Economic evaluation of contrast-enhanced liver MRI in the characterisation of suspected liver lesions
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Abstract

Objectives - To determine the cost effectiveness of contrast enhanced (CE) liver magnetic resonance imaging (MRI) compared to multi-phase computed tomography (CT) scan to characterise suspected liver lesions in patients with known extra-hepatic cancer.

Methods - A decision analytic economic model was built to link diagnostic accuracy to health outcomes in patients with colorectal carcinoma. The model assumed that CE-MRI is diagnostically more accurate, in terms of superior sensitivity and equivalent specificity to CE CT, and patients with a colorectal liver metastasis could be eligible for curative surgery or chemotherapy and palliation. Disutilities were included to capture the impacts of delayed diagnosis (false-negative) or misdiagnosis (false-positive). The cost effectiveness was calculated as the incremental cost relative to the incremental benefit, in which the benefit was estimated using quality-adjusted life-years (QALYs). Sensitivity analyses were conducted to test the robustness of the results.

Results - The clinical evidence supports the increased sensitivity of CE-MRI compared to CT (0.943 versus 0.768). In the base case analysis, CE-MRI was more effective and more costly than CT. The incremental cost effectiveness ratio (ICER) was estimated to be $40,548 per QALY gained. The model is most sensitive to the cost of MRI and palliative treatment and the disutility associated with delayed palliative care in the false negative group.

Conclusions - The results of this paper provide evidence of potential benefits associated with CE-MRI for the diagnosis of liver metastases in patients with identified colorectal carcinoma. CE-MRI can be recommended as cost effective provided that improved diagnostic accuracy results in earlier, curative, disease management.

Keywords

Contrast enhanced liver magnetic resonance imaging (CE-MRI); liver metastasis; cost effectiveness
Introduction

Primary and secondary liver malignancies are a leading cause of mortality and morbidity in Australia [1]. Colorectal cancer (CRC) is the leading cause of liver metastases with 50-60% of liver metastases from this site[2]. One third of colorectal liver metastasis are identified at diagnosis of colorectal cancer and two thirds occur during the course of the disease [2]. In 2014, colorectal cancer was the second most commonly diagnosed cancer in both men and women in Australia [1]. The prognosis for untreated colorectal liver metastasis is poor with a median survival of five to 20 months [3]. The only potentially curative treatment option is hepatic resection, however the majority of patients have unresectable tumours when identified and less definitive therapy is offered [2, 3].

Advancements in medical imaging have aided diagnosis. These advancements include the use of contrast enhanced magnetic resonance imaging (CE-MRI) and contrast-enhanced computed tomography (CE-CT). The use of contrast in MRI and CT improves the image quality and hence accuracy, however, there are additional costs involved[4]. MRI has a number of benefits compared to CT, these include the avoidance of ionising radiation and better image quality in soft tissue[4]. For patients with colorectal cancer, several studies have demonstrated that CE-MRI had superior sensitivity and equivalent specificity to CE-CT [5-9]. This may make MRI better suited to the characterisation of colorectal liver metastasis, however there are concerns with MRI, including possible claustrophobia and agitation as patients are required to lie still during the imaging.[9]

Improved diagnostic accuracy can lead to changes in the management of potential liver malignancies, for example it may identify additional lesions for surgery or identify unresectable lesions, thus avoiding unnecessary surgery. [6, 8, 10, 11]. Therefore, benefits from improved diagnostic accuracy are dependent on changes in management and the availability and effectiveness of treatments for the liver metastasis (and the existing primary cancer). A number of economic evaluations have compared MRI to imaging modalities in patients with suspected liver metastasis [12-17]. Three of these were cost analyses [13, 14, 17] and the remaining were cost-effectiveness analyses [12, 15, 16]. However, the generalisability of these evaluations to the Australian setting is questionable, since some have used inappropriate comparators (e.g. positron emission tomography is not funded for this purpose in Australia)[16], or unavailable contrast agents (e.g. ferucarbotran or superparamagnetic iron oxide (SPIO) [12, 15], or clinical algorithms that are not consistent with Australian practice [15].
This study aims to determine the cost-effectiveness of CE-MRI compared to CE-CT in the detection of liver metastasis in patients with known colorectal cancer in Australia. The realistic contemporary Australian alternatives are considered as comparators. The study includes the health impacts from the potential changes in clinical management due to improved diagnostic accuracy. The inclusion of these characteristics makes our study of increased relevance in contrast to older studies and the international literature.

