



Australian Government

Medical Services Advisory Committee

Public Summary Document

Application No. 1372 – MRI Liver – Scan for the detection and characterisation of focal liver lesions

Applicant: Royal Australian and New Zealand College of Radiologists (RANZCR)

Date of MSAC consideration: MSAC 64th Meeting, 30-31 July 2015

Context for decision: MSAC makes its advice in accordance with its Terms of Reference, see at www.msac.gov.au

1. Purpose of application and links to other applications

An application requesting MBS listing of magnetic resonance imaging (MRI) of the liver was received from the RANZCR. The evidence for assessment of this application was submitted May 2015.

The applicant is seeking the addition of MRI of the liver onto the MBS for two indications:

1. Patients with known extrahepatic malignancy who are being considered by a specialist for hepatic therapies (including but not limited to percutaneous ablation, resection or transplantation); and
2. Patients with known focal liver lesions requiring characterisation.

2. MSAC's advice to the Minister

After considering the available evidence presented in relation to safety, clinical effectiveness and cost-effectiveness of magnetic resonance imaging (MRI) of the liver, MSAC did not support public funding because of the uncertain clinical effectiveness, and cost effectiveness due to weak data associated with change in clinical management and no translation of imaging performance to improved health outcomes.

3. Summary of consideration and rationale for MSAC's advice

MSAC accepted MRI of the liver to be a safe, non-invasive imaging technique for patients who are not contraindicated, noting that the liver-specific contrast agents may cause mild to moderate adverse reactions in a small number of patients and no severe adverse events were directly attributable to any of the contrast agents when the recommended dose was used.

MSAC noted that there was no direct clinical effectiveness evidence for population 1 with the data essentially limited to metastatic colorectal cancer (CRC), and that direct evidence for population 2 was limited to hepatocellular carcinoma (HCC). MSAC acknowledged the preMSAC response which noted that the evidence for population 2 is directed towards hepatocellular carcinoma as this is a common and aggressive malignancy.

MSAC considered that although the diagnostic accuracy data presented indicated that MRI of the liver was more accurate than the comparators, the data for change management indicated there was a limited effect with no demonstrated impact on survival and consequently no health gain. MSAC therefore did not accept the claim of clinical effectiveness due to the lack of direct evidence on patient relevant concerns, and the inconsistency of statistically significant performance of MRI of the liver in the presented data. MSAC was uncertain whether change in management leads to improved patient outcomes for patients.

MSAC agreed with ESC that there may be value in exploring a third population of patients with:

- known CRC with suspected or possible liver metastases who are being considered by a specialist; or
- known HCC identified by MRI for staging and management.

In the base case analysis for population 1, MSAC noted that the cost of imaging with CE-MRI was higher than CE-CT (\$3,739 versus \$3,310; incremental cost \$428.68) over 12 months, and that the model was sensitive to the cost of contrast. The base case for population 2 showed an incremental cost of \$494.07 (CE-MRI versus CE-US) and \$14.14 (CE-CT versus CE-US) over the 12 months, with the model most sensitive to the diagnostic accuracy of CE-US. MSAC noted the resulting ICER for population 1 was approximately \$46,000 with a QALY gain of 0.009 and approximately \$648,000 with a QALY gain of 0.001 for population 2. MSAC considered the economic analysis was highly uncertain due to the limited evidence and was unconvinced of the cost effectiveness particularly considering that the QALY gain represented less than a day.

MSAC considered the financial and budgetary impact to be underestimated as the application assumed that the number of patients requiring MRI or CT would remain constant, despite the ageing Australian population and increasing rates of obesity and diabetes. MSAC noted that MRI is more costly when compared to CT and other MRI scans.

4. Background

There are currently no existing items related to MRI of the liver listed on the MBS. The Applicant advised that MRI of the liver is currently available to patients in the State-based (public) hospital system and most patients at their practice (approximately 70%) accessing this service fall into this category. Currently, other patients receiving MRI of the liver are private patients and pay the full out of pocket cost of the scan.

5. Prerequisites to implementation of any funding advice

There are a large number of MRI devices included on the Australian Register of Therapeutic Goods (ARTG). For the purposes of ARTG classification, MRI machines are classified as active medical devices for diagnosis.

The applicant indicated that a specialist radiologist with expertise in liver imaging would be required to perform an MRI of the liver. The scan would also need to be performed on a Medicare-eligible MRI unit by a Medicare-eligible provider in order to attract a rebate.

