FerriScan®
MRI Measurement of Liver Iron Concentration

FerriScan® R2-MRI Fact Sheet - Hereditary Hemochromatosis

Hereditary Haemochromatosis (HH) and Iron Overload

Hereditary haemochromatosis (HH) is an inherited condition that causes excessive iron absorption from the diet. The condition is caused by an abnormal gene or genes that control iron absorption and is common in countries where the population is largely of Northern European origin.

What is Iron Overload?

In HH excess dietary iron accumulates primarily in the liver. A high Liver Iron Concentration (LIC) over a prolonged period can cause liver damage. This can lead to cirrhosis and an increased risk of hepatocellular carcinoma (HCC).

Early detection is the key to preventing damage from iron overload. Accurate assessment of the iron concentration in the liver can play an important role in the diagnosis and planning of treatment for haemochromatosis

How can I check my Iron Levels?

There are four methods used by clinicians to check for iron overload; MRI, liver biopsy, serum ferritin, and fasting serum TS.

The most widely used biochemical tests for diagnosing iron overload are SF and fasting serum TS. The relationship between excess body iron stores and SF is weak and non-specific[2]. While SF can be used as a screening tool to help identify iron loaded patients, elevated SF levels do not necessarily suggest increased body iron stores. Elevated ferritin concentrations without pathologic iron overload can be observed in acute or chronic inflammatory processes, autoimmune diseases, neoplasias, renal insufficiency, hepatopathies and the metabolic syndrome[5].

SF does not provide an accurate quantitative relationship with body iron stores in hereditary haemochromatosis[1,2,3]. Rather, LIC has a much stronger correlation with body iron stores in HH[2].

The European Association for the Study of the Liver Disease (EASLD) Clinical Practice Guidelines for HFE Haemochromatosis[1] published in 2010 state that **"serum iron concentration and transferrin saturation do not quantitatively reflect body iron stores and should therefore not be used as surrogate markers of tissue iron overload".**

Olynyk and colleagues[2] showed that there was significant inter-individual variability between excess body iron stores (or total phlebotomised iron) and SF concentrations.

A more accurate alternative to these two is the use of FerriScan R2-MRI to quantify liver iron concentration. The risk of liver damage can be assessed by measuring the LIC using FerriScan R2-MRI when a patient is first diagnosed with HH. LIC multiplied by the age at diagnosis has been shown to be a good predictor of liver damage[4]. Unlike blood serum markers, FerriScan®, which can be used repeatedly if required, provides a direct measurement of LIC.

Why use FerriScan in Patients with Hereditary Haemochromatosis?

- FerriScan is the only regulatory cleared (FDA, CE, TGA) method to accurately assess LIC. FerriScan has international regulatory clearance (USA, Europe, Australia);
- FerriScan is non-invasive and can provide information about the distribution of iron within the liver;
- Measurement of LIC provides a definitive diagnosis of haemochromatosis;
- Measurement of LIC before starting iron reduction therapy can help to identify subjects at risk of iron-induced high-grade liver fibrosis[4];
- An accurate measurement of LIC aids in the planning of the phlebotomy regime to ensure adequate iron is removed without the patient becoming anaemic.

I have never had a FerriScan® R2-MRI, what do I need to do?

Your doctor can refer you for a FerriScan® R2-MRI.

- FerriScan is painless, free of ionising radiation, and has a short scan time of about 10 minutes;
- FerriScan can measure LIC over the entire range encountered in clinical practice[2];
- FerriScan results are clinically validated to be unaffected by inflammation, fibrosis or cirrhosis;
- FerriScan requires no breath-hold and may therefore be used for paediatric patients;
- Results are accurate, reliable and reproducible over time and between MRI centres and models of scanner;
- Results are available within a target time of two business days.

What does my FerriScan® Report look like?

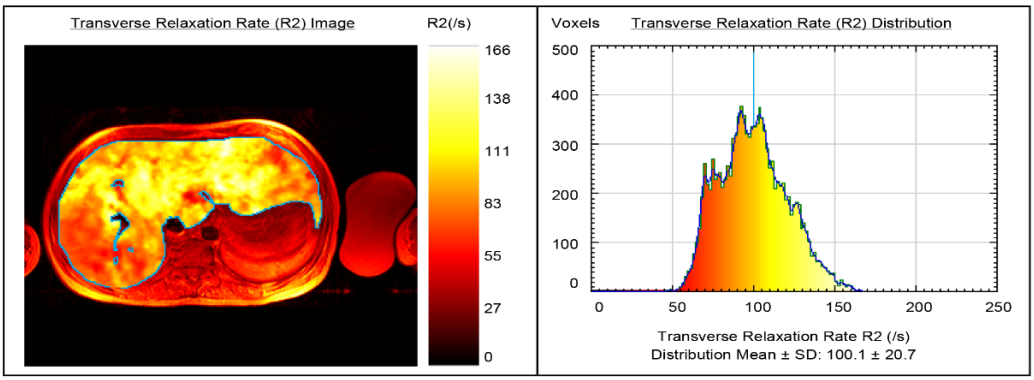
FerriScan®

Liver Iron Concentration Report

Report No:	10000001_S12	Scan Date:	29 May 2016
Patient ID:	ABC-12345678	Analysis Date:	30 May 2016
Name:	PATIENT, Patient	Referrer:	Dr Doctor
Birth Date:	10 Aug 2003	MRI Centre:	MRI Centre Name

Average Liver Iron Concentration	**6.8 mg/g dry tissue**	(NR: 0.17-1.8)
	121 mmol/kg dry tissue	(NR: 3-33)

Normal range (NR) is taken from Bassett et. al., Hepatology 1986; 6: 24-29



Note: The area of the liver image used for the FerriScan analysis excludes large vascular structures and other image artefacts.

Liver Iron Concentration thresholds in Transfusional Iron Overload

Extract from Olivieri et al,Blood 1997; 89, 739-61

LIC Range	Clinical Relevance
0.17-1.8 mg Fe/g dw	Normal range in non-disease patients in healthy population
3.2-7.0 mg Fe/g dw	Suggested optimal range of LIC for chelation therapy in transfusional iron loading
7.0-15.0 mg Fe/g dw	Increased risk of complications
>15.0 mg Fe/g dw	Greatly increased risk of cardiac disease and early death in patients with transfusional iron overload

A follow-up FerriScan may be required every 6 - 12 months.

Authorised by: Service Centre Manager

Resonance Health Analysis Services Pty Ltd www.resonancehealth.com

CE 0805 **CONFIDENTIAL** **ARTG: 116071** **510(k): K043271**

References

1. *European Association for the Study of the liver. EASL Clinical Practice Guidelines for HFE Hemochromatosis.* Journal of Hepatology, 2010. doi: 10.1013/j.jhep.2010.03.001. (C) 2010 European Association for the Study of the Liver.
2. Olynyk, J.K., et al, J Gastroenterol, 1998. **93**. 346-50.
3. Gordeuk, , et al., Am J Hematol, 2008. **83**. 618-26.
4. Olynyk, J.K., et al, Am J Gastroenterol, 2005. **100**. 837-41.
5. Fleming, R.E., et al. N Engl J Med , 2012 366;4 348-354