DMD Muscle Characteristics in the Time and Frequency Domain

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Duchenne muscular dystrophy (DMD) is a lethal muscle degenerative disease affecting 1:3500 male births [1]. It is caused by genetic mutations resulting in dystrophin protein deficiency. Dystrophin maintains membrane integrity; its deficiency causes myofiber damage under mechanical loading [1]. The resulting DMD muscle membrane tears impact its permeability which increases calcium concentration inside the cell and promotes inflammatory reactions and muscle degeneration [2]. Eventually, DMD muscle suffers a loss of mass, and becomes less functional due to inflammation and fibrosis [3]. Current therapies aim to slow disease progression, promote muscle regeneration and growth, and maintain muscle mass [2].

Noninvasive measurements of muscle electrical and mechanical activities using electromyography (EMG) and mechanomyography (MMG) respectively along with muscle force could provide valuable insights about muscle performance and contraction dynamics [4, 5]. The objective of the current study is to investigate the differences in the relation between EMG, MMG, and generated force in healthy and DMD muscles in children. These characteristics could help track DMD progression and effectiveness of therapies and complement other noninvasive measurements like ultrasound and MRI imaging that mainly focus on muscle structure [6]. To the best of authors' knowledge, such characteristics were not fully studied previously.

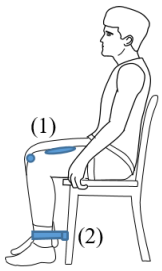

Figure 1. The experimental set up. (1) EMG & MMG, (2) Force gauge

The current study included 14 subjects (5 controls, 4 early ambulatory and 5 late ambulatory) with subject age of 10.2±2.3 years (mean±SD). Subjects rested in the sitting position (Figure 1) with MMG sensor placed over the middle of the rectus femoris muscle. Two EMG electrodes were placed over the same muscle 3 cm distal and proximal to the MMG sensor. The ground EMG electrode was placed over the patella. A force gauge was connected to the distal end of the tibia to measure the force generated from muscle contraction. Subjects were instructed to exert an isometric contraction with maximum voluntary force for 5 seconds against the force gauge while EMG, MMG and generated force were measured at a sampling rate of 2 kHz. This was repeated 5 times with a 30 second rest between contractions.

EMG and MMG signals were bandpass filtered (2-800 Hz and 2-500 Hz respectively); the low cutoff was chosen to remove low frequency noise (e.g., baseline wander) and the high cutoff was chosen such that most of the signal energy is captured. The force was low pass filtered at 50 Hz because most of the force signal energy lied below 50 Hz. Each contraction had three main segments. First, a force buildup segment till reaching a maximum force followed by force plateau and finally force decline, as shown in Figure 2. The onset and end points of the plateau were detected manually using the force characteristics of different segments. Here, the force buildup segment was characterized by a continuous increase in force from its baseline to the onset of a plateau. The force decline segment was characterized by the continuous decrease in force from the end of the plateau until it reaches the baseline. To measure the variability of the force during the plateau, the coefficient of variation (COV) of the force was calculated. All contractions had a COV of < 22%. The current study focuses on feature extraction from the force plateau segment. The other segments will be investigated in future work. The extracted features included the ratio of $force_{RMS}$ to

EMG_{RMS} and the ratio of $force_{RMS}$ to MMG_{RMS}, which are time domain features. For the frequency domain, the EMG mean power frequency was calculated using Equation 1 where f, PSD, and F_s are the frequency, power spectral density, and sampling rate respectively.

$$Mean\ power\ frequency = \frac{\int_0^{Fs/2} f.PSD(f)df}{\int_0^{Fs/2} PSD(f)df} \quad (1)$$

Figure 3 shows the ratio of $force_{RMS}$ to EMG_{RMS} for all contractions. As DMD progresses, this ratio seemed to decrease, which reflects a decline in the muscle ability to generate force for a given activation. There was statistically significant difference between all the groups shown in Figure 3 ($p \leq 0.05$, unpaired t-test). The ratio of $force_{RMS}$ to MMG_{RMS} also decreased with DMD, as shown in Figure 4, with a statistically significant difference between early and late ambulatory and between controls and late ambulatory ($p \leq 0.05$, unpaired t-test). There was no significant difference between controls and early ambulatory for the $force_{RMS}$ to MMG_{RMS} ratio. The results of Figure 4 may also be interpreted as a reduction in muscle force generation efficiency with DMD.

