

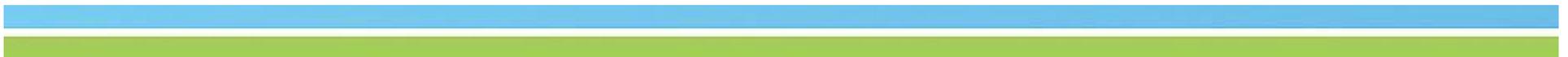
FerriScan[®] : *be better informed*

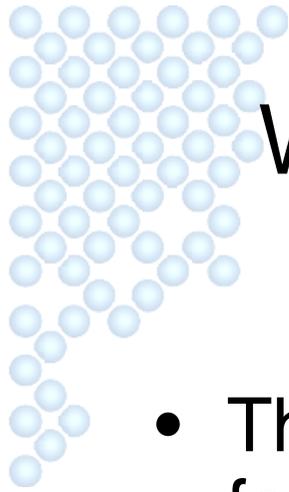
Using FerriScan in the assessment
of liver status in hereditary
haemochromatosis



Hereditary Haemochromatosis

- Hereditary haemochromatosis is an inherited condition that causes high iron absorption from a person's diet. The condition is caused by an abnormal gene or genes that control iron absorption

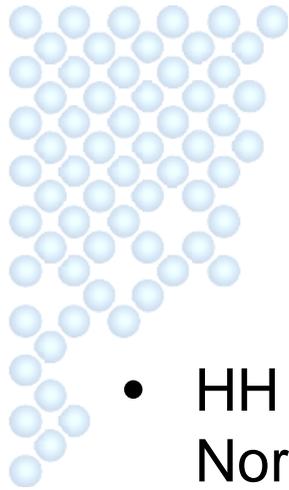




Why is it important to control total body iron stores?

- The human body has no natural mechanism for excreting iron
- Free iron (labile iron) causes tissue damage
- Tissue iron deposits are a source of free iron
- The liver is the primary site of iron storage
- If liver iron storage capacity is exceeded, iron is deposited in other tissues of the body including the heart





Hereditary Haemochromatosis (HH)

- HH is common in countries where the population is largely of Northern European origin
- Approximately 1 in 200 people of Northern European descent are homozygous for the most common HH gene
- Not every individual who has the abnormal gene exhibits symptoms of the disease
- Some people may test negative for the abnormal gene but still suffer from haemochromatosis
- Determination of the magnitude of body iron stores will identify individuals who would benefit from phlebotomy therapy



