Predicting Lung Volumes Using Dynamic MRI in Duchenne Muscular Dystrophy and Unaffected Controls

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INTRODUCTION

- DMD is a fatal X-linked disorder, affecting 1 in every 5,000 male births[1].
- A mutation in the DMD gene totally precludes dystrophin production, a protein responsible for bridging the intracellular actin cytoskeleton to the extracellular matrix, helping muscle cells withstand contraction forces. The protein is found primarily in skeletal and cardiac muscles.
- Cardiac and respiratory muscles are affected in DMD. Fibrosis and fatty infiltration occurs in affected muscle groups.
- Respiratory failure is a major cause of death among individuals, secondary to cardiomyopathies[2]. Ventilatory aids and the use of corticosteroids have ameliorated symptoms and expanded life expectancies, though clinical tests point to a sustained functional decline in lung capacities after the loss of ambulation occurs.
- **AIM:** Given that there is much yet to learn about respiratory impairment in the DMD population, aside from what can be gleaned from clinical tests such as FVC measurements, MRI scans presents a novel way of non-invasively imaging different muscle groups that may be implicated in the disease progression. Unlike clinical tests which provide limited information concerning why or what muscles are involved, MRI scans can yield data regarding chest expansibility and diaphragm function. Thus, we are trying to determine if 2D MRI scans of lung area can accurately measure volumes in 3D systems.

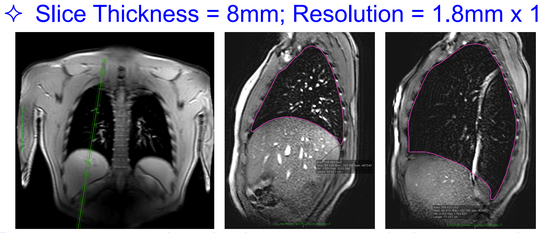
METHODS

N=33 DMD participants (ages 7.3-18.8 years), N=15 controls (ages 6.3-26.4 years)

- DMD Participants: 10/33 ambulatory, 29/33 using corticosteroids

MRI Scans – 3T Philips Achieva (32 Channel Cardiac Coil Used)

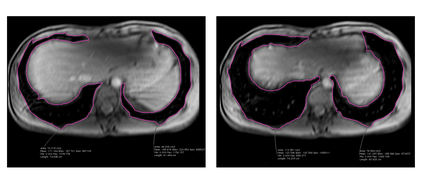
- 2D Scans were taken in the sagittal plane of the right lung. The slice was placed in lung apex, and angled to cross the middle of the lung's base.150 frames were acquired over ~30 seconds → ~5 frames/second. Images were obtained during during normal free breathing, generating tidal volume (TV) and functional residual capacity (FRC) data, and during maximum inspiration/expiration.
  - ✧ Slice Thickness = 8mm; Resolution = 1.8mm x 1.8mm.



Area (Exhalation): 158.620 cm²

Area (Inhalation): 358.620 cm²

- 3D scans were taken in the transversal plane, starting under the lungs and ending just above the apex → multiple cross-sectional slices. Black Blood scans were taken during normal free breathing, while breath hold scans occurred during maximum inspiration/expiration and lasted ~12 seconds.
  - ✧ Black Blood Slice Thickness = 6mm; Resolution = 2mm x 2.5mm.
  - ✧ Breath Hold Slice Thickness = 8mm; Resolution = 2mm x 2.3mm.
- MRI scans were later traced on OsiriX to generate 2D area and 3D volume data.

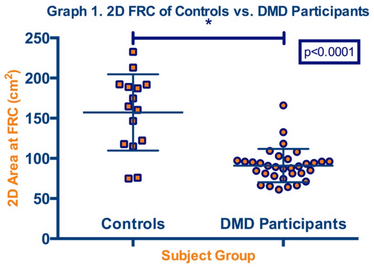


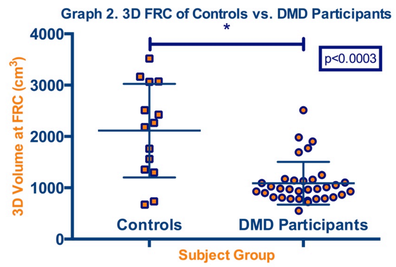
Clinical Spirometry Data Using Forced Vital Capacity

- FVC data was acquired a minimum of 3 times (with some participants being asked to perform the procedure up to 7 times) and the best value was used for analysis.

RESULTS

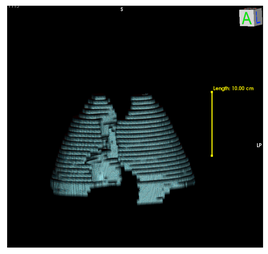
- **A Comparison of 2D Area and 3D Volumes Between Control and DMD Participants:**





Figures 1 and 2: After comparing the 2D lung areas at FRC between controls and participants with DMD, it is apparent that the latter has significantly smaller lung areas, likely due to the progressive weakening of respiratory muscles and the genetic and physiological implications associated with the disease. Similarly, 3D FRC TLV are also smaller among the DMD participant group. Below is a 3D rendering of a set of control lungs compared to those of a DMD participant.

