

Better Trials for Duchenne: How Muscle Fat Measurement and Modeling Are Shaping the Future

**Parent
Project
Muscular
Dystrophy**

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Why We Need Better Trials for Duchenne

- **Sensitive, reliable measures** (endpoints or biomarkers) that can detect meaningful changes **early and over time**
- **Fewer participants needed** to reach clear answers
- **Shorter studies** to reduce burden on individuals with Duchenne and their families

Primary Endpoints Used Widely As “The Standard”



10m Walk/run



4 Stair Climb



Supine to Stand

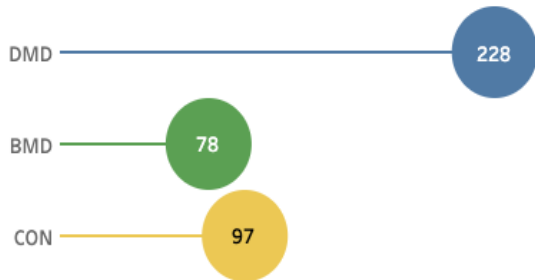
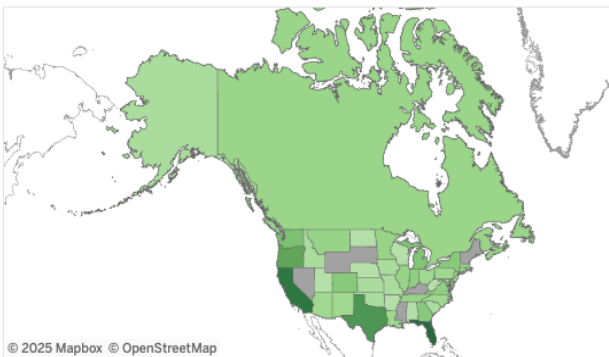


6MWT



ImagingNMD Natural History Study

- 2010-present
- Florida, Oregon, Pennsylvania



Total Subjects

403

Total Visits

1,520

Follow-Up Visits

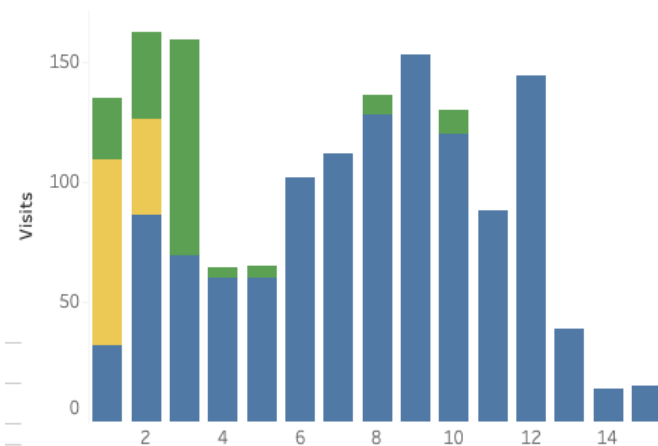
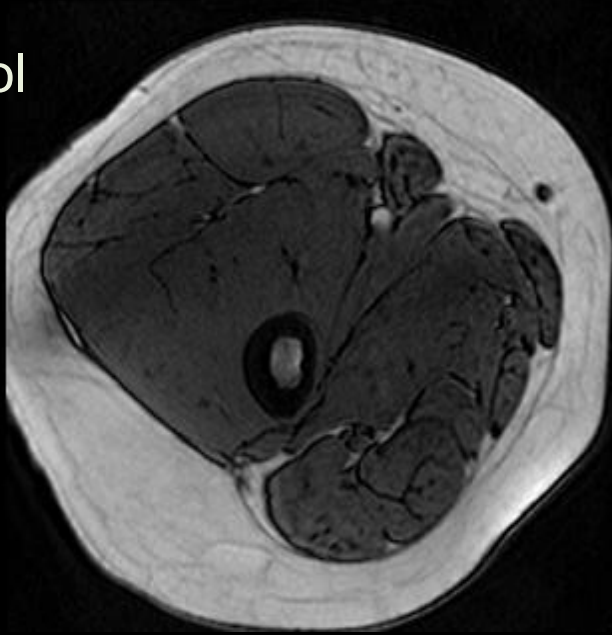


