Introduction to the Quantitative Imaging of Asthma

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Stability of Severe Asthma Phenotypes: Impact of Exacerbations (SARP III)
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Goals

Basic pathophysiology of Asthma
Methods used for quantification of airway size and amount of air trapping
How Hyperpolarized gas MRI visualizes ventilation defects and targets bronchi for treatment

OUTLINE

1. Scope of the problem
2. Pathophysiology
3. Current imaging methods
4. What we have learned from imaging
5. Improving outcomes with image guided therapy

Definition of Asthma

1. Diagnosis based on clinical presentation (cough, dyspnea, wheezing)
2. Spirometry shows evidence of airway obstruction with reversibility after inhaled bronchodilator agents.
3. If spirometry shows no airway obstruction, a methacholine challenge can be performed to provoke bronchoconstriction

Scope of the problem

8.5% of the US population (24 million)

Adult Females > Adult Males
4.6/1000 (women)
3.6/1000 (males)

Pathophysiology

Asthmatic Bronchitis

Wall Thickening (Edema + Sm Muscle Hypertrophy)
Mucous production and Narrowed Lumen

Quantitative Imaging of Asthma

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Pulmonary Function Test Metrics

**TLC** - Total Lung Capacity  
**RV** - Residual Volume  
**FRC** - Functional Residual Capacity

Episodic Progressive Disease

What is the role for imaging?

- **Non-invasive assessment**
  - Phenotyping severity (cross-sectional)  
  - Monitoring progression (longitudinal)
- **Regional assessment of disease**
  - Spatial heterogeneity  
  - Image guidance  
  - Bronchoscopy  
  - Invasive imaging methods

Image Analysis >> Visual interpretation

Highly trained readers agree less than 80% of the time using visual assessment.*

Common Airway Metrics

- a. Wall area percentage (WA%)  
- b. Wall thickness percentage (WT%)  
- c. Lumen Area percentage (LA%)  
- d. Deltalumen  
- e. Ventilation defects (matched with perfusion)  
- f. Low area attenuation (LAA) < -900 HU*

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qCT airway metrics calculated perpendicular to the centerline

inner airway diameter - D1
outer airway diameter - D2

WT = (D2 - D1)/2

Wall Area = (Area C2 - Area C1) x 100%

Lumen area % = (Area C1 / Area C2) x 100%

Deltalumen = 1 - LAFRC / LATLC x 100%

outer circumference - C2 mm²
inner circumference - C1 mm²

Worsened CT airway metrics reflect poorer lung function

Delta Lumen correlates with Outcomes in Severe Asthmatics

Outcome variable
(Number of Subjects)

Airway Metric
Deltalumen

OR (95% CI) p value

Number of ER visits
(63)

0.930 (0.881-0.982) 0.009*

qCT Air Trapping

(TLC - registered FRC) < pixels -850 HU

Stiffer Airways worsened outcomes

Spearman rank correlation coefficient; p = p-value; %p, percent predicted

Female Asthmatics show a BMI dependent change in their deltalumen: SARP cohort data shows that females are more at risk than males for bronchial collapse with an increase in weight.

stiff Airways: worsened outcomes

Increased hospitalization for Asthma (p=0.005)
Increased ICU visits and/or Mechanical Ventilation (p=0.004)
qCT Airway metrics
Normal vs. Asthma

<table>
<thead>
<tr>
<th></th>
<th>Normal</th>
<th>Asthma</th>
</tr>
</thead>
<tbody>
<tr>
<td>L86</td>
<td>-782</td>
<td>-863*</td>
</tr>
<tr>
<td>WA%</td>
<td>53.7</td>
<td>57.7</td>
</tr>
<tr>
<td>WT%</td>
<td>1.61</td>
<td>1.67</td>
</tr>
<tr>
<td>Total Tissue Volume</td>
<td>255</td>
<td>432*</td>
</tr>
<tr>
<td>N. HU</td>
<td>376*</td>
<td>376*</td>
</tr>
<tr>
<td>%</td>
<td>52</td>
<td>55</td>
</tr>
<tr>
<td>Density</td>
<td>0.16</td>
<td>3.8*</td>
</tr>
</tbody>
</table>

Asthma = more air trapping*
= more wall thickening

Quantification of Ventilation

1. Nuclear Medicine (gamma ray)
   - Xenon gas and
   - 99mTc particles
2. CT (HU density)
   - 30% Xenon gas and 30% Xenon + Argon
3. MRI
   - NMR relaxation from laser excited proton spin state
     - Hyperpolarized ³He (Nobel Gas, High gyromagnetic ratio)
     - Hyperpolarized ¹²⁹Xe (Dissolves in blood)
     - Hyperpolarized Fluorine compounds
   - Paramagnetic
     - 100% Oxygen – Room air (difference image)

Airway Tree: Small Airways

Bigger sac = longer ADC (cm²/sec) = less surface area

Diffusion length XD

HP ³He MRI shows heterogeneity in ventilation defects with Asthma

Movie courtesy of Robert Cadman, PhD

HP ³He Diffusion of the terminal bronchiole and alveolar sac size

Diffusion metrics obtained with HP ³He

³He Apparent Diffusion Coefficient (ADC) in COPD patients shows:
- increases
  a. in acinar duct radius (R)
  b. mean chord length (Lm)
- decreases
  c. in alveolar depth (h)
  d. alveolar density (Na)


Diffusion reveals Microstructure

- $^3$He diffuses ~500 μm in 1 ms
- Lung tissue impedes diffusion
- Modified diffusion coefficient reveals structure

Therapy Trial with He-3 MRI

- 44 children ages 9-10 yrs at-risk for asthma
- Upper and lower quartiles of lung function

Response to Therapy

- PVV = 96%, 93%, 96%
- VV = 97%, 81%, 96%
- VV = 97%, 83%, 98%

COAST: Safe Flexible Pediatric Imaging

- 3 Visits: 2 placebo, 1 Rx

Image guided Therapy

- Affected bronchi can POTENTIALLY be treated with thermoplasty
- Candidates must have failed optimized medical therapy.
- Bronchial thermoplasty in subjects with moderate or severe asthma results in an improvement in asthma control.*

Conclusions

1. Post processing of CT and MRI data in Asthmatics shows:
   a. Inc Wall area percentage (WA%)
   b. Inc Wall thickness percentage (WT%)
   c. Dec Lumen Area percentage (LA%)
   d. Less Deltalumen has worsened outcomes
   e. Heterogeneous Ventilation defects over time
   f. Terminal duct size is proportional to HP $^3$He ADC

2. Treatment response can be determined by PFT’s and Imaging biomarkers.

3. Treatment planning can be targeted to the affected bronchi.

Thank you

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References


