

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

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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 COPD² and an estimated 64 million worldwide³
 - National cost of ~\$50 billion⁴



¹CDC. Natl Center for Health Statistics. Final Vital Statistics Report. Deaths: Final Data for 2007.

²CDC. Natl Center for Health Statistics: Natl Health Interview Survey Raw Data, 2008. Analysis by American Lung Assoc.

³The global burden of disease: 2004 update, published 2008.

⁴NIH-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



¹CDC. Natl Center for Health Statistics. Summary Health Statistics: National Health Interview Survey, 2010.

²Condition of Education, NCES, U.S. Department of Education 2001.

³The Costs of Asthma, Asthma and Allergy Foundation 1992 and 1998 Study, 2000 Update.

The burden of lung disease

- CF: cystic fibrosis
 - 2nd most common life-shortening, inherited disorder in U.S. children¹
 - Affects ~30,000, with ~10 million genetic carriers²
 - Median age of survival less than 40 yrs²



¹CDC. Newborn Screening for Cystic Fibrosis. Morbidity and Mortality Weekly Report. October 15, 2004; 53(RR13):1-36.

²Cystic 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



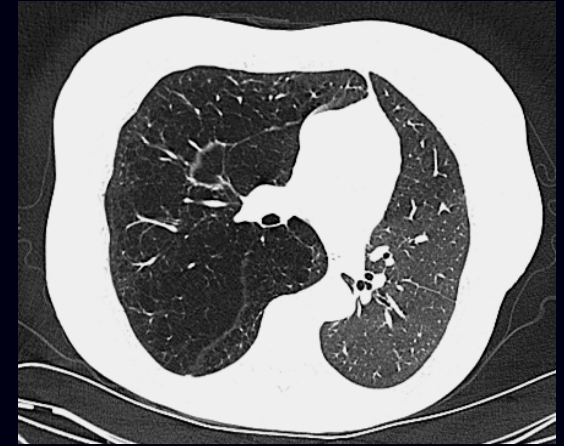
FEV₁: forced expiratory volume in 1 sec.

¹PFTs = 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



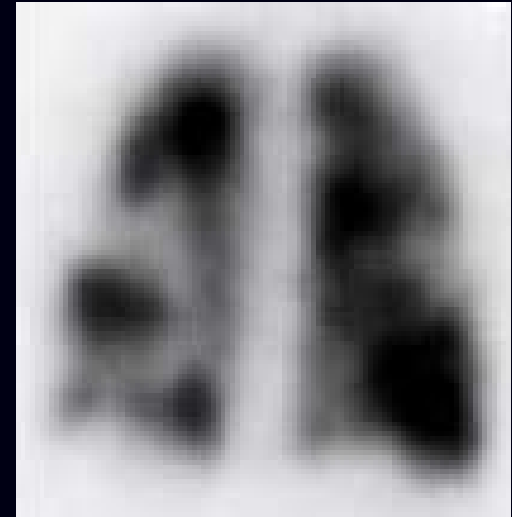
- **Disadvantages**

- ✗ 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**



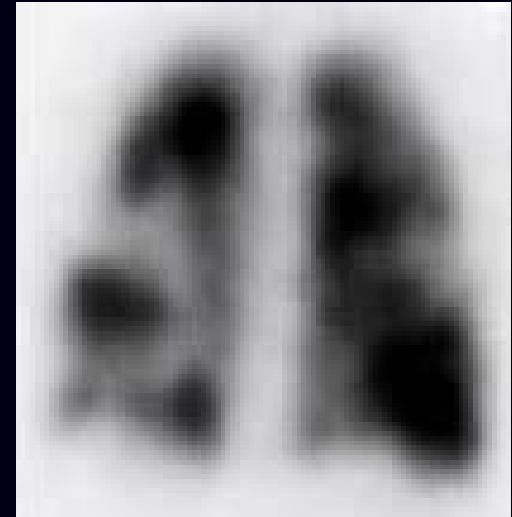
- **Disadvantages**

- ✗ **Radiation (limitation for longitudinal or pediatric studies)**
- ✗ **Poor spatial and temporal resolution**
- ✗ **Very limited structural information**

