Hyperpolarized ^{129}Xe MRI Measures of Gas Exchange in Nonspecific Interstitial Pneumonia (NSIP)

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Introduction

Nonspecific interstitial pneumonia (NSIP) is a distinct form of interstitial lung disease (ILD) with a generally good prognosis [1]. NSIP may be either idiopathic or associated with conditions such as Sjögren's syndrome, rheumatoid arthritis, and connective tissue disorders.

The presentation of NSIP is highly variable. A definitive diagnosis requires a comprehensive clinical assessment, CT, and lung biopsy [1]. **Many features of NSIP may also be exhibited by idiopathic pulmonary fibrosis (IPF),** a disease with a higher incidence rate, far worse prognosis, and different standard of care. **There is a clinical need for tools to better differentiate between NSIP and IPF** and to monitor therapy response longitudinally.

Hyperpolarized (HP) ^{129}Xe MRI enables the quantification of regional gas transfer by single-breath 3D imaging of its distribution in the airspaces, interstitial barrier tissues, and transfer to capillary red blood cells (RBC's), and this technique has previously been applied in IPF [2-4].

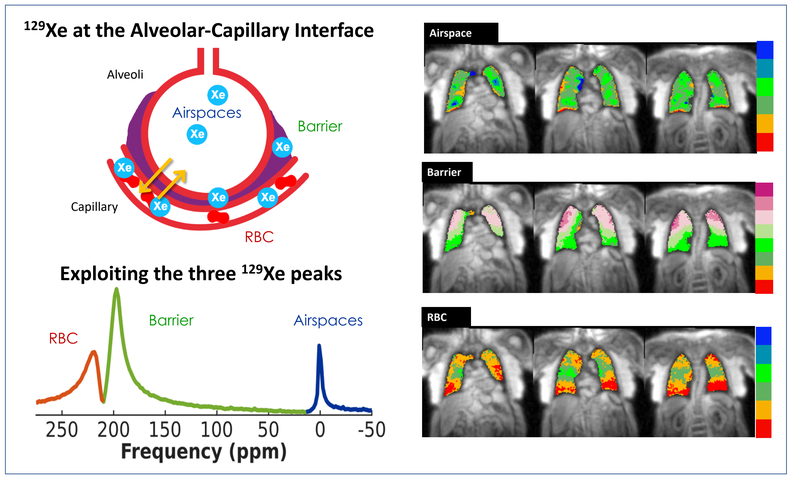
Here, we present the first studies of ^{129}Xe MRI in NSIP.

Methods

HP ^{129}Xe gas exchange MRI was acquired in two cohorts:
- **27 NSIP subjects (7M 20F, 57.3±9.7 yrs)**
- **18 healthy subjects (14M 4F, 32.8±13.4 yrs).**

CT was acquired for all NSIP subjects as part of their standard clinical care.

^{129}Xe Imaging Acquisition Methods
- Subjects inhaled 1L $^{129}Xe/N_2$ blend with ~120 mL ^{129}Xe dose equivalent
- 3D images from 1000 views each interleaved radial gas and dissolved-phase excitations (TR = 15 ms, flip angle = 5/20°, and a TE = TE_{90})
- Dissolved-phase compartments were decomposed using the 1-point Dixon method into RBC and barrier images [5].



Ventilation, tissue barrier, and RBC images were rendered into quantitative maps using a clustering method relative to reference distributions derived from a healthy cohort [2]. Ventilation defect percent (VDP), mean barrier uptake, and mean RBC transfer in NSIP vs. healthy subjects were compared using the Wilcoxon rank-sum test.

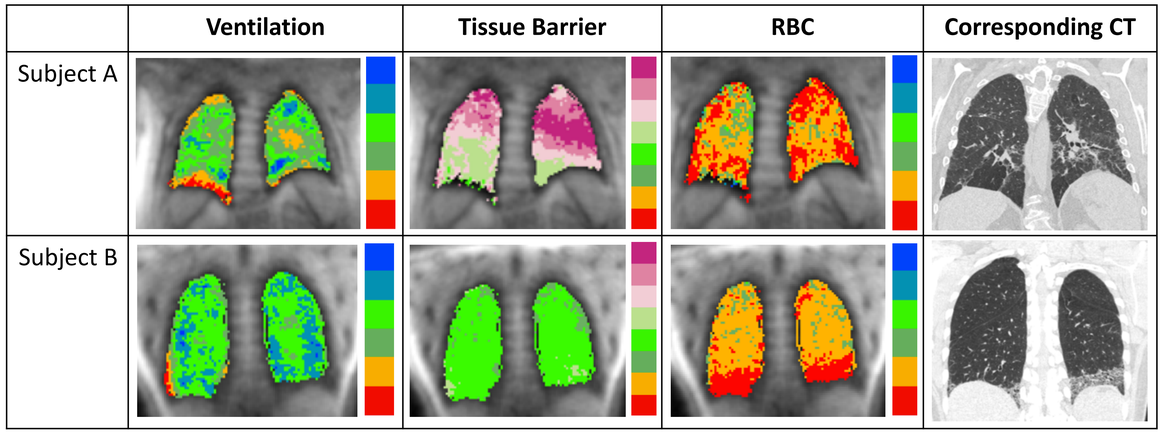


Figure 1. *HP Xe-129 MRI and CT images from two individual NSIP subjects in this cohort. Subject A exhibits preserved ventilation, increased barrier uptake, and widespread reduced RBC transfer with scattered peripheral defects. Subject B exhibits preserved ventilation and barrier uptake, but reduced RBC transfer with focal bibasilar RBC defects.* ***Note that Subject B has uniformly reduced RBC transfer (yellow) in regions which appear normal on CT.*** *Table 1 shows specific clinical, CT, and ^{129}Xe MRI attributes of these subjects.*

