Center for Cancer Research

Xe-129 as a Replacement for He-3 in Hyperpolarized Lung Imaging

Murali Cherukuri (NCI), Simhan Danthi (NHLBI)
Work in my group:

$^{13}$C tracers for hyperpolarized tumor imaging in clinic in prostate, brain, and kidney cancers to define surgical margins.

Slides on hyperpolarized lung imaging with He-3 and Xe-129 presented today are from:
  Prof. John Mugler, U. Virginia
  Prof. Sean Fain, U. Wisconsin
  Prof. Dmitriy A. Yablonskiy, Washington University
Why He-3 MRI?
The burden of lung disease

- COPD: chronic obstructive pulmonary disease
  - 3rd leading cause of death in U.S.\(^1\)
  - More than 10 million adults in U.S. have COPD\(^2\) and an estimated 64 million worldwide\(^3\)
  - National cost of ~$50 billion\(^4\)

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\(^4\)NIH-NHLBI. Morbidity and Mortality: 2009 Chartbook on Cardiovascular, Lung and Blood Diseases.
The burden of lung disease

• Asthma
  ▪ Affects 19 million adults and 7 million children in U.S.1
  ▪ Leading cause of school absences from a chronic illness2
  ▪ National cost of ~$18 billion3

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The burden of lung disease

• CF: cystic fibrosis
  ▪ 2nd most common life-shortening, inherited disorder in U.S. children\(^1\)
  ▪ Affects ~30,000, with ~10 million genetic carriers\(^2\)
  ▪ Median age of survival less than 40 yrs\(^2\)

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\(^{2}\)Cystic Fibrosis Foundation. About Cystic Fibrosis: What You Need to Know. (www.cff.org/AboutCF/).
Standard of care: PFTs

• Advantages
  ✓ Functional information: ventilation, gas-exchange
  ✓ Widely available
  ✓ Inexpensive, easy to administer

• Disadvantages
  ✗ NO regional information
  ✗ Insensitive to early disease and gradual progression
  ✗ Issues with reproducibility

FEV$_1$: forced expiratory volume in 1 sec.

$^1$PFTs = Pulmonary Function Tests (spirometry, body plethysmography, DLCO)
Clinical modalities: CT

- Advantages
  - ✔ High spatial (sub-millimeter) and temporal resolution
  - ✔ Widely available
  - ✔ Quantitative evaluation of tissue density

- Disadvantages
  - ✗ Radiation (limitation for longitudinal or pediatric studies)
  - ✗ Spatial resolution less than alveolar size
  - ✗ Challenging to obtain direct functional information
Clinical modalities: Nuclear medicine

- Advantages
  - Functional information: ventilation, V/Q mismatch
  - Widely available

- Disadvantages
  - Radiation (limitation for longitudinal or pediatric studies)
  - Poor spatial and temporal resolution
  - Very limited structural information
Clinical modalities: Nuclear medicine

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Motivation:

• High health and societal impact of lung disease

• Clear need for improved regional assessment of lung structure & function
Conventional proton MRI

- Signal source
  - Nuclear magnetic moment ("spin") of protons in water & fat molecules
Conventional proton MRI

• Signal strength
  ▪ Alignment (nuclear polarization) of spins in scanner magnet
  ▪ Proportional to magnet strength ($B_o$)
  ▪ Polarization on the order of parts per million ($\sim 10^{-5}$)
Conventional (¹H) MRI
Hyperpolarized-gas MRI

- **Signal source**
  - Nuclear magnetic moment of helium-3 or xenon-129 noble-gas atoms

- **Helium-3 ($^3$He)**
  - Rare isotope of helium
  - Product of tritium ($^3$H) decay

- **Xenon-129 ($^{129}$Xe)**
  - Natural component of atmosphere (0.001%)
  - 26% isotopic abundance
Hyperpolarized-gas MRI

• Signal strength
  ▪ Nuclear polarization created by external laser-based device ("polarizer")
  ▪ Independent of scanner magnet strength
  ▪ Polarization ~50%
Hyperpolarized-gas imaging protocol

