Quantitative Evaluation of Lung Structure and Function Using Magnetic Resonance Imaging and Computed Tomography

Amir Owrangi, MSc

Imaging Research Laboratories, Robarts Research Institute, Graduate Program in Biomedical Engineering, The University of Western Ontario, London, CANADA

February 2, 2012
Research Projects

Questions
Relationship between quantitative CT, $^1$H and $^3$He MRI and established measurements of lung disease?

• Lung Structure
  – Short echo time $^1$H MRI
  – Novel CT analysis techniques

• Lung Function
  – Fourier decomposition $^1$H MRI
  – 4DCT lung imaging
Quantitative measurement of lung disease

- CT
- 3He ADC
- 1H MRI
- 3He MRI SV
- 4DCT
- FD 1H MRI

Diagram shows relationships between different imaging techniques for lung disease quantification.
Challenges in Lung $^1$H MRI

- Inherently low signal intensity
- Substantial MR susceptibility artifacts

Images adapted from Williams A et al. Textbook of Respiratory Medicine 2003
Methods: Lung structural information

FGRE
TR = 4.3ms
TE = 1.0ms
FA = 20
Relationship between Imaging & PFT

Whole lung mean $^1$H SI vs. FEV$_1$/FVC: $r=.65$, $p<.0001$

Whole lung mean $^1$H SI vs. DL$_{CO}$ (%pred): $r=-.39$, $p<.0001$

Whole lung mean $^1$H SI vs. RA$_{950}$: $r=-.58$, $p<.0001$

Whole lung mean $^1$H SI vs. $^3$He ADC (cm$^2$/s): $r=-.58$, $p<.0001$
Respiration and tissue density

Zapke M, Respir Res 2006
Fourier Decomposition

- Time [s]
- Frequency (Hz)
- $I(\omega)^2$ [a.u.]
- $S_l$ [a.u.]

- $^1$H Ventilation-weighted
- $^3$He Static ventilation

- Ventilation 0.25 Hz
- Perfusion 0.95 Hz
RA (-950) and HU at 15\(^{th}\) percentile

Relative frequency (%)
Extent of Emphysema: Low Attenuation Cluster Analysis

Mishima M et al 1999

Coxson HO et al 2003
Correlations: CT LAC, $^3$He ADC and DL$_{CO}$

- $r = 0.79$, $p < 0.0001$
- $r = -0.60$, $p < 0.0001$
Three Dimensional Ultrasound Measurements of Carotid Atherosclerosis in Vulnerable Patient Populations

D. Buchanan, ¹,² I. Gyacskov,¹ E. Ukwatta,¹,³ T. Lindenmaier,¹ S. McKay,¹ Y. Bureau,² D.G. Hackam,⁴,⁵ A. Fenster¹-³ and G. Parraga¹-³

¹Imaging Research Laboratories, Robarts Research Institute, ²Department of Medical Biophysics, ³Biomedical Engineering Graduate Program, ⁴Division of Clinical Pharmacology, ⁵Department of Epidemiology and Biostatistics, The University of Western Ontario, London, CANADA

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Imaging Phenotypes of Carotid Atherosclerosis

Intima-Media Thickness

Total Plaque Area

Total Plaque Volume


Vessel Wall Volume

Total Plaque Volume

Intima-Media Thickness

Total Plaque Area

Total Plaque Volume


Vessel Wall Volume
Semi-automated TPV Pipeline

- Locate plaque
- Set bifurcation point

**Longitudinal view (long axis):**
- Define minimum and maximum z-axis values (contour 1)
- Find center of plaque
- Draw contour

**Axial view (short axis):**
- Establish cross-sectional area near end of plaque (contour 2)
- Establish cross-sectional area near opposing end of plaque (contour 3)

**Polyhedron Volume Calculation**
TPV Segmentation – Large Plaque

Axial View
Longitudinal View

(Orange Line Indicates 10mm)

Manual Segmentation = 209.6 mm³
Semi-automated Segmentation = 201.7 mm³
### Carotid Ultrasound Imaging Phenotypes and Age