6. Proposal for public funding

The proposed MBS item descriptors as determined by PASC are presented below.

| Category 5 – DIAGNOSTIC IMAGING SERVICES |
|--|
| <p>Item [proposed MBS item number 1] (specialist referral)</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a specialist or by a consultant physician – scan of liver for:</p> <ul style="list-style-type: none"> - known extrahepatic malignancy with suspected or possible liver metastases who are being considered by a specialist for hepatic therapies (R) (Contrast), or - known liver lesion(s) identified by a prior diagnostic imaging technique, which requires additional information to characterise (R) (Contrast) (Anaes.) <p>Bulk bill incentive</p> <p>Fee: \$TBA:</p> <p>(See para DIQ of explanatory notes to this category)</p> |
| <p>Item [proposed MBS item number 2] (GP referral)</p> <p>MAGNETIC RESONANCE IMAGING performed under the professional supervision of an eligible provider at an eligible location where the patient is referred by a medical practitioner (excluding a specialist or consultant physician) – scan of liver for:</p> <ul style="list-style-type: none"> - known liver lesion(s) identified by a prior diagnostic imaging technique, which requires additional information to characterise (R) (Contrast) (Anaes.) <p>Bulk bill incentive</p> <p>Fee: \$TBA</p> <p>(See para DIQ of explanatory notes to this category)</p> |
| <p>Item [proposed MBS item number 3]</p> <p>NOTE: Benefits in Subgroup 22 are only payable for modifying items where claimed simultaneously with MRI services. Modifiers for sedation and anaesthesia may not be claimed for the same service.</p> <p>Modifying items for use with MAGNETIC RESONANCE IMAGING or MAGNETIC RESONANCE ANGIOGRAPHY performed under the professional supervision of an eligible provider at an eligible location where the service requested by a medical practitioner. Scan performed:</p> <ul style="list-style-type: none"> - involves the use of HEPATOBILIARY SPECIFIC contrast agent for [proposed MBS item numbers 2 and 3] <p>Bulk bill incentive</p> <p>Fee: \$TBA</p> |

The applicant noted that specialist referral is generally required for MRI procedures due to the complexity of the test and the necessity of the referrer understanding the uses and limitations of MRI procedures. There are a small number of items that general practitioners (GPs) can request for specific indications.

Current legislative requirements stipulate that Medicare-eligible MRI items must be reported on by a trained and credentialed specialist in diagnostic radiology. The specialist radiologist must be able to satisfy the Chief Executive Medicare that they are a participant in the RANZCR Quality and Accreditation Program (Health Insurance Regulation 2013 – 2.5.4 –

Eligible Providers) (Australian Government 2013). The applicant noted that the costs for the proposed items were investigated as part of this assessment.

7. Summary of Public Consultation Feedback/Consumer Issues

Consultation feedback was received from one consumer organisation, two professional organisations and one general practitioner. The feedback received was generally supportive of the application.

8. Proposed intervention's place in clinical management

The applicant has provided the below clinical management pathways (Figure 1 & Figure 2) that were developed in conjunction with, and agreed upon by PASC.

Figure 1 describes the clinical pathway for patients with a known extrahepatic malignancy with suspected or possible liver metastases and who are being considered for hepatic therapies (population 1).

Figure 2 describes the clinical pathway for patients with known focal liver lesions requiring characterisation (population 2).

Figure 1 Clinical decision pathway for patients with a known extrahepatic malignancy with suspected or possible liver metastases, and who are being considered for hepatic therapies (population 1)

