Cardiac MRI Assessment of Rejection and Cardiac Allograft Vasculopathy in Pediatric Heart Transplant Recipients
PI: Soslow, Jonathan H

PROGRESS REPORT

Specific Aims:
Aim 1: Create a model for non-invasive detection of rejection in pediatric heart transplant patients using advanced cardiac MRI (CMR) imaging techniques.
Hypothesis 1: A regression model combining advanced CMR sequences, including T_1, T_2, and extracellular volume (ECV) mapping, non-invasively detects acute rejection.

Aim 2: Identify non-invasive methods of detecting cardiac allograft vasculopathy (CAV) in pediatric heart transplant recipients.
Hypothesis 2: CMR regadenoson stress testing detects CAV diagnosed by coronary angiography.
Hypothesis 3: Regadenoson stress testing will detect CAV in setting of negative coronary angiography and abnormal findings on intravascular ultrasound (IVUS).

Current enrollment:
At this point, we have enrolled 18 patients, 5 of whom had rejection and 5 of whom underwent regadenoson CMR. Preliminary analysis of the patients with rejection suggests that native T1 and T2 are elevated in patients with rejection in the short axis and 4 chamber views. See Figure 1 for preliminary data. We are analyzing the data with plans for abstract submission, though we hope to increase enrollment over the next year to strengthen these results. We are also pursuing more complex analyses that may be better able to separate patients with and without rejection. Long-term, we feel that a model will be the best way to determine presence or absence of rejection, but a larger cohort of patients with rejection will be necessary.

Challenges and how these challenges were addressed:
The number of patients with rejection remains lower than anticipated, though the rate of enrollment has improved since our last progress report. The second site is up and running and has enrolled 4 patients, all of whom underwent regadenoson CMR. As with the prior progress report, we have not had difficulty enrolling patients without rejection, but have slowed our enrollment of these patients to leave funds for patients with acute rejection.

We have moved forward with adding Colorado Children's Hospital as a second site. They have been sent a phantom and have scanned the phantom but have not finished regulatory documentation.

Dissemination of results:
The goal at our last progress report in July of 2018 was to have an abstract submitted by July of 2019. We plan to submit at least one abstract in the next year detailing our use of T1, T2, and ECV mapping to identify patients with acute rejection. We are currently working on analysis of stress regadenoson studies.

Timeline for future grants:
Based on our preliminary work, I have initiated a multi-center collaboration. The primary investigators will be myself and Dr. Samyn (Children's Wisconsin). We are developing the protocol to begin retrospective collection of CMRs in transplant patients from multiple sites. We plan to begin by applying for multiple Foundation grants to cover infrastructure for a multi-center collaboration, including image analysis and statistical analysis. Once we have established the multi-center collaboration and infrastructure, will apply for a larger NIH grant to prospectively assess the utility of CMR for detection of acute rejection. CMR researchers from the following sites have expressed interest in collaborating: Vanderbilt University Medical Center, Children's Hospital of Wisconsin, Lurie Children's Hospital, Joe DiMaggio Children's Hospital, Children's Hospital of Colorado, University of Michigan, Children's National Medical Center, Seattle Children's Hospital, Riley Children's Hospital, Children's Hospital at Montefiore, Children's Hospital of Atlanta, Toronto Hospital for Sick Children, and Lucile Packard Children's Hospital at Stanford.

Cardiac MRI Assessment of Rejection and Cardiac Allograft Vasculopathy in Pediatric Heart Transplant Recipients
PI: Soslow, Jonathan H

We feel that a large consortium of hospitals prospectively evaluating the utility of CMR in pediatric heart transplant patients could have a significant impact on the health of pediatric heart transplant recipients.