Methods

Model Design
A decision analytic model (Excel, 2010) was constructed to estimate the cost-effectiveness of CE-MRI (specifically gadoxetic acid contrast agent) to CE-CT in the detection of liver metastases of patients with colorectal cancer (Figure 1). Using this model, the incremental cost per additional case detected and cost per QALY gained were estimated. Due to the absence of long term clinical data, only short-term costs were considered. QALYs were calculated over a 12 month time horizon with no discounting in the model. A health care perspective was applied, taking into account the intervention and subsequent health care resource costs incurred by health care providers.

[Insert Figure 1: Decision tree of cost-effectiveness model]

The model is designed to estimate the short term clinical impacts of the performance of the diagnostic tests on early healthcare resource use. The population of interest are patients with known colorectal cancer with a suspected liver metastasis. This could occur either because the staging CT revealed a potential lesion or abnormality in the liver or there has been the subsequent detection of a liver abnormality after diagnosis, staging and potentially treatment. At this point, patients can receive CE-CT (current practice) or CE-MRI to identify and characterise liver metastases. Patients with liver metastasis (true positive) will receive curative treatment (i.e. surgery) or non-curative treatment (palliative care or chemotherapy) as necessary. Patients that are incorrectly diagnosed with liver metastasis (false positive) will receive an additional CE-MRI and unnecessary surgical treatment, which is associated with a utility decrement and additional cost. The patients with no metastases (true negative) will continue with a watch and wait strategy. Finally, patients who
receive a false negative test will eventually be diagnosed with liver metastases and receive either delayed surgery (if potentially curative) or palliative care.

**Model inputs**

**Diagnostic accuracy**

The diagnostic accuracy of MRI and CT for detecting liver metastasis has been established in patients with colorectal cancer [5-9] and other cancers [18-20]. Several studies have found that CE-MRI is superior sensitivity to CE-CT, with equivalent specificity [5-9]. A linked evidence approach was taken to inform the diagnostic accuracy and change in management associated with CE-MRI. The pooled sensitivity for MRI (contrast agent gadoxetic acid) was 0.943 (95% CI 0.91, 0.96) and CE-CT was 0.768 (95% CI 0.67, 0.84) [5-9]. Specificity was based on a single head-to-head prospective trial between CT and MRI (n=35) [9]. The averages from the 3 readers and the lowest and highest specificity results were used in the base case model; 0.971 (0.967 – 0.973) for MRI and 0.965 (0.945 to 1.000) for CE-CT.

**Estimation of resource use and costs**

Costs were composed of two parts; diagnostic costs and the subsequent treatment of the liver metastasis. The costs of treating the existing colorectal cancer were not included as these costs would be the same in both arms. All costs are in Australian 2015 prices and where relevant were inflated to 2014-2015 prices using the AIHW Total Health Price Index, calculated using the average inflation rate from 2002-2012 [21].

The Medicare Benefits Schedule (MBS), list of services subsidised by the Australian Government, was used to estimate the item costs. The MBS lists a wide range of consultations, procedures and tests, and a schedule fee for each of these items[22]. The cost of the CE-MRI ($500) was based on a proposed MBS fee for MRI (since this test is currently not funded by the MBS) and the cost of contrast ($300) was based on the use of gadoxetic acid (Primovist®)[23]. As an alternative, use of another gadolinium based contrast gadobenate dimeglumine (MultiHance®) ($20) was tested in a sensitivity analysis. It was assumed that anaesthesia and sedation would be required for 5% of patients undergoing MRI (based on expert advice). The costs for general anaesthesia with fentanyl (weighted average of MBS items 17610, 17615, 17620, 17625), referred consultation (weighted average of MBS items 17640, 17645, 17650, 17655) and the initiation of management of anaesthesia (MBS item 21922) and the oral and intravenous sedative (oral diazepam, intravenous midazolam (10178Q)).
The cost of the comparator CE-CT ($294.25) was based on the weighted average of MBS items with and without contrast on equipment greater or less than 10 years old (56401, 56407, 56441 and 56447). Some patients may be contraindicated to contrast (either for MRI or CT and imaging can be performed without contrast).

The cost of surgery was based on public hospital costs published by the National Hospital Cost Data Collection (weighted average H61A and H61B)[24]. The cost of palliative treatment was an average cost of best supportive care and chemotherapy, a simplifying assumption was made with 50% for palliative care [25] and 50% chemotherapy (PBS items 7253R, 75234R and MBS item 13918).