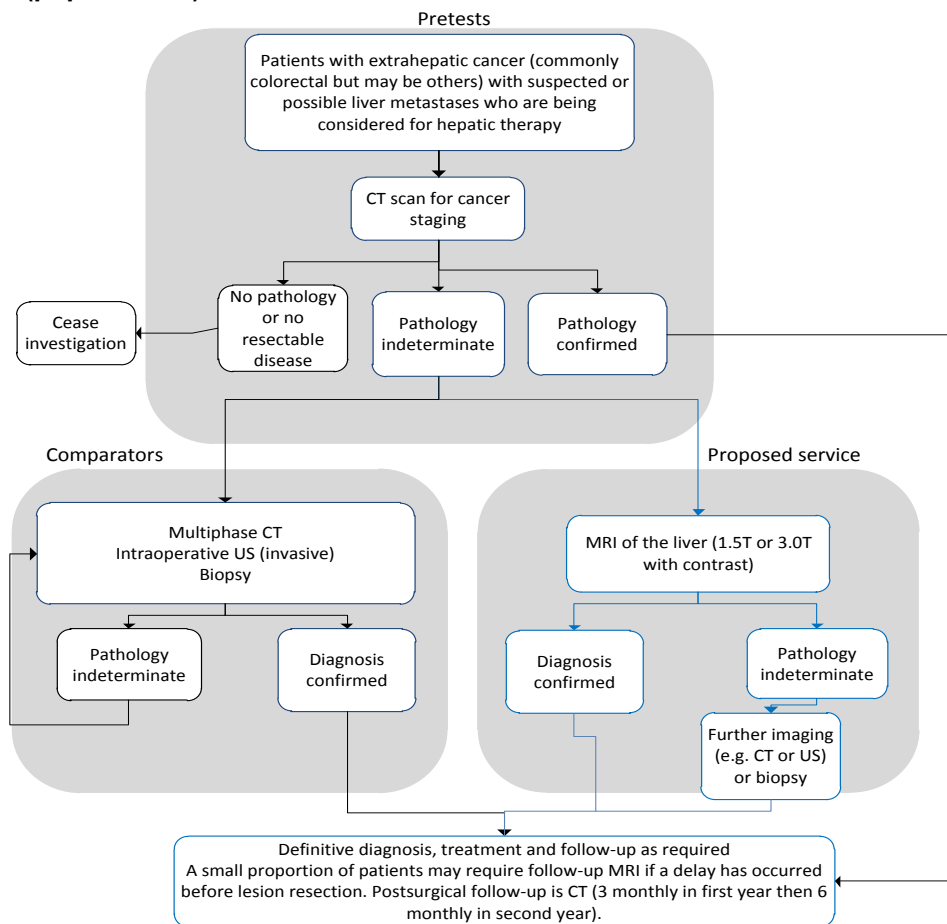
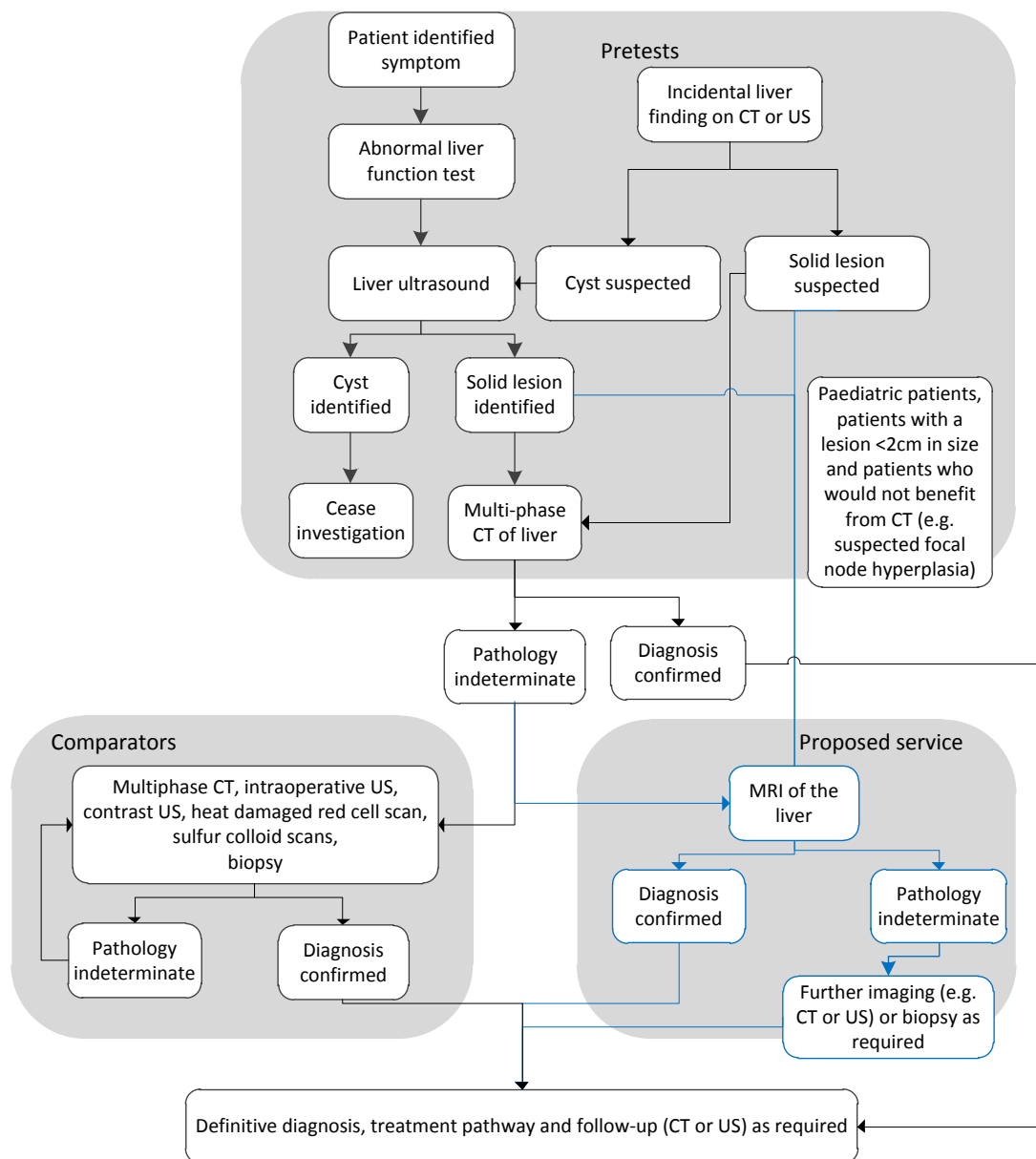


