# Medical Services Advisory Committee

# Public Summary Document

## *Application No. 1131 - Assessment of Liver Iron by R2-Magnetic Resonance Imaging (R2-MRI)*

**Sponsor/Applicant/s: Resonance Health Analysis Services Pty Ltd**

**Date of MSAC consideration: 49th MSAC meeting, 29-30 July 2010**

### 1. Purpose of Application

On 30 June 2008, Resonance Health Analysis Services Pty Ltd, requested MSAC to undertake an assessment of liver iron by R2-Magnetic Resonance Imaging (MRI) for transfusional dependent patients. The procedure uses data from MRI images to calculate iron concentration in the liver.

Although not requested by the applicant, the MSAC Advisory Panel broadened the scope of the assessment to include non-transfusional iron overload.

### 2. Current arrangements for public reimbursement

There is no Medicare Benefits Schedule (MBS) item for assessment of liver iron by MRI data analysis.

### 3. Background

The majority of transfusion dependent patients have thalassaemia major, a genetic disorder characterised by defective haemoglobin production. Sufferers require regular blood transfusions, and consequently receive excess iron which accumulates causing irreversible tissue damage. The MRI data analysis system is designed to optimise iron chelating therapy, a treatment used to remove excess iron from the body, by providing accurate liver iron measurements to determine optimal chelation dose (appropriate chelation dose is currently based on the judgement of the physician through the use of other diagnostic tests such as measurement of serum ferritin).

The service uses data collected from a suitably calibrated standard MRI scanner that are then electronically transferred to a central, offsite facility for analysis and report. The software application is intended to be used as a measuring device, and does not come into direct contact with patients. Following analysis at the central facility, a report detailing results is then returned to the radiologist at the centre where the MRI was conducted.

The service is indicated for individuals with, or suspected of, systemic iron overload where a definitive diagnosis of iron overload is required or where monitoring of the liver iron burden is required for ongoing clinical management.

## 4. Clinical need

Whether iron overload is due to blood transfusions or haemochromatosis, excess iron can accumulate in nearly all tissues and the ultimate pattern of organ injury is the same. Iron overload is not currently routinely monitored, but overload can cause death. Morbidity results from deposition in the liver, endocrine organs, heart, pancreas, and joints. Iron cardiomyopathy is of particular concern, and remains the leading cause of death in patients with thalassaemia major.

The assessment of liver iron by MRI data analysis may result in more efficient usage of chelation therapy and possibly a reduction in morbidity.

## 5. Comparator

The procedure was intended to substitute liver biopsy, which is the current gold standard test to ascertain liver iron levels. Because of the risks of the procedure, many physicians or their patients choose not to undertake a liver biopsy, but how often this choice is made is unknown. Without a liver biopsy, iron levels can be estimated indirectly through measurement of serum ferritin.

MSAC noted that liver iron assessment by R2-MRI analysis would not necessarily replace liver biopsy where biopsy is currently undertaken in patients with haemochromatosis because biopsy also provides information about histopathological changes which might be important for patient management.

## 6. Scientific basis of comparison

On the basis that no studies could be found that investigated the implications of inclusion of R2-MRI data analysis in algorithms for managing patients at risk of iron overload for final patient outcomes, a linked search of the available literature was undertaken to identify studies addressing safety, accuracy, and whether the test changed patient management.

## 7. Safety

As MRI does not involve ionising radiation, it has generally been accepted as a safe imaging modality as long as proper precautions are taken. MRI is not appropriate for a small number of patients (e.g. patients with implanted devices). There is no evidence of cumulative health effects of repetitive exposure to magnetic fields.

When compared to liver biopsy to determine liver iron concentration, MRI is safer.

## 8. Clinical effectiveness

During the assessment phase, only a single study was available to assess the clinical effectiveness of the procedure. This study appeared to be subsequently supported through the provision (by the applicant) of unpublished data prior to the application being considered by MSAC.

MSAC agreed that, based primarily on unpublished results from 233 patients with beta-thalassemia and transfusional haemosiderosis, assessment of R2-MRI data accurately reflects hepatic iron concentration, when compared to measurement of iron concentrations in liver biopsy specimens.

However, no evidence was provided that liver iron concentration reflected cardiac iron levels, or that measurement of liver iron by R2-MRI analysis affected the use of chelation therapy or resulted in improved outcomes in patients with transfusional iron overload.

## 9. Economic evaluation

Assessment of liver iron concentration by MRI data analysis was considered by MSAC as cheaper than liver biopsy per procedure. However, MSAC noted that utilisation of liver biopsy is very low possibly due to patients opting not to undergo the procedure after receiving the referral. Additionally, liver biopsy is commonly undertaken in the public hospital setting and therefore has no associated MBS cost.

