MRI of the airways and lungs
Including hyperpolarized techniques

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Neither financial relationship relates directly to the work discussed.
Lung is most challenging solid organ to image

1. Large and moves with respiration (motion artifacts)
2. Low density ($\rho = 0.2$ g/cm$^3$ at TLC)
3. Multiple air-tissue interfaces (alveoli) cause fast MRI decay of signal

Techniques we use

X-ray (not tomographic)

X-ray CT (fairly high ionizing radiation)

A few other techniques like ultrasound (streaky results)


MRI (no radiation, but historically bad for parenchyma)

(now pretty good!)
Challenges led to new innovation for in-vivo imaging

1. UTE and FT MRI sequences (short echo time)
   Mostly structural imaging (& self gating)
   Some functional techniques
   Oxygen enhanced & multi-volume matching

2. Neonatal MRI
   1.5T ONI / GE hybrid
   (Cincinnati Children’s for 5 yrs, now at Sheffield)

3. Hyperpolarized-gas MRI ($^3$He or $^{129}$Xe)
   Realtime ventilation (breath hold for 10-15 s)
   Measure of alveolar-airspace size
   Measures of gas exchange

Healthy: $\text{FEV}_1 = 98%$
Cystic Fibrosis: $\text{FEV}_1 = 102%$
Complementary Techniques: UTE and HP-gas MRI

CF is a “model” lung disease, since structure+function abnormalities

Structure via UTE MRI
Lung parenchymal signal decays quickly with time
Radial k-space techniques allow short echo time

Lung parenchymal signal

Function (ventilation): $^{129}$Xe MRI
Gas with strong magnetic signal
Score both MRI and CT via Brody Score

Lung Abnormalities
- Bronchiectasis (BR)
- Ground glass opacity (GGO)
- Bronchial wall thickening (BWT)
- Mucus Plugging (MP)
- Consolidation (Con)
- Air trapping (AT)

**CF: UTE MRI comparison to CT: 1-3 yr olds**

![Image showing UTE MRI and CT comparisons with various lung abnormalities highlighted.](image)

- Equation: \( y = 0.47x + 0.87 \)
- \( R^2 = 0.81 \)
Hyperpolarized $^{129}$Xe MRI

Subject in MRI Scanner

Axial Slices Acquired

Inhaled $^{129}$Xe

Control, 6 y.o. female
FEV$_1$ = 95%, VDP = 1.8%

Cystic Fibrosis, 15 y.o. female
FEV$_1$ = 72%, VDP = 32.2%

Cystic Fibrosis, 11 y.o. male
FEV$_1$ = 102%, VDP = 27.5%

$^{129}$Xe MRI in a control subject, and in a patient with CF

14 y.o. male control subject, $FEV_1 = 103\%$ (normal lung function)

All control subjects: uniform $^{129}$Xe ventilation and low $^{129}$Xe ventilation defect percentage (VDP)

15 y.o. female CF subject, $FEV_1 = 73\%$
$^{129}$Xe Ventilation Defect Percentage (VDP) in CF

$^{129}$Xe ventilation MRI is a very sensitive technique for measuring airway obstruction.

**Control**
- FEV$_1$ = 115%

**CF**
- FEV$_1$ = 81%
- FEV$_1$ = 102%

N = 10
N = 11

Ages 6-16

Together get function, structure, and microstructure

Quantify by lobe, segment, or region
Self-gating proton MRI: motion correction and respiration gating

Neonatal Respiratory Cycle via Initial FID Phase
(data binned into 25% quartiles)

Period of quiescence

Period of bulk motion

Quiescence resumed

Tidal expiration

Tidal inspiration

High-resolution pulmonary MRI in neonates is feasible (no sedation, free breathing or normal resp support)

After new sequences and 2-yr optimization:
High-resolution images, high signal

Lung parenchymal signal

MRI signal

time after rf pulse (ms)

NICU control patient – no lung abnormalities

Use to quantify density, like CT?

5 Neonates (~ 40 wks PMA), clinical CT + research MRI

- BPD (Bronchopulmonary Dysplasia)
- Pulmonary Intersitial Glycogenosis
- Poland Syndrome

CT

UTE MRI

BPD, $R^2 = 0.81$

PIG, $R^2 = 0.79$

PoS, $R^2 = 0.23$

PIG, $R^2 = 0.82$

TEF*, $R^2 = 0.73$


Now we can, with MRI gating and motion correction:

1. Calculation of parenchymal densities and opacities, left & right-lung tidal volumes
2. Visualization of ventilation via ciné loops (from binned reconstructions)
3. Visualization and measurement of airway-walls (structure, malacia)
4. Measure ventilation and gas exchange via $^{129}$Xe MRI
Does pulmonary imaging matter?

1. Does imaging relate to
   a. disease severity?
   b. interventional efficacy?
2. Can we meaningfully phenotype?
3. Does imaging or image-phenotyping help predict outcomes?
4. Do we get unexpected new knowledge?
Parenchymal score stratifies clinical BPD severity

**Clinical severity?**

<table>
<thead>
<tr>
<th>BPD severity (NICHD/NHLBI)</th>
<th>Cohort size N=41 total</th>
</tr>
</thead>
<tbody>
<tr>
<td>Term control</td>
<td>N = 5</td>
</tr>
<tr>
<td>Preterm control</td>
<td>N = 4</td>
</tr>
<tr>
<td>Mild BPD</td>
<td>N = 7</td>
</tr>
<tr>
<td>Moderate BPD</td>
<td>N = 6</td>
</tr>
<tr>
<td>Severe BPD</td>
<td>N = 20 (2 are deceased)</td>
</tr>
</tbody>
</table>

![Box plot showing BPD MRI scores for different BPD severity levels]
Conclusions

Pulmonary MRI is feasible, practical (even in NICU)

• In BPD we can quantify prematurity-associated pulmonary abnormalities
• Predictive of severity and outcomes

New UTE methods with self-gating

• Resolution approaching CT (0.7mm), signal ~ density
• Removal of bulk motion
• Respiratory gating, regional physiology

Hyperpolarized gas MRI

• Very sensitive measure of early lung obstruction
• Quantification of airspace size possible even in neonates