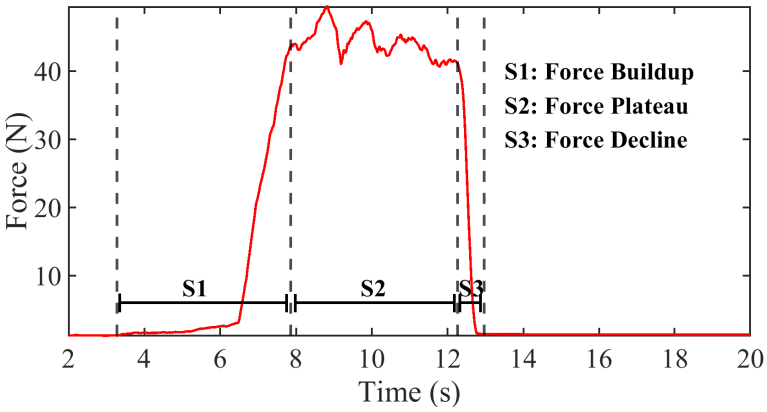

Figure 2. Segments of a typical muscle contraction force profile

Dystrophin is known to play a role in forming dystrophin-glycoprotein complex, which maintains muscle integrity and helps transmit the force generated by muscle contraction. Consequently, dystrophin deficiency with DMD could negatively impact force transmission [2, 7]. This may further explain the decreased force with DMD.

Figure 5 shows the distribution of the EMG mean power frequency, which decreased with DMD ($p \leq 0.05$, unpaired t-test) between the 3 groups shown in the figure. Fast-twitch fibers are known to be affected by DMD first [8] and are characterized by high firing rates compared to slow-twitch fibers [9]. Since EMG

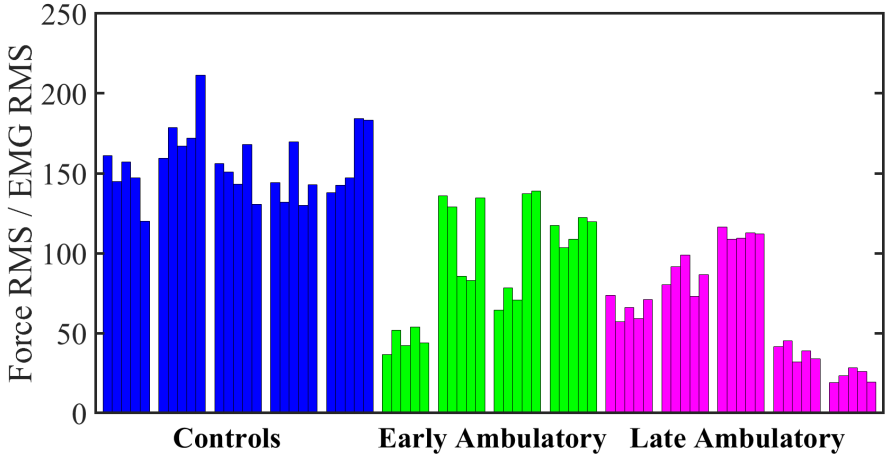

Figure 3. Ratio of force RMS to EMG RMS for the force plateau for all contractions in all subjects

frequency content is a function of the firing rate [9], the loss of fast-twitch fibers is consistent with the reduction in the EMG mean power frequency with DMD shown in Figure 5.

The results highlighted potential time and frequency domain features that could differentiate between healthy and DMD muscles and between early and late ambulatory DMD states in children. These features were extracted from noninvasive measurements of EMG, MMG, and force. Such features may prove helpful to clinically track DMD progression and monitor the effectiveness of emerging or current therapies. Limitations of the current pilot study include the small number of subjects tested and inter-and intra-subject variabilities. Testing the presented approach in more subjects is warranted to confirm the study results. Future work may also investigate the utility of time-frequency domain features.