Clinical modalities: Nuclear medicine

- **Advantages**

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



- **Disadvantages**

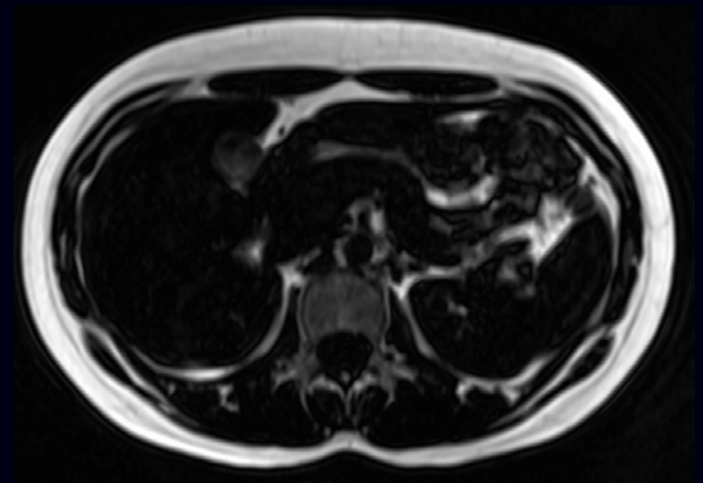
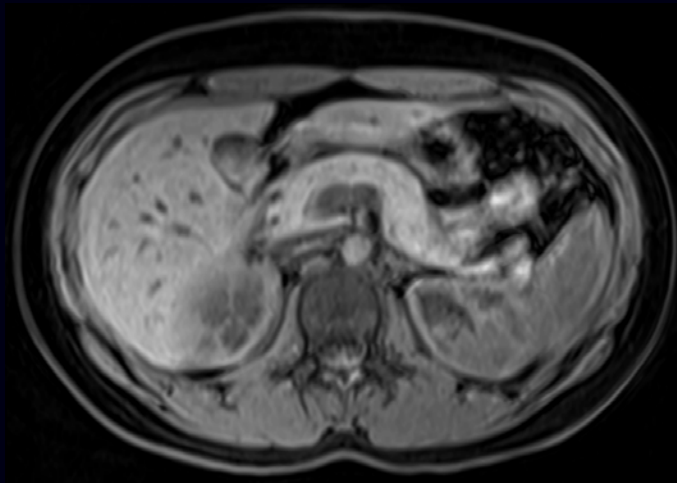
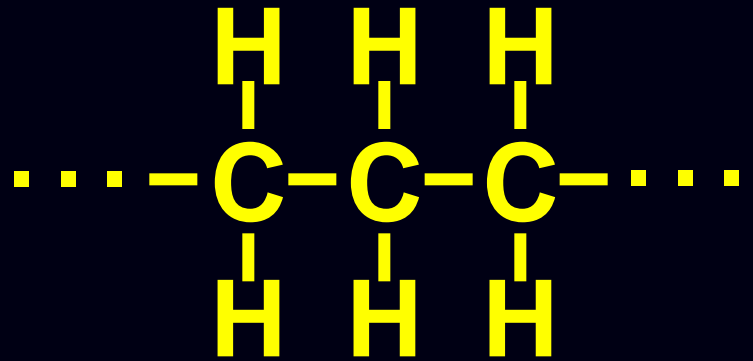
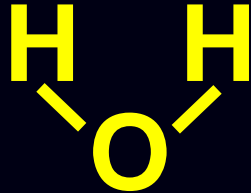
- ✗ **Radiation (limitation for longitudinal or pediatric studies)**
- ✗ **Poor spatial and temporal resolution**
- ✗ **Very limited structural information**

Motivation:

- High health and societal impact of lung disease
- Clear need for improved regional assessment of lung structure & function

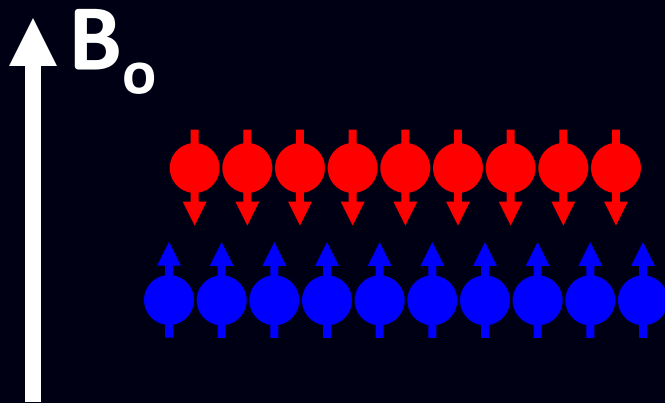
Conventional proton MRI

- Signal source
 - Nuclear magnetic moment (“spin”) of protons in water & fat molecules

