T1 Mapping and ECV Estimates at 3T in Pediatric Subjects with Duchenne Muscular Dystrophy and Healthy Controls

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I have nothing to disclose
Duchenne Muscular Dystrophy (DMD)

Incidence of 1:3500 boys\(^1\)

\[1\] McNally EM et al., Circulation (2015)
Duchenne Muscular Dystrophy (DMD)

The genotype is variable, therefore the phenotype is variable.

> 2,000 mutations in the DMD gene have been identified\(^2\)

The genotype is variable, therefore the phenotype is variable.

Duchenne Muscular Dystrophy (DMD)

Dystrophin Protein

- Links sarcomere and extracellular matrix
- Mutation disrupts link to extracellular matrix
  - Causing tears in cellular membrane during myocyte contraction
DMD - Histology

DMD Muscle

- Myofiber size variation
- Fatty replacement, myofiber splitting, and hypertrophy
- Atrophic fibers and fibrofatty replacement

DMD - Progression

Skeletal Muscle

- Gowers Sign
- Using hands to push on legs to stand
- Corticosteroids

Respiratory Muscle

- Airway Clearance
- Muscle Training
- Ventilation

Cardiac Muscle

- DCM
- ~25 Years
- ACE Inhibitors
- ß-blockers
- Resynchronization

Mayo Clinic

~20 Years

~12 Years

~25 Years
Imaging shows that there is clearly disease in the myocardium long before onset of clinical symptoms\textsuperscript{4}.

The genotypic/phenotypic variations blur the line of cardiac involvement. Important to determine biomarkers most sensitive to cardiac involvement in DMD.

Often noted as late outcomes in DMD.

\textsuperscript{4} Bushby et al., Lancet Neurol. (2010)
Pre-contrast T1 is a non-invasive measure of myocardial remodeling and potential early indicator of cardiac disease.

T1 measurements in boys with DMD acquired at 1.5T may identify myocardial changes and assess disease severity\(^5\).

Extracellular volume (ECV) can be calculated and used to quantify diffuse fibrosis\(^6\).

<table>
<thead>
<tr>
<th></th>
<th>Native T1 (ms)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Lateral</td>
</tr>
<tr>
<td>DMD</td>
<td>1075.1(71.8)</td>
</tr>
<tr>
<td>CONTROL</td>
<td>978.2(36.4)</td>
</tr>
<tr>
<td>p</td>
<td>0.000</td>
</tr>
</tbody>
</table>

Mavrogeni et al, JCMR 2016

To characterize differences in global and septal myocardium between boys with DMD and healthy controls at 3T. Pre-contrast T1, post-contrast T1, and ECV estimates.
## Results: Demographics

<table>
<thead>
<tr>
<th></th>
<th>DMD (N=26) Median (IQR)</th>
<th>Control (N=17) Median (IQR)</th>
<th>Mann-Whitney P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age (years)</td>
<td>13(5.0)</td>
<td>13(4.0)</td>
<td>&gt;0.05</td>
</tr>
<tr>
<td>Height (cm)</td>
<td>134(26.0)</td>
<td>165(20.3)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Weight (kg)</td>
<td>50(26.3)</td>
<td>51.3(15.3)</td>
<td>0.61</td>
</tr>
<tr>
<td>Body mass index (kg/m²)</td>
<td>25.9(9.5)</td>
<td>18.2(3.38)</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Heart rate (bpm)</td>
<td>87(24)</td>
<td>69(30)</td>
<td>0.02</td>
</tr>
<tr>
<td>Hematocrit (%)</td>
<td>43.5(3.6)</td>
<td>-</td>
<td>-</td>
</tr>
</tbody>
</table>
Methods - DMD MRI EXAM at 3T

