T_1-Mapping and ECV Estimates at 3T in Pediatric Subjects with Duchenne Muscular Dystrophy and Healthy Controls

Nyasha G. Maforo[1,2], Patrick Magrath[1,3], Kévin Moulin[5], Jiaxin Shao[1], Kavya Umachandran[3], Grace Kim, Pierangelo Renella[1], Nancy Halnon[4], Holden Wu[1], and Daniel B. Ennis[5]

[1]Department of Radiological Sciences, [2]Physics and Biology in Medicine Interdepartmental Program, [3]Department of Bioengineering, [4]Department of Pediatrics (Cardiology), University of California, Los Angeles, California. [5]Department of Radiology, Stanford University, Stanford, California.

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) T_1, to evaluate the on-set of microstructural remodeling. Native T_1 measurements in boys with DMD acquired at 1.5T identify myocardial changes and assess disease severity[2]. Moreover, from pre- and post-contrast T_1 measurements, extracellular volume (ECV) can be calculated and used to quantify diffuse fibrosis[3]. The 3T MRI study herein aims: 1) to characterize pre-contrast (native) T_1 differences between boys with DMD and healthy controls; 2) to report post-contrast T_1 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/m^2, HR=97±14.5 bpm) and healthy boys (N=16, 13.5±3.1 years, BMI=19.8±5.9 kg/m^2, HR=76±18.5 bpm) were prospectively enrolled (IRB-approved, informed consent) and underwent 3T cardiac MRI (cMRI). T_1 measurements were acquired with a MOtion COrrection (MOCO) gradient echo inversion recovery MOLLI 5(3)3 (pre-contrast) and 4(1)-3(1)-(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 T_1 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 T_1 in DMD boys (pre-contrast only for healthy). Data is reported as median and IQR and as standard deviation (SD) for assessing myocardial heterogeneity.
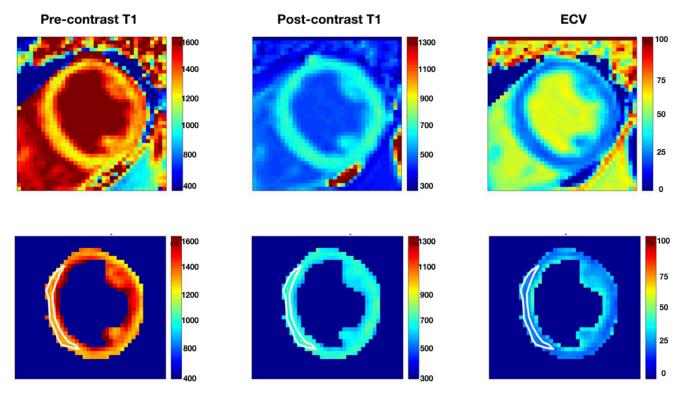
Results
DMD subjects exhibited increased native T_1 [1334(60) ms vs. 1290(51) ms, p<0.001, FIG. 2A] and increased SD [131(37) ms vs. 85(26) ms, p<0.001] when compared to the healthy controls. Multiple regression showed no significant dependency of native and post-contrast T_1 on age, HR, and BMI in the 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 T_1 with HR and BMI are possible (FIG. 2A to 2C). For boys with DMD, the regional analyses showed increased pre-contrast T_1 [1334(61) ms vs. 1270(37) ms p<0.001], decreased post-contrast T_1 [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).
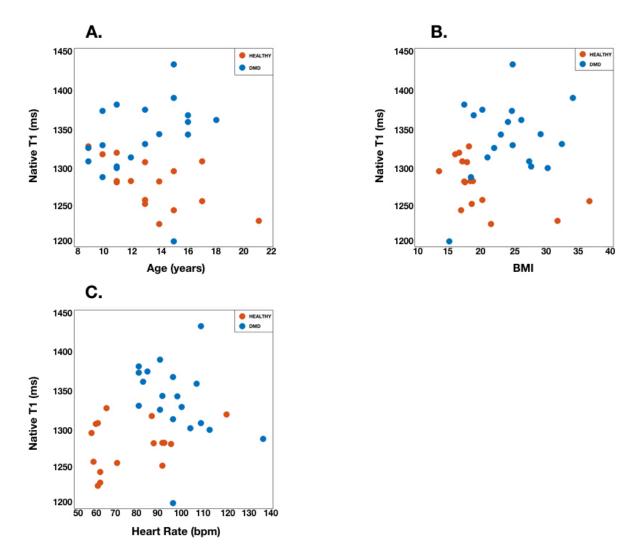
Conclusion
Boys with DMD have elevated pre-contrast T_1 compared to their healthy, age-matched controls. As expected the reported 3T T_1 values from this study are longer relative to previously reported 1.5T values for DMD and healthy groups (e.g. [1045ms vs 988ms, p=0.001])[4]. Hence, the reported values 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_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.

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 T_1 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.
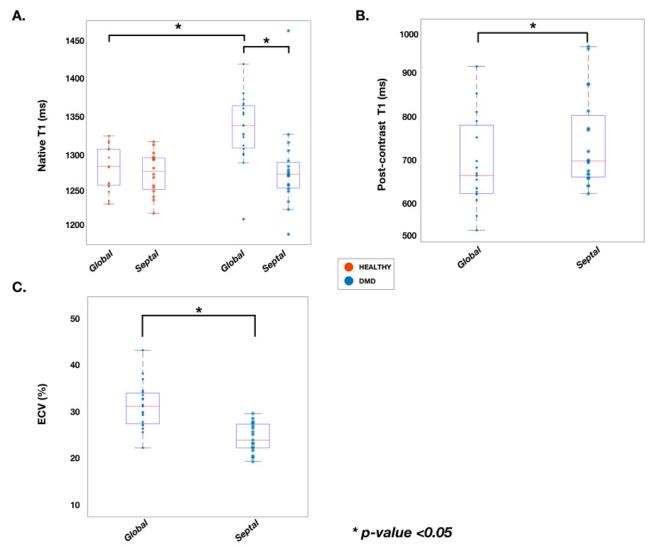
FIG. 3A-C: Box plots of regional (septal wall) compared to global (entire short-axis slice) native T$_1$, post-contrast T$_1$, and ECV. (A) Boys with DMD present with elevated native T1 compared to healthy controls. Significant regional differences present in (A) pre-contrast, (B) post-contrast T1, and (C) ECV for DMD boys measured at 3T.