Integrated Spectroscopic Imaging (CSI) and Chemical Shift Saturation Recovery (CSSR) of Hyperpolarized ^{129}Xe in the Human Lungs

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Target Audience: Hyperpolarized gas MRI community; respiratory clinicians and physiologists.

Introduction & Purpose: Recent developments in hyperpolarized (HP) ^{129}Xe MR for studies of pulmonary gas exchange in humans have focused on two principal themes: i) Dixon-based [1] or "IDEAL" chemical shift imaging (CSI) [2] methods, for regional depiction of the chemically-distinct resonances of ^{129}Xe dissolved in lung tissues and blood plasma (T/P) and red blood cells (RBC); (ii) acquisition of time-series of NMR spectra via the chemical shift saturation recovery (CSSR) technique [3, 4]. These methods provide complementary regional and temporal information about gas exchange, however the former methods are limited to providing pseudo-quantitative data in terms of ratios of signal intensities from ^{129}Xe in different spectral compartments, whilst the latter method permits quantification of pulmonary blood flow and lung microstructure, such as alveolar septal thickness, but the necessity for multiple repetition times constrains spatial resolution achievable within a breath-hold. Crucially, most lung diseases have a spatially heterogeneous pattern, e.g. idiopathic pulmonary fibrosis is concentrated at the lung base and periphery [5]. Furthermore, there are well-known gravitational effects in the lung, in terms of tissue density [6] and ventilation-perfusion ratio (V/Q) [7]. The expected decrease in V/Q from anterior to posterior (A-P) has been measured using ^{129}Xe MR by calculating the ratio of gaseous and dissolved ^{129}Xe signals in an imaging experiment as a function of A-P position [8], however, in that work, the dissolved-phase ^{129}Xe signal was not separated into its constituent components. In this work, we implement a free induction decay (FID) based CSI method with multiple spectral acquisitions at different delay times (CSSR) for each spatial position, to study the regional variation in gas exchange dynamics from anterior to posterior, with spectral-selectivity of T/P and RBC components.

Methods: A FID-based CSI sequence with a variable repetition time (TR) CSSR acquisition for each phase encode was programmed in-house (Fig 1). Two healthy subjects were scanned on a whole-body 1.5 T GE (Signa HDx) MR system. Enriched xenon gas (86% ^{129}Xe, polarized to ~ 50% using an in-house polarizer [9]) was delivered to subjects in 1 L doses of either 100% xenon or 50:50 xenon-nitrogen mixtures. Subjects were scanned on two occasions, with 1D phase-encoding implemented in both the anterior-posterior (A-P) and right-left (R-L) directions. To limit the sequence breath-hold time to ~ 15 sec, eight TRs (20 ms – 320 ms) were selected, with 16 CSI phase encodes and a field-of-view of 26 cm for A-P (36 cm, R-L); each encode corresponding to ~ 16 (22.5) mm. Additional sequence parameters: binomial-composite radiofrequency pulses were utilized to provide selective saturation of dissolved ^{129}Xe [10]; 128 spectral points were sampled over a bandwidth of 12 kHz.

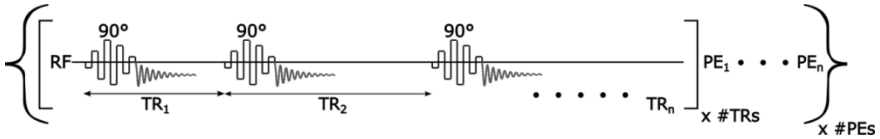

Figure 1: Interleaved CSI-CSSR pulse sequence, as implemented in this work. For each CSI phase encoding step (PE), 90° radiofrequency pulses were used to saturate dissolved ^{129}Xe magnetization and generate FIDs at multiple different inter-pulse delay times (TR) in order to sensitize the MR acquisition to xenon uptake dynamics for each pixel.