The required frequency of MRI scanning to monitor iron concentration levels was unknown.

## 10. Financial/budgetary impacts

Based on anticipated patient utilisation if listed on the MBS, MSAC estimated a cost for the MBS of $1.1 million to $3.3 million per annum, with potential additional costs due to the need for some patients to be sedated prior to the MRI scan.

MSAC agreed that that since a MRI scan is much less invasive than a liver biopsy, it is reasonable to expect that the utilisation rate would be higher than existing liver biopsy utilisation rates.

## 11. Other significant factors

MSAC suggested a need for a future “fit-for-purpose” application for cardiac iron measurement.

## 12. Summary of consideration and rationale for MSAC’s advice

MSAC considered the evidence in relation to the assessment of liver iron by R2-MRI data analysis for patients with both transfusional and non-transfusional iron overload.

MSAC agreed that, based primarily on unpublished results from 233 patients with beta-thalassemia and transfusional haemosiderosis, assessment of R2-MRI data accurately measures hepatic iron concentration, when compared to measurement of iron concentrations in liver biopsy specimens.

In relation to the use of the test for the non-transfusional iron overload group (mainly patients with primary haemochromatosis), MSAC concluded that there was insufficient evidence to determine the utility of the test in this group (ie whether a beneficial change in clinical management is likely to occur as a result of using the test), as the test would only partially substitute for liver biopsy in the management of these conditions (because liver biopsy also provides other important diagnostic and prognostic information [eg. detection of fibrosis and cirrhosis] for these patients). It was also noted that the applicant had not sought public funding for the use of the test in this group.

In relation to the use of the test in patients with transfusional iron overload, MSAC did not consider that there was sufficient evidence to conclude that the information obtained from using the test would result in either cost savings or improved patient health outcomes through informing changes to patient management.

MSAC noted that liver iron assessment by R2-MRI analysis would not necessarily replace liver biopsy where biopsy is currently undertaken in transfusion-dependent patients because biopsy also provides information about histopathological changes caused by iron overload which might be important for patient management, and liver biopsy in this patient group would not be a frequent indication.

MSAC considered that liver iron assessment by R2-MRI analysis may become be a useful and non-invasive means of monitoring iron levels to inform appropriate chelation therapy dosage, but that further evidence is required to support this hypothesis, including evidence of any consequential impact of such changes in patient management for chelation therapy costs and patient health outcomes. MSAC also considered that there was insufficient evidence to determine the optimal intervals between repeated R2-MRI analyses in this patient group.

MSAC also noted that no evidence was presented that iron concentration in the liver correlates with cardiac iron concentration, given that the leading cause of death for thalassemia patients with transfusional iron overload is iron cardiomyopathy. MSAC was therefore unable to conclude that the R2-MRI measurement of hepatic iron concentration levels was a better surrogate for cardiac iron estimation than serum ferritin, which itself is not regarded as a useful indicator of cardiac iron concentration. Further evidence on the role of R2-MRI data analysis in changing patient management and patient outcomes would be useful.

Therefore, MSAC does not support public funding for the assessment of liver iron by R2-MRI data analysis in transfusion-dependent patients, on the basis of insufficient evidence that measuring hepatic iron concentration results in any change to patient management and/or patient health outcomes.

## 13. MSAC's advice to the Minister

On the strength of the available evidence for safety, effectiveness and cost-effectiveness, MSAC does not support public funding for assessment of hepatic iron content by analysis of R2-MRI data obtained from scans of the liver.

## 14. Context for Decision

This advice was made under the MSAC Terms of Reference:

- Advise the Minister for Health and Ageing on the strength of evidence pertaining to new and emerging medical technologies and procedures in relation to their safety, effectiveness and cost-effectiveness and under what circumstances public funding should be supported;

- Advise the Minister for Health and Ageing on which new medical technologies and procedures should be funded on an interim basis to allow data to be assembled to determine their safety, effectiveness and cost-effectiveness;

- Advise the Minister for Health and Ageing on references related either to new and/or existing medical technologies and procedures; and

- Undertake health technology assessment work referred by the Australian Health Ministers' Advisory Council (AHMAC) and report its findings to the AHMAC.

## 15. Linkages to Other Documents

MSAC's processes are detailed on the MSAC Website at: www.msac.gov.au.

The MSAC Assessment Report is available at [*link inserted when published and agreed by Minister to publicly release outcomes*].