Figure 2 Clinical decision pathway for patients with known focal liver lesions requiring characterisation (population 2)



9. Comparator

The applicant has indicated that for population 1, the comparators to liver MRI as listed in the PASC-ratified protocol are multiphase CT, IOUS and liver biopsy.

For population 2, the applicant has indicated that the comparators are as follows:

- liver biopsy
- multiphase CT
- CE-US
- IOUS
- sulphur colloid scans (for FNH)
- labelled red cell scan (haemangioma)

Following feedback from the applicant, radiologist, oncologist and a liver surgeon, it was determined that, for the purpose of this assessment, MRI with gadoxetic acid (GA-MRI) is expected to mostly replace the alternative non-invasive tests of multiphase CT and/or CE-US.

Expert input has advised that biopsy may be a comparator in certain instances. Specifically, it would be a comparator when disperse lesions are present, and the risk of the cancer seeding along the length of the biopsy needle is acceptable. Sulphur colloid scans and labelled red cell scans would more commonly be used as follow-up tests when FNH or haemangioma are suspected. IOUS is usually undertaken once the decision for resection has been made, for perioperative confirmation of lesion location and surgical margins.

10. Comparative safety

Eleven studies with a total of 3,837 participants reported data on the safety of gadoxetic acid. The most common adverse events (AEs) were nausea, dyspnoea, headache, and flushing. The rate of severe respiratory motion artefact related to dyspnoea was significantly correlated to a high (20 ml) dose of gadoxetic acid, which is more than would reasonably be used (10 ml).

One non-randomised comparative trial investigated the relative incidence of dyspnoea between gadoxetic acid and gadobenate dimeglumine (MultiHance®). The trial found that patients administered with gadoxetic acid had significantly higher rates of dyspnoea, although all cases subsided without medical treatment. There was no difference in other AEs between groups. Evidence from single-arm studies indicated that gadobenate dimeglumine is well-tolerated and has a low incidence of AEs.

Liver MRI with hepatocellular-specific contrast agents was considered to be safe, and no severe AEs were directly attributable to any hepatobiliary-specific contrast agent when the recommended dose was used.

11. Comparative effectiveness

Population 1

Direct evidence

Two studies which reported on patient outcomes following MRI with no contrast. One study compared MRI (no contrast) with CT and found no difference between the groups in terms of intrahepatic recurrence of disease or recurrence-free survival. The second study compared MRI to traditional follow-up (liver function and carcinoembryonic antigen tests) in diagnosing resectable lesions. Out of 293 patients undergoing surgery for CRC; 37 patients had liver metastases and nine patients were identified by MRI as having resectable tumours. In comparison, liver function and carcinoembryonic antigen tests identified six patients as having resectable disease. Patients who had tumour resection had a significantly longer median survival time than those who were not eligible for resection.

While these studies provided direct evidence on patient outcomes following MRI, the studies had a high risk of bias and did not use contrast enhanced MRI. A linked evidence approach was taken to inform the diagnostic accuracy of and change in management associated with GA-MRI.

Linked evidence - Diagnostic accuracy: liver metastases from CRC

CRC is the most common source of liver metastases and was the most commonly reported indication in the literature. Five diagnostic accuracy studies were identified. The studies were

classified as National Health and Medical Research Council (NHMRC) level III-1 or III-2 and represent a total of 264 patients. The studies were deemed to be of mixed quality (Whiting et al. 2011) although there were no applicability issues with the study populations.

Area under curve (AUC) data was reported by three studies. GA-MRI had consistently improved diagnostic accuracy in all studies ($p < 0.05$ where reported). Results from one study showed that GA-MRI was more accurate than CE-US (0.992 vs 0.844, $p < 0.05$). GA-MRI was equivalent to unenhanced diffusion-weighted MRI (DW-MRI) (0.992 vs 0.890, $p > 0.05$) in the one study that reported this comparison.