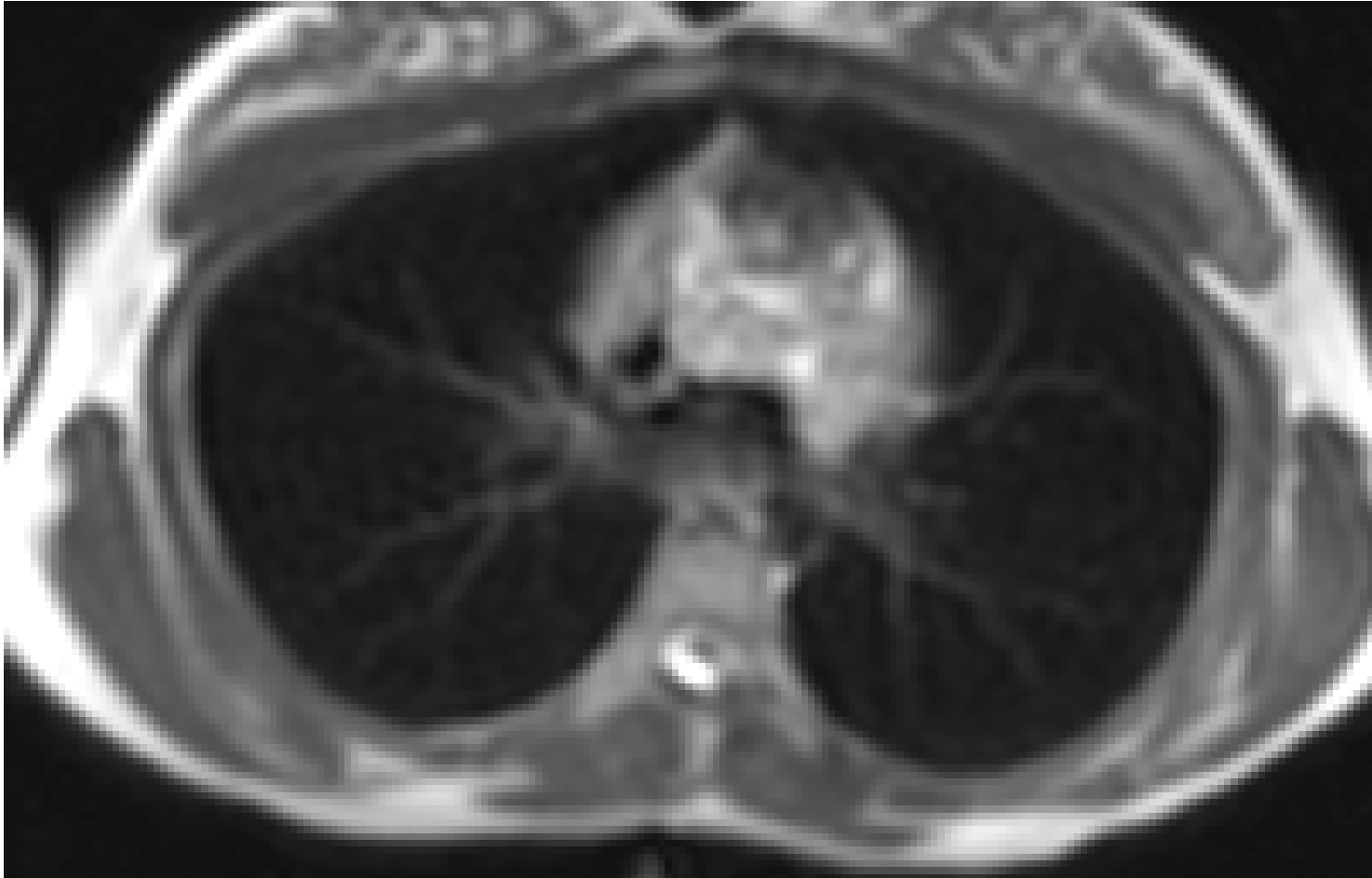


Conventional proton MRI

- Signal strength
 - Alignment (nuclear polarization) of spins in scanner magnet
 - Proportional to magnet strength (B_0)
 - Polarization on the order of parts per million ($\sim 10^{-5}$)

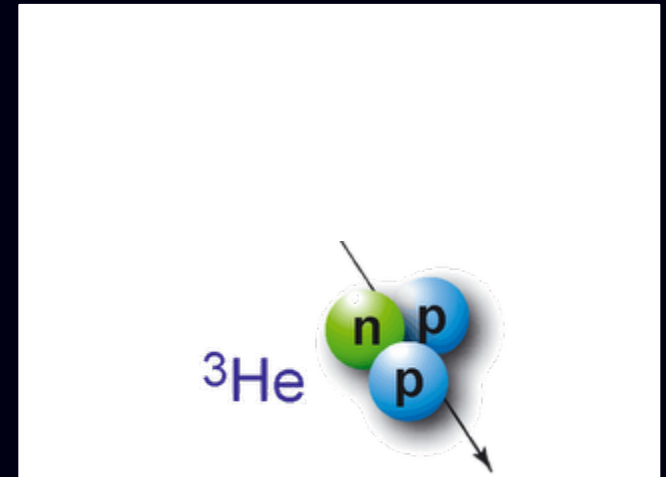


Conventional (^1H) MRI



Hyperpolarized-gas MRI

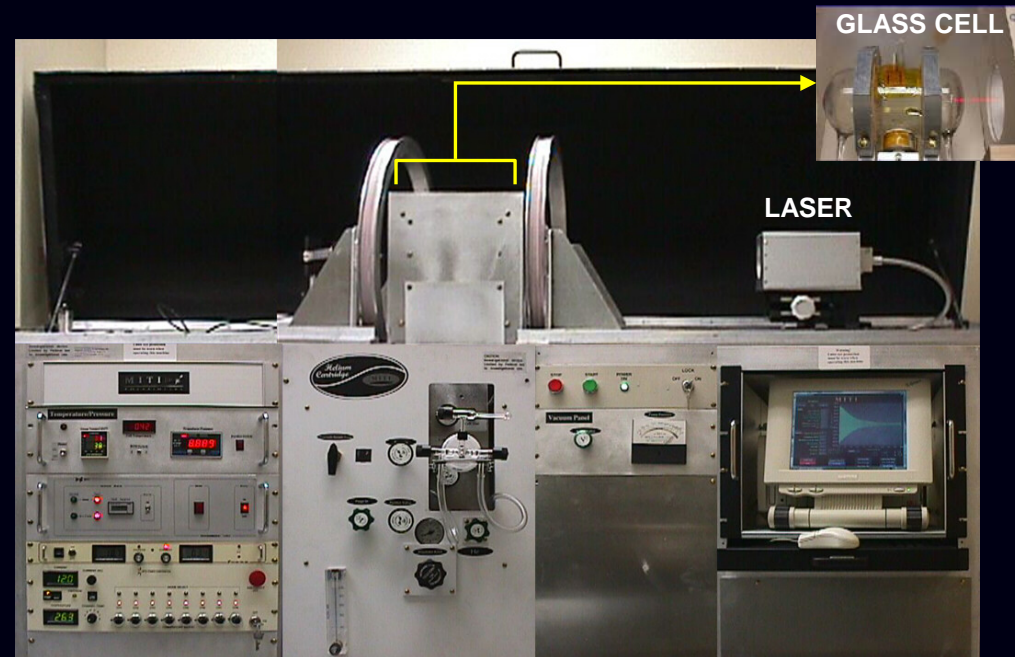
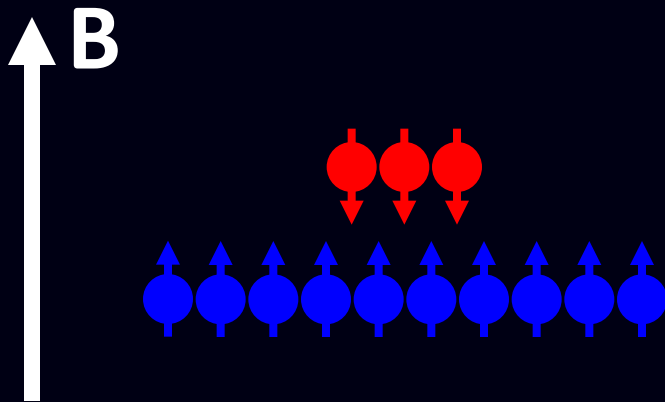
- Signal source
 - Nuclear magnetic moment of helium-3 or xenon-129 noble-gas atoms
- Helium-3 (^3He)
 - Rare isotope of helium
 - Product of tritium (^3H) decay
- Xenon-129 (^{129}Xe)
 - Natural component of atmosphere (0.001%)
 - 26% isotopic abundance