Probabilities

It was estimated that 40% of patients with colorectal cancer being investigated for a liver lesion would have a liver metastasis. (Saunders et al (2002), other studies have reported lower estimates of 20-25% which was tested in the one-way sensitivity analysis [26, 27]. It was assumed that 20% of patients identified with a liver metastasis (true positive) would be eligible for curative treatments [27], and that patients mis-diagnosed (false negative) would be identified with liver metastasis within the year, but have lower chance of being eligible for curative treatment. In the base case this was estimated to be 10% (half of the true positive rate). This was tested in the sensitivity analysis by assuming the rate of curable disease was the same for true positive cases.

Quality of life

Utilities were derived from the literature for patients receiving surgery [15] or palliative treatments [28]. For patients with no liver metastases (true negative and false positive), their utility was based on patients with stage III colorectal cancer[29]. Utility decrements were applied to patients with a false negative result who received delayed curative treatment or palliative treatment [15, 28].

Survival

The median survival estimates are based on five year overall survival rates in Westwood et al. 2013. These were; metastatic disease requiring curative surgery (0.24; SE 0.03), metastatic disease requiring palliative care (0.06; SE 0.04), and no metastatic disease 0.85 (SE 0.01)[15]. The 5 year overall survival rates were converted to one year probabilities of survival (assuming a constant hazard rate, and exponentiated back to probabilities) and the resulting 1 year probabilities of survival for curable liver metastases is 75%, non-curable liver metastases is 57% and no liver metastases is 97%.
Sensitivity Analysis

Univariate sensitivity analysis was performed using the upper and lower 95% confidence interval to test parameter uncertainty in the model. Uncertainty in the cost estimates for treatment and additional MRI costs was tested by assuming lower and upper estimates by calculating the inverse of the gamma cumulative distribution. Probabilistic sensitivity analysis was also conducted to test the joint uncertainty across all model parameters. Beta distributions were applied to probabilities, utilities and survival rates, and gamma distributions were applied to utilities and costs[30]. Distributions were applied to all parameters and Monte Carlo simulation was conducted (1,000 iterations).

Scenario analysis was also performed to test the impact of the assumptions made in the model. The scenarios tested included: 1) all patients receive cheaper contrast (MultiHance®) with same diagnostic accuracy; 2) false positive patients do not receive unnecessary surgical treatment and have same costs and benefits as true negative patients; 3) no difference in probability of having curable liver metastases between true positive and false negative patients; and 4) same specificity was used for both MRI and CT.

Table 1 summarises the parameter estimates used in the model, along the distributions assumed in the PSA analysis.

[Insert Table 1: Model inputs for base case analysis and sensitivity analysis]

Results

The total cost (imaging plus health care) of imaging with CE-MRI was higher than CE-CT ($3,740 versus $3,311; incremental cost $429) over 12 months (Table 2). The incremental cost is mainly due to the additional cost of MRI ($508.24), but this is offset somewhat because there are fewer false negative test results (from superior sensitivity) which is associated with avoided future imaging. The corresponding QALYs were higher in the CE-MRI strategy compared with CE-CT (0.658 QALY versus 0.647 QALY), giving an incremental gain of 0.011 QALYs. This QALY gain is due to the improved survival associated with more curative surgery.

The incremental cost-effectiveness ratio (ICER) for CE-MRI compared to CE-CT was $40,548 per QALY gained. A willingness-to-pay threshold indicates how much a decision-maker is willing to pay for one
additional QALY. In this analysis we assumed a $50,000/QALY gained threshold. Consequently, since the ICER is below the $50,000/QALY threshold, CE-MRI is considered cost-effective.

This estimate is conservative since the model did not capture health benefits beyond 12 months. Based on a simplified decision tree (ignoring curative and non-curative treatments) the cost per additional case detected between CE-MRI and CE-CT was calculated. Compared to CE-CT, CE-MRI results in an additional 0.07 case (7 per 100) of liver metastasis detected or $6,929 per additional case detected.

**Scenario analysis**

In the scenario analysis it was assumed that all patients would receive dimeglumine gadobenate (MultiHance®) rather than gadoxetic acid (Primovist®) and the resulting cost for contrast was reduced from $300 (including co-payment) to $44.80 (100% MBS fee for item 63491). Using MultiHance® rather than Primovist® reduced the ICER to $29,404 per QALY gained relative to CE-CT. Assuming that no unnecessary surgical treatment was performed in patients receiving a false positive test (i.e. impact is closer to true negative patients, but these patients still receive an additional MRI) increased the ICER to $44,827 per QALY gained. Similarly, assuming that the probability of curable metastasis (20%) was same for all positive results increased the ICER to $42,448 per QALY gained. Assuming that the base case specificity was the same in both MRI and CT (0.971), this increased the ICER to $45,111 per QALY gained.