<table>
<thead>
<tr>
<th></th>
<th>All (n = 316)</th>
<th>Male (n = 236)</th>
<th>Female (n = 80)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>IMT mm</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r (p-value)</td>
<td>0.18 (0.0012)</td>
<td>0.19 (0.0028)</td>
<td>0.30 (0.0071)</td>
</tr>
<tr>
<td>R²</td>
<td>0.03 (0.0012)</td>
<td>0.04 (0.0028)</td>
<td>0.09 (0.0071)</td>
</tr>
<tr>
<td><strong>VWV mm³</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r (p-value)</td>
<td>0.24 (0.0001)</td>
<td>0.34 (0.0001)</td>
<td>0.10 (0.37)</td>
</tr>
<tr>
<td>R²</td>
<td>0.06 (0.0001)</td>
<td>0.12 (0.0001)</td>
<td>0.01 (0.37)</td>
</tr>
<tr>
<td><strong>TPV mm³</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>r (p-value)</td>
<td>ND</td>
<td>ND</td>
<td>0.15 (0.19)</td>
</tr>
<tr>
<td>R²</td>
<td></td>
<td></td>
<td>0.02 (0.19)</td>
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</table>
Carotid Ultrasound Phenotypes in Females

**All**

\[ y = 339.7x + 191.4 \]

\[ r^2 = 0.30 \]

\[ r = 0.55 \]

\[ p < 0.0001 \]

**Females**

\[ y = 17.41x - 0.8645 \]

\[ r^2 = 0.012 \]

\[ r = 0.11 \]

\[ p = 0.34 \]

**Females**

\[ y = 259.4x + 206.2 \]

\[ r^2 = 0.14 \]

\[ r = 0.37 \]

\[ p = 0.0008 \]

**Females**

\[ y = 0.0829x - 20.99 \]

\[ r^2 = 0.13 \]

\[ r = 0.36 \]

\[ p = 0.0012 \]
Safety and Tolerability of Hyperpolarized $^{129}$Xe in Healthy and Lung Disease Patients

Yajur Shukla MD$^{1,2}$, Andrew Wheatley BSc$^1$, Adam Farag MSc$^1$, Alexei Ouriadov PhD$^1$ David McCormack MD$^2$, Giles Santyr PhD$^{1,3}$, Grace Parraga PhD$^{1,3-5}$

$^1$Imaging Research Laboratories, Robarts Research Institute, London, Canada;
$^2$Division of Respirology, Department of Medicine, The University of Western Ontario, London, Canada;
$^3$Department of Medical Imaging, The University of Western Ontario, London, Canada;
$^4$Department of Medical Biophysics, The University of Western Ontario, London, Canada;
$^5$Graduate Program in Biomedical Engineering, The University of Western Ontario, London, Canada;

February 2$^{nd}$, 2012
Motivation

• Cost of $^3$He has gone up considerably because of the supply-demand discrepancy from increased use for homeland security applications$^1$
• Advances in counter-current polarizer technology responsible for producing HP-\textsuperscript{129}Xe allows for higher quality MR imaging protocols compared to the first human studies back in 1997$^{2,3}$

Objective

• To assess the safety and tolerability of 500ml inhalation of 50-60\% HP-\textsuperscript{129}Xe in healthy volunteers and lung disease patients

Methods

- 12 healthy volunteers (HV), 7 asthma subjects, 10 COPD subjects, 3 CF subjects, 1 radiation-induced lung injury (RILI) subject
- Monitored for adverse events from t=0 to 24 hours after HP-$^{129}$Xe administration
- SpO2 and HR also monitored at baseline, after HP-$^{129}$Xe inhalation and one-minute recovery from inhalation
Results

Xenon Doses & Adverse Events

<table>
<thead>
<tr>
<th>Parameter</th>
<th>All n=33</th>
<th>HV n=12</th>
<th>Asthma n=7</th>
<th>COPD n=10</th>
<th>CF n=3</th>
<th>RILI n=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of Visits</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1</td>
<td>26</td>
<td>10</td>
<td>7</td>
<td>5</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>≥ 2</td>
<td>7</td>
<td>2</td>
<td>0</td>
<td>5</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Number of HP-(^{129})Xe Doses</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>2-4</td>
<td>27</td>
<td>10</td>
<td>7</td>
<td>6</td>
<td>3</td>
<td>1</td>
</tr>
<tr>
<td>5-9</td>
<td>4</td>
<td>0</td>
<td>0</td>
<td>4</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>≥ 10</td>
<td>2</td>
<td>2</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 1. Subject Clinical Visits & Total Xenon Doses
HP-\(^{129}\)Xe=hyperpolarized xenon

