Early Detection of Iron Cardiomyopathy in Thalassemia (EDICT)

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Synopsis:
Iron overload is a serious and relatively common health problem resulting from a wide range of clinical pathologies including transfusion-dependent anemias such as β thalassemia, sickle cell disease, aplastic anemia, renal failure, and malignancies as well as disorders of iron metabolism including hemachromatosis and porphyrias. These disorders are common and have significant social and economic costs. Unfortunately, iron toxicity is often clinically silent until significant and irreversible organ damage has occurred. Particularly at risk are the liver, heart and pancreas. The most feared and deadly complication results from cardiac iron deposition. Typically, cardiac iron deposition produces arrhythmias, systolic and diastolic dysfunction, and congestive heart failure in the second or third decade of life. Death often occurs within six months of symptom onset. Progressive iron overload is universally fatal, although early recognition and treatment (chelation therapy) significantly improves prognosis.

Subcutaneous iron chelation therapy is a method of reducing iron overload, dramatically improving the length and quality of life for thalassemia patients, however cardiac complications remain common. Despite apparently adequate chelation therapy (measured by liver iron concentration by Superconducting Quantum Interference Devices (SQUID) and/or biopsy), cardiac failure and arrhythmias remain the leading cause of death in this population. Development of sensitive techniques to assess cardiac iron load and its response to chelator therapy is in critical need to improve patient management.

Conventional cardiac surveillance consisting of annual Holter monitoring, echocardiogram, and electrocardiogram, has proved ineffective in detecting pre-clinical cardiac iron overload. Standard cardiac monitoring detects physiologic response to myocardial iron, which occurs late in the disease process, often concurrent with symptoms. Therefore, a clinical tool to assess the level of cardiac iron, independent of cardiac symptoms, offers tremendous clinical advantages. In addition to measuring liver iron, MR can also be used to measure myocardial iron content. Recent work suggests that MRI is the best predictor of cardiac functional degeneration in response to iron overload. Liver iron, myocardial iron, and cardiac function can be measured in a single, one-hour MR exam.

The specific aims of this study are:
1. To determine the relationship between cardiac function, exercise capacity, and cardiac rhythm to cardiac and liver iron loading in patients with transfusion dependent thalassemia.
2. To determine the reproducibility of cardiac MRI in patients with transfusion dependent thalassemia.
3. To establish references ranges for measures of cardiac function, exercise capacity, and cardiac rhythm in patients with transfusion dependent thalassemia.