

DISSOLVED HYPERPOLARISED ^{129}Xe AS A PROBE OF LUNG FUNCTION IN IDIOPATHIC PULMONARY FIBROSIS AND SYSTEMIC SCLEROSIS

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Target Audience: Hyperpolarised gas MRI community; clinicians, scientists and specialists with an interest in lung function and rare lung diseases.

Purpose & Introduction: The degradation of gas exchange function in Idiopathic Pulmonary Fibrosis (IPF) and Systemic Sclerosis (SSc) has varying contributions from structural and functional changes in the alveolar, interstitial and pulmonary-vascular components. Pulmonary Function Tests (PFTs, e.g. DL_{CO}) provide limited functional information and the extent of interstitial change on High Resolution Computed Tomography (HRCT) correlates poorly with symptoms. Novel techniques are therefore required to characterise structural changes to the gas exchange surface in the lungs and assess efficacy of possible treatments. Recent work has highlighted the potential of Chemical Shift Saturation Recovery (CSSR) NMR spectroscopy with hyperpolarised (HP) ^{129}Xe for detecting changes in alveolar-capillary septum thickness, characteristic of interstitial pulmonary pathologies¹⁻³. In this work, we demonstrate the practicability of the CSSR method for non-invasive quantification of lung microstructure, gas uptake and pulmonary-vascular function in subjects with IPF and SSc.

Methods: All whole-lung CSSR spectroscopy experiments were performed on a 1.5T scanner (GE Signa HDx), with a flexible transmit-receive vest coil tuned to the xenon resonant frequency (17.66MHz). Subjects comprised eight healthy controls, three subjects with IPF and three with SSc. Each subject inhaled a mixture of 500mL of cryogenically-accumulated, isotopically-enriched xenon gas (10-15% nuclear polarisation achieved by spin exchange optical pumping)⁴ and 500mL N₂. CSSR sequence parameters were as follows: 14-element pulse-width modulated binomial composite RF pulse, providing perfect saturation of dissolved-phase HP ^{129}Xe (90°) in the lung region and minimal gas excitation (1°)⁵; 25 different repetition times in order to sensitise the NMR acquisition to gas uptake (20ms to 1s, sequentially swept through three times); 64 spectral points per scan; total breath-hold, 15s. CSSR uptake curves (described by F(TR), the ratio of dissolved HP ^{129}Xe signal intensity at time t=TR to gas signal intensity at t=0) were fitted with the models of Patz *et al.*^{1,2}, Månsson *et al.*⁶ and Chang⁷. These models were rigorously compared and utilised to estimate parameters relevant to lung physiology. Results were analysed with reference to standard PFTs (DL_{CO}) as well as 3D-inspiratory CT, ^3He MR ventilation and apparent diffusion coefficient (ADC) mapping, and dynamic contrast-enhanced (DCE) ^1H MRI.

Results & Discussion: Assessment of NMR spectra showed an increased peak due to ^{129}Xe dissolved in parenchymal tissues and blood plasma (T/P) with a diminished peak from ^{129}Xe in erythrocytes (RBC) in patients when compared to healthy volunteers (Figure 1). ^{129}Xe uptake curves indicated that gas transfer is impaired and delayed in these patients, attributable to underlying changes in lung microstructure, e.g.

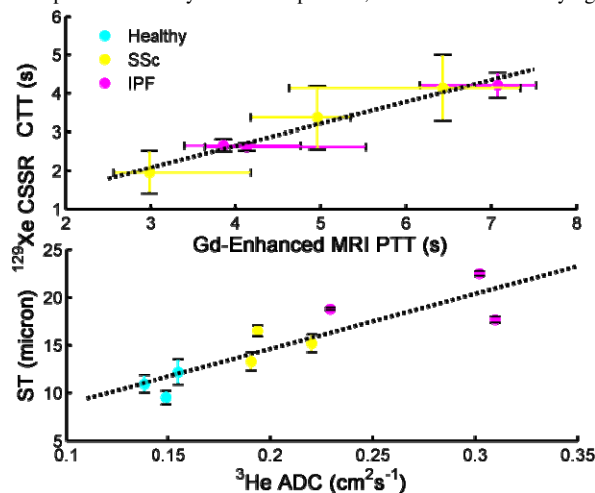


Figure 3: ^{129}Xe CSSR compared with clinically-accepted techniques: capillary transit time (CTT) versus pulmonary transit time (PTT) from DCE-MRI; septal thickness (ST) versus ^3He ADC. Note: only the Patz model displayed a clear correlation between CTT and PTT.

