FerriScan®

MRI Measurement of Liver Iron Concentration

FerriScan® R2-MRI Fact Sheet - Iron Chelation

FerriScan (R2-MRI) is an accurate, non-invasive MRI based technique for measuring liver iron concentration (LIC). It has been used in clinical trials of iron chelators since its launch in 2004.

FerriScan is provided to the international clinical community as an image analysis service. Following a 10 minute patient scan, the image data is sent electronically to Resonance Health and analysed centrally at a quality controlled facility. The FerriScan LIC Report is returned within 48 hours with the patient's LIC measurement.

FerriScan has regulatory clearance in most international jurisdictions including the USA, Europe and Australia, and has been established at over 100 centres.

FerriScan is unaffected by inflammation and fibrosis and is safer and more cost-effective than biopsy. FerriScan has been validated in multiple studies across both primary and secondary iron-loading conditions. Blood serum markers such as serum ferritin and transferrin saturation are unable to provide a consistent and reliable estimation of total body iron, particularly where confounding factors may be present. Evidence of the unreliability of serum ferritin has been found in β thalassaemia major[1], thalassaemia intermedia[2], sickle cell disease[3,4], hereditary haemochromatosis[5,6] and myelodysplastic syndrome[7,8].

Sensitivity and Specificity

FerriScan's high sensitivity, specificity and reproducibility between centres and different MRI scanners give it considerable advantages over other MRI-based methods of measuring iron overload.

FerriScan was originally calibrated against liver biopsy on 105 patients on five different MRI scanners to accurately measure LIC in a range from 0.3 – 42.7 mg Fe/g dry weight. This range is larger than that achievable by any other published MRI-based method.

FerriScan Validation

A FerriScan validation study of 233 patients was presented at ASH 2010 and concluded:

- the FerriScan technique was robust and no deviation had occurred from the original calibration to the subsequent validation
- No statistically significant differences in accuracy or precision of LIC measurements across the five scanners
- No detectible change in the FerriScan technique caused by the use of deferasirox, the presence of fibrosis, or use in very young children.

These finding confirmed the clinical usefulness of FerriScan as a monitoring tool for iron overload.

LIC threshold (mg Fe/g dw)	Clinical relevance*	FerriScan R2-MRI	
		Sensitivity (95% confidence limits) %	Specificity (95% confidence limits) %
1.8	Upper 95% of normal	94 (86-97)	100 (88-100)
3.2	Suggested lower limit of optimal range for LICs for chelation therapy in transfusional iron loading	94 (85-98)	100 (91-100)
7.0	Suggested upper limit of optimal range for LICs for transfusional loading and threshold for increased risk of iron-induced complications	89 (79-95)	96 (86-99)
15	Threshold for greatly increased risk for cardiac disease and early death in patients with transfusional iron overload	85 (70-94)	92 (83-96)

**Taken from Olivieri and Brittenham, Blood 1997; 89:739-61*

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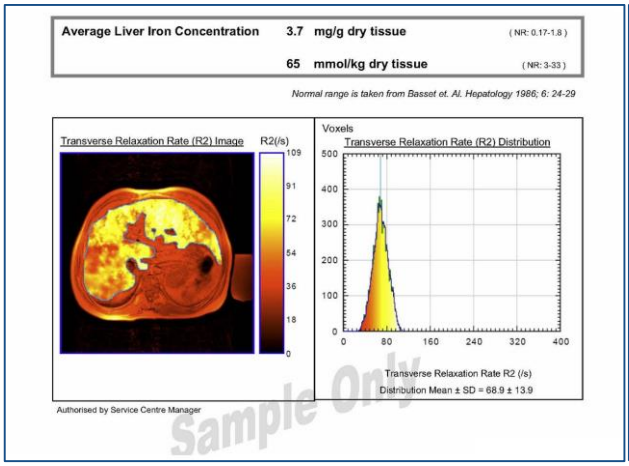
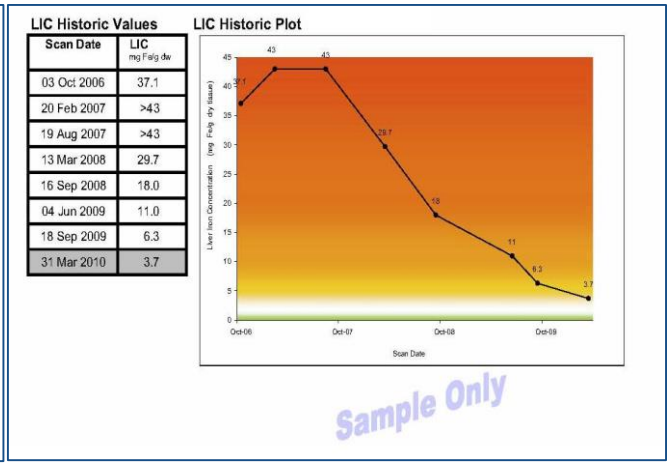
Diagnosis and Management of Iron Overload

