Seeing is Believing: New Imaging Physics to Transform Asthma Patient Outcomes

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May 13, 2018 1200-1230hrs Halifax NS CANADA

Schulich MEDICINE & DENTISTRY

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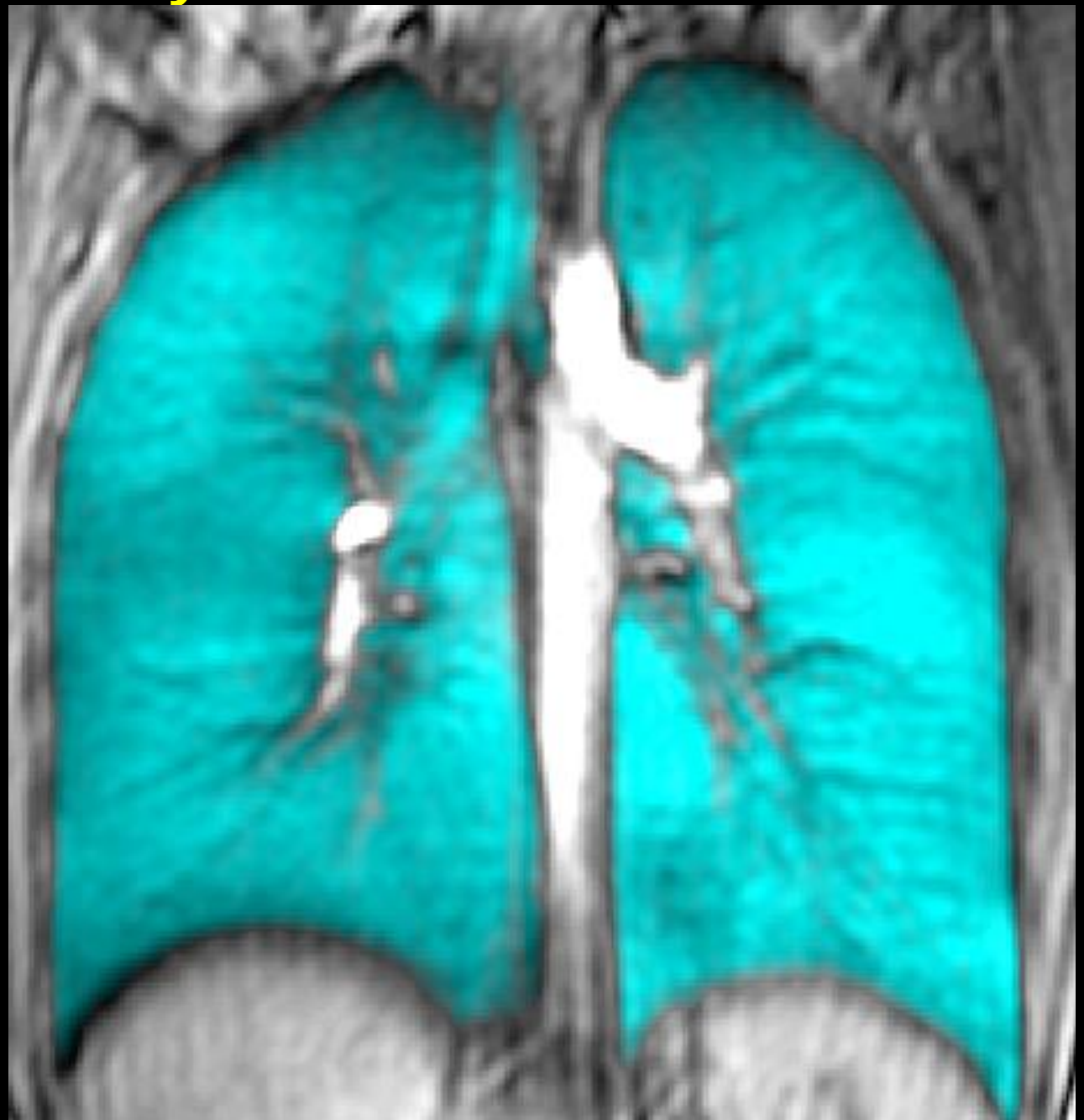
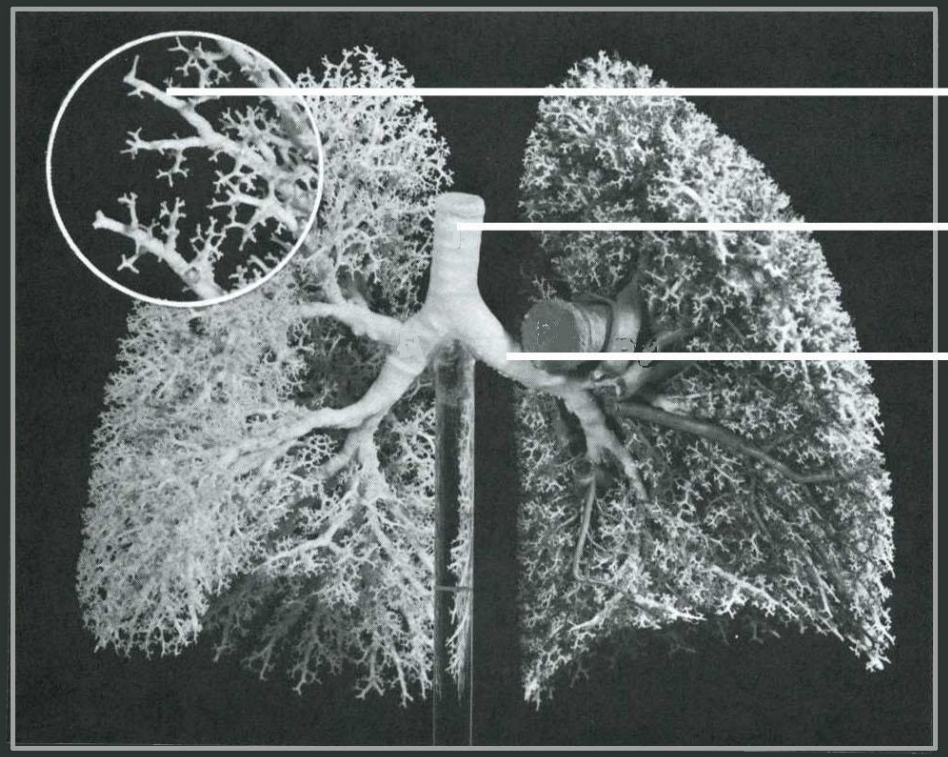
Pulmonary MRI: Structure & Function

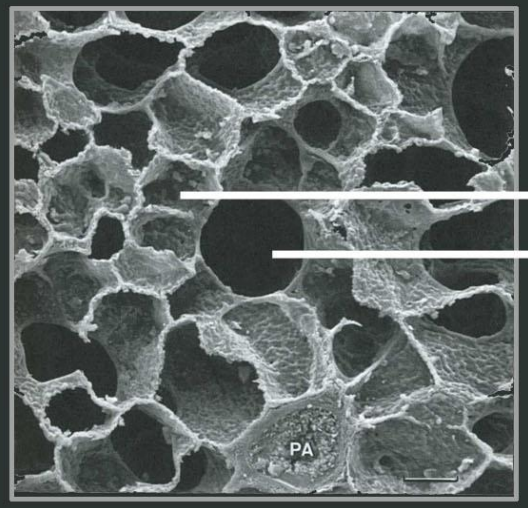


- Conventional MRI measures environment of protons in tissue
- No ionizing radiation
- Inhaled $^{3}He/^{129}Xe/^{19}F$ functional MRI



- 2400km airways

- ~15 breaths/min
- ~450 breaths/this talk!
- ~1B breaths/lifetime



- 300M alveoli d=300nm

Breathing: When things go wrong

World Health Organization

The Burden of Lung Disease: Asthma

→ ***Most common*** chronic childhood disease[1]

→ ***Single largest*** cause of hospitalization of Canadian kids[3]