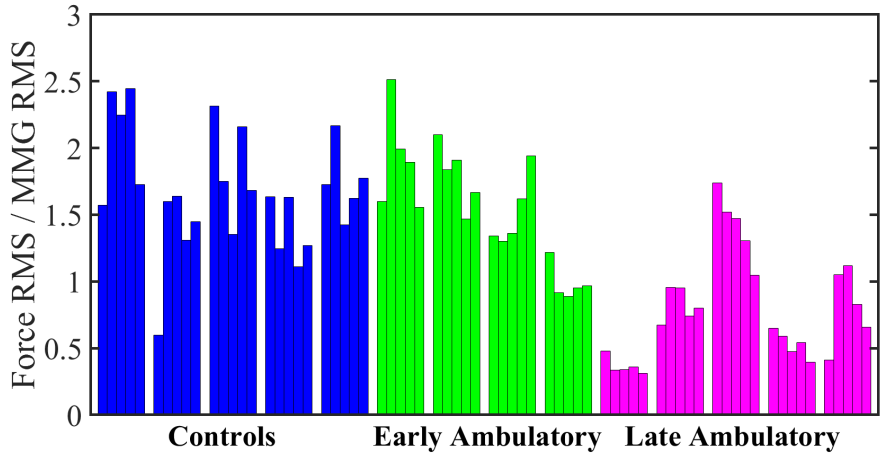

Figure 4. Ratio of force RMS to MMG RMS for the force plateau for all contractions in all subjects

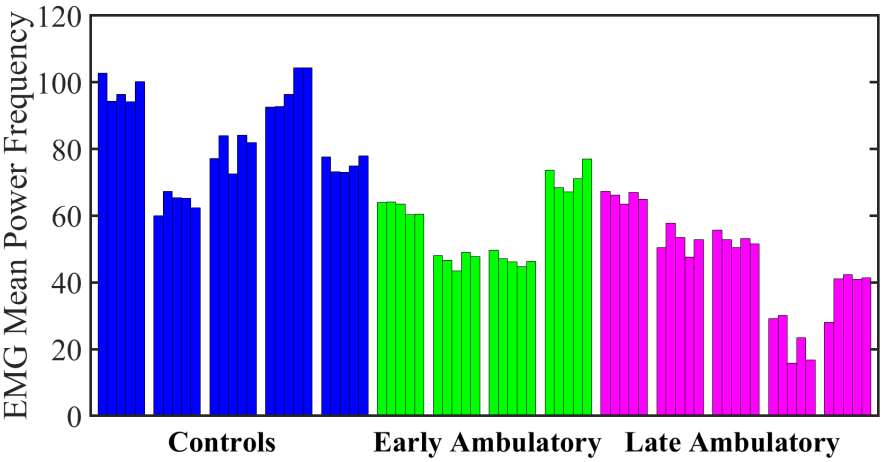

Figure 5. EMG mean power frequency for the force plateau for all contractions in all subjects

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REFERENCES

[1] R. L. Filippelli and N. C. Chang, "Empowering Muscle Stem Cells for the Treatment of Duchenne Muscular Dystrophy," *Cells Tissues Organs,* vol. 211, no. 6, pp. 4-17, 2022.

[2] K. Swiderski, J. P. Hardee, and G. S. Lynch, "Regenerative Rehabilitation for Duchenne Muscular Dystrophy," in *Regenerative Rehabilitation: From Basic Science to the Clinic*, S. M. Greising and J. A. Call Eds. Cham: Springer International Publishing, 2022, pp. 85-119.

[3] Y. Kharraz, J. Guerra, P. Pessina, A. L. Serrano, and P. Muñoz-Cánoves, "Understanding the Process of Fibrosis in Duchenne Muscular Dystrophy," *BioMed Research International,* vol. 2014, p. 965631, 2014/05/04 2014.

[4] T. W. Beck *et al.*, "Does the frequency content of the surface mechanomyographic signal reflect motor unit firing rates? A brief review," *Journal of Electromyography and Kinesiology,* vol. 17, no. 1, pp. 1-13, 2007/02/01/ 2007.

[5] S. Fukuhara, T. Kawashima, and H. Oka, "Indices reflecting muscle contraction performance during exercise based on a combined electromyography and mechanomyography approach," *Scientific Reports,* vol. 11, no. 1, p. 21208, 2021/10/27 2021.

[6] N. G. Simon, Y.-i. Noto, and C. M. Zaidman, "Skeletal muscle imaging in neuromuscular disease," *Journal of Clinical Neuroscience,* vol. 33, pp. 1-10, 2016/11/01/ 2016.

[7] J. M. Ervasti and K. P. Campbell, "A role for the dystrophin-glycoprotein complex as a transmembrane linker between laminin and actin," *Journal of Cell Biology,* vol. 122, no. 4, pp. 809-823, 1993.

