Liver Fat Quantification

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Disclosure

• Research agreement with Siemens Medical Solutions
Background

• Non-alcoholic fatty liver diseases (NAFLD)
  – Most common cause of liver disease in the children and adolescents in the United States.
  – High risk for cardiometabolic complications and more severe liver-related morbidity.

• NAFLD spectrum
  – Simple steatosis: nonalcoholic fatty liver (NAFL)
  – Nonalcoholic steatohepatitis (NASH)
  – Liver fibrosis and cirrhosis

• Clinical diagnosis
  – Elevated alanine aminotransferase (ALT): sensitivity 45%, specificity 85%
  – Liver biopsy: hepatic inflammation and fibrosis for diagnosis of NASH
## Role of Radiology

### Fat Quantification

<table>
<thead>
<tr>
<th>Modality</th>
<th>Pros</th>
<th>Cons</th>
</tr>
</thead>
</table>
| **Ultrasound** | • Widespread  
• Low cost | • Highly operator dependent  
• Abdominal gas and body habitus  
• Not quantitative |
| **CT** | • High resolution  
• Anatomic image | • Semi-quantitative  
• Insensitive to low fat deposition  
• Ionizing radiation |
| **MRI** | • Quantitative measurement of fat percentage  
• No ionizing radiation | • MRI contradictions  
• Longer setup and imaging time |
MRI Liver Fat Quantification
Chemical shift Imaging (Dixon MRI)

- Water and fat protons have different resonance frequency (precession rate)
- Δf = 3.5 ppm → 220 Hz at 1.5T, 440 Hz at 3.0T
- Water and fat signals will be in- and out-of-phase at certain TE

![Diagram showing Chemical shift Imaging](image-url)
In-phase (IP)  
\[ |W + F| \]

Out-of-phase (OP)  
\[ |W - F| \]
Two-point Dixon

Signal Fat Fraction (FF)

- Fraction of the liver MR signal attributable to liver fat

\[
S_{IP} = |S_w + S_F| \\
S_{OP} = |S_w - S_F|
\]

\[
FF_{2pt} = \frac{S_F}{S_F + S_w} = \frac{S_{IP} - S_{OP}}{2S_{IP}}
\]

Limitation

- Water/fat ambiguity
  - Which one is dominant?
- T2* signal decay is ignored
  - Under-estimate FF
Three-point Dixon

**Purpose**
- Correct T2* decay of signal intensity

\[
T2^* = (TE_{IP2} - TE_{IP1}) \cdot \log \frac{S_{IP1}}{S_{IP2}} \Rightarrow S_{IP1\_CORR} = S_{IP1} \cdot e^{(TE_{IP2} - TE_{IP1})/T2^*}
\]

\[
FF_{3pt} = \frac{S_{IP1\_CORR} - S_{OP}}{2S_{IP1\_CORR}}
\]

Signal-based, not model-based, how accurate is it?
Model-based PDFF Calculation

Proton Density Fat Fraction (PDFF)
• fraction of the proton density attributable to liver fat

\[ PDFF = \frac{\rho_F}{\rho_W + \rho_F} \]
Fat Spectrum

*in vivo* liver MR spectrum of a fatty liver

How many fat peaks should be included in the model to achieve best accuracy?

1. \(-\text{CH}=\text{CH}^-\) and \(-\text{CH}–\text{O}–\text{CO}^-\)
2. \(-\text{CH}_2–\text{O}–\text{CO}^-\)
3. \(-\text{CH}=\text{CH}–\text{CH}_2–\text{CH}=\text{CH}^-\)
4. \(-\text{CO}–\text{CH}_2–\text{CH}_2–\) and \(-\text{CH}_2–\text{CH}–\text{CH}–\text{CH}_2–\)
5. \(-\text{CO}–\text{CH}_2–\text{CH}_2–\) and \(-\text{(CH}_2)_n^-\)
6. \(-(\text{CH}_2)_n–\text{CH}_3\)

Magnitude Data Fitting

- Use magnitude data acquired from multi-echo acquisition.

**Pros**
- Not sensitive to field inhomogeneity and phase errors

**Cons**
- Sensitive to water/fat ambiguity
- Initial FF value for non-linear data fitting (> or < 0.5) affect the results
Complex Data Fitting

• Use **complex data** acquired from multi-echo acquisition.

• **Pros**
  – Not sensitive to initial FF value
  – More robust to avoid water/fat ambiguity

• **Cons**
  – Needs information regarding B0 field inhomogeneity
  – Sensitive to phase errors
  – More complicated algorithms

![Real part of signal](image1)

![Imaginary part of signal](image2)
Equations

\[
S(TE)_{\text{magnitude}} = \rho_W \cdot \exp \left( -\frac{TE}{T_{2W}^*} \right) + \rho_F \cdot \exp \left( -\frac{TE}{T_{2F}^*} \right) \cdot \sum_{n=1}^{N_p} C_n \cdot \exp(2\pi i \cdot f_n \cdot TE)
\]

\[
S(TE)_{\text{complex}} = \left\{ \rho_W \cdot \exp \left( -\frac{TE}{T_{2W}^*} \right) + \rho_F \cdot \exp \left( -\frac{TE}{T_{2F}^*} \right) \cdot \sum_{n=1}^{N_p} C_n \cdot \exp(2\pi i \cdot f_n \cdot TE) \right\} \cdot \exp(2\pi i \cdot \Delta B_0 \cdot TE)
\]