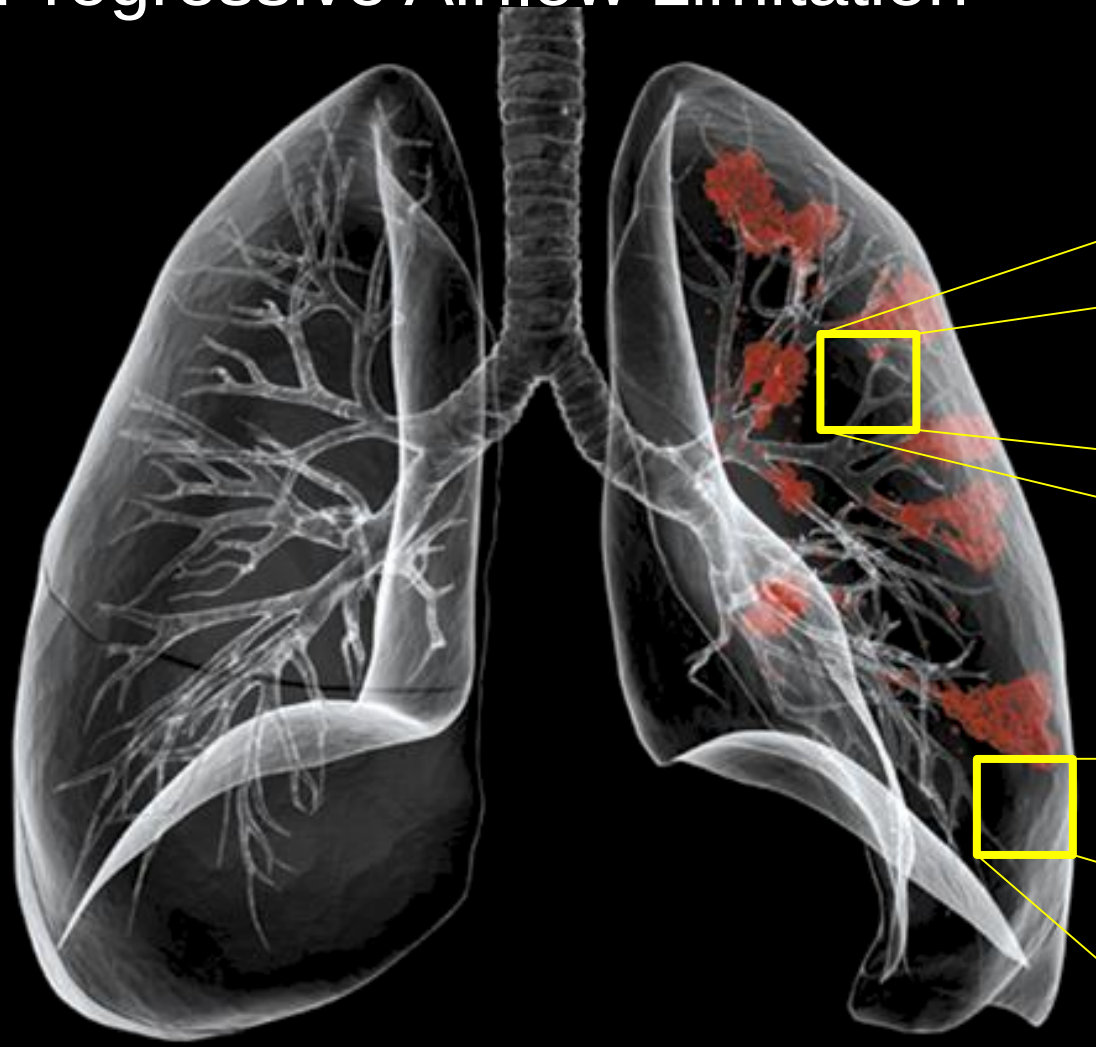
→ ***Single largest*** cause of school absence & ***3rd*** leading cause of work loss[4] ~2M Ontarians ~ 25% children

Ontario Total Health Care Costs		
	2011	**2041**
Lung Cancer	$293.9 million	$33.5 billion
Asthma	$1.8 billion	$100 billion
COPD	$3.9 billion	$311 billion

1. Garner et al. *2008*. 2. GINA 2014, 3. Harrison et al. *1992*. 4. OASIS, *2013*.

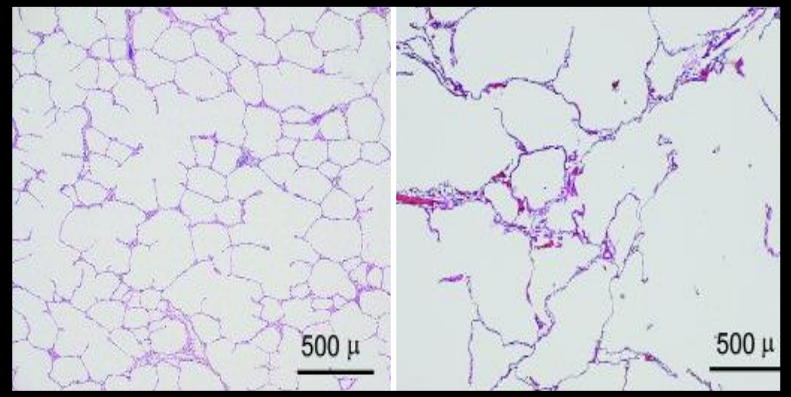
Diseased Airways and Airspaces

Progressive Airflow Limitation



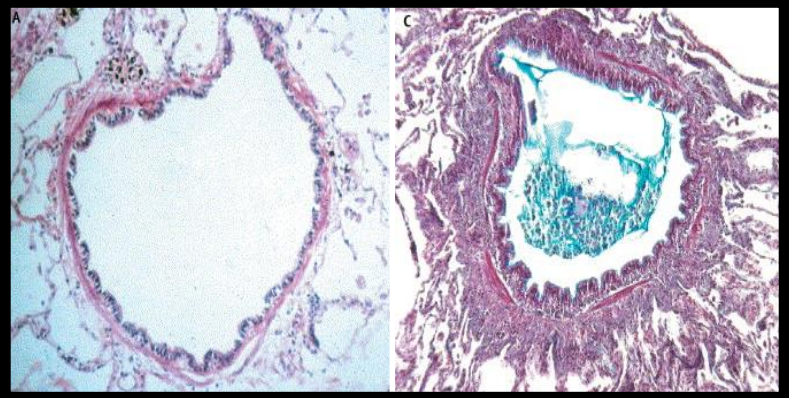
Parenchyma

Healthy Disease



Airways

Healthy Disease



Images adapted from: Hogg *et. al. Lancet (*2004) ; Woods *et. al. MRM (*2006)

Can imaging biomarkers help?

- *Provide sensitive, specific, precise & accurate measurements that can be used to:*

- Directly measure disease pathologies
- Quantify Tx response / Discover & develop new Tx

- Phenotype patients for personalized treatment
- Guide treatment decisions

- Predict & improve patient outcomes

Hyperpolarized Inhaled Gas Pulmonary MRI

Advantages

→ Functional information
→ Objective and independent of patient effort
→ High temporal & spatial resolution
→ FAST, 7-15s image acquisition!!!
→ No ionizing radiation = safe for serial & longitudinal evaluation

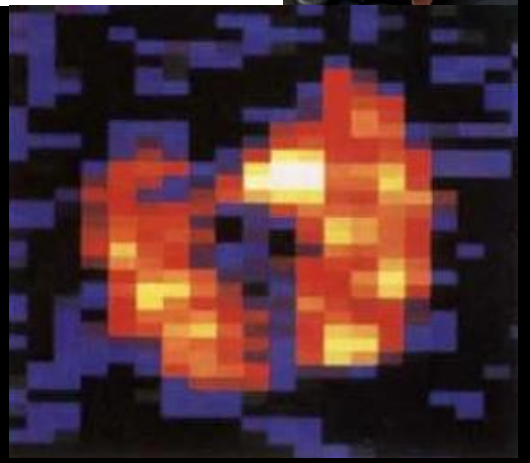
Letter

Biological magnetic resonance imaging using laser-polarized ^{129}Xe

M. S. Albert, G. D. Cates, B. Driehuys, W. Happer, B. Saam, C. S. Springer Jr & A. Wishnia

Nature **370**, 199–201 (21 July 1994)
doi:10.1038/370199a0

Received: 07 February 1994
Accepted: 07 June 1994



Canadian Centres

→ 2004: Robarts Research Institute, Western University
→ 2011: Thunder Bay Regional Research Institute, Lakehead University
→ 2013: SickKids, University of Toronto
→ **2018: St. Joseph's Healthcare Hamilton, McMaster University**

^{129}Xe and ^{3}He MRI: Requirements/Challenges

Requirements…

→ Coils, polarizer, gas, expertise

Challenges…

→ Relatively expensive ($200/dose)

→ Current access to methods are limited

→ Regulatory approval needed (& underway)

→ Divergent, disruptive (why bother: FEV_1 is OK)

