Medical Imaging of Hyperpolarized Gases

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Nuclear Magnetic Resonance

- Excitation
- RF pulse
- Magnetization vector

- Net alignment
Nuclear Magnetic Resonance

Precesses at resonance frequency

\[ \omega = \gamma B \]

Magnetization vector

Net alignment
Nuclear Magnetic Resonance

Precesses at resonance frequency

\[ \omega = \gamma B \]

\[ T = \frac{2\pi}{\omega} \]

RF coil

NMR Signal
Nuclear Magnetic Resonance

Boltzmann distribution

\[ P_{\text{thermal}} = \frac{|N_{\uparrow} - N_{\downarrow}|}{N_{\uparrow} + N_{\downarrow}} = \tanh\left(\frac{\gamma h B}{4\pi k T}\right) \]

Large magnetic field
(1.5 ~ 3.0 Tesla)
Nuclear Magnetic Resonance

Boltzmann distribution

$^1\text{H Polarization}$

Thermal polarization:
$\sim 0.0005\ %$ at 1.5 T
(5 parts per million)

Large magnetic field
(1.5 ~ 3.0 Tesla)
Magnetic Resonance Imaging

Frequency encoding:
Gradient maps spatial location to frequency

\[ x \leftrightarrow \omega \]

Signal is Fourier transform:

\[ s(t) = \int \rho(x) e^{-i\omega(x)t} \, dx \]

Magnetic field gradient:

\[ \vec{B} = (B_0 + xG_x)\vec{z} \]
Magnetic Resonance Imaging

2003 Nobel Prize in medicine!

Frequency encoding:
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Hyperpolarized Noble-Gas MRI

- Spin-exchange optical pumping (SEOP)
- Polarization: \(~0.0005\% \rightarrow 50\%\)
- Stable spin-1/2 noble gases: \(^3\text{He}, \ ^{129}\text{Xe}\)
- $^{129}$Xe: 500 mL ~10% (1 hour)
- $^3$He: 1 L, 30~40% (15 hours)
Polarization Cell
Polarize overnight

- Current polarizer: 30-40% polarization
  1 liter $^3$He per day
- New polarizer: 40-% polarization
  3 liters $^3$He per day

Dispense into bag

![Graph showing $^3$He spin-up with $T_{fit} = 4.6$ hrs]
Siemens Avanto (1.5 Tesla)

Vest-shaped RF coil
(48.5 MHz for $^3$He)

Inhale gas from bag
Hyperpolarized Noble-Gas MRI

- Contrast agent?
- Directly image the inhaled gas

Static Ventilation Imaging

Healthy Subject

Asthmatic

Static Ventilation Imaging

- Severe-persistent asthmatic

Pre Albuterol  Post Albuterol

Chest radiograph

Unusual Subject

3He MRI

Pneumatocele
3D Static Ventilation Imaging

Axial

Coronal

Sagittal

Isotropic 3mm resolution

3D Static Ventilation Imaging
Ventilation Imaging Applications

- Asthma
- Chronic obstructive pulmonary disease (COPD)
- Cystic Fibrosis
- Lung transplant / rejection
MR Grid Tagging

“Tag” the magnetization

End-inspiration

End-expiration

Displacement
2-Phase Grid Tagging

- Temporal resolution of displacement vectors achieved via linear interpolation

Pulse sequence parameters:
- Tag spacing 22 mm
- 5 coronal slices (TH 25 mm), flip angle 4°
- 50% angular density, heavily interleaved
- TR / TE = 3.4 / 1.2 ms
- 870 ms per full image set
- Temporal pseudo-resolution 50 ms
GW Miller et al. Regional quantification of pulmonary biomechanics using dynamic MRI of grid-tagged hyperpolarized $^3$He. ISMRM 15:945 (Berlin, 2007).
Tagging Applications

• Pulmonary Biomechanics
  ➢ Chronic obstructive pulmonary disease (COPD)

• Radiation Therapy
T1-Weighted Contrast

- Hyperpolarized nuclei
  - T1 in bag is tens of minutes
  - T1 in lung is \( \sim 20 \) seconds, due to \( \text{O}_2 \)
  - T1-weighted \(^3\text{He}\) imaging provides
    - \( P_{\text{A} \text{O}_2} \) contrast

Thermally polarized nuclei
Quantitative PO$_2$ Mapping

Phantom experiments

\begin{align*}
\text{pO}_2 \text{ [atm]} & \quad \text{3He image} \\
\text{0.00} & \quad \text{0.20} \\
\text{0.10} & \quad \text{0.15} \\
\text{0.05} & \quad \text{0.05} \\
\text{0.00} & \quad \text{0.00}
\end{align*}

\begin{align*}
\text{Measured pO}_2 \text{ [atm]} & \quad \text{Prepared pO}_2 \text{ [atm]} \\
0 & \quad 0 \\
0.1 & \quad 0.1 \\
0.2 & \quad 0.2
\end{align*}
$P_AO_2$ Mapping in Human Lungs

Healthy volunteer – inhaled $^3$He plus room air

- Coronal projection
- 3 cm slice
$P_AO_2$ Mapping in Human Lungs

Healthy volunteer – 2 different inhalations

$^3$He + room air  $\quad$ $^3$He + $O_2$

Mean = 101 mm Hg  $\quad$ Mean = 227 mm Hg

GW Miller et al. Short-breath-hold lung pO$_2$ mapping with hyperpolarized $^3$He MRI. ESMRMB 22 (Basle, 2005).
PAO₂ Mapping in Human Lungs

