IMPACT: This work investigates the intra-exam repeatability of Circumferential Strain measured by CINE DENSE in boys with Duchenne Muscular Dystrophy. Circumferential strain ($E_{cc}$) is a promising biomarker for improved diagnosis and evaluation of patient therapy, but its repeatability has not been validated in a DMD or pediatric cohort. Intra-scan repeatability was high, with a smallest detectable change in strain of 0.005 for patients and volunteers, well under the previously reported $0.013 \pm 0.015$ decrease in $E_{cc}$/year reported in DMD boys.
Duchenne Muscular Dystrophy (DMD) is the most common fatal inherited genetic disorder (1 in 3800 boys).

Heart failure is the leading cause of mortality.

The most commonly used cardiac MRI biomarkers (LV ejection fraction, and LGE-positivity) are primarily effective at detecting late-stage disease and are highly variable.

**Study Aim:** Quantify the intra-exam repeatability of peak mid-wall circumferential (Ecc) strain derived from CINE DENSE in boys with DMD compared to age-matched healthy controls.

**References:**

**Acknowledgements:**
Funding for this work was provided by NIH R01 HL131975 to DBE.

For more information regarding our work on the intra-exam repeatability of CINE DENSE in DMD, please see Program #2164.
• Recently, peak systolic circumferential strain (Ecc) in the LV derived from MRI tagging has been reported to effectively distinguish DMD patients and normal volunteers despite no significant differences in LVEF3-5

• However, patients with DMD can have difficulty with the breath-holding required for tagged images

• CINE DENSE is a free-breathing method for measuring myocardial strain with notable imaging and post-processing advantages6

• Sensitive biomarker of cardiac dysfunction in DMD
• Patients experience difficulty with tagging breath-holds

STUDY AIM:
Quantify the intra-exam repeatability of peak mid-wall circumferential (Ecc) strain derived from CINE DENSE in boys with DMD compared to age-matched healthy controls.

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For more information regarding our work on the intra-exam repeatability of CINE DENSE in DMD, please see Program #2164.
CINE DENSE is a free-breathing method for measuring myocardial strain with notable imaging and post-processing advantages.

While previous studies have assessed the segmental reproducibility of CINE DENSE in adult patients and volunteers, none have considered pediatric patients.

In fact, CINE DENSE strain in a DMD cohort has not been reported. Defining the intra-exam repeatability of strain with CINE DENSE in this cohort is important to quantifying longitudinal disease progression.

Quantify the intra-exam repeatability of peak mid-wall circumferential ($E_{cc}$) strain derived from CINE DENSE in boys with DMD compared to age-matched healthy controls.

**STUDY AIM**

Quantify the intra-exam repeatability of peak mid-wall circumferential ($E_{cc}$) strain derived from CINE DENSE in boys with DMD compared to age-matched healthy controls.

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For more information regarding our work on the intra-exam repeatability of CINE DENSE in DMD, please see Program #2164.
METHODS

Intraclass Correlation Coefficient (ICC)

Standard Error of Measurement (SEM) = SD \times \sqrt{(1 - ICC)}

Smallest Detectable Change (SDC) = 1.96 \times SEM \times \sqrt{2}

Study Population: IRB-approved prospective study; boys with DMD (N=11) and age matched healthy volunteers (N=10) underwent a cMRI examination after obtaining informed consent.

MRI Protocol: A single, ECG-triggered, navigator gated, mid-ventricular LV short-axis slice was acquired with balanced 3-point encoding, 2.5x2.5x8mm, TE/TR=1.04/15, K_s=0.06cycles/mm, N_avg=3, spiral interleaves=10, scan time=2min/slice. To define a lower bound on repeatability each acquisition was repeated to assess intra-exam repeatability without patient repositioning.

Data Processing: All CINE DENSE data were imported into custom software \(^6\) used to extract the x, y, and z Lagrangian displacements that ultimately compute E_{cc}. The intraclass correlation coefficient (ICC) between repeated scans was used to compute the standard error of measurement (SEM), and the smallest detectable change (SDC) in strains \(^9\).

Bland-Altman analysis was used to assess and visualize bias and limits-of-agreement between repeated exams.

Study AIM: Quantify the intra-exam repeatability of peak mid-wall circumferential (E_{cc}) strain derived from CINE DENSE in boys with DMD compared to age-matched healthy controls.

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Funding for this work was provided by NIH R01 HL131975 to DEB.

For more information regarding our work on the intra-exam repeatability of CINE DENSE in DMD, please see Program #2164.
RESULTS

In both patients and volunteers, the intraclass correlation coefficient is high (93.6% and 91.0%), and the standard error of measurement is quite low (0.0019 and 0.0019 for $E_{cc}$).

The smallest detectable change (a threshold above which a change in measurement exceeding the threshold is true and reliable at a 95% confidence interval, not simply measurement error) was 0.0052 and 0.0054 $E_{cc}$, respectively.

Bland-Altman analysis shows good agreement between repeated scans, with a mean difference and limits of agreement (1.96xSD) of 0.0025±0.014 and -0.0048±0.0126 for patients with DMD and volunteers respectively.

Table 1. Intra-Scan Repeatability of $E_{cc}$

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ACKNOWLEDGEMENTS: Funding for this work was provided by NIH R01 HL131975 to DBE.

For more information regarding our work on the intra-exam repeatability of CINE DENSE in DMD, please see Program #2164.
This data suggests that peak midwall E\textsubscript{cc} measured with navigator-gated CINE DENSE has high intra-scan reproducibility and can be used to measure changes in E\textsubscript{cc} as low as 0.005 (0.5%).

Previous reports using MRI tagging suggest that peak systolic E\textsubscript{cc} decreases uniformly amongst DMD patients at a rate of 0.013±0.015 (1.3±1.5%) strain per year \textsuperscript{5}

The smallest detectible change (considering inter-study error) in mid-ventricular E\textsubscript{cc} as measured by MRI tagging is an absolute decrease of 0.027 (2.7%) \textsuperscript{10}.

The intra-exam SDC of CINE DENSE is capable of resolving this change and is well below the total tagged SDC.

### Table 1. Intra-Scan Repeatability of E\textsubscript{cc}

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### DISCUSSION

#### Table 1. Intra-Scan Repeatability of E\textsubscript{cc} in DMD Patients Compared to Normal Volunteers

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#### Study Aim:
Quantify the intra-exam repeatability of peak mid-wall circumferential (E\textsubscript{cc}) strain derived from CINE DENSE in boys with DMD compared to age-matched healthy controls.

#### References:

#### Acknowledgements:
Funding for this work was provided by NIH R01 HL131975 to DBE.

For more information regarding our work on the intra-exam repeatability of CINE DENSE in DMD, please see Program #2164.
The characterization of repeatability of CINE DENSE E\textsubscript{cc} is novel both in a pediatric cohort and in a DMD population, and may be useful for quantifying longitudinal progression of disease and response to therapy.

This study did not assess intra or inter-observer variability or inter-study repeatability.

However intra-scan repeatability without repositioning is important because it provides a reasonable lower bound on our confidence in E\textsubscript{cc} measured with CINE DENSE and in quantifying the repeatability of the measurement itself.

- E\textsubscript{cc} measured with navigator-gated CINE DENSE has high intra-scan reproducibility and can be used to measure changes in E\textsubscript{cc} as low as 0.005 (0.5%).
- The intra-exam SDC of CINE DENSE is capable of resolving the reported annual decrease of E\textsubscript{cc} in DMD (0.013±0.015 strain).

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