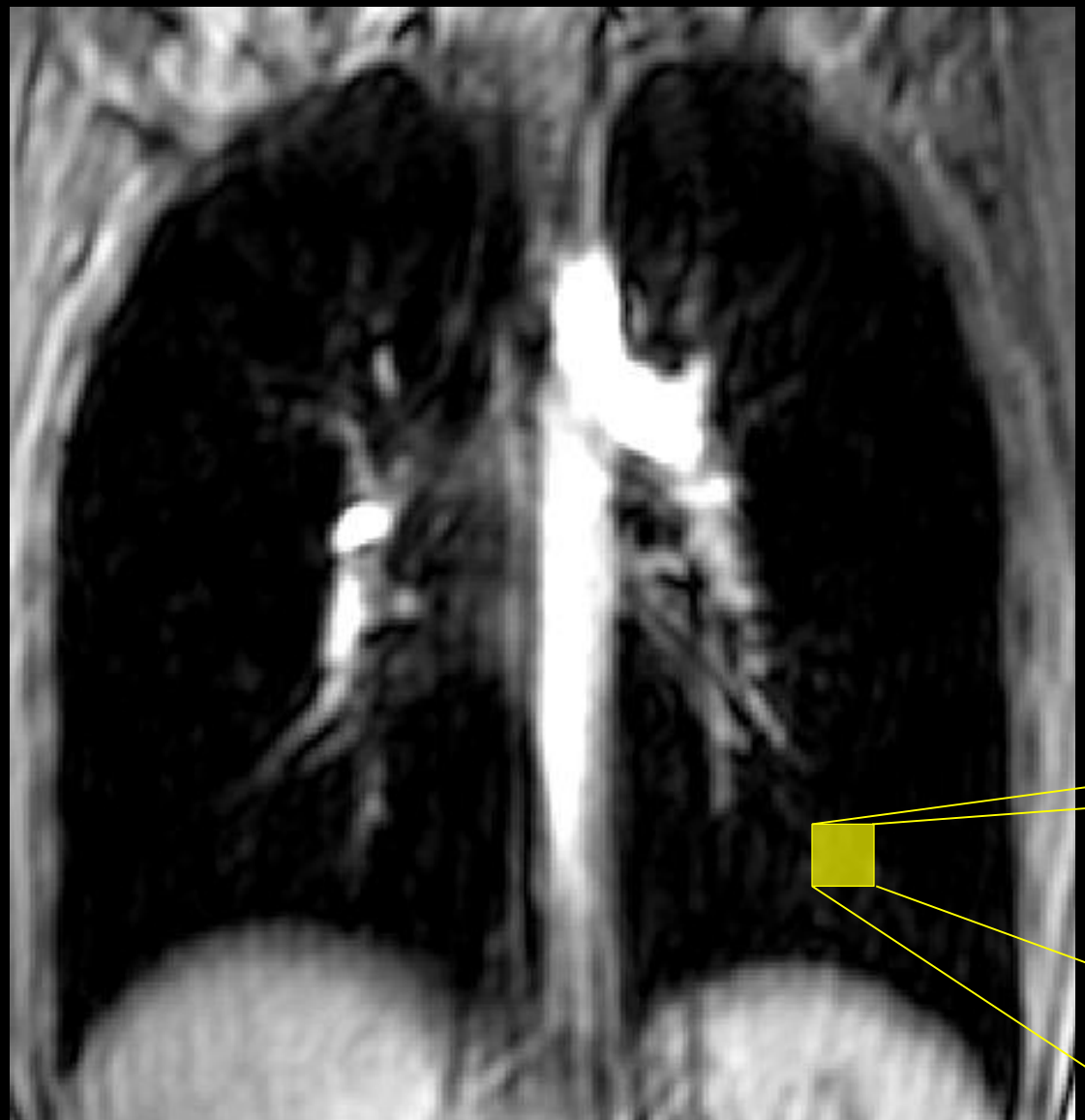
→ Validation still required

→ Image processing pipelines still required

→ Driven by Physics, Engineering? Respirology? Radiology?

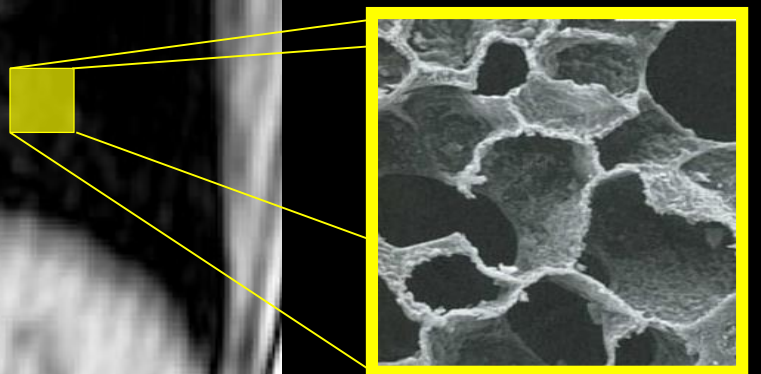
Conventional Pulmonary ^{1}H MRI

Conventional ^{1}H MRI

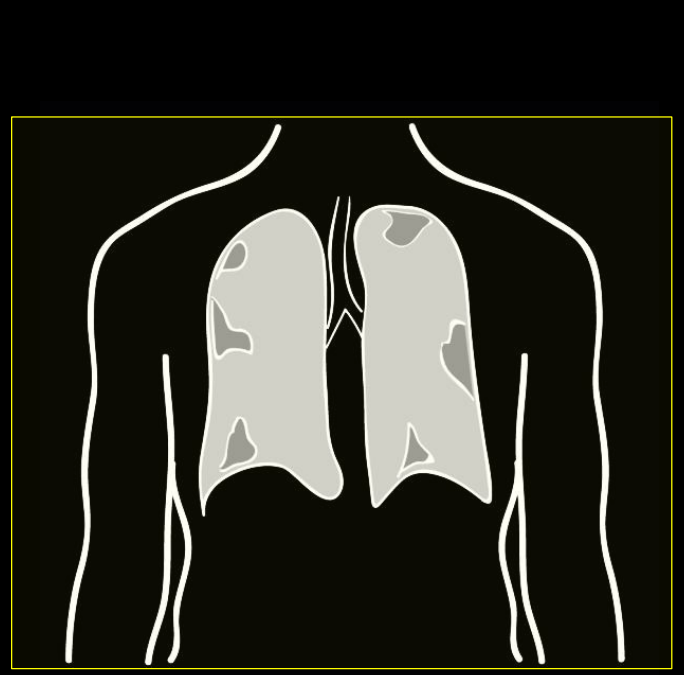


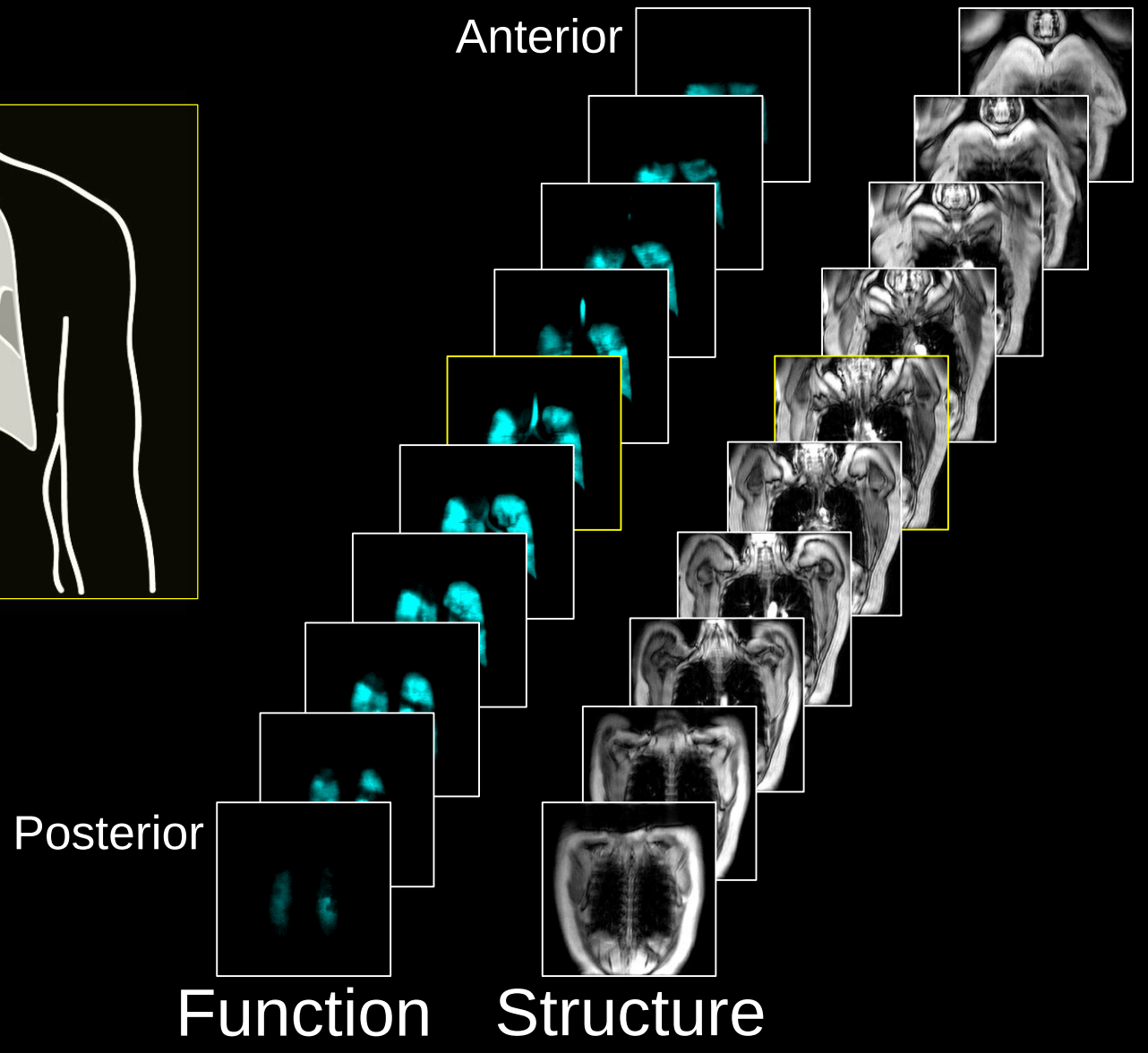
Measures environment of protons → lung structure