References: [1] S. Patz *et al.*, Academic Radiology, **15**, 713 (2008). [2] S. Patz *et al.*, New Journ Phys, **13**, 015009 (2011). [3] K. Ruppert *et al.*, Proc ISMRM, **21**, 1455 (2013). [4] G. Norquay *et al.*, Journ Appl Phys, **113**, 044908 (2013). [5] G. Leung *et al.*, Proc ISMRM, **21**, 1449 (2013). [6] S. Månsson *et al.*, Mag. Res. Med, **50**, 6, 1170-9 (2003). [7] Y. Chang, Mag. Res. Med, **69**, 3, 884-890 (2013).

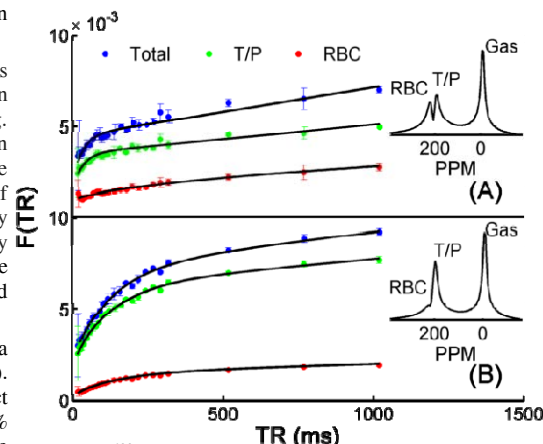


Figure 1: ^{129}Xe uptake dynamics for (A) a healthy volunteer and (B) a subject with IPF. Insets: typical post-processed spectra obtained from CSSR experiment.

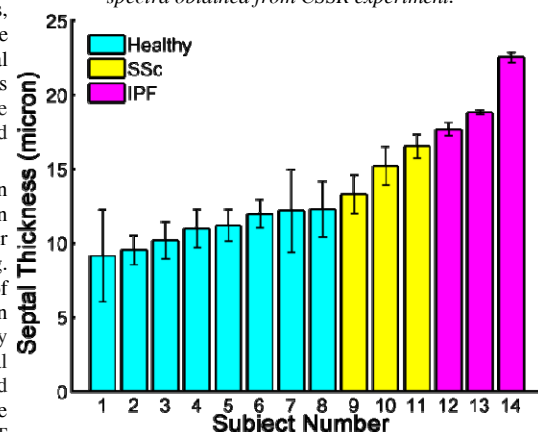


Figure 2: Mean alveolar septal thicknesses for healthy volunteers and subjects with IPF and SSc, as derived from the Patz model, displayed in increasing order.

inflammation and thickening of parenchymal tissue. Diffusion modelling exhibited a significantly increased mean alveolar septal thickness in patients with IPF and SSc, versus healthy controls (Figure 2). HP ^3He , ^1H UTE, and CT imaging highlighted distinct regional fibrosis and heterogeneity in the lungs of IPF patients; however SSc subjects appeared comparatively normal (except for some small ^3He ventilation defects in one subject), despite noticeable septal thickening detected by CSSR, and severely reduced DL_{CO}. An elevated xenon capillary transit time (average time a xenon atom resides in the gas exchange region) was observed in almost all patients; this parameter correlated well with the pulmonary transit time (time taken for one pass of gadolinium (Gd) from pulmonary artery to left atrium) determined from DCE-MRI (Figure 3). Also shown in this figure, preliminary data suggests a correlation between septal thickness and the ADC value from ^3He diffusion MRI.

Conclusions: Whole-lung CSSR spectroscopy with HP ^{129}Xe is capable of detecting alterations in lung structure-function, allowing non-invasive measurement of alveolar-capillary septum thickness and pulmonary-capillary transit times. We have shown clinically-important septal thickening and reduced DL_{CO} in SSc subjects with very little / no known interstitial or pulmonary-vascular involvement. Further clinical benefits may be achieved with the use of multi-channel receiver array coils, or by adapting the technique to a “gas exchange imaging” experiment, in order to quantify regional variations in gas exchange impairment.