tecno-chemistry.blogspot.com

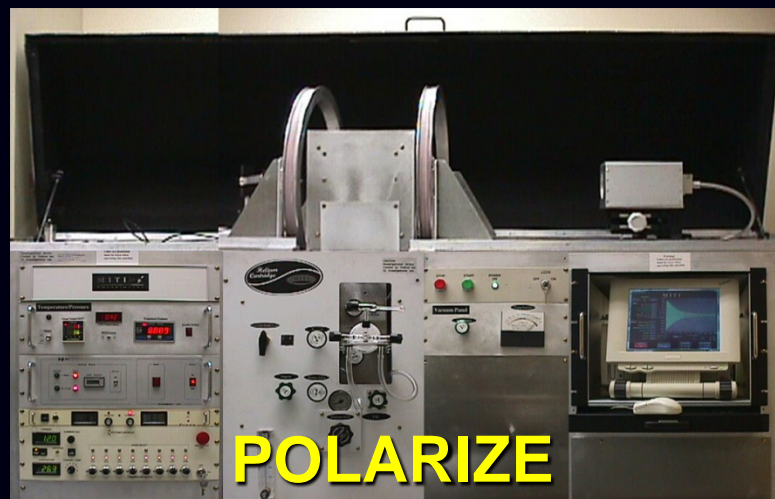
Hyperpolarized-gas MRI

- Signal strength
 - Nuclear polarization created by external laser-based device (“polarizer”)
 - Independent of scanner magnet strength
 - Polarization ~50%



Hyperpolarized-gas imaging protocol

1



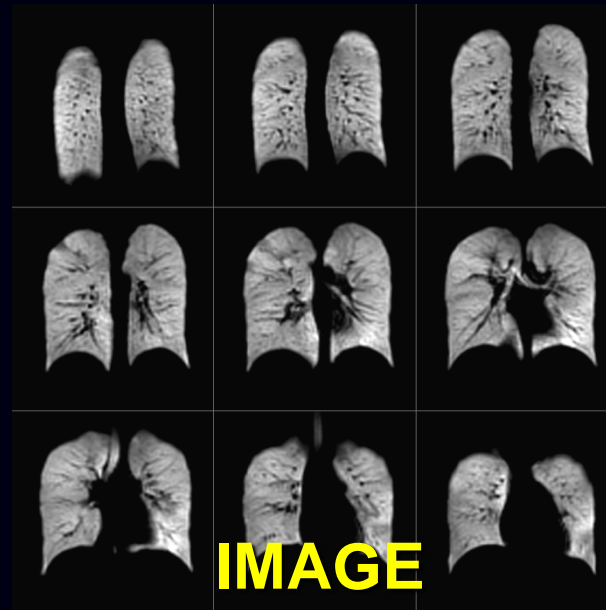
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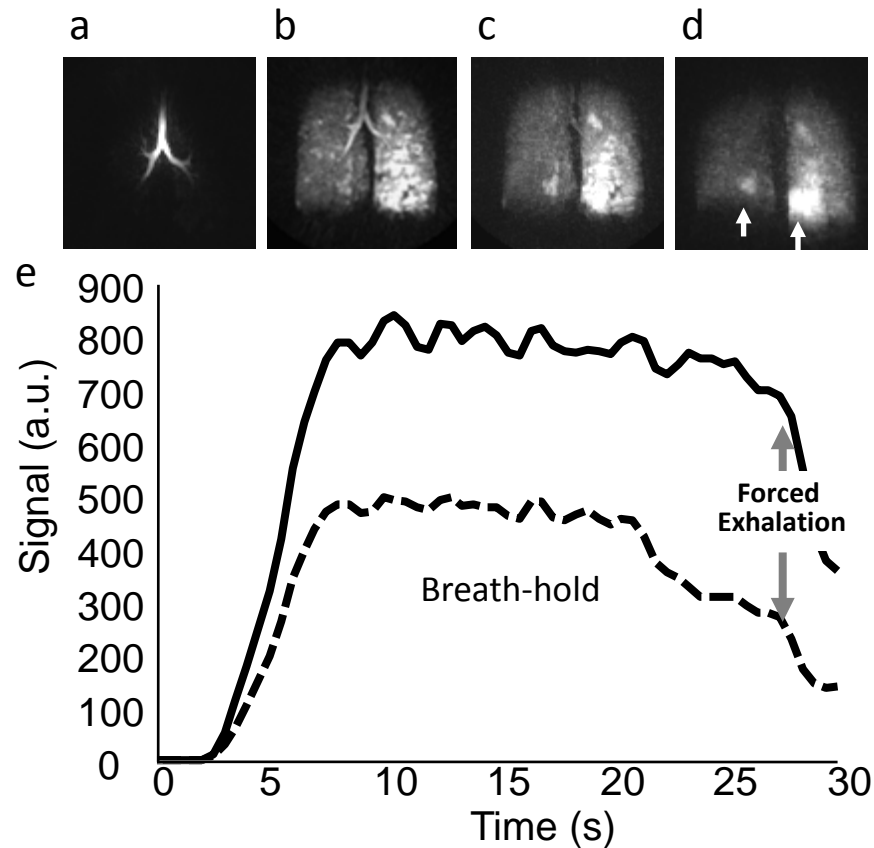
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4



Dynamic Imaging of Respiratory Maneuvers



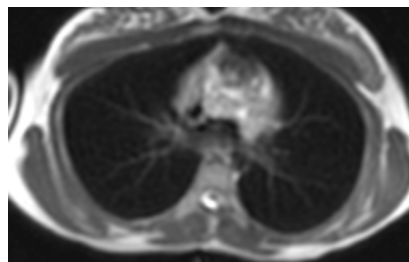
Holmes, JH et al. Magn Reson Med. 2009 Dec;62(6):1543-56.