Proton density
\(T_2^*\) decay
Frequency shift of fat peak

\[
PDFF = \frac{\rho_F}{\rho_W + \rho_F}
\]
T2* and T1 Correction

- T2* signal decay should be counted in the multi-echo fat/water interference model
  - Valuable to measure concurrent liver iron deposition
  - Mono-exponential T2* decay (T2*_{water} = T2*_{fat})
  - Bi-exponential T2* decay (T2*_{water} ≠ T2*_{fat})

- T1 weighting will affect water and fat proton density measurements
  - To be corrected in the multi-echo fat/water interference model
  - To reduce T1 weighting by using small flip angle
# Fat Quantification Protocol at Lurie Children’s Hospital

<table>
<thead>
<tr>
<th>MRI Acquisition</th>
<th>2D</th>
<th>3D</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sequence</td>
<td>Six echo gradient echo</td>
<td></td>
</tr>
<tr>
<td>Echo time (TE) (ms)</td>
<td>2.3, 4.6, 6.9, 9.2, 11.5, 13.8</td>
<td></td>
</tr>
<tr>
<td>Flip angle</td>
<td>10</td>
<td>6</td>
</tr>
<tr>
<td>Repetition time (TR) (ms)</td>
<td>120</td>
<td>15.6</td>
</tr>
<tr>
<td>Matrix</td>
<td>256×166</td>
<td>192×133</td>
</tr>
<tr>
<td>Slice thickness/gap (mm)</td>
<td>10/10</td>
<td>4/0</td>
</tr>
<tr>
<td>Parallel imaging</td>
<td>2</td>
<td>4</td>
</tr>
<tr>
<td>Coverage in one breath-</td>
<td>Single slice</td>
<td>Whole liver coverage</td>
</tr>
<tr>
<td>hold</td>
<td></td>
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</tr>
</tbody>
</table>
Fat Quantification Protocol at Lurie Children’s Hospital

### Post processing Model

<p>| | |</p>
<table>
<thead>
<tr>
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</tr>
</thead>
<tbody>
<tr>
<td>Number of fat peaks</td>
<td>5 peaks (1.3, 2.1, 0.9, 5.3, 4.2 ppm)</td>
</tr>
<tr>
<td>Non-linear curve fitting</td>
<td>Signal magnitude fitting</td>
</tr>
<tr>
<td>T2* decay</td>
<td>Bi-exponential (T2<em>_water, T2</em>_fat)</td>
</tr>
<tr>
<td>Initial FF and T2* for curve fitting</td>
<td>FF and T2* calculated by 3-point Dixon Liver FF&lt;0.5 as prior knowledge</td>
</tr>
</tbody>
</table>

![Graphs showing HIGH FF (~30%) and LOW FF (~5%) signal magnitude over time.](image-url)
Phantom Validation

- Ex-vivo pork liver-fat homogenate phantom
  - Ex-vivo pork liver samples mixed with 0-50% pork visceral fat
  - Proximate analyses to determine the true chemical fat composition for each liver-fat homogenate
The parametric PDFF map indicates the non-uniform distribution of hepatic fat.

**PDFF**

- **Patient Example 1**
  - PDFF = 14.9 ± 2.5%

- **Patient Example 2**
  - PDFF = 22.9 ± 6.4%
Your child recently had an MRI scan to measure the amount of fat present in the liver.

The picture on the left side shows a normal liver. The amount of fat in a normal liver is less than 5%. This amount of fat causes the liver to look pink.

The picture on the right side is your child’s liver. The amount of fat in your child’s liver is X %. Fat build up in the liver causes the liver to look more yellow. This condition is known as fatty liver. The picture does not show inflammation or scarring of the liver that are other injuries associated with fatty liver. Permanent scarring (cirrhosis) is a serious condition of the liver that may result from untreated disease.

Weight loss is the recommended treatment for this condition. A successful weight loss program should change the liver color from dark yellow to light yellow to pink.
Monitoring Liver Fat

Patient 1
17 yo, male, with an increase in weight and BMI
PDFF ➡
Fatty liver disease progression

Patient 2
13 yo, male, with 2 hours exercising per day and healthy diet.
PDFF ➩
Resolved fatty liver disease
Signal-voxel MRS

- Single breath-hold STEAM acquisition.
- Multiple TEs to fit signal to get transverse relativity R2 and corrected PDFF.
- Can be used as a reference measurement and compared with the Dixon method.
Take-home Message

• The multi-echo Dixon MRI method is highly useful in the evaluation of pediatric NAFLD by generating whole liver PDFF maps within a single breath-hold.

• At Lurie Children's, we use 3D T1w 6-echo gradient echo sequence for acquisition and magnitude signal + 5-fat-peak + biexponential T2* model for fat quantification.

• Single-voxel, single breath-hold, MRS can be used as a reference for local FF measurement.

• Fat deposition color images provide personalized patient education materials to promote healthy life style.