<table>
<thead>
<tr>
<th>Type</th>
<th>All n=33</th>
<th>HV n=12</th>
<th>Asthma n=7</th>
<th>COPD n=10</th>
<th>CF n=3</th>
<th>RILI n=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2</td>
<td>0</td>
<td>1</td>
<td>1</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Serious</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Hypoxic</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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<tr>
<td>Withdrawn</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
</tbody>
</table>

Table 2. All Adverse Events.
*Light headedness, slight voice change
†Headache and nausea

<table>
<thead>
<tr>
<th>Intensity</th>
<th>All n=33</th>
<th>HV n=12</th>
<th>Asthma n=7</th>
<th>COPD n=10</th>
<th>CF n=3</th>
<th>RILI n=1</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>0</td>
<td>0</td>
<td>1*</td>
<td>1†</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Moderate</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Severe</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
<td>0</td>
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</table>

<table>
<thead>
<tr>
<th>Relationship</th>
<th>HP-(^{129})Xe related</th>
<th>Unrelated</th>
</tr>
</thead>
<tbody>
<tr>
<td>All n=33</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>HV n=12</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>Asthma n=7</td>
<td>1</td>
<td>0</td>
</tr>
<tr>
<td>COPD n=10</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>CF n=3</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>RILI n=1</td>
<td>0</td>
<td>0</td>
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</tbody>
</table>
Results

**Sp02 & HR Monitoring**

<table>
<thead>
<tr>
<th>Parameter</th>
<th>HV n=12</th>
<th>Asthma n=7</th>
<th>COPD n=10</th>
<th>CF n=3</th>
<th>RILI n=1</th>
<th>P value*</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sp02 Mean drop after HP-129Xe Inhalation (%) (±SD)</td>
<td>-3 (1.4)</td>
<td>-3 (2.3)</td>
<td>-4 (1.4)</td>
<td>-6 (2.1)</td>
<td>-11 (0.7)</td>
<td>0.329</td>
</tr>
<tr>
<td>Mean Recovery from HP-129Xe Inhalation (%) (±SD)</td>
<td>0 (0.7)</td>
<td>0 (1.2)</td>
<td>0 (0.7)</td>
<td>-1 (0.5)</td>
<td>-1 (0.0)</td>
<td>0.329</td>
</tr>
<tr>
<td>HR Mean change after HP-129Xe Inhalation (±SD)</td>
<td>1 (4.1)</td>
<td>2 (3.8)</td>
<td>0 (3.4)</td>
<td>-2 (7.1)</td>
<td>1 (5.6)</td>
<td>0.518</td>
</tr>
<tr>
<td>Mean Recovery from HP-129Xe Inhalation (±SD)</td>
<td>1 (4.5)</td>
<td>1 (4.6)</td>
<td>-1 (3.1)</td>
<td>-2 (5.4)</td>
<td>1 (3.5)</td>
<td>0.565</td>
</tr>
</tbody>
</table>

Table 3. Sp02/HR changes following inhalation of hyperpolarized 129Xe
HP-129Xe=hyperpolarized Xe 129, SD=Standard Deviation
*p value determined with ANOVA

Figure 1. Mean/Standard Deviation of Sp02 and HR at baseline, Post-HP129Xe Inhalation and One-Minute Recovery.

*BL=Baseline, P-Xe=Post-HP129Xe Inhalation, R=One minute recovery after inhalation
Conclusions

- Healthy and lung disease subjects had minimal adverse events when administered multiple doses of 500ml of 50-60% HP-$^{129}$Xe
- Subjects’ vital parameters (sp02 and HR) remained stable throughout each of the scans

Future Direction

- Reproducibility of VDV and ADC in HP-$^{3}$He MRI vs. HP-$^{129}$Xe MRI in healthy and lung disease subjects
Hyperpolarized Noble Gas Magnetic Resonance Imaging of Chronic Obstructive Pulmonary Disease

M Kirby, S Svenningsen, D Buchanan, A Wheatley, A Farag, GE Santyr, NAM Paterson, DG McCormack and G Parraga

Imaging Research Laboratories,
Robarts Research Institute
Department of Medical Biophysics,
The University of Western Ontario
1. Is there a relationship between carotid atherosclerosis and COPD?