**One-way sensitivity analysis**

The sensitivity analysis demonstrated that the main drivers of the model is the cost of the MRI contrast agent used ($20 to $300 per patient). The model is also sensitive to the cost of palliative treatment, additional MRI costs (general anaesthesia, sedation), prevalence of liver metastases, diagnostic accuracy of CE-CT and disutility for delayed non curative care. These are summarised in Figure 2.

[Insert figure 2: One-way sensitivity analysis for CE-MRI and CE-CT]

**Probabilistic sensitivity analysis**

The likelihood of an intervention being considered cost-effective relative to alternatives at various willingness-to-pay thresholds can be illustrated by a cost-effectiveness acceptability curve (CEAC) (Figure 3). The CEAC shows that if the willingness-to-pay is lower than $60,000/QALY, the control
group was more likely to be favoured, but it became the least favoured option once the willingness-to-pay rises above $60,000/QALY. At $50,000/QALY, the assumed threshold in the model, CE-MRI had a lower chance of being regarded as cost-effective compared to CE-CT.

[Insert Figure 3: Cost-effectiveness acceptability curve]

Discussion

This study provides evidence of the potential benefits associated with using CE-MRI for the diagnosis of liver metastases in patients with identified colorectal carcinoma. These benefits eventuate because of demonstrated improvements in diagnostic accuracy, particularly the sensitivity of imaging, which results in more cases of liver metastases detected, definitive therapy undertaken, and improved quality of life. CE-MRI was more expensive than CE-CT, and based on an upper threshold for acceptable cost effectiveness of $50,000 per QALY, this analysis demonstrates that CE-MRI is potentially cost-effective provided that improved diagnostic accuracy results in earlier, curative, disease management.

There are additional challenges in assessing the cost-effectiveness of diagnostic technology. Diagnostic technologies do not impact patients outcomes directly. Rather, they give information that may be valued, either by the treating clinician or the patient. Alternatively, the diagnostic technology may lead to a change in the treatment of patients which may alter the long term outcomes of the patient. It is unclear if an improvement in diagnostic accuracy will necessarily translate into improved clinical outcomes for the patient. This may be due to the requirement of behavioural change by clinicians.

It is evident from the model that the sequelae of testing are key drivers of the costs-effectiveness results. These sequelae include the cost of palliative care and the disutility associated with delayed diagnosis. This is interesting because many cost effectiveness studies of diagnostics tests only present a surrogate endpoint, such as cost per case detected, which often omit longer-term impacts. Yip et al (2014) compared three different imaging strategies using a combination of CT, PET and MRI and presented the analysis in terms of the time to decision (weeks). The authors found that a CT scan followed by both a PET and MRI as necessary led to the shortest time to decision[16]. However, whilst it is easy to interpret the best outcome (shortest time to decision) it is difficult to assess value for money. In this study the modelled benefit extended beyond the cost per additional case detected usually seen in cost-effectiveness analyses of diagnostic technologies. This was performed in order to translate improvements in diagnostic accuracy to improved clinical utility. Our study reported
health gains in terms of QALYs, these capture health benefits associated with the sequelae of testing and are more readily comparable across interventions and diseases.

There is limited direct evidence on patient outcomes. A retrospective analysis by Wiggans et al. (2014), in patients receiving CT with MRI versus CT alone found no difference in intra-hepatic recurrence of disease and no difference in the recurrence-free survival between the two groups, this was based on similar diagnostic accuracy [31]. A number of different treatment options were employed including pre-operative chemotherapy, surgery (open or laparoscopic), wedge resection or no surgery [31]. Unlike the Wiggans study we used a linked evidence approach to inform the change in management associated with CE-MRI improved diagnostic accuracy.

In the absence of long term clinical outcome data, the model assessed the short term impacts of the performance of the diagnostic tests on early healthcare resource use limiting the time horizon to 12 months. The assumption regarding change in management was addressed by two scenario analyses which reduced the difference in outcomes between patients with and without liver metastasis despite the test result. The resulting ICERS were both slightly higher than the base case result but remained below the assumed threshold for cost-effectiveness of $50,000 per QALY gained in the deterministic analysis. Differences in specificity were minimised by assuming the same outcomes in false positive and true negative results, given this was based on a single study (no statistically significant difference) [9], however, this still assumed an additional MRI in both arms. Differences in sensitivity were reduced by assuming no difference in probability of curative treatment between true positive and false negative in a scenario analysis.

