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Australia and New Zealand Horizon Scanning Network

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National Horizon Scanning Unit
Horizon scanning prioritising summary

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MRI for the assessment of liver iron stores: Management of patients with suspected or diagnosed haemochromatosis.

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PRIORITISING SUMMARY

REGISTER ID: **000083**

NAME OF TECHNOLOGY: **MAGNETIC RESONANCE IMAGING FOR THE ASSESSMENT OF LIVER IRON STORES**

PURPOSE AND TARGET GROUP: **MANAGEMENT OF PATIENTS WITH SUSPECTED OR DIAGNOSED HAEMOCHROMATOSIS**

STAGE OF DEVELOPMENT (IN AUSTRALIA):

☐	Experimental	☐	Established
☐	Investigational	☒	Established *but* changed indication or modification of technique
☐	Nearly established	☐	Should be taken out of use

AUSTRALIAN THERAPEUTIC GOODS ADMINISTRATION APPROVAL

☐	Yes	ARTG number	
☐	No	☒	Not applicable

INTERNATIONAL UTILISATION:

COUNTRY	LEVEL OF USE		
	Trials Underway or Completed	Limited Use	Widely Diffused
France	✓		
United States	✓		
Spain	✓		

IMPACT SUMMARY:

Larger health care institutions provide Magnetic Resonance Imaging (MRI) for the diagnosis and monitoring of a variety of health conditions (eg cancer). MRI is now being considered as a non-invasive diagnostic and management tool for haemochromatosis.

Haemochromatosis is a condition of multiple aetiologies in which iron overload results from an excessive absorption of iron in the intestine followed by cellular deposition, primarily in the liver but also in the heart, pancreas and other tissues (Braunwald et al 2001; Whittington & Kowdley 2002). This condition may be an autosomal recessive disorder, as a result of mutations to the HFE gene (C282Y and H63D mutations), or it may have idiopathic origins associated with such conditions as viral hepatitis or cirrhosis of the liver (Whittington & Kowdley 2002).

In Australia in 2001-2002, 5773 patients were diagnosed with iron metabolism disorders that required hospitalisation (AIHW 2001). What proportion of these patients were diagnosed with haemochromatosis is not evident. However, haemochromatosis is reported to be one of the most common genetic diseases, with a prevalence of 1:200 to 1:500 in people of European decent having the homozygotic genotype (Whittington & Kowdley 2002). Approximately 60% of C228Y homozygotes experience an iron overload, but it is unknown how many of these patients will develop serious disease.

If untreated, iron overload can result in conditions such as liver cirrhosis, hepatic cancer, heart failure or diabetes mellitus.

Presently the most accurate measure of liver iron concentration involves chemical and histochemical analysis of liver biopsy specimens. However, biopsy is an invasive procedure that carries with it the inherent risks of a surgical procedure. Further, there can exist large variability in the measured iron concentration from one sampled region of the liver to another. Serum ferritin measurements may also be used to determine extent of iron overload (Whittington & Kowdley 2002).

The rationale for conducting MRI is that it provides an overall view of iron concentrations in the liver. In theory, the accumulation of iron reduces the signal intensity, making the liver appear darker than surrounding tissues. Recent studies have attempted to correlate this signal intensity with biochemically determined iron concentrations from liver biopsy samples.

A prospective cross-classification study of 38 patients with hereditary or idiopathic haemochromatosis underwent liver biopsy within 1 month of an MRI (Bonkovsky et al 1999). There was no mention of blinding, however for all but five patients the results of MR images were assessed prior to liver biopsy. This study found a high negative correlation between hepatic iron concentrations determined by biopsy and the signal intensity on a MRI ($r=-0.94$).

In a larger prospective cross-classification study, 112 patients with suspected iron metabolism abnormalities were recruited for a combined liver biopsy and MRI scan (Alustiza et al 2004). A radiologist, blinded to biopsy results, performed the assessment of MR imaging data. An identical inverse linear relationship to the Bonkovsky study (above) was found between liver biopsy iron concentrations and MR imaging data ($r= -0.94$).

In a prospective cross-classification study of 80 patients with ideopathic haemochromatosis, iron concentrations of liver and pancreas were determined by MRI and by measuring serum ferritin (Kim et al 2001). Two experienced readers, blinded to the results of the clinical tests, performed assessment of MR images. A moderate correlation was determined between mean ferritin concentration and signal intensity grades on MR images ($r = 0.49$, $p<0.001$).

Finally, in a prospective cross-classification study of 174 subjects suspected of hepatic iron overload or being managed for chronic hepatitis C, biochemical determination of hepatic iron concentration from biopsy was compared to an MRI assessment of iron stores (Gandon et al 2004). Two independent radiologists performed the measurements of liver to muscle iron concentration ratios. This study found that using the most sensitive MRI technique of T2 gradient recalled echo sequence resulted in a sensitivity of the test of 89% and a specificity of 80%. The MRI was able to identify iron overload in all patients with a biochemically measured hepatic iron concentration greater than 60 μmol/g.

No cost-effective studies have been performed on the use of MRI as a tool for determining tissue iron concentrations. It would be expected that the cost of a single MRI scan for the purpose of determining tissue iron concentration would be similar to that performed on the liver for other conditions (fee of $475, MBS item # 63000 - 63946). In comparison the MBS fee for a liver biopsy is $145.05 (MBS# 30409) and the biochemical determination of iron concentration in liver tissue is $33.10 (MBS# 66596).

CONCLUSION:

There is a high level of diagnostic evidence for the assessment of liver iron stores using MRI. The non-invasive nature of the procedure and the existing use of MRI technology in Australia, give this technology the potential for rapid uptake.

HEALTHPACT ACTION:

It is therefore recommended that a Horizon Scanning report be conducted. However, in the interim period since this decision an application was made to MSAC for a full HTA on this technology.

SOURCES OF FURTHER INFORMATION:

AIHW (2001), *The AIHW national hospital morbidity database* [Internet]. Australian Institute of Health and Welfare. Available from: http://www.aihw.gov.au/ [Accessed 16/03/04]

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Bonkovsky, H. L.,Rubin, R. B.et al (1999). 'Hepatic iron concentration: noninvasive estimation by means of MR imaging techniques', *Radiology,* 212 (1), 227-234.

Braunwald, E.,Fauci, A. S.et al (2001), *Harrison's (15th Edition) prinicples of internal medicine,* 2. 15, New York.

Gandon, Y.,Olivie, D.et al (2004). 'Non-invasive assessment of hepatic iron stores by MRI', *Lancet,* 363 (9406), 357-362.

Kim, M. J.,Mitchell, D. G.et al (2001). 'Hepatic iron deposition on MR imaging in patients with chronic liver disease: correlation with serial serum ferritin concentration', *Abdom Imaging,* 26 (2), 149-156.

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SEARCH CRITERIA TO BE USED:

Iron
Magnetic-resonance-imaging
MRI
H?emochromatosis
Sensitivity-and-specificity
Prevalence