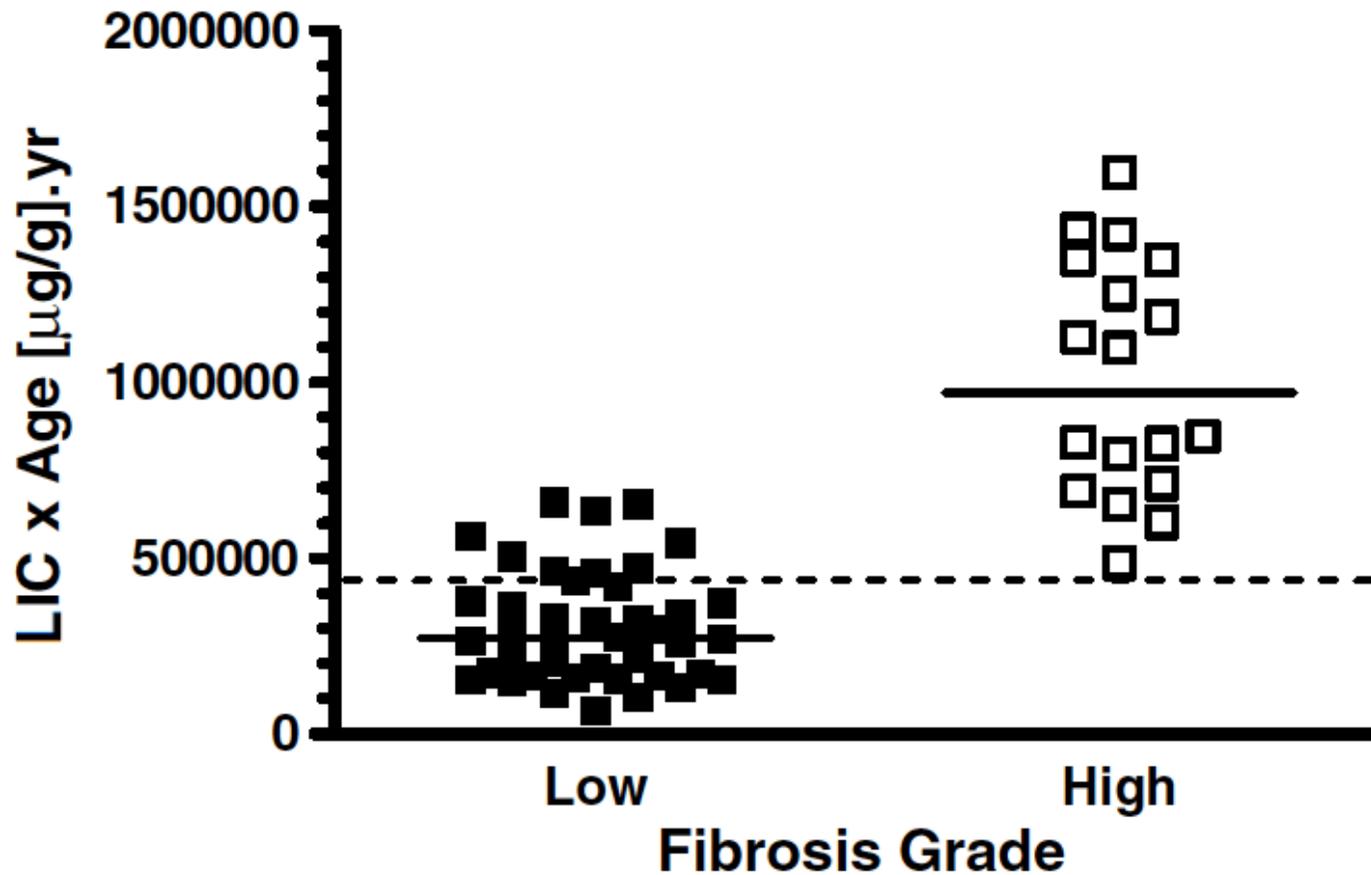


When is measurement of liver iron concentration (LIC) important?

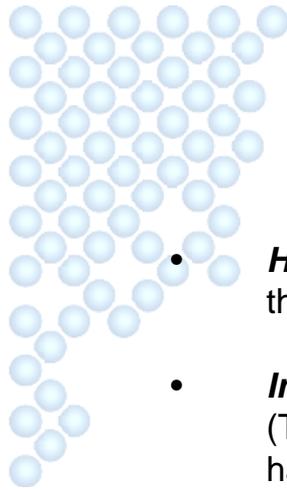
- High LIC over a prolonged period causes liver damage
- Measurement of LIC at diagnosis enables risk of liver damage to be assessed
- Liver damage (high grade fibrosis) is a risk factor for hepatocellular carcinoma (HCC)
- Biopsy and/or regular monitoring for HCC may be recommended for patients who have had high LIC over a prolonged period