In a meta-analysis of sensitivity GA-MRI was found to be more sensitive than CE-CT (Table 1). Only one study reported specificity data and the specificity of the techniques was equivalent. Summary receiver operating characteristic (SROC) analysis was not possible. Another study found GA-MRI to be of higher but statistically equivalent specificity to DW-MRI (0.95 and 0.88 respectively, $p > 0.05$).

Table 1 Meta-analysis results for population 1, CRC

| Results | Sensitivity ratio [95% CI] | Sensitivity tau [prediction interval] | Specificity ratio [95% CI] | Specificity tau [prediction interval] |
|----------------|----------------------------|---------------------------------------|----------------------------|---------------------------------------|
| GA-MRI v CE-CT | 1.24 [1.12, 1.37] | 0.093 [1.01, 1.53] | N/A | N/A |

N/A = data was not available for meta-analysis

Diagnostic accuracy - other secondary liver metastases

Three diagnostic accuracy studies, involving a total of 280 patients, were identified that included diagnostic accuracy data on GA-MRI in patients with extrahepatic metastases other than those originating from CRC. The studies were of mixed quality and all were classified as NHMRC level III-2. Meta-analysis was not conducted due to the heterogeneity of the studies. Results from the studies that reported on other secondary lesions were consistent with the results for CRC metastases. Overall, GA-MRI had a higher diagnostic accuracy than CE-CT (informed by AUC results from 2 studies). GA-MRI was more accurate than unenhanced dynamic MRI (D-MRI), although this result was borderline statistically significant ($p = 0.05$; 1 study). D-MRI had a greater diagnostic accuracy than CE-CT (informed by 1 study). GA-MRI was associated with higher or equivalent sensitivity than CE-CT (3 studies). There was no marked difference in specificity, positive predictive value (PPV) or negative predictive value (NPV) between the two techniques.

Change in management

Four studies reported on change in management of patients with CRC metastases following GA-MRI compared with CT alone. Across a combined total of 917 patients, five patients avoided surgery for unresectable disease following GA-MRI and one patient was indicated for resection following GA-MRI (having previously been deemed ineligible on the basis of CT). The most commonly reported management change following GA-MRI was a modification to the planned surgery to include newly detected lesions in the resection, and this was reported in 15 patients. MRI was able to characterise 90 per cent of lesions that were equivocal on CE-CT. Two studies compared the change in management following GA-MRI to DW-MRI but no statistical difference was found.

No change in management studies were identified for any other primary source of liver metastases.

Overall, the key results for population 1 were:

- Five diagnostic accuracy studies were identified for CRC and three were identified for other liver metastases.
- GA-MRI was found to be more sensitive than CE-CT in the detection of CRC liver metastases (result from meta-analysis of 5 studies). GA-MRI had equivalent specificity to CE-CT in patients with CRC liver metastases (result from 1 study)
- Compared with unenhanced MRI, it is unclear whether GA-MRI offers significantly superior diagnostic accuracy for the detection and characterisation of liver lesions (result from 1 study).
- The enhanced diagnostic accuracy of GA-MRI compared with CE-CT appeared to lead to more appropriately targeted surgery for CRC liver metastases.
- It is unclear whether change in management leads to improved patient outcomes for patients with CRC liver metastases.

Population 2

Direct evidence

Two primary studies (NHMRC level III-3) that provided direct evidence on the effect of GA-MRI on the survival of patients with HCC (Kim et al. 2015a; Matsuda et al. 2014). Kim et al. (2015) reported a statistically significant increase in overall survival at 3 years follow-up for GA-MRI compared with CE-CT (82.2% compared with 73.7% respectively, $p = 0.001$). Similarly, recurrence-free survival was higher in the GA-MRI group compared with the CT group (56.2% and 42.0% respectively, $p = 0.003$).

Matsuda et al. (2014) assessed the overall and recurrence-free survival in patients undergoing unenhanced MRI and those undergoing GA-MRI. GA-MRI was associated with higher recurrence-free survival compared with conventional MRI (hazard ratio [HR] = 0.57, 95% confidence interval [CI] = [0.37, 0.87], $p < 0.01$). Overall survival was higher in the GA-MRI group although this did not reach the level of statistical significance (HR = 0.72, 95% CI = [0.34, 1.15], $p = 0.38$).

As the direct evidence of the effectiveness of GA-MRI compared with CE-CT and D-MRI were each informed by a single study with a risk of bias, a linked evidence approach was also undertaken to inform the results of this assessment.