1. POLARIZE
2. DISPENSE
3. INHALE
4. IMAGE

3He flexible chest coil
Dynamic Imaging of Respiratory Maneuvers

Imaging of Ventilation

Conventional (¹H) and Hyperpolarized ³He MRI

³He MRI
Moderate Asthma

³He MRI Normal

³He MRI Normal

³He MRI Normal

³He MRI Normal

¹H MRI Normal

¹H MRI Normal

¹H MRI Normal

Severe Asthma

Severe Asthma

Lung function & structure with $^3\text{He}$

- Ventilation
- Microstructure
- Alveolar oxygen concentration
- Pulmonary biomechanics
**Ventilation**

- **Static**: distribution of gas following inhalation
  - Low-flip-angle gradient-echo pulse sequence during breath hold
- Pathology induces ventilation “defects”
Ventilation

• Dynamic: distribution of gas during respiration
  ▪ Repeated acquisition using low-flip-angle GRE pulse sequence
  ▪ Spiral or radial $k$-space sampling

• Air trapping

• Gas washout rate and quantitative (specific) ventilation

Fig. 3 from MH Deppe et al. ISMRM 2011; 910
Ventilation: Applications in disease

- COPD / Emphysema
- Asthma
- Cystic fibrosis
- Lung transplant / rejection
Asthma: Provocation & treatment

Provocation: Exercise

Baseline: FEV$_1$ 103%
Post-exercise: FEV$_1$ 40%

Treatment: Albuterol

Baseline: FEV$_1$ 36%
Post-Albuterol: FEV$_1$ 57%

$^3$He in short supply.

Supply issue focuses attention on the alternative agent: $^{129}\text{Xe}$
$^{129}$Xe to the rescue:

Is $^{129}$Xe a viable replacement for $^3$He?
### $^{129}$Xe vs. $^3$He for lung MRI

<table>
<thead>
<tr>
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<th>$^{129}$Xe</th>
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<td>32.4</td>
<td>11.8</td>
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<td>Diffusivity in air [cm$^2$/s]</td>
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- $^3$He easier to polarize
- Advances in $^{129}$Xe polarization needed
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- $^{129}$Xe can probe pulmonary gas exchange
- $^{129}$Xe has anesthetic side effects
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<td>Sensitivity to local environment</td>
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- ~200 ppm range of chemical shifts for $^{129}$Xe
$^{129}\text{Xe}$ vs. $^{3}\text{He}$: Ventilation
129Xe ventilation in disease

Asthma

COPD

Cystic Fibrosis
$^{129}\text{Xe}$ vs. $^{3}\text{He}$: ADC

$^{129}\text{Xe}$

Healthy  COPD

$^{3}\text{He}$

Healthy  COPD

0.0 cm²/s  0.12 cm²/s  0.85 cm²/s
$^{129}\text{Xe in the lung}$

- "gas phase" → ventilation
  - ~98% of $^{129}\text{Xe}$
- "dissolved phase" → gas uptake
  - ~2% of $^{129}\text{Xe}$

Amplitude vs. Chemical shift [ppm] (∝ frequency)

Airspaces, lung parenchyma/plasma, red blood cells
$^{129}$Xe to the rescue:

- For applications pioneered with $^3$He, $^{129}$Xe can provide comparable results.
- Added value of $^{129}$Xe in providing regional quantification of gas uptake or exchange.
Motivation

COAST
Childhood Origins of ASThma

A prospective birth cohort study designed to evaluate genetic and environmental factors contributing to the development of childhood asthma

• 287 children enrolled at birth
• At-risk: Parental allergies and asthma
• Key Collaboration – PI Dr. Robert Lemanske, Pediatrics and Allergy and Immunology, Medical Physics, Radiology

Funded by the NHLBI
Summary

• Lung disease is a major worldwide health issue with substantial societal impact.

• Hyperpolarized-gas MRI offers unique functional & structural information about the healthy & diseased lung.

• Xe-129 can be used as an alternate to He-3

• He-3 is the only choice for pediatrics.