Single-Breath Gas and Dissolved-Phase ^{129}Xe MRI in Healthy Subjects using a 3D Radial Sequence: Effect of Posture on Signal Distribution

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PURPOSE: When dissolved in lung tissue, the resonance frequency of hyperpolarized (HP) ^{129}Xe shifts significantly, displaying unique peaks associated with barrier tissues at 197 ppm and red blood cells (RBC) at 211 ppm. Thus, HP ^{129}Xe provides a unique window on pulmonary gas-exchange. In particular, this property was used to image dissolved-phase ^{129}Xe in human subjects[1,2]. These first images showed substantial regional heterogeneity, suggesting true pulmonary gas exchange is similarly heterogenious[1]. However, because ^{129}Xe in the alveolar spaces is the source of dissolved-phase magnetization, quantifying heterogeneity requires that gas- and dissolved-phase images be acquired in the same breath[2]. Mugler *et al*., elegantly achieved this goal by exploiting the chemical shift "artifact" of dissolved ^{129}Xe in slice selective GRE imaging. Unfortunately, this approach required high ^{129}Xe polarization (~40%), due to the rapid T2* (~2 ms) decay of ^{129}Xe dissolved in the pulmonary tissues[3]. As an alternative, we introduce an interleaved, 3D radial sequence to images both gas- and dissolved-phase in a single breath. This sequence intrinsically overcomes the short T2* of the dissolved-phase[3] and readily lends itself to the separation of the RBC and barrier tissue components using Dixon imaging[4]. Further we investigate physiological contributions to dissolved-phase heterogeneity by imaging subjects in both the prone and supine position.

METHODS: This IRB-approved study was conducted under an FDA IND (109490), and subjects provided written informed consent. Images were acquired in 9 healthy subjects (8 men, 1 woman, age=45.6±18.7 years, both supine and prone) on a 1.5 T GE scanner (EXCITE15M4). MRI employed 1-L of enriched (86%) ^{129}Xe polarized to 7–10% with a Rb-vapor polarizer (Polarean, Durham, NC). To acquire gas- and dissolved-phase images, [FOV=40 cm, Matrix=32×32×32, 1.2-ms sinc pulse, TE/TR=0.932/7.5 ms, 1,001 rays per resonance, flip angle=22° (dissolved), and 0.5° (gas)] each ray of k-space was acquired twice—once with transmit and receive frequencies on the gas-phase resonance (0 Hz) and once on the dissolved-phase (+3832 Hz). Data were then individually reconstructed using the NUFFT[5] algorithm. 3D ^{1}H images of the thoracic cavity were also acquired using the radial sequence (FOV=40cm, 64×64×64, TE/TR=0.334/2.4 ms, 5,647 rays, flip angle=5°). The intensities of both images were individually normalized, and the dissolved-phase image was divided by the gas-phase image to create a gas-transfer map. Mean gas-transfer in the thoracic cavity (as defined by the ^{1}H image) for each image slice was subjected to a linear regression, weighted by number of pixels, to assess gas-transfer gradients for each posture.

RESULTS: Dual acquisitions were successfully acquired in both postures for all subjects (see **Figure A**). Gas and dissolved-phase images exhibited substantial heterogeneity, with higher signal intensities in the gravitationally dependent lung, and this gradient persisted in the normalized gas-transfer maps. When supine, the mean gas-transfer gradient was -1.99±0.74% cm^{-1}, which reversed to 1.94±1.14% cm^{-1} when prone ($p<0.001$) (representative gradient in **Figure B**). Differences in supine and prone gradients increase with subject TLC ($r=0.62$), suggesting larger gas-transfer gradients occur at lower lung inflation (i.e., when 1-L doses were diluted in larger lungs). Also, in preliminary studies of subjects with pulmonary disease (not shown), this gas-transfer gradient was reduced, in agreement with the observations of Mugler *et al*.[2] However, our studies of healthy subjects also showed significant in-plane gas-transfer heterogeneity, and nearly all subjects had higher gas-transfer values in slices iso-gravitational with the heart. Finally, while gas-transfer varied substantially, the mean gas-transfer value was ~1 in all subjects, regardless of body position.

DISCUSSION AND CONCLUSIONS: This interleaved 3D radial sequence enabled imaging of both the gas- and dissolved-phase ^{129}Xe in a single breath with sub-ms TEs and required only modest polarization (~10 %). The increased gas and dissolved-phase signal observed from the dependent lung could be attributed to intra-pleural pressure[6] and tissue density gradients[7]. The persistence of this gradient in gas-transfer maps indicates ventilation is not the sole source gravitational heterogeneity in the images. This non-monotonic variability of gas-transfer in normal subjects may indicate a significant reserve capacity for gas exchange in the healthy, resting lung and a heterogeneous filling of the lung capillary beds at rest. The additional heterogeneity contributed by the variable expansion of the lungs could be mitigated in the future with volume-controlled experiments. These preliminary results show that dissolved-phase imaging, while an interesting new avenue, is intrinsically heterogeneous in healthy lungs. To understand the capillary blood component of these images, it will be valuable to further separate dissolved images into their RBC and tissue components[4].

REFERENCES: 1. Cleveland *et al*., PLoS One, 2010. **2.** Mugler *et al*., PNAS, 2010. **3.** Mugler *et al*., ISMRM 2012. **4.** Driehuys *et al*., PNAS, 2006. **5.** Song *et al*., IEEE 2009. **6.** West *et al*. Respiratory Physiology, 1995. **7.** Prisk *et al*., JAP, 2007.

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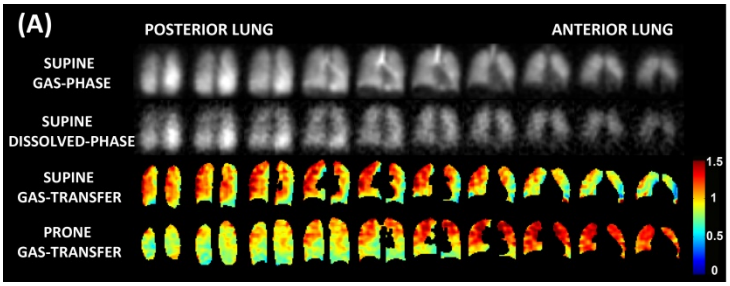

Figure: **(A)** Gas and dissolved-phase ^{129}Xe images from a representative healthy volunteer. In addition to the gradient in the source images, the gradient is retained in the gas-transfer map in both postures, with higher values in the dependent lung. **(B)** The mean gas-transfer per slice in the two postures.