LIC x age at diagnosis is good predictor of liver damage



Olynyk et al (2005) Am. J. Gastroenterol 100, 837



Case Study: Cause of lethargy – iron overload confirmed by FerriScan

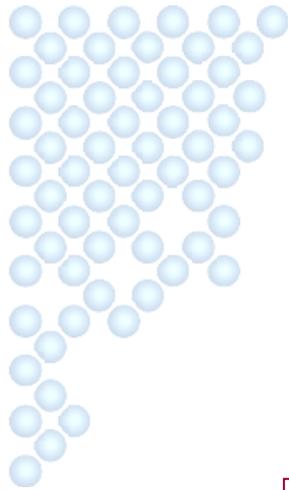
- **History and examination:** A 39 year old Caucasian man presented with lethargy and fleeting aches in the small joints of the hands. Physical examination was completely normal.
- **Investigations for diagnosis:** Full blood picture, ESR, LFTs were normal. Serum transferrin saturation (TS) was 85% and ferritin (SF) levels 890 (g/L). Testing for the C282Y and H63D mutations in the haemochromatosis (HFE) gene were negative. Patient referred for quantitative measurement of liver iron concentration (LIC) using non-invasive MRI (FerriScan®). Hepatic iron concentration was elevated: 90 mmol/kg dry tissue (NR: 3-33[1]).
- **Diagnosis:** Iron overload (haemochromatosis – not HFE related), confirmed by increased liver iron concentration.
- **Management:** Refer patient for phlebotomy therapy. FerriScan used to monitor LIC.
- **Discussion:**
 - The most common symptoms associated with iron overload in adults include unexplained fatigue, malaise and arthralgia [2,3]
 - Elevated transferrin saturation and ferritin levels suggest body iron accumulation[3]
 - Although testing for C282Y and H63D mutations in the HFE gene were negative, this does not completely rule out genetic hemochromatosis[2]
 - Measuring LIC using non-invasive MRI (FerriScan) assists in the diagnosis of iron overload. The outcome from quantitative LIC will also assist in monitoring treatment in the early stages [4]

Professor John K Olynyk, Professor of Gastroenterology, School and Medicine and Pharmacology (UWA). Fremantle Hospital Campus

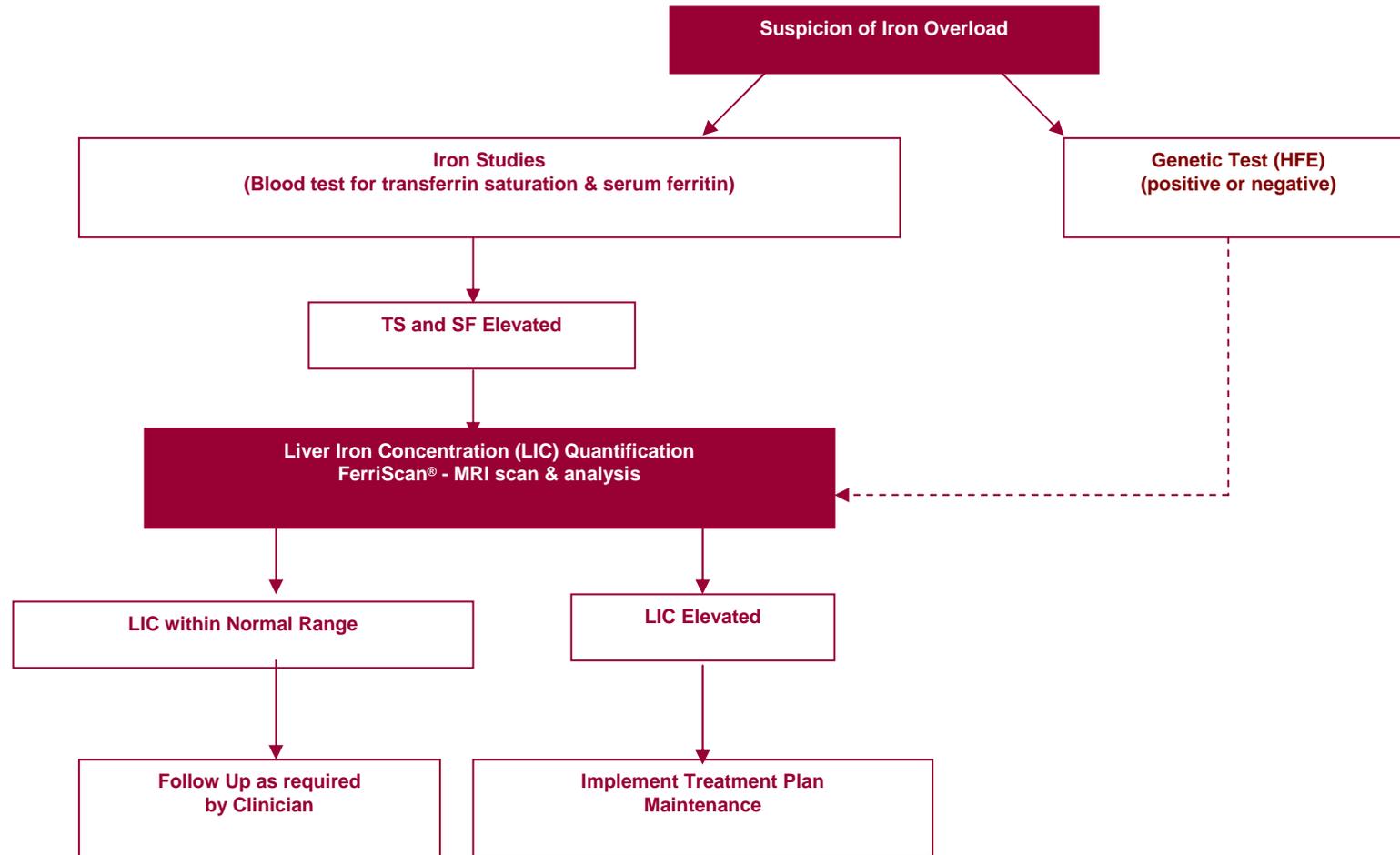
[1] Normal range (NR) is taken from Bassett et. al., Hepatology 1986; 6: 24-29.