Linked evidence - Diagnostic accuracy

HCC is the most common type of primary liver lesion and was the most commonly reported primary liver lesion. A total of 24 studies with 1,471 patients were identified. The studies were classified as NHMRC level II (2 studies), level III-1 (1 study) or level III-2 (21 studies). The studies were deemed to be of mixed quality (Whiting et al. 2011), although there were no applicability issues with the included population of the studies.

SROC analysis was undertaken for studies reporting the sensitivity and specificity of GA-MRI, D-MRI and CE-CT (receiver operating characteristic [ROC] analysis was not possible for CE-US and CT arterial portography/CT hepatic arteriography [CTAP/CTHA]). GA-MRI was more accurate than D-MRI (AUC of 0.95 and 0.92 respectively) which was in turn more accurate than CE-CT (AUC of 0.88).

Comparative sensitivity and specificity data are shown in Table 2. GA-MRI was more sensitive than CE-CT and this effect was amplified in studies of patients with lesions less than 3 cm in diameter. There was no statistical difference in sensitivity between GA-MRI and D-MRI. D-MRI was more sensitive than CE-CT and this result was bordering on statistical significance. There was no difference in specificity between GA-MRI, D-MRI and CE-CT.

Table 2 Sensitivity and specificity data for HCC

| | Sensitivity ratio [95% CI] | Sensitivity tau, [predication interval] | Specificity ratio [95% CI] | Specificity tau, [predication interval] |
|----------------------------------|-----------------------------------|--|-----------------------------------|--|
| GA-MRI v CE-CT (any size) | 1.14 [1.08, 1.20] | 0.0574 [1.01, 1.29] | 0.98 [0.95, 1.01] | 0.00 [0.960, 1.049] |
| GA-MRI v CE-CT (small lesions) (| 1.38 [1.25, 1.53] | 0.0573 [1.186, 1.617] | NA | NA |
| D-MRI v GA-MRI | 1.04 [0.96, 1.13] | 0.002 [0.961, 1.134] | 0.98 [0.90, 1.07] | 0.00 [0.905, 1.065] |
| D-MRI v CE-CT | 1.12 [1.00, 1.24] | 0.00 [1.00, 1.24] | 0.99 [0.92, 1.06] | 0.00 [0.917, 1.061] |

NA = not applicable (specificity data for all lesion sizes was combined for the meta-analysis due to the per-patient, rather than per-lesion, nature of the data)

The comparative diagnostic accuracy of gadoxetic acid and gadobenate dimeglumine (MultiHance®) found no statistical difference between the two modalities. However, care should be taken in interpreting these conclusions as this was a small study involving 18 patients. Two additional studies compared lesion enhancement with each contrast, reporting conflicting results.

Two retrospective studies directly compared the diagnostic accuracy of GA-MRI with gadopentetate dimeglumine (Magnevist®)-enhanced MRI. One study found no significant difference in diagnostic accuracy between each modality, while the other reported significantly higher sensitivity in GA-MRI (0.90 vs 0.88 $p < 0.05$).

Meta-analysis was not undertaken for CE-US due to the small number of studies reporting data for this comparator. The sensitivity of CE-US was equivalent to GE-MRI in lesions of any size (Alaboudy et al. 2011; Sugimoto et al. 2012). For small lesions one study reported statistically higher sensitivity (0.87 vs 0.44, $p < 0.05$) for GA-MRI (Takahashi et al. 2013) while the other study reported statistically higher sensitivity (0.60 vs 0.67, $p < 0.05$) for CE-US (Kawada et al. 2010). Two studies reported higher specificity in CE-US compared with GA-MRI (0.46 vs 1.00, $p < 0.05$ and 0.84 vs 0.92, $p < 0.05$) (Sugimoto et al. 2012; Takahashi et al. 2013). PPV and NPV were reported by one study (Takahashi et al. 2013) that found that PPV was higher (0.87 vs 1.00, $p < 0.05$) in CE-US while NPV was statistically higher (0.462 vs 0.302, $p < 0.05$) in GA-MRI.

Three diagnostic accuracy studies reported results for GA-MRI compared with CTAP/CTHA. Two of the studies included patients with any sized lesions (Kakihara et al. 2013; Ooka et al. 2013) while one study was restricted to patients with small lesions (Sano et al. 2011). Meta-analysis of these results was not performed. All three studies found that GA-MRI had a higher sensitivity than CTAP/CTHA (mean sensitivity 0.54, 0.94 and 0.96 vs 0.54, 0.84 and

0.65, all $p < 0.05$). There was no difference in specificity. Mixed results were reported for PPV and NPV.