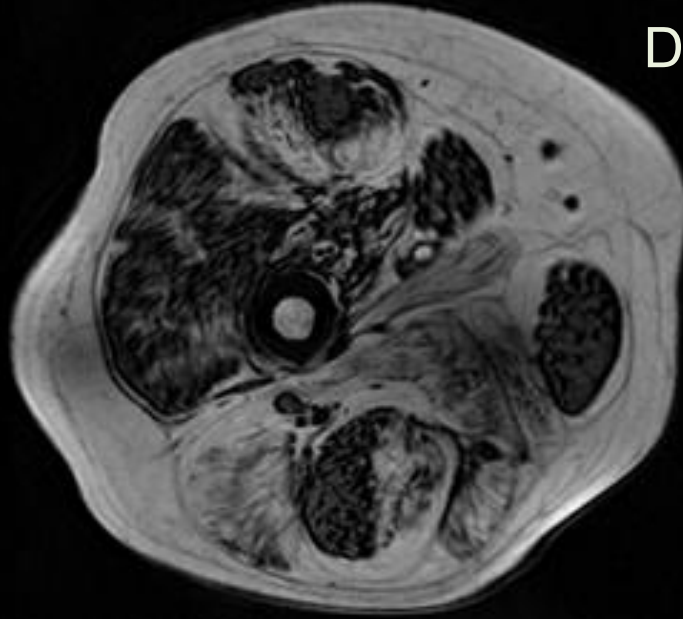
Image Source: imagingnmd.org/research-dashboard

MR Imaging Detects Muscle Pathology

Control



Duchenne

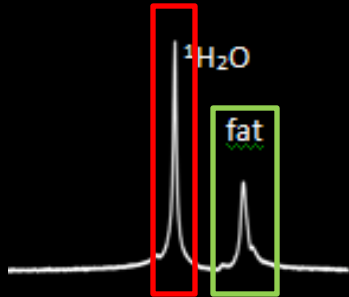
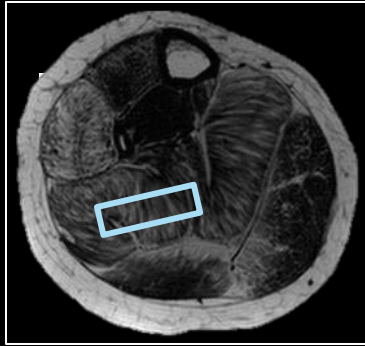


Visual inspection → Quantitative Imaging



Image Source: ImagingNMD

Spectroscopy (MRS) provides a precise and reliable measure of muscle fat

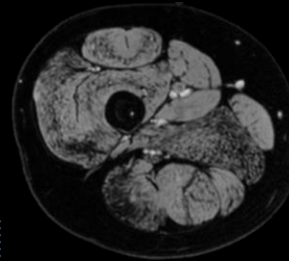


Fat fraction = the ratio of the peak areas of fat (green) to the sum of the peak areas of fat (green) and water (red).

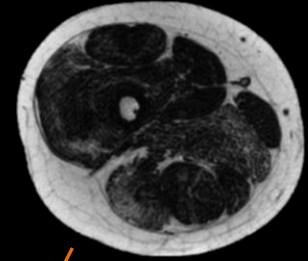
$$\text{Fat Fraction (FF)} = \frac{\text{Fat}}{\text{H}_2\text{O} + \text{Fat}}$$