Liver iron concentration provides the best measure of total body iron stores and is a validated predictor of the risks a particular patient faces from the complications of iron toxicity.[9, 10] FerriScan can assist in providing a definitive diagnosis of iron overload where this may be indicated by increased serum ferritin trends, genetic testing or a history of blood transfusions. Monitoring of iron stores can improve patient outcomes.[11]





The FerriScan Report provides a definitive LIC measurement. A historic report of the patient's LIC measurement is currently available in some regions.

Iron Chelator Management

- Regular monitoring with serum ferritin can provide useful trending information in some diseases, but does not provide a measure of how iron-loaded a patient is. In thalassaemia intermedia there is no useful correlation between serum ferritin and liver iron.[2] In sickle cell disease fluctuations in serum ferritin are caused by a range of factors providing little useful information to clinician.
- FerriScan provides a reliable indication of total body iron on which to base chelator dose adjustment decisions. An annual FerriScan is recommended to benchmark the patient's progress under chelation.
- The longitudinal monitoring of individual patients requires a technique with an accuracy and precision high enough to confidently detect clinically relevant changes. FerriScan is able to fulfil this criterion.
- An additional feature on some FerriScan LIC reports is a graph tracking the patients LIC history, which may assist with patient's compliance to chelator therapy. This is available in some jurisdictions only.
- The sensitivity and specificity of FerriScan at both very high and very low levels of LIC enables chelation therapy to be optimised, minimising the risk of chelator toxicity.

Cardiac Iron

Some iron-loading disorders such as β thalassaemia major can also result in secondary iron loading in other organs, including the heart, with very serious implications for the risk of cardiac disease or death.[12] In these circumstances, clinicians may also require a Cardiac T2* measurement to indicate the degree of cardiac iron loading.

The FerriScan and Cardiac T2 * Dual Analysis Service is available at selected Radiology Centres internationally to provide this additional information on which clinicians can base their treatment decisions. The two sets of scan data can be collected during the one patient visit at suitably equipped MRI scanners.

References

1. Brittenham, G et al. Am J Hematol. 1993;42(1):81-5.
2. Taher, A. et al. Haematologica, 2008. 93. 1584-6.
3. Kwiatkowski, J. et al Hematol Oncol Clin North Am, 2004. 18. 1355-77, ix.
4. Karam, L et al Pediatr Blood Cancer 2008;50:62-65
5. Olynyk, J. et al Am J Gastroenterol, 1998. 93. 346-50
6. Gordeuk, V. Am J Hematol, 2008. 83. 618-26.
7. Jensen, P.D., F.T. Jensen, T. Christensen, J.L. Nielsen, and J. Ellegaard, Blood, 2003. **101**. 91-6.
8. Porter, J., R. Galanello, G. Saglio, E.J. Neufeld, E. Vichinsky, et al, Eur J Haematol, 2008. **80**. 168-76.
9. Angelucci E et al N Engl J Med. 2000; 343:327-31
10. Cappellini MD, Cohen A, Eleftheriou A, et al. Guidelines for the Clinical Management of Thalassaemia. 2nd ed. Nicosia, Cyprus:
11. Thalassaemia International Fed deration; 2007
12. Pakbaz Z, Fischer R, Treadwell M, R. Y, Fung EB, Calvelli L, Quirolo K, Foote D, Harmatz P, Vichinsky EP. Ann NY Acad Sci 2005;1054:486-491.
13. Kirk et al, Circulation. 2009;120:000-000

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