Diagnostic accuracy for other primary liver lesions

Seven studies, which included a total of 742 patients, were identified that included diagnostic accuracy data on GA-MRI in patients with primary liver lesions other than HCC. The studies were NHMRC level III-2 and of mixed quality.

Sensitivity results from the studies that reported on primary lesions other than HCC were consistent with the results for HCC, with GA-MRI associated with statistically higher sensitivity than CE-CT in two studies (mean sensitivity 0.87 and 0.69 vs 0.66 and 0.63, both $p < 0.05$) and statistically equivalent sensitivity in two studies. Two studies did not report the statistical significance of their results.

Six studies found an increase in specificity for GA-MRI compared with CE-CT. This was statistically significant in two studies (0.95 and 0.74 vs 0.79 and 0.59, both $p < 0.05$).

Change in management

Three studies were identified that reported on a change in management for patients with HCC. In each of the studies the patients undergoing GA-MRI were compared with patients who underwent CE-CT (Cha et al. 2014; Hammerstingl et al. 2008; Yoo et al. 2013). Across a combined total of 328 patients, 11 patients were found to be outside the Milan criteria following GA-MRI and 16 patients avoided surgery for unresectable disease. Changes to the surgical plan, including expansion of surgical margins, were required for 12 patients following GA-MRI. Changes to planned radiofrequency ablation (RFA) or transarterial chemoembolisation (TACE) therapy were required for 57 patients.

No change in management studies were identified for any primary lesions other than HCC.

The key results for population 2 were:

- Population 2: 24 diagnostic accuracy studies were identified for HCC and seven were identified for other primary lesions.
- GA-MRI was found to have a higher AUC and sensitivity than CE-CT in patients with HCC. There was no difference in specificity between GA-MRI and CE-CT.
- GA-MRI was found to have a higher AUC than D-MRI; however, meta-analysis of sensitivity and specificity data showed no statistical difference between the two imaging techniques. Therefore, the superiority of GA-MRI over D-MRI is not established.
- GA-MRI appears to be more sensitive than CE-CT and to have equivalent or superior specificity than CE-CT in patients with primary liver lesions other than HCC.
- The relative diagnostic accuracy of GA-MRI is equivalent to gadobenate dimeglumine (MultiHance®)-enhanced MRI. The relative diagnostic accuracy of GA-MRI is equivalent to, or statistically higher than, gadopentetate dimeglumine (Magnevist®)-enhanced MRI. However, this data is from a small evidence base. There is currently insufficient evidence to adequately assess the relative diagnostic accuracy of GA-MRI and gadobenate dimeglumine-enhanced MRI or gadopentetate dimeglumine-enhanced MRI.

12. Economic evaluation

A cost utility analysis approach was used with two decision analytic models being developed, one for each population. Population 1 included patients with a suspected liver metastasis from an extra-hepatic malignancy after initial staging by an unenhanced CT or US scan, while population 2 included patients with a focal liver lesion incidentally detected from an unenhanced CT or US scan.

Population 1

- The cost of a CEMRI was estimated to be \$802.49 (cost of proposed MRI MBS item (\$500) and additional costs including contrast (\$300) and sedation (\$2.49). The cost of CT was estimated to be \$294.25 (weighted average of MBS items 56401, 56407, 56441, 56447). The incremental cost of performing the procedure was \$508.24.
- In the base case analysis, the treatment and imaging costs were higher in the CEMRI cohort relative to the CECT cohort (\$3,739 versus \$,3110; incremental cost \$428.68) over the 12 months
- The corresponding QALYs were slightly higher in the CEMRI strategy compared with CECT (0.622 QALY versus 0.612 QALY, incremental gain 0.009 QALY) over the 12 months.
- The CEMRI strategy is more effective and more costly than CECT. The ICER is \$46,443.87 per QALY gained over the 12 months.
- The model is sensitive to the cost of the contrast agent used. Using MultiHance® rather than Primovist® reduced the ICER to \$27,606.84 per QALY gained relative to CECT.