2. Can $^3$He MRI detect improvements following an acute exacerbation of COPD before spirometry?

3. How does the distribution of $^{129}$Xe gas in the lung compare with $^3$He MRI?

4. Can $^3$He MRI detect ventilation abnormalities in subjects with non-obstructive emphysema?
$	extsuperscript{3}$He MRI Measurements in Subjects with Low versus High Total Plaque Area (TPA)

Low TPA

Static Ventilation

$	extsuperscript{3}$He ADC Map

VDP=8%

ADC=0.29 cm$^2$/s
Relationship between COPD and atherosclerosis?

$n=49$

$r=.32, p=.03$

$r=.22, p=.13$

$VDP$ vs $TPA$

$ADC$ vs $TPA$
1. Is there a relationship between carotid atherosclerosis and COPD?

2. Can $^3$He MRI detect improvements following an acute exacerbation of COPD before spirometry?

3. How does the distribution of $^{129}$Xe gas in the lung compare with $^3$He MRI?

4. Can $^3$He MRI detect ventilation abnormalities in subjects with non-obstructive emphysema?
$^3$He MRI of COPD Exacerbation

Pre-Exacerbation
29.1 months

$\text{FEV}_1 = 41\%_{\text{pred}}$
$\text{FVC} = 66\%_{\text{pred}}$
$\text{FRC} = 95\%_{\text{pred}}$
$\text{VDP} = 16\%$
$\text{ADC}=0.34\text{cm}^2/\text{s}$

Kirby et. al. CHEST (In preparation)
$^3$He MRI of COPD Exacerbation

Pre-Exacerbation

29.1 months  5.6 months
$^3\text{He}$ MRI of COPD Exacerbation

Pre-Exacerbation

29.1 months

FEV$_1$ = 41%$_{\text{pred}}$
FVC = 66%$_{\text{pred}}$
FRC = 95%$_{\text{pred}}$
VDP = 16%
ADC = 0.34 cm$^2$/s

5.6 months

FEV$_1$ = 47%$_{\text{pred}}$
FVC = 70%$_{\text{pred}}$
FRC = 105%$_{\text{pred}}$
VDP = 29%
ADC = 0.38 cm$^2$/s

Kirby et. al. CHEST (In preparation)
$	extsuperscript{3}$He MRI of COPD Exacerbation

Pre-Exacerbation: 29.1 months
Post-Exacerbation: 15.7 months

ADC (cm$^2$/s) vs. Slice Number

Pixel Count vs. ADC (cm$^2$/s)
1. Is there a relationship between carotid atherosclerosis and COPD?

2. Can $^3$He MRI detect improvements following an acute exacerbation of COPD before spirometry?

3. How does the distribution of $^{129}$Xe gas in the lung compare with $^3$He MRI?

4. Can $^3$He MRI detect ventilation abnormalities in subjects with non-obstructive emphysema?
$^{3}\text{He}$ and $^{129}\text{Xe}$ MRI: Comparison
$^{3}\text{He}$ and $^{129}\text{Xe}$ MRI: Correlation with PFTs

