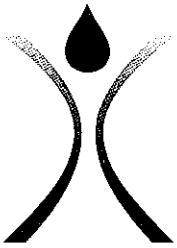

Cooley's Anemia
FOUNDATION

Leading the Fight Against Thalassemia

Position Statement on MRI-based Hepatic Iron Assessment Methods, including FerriScan®

The Cooley's Anemia Foundation recommends FerriScan for the measurement of liver iron concentration in patients with thalassemia.

The Cooley's Anemia Foundation is dedicated to serving people afflicted with various forms of thalassemia, most notably the major form of this genetic blood disease, Cooley's Anemia (also known as thalassemia major). Our mission is to advance the treatment and cure for this serious blood disease, enhancing the quality of life of patients and educating the medical profession, trait carriers and the public about thalassemia major. The Cooley's Anemia Foundation supports research and medical advancements for patients and their families. To this end, the Foundation supports the use of MRI methods, as important, patient-friendly alternatives to liver biopsy.

Among the published MRI methods for iron detection in patients with transfusional (and non-transfusional) iron overload, Ferriscan is unique because of regulatory approval in several countries.

FerriScan received FDA approval in 2005 and is also regulatory approved in Canada, Europe, Australia and New Zealand. To date, FerriScan has been implemented successfully in over 20 countries and more than 8,000 patients have had their liver iron concentrations measured using this technique. It is easy to set up on most MRI scanners and requires no additional hardware or software to be purchased.

FerriScan and other MRI iron assessment methods provide a non-invasive and cost-effective means to monitor liver iron concentration in transfused patients with thalassemia, sickle cell disease and other blood disorders as well as patients with hemochromatosis. FerriScan is an MRI-based technology capable of accurately measuring liver iron concentrations in all patients regardless of the amount of iron in their liver, a feature particularly important for patients with heavy iron loading often found with thalassemia. Some of the other MRI-based methods are less accurate at higher iron concentrations. MRI image data are acquired on a local scanner and electronically transmitted to a central data analysis center that is ISO 9001 and ISO 13485 certified. Several centers measure using both Ferriscan and local MRI measures. Comparison between hospitals is facilitated by Ferriscan, which is standardized and centrally read.

The Cooley's Anemia Foundation believes that MRI iron assessments, including FerriScan, should be available to all patients who rely on iron overload measuring to identify excess iron which accumulates in the liver and which leads to serious complications such as liver fibrosis and organ failure. Regular monitoring of liver iron can improve the management of iron overload leading to prolonged and improved quality of life.

Traditional techniques for monitoring the body iron burden include serum ferritin and liver biopsy. Serum ferritin provides a general indication on how well chelation therapy is working by providing useful trending information. However, serum ferritin is an unreliable indicator of the magnitude of iron overload, as results can be confounded by inflammation, infection or other underlying diseases.

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Liver biopsy has traditionally been regarded as the gold standard for assessing liver iron in patients with iron overload, and published data confirm that liver iron is closely correlated with total body iron stores. However, a liver biopsy is invasive, can be painful and carriers the risk of complications. Furthermore, since iron is deposited in the liver in a non-uniform manner, the small amount of liver tissue obtained via a liver biopsy may not be representative of the entire liver, often making this technique inaccurate. It is also not possible to obtain liver biopsies as often as required to effectively monitor iron levels in patients who are being regularly transfused. Liver biopsies are substantially more expensive than Ferriscan MRI, which amounts to the combined cost of an abdominal MRI without contrast, plus the cost of the ferriscan analysis, which is similar to a "send out" laboratory test.

MRI iron assessment has several advantages over both serum ferritin and liver biopsy including:

- Non-invasive and therefore, not painful or harmful to the patient.
- Provides a measurement of the amount of iron across a large section of the liver.

When FerriScan is employed to measure liver iron concentrations it helps physicians:

- Determine if and when chelation therapy should begin.
- Monitor how chelation therapy is working.
- Adjust therapy accordingly.
- Provide accurate feedback to the patient to address potential compliance issues.

There is significant clinical and scientific evidence available to support this technique as a means to monitor liver iron concentrations in patients with thalassemia.

MRI based iron assessment represents the type of medical breakthrough our members depend on. Ferriscan itself is a high-quality (clinical grade, FDA approved) method of accomplishing this assessment Based on our review of the peer-reviewed literature (listed below), Cooley's Anemia Foundation recommends that third party insurance companies develop positive coverage policies so that consumers can access this test, providing more accurate and cost-effective results than liver biopsy.

Transfusional Iron Overload

1. Adlette I et al, Absence of cardiac siderosis by MRI T2* despite transfusion burden, hepatic and serum iron overload in Lebanese patients with sickle cell disease. Eur Journal of Haematology 2009; "Accepted Article"; doi: 10.1111/j.1600-0609.2009.01345.x. [Abstract]
2. Porter J, Concepts and goals in the management of iron overload. American Journal of Hematology 2007;82:1136-39.
3. Karam LB et al, Liver biopsy results in patients with sickle cell disease on chronic transfusions: poor correlation with ferritin levels. Pediatric Blood and Cancer 2008;50:62-65.
4. Min Y et al, A multi-center, open label study evaluating the efficacy of iron chelation therapy with deferasirox in transfusional iron overload patients with myelodysplatic syndromes or aplastic anemia using quantitative R2 MRI. Leukemia Research 2009;33 (Supp1):S118-119.
5. Greenberg P.L et al, Change in liver iron concentration (LIC), serum ferritin (SF) and labile plasma iron (LPI) over 1 year of deferasirox (Exjade®) therapy in a cohort of patients with MDS. Leukemia Research 2009;33 (Supp1):120.

Hereditary Hemachromatosis

1. Olynyk JK et al, Predicting iron overload in hyperferritinemia. Clinical Gastroenterology and Hepatology 2009; 7:359-362. [Abstract]

2. Olynyk JK et al, Duration of hepatic iron exposure increases the risk of significant fibrosis in hereditary hemochromatosis: a new role for magnetic resonance imaging. American Journal of Gastroenterology 2005; 100:837-841.
3. St. Pierre TG et al, A new model for predicting venesection therapy requirement in hereditary hemochromatosis using non-invasive liver iron concentration measurement. Blood (ASH abstracts) 2005; 105:3596. [Abstract]

Liver Iron Concentration

1. St. Pierre TG, Using MRI to measure liver iron concentration levels. TIF Magazine, Mar 2009; 42-44.
2. St. Pierre TG et al, Non-invasive measurement and imaging of liver iron concentrations using proton magnetic resonance. Blood 2005; 105:855-61.
3. Angelica E et al, Hepatic iron concentration and total body iron stores in thalassemia major. New England Journal of Medicine 2000; 343:327-31.
4. Teller PT et al, Hepatic iron concentration combined with long-term monitoring of serum ferritin to predict complications of iron overload in thalassemia major. British Journal of Haematology 2000; 110: 971-77.
5. Kowdley KV et al, Survival after liver transplantation in patients with hepatic iron overload; the national hemochromatosis transplant registry. Gastroenterology 2005; 129:494-503 [Abstract].
6. Piga A et al, Comparison of LIC obtained from biopsy, BLS and R2-MRI in iron overload patients with β-thalassemia, treated with deferasirox (Exjade®, ICL670). Blood (ASH abstracts) 2005; 106:2689. [Abstract]