Dixon Imaging provides high spatial resolution of multiple muscles

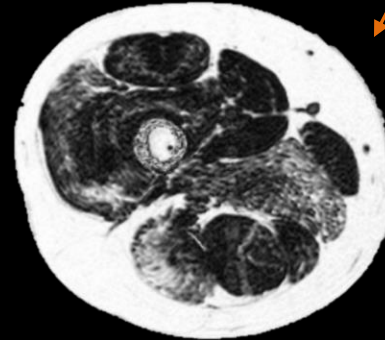
WATER IMAGE



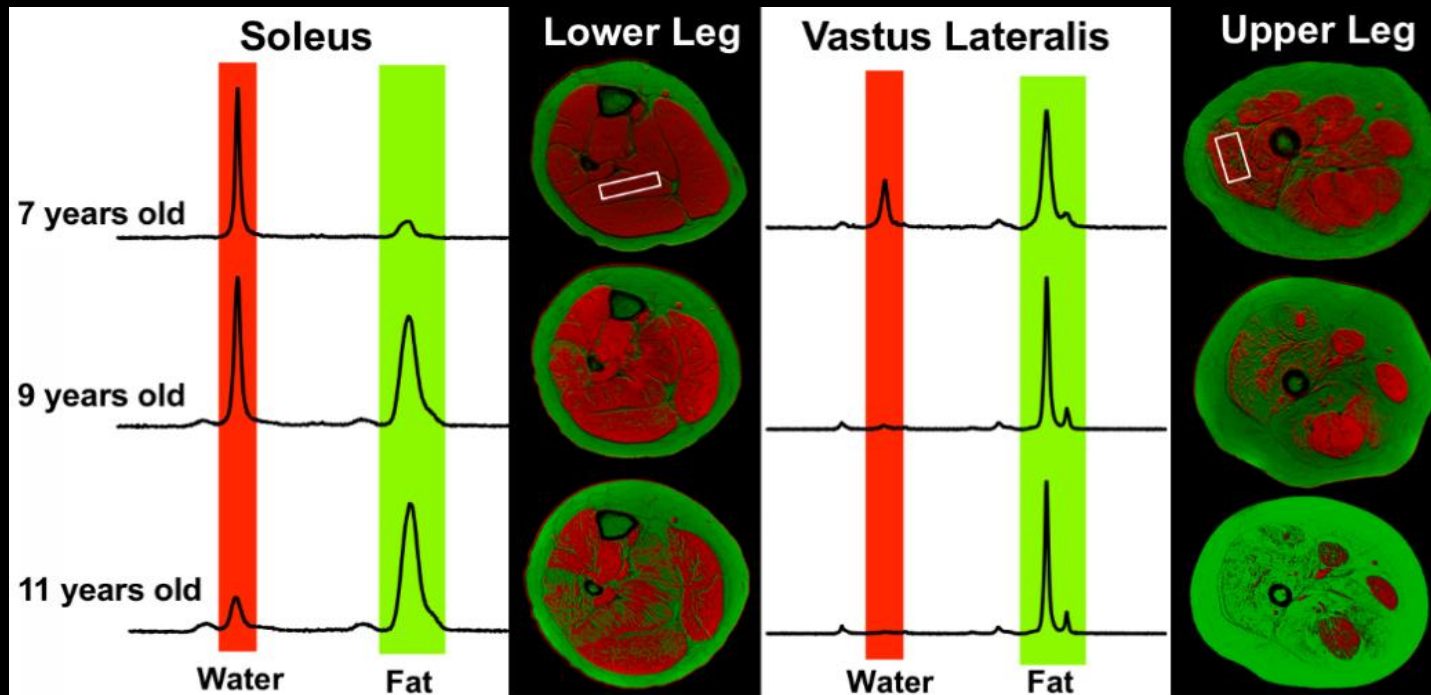
FAT IMAGE



DERIVED
FF MAP



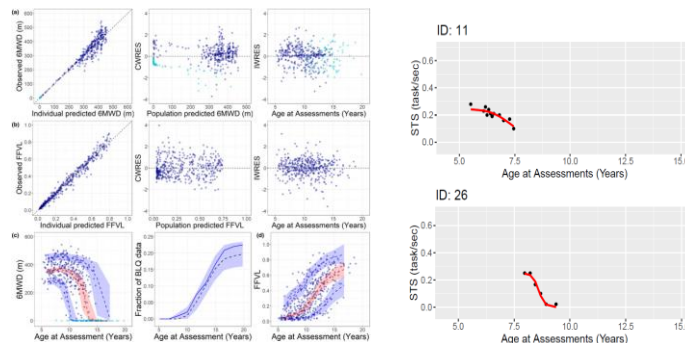
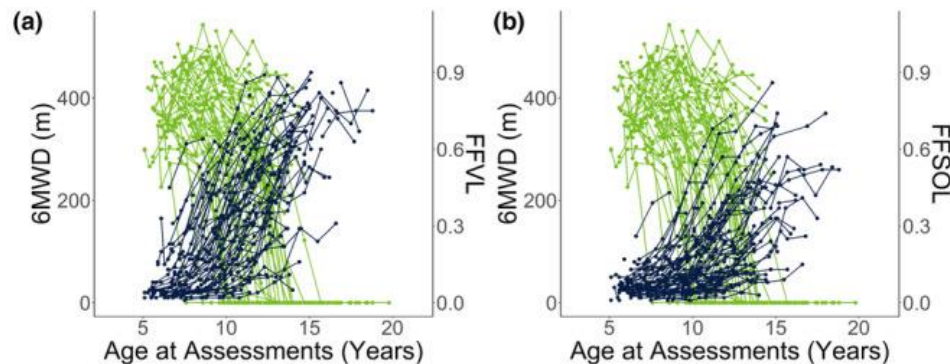
Muscle Fat Fraction as Measure of DMD Progression



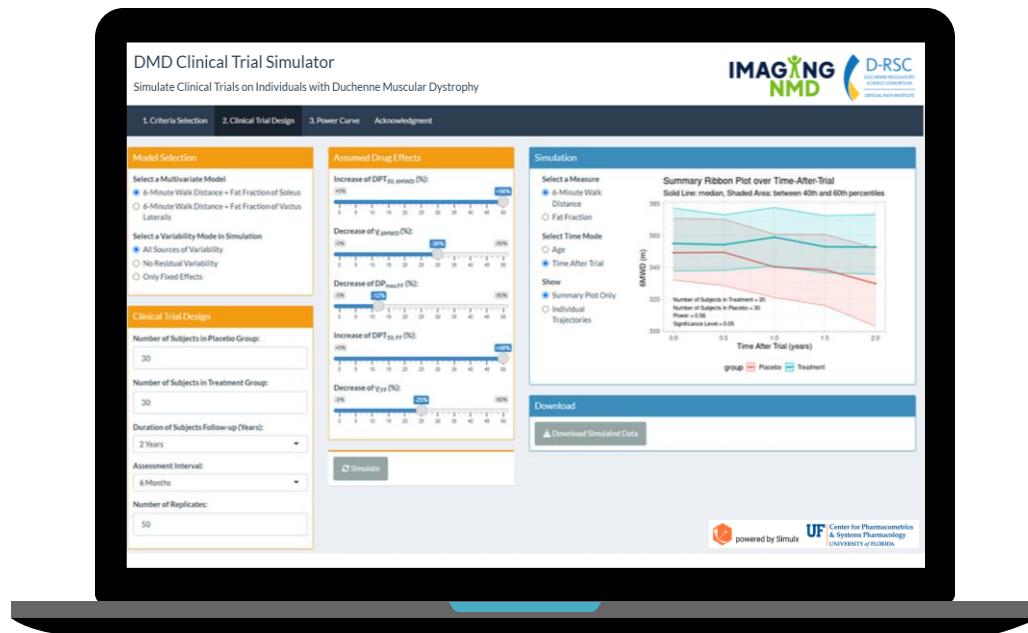
How can we use modeling to maximize the value of fat fraction in clinical trials— and design smaller, shorter studies?

Regulatory-Grade Multivariate Disease Progression Models

- Quantify the longitudinal associations between 6MWD and fat fraction measures in the leg muscles.
- Accurately predict **how baseline characteristics** influence individual-level trajectories.
- Provide clinically interpretable parameters.