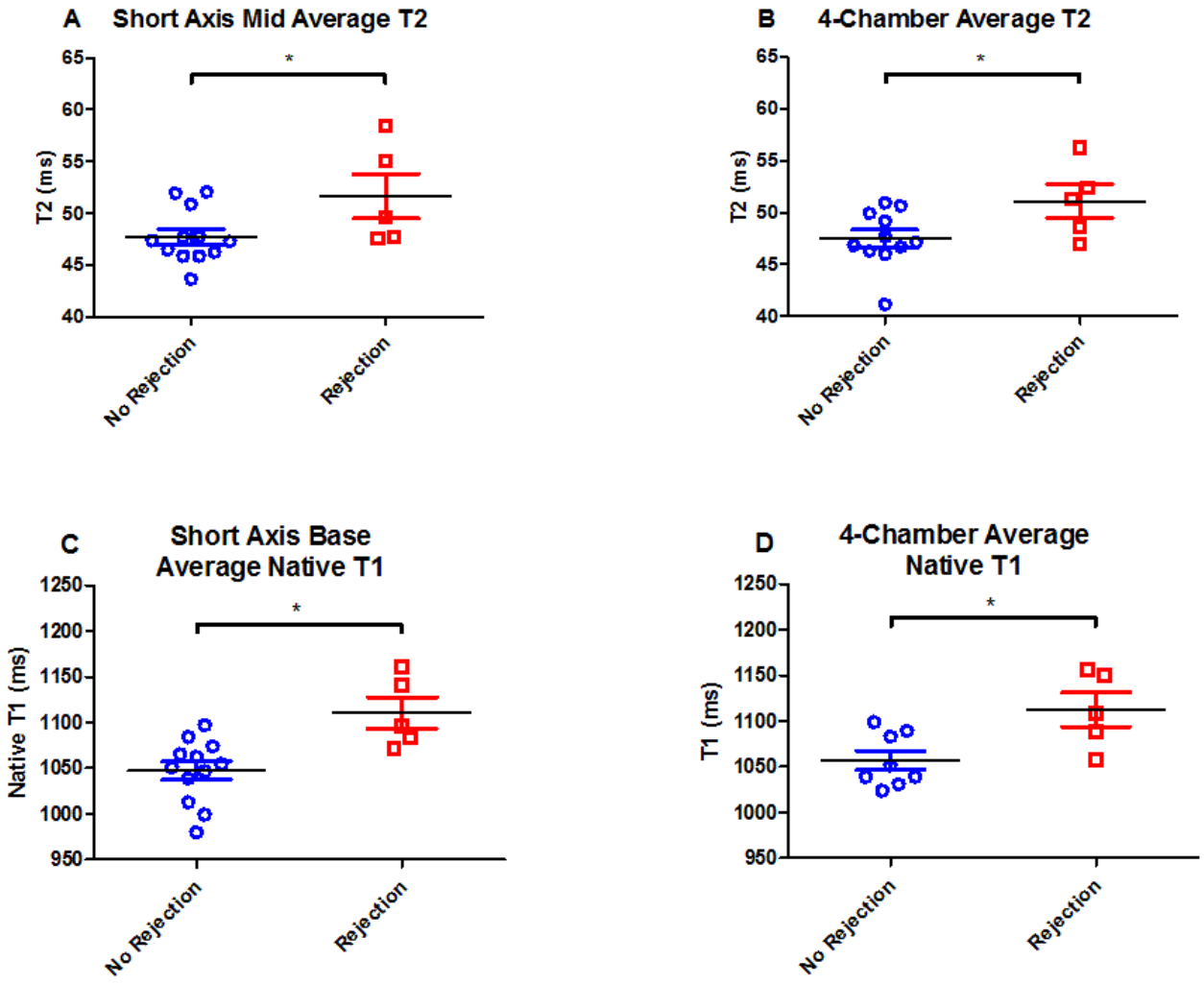

Figure 1: Preliminary results demonstrating a significant difference between patients with and without rejection of average T2 at the mid-LV short axis slice (A) and in the 4-chamber (B) and native T1 at the base LV short axis slice (C) and 4-chamber (D). Student's T-test used to perform statistical analysis.