[8] J. Talbot and L. Maves, "Skeletal muscle fiber type: using insights from muscle developmental biology to dissect targets for susceptibility and resistance to muscle disease," *WIREs Developmental Biology,* vol. 5, no. 4, pp. 518-534, 2016/07/01 2016.

[9] Y. B. Seven, C. B. Mantilla, W.-Z. Zhan, and G. C. Sieck, "Non-stationarity and power spectral shifts in EMG activity reflect motor unit recruitment in rat diaphragm muscle," *Respiratory Physiology & Neurobiology,* vol. 185, no. 2, pp. 400-409, 2013/01/15/ 2013.

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Abstract

- Duchenne muscular dystrophy (DMD) is a lethal muscle degenerative disease affecting 1:3500 male births. DMD is caused by genetic mutations resulting in dystrophin protein deficiency.
- DMD is a progressive disease that leads to a loss of muscle mass and function due to inflammation and fibrosis.
- Noninvasive measurements of muscle electrical and mechanical activities using electromyography (EMG) and mechanomyography (MMG) respectively along with muscle force could provide valuable insights about muscle performance and contraction dynamics.
- The rectus femoris muscle was considered in the current study. EMG, MMG, and force were acquired simultaneously from 14 subjects who were instructed to perform maximum voluntary isometric contractions for 5 seconds with 30 seconds rest in between.
- The results showed a decrease in the ratio of force RMS to EMG RMS and force RMS to MMG RMS with DMD which might indicate a reduction in muscle force generation efficiency .
- The EMG mean power frequency decreased with DMD which reflected the loss of fast-twitch fibers; which are known to be more affected by DMD than slow-twitch fibers.

Objectives

- The objective of the current study is to investigate the differences in the relation between EMG, MMG, and generated force in healthy and DMD muscles in children. These characteristics could help track DMD progression and effectiveness of therapies and complement other noninvasive measurements like ultrasound and MRI imaging that mainly focus on muscle structure.

Methodology

- The current study included 14 subjects (5 controls, 4 early ambulatory and 5 late ambulatory, 10.2±2.3 years old) after IRB approval.
- Subjects were instructed to exert an isometric contraction with maximum voluntary force for 5 seconds against the force gauge while EMG, MMG and generated force were simultaneously measured (see Figure 1) at a sampling rate of 2 kHz. This was repeated 5 times with a 30 second rest between contractions.
- Signals were filtered (EMG: 2-800 Hz, MMG: 2-500 Hz, Force: lowpass at 50 Hz).
- Features were extracted from the force plateau, See Figure 2. They included the ratio of force RMS to EMG RMS and the ratio of force RMS to MMG RMS and the EMG mean power frequency.

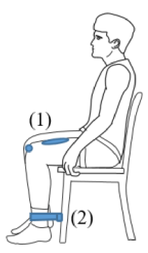

Figure 1. The experimental set up. (1) EMG & MMG, (2) Force gauge

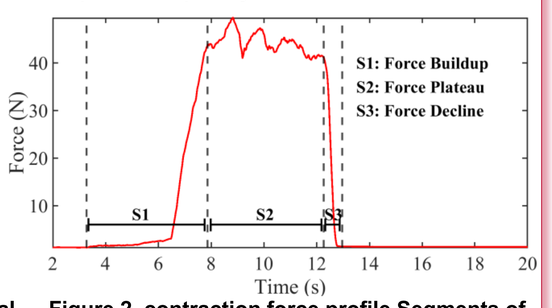

Figure 2. contraction force profile Segments of a typical muscle

Results

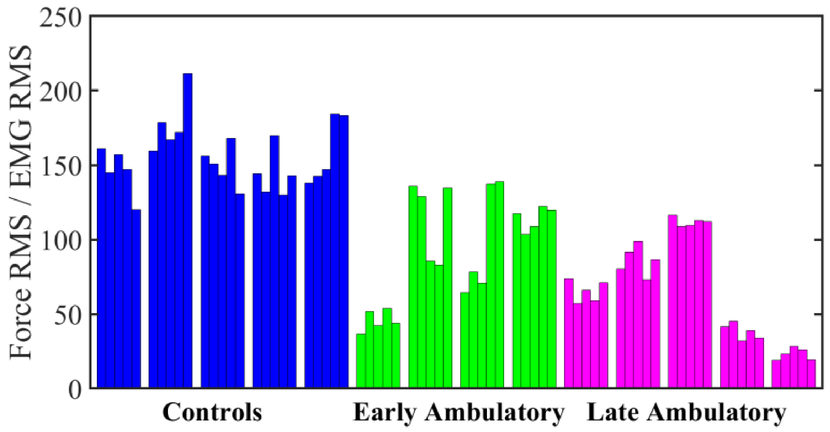

Figure 3. Ratio of force RMS to EMG RMS during the force plateau for all contractions in all subjects. The ratio decreased with DMD.