A. Localizers

B. Short Axis Tagging

C. Pre-Contrast T1-Mapping

D. T2-Mapping

E. Perfusion

F. Short & Long-Axis CINE

G. LGE Imaging

H. Post-Contrast ECV

<table>
<thead>
<tr>
<th>Sequence Parameter</th>
<th>MOLLI HR &lt; 90</th>
<th>MOLLI HR &gt; 90</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOV (mm)</td>
<td>360 x 270</td>
<td>360 x 270</td>
</tr>
<tr>
<td>Matrix (mm$^2$)</td>
<td>192x164</td>
<td>192x164</td>
</tr>
<tr>
<td>Resolution (mm$^3$)</td>
<td>2x2x8</td>
<td>2x2x8</td>
</tr>
<tr>
<td>Slice thickness (mm)</td>
<td>8</td>
<td>8</td>
</tr>
<tr>
<td>TE (ms)</td>
<td>1.12</td>
<td>1.01</td>
</tr>
<tr>
<td>TR (ms)</td>
<td>2.7</td>
<td>2.44</td>
</tr>
<tr>
<td>Flip angle (°)</td>
<td>20</td>
<td>20</td>
</tr>
</tbody>
</table>
Methods - Data Analysis

CMR

- **Patients**
  - Pre- & Post-contrast T1
  - ECV

- **Volunteers**
  - Pre-contrast

Single mid-ventricular slice

ROI Selection

- **Global**
- **Septal**

Extract summary statistics
**Methods - Data Analysis**

**CMR**

**Patients**
- Pre- & Post-contrast T1

**Single mid-ventricular slice**

**ROI Selection**

**Pre-Contrast**

**Register Pre+Post Blood pool T1 Hematocrit**

**Post-Contrast ECV**

**Extract summary statistics**

**Report Median (IQR)**
Results - Increased Pre-contrast T1 in DMD Subjects

CONTROL

DMD

Native T1 (ms)

Global Myocardium

MEDIAN (IQR)

HEALTHY

* p<0.05

1291(62)

1301(39)
Results - Decreased Pre-contrast T1 in Septal Region

- **HEALTHY**
  - Global Myocardium: 1291 (62)
  - Septal Myocardium: 1301 (53)

- **DMD**
  - Global Myocardium: 1331 (58.3)
  - Septal Myocardium: 1301 (39)

* p<0.05
Results - Decreased Pre-contrast T1 in Septal Region

* p<0.05

MEDIAN (IQR)
Results - Increased Post-contrast T1 in DMD Septum

- **Post-contrast (ms)**
  - Global: 596 (92)
  - Septal: 631 (108)

- Pre-contrast vs. Post-contrast:
  - **Global Myocardium**
  - **Septal Myocardium**

- *p < 0.05

MEDIAN (IQR)
Results: Decreased ECV in DMD Septum

Previously reported ECV values⁵:
DMD: 31.3(6.7)
CONTROL: 24.4(3.5)

Discussion - Variable Disease Progression

- **Native T1**
  - Control: EF > 55%
  - DMD Early Stage: EF > 55%
  - DMD Late State: EF < 55%
- **LGE**
  - Control: EF > 55%
  - DMD Early Stage: EF > 55%
  - DMD Late State: EF < 55%
- **Post-contrast**
  - Control: EF > 55%
  - DMD Early Stage: EF > 55%
  - DMD Late State: EF < 55%
- **ECV**
  - Control: EF > 55%
  - DMD Early Stage: EF > 55%
  - DMD Late State: EF < 55%

**HLA CINE**

- Control: EF > 55%
- DMD Early Stage: EF > 55%
- DMD Late State: EF < 55%
Discussion & Conclusions

- Boys with DMD present with significantly elevated pre-contrast $T_1$ compared to healthy boys.

- As expected, 3T $T_1$ values here are elevated relative to previously reported 1.5T values for DMD and healthy groups.

- Post-contrast $T_1$ and ECV estimates are reported here for boys with DMD at 3T for the first time.

- Global myocardial values more elevated compared to the septum for DMD boys.
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