Low signal due to high gas density



Hyperpolarized Gas MRI Acquisition Fundamentals



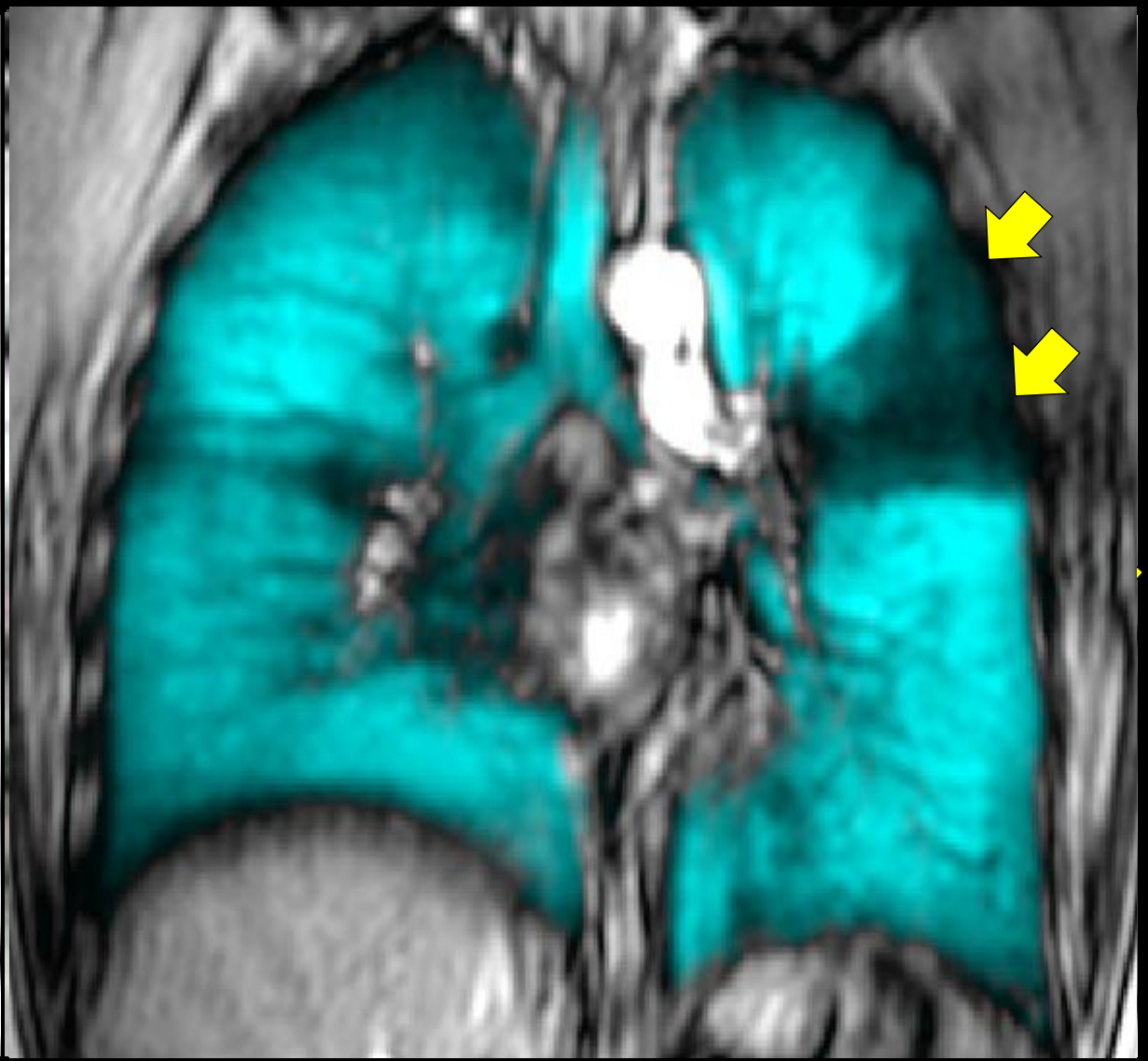


This is what Asthma looks like: MRI & CT

Healthy

26 y/o F; FEV_1=102%$_{pred}$

Asthma



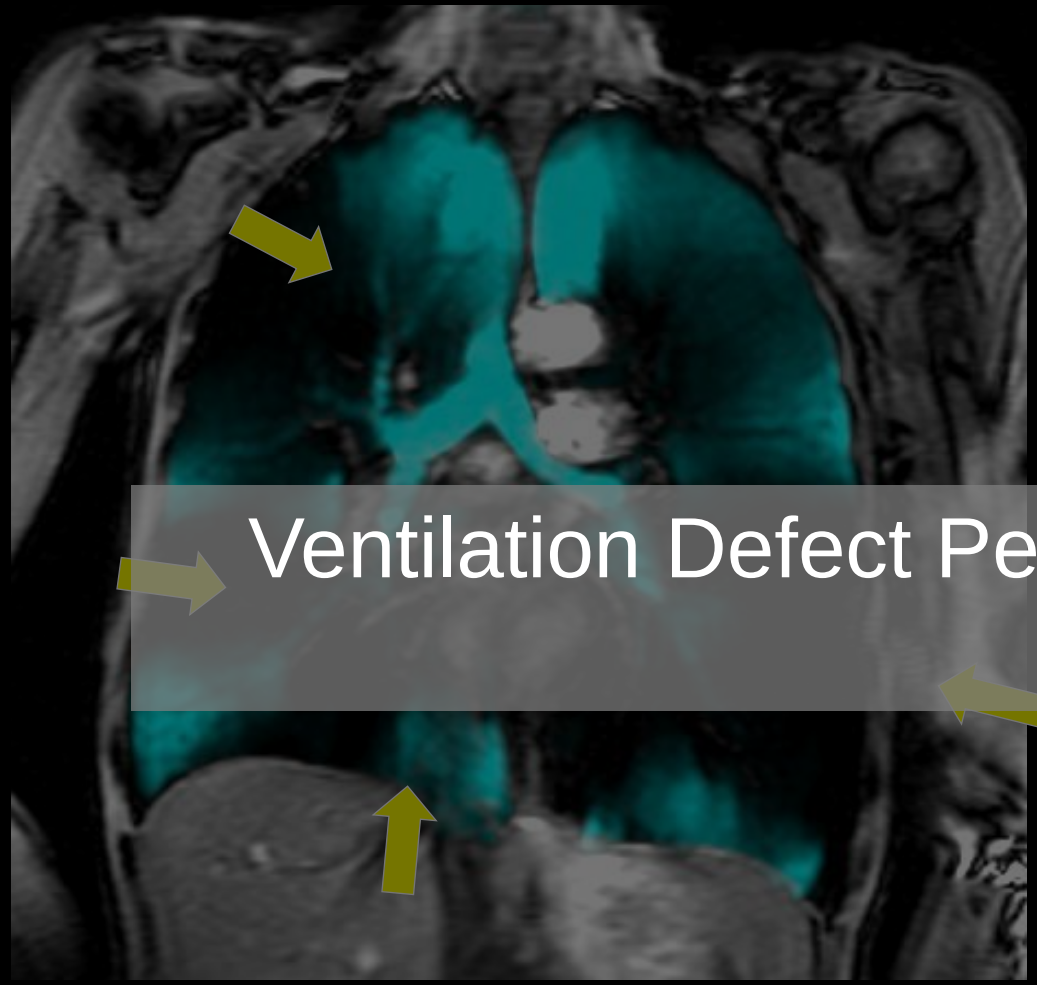
44 y/o F; FEV_1=95%$_{pred}$

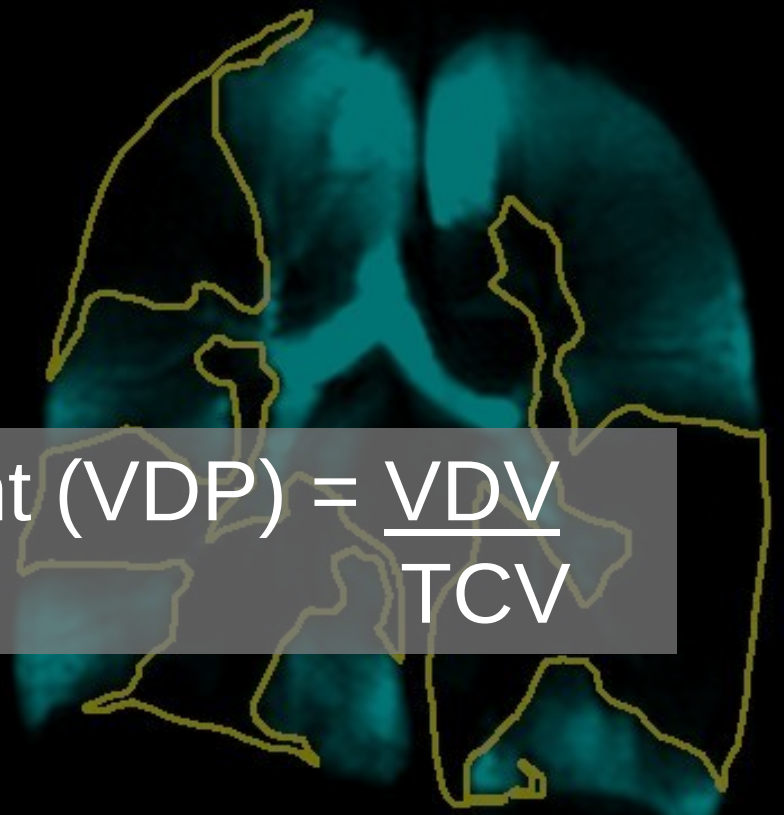
Can we Quantify and Automate
Ventilation Defect Measurements?

Quantitative MRI Biomarkers of Lung Ventilation

Co-Registration

Segmentation





$$\text{Ventilation Defect Percent (VDP)} = \frac{\text{VDV}}{\text{TCV}}$$

TCV = Thoracic Cavity Volume

VDV = Ventilation Defect Volume

Mathew *et. al. Acad Radiol*. 2008

Kirby M et al. Acad Radiol 2011

Functional MRI Biomarker Development

nber of classes:

Published in final edited form as:
Acad Radiol. 2014 December ; 21(12): 1530–1541. doi:10.1016/j.acra.2014.07.017.