Population 2

- The cost of CEMRI was estimated to be \$776.52 due to the use of other contrast agents that would be eligible for the existing contrast item. The cost of CT was estimated to be \$294.25 (weighted average of MBS items 56401, 56407, 56441, 56447). The cost of CEUS was estimated to be \$280.67 (weighted average of MBS items 55036, 55037 with contrast cost of \$170 based on advice from Applicant). The incremental cost of CEMRI to CECT is \$495.85 and of CEMRI to CEUS is \$498.85.
- In the base case analysis, CEUS (\$838.27) was the least costly option followed by CECT (\$852.67) and CEMRI (\$1,332.96). This gives an incremental cost of \$494.07 (CEMRI versus CEUS) and \$14.14 (CECT versus CEUS) over the 12 months.
- The incremental QALYs gained from CECT were lower than CEUS by 0.001 QALYs, therefore, as CECT was more costly and less effective than CEUS, it is dominated by CEUS. The corresponding QALYs were slightly higher in the CEMRI strategy compared with CEUS (0.001) over the 12 months.
- Therefore, the CEMRI strategy was more costly and more effective than CEUS. The estimated ICER is \$648,408 per QALY gained) over the 12 months.
- The use of existing contrast MBS item 63491 reduced the ICER to \$344,097 per QALY gained over the 12 months.
- This model was most sensitivity to the diagnostic accuracy of CEUS.

13. Financial/budgetary impacts

The financial impact of public funding for MRI liver imaging was estimated as the potential incremental costs to the MBS from the displacement of CT abdominal services using contrast (includes liver, spleen, biliary and other procedures). The analysis only included the use of CT as this is a comparator in both populations. This included all the intended uses of MRI (population 1 and population 2) and represents the upper limit of costs to the MBS. Scenarios were analysed showing that a lower substitution of CT services with MRI would result in lower incremental costs to the MBS. These values are dependent on the future uptake rate of MRI services.

- Assuming that all patients receive MRI and a CT (0% substitution, 100% addition), the incremental cost was estimated to be \$8.7 million (\$7.4 million excluding co-payment)
- Assuming that 100 % of patients receive MRI (100% substitution of CT services), the incremental cost was estimated to be \$6 million (\$4.5 million excluding co-payment)
- Assuming that 20% of patients receive MRI (20% substitution of CT services), the incremental cost was estimated to be \$1.1 million (\$911,018 excluding co-payment)
- If the cost of MRI uses the existing MBS item for contrast 63491, then the incremental financial impact of listing MRI is expected to be reduced.

14. Key issues from ESC for MSAC

ESC noted that there was no direct evidence for population 1 and that direct evidence for population 2 was limited to hepatocellular carcinoma. The evidence in the assessment report for Population 1 was essentially limited to metastatic CRC. It is therefore unclear how this proposal is different, unless it is suggested that the initial staging CT scan (see clinical decision pathway Fig 1) is bypassed, and patients with CRC go straight to staging MRI – this is unlikely to happen in practice.

ESC also noted that the QALY gains of 0.009 and 0.001 for populations 1 and 2 respectively represented less than a day.

ESC noted that MRI was generally considered safe for patients who are not contraindicated. ESC concluded that the clinical evidence provided indicated that the intervention was more accurate than the comparators, but noted that there was a lack of data on patient relevant outcomes.

ESC concluded that the economic model was reasonable and applicable to the populations and the Australian context. In considering the translation issues for the model, ESC considered that it was reasonable for the time horizon to be limited to 12 months as outcomes were based on diagnostic accuracy rather than long term health impacts. ESC also noted that some of the assumptions were simplistic, but considered the impact on the model would be limited given the 1 year time horizon.

ESC suggested, in light of the lack of evidence for either proposed populations, that there may be value in exploring a third population, of patients with:

- known CRC with suspected or possible liver metastases who are being considered by a specialist; or
- known HCC identified by MRI for staging and management.

ESC advised additional financial modelling on this population would be required to review, in particular, why the proposed MRI scan and contrast agent has a higher cost compared to other similar MRIs and also the contrast agent. The pre-MSAC response noted that liver MRI is more complicated than small bowel MRI and MRI of the pancreas, therefore it is difficult to identify a similar MRI that currently has a rebate.

ESC noted that other matters were raised in the Applicant's comments on the Final Assessment Report, but judged that addressing these would not substantially alter its advice to MSAC.

15. Other significant factors

Nil.

16. Applicant's comments on MSAC's Public Summary Document

The initial application proposed evaluating 3 patient populations: 1) patients with extrahepatic malignancy being considered for hepatic intervention; 2) patients with chronic liver disease and a new lesion over 10mm found at screening; and 3) patients with incidental liver lesions. Populations 2 and 3 should be kept separate for economic analysis, as population 3 is likely to be the least economically viable group. Data linking survival to imaging modality is limited, however a substantial body of evidence exists that shows the greater diagnostic accuracy of contrast enhanced MRI compared with other modalities. Appropriate stratification of patients into various therapies is enhanced by MRI. I encourage MSAC to review the economic analysis separating populations 2 and 3.

17. Further information on MSAC

MSAC Terms of Reference and other information are available on the MSAC Website at: www.msac.gov.au.