Model-Based Clinical Trial Simulator



← This model-based clinical trial simulation tool can be accessed via the link:

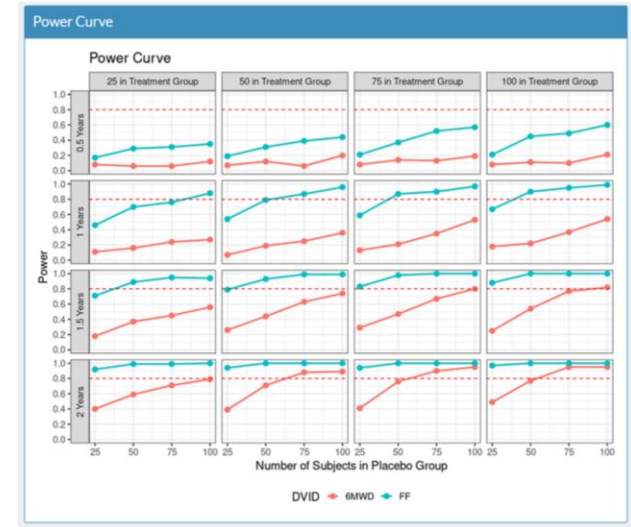
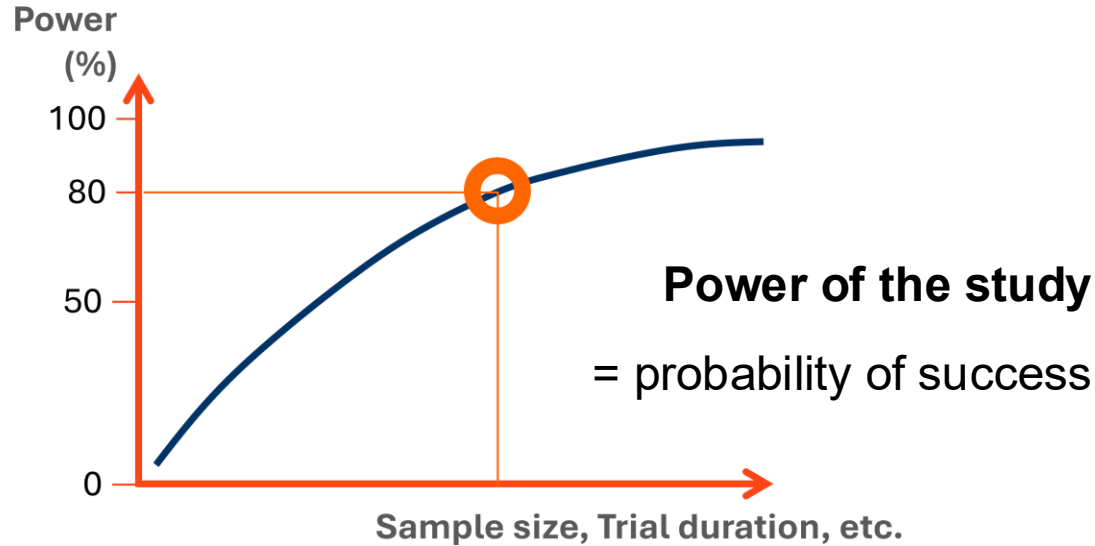
<https://app.cop.ufl.edu/dmd>

... And more to come!

PP
MD

PMID: 39360574 (DOI: [10.1002/psp4.13246](https://doi.org/10.1002/psp4.13246))

Model-Informed Clinical Trial Optimization



Takeaways

- Measuring muscle fat gives us a clear and reliable way to track changes in Duchenne.
- By using existing data and modeling, we can design better trials through simulation before they even begin.
- This helps create smaller, shorter studies reducing burden on individuals with Duchenne and their families.

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**Parent
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- UF Startup Fund
- UF CTSI Pilot Fund



- ASCPT Abernethy ESI Award



Questions?

The background features large, bold, dark red letters 'P' and 'M' in a sans-serif font. The 'P's are positioned at the top, and the 'M' is at the bottom, with a vertical red line separating them. The text 'Thank you!' is centered in the middle of the image.

Thank you!