T₁-Mapping and ECV Estimates at 3T in Pediatric Subjects with Duchenne Muscular Dystrophy and Healthy Controls

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Background
Cardiovascular disease is the leading cause of death in patients with Duchenne muscular dystrophy (DMD) – a fatal X-linked genetic disorder.¹ Current research aims to investigate cardiac MRI biomarkers, including native (pre-contrast) T₁, to evaluate the on-set of microstructural remodeling. Native T₁ measurements in boys with DMD acquired at 1.5T identify myocardial changes and assess disease severity². Moreover, from pre- and post-contrast T₁ measurements, extracellular volume (ECV) can be calculated and used to quantify diffuse fibrosis³. The 3T MRI study herein aims: 1) to characterize pre-contrast (native) T₁ differences between boys with DMD and healthy controls; 2) to report post-contrast T₁ values and ECV estimates in boys with DMD; and 3) to assess both myocardial heterogeneity and regional differences in boys with DMD and healthy controls.

Methods
Pediatric boys with DMD (N=19, 13.2±3.1 years, BMI=24.2±5.1 kg/m², HR=97±14.5 bpm) and healthy boys (N=16, 13.5±3.1 years, BMI=19.8±5.9 kg/m², HR=76±18.5 bpm) were prospectively enrolled (IRB-approved, informed consent) and underwent 3T cardiac MRI (cMRI). T₁ measurements were acquired with a MOtion CORrection (MOCO) gradient echo inversion recovery MOLLI 5(3)3 (pre-contrast) and 4(1)-3(1)-2(2) (post-contrast) sequence. Contrast (3cc, Multihance) was only administered to the DMD cohort. Post-contrast images were acquired ~10 minutes after contrast injection. The pre- and post-contrast T₁ maps were combined with the patient’s hematocrit to calculate an ECV map (MATLAB, MathWorks). All maps were used to determine global and septal measurements for the left ventricular (LV) myocardium (FIG. 1). Group-wise comparisons were performed with a two-tailed t-test. Multiple regression assessed the dependency of age, heart rate (HR), and BMI on pre- and post-contrast T₁ in DMD boys (pre-contrast only for healthy). Data is reported as median and IQR and as standard deviation (SD) for assessing myocardial heterogeneity.

Results
DMD subjects exhibited increased native T₁ [1334(60) ms vs. 1290(51) ms, p<0.001, FIG. 2A] and increased SD [131(37) ms vs. 85(26) ms, p<0.001] when compared to the healthy controls. Multiple regression showed no significant dependency of native and post-contrast T₁ on age, HR, and BMI in the healthy nor DMD groups. However, HR and BMI were both higher in DMD (p<0.001 and p=0.02) and a trend toward elevated native T₁ with HR and BMI are possible (FIG. 2A to 2C). For boys with DMD, the regional analyses showed increased pre-contrast T₁ [1334(61) ms vs. 1270(37) ms p<0.001], decreased post-contrast T₁ [652(168) ms vs. 697(152) ms p<0.001], and increased ECV [30(6)% vs. 24(4)% p<0.001] for the entire myocardium relative to the septum (FIG. 3A to 3C).
Conclusion
Boys with DMD have elevated pre-contrast T\textsubscript{1} compared to their healthy, age-matched controls. As expected the reported 3T T\textsubscript{1} values from this study are longer relative to previously reported 1.5T values for DMD and healthy groups (e.g. [1045ms vs 988ms, p=0.001])\textsuperscript{4}. Hence, the reported values help establish 3T reference values for both boys with DMD and healthy subjects. Furthermore, post-contrast T1 and ECV estimates are reported here for boys with DMD at 3T for the first time. Increased SD of pre-contrast T\textsubscript{1} within each DMD boy could be a potential marker of tissue heterogeneity. Lastly, we find that the myocardial free wall is more affected than the septum for boys with DMD.

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FIG. 1: An example of Pre- and Post-contrast T1 and EVC maps for a subject with DMD. Top Row: Mid-ventricular short-axis maps. Bottom row: Example myocardial and septal (white contour) ROIs used for both DMD and healthy subjects.
FIG. 2A-C: Native T1 as a function of possible covariates (Age, BMI and HR) for boys with DMD and healthy subjects. No significant relationship found, but a trend toward elevated native T1 with BMI and HR are possible.
FIG. 3A-C: Box plots of regional (septal wall) compared to global (entire short-axis slice) native $T_1$, post-contrast $T_1$, and ECV. (A) Boys with DMD present with elevated native $T_1$ compared to healthy controls. Significant regional differences present in (A) pre-contrast, (B) post-contrast $T_1$, and (C) ECV for DMD boys measured at 3T.