MRI/MRS assessment of the status of skeletal muscle in DMD patients

H. Lee Sweeney, Ph.D.
Professor of Physiology
Director, Penn Wellstone Muscular Dystrophy Cooperative Research Center
Perelman School of Medicine
University of Pennsylvania
MRI/MRS assessment of the status of skeletal muscle in DMD patients

H. Lee Sweeney, Ph.D.
Professor of Pharmacology & Therapeutics
Director, UF Myology Institute
University of Florida
## Natural History

<table>
<thead>
<tr>
<th></th>
<th>Controls</th>
<th>DMD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number</td>
<td>36</td>
<td>136</td>
</tr>
<tr>
<td>Mean Age (years)</td>
<td>9.7 (±2.3)</td>
<td>8.3 (±2.2)</td>
</tr>
<tr>
<td>Steroid positive (number)</td>
<td>NA</td>
<td>100</td>
</tr>
<tr>
<td>BMI</td>
<td>17.3 (±3.5)</td>
<td>18.8 (±4.1)</td>
</tr>
</tbody>
</table>

- **CHOP** - Philadelphia, PA
- **OHSU/Shriner’s** – Portland, OR
- **UF** - Gainesville, FL

- Krista Vandenborne (UF), Director
- Lee Sweeney (UPenn/CHOP), Co-Director
Muscle damage
Inflammation
Atrophy and Hypertrophy
Fiber replacement

Magnetic Resonance Biomarker

Secondary processes

Disease Progression
Muscle damage

Atrophy and Hypertrophy

Inflammation

Fiber replacement

Disease Progression

Most useful MR parameters:
- Fat fraction (% of muscle replace by fat)
- Quantitative $T_2$ imaging

Secondary processes
T1 weighted MR Image

Control

Duchenne

Lower leg muscles

TA

LG

Sol

MG
Quantitative imaging - T1 weighted images

- Maximal muscle CSA
- Contractile vs non-contractile area
- Specific force production (force/muscle CSA)

➢ Specific force production (force/muscle CSA)
Non-contractile Area - Signal Intensity Thresholding

% Non-contractile component by age:

- BF1
- RF
- AM
- Gr

Age (yrs):
- <8
- 8-10
- 10-12
- >12

Image showing MR scan with highlighted regions for AM and Gr.
Quantitative imaging – T2 weighted images

T1

T2 + FS
$T_2$ as Marker of Muscle Damage/Inflammation

$T_2$ is very sensitive to local tissue chemistry

- Changes in tissue compartmentation, i.e. membrane permeability
- Water content; edema, inflammation/regeneration
- Fat content, fibrosis,…

$S(TE) = A \cdot e^{-\frac{TE}{T2}}$

$T_2$ Map

$T_2$ as Marker of Muscle Damage/Inflammation

$T_2$ is very sensitive to local tissue chemistry

- Changes in tissue compartmentation, i.e. membrane permeability
- Water content; edema, inflammation/regeneration
- Fat content, fibrosis,…

$T_2$ as Marker of Muscle Damage/Inflammation

$T_2$ is very sensitive to local tissue chemistry

- Changes in tissue compartmentation, i.e. membrane permeability
- Water content; edema, inflammation/regeneration
- Fat content, fibrosis,…
MRI Monitoring Efficacy of Treatment

T2 Contrast

Elevated T2
Untreated
rAAV1-tMCK-LacZ

Secondary processes

- Membrane Integrity
- Inflammation
- Apoptosis and atrophy
- Fiber replacement

Disease Progression

H-Spectroscopy

3 point Dixon Imaging
Comparison of Fat Fraction ± Corticosteroids

- Control
- Corticosteroid-naive
- Corticosteroid

![Graph showing fat fraction comparison](image)
1 year Progression in Fat Fraction ± Corticosteroids

Change in fat fraction (%)
Progression of Fat Fraction with Corticosteroids

- **Soleus**
- **Vastus Lateralis**

*Control mean and 95% CI*
How can MRI be useful for dystrophin replacement therapies?

- MRI can identify areas of intact muscle to guide biopsies.
- Dystrophin expression should result in a slower progression in intramuscular Fat Fraction compared to untreated patients.
- The initiation of dystrophin expression may be associated with an acute decline in $T_2$, which can be detected by both MRI and $^1$H-MRS. However, in older boys with high fat fractions, it may be necessary to use $^1$H-MRS to visualize only the $T_2$ component specifically due to inflammation and/or damage.