

MRI muscle segmentation in Duchenne muscular dystrophy: Stepwise region of interest (ROI) contractions to minimize fat fraction variability

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1 INTRODUCTION

- Muscle MR imaging provides important efficacy-response biomarkers for DMD and other neuromuscular trials¹
- MRI proton density fat fraction (PDFF) is a sensitive and objective endpoint² for quantifying fat replacement in affected muscle
- The largest source of variability in MRI-PDFF measurements of the vastus lateralis (VL) is segmentation errors between analysts at the cross-sectional boundaries of muscles,³ which can be reduced by an axial contraction of segmentation boundaries⁴
- To minimize MRI-PDFF measurement variability, the optimal axial contraction may be different for different muscles

2 AIMS

- Test a strategy for optimizing muscle ROIs to minimize fat fraction variability and maximize ROI volume for muscles of different size, location, and depth

3 METHODS

- MRI scans of the VL (N=13) and soleus (N=14) optimized for PDFF quantitation^{5,6} were randomly extracted from an anonymous clinical trial data repository
- Muscle bellies were segmented from T1-weighted images by 2 independent analysts and the center 3 axial slices were extracted as the original ROI for fat fraction quantitation
- Each original ROI was automatically contracted in 0.2 mm increments from 0 to 2 mm and fat fraction was computed from the PDFF map using each contracted contour as a ROI

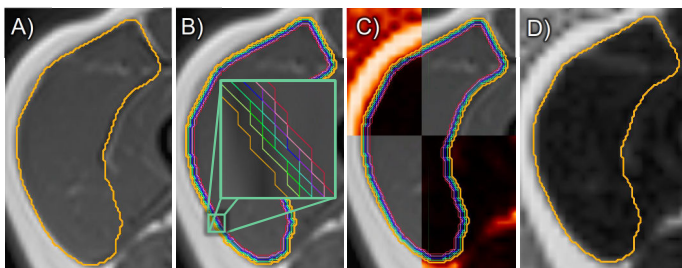


Fig. 1: Fat fraction quantitation A) Muscle segmented on T1 B) Stepwise contraction from 0 mm to 2 mm in steps of 0.2 mm C) T1 and PDFF map co-registered D) ROIs from T1 overlaid on PDFF map, fat fraction is average value of PDFF map within each ROI

- 1-way/2-way random effects, single-rating, absolute agreement intraclass correlation coefficient (ICC) was calculated between 2 analysts (soleus) or 2 analysts with physician overread (VL) fat fraction values
- Fat fraction minimum detectable change (MDC) and Dice coefficient calculated at each stepwise contraction

$$\text{MDC} = 1.96 \times \sqrt{2} \times \text{SD} \sqrt{1 - \text{ICC}}$$

SD = standard deviation

$$\text{Dice} = \frac{2 \times \text{Contracted ROI}}{\text{Original ROI} + \text{Contracted ROI}}$$

- Optimal contraction determined by coincidence of MDC, Dice, and fat fraction vs contraction

4 RESULTS AND DISCUSSION

- Average fat fraction appeared to approach an asymptote after the initial 0.6 mm contraction in the VL (Fig. 2) and soleus (Fig. 3)
- Fig. 2 shows fat fraction MDC reduced by 75% in the VL with 1.2 mm contraction (MDC = 1.0%, Dice 0.91)
- Fig. 3 shows fat fraction MDC reduced by 29% in the soleus with 1.0 mm contraction (MDC = 1.3%, Dice 0.90)

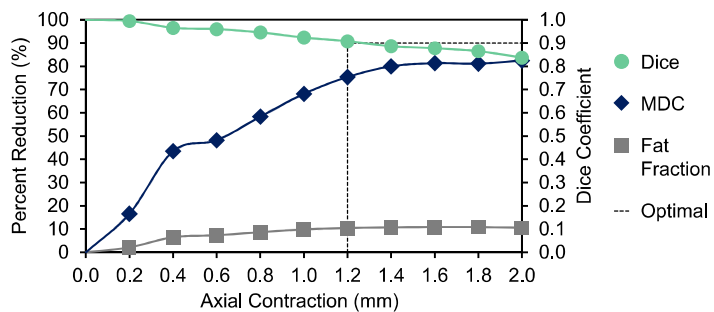


Fig. 2: MDC and fat fraction percent reductions in the VL and Dice coefficient at each contraction increment from 0 to 2 mm

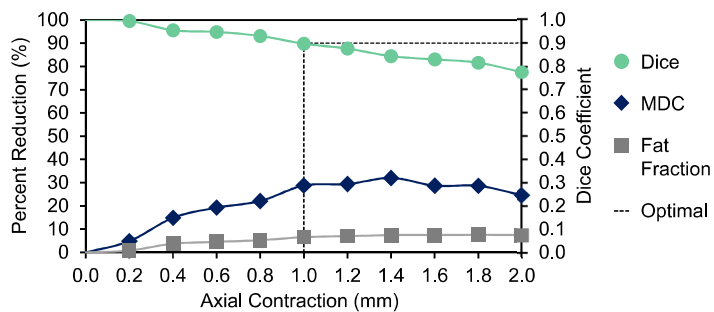


Fig. 3: MDC and fat fraction percent reductions in the soleus and Dice coefficient at each contraction increment from 0 to 2 mm

- Variability approached a minimum as demonstrated by convergence of MDC reduction and a Dice coefficient nearing 0.9 for both muscles in Figs. 2 and 3
- Further axial contraction of the ROI had minimal effects on MDC and average fat fraction values

5 CONCLUSIONS

- Axial contraction of ROI that represents a Dice coefficient of 0.9 (82% of the segmented muscle volume) is optimal for maximizing interrogated volume and ability to demonstrate efficacy for disease-modifying therapeutics

6 REFERENCES

1. Duchenne Muscular Dystrophy and Related Dystrophinopathies: Developing Drugs for Treatment Guidance for Industry. 2018; FDA-2015-D-1884
2. Burakiewicz J, et al. *J Neurol.* 2017; 264(10):2053-67
3. Hammond M, et al. *Neuromuscul Disord.* 2020; 30(1):S92
4. Hammond M, et al. *Neuromuscul Disord.* 2021; 31:S152
5. Berglund J, et al. *Magn Reson Med.* 2017; 78(3):941-9
6. Yu H, et al. *Magn Reson Med.* 2008; 60(5):1122-34

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