#### **1. Introduction**

# Whole-Body MSK MRI Evaluation of FSHD Disease **Heterogeneity and Progression**

Fulcrum

Therapeutics



- WB-MSK-MRI Captures
- Holistic evaluation of skeletal musculature
- Small quantitative changes in muscle health
- that correlate with functional measures Disease Heterogeneity
- Non-invasive
- Minimal burden on patient participation
- Changes in MSK MRI may be detected earlier than changes in clinical outcome assessments (COAs)

Affected Muscle

**Study Objective:** The aim of this study was to develop a quantitative whole-body (WB) musculoskeletal MRI protocol in facioscapulohumeral muscular dystrophy (FSHD), evaluate the reliability of longitudinal WB composite scores and assess correlations with clinical outcomes.

### **New Paradigm of Image Analysis in Neuromuscular** Disease



Imaging a slice(s) of select muscles in lower limbs



Imaging of whole muscle, proximal to distal, in the whole body



Personalized set of muscles to follow over time

## 2. Study Design

- Two Visits 4-12 weeks apart
- Assessments included:
- WB-MSK-MRI
- Clinical Outcome Assessments
- Muscle Biopsy
- TUG
- FSHD TUG
- Reachable Workspace (RWS)







# Quantitative Muscle Analysis in FSHD Using Whole-Body MRI: **Composite Muscle Measurements for Cross-Sectional Analysis**

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## Main Inclusion Criteria

- Age 18-65 years old
- Confirmed diagnosis of FSHD1 with 1-7 repeats
- CSS 2 to 4 on Ricci's scale (range 0-5)
- Presence of STIR positive signal in at least one leg muscle eligible for muscle biopsy

Subject Demographics (N=17)			
Variable	Mean(SD); Range		
Age	49.4 (13.02); 23-65		
Gender (Female) %	29.4%		
Clinical Severity Score (CSS)	3.0 (0.71); 2-4		
Average Repeats	5.2 (1.46); 3-7		

# Imaging Protocol for Whole Body MRI



Total examination time ~30 min

# Muscles Studied: 18 muscles bilaterally; 36 total

#### Arm

- Deltoid
- Biceps Brachii
- Triceps Brachii

#### Torso

- Pectoralis Major
- Rhomboideus
- Latissimus Dorsi & Teres Major
- Trapezius
- Serratus Anterior
- Paraspinal (C3-Sacrum)

#### Neck

- Supraspinatus
- Infraspinatus
- Subscapularis
- Teres Minor

#### Legs

- Quadriceps
- Hamstrings
- Adductors
- Tibialis Anterior
- Gastrocnemius
- Medialis

478 out of 612 muscles analyzed;134 not analyzable: 64 Image Artifacts (technical issues; e.g. streak artifact); 70 due to complete fat replacement



Biomarker	Category	(%)	Sw
LMV	Normal	1.9	4.8 cl
	Intermediate	3.4	6.2 cl
MFF	Normal	4.6	0.5%
	Intermediate	4.8	1.5%
MFI	Normal	4.8	0.3%
	Intermediate	3.0	0.4%











