

## FerriScan<sup>®</sup> R2-MRI Fact Sheet - Hereditary Haemochromatosis and Iron Overload

### 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.

### Genetic Testing

The two most frequently occurring mutations in the HFE gene are known as C282Y (occurs in approximately 70-80% of subjects with HH) and H63D (in approximately 5% of subjects with HH). While a diagnosis of HH can be made in the majority of patients through readily available genetic testing, 20-30% of patients who display symptoms of HH do not have a mutation in the HFE gene. Therefore, alternative techniques are required to diagnose HH<sup>1</sup>.

Furthermore, even though a patient might be identified as having a HFE gene mutation, the presence of the gene does not necessarily result in iron overload. **Therefore, an alternative technique is required to diagnose iron overload in HH patients.**

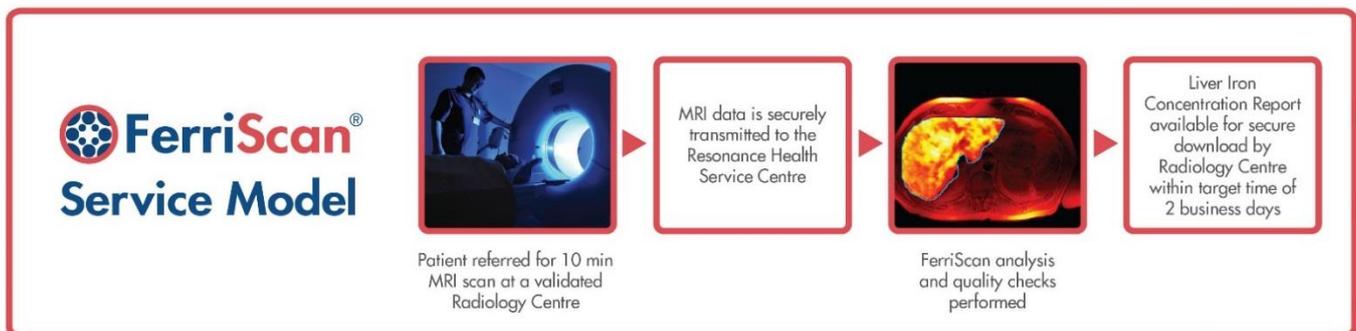
*Early detection is the key to preventing damage from iron overload. Accurate assessment of the iron concentration in the liver can play an important role in the diagnosis and planning of treatment for haemochromatosis*

### Measurement of Liver Iron Concentration (LIC)

In HH excess dietary iron accumulates primarily in the liver. High LIC over a prolonged period causes liver damage (high-grade fibrosis). This can lead to cirrhosis and is a risk factor for hepatocellular carcinoma (HCC). The risk of liver damage can be assessed through measurement of LIC by 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<sup>8</sup>. FerriScan R2-MRI provides a direct measurement of LIC, unlike blood serum markers and can be used repeatedly if required.

### Key FerriScan Features

- ✓ FerriScan provides an accurate, validated MRI-based measurement of liver iron concentration
- ✓ FerriScan is non-invasive, requires no contrast agents and has a scan time of approximately 10 minutes
- ✓ FerriScan has high sensitivity and specificity for measuring LIC
- ✓ Image analysis and LIC reporting is performed at a central ISO 13485 certified Service Centre
- ✓ FerriScan has international regulatory clearance (USA, Europe, Australia)
- ✓ Results are available within a target time of two business days
- ✓ FerriScan can measure LIC over the entire range encountered in clinical practice<sup>3</sup>
- ✓ 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
- ✓ There is no requirement for customers to purchase new software or hardware
- ✓ FerriScan is suitable for 1.5 Tesla MRI scanners
- ✓ FerriScan is charged per scan only



## Why use FerriScan in Patients with Hereditary Haemochromatosis?

- FerriScan is the only regulatory cleared (FDA, CE, TGA) method to accurately assess LIC
- 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<sup>8</sup>
- An accurate measurement of LIC aids in the planning of the phlebotomy regime to ensure adequate iron is removed without the patient becoming anaemic

## Clinical Guidelines

Many algorithms have been proposed for the diagnosis of HH. The EASL Clinical Practice Guidelines for HH<sup>2</sup> recommend the following:

- Patients with suspected iron overload should first receive measurement of fasting transferrin saturation (TS) and serum ferritin (SF)
- If transferrin saturation is increased, HFE testing for C282Y and H63D polymorphisms should be performed
- Diagnosis of HFE-haemochromatosis should not be based on C282Y homozygosity alone, but requires evidence of increased iron stores
- Direct assessment of liver iron stores in patients who have elevated SF concentrations and/or transferrin saturation should be performed. This approach is supported by the Dutch Guidelines for the diagnosis and treatment of HH<sup>5</sup> and publications by Swinkels et al<sup>6</sup>, Camaschella<sup>7</sup> and Gan et al.<sup>9</sup> (see Figure 4 in ref)

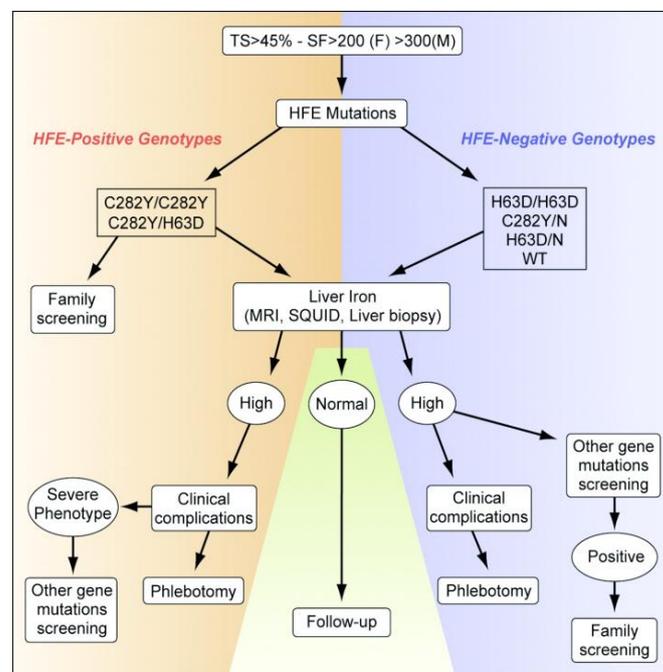


Fig 2: Flow chart for haemochromatosis diagnosis based on genotype at risk and liver iron content. Taken from Camaschella, C. Blood. 2005<sup>7</sup>

## Limitations of SF and 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<sup>3</sup>. 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<sup>10</sup>.

SF does not provide an accurate quantitative relationship with body iron stores in hereditary haemochromatosis<sup>2,3,4</sup>. Rather, LIC has a much stronger correlation with body iron stores in HH<sup>3</sup>.

The European Association for the Study of the Liver Disease (EASLD) Clinical Practice Guidelines for HFE Haemochromatosis<sup>2</sup> 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<sup>3</sup> showed that there was significant inter-individual variability between excess body iron stores (or total phlebotomised iron) and SF concentrations.

## References

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