Extending Semi-Automatic Ventilation Defect Analysis for Hyperpolarized ^{129}Xe Ventilation MRI

Ventilation Defect Percent (VDP)

TECHNICAL DEVELOPMENT

Spatial Fuzzy C-Means Thresholding for Semiautomated Calculation of Percentage Lung Ventilated Volume From Hyperpolarized Gas and ^{1}H MRI

Paul J.C. Hughes, MEng,[1] Felix C. Ho
Alberto Biancardi, PhD,[1,2] Helen Mars

Automated Segmentation & Registration: 2017

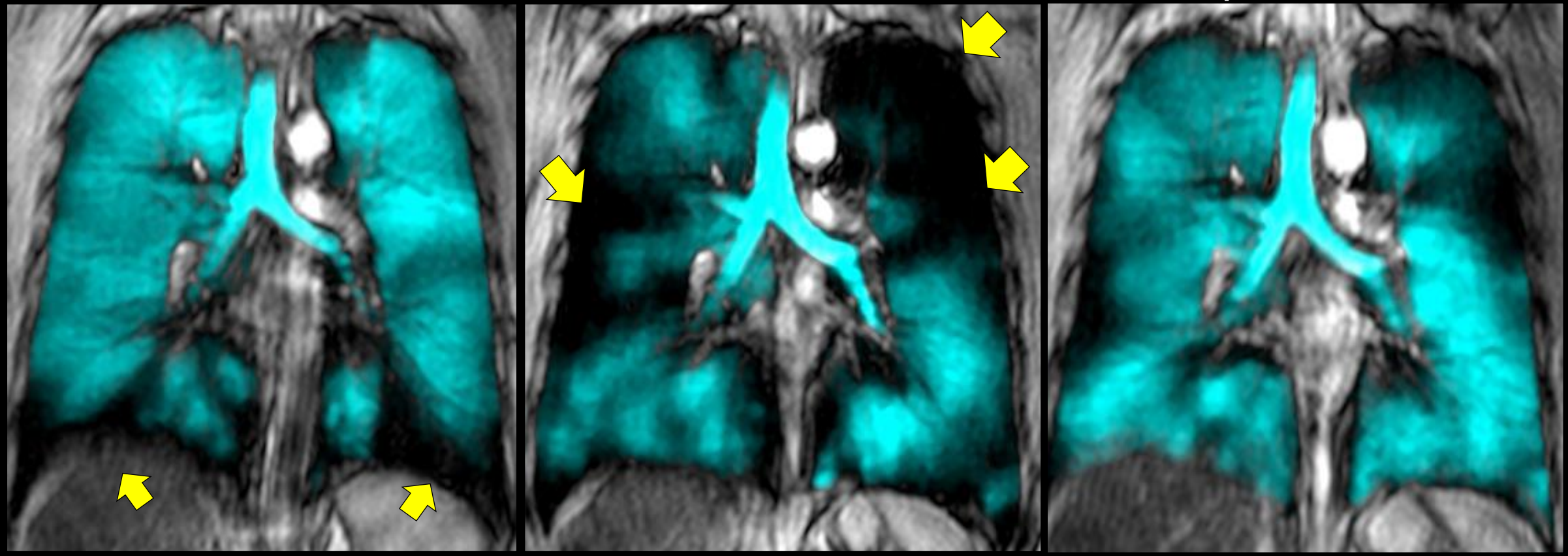
Guo et al Med Phys 2017

Globally optimal co-segmentation of three-dimensional pulmonary ^{1}H and hyperpolarized ^{3}He MRI with spatial consistence prior

Fumin Guo[a,b], Jing Yuan[a,c], Martin Rajchl[a,b], Sarah Svenningsen[a,c], Dante PI Capaldi[a,c], Khadija Sheikh[a,c], Aaron Fenster[a,b,c], Grace Parraga[a,b,c,*]