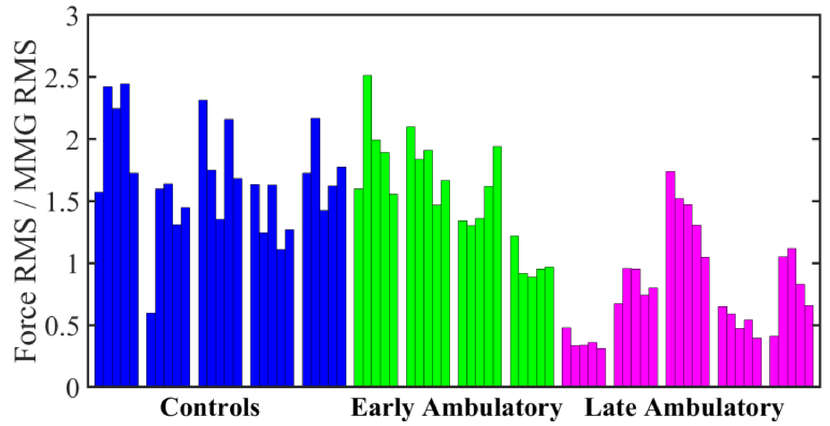

Figure 4. Ratio of force RMS to MMG RMS during the force plateau for all contractions in all subjects. The ratio decreased with DMD.

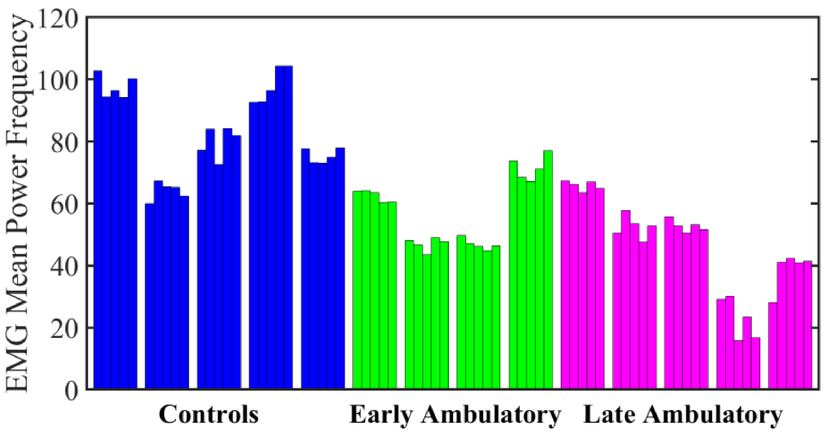

Figure 5. EMG mean power frequency during the force plateau for all contractions in all subjects. The frequency decreased with DMD.

Conclusions

- The results highlighted potential time and frequency domain features that may help differentiate between healthy and DMD muscles (and possibly DMD stages) in children. These features were extracted from noninvasive measurements of EMG, MMG, and force.
- Such features may prove helpful to clinically track DMD progression and monitor the effectiveness of emerging or current therapies.
- Limitations of the current pilot study include the small number of subjects tested and inter-and intra-subject variabilities. Testing the presented approach in more subjects is warranted to confirm the study results.
- Future work may also investigate the utility of time-frequency domain features.

ACKNOWLEDGMENTS

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REFERENCES

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[3] Y. Kharraz, J. Guerra, P. Pessina, A. L. Serrano, and P. Muñoz-Cánoves, "Understanding the Process of Fibrosis in Duchenne Muscular Dystrophy," BioMed Research International, vol. 2014, p. 965631, 2014/05/04 2014.

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[9] Y. B. Seven, C. B. Mantilla, W.-Z. Zhan, and G. C. Sieck, "Non-stationarity and power spectral shifts in EMG activity reflect motor unit recruitment in rat diaphragm muscle," Respiratory Physiology & Neurobiology, vol. 185, no. 2, pp. 400-409, 2013/01/15/ 2013