Imaging of Ventilation

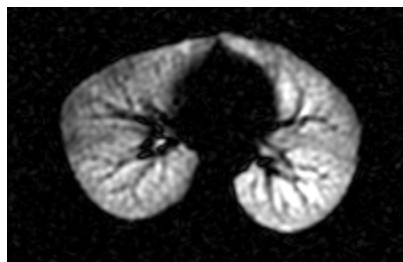
Conventional (^1H) and Hyperpolarized ^3He MRI

^3He MRI

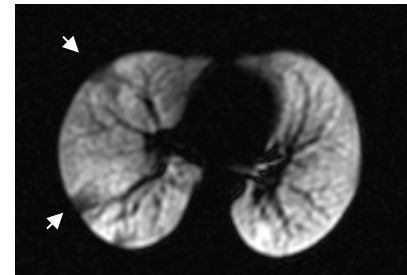
^1H MRI Normal



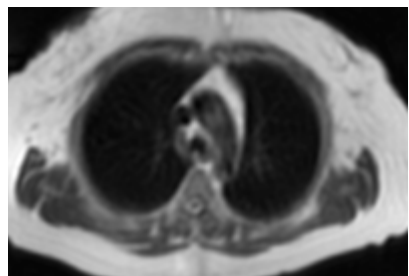
^3He MRI Normal



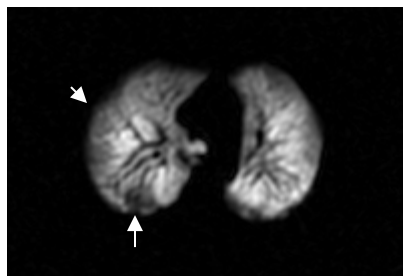
Moderate Asthma



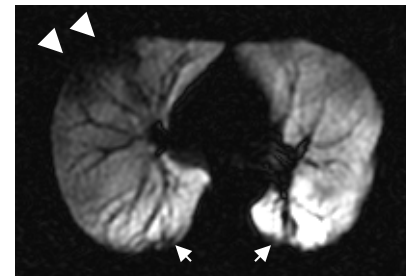
^1H MRI Normal



^3He MRI Normal



Severe Asthma



Castro et al., "Lung imaging in Asthma: The picture is clearer," JACI J Allergy Clin Immunol. 2011 May 31.

Lung function & structure with ^3He

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

Ventilation

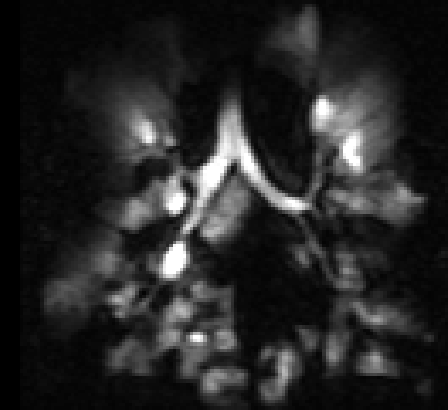
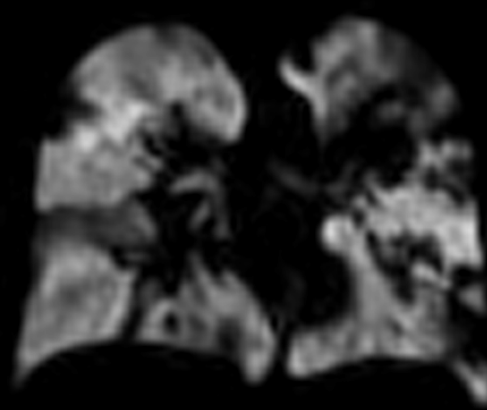
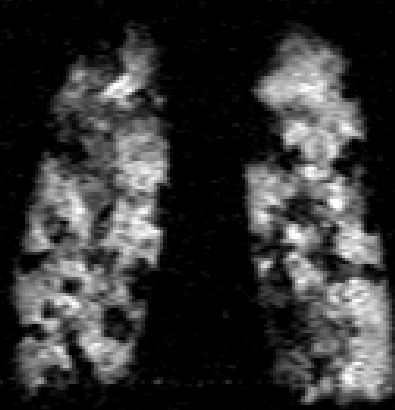
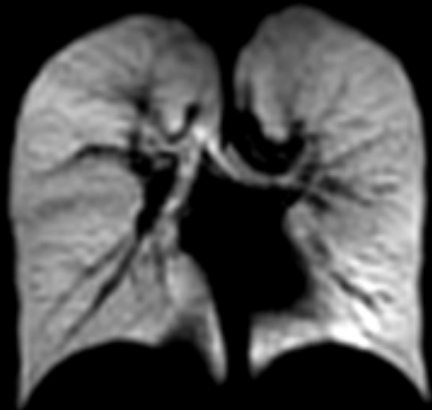
- **Static: distribution of gas following inhalation**
 - Low-flip-angle gradient-echo pulse sequence during breath hold
- **Pathology induces ventilation “defects”**

Healthy

Heavy Smoker

Cystic Fibrosis

COPD



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**

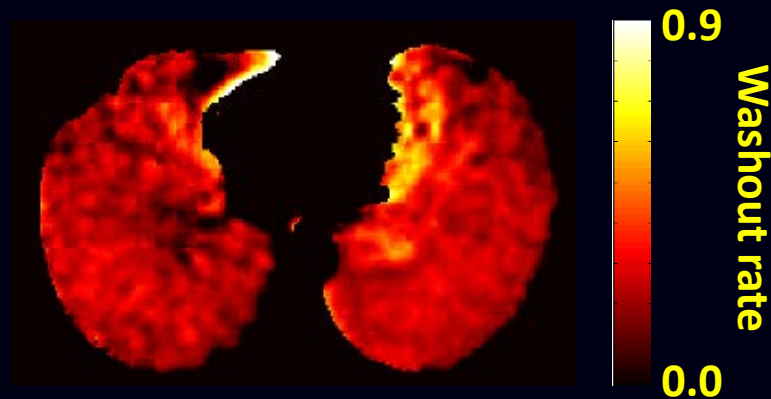


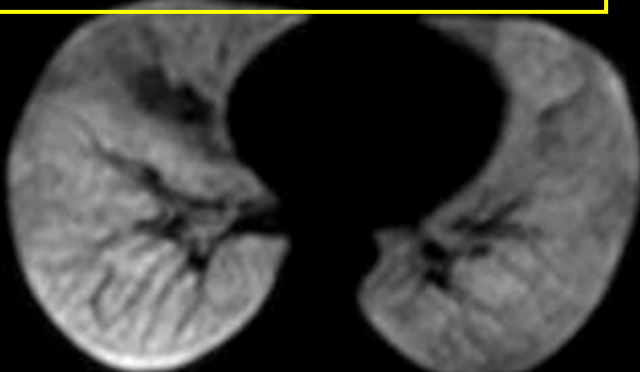
Fig. 3 from MH Deppe et al. ISMRM 2011; 910