In Westwood et al. (2013), four diagnostic tests were compared, CE-MRI, SPIO-CE-MRI, CE-US and CE-CT. Based on a single study (n=34, where all four tests were given), the authors assumed similar sensitivity and higher specificity in MRI (100%) over CECT (96%) [15, 32]. The base case assumed that patients that received a positive test received a full body CT scan and a biopsy, therefore no unnecessary surgeries were performed and any difference in specificity would not impact on outcomes[15]. Our model does not assume that all patients receive a biopsy prior to surgery; hence differences in diagnostic accuracy could lead to different patient outcomes. Further, based on a review of the literature, MRI was found to have superior sensitivity to CE-CT, with equivalent specificity [5-9]. Westwood et al (2013) does not use the treatment algorithm that is assumed to be used in Australia [15].
There is considerable uncertainty in the costs of treatments following imaging, for example, surgery and non-curative treatments such as palliative care and chemotherapy. Simplifying assumptions were used to estimate these costs, including the type and proportion of palliative care and chemotherapy and the model ignored other treatment options (chemotherapy as neo-adjuvant therapy prior to surgery). These were addressed using a gamma distribution (for the PSA and estimating the upper and lower estimates), this led to conservative estimates and added to the uncertainty in the model as represented by the shallow slopes in the PSA CEAC (Figure 3).

This model has a clearly defined patient population (patients with known colorectal cancer and a suspicion of liver metastasis) and therefore a proposed clinical algorithm can be tested. The model inputs are based on a review of the clinical evidence, in particular, the specific use of gadoxetic acid (Primovist®) contrast enhanced MRI compared to CT. Unenhanced MRI was not considered an appropriated comparator for the study because it was not part of the Australian clinical algorithm, however, some patients may be contraindicated for contrast. That said, compared to unenhanced MRI it is unclear if CE-MRI offers significantly superior diagnostic accuracy for the detection and characterisation of liver lesions [6]. For this reason, a scenario analysis was included to reflect the use of a different contrast agent and how this impacts (reduced) on the ICER. Assuming identical diagnostic accuracy, MRI without contrast is still more expensive than CE-CT.

Newer diagnostic technologies are expensive in comparison to older technologies. Recently, a review had found that an MRI scan is approximately seven times more expensive than an X-ray and 20 per cent more expensive than a CT scan[22]. Hence, the Australian Government has sought to improve ‘Appropriate requesting’, defined as ‘Requests by medical practitioners for diagnostic imaging services that are clinically appropriate and cost-effective’[22]. Cost-effectiveness considerations are becoming progressively important in decision making for public funding. In Australia, the Medical Services Advisory Committee (MSAC) provides advice on the strength of the evidence relating to the comparative safety, clinical effectiveness and cost-effectiveness of any new medical service, and the circumstances under which public funding (listing on the MBS) should be supported[33]. In this context, funding had been sought for the listing of liver MRI in the characterisation of liver lesions in patients with known extra-hepatic malignancy (e.g. colorectal cancer). MRI have already been listed on the MBS for biliary and pancreatic imaging[34]. CT services with and without the use of contrast have already been listed for use in this patient population on the MBS[34]. In the meeting of July 2015 MSAC did not recommend the funding of CE-MRI for extra-hepatic malignancy being considered for liver therapy. Included amongst the reasons were the lack of direct evidence of benefit and a lack of evidence in the management changes required.
There are a number of limitations with the modelling approach used. This model focuses only on liver metastases that are secondary to colorectal cancer. Other primary cancers that cause liver metastases including neuroendocrine and non-neuroendocrine (pancreatic and breast cancer) were ignored for simplicity. These cancers are likely to have different outcomes and treatments so the results of this study are not transferable to those populations. Other populations may include primary liver malignancies [13-15, 35-39] or cirrhosis surveillance for the development of hepatocellular carcinoma [15]. All of these could also be imaged using MRI and CE-MRI but the current study does not provide any evidence for the cost-effectiveness of the technology for these indications. Also, the modelling assumed that the diagnosis of an isolated liver metastasis will result in a treatment change. It may be that the information derived by the clinician and/or patient on the prognosis of the cancer from a CE-MRI may be valued irrespective of a treatment change. The impact of the information on prognosis is one aspect which would be valuable to patient and clinician irrespective of treatment changes. The value of this information has not been captured in the model.