MRI of Asthma: What we discovered

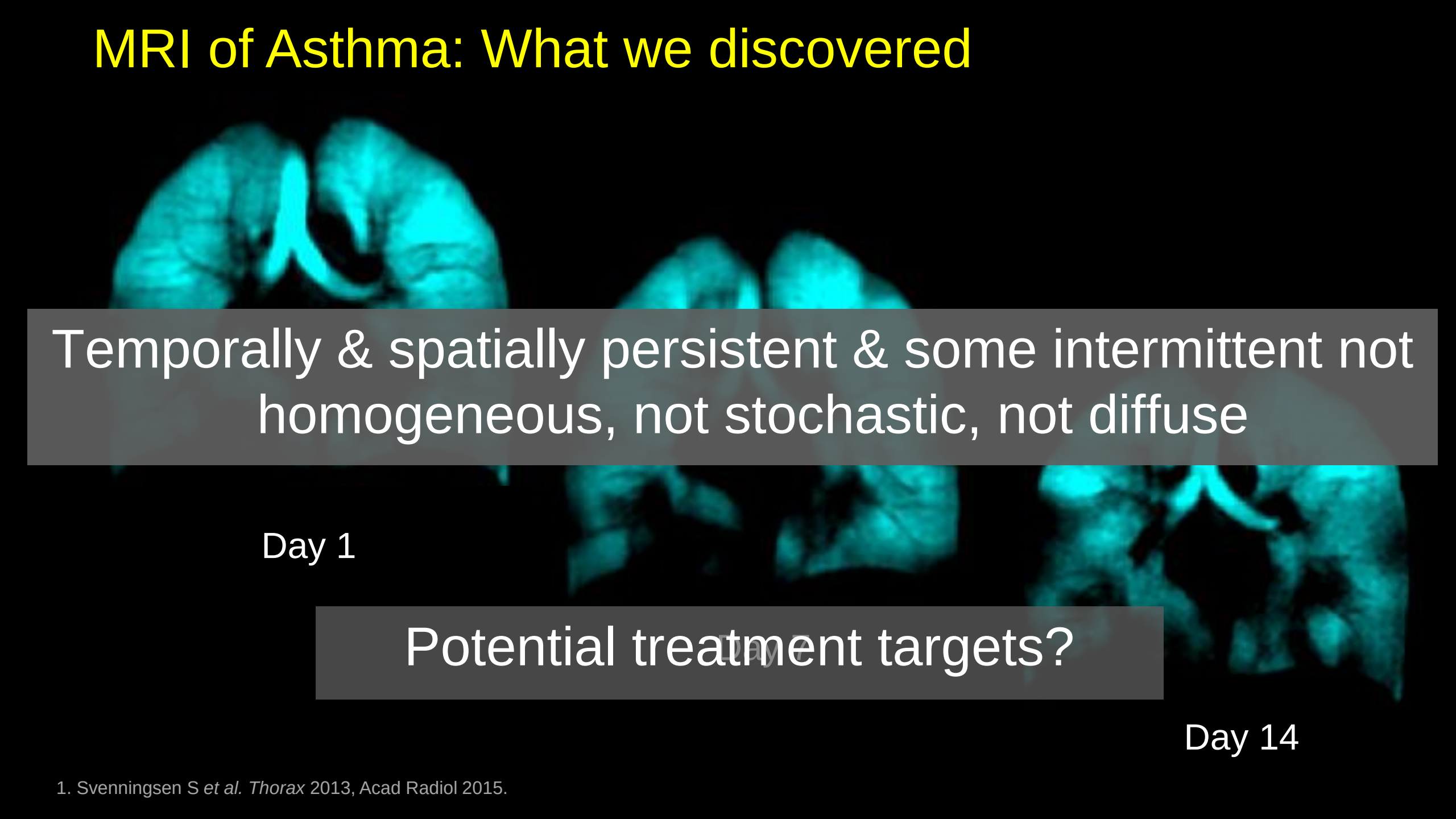
Baseline | Response to Trigger | Response to Tx



MRI ventilation defects worsen in response to different triggers and respond to Tx

1. Costella S *et al. Respirology* 2012.; Samee; DeLange; DeLange; Altes

MRI of Asthma: What we discovered



Temporally & spatially persistent & some intermittent not homogeneous, not stochastic, not diffuse

Day 1

Potential treatment targets?

Day 14

1. Svenningsen S *et al. Thorax* 2013, Acad Radiol 2015.

MRI of Asthma: What we collectively discovered

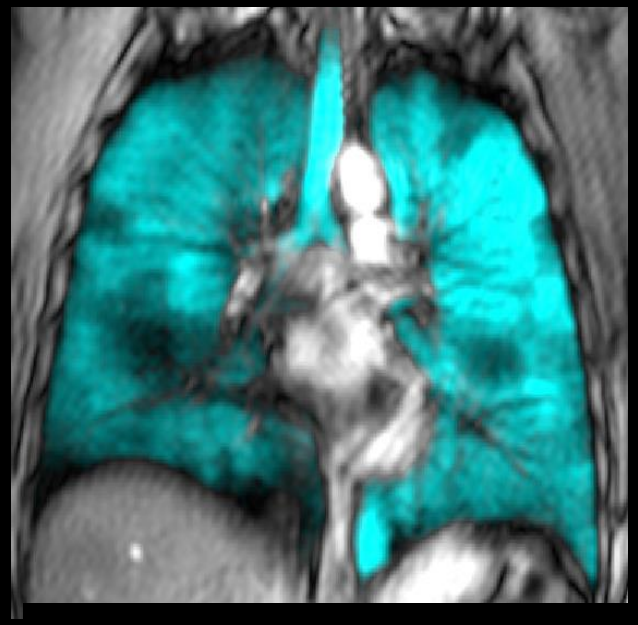
- Temporal and spatially persistent/intermittent abnormalities
- Sensitive to treatment
- Reflect airway remodeling, inflammation
- Correlate with indices of disease severity
- Worsen after triggers and bronchoconstriction

But….

Can MRI predict outcomes that matter to patients?
Asthma control & symptoms

Ventilation Defects & Asthma Control/ Quality of Life

ACQ ≤2 (n=7)

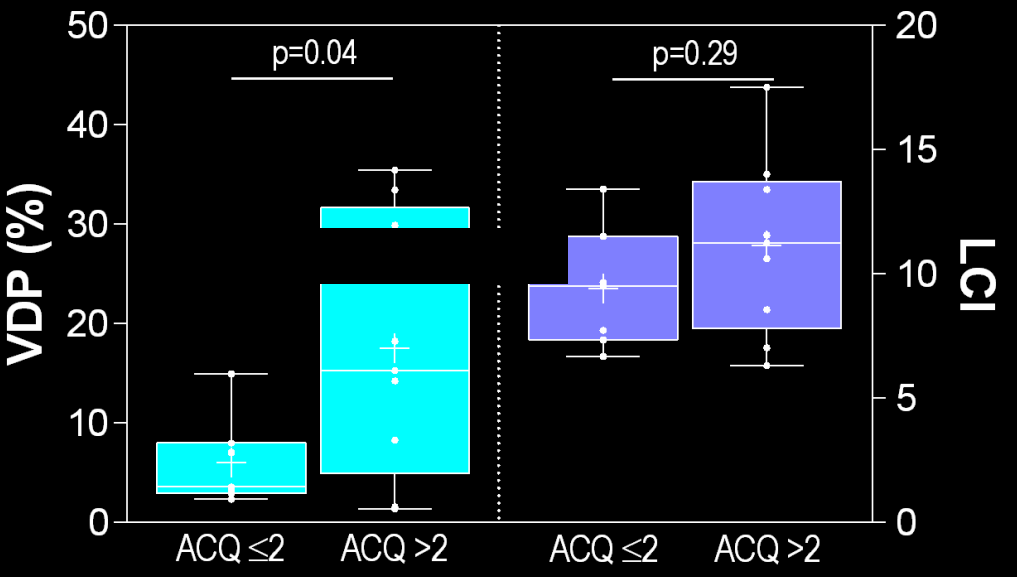


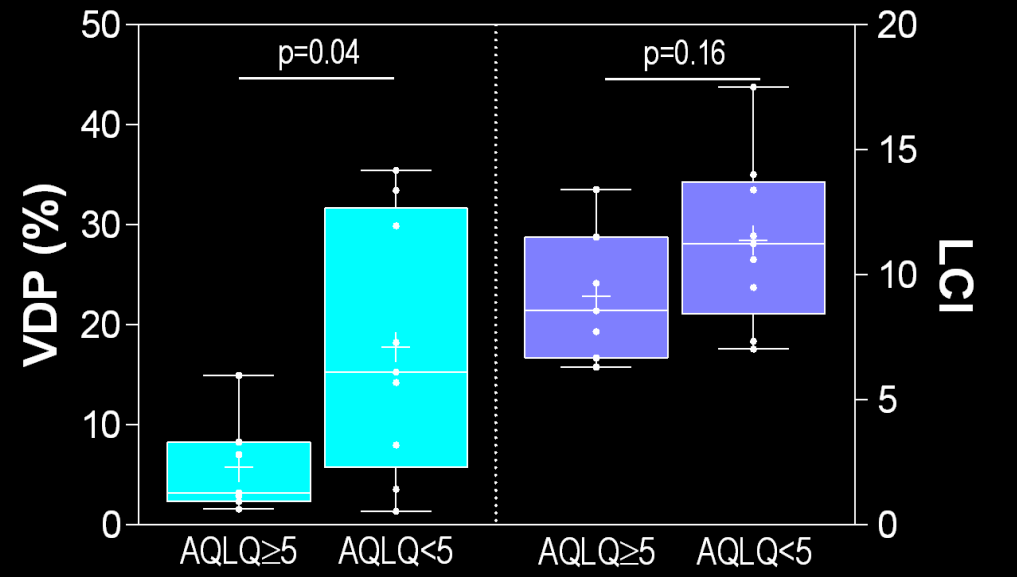
ACQ>2 (n=9)

Worse asthma control (↑ACQ)

Worse VDP

Worse quality-of-life (↓AQLQ)





Svenningsen S *et al. Eur Resp J 2016*.

Can we use MRI function to
Guide Therapy Decisions?