Ventilation: Applications in disease

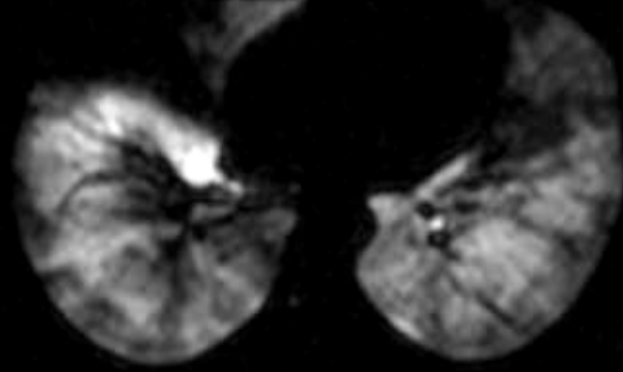
- **COPD / Emphysema**
- **Asthma**
- **Cystic fibrosis**
- **Lung transplant / rejection**

Asthma: Provocation & treatment

Provocation: Exercise

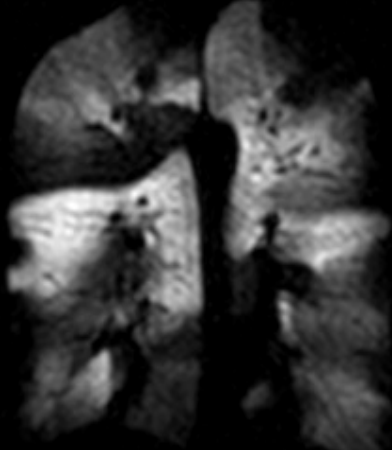


Baseline: FEV₁ 103%

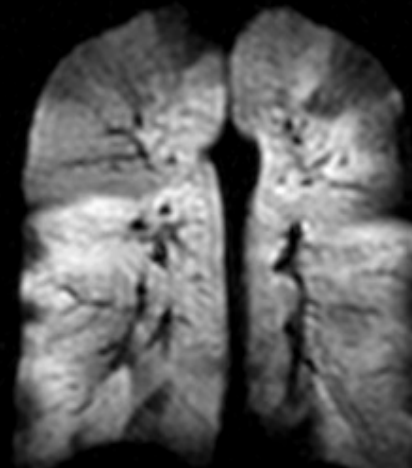


Post-exercise: FEV₁ 40%

Treatment: Albuterol



Baseline: FEV₁ 36%



Post-Albuterol: FEV₁ 57%

^3He in short supply.

**Supply issue focuses attention
on the alternative agent: ^{129}Xe**

^{129}Xe to the rescue:

Is ^{129}Xe a viable replacement for ^3He ?

^{129}Xe vs. ^3He for lung MRI

	^3He	^{129}Xe
Gyromagnetic ratio (γ) [MHz/T]	32.4	11.8
Diffusivity in air [cm^2/s]	~0.9	~0.1
Polarization for ~1 L (historic)	~50%	~10%

- ^3He easier to polarize
- Advances in ^{129}Xe polarization needed

^{129}Xe vs. ^3He for lung MRI

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Diffusivity in air [cm²/s]	~0.9	~0.1
Polarization for ~1 L (historic)	~50%	~10%
Solubility	negligible	high in lipids

- ^{129}Xe can probe pulmonary gas exchange
- ^{129}Xe has anesthetic side effects

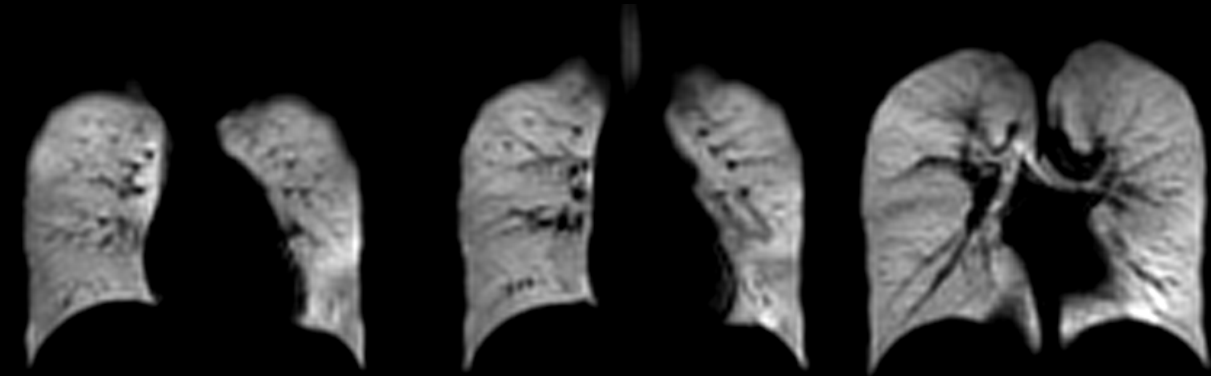
^{129}Xe vs. ^3He for lung MRI

	^3He	^{129}Xe
Gyromagnetic ratio (γ) [MHz/T]	32.4	11.8
Diffusivity in air [cm^2/s]	~ 0.9	~ 0.1
Polarization for ~ 1 L (historic)	$\sim 50\%$	$\sim 10\%$
Solubility	negligible	high in lipids
Sensitivity to local environment	negligible	exquisite