Results & Discussion: In the R-L direction, the dissolved and gaseous ^{129}Xe signal intensities were symmetrically distributed about a region of low signal (in between the two lungs) at all repetition times, with little R-L variation in ventilation, perfusion or tissue density. Fig 2 depicts typical results acquired from one

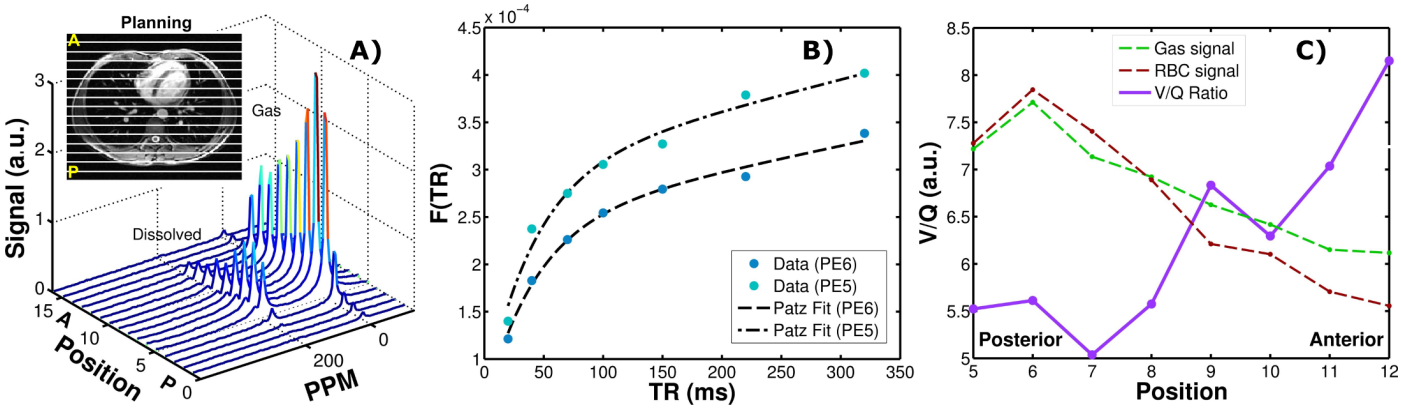

Figure 2: A) ^{129}Xe spectra acquired from one subject at a TR of 100 ms, as a function of A-P position (planning shown in inset). B) Example ^{129}Xe CSSR uptake curves from two posterior sections of the lung (5 and 6 in A)), fitted with the model of Patz et al. C) A-P position dependence of signal from gaseous (green) and RBC-dissolved ^{129}Xe (red), and the corresponding ratio of gas/RBC signal (V/Q, purple). In A) and C), each position step represents ~ 16 mm.

subject in the A-P orientation, highlighting elevated signal from both gaseous and dissolved ^{129}Xe in the posterior regions. At TRs > 50 ms, the total dissolved ^{129}Xe signal from the most posterior regions was greater than that from anterior regions. Fig 2B shows example ^{129}Xe uptake curves from two posterior positions, modelled using the method of Patz et al. [3], exhibiting a good agreement between model fit and data. However, CSSR data fitting from the anterior regions where signal-to-noise ratio was low was challenging, and meaningful differences in fit parameters as a function of A-P position could not be derived. Nevertheless, we would not necessarily expect to observe an A-P variation in alveolar septal thickness in normals, and in future work it may be more instructive to better quantify long TR (> 100 ms) data to directly measure regional perfusion changes. Finally, to validate the proposed method with a standard clinical observation, the integrated signal intensities from gaseous and RBC-dissolved ^{129}Xe at the longest TR value were divided for each location to determine the ventilation-perfusion ratio (Fig 2C). These findings indicated a noted increase in V/Q in the most anterior slices, in agreement with previously-published imaging measurements [8].

Conclusion: A proposed method for regional quantification of pulmonary gas exchange dynamics has been demonstrated through a combined CSI and CSSR approach with hyperpolarized ^{129}Xe. The method enables acquisition of CSSR uptake curves at different spatial positions and has been validated by calculating the A-P gradient in V/Q ratio from the ratio of gaseous to RBC-dissolved ^{129}Xe MR signals. In future work, an application of the technique to measure superior-inferior differences in alveolar septal thickness in fibrotic lung disease with a basal predominance can be envisaged.

References: [1] B. Driehuys et al., PNAS. 2006;103(48):18278-18283. [2] K. Qing et al., MRM. 2014;39:346-359. [3] S. Patz et al., New J Phys. 2011;13:015009. [4] Y. V. Chang et al., MRM. 2013;69:884-890. [5] T. E. King et al., Lancet. 2011;378:1949-61. [6] H. Hatabu et al., Eur J Rad. 1999;29(3):245-252. [7] J. B. West & C. T. Dollery, Journ Appl Physiol, 1960.15(3):405-410. [8] J. P. Mugler III et al., PNAS. 2010;107(50):21707-21712. [9] G. Norquay et al., In: Proc PING14: Hyperpolarised Noble Gases, Les Houches, 2014. [10] G. Leung et al., MRM. 2014; doi:10.1002/mrm.25089.