Personalized Treatment: Targeting Inflammation

Inflammation Not Controlled

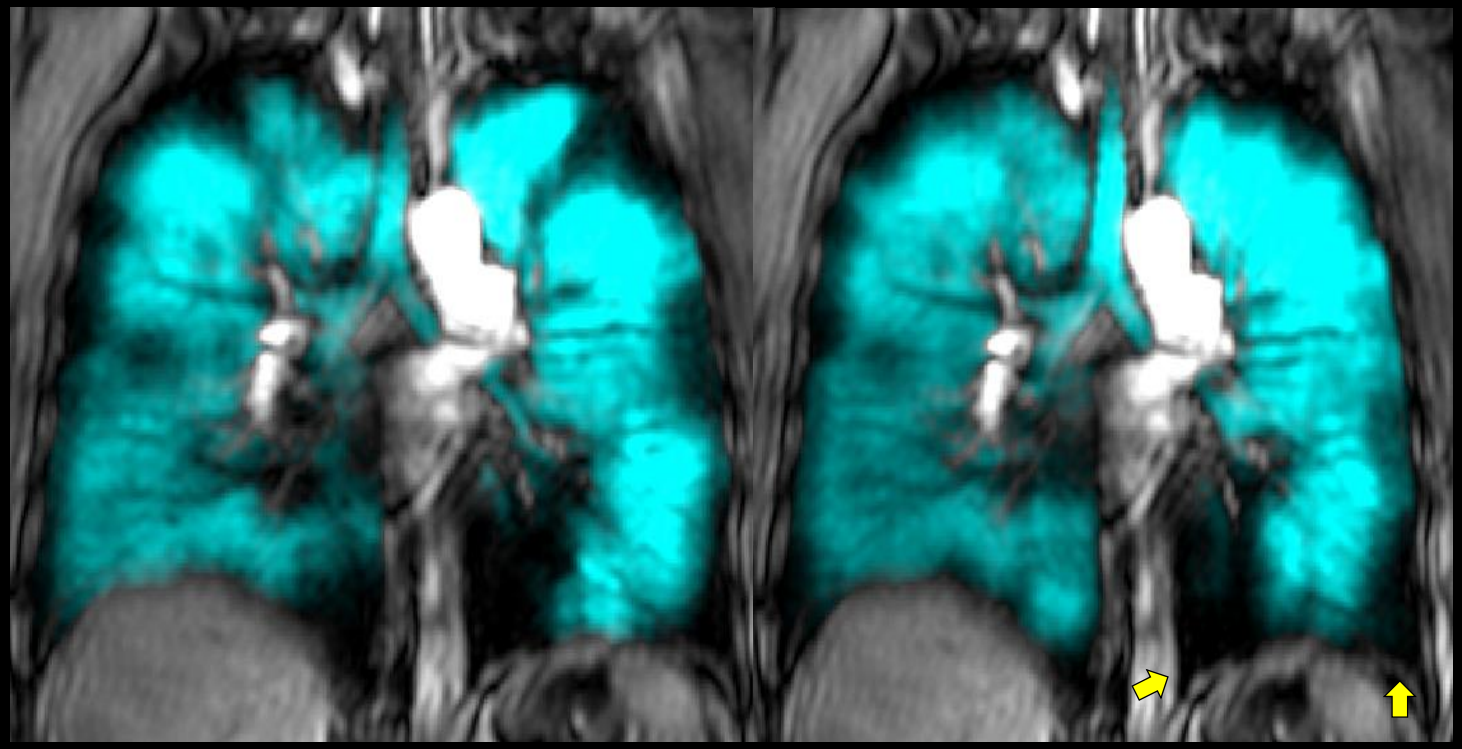
Benralizumab (Anti-IL5Rα) →

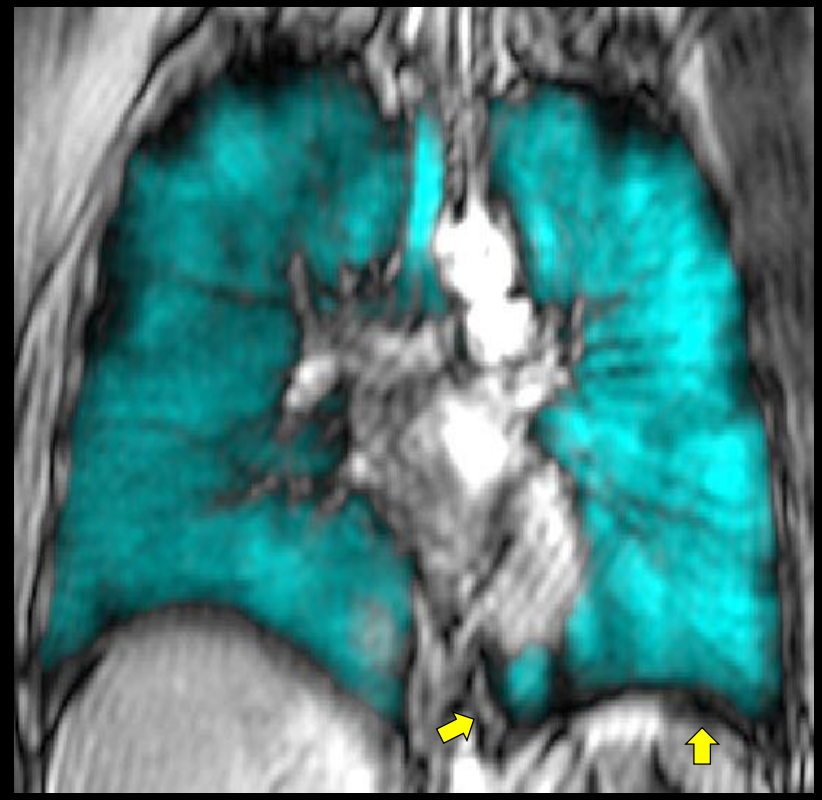
Inflammation Controlled

Pre-BD

Post-BD

Post-BD





VDP=19%
FEV_1=67%$_{pred}$, ACQ=2.3

VDP=10%
FEV_1=76%$_{pred}$, ACQ=2.3

VDP=3%
FEV_1=84%$_{pred}$, ACQ=0.4

Nair, Svenningsen and Parraga Unpublished data

➡BD non-responsive , anti-IL5Rα responsive

Personalized Treatment: Image-guided Bronchial Thermoplasty

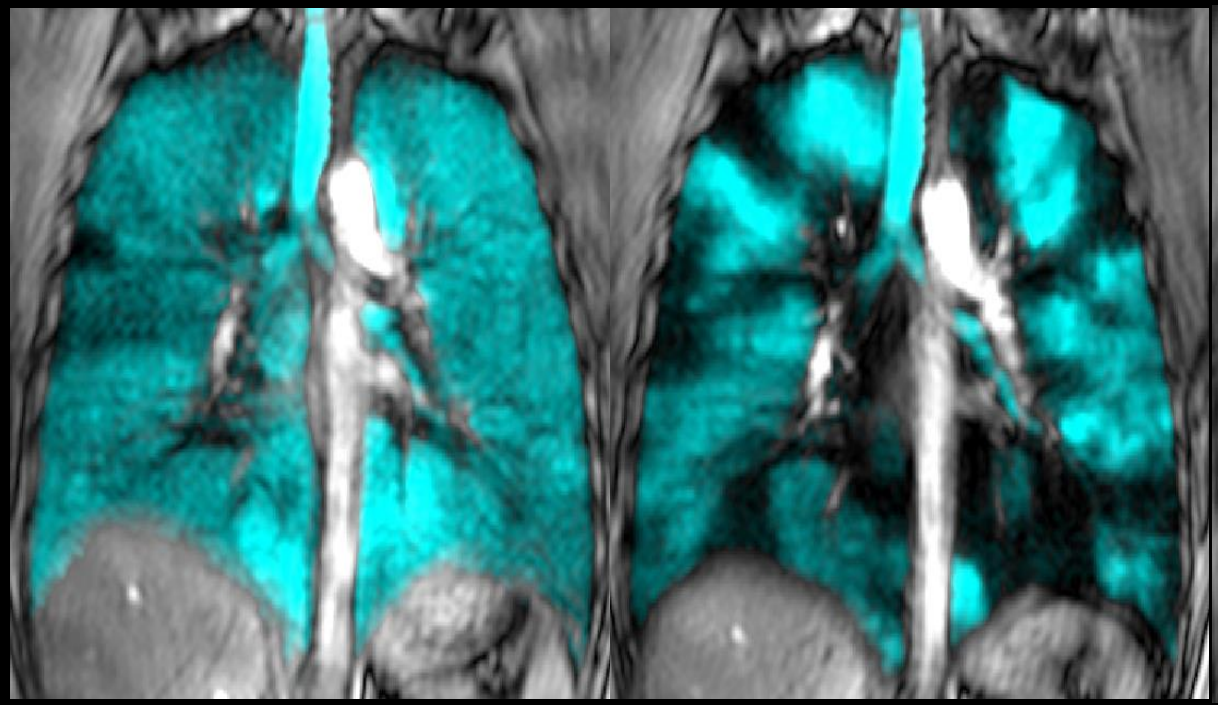
Inflammation Controlled

Bronchial Thermoplasty (BT)