[2] Pietrangelo, A. **Hereditary Hemochromatosis – A New Look at an Old Disease**. The New England Journal of Medicine, 2004; 350:2383-2392.

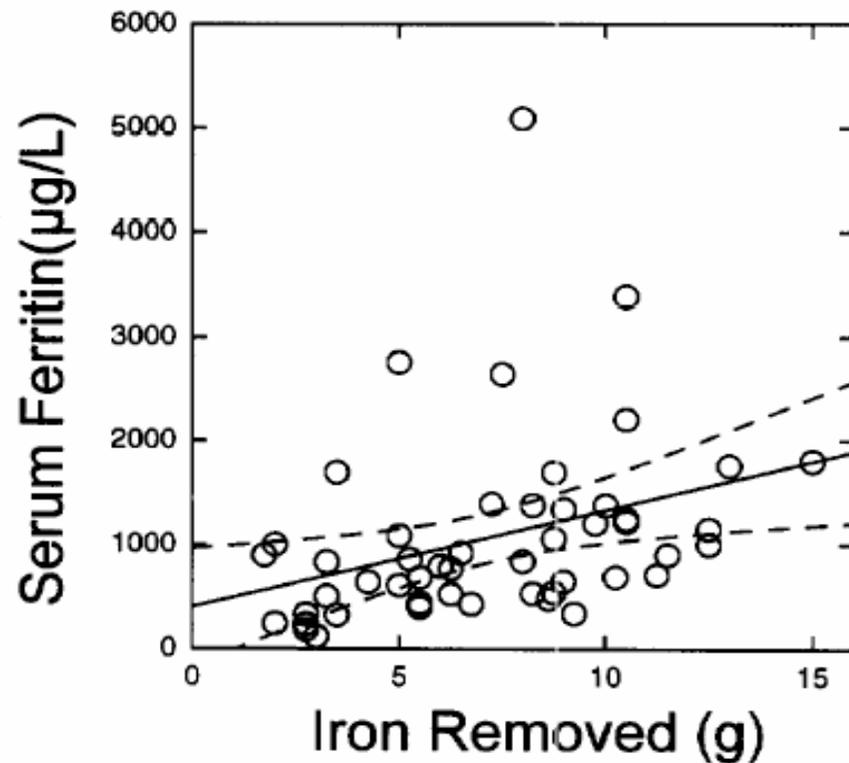
[3] Dooley, J. & Worwood, M. **Guidelines on diagnosis and therapy: Genetic Haemochromatosis**. British Committee for Standards in Haematology. 2000. Abingdon, Oxford, Darwin Medical Communications Ltd. [4] St. Pierre, T.G., Clark, P.R., Chua-anusorn, et al. **Non-invasive measurement and imaging of liver iron concentrations using proton magnetic resonance**. Blood, 2005; 105:855-861.