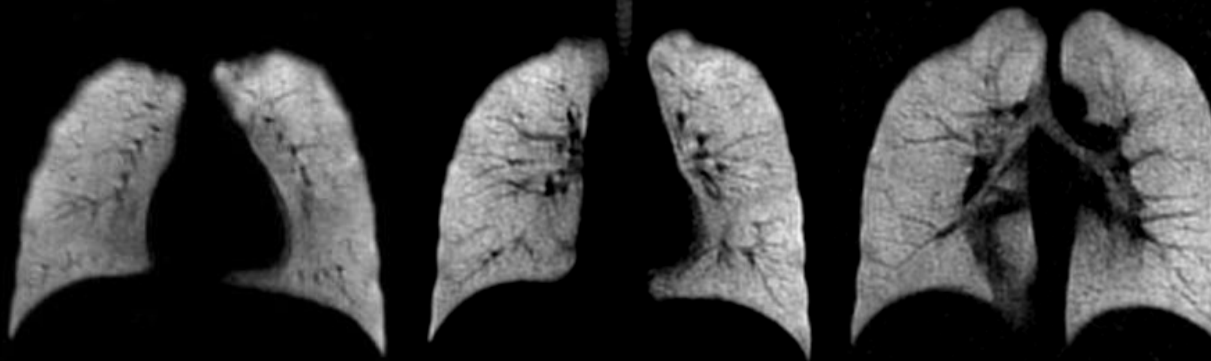
- ~ 200 ppm range of chemical shifts for ^{129}Xe