$r = -0.84, p < 0.0001$

$r = -0.54, p = 0.02$

$r = -0.83, p < 0.0001$
Hyperpolarized Noble Gas MRI of COPD

1. Is there a relationship between carotid atherosclerosis and COPD?

2. Can $^3$He MRI detect improvements following an acute exacerbation of COPD before spirometry?

3. How does the distribution of $^{129}$Xe gas in the lung compare with $^3$He MRI?

4. Can $^3$He MRI detect ventilation abnormalities in subjects with non-obstructive emphysema?
Non-obstructive Emphysema

Static Ventilation

$\text{FEV}_1 = 104\%_{\text{pred}}$

$\text{FVC} = 132\%_{\text{pred}}$

$D_{\text{LCO}} = 37\%_{\text{pred}}$

ADC Map

$^3\text{He VDP} = 15\%$

$^3\text{He ADC} = 0.55\text{cm}^2/\text{s}$
## Subject Demographics

<table>
<thead>
<tr>
<th></th>
<th>Healthy Ex-smokers (n=29)</th>
<th>Non-obstructive Emphysema (n=17)</th>
<th>Significance of Difference (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age yrs (±SD)</td>
<td>69 (10)</td>
<td>74 (9)</td>
<td>0.15</td>
</tr>
<tr>
<td>Female Sex</td>
<td>5</td>
<td>13</td>
<td>0.0001</td>
</tr>
<tr>
<td>Pack years (±SD)</td>
<td>28 (17)</td>
<td>28 (19)</td>
<td>0.88</td>
</tr>
<tr>
<td>Years since quit (±SD)</td>
<td>21 (12)</td>
<td>25 (14)</td>
<td>0.36</td>
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Hyperpolarized Helium-3 and Xenon-129 Magnetic Resonance Imaging

Nikhil Kanhere, M Kirby, A Wheatley, D McCormack and G Parraga

Imaging Research Laboratories, Robarts Research Institute, Graduate Program in Biomedical Engineering, The University of Western Ontario, London, CANADA

February 2, 2012
Research Questions:

- Is $^{129}$Xe MRI more sensitive than $^3$He MRI to functional alterations of the lung following radiation damage in RILI?
- Is there reproducibility in hyperpolarized $^{129}$Xe MRI of COPD subjects?
Whole lung $^3$He and $^{129}$Xe MRI Measurements

<table>
<thead>
<tr>
<th></th>
<th>$^3$He MRI</th>
<th>$^{129}$Xe MRI</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Ipsilateral</td>
<td>Contralateral</td>
</tr>
<tr>
<td>VDP(%)</td>
<td>6</td>
<td>2</td>
</tr>
<tr>
<td>C2(%)</td>
<td>22</td>
<td>10</td>
</tr>
<tr>
<td>C3(%)</td>
<td>64</td>
<td>28</td>
</tr>
<tr>
<td>C4(%)</td>
<td>8</td>
<td>42</td>
</tr>
<tr>
<td>C5(%)</td>
<td>0</td>
<td>18</td>
</tr>
</tbody>
</table>
Research Questions:

• Is $^{129}$Xe MRI more sensitive than $^3$He MRI to functional alterations of the lung following radiation damage in RILI?

• Is there reproducibility in hyperpolarized $^{129}$Xe MRI of COPD subjects?
129Xe functional measurements:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Scan (n=9)</th>
<th>5-min Rescan (n=9)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDP % (±SD)</td>
<td>26 (12)</td>
<td>26 (12)</td>
<td>0.80</td>
</tr>
<tr>
<td>C2 % (±SD)</td>
<td>17 (5)</td>
<td>16 (5)</td>
<td>0.20</td>
</tr>
<tr>
<td>C3 % (±SD)</td>
<td>20 (13)</td>
<td>24 (11)</td>
<td>0.14</td>
</tr>
<tr>
<td>C4 % (±SD)</td>
<td>20 (13)</td>
<td>24 (11)</td>
<td>0.14</td>
</tr>
<tr>
<td>C5 % (±SD)</td>
<td>12 (6)</td>
<td>11 (5)</td>
<td>0.08</td>
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</table>
$^{129}$Xe functional measurements:

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Scan (n=3)</th>
<th>5-min Rescan (n=3)</th>
<th>7-day Rescan (n=3)</th>
<th>P-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDP % (±SD)</td>
<td>22 (6)</td>
<td>19 (9)</td>
<td>22 (9)</td>
<td>0.06</td>
</tr>
<tr>
<td>C2 % (±SD)</td>
<td>17 (4)</td>
<td>15 (2)</td>
<td>14 (0)</td>
<td>0.10</td>
</tr>
<tr>
<td>C3 % (±SD)</td>
<td>26 (13)</td>
<td>31 (6)</td>
<td>29 (8)</td>
<td>0.15</td>
</tr>
<tr>
<td>C4 % (±SD)</td>
<td>23 (5)</td>
<td>24 (9)</td>
<td>23 (10)</td>
<td>0.81</td>
</tr>
<tr>
<td>C5 % (±SD)</td>
<td>13 (5)</td>
<td>11 (7)</td>
<td>11 (10)</td>
<td>0.18</td>
</tr>
</tbody>
</table>
Development of 3D Lung Atlas

