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

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1. Introduction

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

- WB-MSK-MRI Captures
- Holistic evaluation of skeletal muscle
- Small quantitative changes in muscle health that correlate with functional measures
- Disease Heterogeneity
- Non-invasive
- Minimal burden on patient participation
- Non-invasive
- WB-MSK-MRI has a small quantitative changes in muscle health
- Holistic evaluation of skeletal musculature that correlate with functional measures

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

1.2 Study Design

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

Muscles Studied: 18 muscles bilaterally; 36 total

- Arm
  - Deltoid
  - Biceps Brachi
  - Triceps Brachi
- Neck
  - Supraspinatus
  - Infraspinatus
  - Subscapularis
  - Teres Minor
- Torso
  - Pectoralis Major
  - Rhomboid
  - Latissimus Dorsi & Teres Major
  - Trapezius
  - Serratus Anterior
  - Paraspinal (C3-Sacrum)
- Legs
  - Quadriceps
  - Hamstrings
  - Adductors
  - Tibialis Anterior
  - Gastrocnemius
  - Medials

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

2. Study Design

2.1 Imaging Protocol for Whole Body MRI

- Total examination time ~30 min

3. Results

3.1 Variability of WB-Composites in Normal and Intermediate Muscles

- WB-MSK-MRI Captures Disease Heterogeneity as Shown in Representative Avatars of Each Enrolled Subject

- Good Reproducibility for All Individual Muscle Measurements

- Reproducibility Statistics for the Longitudinal Composites, MFI, MFF

- Strong correlations with clinical outcome assessments support meaningfulness of each quantitative MRI metric

4. Conclusion

- Developed WB-MSK-MRI protocol, currently being performed in all Phase 2 clinical trials of losmapimod.
- Reproducibility of quantitative muscle measurements was excellent.
- Strong cross-sectional correlation between Regional Composite Measurement (MFFtot & MFItot) and TUG, FSHD-TUG and RWS.
- Whole-Body MSK MRI can capture the heterogeneity and provide important information about disease severity as it correlates with FSHD relevant clinical endpoints.

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