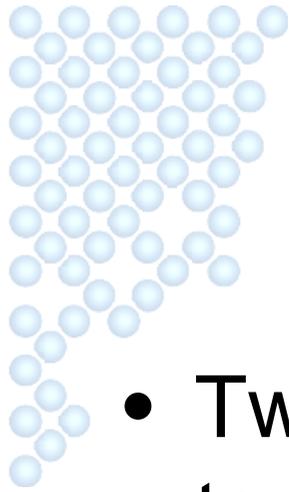
A suggested algorithm for clinical management of iron overload



Is serum ferritin a reliable indicator of body iron stores in HH?



- There is a weak correlation between SF and iron stores in a cohort of HH subjects
- For individuals, SF is an unreliable indicator of body iron stores



Genetic Testing (HFE)

- Two major mutations of HFE attributable to iron loading are C282Y and H63D
- People who inherit the HFE gene mutation from both parents are at the greatest risk of developing haemochromatosis
- Negative genetic testing may not rule out hereditary haemochromatosis





FerriScan[®]

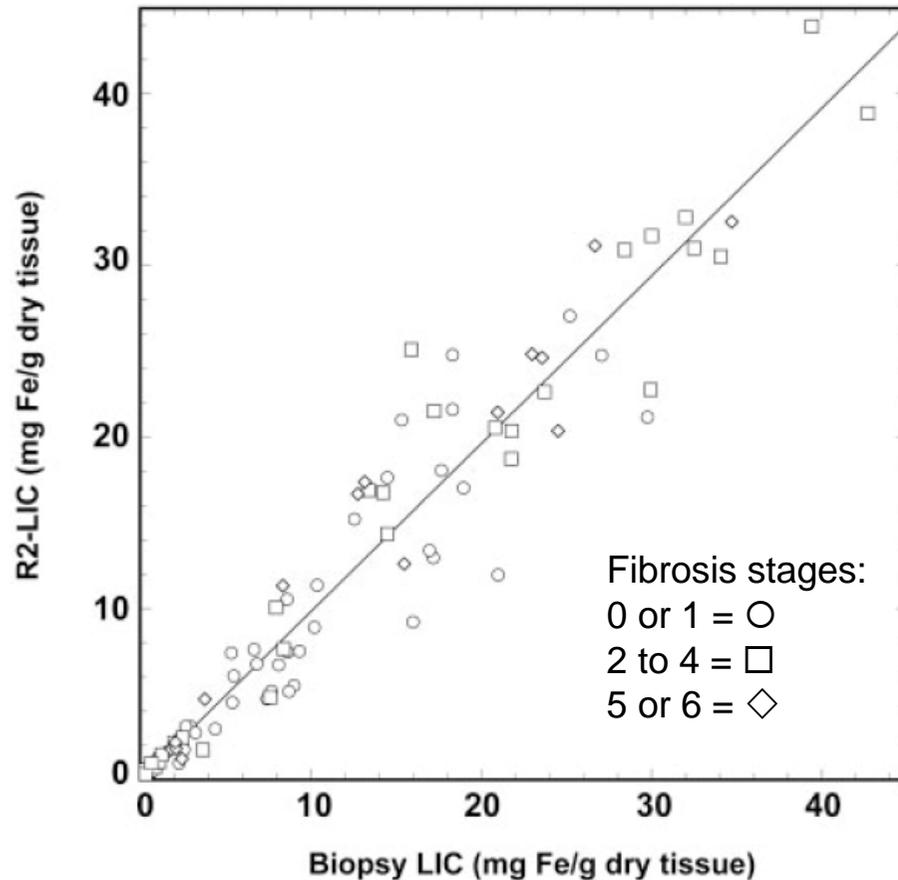
non-invasive measurement of LIC



- FerriScan uses MRI to measure LIC
- FerriScan is based on the R2-MRI technique

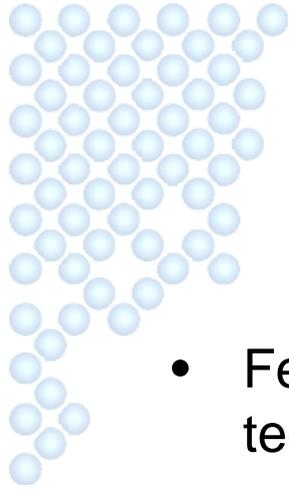


FerriScan[®] is a reliable measure of LIC



- High sensitivity and specificity over entire range of LIC encountered
- Unaffected by presence of fibrosis/cirrhosis