• Spirometry- Global measurement of disease, not regional measurement

• Goal: GOLD stage specific lung atlas
Thoracic cavity
Hypo-ventilated
Normal

Stage 2 (n=5)
Hyperpolarized Noble Gas Magnetic Resonance Imaging of Asthma

Sarah Svenningsen\textsuperscript{1,2}, Miranda Kirby\textsuperscript{1,2}, Andrew Wheatley\textsuperscript{1}, David G McCormack\textsuperscript{3} and Grace Parraga\textsuperscript{1,2}

\textsuperscript{1}Imaging Research Laboratories, Robarts Research Institute; \textsuperscript{2}Department of Medical Biophysics; \textsuperscript{3}Division of Respirology, Department of Medicine, The University of Western Ontario, London, Canada.

February 2, 2012
Hyperpolarized Noble Gas MRI of Asthma

1. Can we provide a way to display lung function abnormalities that endure over time?

2. Is there a relationship between hyperpolarized $^3$He and $^{129}$Xe MRI measurements?

3. Is there a relationship between anatomical location and $^3$He and $^{129}$Xe ADC in asthma?
4D Gas Distribution Map

Baseline 1

4D Gas Distribution Map

Intermittent Defect Percent (%)

Exercise

Ventilation Defect Percent (%)

$r = 0.66$, $r^2 = 0.44$

$p = 0.01$

$N = 14$
Hyperpolarized Nobel Gas MRI of Asthma

1. Can we provide a way to display lung function abnormalities that endure over time?

2. Is there a relationship between hyperpolarized $^3$He and $^{129}$Xe MRI measurements?
3He and $^{129}$Xe MRI Comparison

3He MRI

VDP = 17%

$^{129}$Xe MRI

VDP = 27%
# Whole lung $^3$He and $^{129}$Xe MRI Measurements

<table>
<thead>
<tr>
<th></th>
<th>$^3$He MRI (n=7)</th>
<th>$^{129}$Xe MRI (n=7)</th>
<th>Mean Difference (p)</th>
</tr>
</thead>
<tbody>
<tr>
<td>VDP (%) (±SD)</td>
<td>10 (7)</td>
<td>19 (5)</td>
<td>-9 (0.002)</td>
</tr>
<tr>
<td>C2P (%) (±SD)</td>
<td>12 (1)</td>
<td>12 (2)</td>
<td>0 (NS)</td>
</tr>
<tr>
<td>C3P (%) (±SD)</td>
<td>35 (4)</td>
<td>24 (5)</td>
<td>11 (0.002)</td>
</tr>
<tr>
<td>C4P (%) (±SD)</td>
<td>28 (3)</td>
<td>29 (3)</td>
<td>-1 (NS)</td>
</tr>
<tr>
<td>C5P (%) (±SD)</td>
<td>14 (3)</td>
<td>15 (3)</td>
<td>-1 (NS)</td>
</tr>
</tbody>
</table>
Hyperpolarized Nobel Gas MRI of Asthma

1. Can we provide a way to display lung function abnormalities that endure over time?

2. Is there a relationship between hyperpolarized $^3$He and $^{129}$Xe MRI measurements?

3. Is there a relationship between anatomical location and $^3$He and $^{129}$Xe ADC in asthma?
AP ADC Gradient: $^3\text{He}$ and $^{129}\text{Xe}$
Regional Pulmonary Functional Imaging Measurements in Asthma after Methacholine Challenge using Hyperpolarized $^3$He Magnetic Resonance Imaging

Stephen Costella$^{1,2}$, Miranda Kirby$^{1,3}$, Geoffrey N Maksym$^4$, David G McCormack$^5$, Nigel AM Paterson$^5$, Grace Parraga$^{1-3}$

$^1$Imaging Research Laboratories, Robarts Research Institute
$^2$Graduate Program in Biomedical Engineering, Western University
$^3$Department of Medical Biophysics, Western University
$^4$School of Biomedical Engineering, Dalhousie University
$^5$Division of Respirology, Department of Medicine, Western University

February 2$^{nd}$, 2012
Motivation

• Small airways are the major site of airflow obstruction in asthma\(^1\) but spirometry is insensitive to distal airway function\(^2\)
• Spirometry and plethysmography only provide global measures of lung function and volume