Female, age 65, left-lung transplant

GW Miller et al. Short-breath-hold pO₂ imaging with ³He: Initial experience in lung disease. ISMRM 14:1289 (Seattle, 2006).
$P_{A}O_2$ Applications

- Pulmonary embolus
- Sickle Cell disease
- High-Altitude Pulmonary Edema
Lung Structure vs. Imaging Resolution

Pixel resolution ~ 3 mm

3He image of rabbit lung
Lung Structure vs. Imaging Resolution

Fine lung structure

acinus ~3 mm

Alveoli ~200 µm
Diffusion as a Probe of Microstructure

“Apparent Diffusion Coefficient” (ADC)

Normal Alveolar Sac

small, healthy airspaces

Low $^3$He ADC

Emphysematous Alveolar Sac

enlarged, diseased airspaces

High $^3$He ADC
How do we measure diffusion using NMR?

- Use magnetic-field gradients to encode displacement
Diffusion-Weighted Pulse Sequence

Precessing spins in lab frame

Vector sum in rotating frame
Diffusion-Weighted Pulse Sequence

Precessing spins in lab frame

Vector sum in rotating frame
Diffusion-Weighted Pulse Sequence

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Vector sum in rotating frame
Diffusion-Weighted Pulse Sequence

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Vector sum in rotating frame

G_x

Precessing spins in lab frame
Diffusion-Weighted Pulse Sequence

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Vector sum in rotating frame
Diffusion-Weighted Pulse Sequence

Precessing spins in lab frame

Vector sum in rotating frame
Diffusion-Weighted Pulse Sequence

Precessing spins in lab frame

Vector sum in rotating frame

$G_x$

$B_x$

time
**Diffusion-Weighted Pulse Sequence**

Vector sum in rotating frame

\[ S_1 = S_0 e^{-b \cdot ADC} \]

- Use this equation to extract ADC
- So-called “b value” can be calculated from gradient waveform (free diffusion)
3He ADC: Lung Transplant

- 3He free diffusion coefficient: ~0.9 cm²/s in air
Time-Dependent Diffusivity

Normal Lung

Emphysema

Histology is “gold standard” for characterizing microstructure
Time-Dependent Diffusivity

Emphysema

Normal

Simulated Brownian motion

\[ D(t) \]

\[ D_0 \]

\[ t \]

free diffusion

restricted diffusion

very restricted diffusion
Time vs. Length Scales

\[ \Delta x \sim \sqrt{2D \cdot \Delta t} \]

Time vs. Length Scales

\[ \Delta x \sim \sqrt{2D \cdot \Delta t} \]

- Structural sensitivity determined by diffusion time
Diffusion Applications

Structural information!

- Emphysema
- Lung development
- Asthma?
- Smoking-related lung disease
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<thead>
<tr>
<th></th>
<th>Low Exposure</th>
<th>High Exposure</th>
<th>Smoker</th>
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<tbody>
<tr>
<td><strong>Short time scale</strong> (~1 ms)</td>
<td><img src="image1.png" alt="Image" /></td>
<td><img src="image2.png" alt="Image" /></td>
<td><img src="image3.png" alt="Image" /></td>
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<tr>
<td><strong>Long time scale</strong> (~1 s)</td>
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<td><img src="image5.png" alt="Image" /></td>
<td><img src="image6.png" alt="Image" /></td>
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C Wang et al. Detection of the Changes in the Lungs of People who had High Exposure to Secondhand Cigarette Smoke Using Long-time-scale Global \(^3\)He Diffusion MRI. RSNA 93 (Chicago, 2007).
What about $^{129}$Xe?

- **Cons**
  - Intrinsically lower MR signal
  - Absorbed into tissues and blood

- **Pros**
  - Naturally abundant
  - Absorbed into tissues and blood
Dissolved-Phase Imaging

- Solubility ~1%
- Resonance frequency in dissolved phase is different by ~200 ppm (chemical shift)
- Blood, tissue frequencies slightly different
Chemical-Shift Imaging (CSI)

- Image both gas and dissolved phases, separate based on frequency
- Rabbit with pulmonary embolus

J Mata et al. High-resolution Chemical Shift Imaging of the lungs with Xe-129 during a single 6 second breath-hold: Results from a rabbit model of pulmonary embolism. ISMRM 16:2679 (Toronto, 2008).
Dixon-based CSI

- Separately image both dissolved-phase resonances
- Rat with pulmonary fibrosis
Dixon-Based CSI

Airspaces  Barrier (tissue)  Red Blood Cells

Control

Left lung treated with Bleomycin (day 11 post)

Indirect Imaging of Gas Exchange

Xenon Transfer Contrast (XTC)

- Dynamic equilibrium among compartments
- Repeated, selective destruction of non-equilibrium dissolved magnetization
- Exploit large gas-phase magnetization as an amplifier for weak dissolved-phase signals

Effects of Exchange on Gas Signal

Gas Peak: Exchange

Gas Peak: Control

Effects of Exchange on Gas Signal
Applications of $^{129}$Xe Transfer

- Opens up lots of new possibilities
  - Direct window into gas exchange
  - Tissue density
  - Surface-to-Volume ratio (S/V)
- Fibrosis
- Pulmonary edema
- Radiation injury
Hyperpolarized-Gas MRI

- New insight into lung function and disease
- Earlier detection of lung disease
- Regional assessment of microstructure
- Regional maps of gas exchange
- Efficacy of therapy → drug development
- Minimally invasive
- Safely repeated