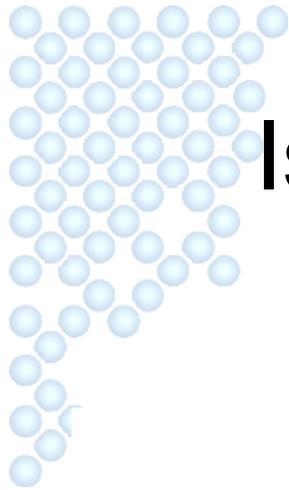
St Pierre et al, Blood. 2005; 105:855-861.



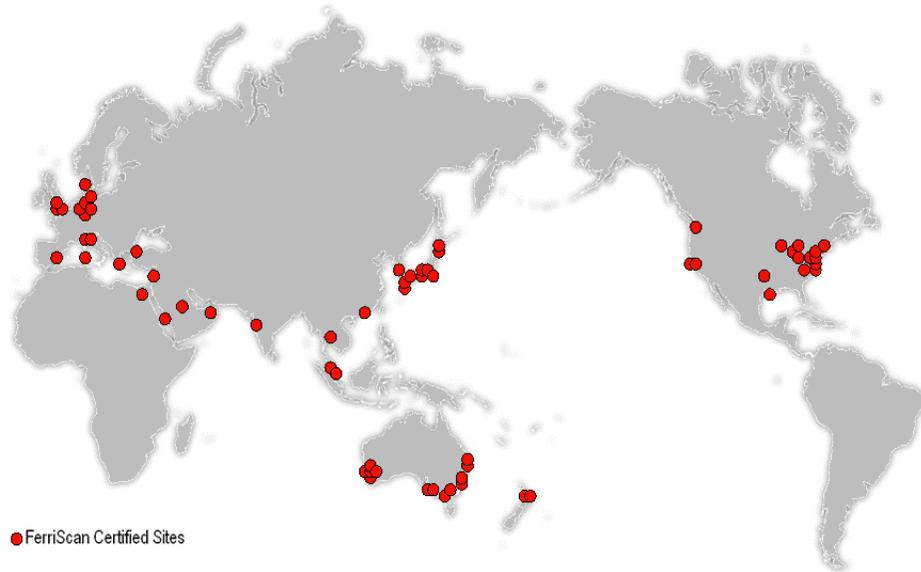
Why choose FerriScan®?

- FerriScan is the world's leading liver iron measurement technology
- FerriScan has a proven dynamic range of LIC measurement greater than any other MRI technique
- All MRI scanners using FerriScan are regularly validated with standards
- Centralised global data analysis service ensures results that can be compared between clinics
- FerriScan provides quality assured data acquisition and analysis
- FerriScan has FDA, Health Canada, TGA, MedSafe clearances and CE Mark





Is FerriScan[®] easy to implement?



- FerriScan works on most clinical MRI scanners available today
- The FerriScan team provides clear instructions and on-line support to help radiologists implement the technique
- FerriScan has been successfully implemented in over 20 countries.



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