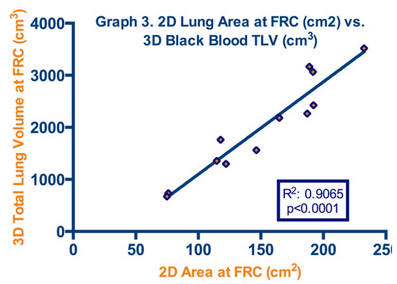
Control Lungs

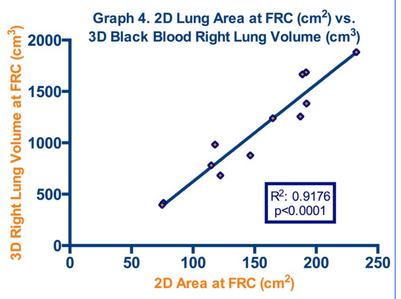


DMD Participant Lungs

The 3D volume renderings are from gender- and age-matched individuals. The lungs from the DMD participants are much smaller, and have a more cone-like shape.

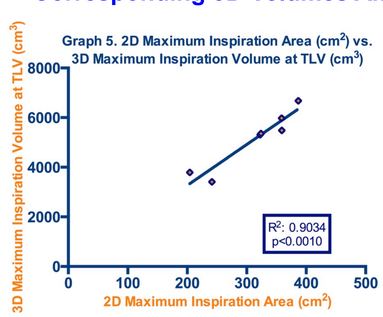
- **A Comparison of 2D Lung Area at FRC with 3D Black Blood FRC Scans Among Controls:**

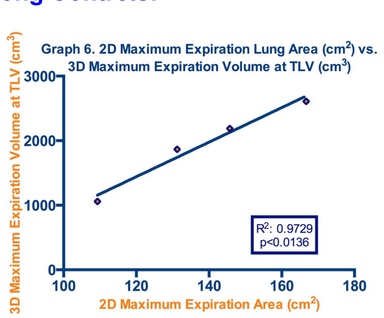




Figures 3 and 4: A strong correlation is present between 2D right lung area and both 3D TLV and right lung volume, suggesting that 2D scans can predict volumes.

- **A Comparison of 2D Maximum Inspiration/Expiration with the Corresponding 3D Volumes Among Controls:**





Figures 5 and 6: Both 2D maximum inspiration and expiration areas show strong correlations with 3D measurements of maximum inspiration and expiration volumes respectively, also indicating that 2D scans can accurately measure 3D volumes.

RESULTS CONTINUED

- **The Correlation of 2D Area Differences with Seated FVC Among Controls:**

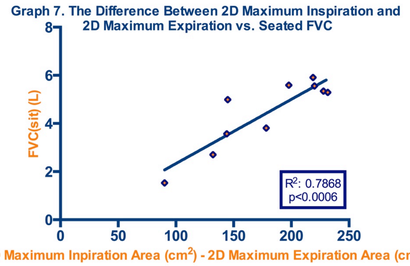
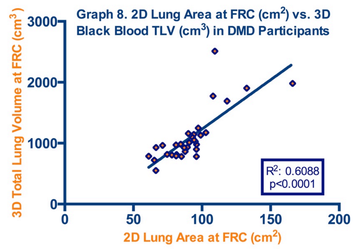
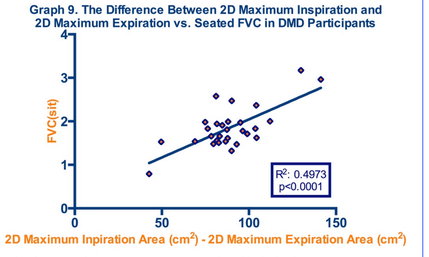


Figure 7: When 2D maximum expiration areas were subtracted from maximum inspiration areas, the difference was then plotted against seated FVC values from the same subjects, yielding a positive correlation, though not as strong as previous correlations.

- **A Comparison of 2D Lung Area at FRC with 3D Black Blood FRC Scans, and the Correlation of 2D Area Differences with Seated FVC Among DMD Participants:**





Figures 8 and 9: DMD data comparing 2D right lung volume to 3D total lung volume showed a lower correlation than control data, though still positive. Likewise, when the difference in 2D maximum inspiration and expiration was compared to seated FVC, the correlation was still lower than that of the controls.

CONCLUSION

- Analysis of control data indicates strong correlations between multiple 2D areas and corresponding 3D volumes, suggesting that 2D scans may be used to infer 3D values.
- The same correlations among DMD participants were not as strong as those of the controls, though still positive. This may be due to the fact that boys with DMD have different lung and rib cage morphology.
- More exploration is needed into why the relationships are not as strong in DMD participants as in controls.

REFERENCES

[1] Bishop, CA, et al. *Frontiers in Neurology*. 2018;9:9.
[2] Cheeran, D, et al. *Journal of the American Heart Association: Cardiovascular and Cerebrovascular Disease*. 2017;6(10):e006340.

ACKNOWLEDGEMENTS

The research was funded by DMR 1644779, as well as the Senator Paul D. Wellstone Muscular Dystrophy Cooperative Research Center (U54R052646). A portion of this work was performed in the McKnight Brain Institute at the National High Magnetic Field Laboratory's AMRIS Facility, which is supported by National Science Foundation Cooperative Agreement No. DMR-1157490 and the State of Florida. I would also like to thank Dr. Walter, Alison Barnard, and the rest of the Walter lab for all their help, as well as all the patients for their continued support for our work.