Inner Spaces
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Points

- Thalassemia major patients need constant blood transfusions, which leads to iron overload, in the heart and liver
- Chelation agents such as DFO and DFP are able to control, prevent and reverse iron overload
- Iron overload in the heart does not correlate with Fe levels in the liver or serum ferritin levels
- T2* measurement in the LV septum is the best, current, non-invasive method of measuring Fe overload in the heart, using special sequences in a cardiac MRI scanner

Cardiac MRI for Myocardial Iron Estimation in Thalassemia Major

Thalassemia is a well-known and relative common inherited disorder of hemoglobin (Hb) synthesis. Due to a global deficiency in the synthesis of beta-globin chains, there is severe anemia in the classic form of beta-thalassemia, i.e. thalassemia major. Minor grades also exist, but are not relevant to this discussion. The prevalence of beta-thalassemia in India ranges from 3.5-15% in the general population and every year, 10,000 children with thalassemia major are born in India, responsible for 10% of the total number in the world.

The mainstay of treatment remains blood transfusions. However, it was realized early on, that significant iron (Fe) overload develops in many organs of the body following long-term transfusion therapy. Hence, associated treatment with chelating agents, such as deferoxamine (DFO) and deferiprone (DFP) is also now concurrently instituted to prevent and/or to control Fe overload.

Of the various organs in which Fe load occurs, the liver and the heart are the most important. In unchelated, transfused patients, by age 10 the heart becomes enlarged and patients develop heart block and pericarditis, with heart failure by age 16. Once heart failure occurs, the mean period of survival is 3 months. Even in this modern era of chelation treatment, cardiac complications are still responsible for 71% of deaths.

Diagnosing iron overload in the heart is important, so that the intensity of the chelation therapy can be monitored accordingly. The most accurate way to do so, would be an endomyocardial biopsy, but this is not clinically practical. Liver Fe measurements can be performed with a liver biopsy, but there is a very weak correlation between iron levels in the liver and the heart. Serum ferritin levels also do not correlate with Fe overload in the heart. Echocardiography is insensitive as well.

As a result, a non-invasive test for estimating iron in the heart is required. MRI is able to fulfill this need. One parameter that can be relatively easily measured is T2*, which is a relaxation parameter and can be studied using gradient-echo techniques. The use of T2* measurements, has been validated in the liver, by comparing Fe in liver biopsies with T2* measurements (Fig.1) and further by comparing T2* values in the heart with cardiac function, both at baseline and after chelation therapy (Fig. 2).

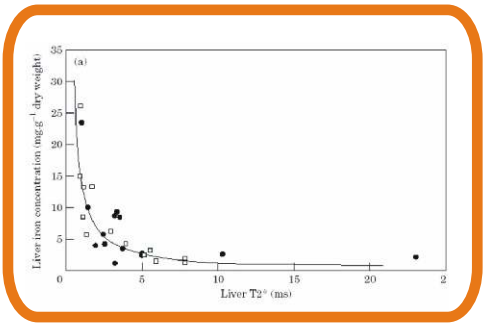

Fig. 1

Fig. 1: Graph showing the strong inverse correlation between liver Fe concentration and T2 values (courtesy Dr. Pennell D J, RBH, London).*

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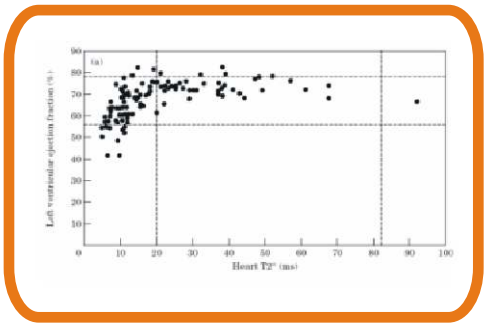

Fig. 2

Fig. 2: Graph showing the strong direct correlation between reduced T2 values and decreasing ejection fraction (courtesy Dr. Pennell D J, RBH, London)*

T2* is measured in the septum, using a multi-echo technique (Fig. 3) A T2* value of less than 20 (Fig. 4) suggests significant Fe overload and a value of less than 10 suggests severe Fe overload. Low values are usually associated with evidence of cardiac dysfunction, in the form of areas of segmental wall dysfunction, dilatation and reduced ejection fraction, as well. With intense treatment, T2* values are seen to improve, along with improvement in other parameters of cardiac function.

To measure T2*, we need a 1.5T MRI scanner, along with special hardware and software, which allows us to perform dedicated cardiac MRI examinations. We measure T2* values, using a special sequence developed by the Royal Brompton Heart & Lung Institute in London, along with dedicated measurement software.

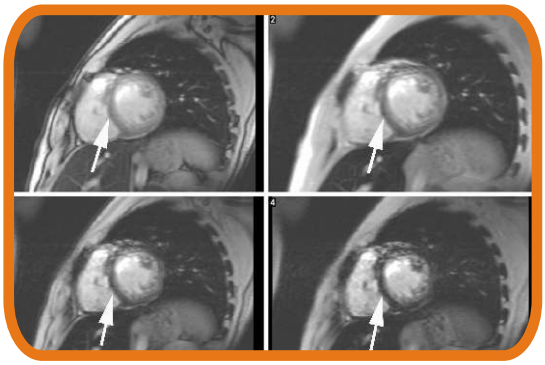

Fig. 3

Fig. 3: Four (out of the usual eight) images obtained at different echo times, showing reduction in signal in the septum (white arrows) with increasing echo time due to Fe overload.

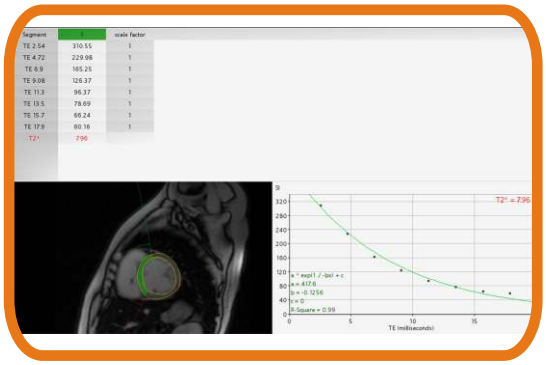

Fig. 4

Fig. 4: A typical report in this patient with severe Fe overload (T2 of 7.96)*

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