I clinical trial for ^{129}Xe MRI. 10 COPD patients and 10 age-matched controls were imaged during the efficacy portion of the trial. All subjects gave informed consent. Studies were conducted under a GE Healthcare IND and approved by the Duke University Medical Center IRB. MRI was performed at 1.5 T using a GE EXCITE 14M5 system. Studies consisted of a calibration scan (200 ml Xe) and 4 (healthy subjects) or 3 (COPD patients and controls) 1-L doses of isotopically enriched xenon (83% ^{129}Xe) polarized to 6-9% using prototype GE polarizers. Slice selective ventilation images (matrix=128×128, FOV=40×40 cm, slice thickness=15 mm, TR/TE=7.9/1.9 ms, BW=8 kHz) were acquired using a SPGRE sequence. Dissolved ^{129}Xe images were acquired using a 3D radial sequence (3751 views, matrix=32×32×32, FOV= 40×40×48 cm^3, TR/TE=4.2/0.9 ms, BW=15.6 kHz). Dissolved ^{129}Xe was selectively excited with a 1.2 ms, 3-lobe sinc pulse applied 3826 Hz above the gas phase ^{129}Xe frequency.

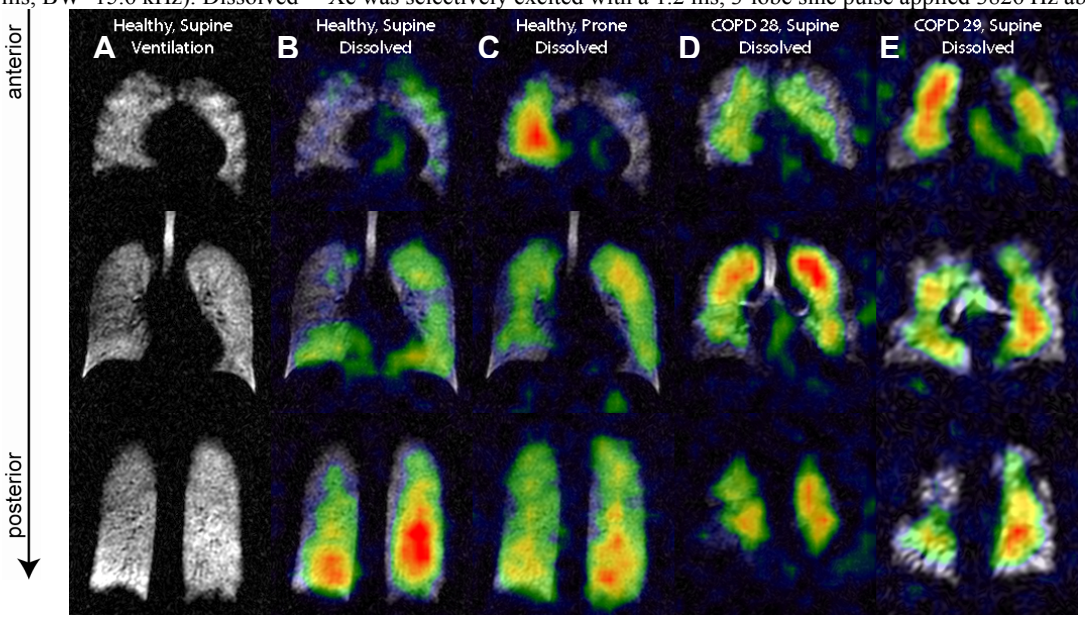

Fig. 1. HP ^{129}Xe MR images. **(A)** Representative slices from the ventilation image of a healthy subject. **(B)** Dissolved ^{129}Xe image (color) overlaid on (A). Image was acquired after the subject had been supine for 1 hr. Despite homogeneous ventilation, the dissolved ^{129}Xe image displays a heterogeneous signal intensity pattern consistent with a gravity-dependent distribution of capillary blood volume. **(C)** Same subject as in (B) imaged 10 min after moving to the prone position. Now the gravitationally dependent (anterior) slices display increased signal intensity. **(D)** Dissolved ^{129}Xe image from a supine COPD patient. The signal intensity pattern is also heterogeneous, but displays less gravitational dependence than is seen in (B) and (C). **(E)** Dissolved image from a second COPD patient. Again a heterogeneous, but less gravitationally dependent, pattern is observed.

Results: Optimized dissolved ^{129}Xe images were obtained using relatively large flip angle (~8° at TR=4.2 ms) RF pulses made possible by the rapid, diffusive magnetization replenishment from gaseous ^{129}Xe, which occurs with a time constant of ~100 ms[2,3]. This replenishment partially overcomes the low pulmonary tissue density, enabling dissolved, 3D MRI with acceptably high SNR. In all subjects, significant dissolved ^{129}Xe intensity was visible in the left side of the heart. Increasing the TR or the decreasing the flip angle allowed more HP ^{129}Xe to reach the heart without RF attenuation and, thus, provided increased signal intensity from this region. In healthy volunteers, the dissolved ^{129}Xe images largely matched the normal ventilation pattern but showed significant directional heterogeneity. Specifically, in supine subjects, the dissolved ^{129}Xe signal was notably increased in the posterior slices, which represent the gravitationally dependent portions of the lungs (Fig. 1B). Imaging in the prone position (Fig. 1C), resulted in a substantial signal increases in the anterior (now dependent) image slices. Images obtained from COPD patients (Fig. 1D&E) also displayed significant signal heterogeneity. However, the pattern of the heterogeneity was strikingly different and displayed less obvious directionality.

Discussion and Conclusions: We have demonstrated the feasibility of directly imaging ^{129}Xe dissolved in human pulmonary tissues and show that 3D resolution (12.5×12.5×15 mm^3) can be obtained within a 16 s breath-hold. In healthy volunteers, these images display heterogeneity that is consistent with known physiology[4] and other imaging studies[5] and that likely resulted from a gravity-dependent distribution of capillary blood volume. The appearance of this pattern in the images suggests that dissolved ^{129}Xe MRI reflects pulmonary function at a fundamental level. The signal intensity pattern observed from COPD patients, however, does not seem to follow a purely gravitationally-dependent pattern. We speculate that this non-directional heterogeneity results from the redistribution of capillary blood volume in response to pulmonary disease progression. Although additional work is needed to quantify the various aspects of perfusion heterogeneity and their influence on dissolved HP ^{129}Xe MRI, this work suggests that direct imaging of dissolved ^{129}Xe could provide analogous, but spatially resolved, information to that provided by conventional DL_{CO} tests and provide a non-invasive means to longitudinally evaluate pulmonary diseases affecting gas exchange.

Acknowledgements: GE Healthcare**,** HL 5R21HL87094, Philip Morris External Research Fund, Center for In Vivo Microscopy P41 RR005959
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