^{129}Xe vs. ^3He : Ventilation

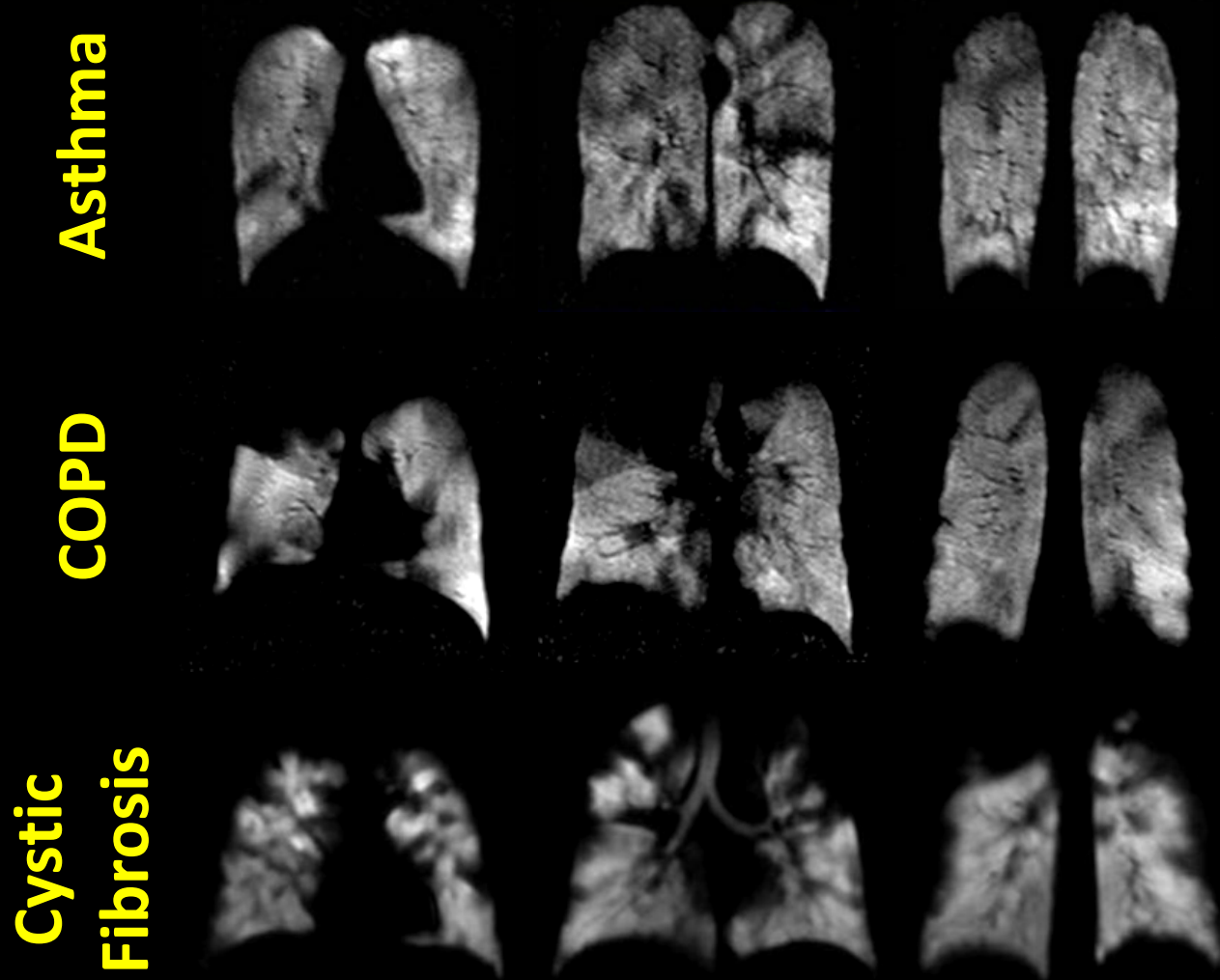
^3He



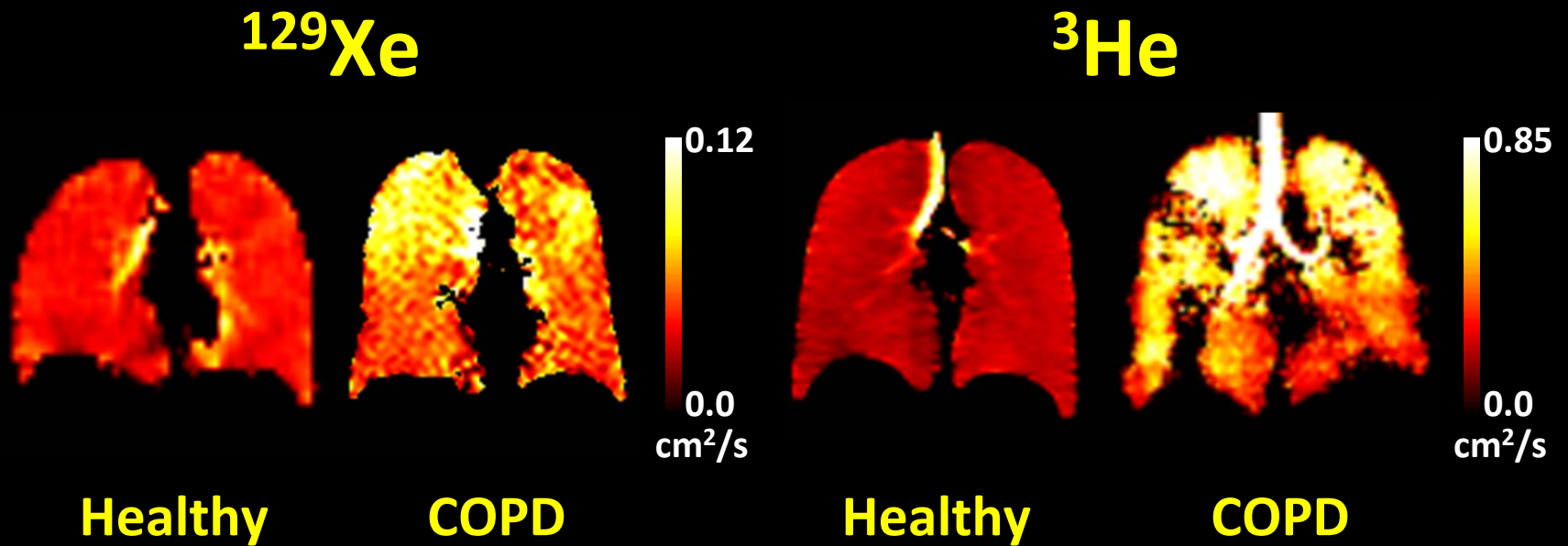
^{129}Xe



^{129}Xe ventilation in disease



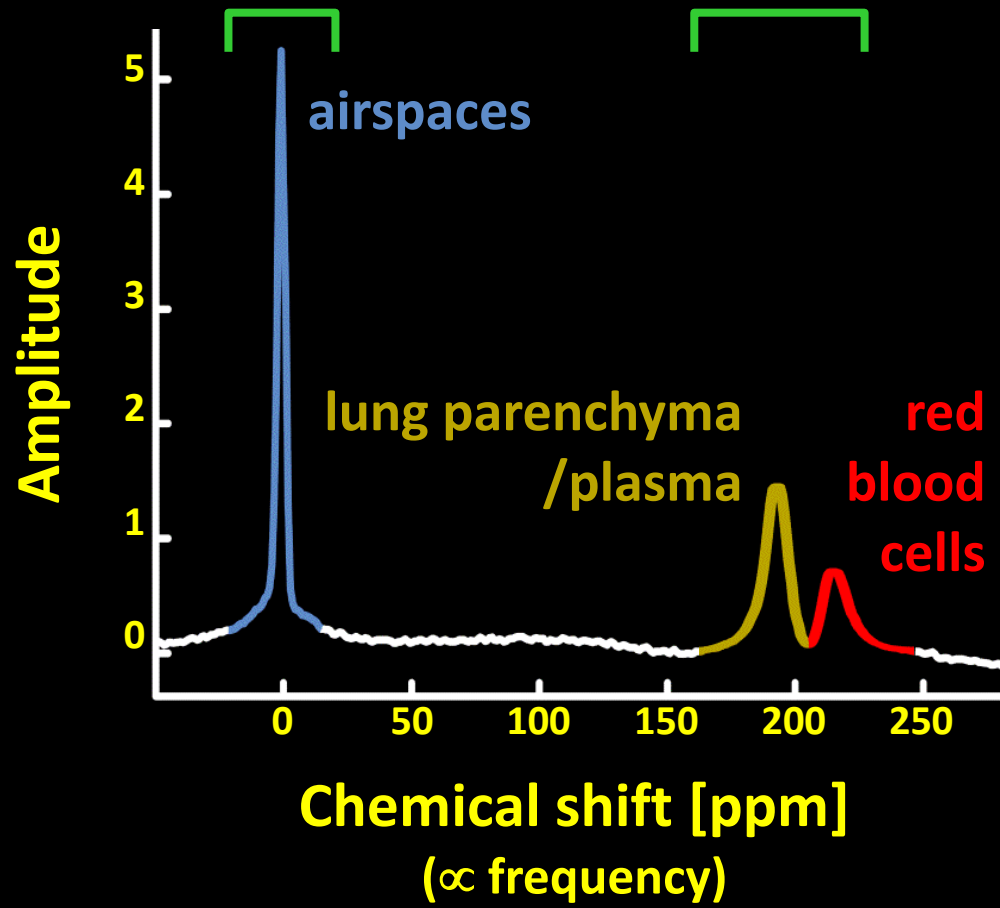
^{129}Xe vs. ^3He : ADC



^{129}Xe in the lung

“gas phase”
→ ventilation
~98% of ^{129}Xe

“dissolved phase”
→ gas uptake
~2% of ^{129}Xe



^{129}Xe to the rescue:

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



C O A S T

Childhood

Origins of

A S T h m a

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*

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.