	Subject A	Subject B
FVC % Predicted	59%	81%
DLCO	10.0	14.6
Concurrent Diagnoses	Unknown etiology. Likely underlying inflammatory disorder. HP-like appearance, but ruled out by pathology.	Rheumatoid arthritis
ILD-Related Medications at imaging (time period)	Prednisone: 13mo Mycophenelate (CellCept): 37mo	Rituximab (Rituxan), periodic infusions over 18mo Prednisone: 39mo
CT Findings	Peribronchovascular ground glass & consolidation Air trapping	Lower lobe ground glass with bronchiectasis/ bronchiolectasis
Hyperpolarized ^{129}Xe MRI Measurements		
Ventilation defect percent (healthy ref. 5.0% ± 4.7%)	4%	1%
Mean barrier uptake (healthy ref. 0.76 ± 0.19)	1.61	0.71
Mean RBC transferl (healthy ref. 0.42 ± 0.14)	0.12	0.17

Table 1. *Diagnosis, treatment , and imaging characteristics of the two individual NSIP subjects shown in Figure 1.*

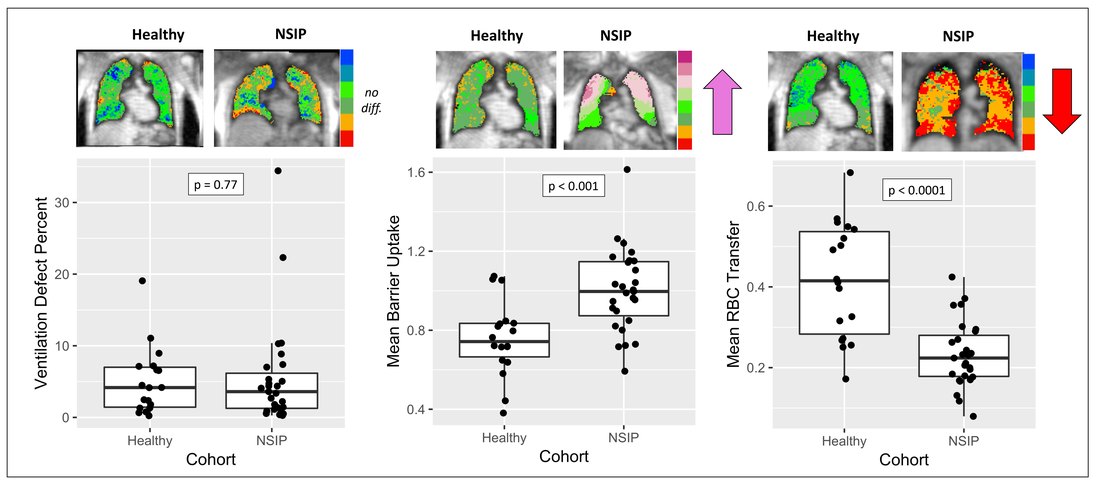


Figure 2. *Distributions of ventilation defect percent (VDP), mean barrier uptake, and mean RBC transfer in healthy (N = 18) vs. NSIP (N = 27) subjects. There was no significant difference in VDP (p = 0.77) but barrier uptake was elevated in NSIP subjects (p < 0.001) and RBC transfer was reduced (p < 0.0001).*

Results

Hyperpolarized ^{129}Xe MRI gas exchange images of two typical NSIP subjects (Table 1) from this study together with CT are shown in Figure 1.

In the overall NSIP population (N = 27), we observed patterns of
(1) **Preserved ventilation** (p = 0.77 vs healthy),
(2) **Increased barrier uptake** (p < 0.001), and
(3) **Severely reduced RBC transfer** (p < 0.0001)
as shown in Figure 2.

Study subjects are on a variety of different drugs as part of their clinical treatment for NSIP, including prednisone, mycophenolate (CellCept), and rituximab (Rituxan). Ongoing analyses will assess correlations between imaging measurements, treatment history, and concomitant conditions associated with NSIP.

Discussion

- **Barrier uptake and RBC transfer were impacted in NSIP** despite **no measured differences in ventilation** relative to healthy subjects.
- **Direct comparisons of NSIP vs. IPF** on ^{129}Xe MRI may provide a means of **characterizing functional differences between these two diseases** and aiding diagnosis, prognosis, and clinical decision-making.
- The non-ionizing nature of MRI makes this technique suitable for **repeated, longitudinal monitoring** of disease progression and rapid assessment of treatment response.
- Since ^{129}Xe MRI enables the assessment of functional phenomena occurring **at the alveolar level,** it may be sensitive to **early *functional* abnormalities before corresponding *structural* abnormalities are visible on CT.**

Conclusion

Hyperpolarized ^{129}Xe MRI is capable of detecting characteristic functional abnormalities in NSIP.

Further work in this area will explore the ability of ^{129}Xe in NSIP to
- Distinguish NSIP from other forms of ILD such as IPF
- Determine possible disease subtypes and treatable traits
- Monitor response to targeted therapies
- Guide clinical decision making.

References:
[1] Travis et al., *Am J Respir Crit Care Med*, Vol 177. pp 1338-1347, 2008.
[2] Wang, JM, Robertson SH, Wang Z, et al. Thorax 2018;73:21-28
[3] Mammarappallil JG, et al. J Thorac Imaging 2019;34(2):136-150.
[4] Rankine LJ et al., American Thoracic Society [In Press.]
[5] Kaushik et al., MRM, 2016.

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