Simultaneous Imaging of Ventilation Distribution and Gas Exchange in the Human Lung using Hyperpolarized Xe129 MRI

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Introduction: The high solubility of xenon in biological tissues, combined with an exquisite sensitivity to its environment that results in an enormous range of chemical shifts upon solution, make hyperpolarized Xe129 particularly attractive for exploring characteristics of lung function, such as gas exchange, that are not accessible by using hyperpolarized He3. With improvements in gas-polarization hardware [1], liter quantities of hyperpolarized Xe129 can be obtained with sufficient polarization to make direct dissolved-phase imaging in humans feasible during a single breath-hold period. Recently, Driehuys et al demonstrated breath-hold images of dissolved-phase Xe129 in humans following inhalation of 1 liter of Xe129 polarized to approximately 8% [2]. The large difference in chemical shift, and hence resonant frequency, between gas-phase and dissolved-phase Xe129 presents the opportunity to capture both components in the same image, thus potentially yielding, from a single breath-hold acquisition, simultaneous depiction of the regional distributions of the gas following inhalation and of the fraction of gas that exchanges into the lung parenchyma and blood. The purpose of this work was to demonstrate the feasibility of such a method in the healthy and diseased human lung.

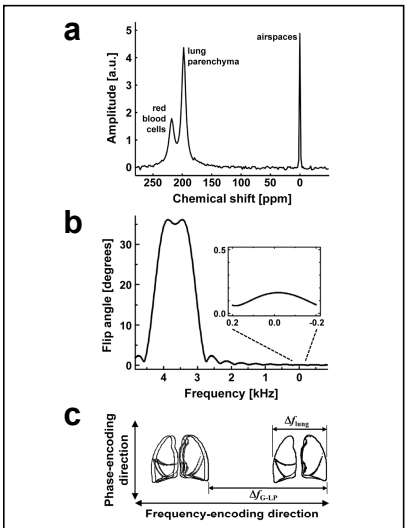

Fig. 1. Relationships between the gas and dissolved spectral peaks of Xe129 and the excitation and frequency-encoding characteristics of a pulse sequence designed to simultaneously acquire images of gas- and dissolved-phase xenon.

Methods: Figure 1 illustrates the relationships between the gas and dissolved peaks of Xe129, and the excitation and frequency-encoding characteristics of a pulse sequence designed to generate an image that shows, side-by-side along the frequency-encoding direction, both Xe129 in the lung airspaces and Xe129 dissolved in the lung parenchyma and blood. Figure 1a shows a representative spectrum of Xe129 from a healthy human lung. Figure 1b illustrates the frequency response of an RF pulse suitable for simultaneous imaging of the gas and dissolved components. Since the amount of Xe129 in the dissolved-phase compartments is much less than that in the airspaces, and because Xe129 in the airspaces acts as a reservoir for the dissolved-phase compartments, it is desirable to apply a relatively high flip angle to Xe129 in the dissolved-phase compartments but a relatively low flip angle to that in the airspaces. Finally, Fig. 1c shows how the dissolved-phase and gas-phase components appear separated along the frequency-encoding direction for appropriately selected pulse-sequence parameter values.

Two- and three-dimensional versions of the simultaneous gas-phase, dissolved-phase technique were implemented based on an RF-spoiled gradient-echo sequence. Flexible chest (Clinical MR Solutions, Brookfield, WI) and vest-shaped (custom built) RF coils were used for imaging on a 1.5T scanner (Avanto, Siemens). Enriched xenon gas (87% Xe129) was polarized by collisional spin exchange with an optically-pumped rubidium vapor using a prototype commercial system (Xemed LLC, Durham NH). Images were acquired in 11 subjects: 6 healthy subjects, 3 asthmatics, and 2 subjects with mild COPD. Each subject inhaled a gas mixture having a total oxygen concentration of 21% and containing 0.5 or 1 L of hyperpolarized Xe129 polarized to 20-40%, room air and oxygen. Sequence parameters were: TR, 35-300 ms; TE, 2.7-2.8 ms; flip-angle at dissolved phase, 16-80°; bandwidth, 90-120 Hz/pixel; PE order, sequential; spatial resolution, 9-12 x 9-12 x 12-20 (for 3D) mm^3; acquisition time, 2-18 s. All experiments were performed under a Physician's IND for imaging with hyperpolarized Xe129 using a protocol approved by our institutional review board. Informed consent was obtained in all cases.

Results and Discussion: Images simultaneously demonstrating ventilation (gas-phase Xe129) and gas exchange (dissolved-phase Xe129) were successfully obtained in all subjects. A representative 2D projection image from a healthy volunteer is shown in Fig. 1, illustrating uniform distributions of both the gas- and dissolved-phase signals, indicating uniform distributions of ventilation and gas exchange, respectively, as expected. In contrast, in subjects with lung disease, signal-intensity variations seen in the dissolved-phase components of the images were similar, but not identical, to those seen in the corresponding gas-phase components. This is demonstrated in Fig. 3, which compares an image from a 3D acquisition in a healthy subject (Fig. 3a) to that from a subject with severe asthma (Fig 3b). In the asthmatic, ventilation defects are seen in the gas-phase component (Fig. 3b, left). The pattern of signal-intensity variations in the dissolved-phase component (Fig. 3b, right) is somewhat different than that for the gas-phase component (see Fig. 3 caption), suggesting that the dissolved-phase component reflects more information than simply the local concentration of gas.

Conclusions: This work demonstrates the feasibility of using MRI of hyperpolarized Xe129 to acquire images in a single, short breath-hold period that simultaneously depict ventilation distribution and gas exchange in the human lung with matched resolution. The method presents new opportunities for quantifying relationships among gas delivery, exchange and transport, and shows significant potential to provide new insights into lung disease.

References: **1.** Hersman FW et al. Acad Radiol 2008;15:683-692. **2.** Driehuys B et al. 4th IWPFI, Boston, 2009.

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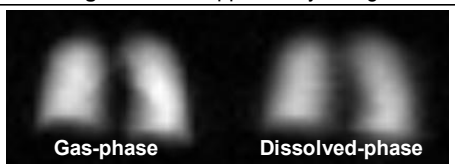

Fig. 2. Coronal 2D projection image demonstrating simultaneous depiction of the distributions of ventilation following inhalation and gas exchange (TR/TE/FA 160/2.8/35°; resolution 12 x 12 mm^2).

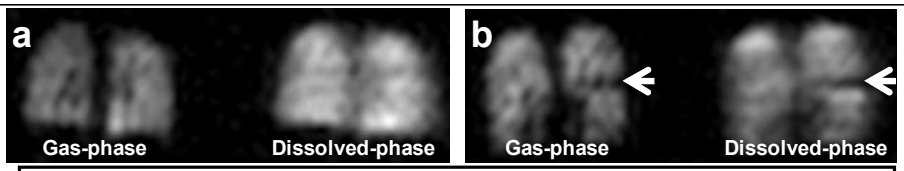

Fig. 3. Images from 3D acquisitions in (**a**) a healthy subject and (**b**) a severe asthmatic demonstrating simultaneous depiction of the distributions of ventilation following inhalation and gas exchange (TR/TE/FA 50/2.8/20°; resolution 12 x 12 x 20 mm^3). While both images in (b) show a signal dropout at the location of a ventilation defect (arrows), a band of elevated signal is seen just below this defect in the dissolved-phase image.