Objective

• Evaluate regional lung structure and function before, during and after methacholine challenge (MCh) using hyperpolarized \(^3\)He spin density and diffusion-weighted MRI

2. Macklem PT and Mead J. *JAP.* 1967
Methods

- Twenty-five asthma subjects and 8 healthy volunteers (HV)
- Spin density and DWI ($b = 1.6 \text{s/cm}^2$) performed at baseline, post-MCh and after recovery
- Ventilation Defect Percent (VDP) and Apparent Diffusion Coefficients (ADC) were calculated from each image set
Results

Global Measurements
Results

Regional Measurements

Asthma (n = BL Post-MCh)

<table>
<thead>
<tr>
<th></th>
<th>Posterior</th>
<th>Anterior</th>
</tr>
</thead>
<tbody>
<tr>
<td>ADC</td>
<td></td>
<td></td>
</tr>
<tr>
<td>ΔPA</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>PAG</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>ΔSI</td>
<td>*</td>
<td>*</td>
</tr>
<tr>
<td>SI G</td>
<td>NS</td>
<td>NS</td>
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Healthy

<table>
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VDP

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Baseline | Post-MCh | Recovery

PA G

SI G
Discussion

Global
• Whole lung VDP increases post-MCh in both groups and baseline VDP is significantly higher in asthma
• Whole lung ADC is significantly greater in asthma post-MCh compared to recovery with similar trend towards significance between baseline and post-MCh
• Baseline VDP significantly larger in asthma

Regional
• Significantly higher VDP in posterior and inferior ROI at all time-points
• Significantly higher ADC in anterior and superior ROI at all time-points
• Increase in global VDP mainly due to posterior slices in HV but whole lung in asthma
• Defects and elevated ADC tend towards periphery of lung
Development and Proof-of-Concept of Three-Dimensional Histology Lung Volumes

L Mathew¹, M Alabousi¹, A Wheatley¹, U Aladl¹, D Slipetz², JC Hogg³, A Fenster¹ and G Parraga¹

¹Imaging Research Laboratories, Robarts Research Institute, The University of Western Ontario, London, CANADA,
²Merck Research Laboratories, Boston, USA
³UBC James Hogg iCapture Centre, St. Paul’s Hospital, The University of British Columbia, Vancouver, CANADA
Tissue Processing

- Sample
- Remove
- Section
- Digitize
- Image Processing
- 3D Volume
- Measure

- 2 male C57BL/6 mice
- Wildtype, Elastase
- 20-25 grams
Tissue Processing

- Sample
- Remove
- Section
- Digitize
- Digitize
- Image Processing
- 3D Volume
- Measure

- Maximally inflated
- Fixed with paraffin wax
Tissue Processing

- Sample
- Remove
- Section
- 5 μm thickness
- 10 μm gap
- Digitize
- Image Processing
- 3D Volume
- Measure
Tissue Processing

1. Sample
2. Remove Section
3. Digitize
4. Image Processing
5. Measure

- 2 μm in-plane
3D Volume

Sample

Remove

Section

Digitize

Image Processing

Measure
3D Volume

- Sample
- Remove
- Section
- Digitize
- Image Processing
- Measure
## Results: Wildtype vs Elastase

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<th>Elastase</th>
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<td>64.5 ± 14.0*</td>
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<td>Total Lung Volume (mm$^3$)</td>
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<td>Tissue Lung Volume (mm$^3$)</td>
<td>41.5**</td>
<td>49.8**</td>
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<td>75.9 ± 5.6**</td>
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<td>Tissue:Airspace Volume %</td>
<td>38.3 ± 13.2**</td>
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*p<0.001, **p<0.0001
## Results: Wildtype vs Elastase

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*\( p<0.001 \), **\( p<0.0001 \)
Results: 1D to 3D Correlation

- **Airspace Volume / Total Lung Volume (%)**
  - \( R^2 = 0.56 \)
  - \( R = 0.75 \)
  - \( p = 0.012 \)
  - \( y = 0.23x + 60.97 \)
  - • Wildtype
  - × Elastase

- **Tissue Volume / Airspace Volume (%)**
  - \( R^2 = 0.54 \)
  - \( R = -0.73 \)
  - \( p = 0.016 \)
  - \( y = -0.43x + 60.26 \)
  - • Wildtype
  - × Elastase