Post-BT

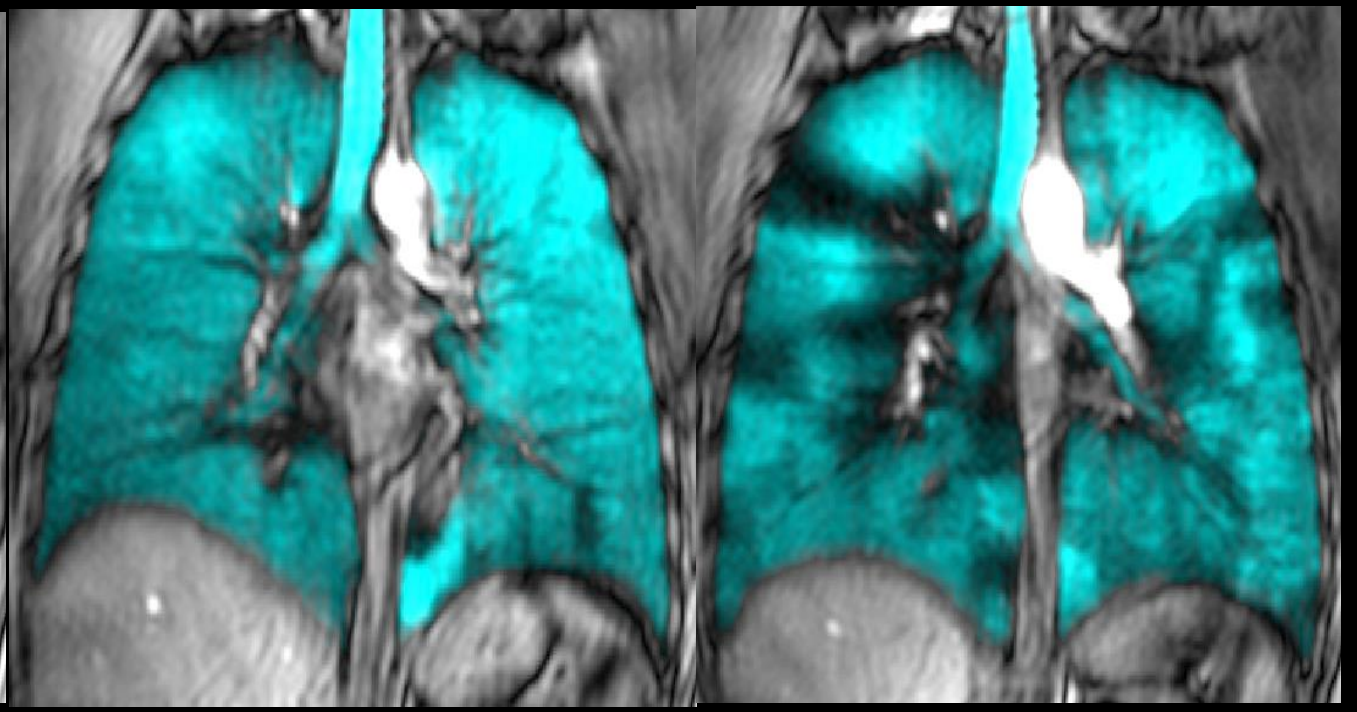
Baseline

Post-MCh



Baseline

Post-MCh



ACQ=1.6

PC_{20}=0.05mg/mL

SABA= 4 puffs/day

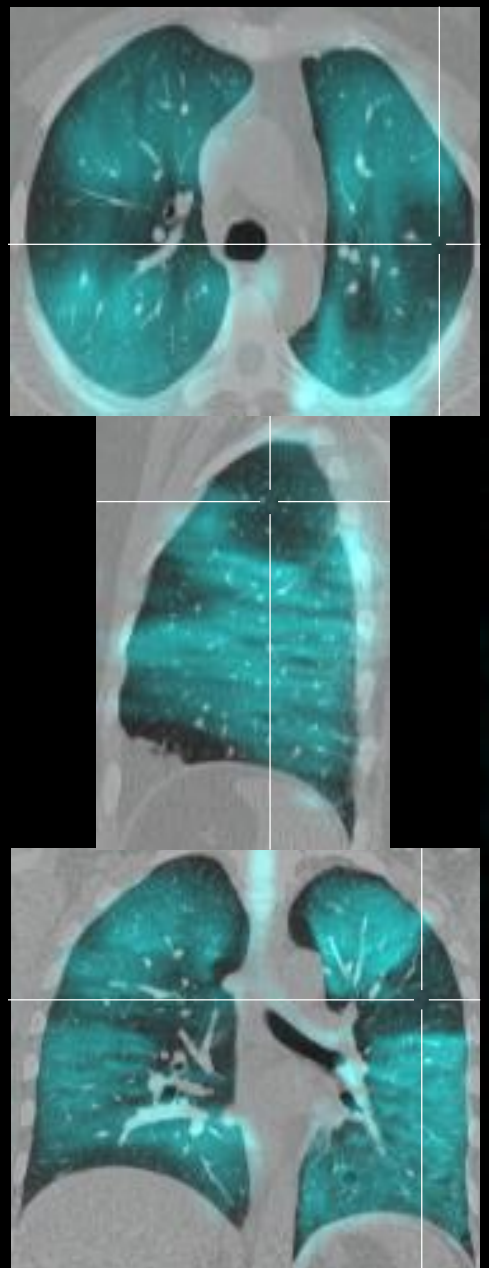
ACQ=0.0

PC_{20}=1.50mg/mL

SABA= 1-2 puffs/14 days

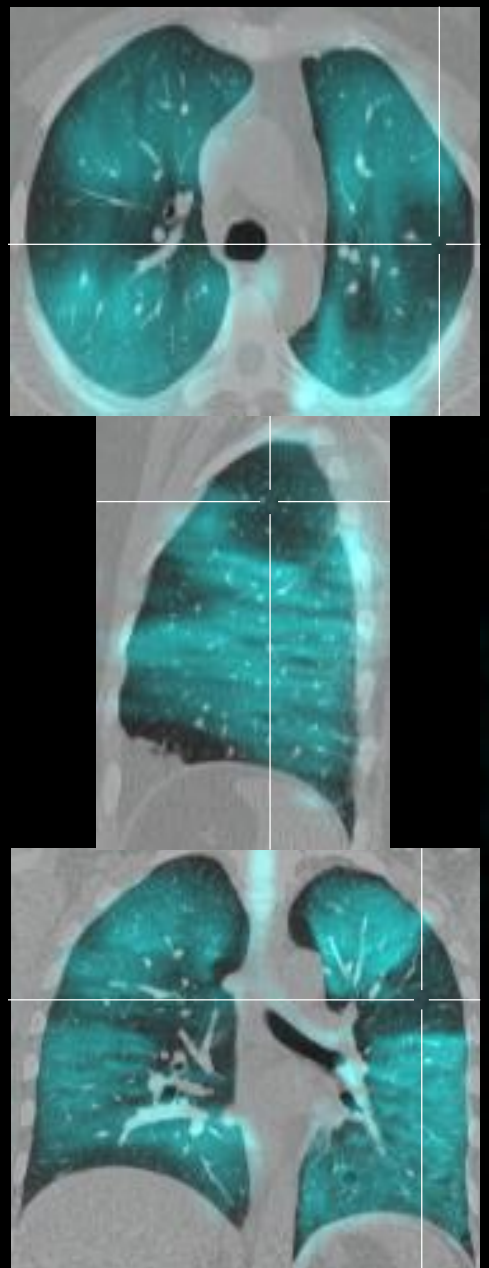
Nair, McCormack, Cox, Svenningsen and Parraga Unpublished data

Translation: Image-Guided Interventions



Now approved for image-guided Biopsy to confirm and validate MRI findings

Relationship of Ventilation & Airway Abnormalities



London Lung Imaging Research Team

robarts RESEARCH

NSERC CRSNG

CIHR IRSC
Canadian Institutes of Health Research
Instituts de recherche en santé du Canada

CRRN RCRR
Canadian Respiratory Research Network
Réseau canadien de recherche respiratoire

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CATT
Complex Airways-disease Translational Team

Impact?