**Conclusion**

The results of this paper provide evidence of potential benefits associated with CE-MRI for the diagnosis of liver metastases in patients with identified colorectal carcinoma. CE-MRI can be recommended as cost effective provided that improved diagnostic accuracy results in earlier, curative, disease management.
Figure 1: Model structure
Table 1: Model inputs for base case analysis and sensitivity analysis

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Mean</th>
<th>Lower</th>
<th>Upper</th>
<th>SE</th>
<th>Distribution</th>
<th>α</th>
<th>β/λ*</th>
<th>Source</th>
</tr>
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<tbody>
<tr>
<td>Prevalence of liver metastases</td>
<td>0.40</td>
<td>0.20</td>
<td>0.80</td>
<td>0.10</td>
<td>Beta</td>
<td>9.20</td>
<td>13.80</td>
<td>[15]</td>
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<tr>
<td>Sensitivity of MRI</td>
<td>0.943</td>
<td>0.912</td>
<td>0.964</td>
<td>0.01</td>
<td>Beta</td>
<td>288.22</td>
<td>17.42</td>
<td>[5-9]</td>
</tr>
<tr>
<td>Specificity of MRI</td>
<td>0.971</td>
<td>0.967</td>
<td>0.973</td>
<td>0.00</td>
<td>Beta</td>
<td>11669.98</td>
<td>348.54</td>
<td>[9]</td>
</tr>
<tr>
<td>Sensitivity of CT</td>
<td>0.768</td>
<td>0.673</td>
<td>0.841</td>
<td>0.04</td>
<td>Beta</td>
<td>73.64</td>
<td>22.25</td>
<td>[5-9]</td>
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<td>Specificity of CT</td>
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<td>0.945</td>
<td>1</td>
<td>0.01</td>
<td>Beta</td>
<td>163.14</td>
<td>5.86</td>
<td>[9]</td>
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<td>Probability curative treatment if TP</td>
<td>0.20</td>
<td>0.10</td>
<td>0.40</td>
<td>0.08</td>
<td>Beta</td>
<td>5.26</td>
<td>21.05</td>
<td>[27]</td>
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<td>Probability curative treatment if FN</td>
<td>0.10</td>
<td>0.05</td>
<td>0.20</td>
<td>0.04</td>
<td>Beta</td>
<td>6.05</td>
<td>54.42</td>
<td>Expert opinion</td>
</tr>
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<td>Cost of MRI</td>
<td>$500.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>[23]</td>
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<td>Cost of MRI additional</td>
<td>$302.49</td>
<td>$7.66</td>
<td>$1,115.85</td>
<td>302.49</td>
<td>Gamma</td>
<td>1.00</td>
<td>0.00</td>
<td>[23, 40, 41]</td>
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<tr>
<td>Cost of CT</td>
<td>$294.25</td>
<td>$110.71</td>
<td>$336.03</td>
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<td>Gamma</td>
<td>25.94</td>
<td>0.09</td>
<td>[41]</td>
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<td>Cost of surgery TP</td>
<td>$7,794.20</td>
<td>$197.33</td>
<td>$28,751.85</td>
<td>7794.20</td>
<td>Gamma</td>
<td>1.00</td>
<td>0.00</td>
<td>[24] H61A and H61B</td>
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<tr>
<td>Cost of palliative treatment TP</td>
<td>$6,713.25</td>
<td>$169.96</td>
<td>$24,764.37</td>
<td>6713.25</td>
<td>Gamma</td>
<td>1.00</td>
<td>0.00</td>
<td>[40] 7253R, 75234R, 13918, [25]</td>
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<tr>
<td>Cost of surgery FN</td>
<td>$8,596.69</td>
<td>$217.65</td>
<td>$31,712.15</td>
<td>8596.69</td>
<td>Gamma</td>
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<td>0.00</td>
<td>[24] H61A and H61B, MRI cost</td>
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<td>$190.28</td>
<td>$27,724.66</td>
<td>7515.74</td>
<td>Gamma</td>
<td>1.00</td>
<td>0.00</td>
<td>[40] 7253R, 75234R, 13918, [25], MRI cost</td>
</tr>
<tr>
<td>Cost of no metastases FP</td>
<td>$802.49</td>
<td>$20.32</td>
<td>$2,960.29</td>
<td>802.49</td>
<td>Gamma</td>
<td>1.00</td>
<td>0.00</td>
<td>Cost of MRI</td>
</tr>
<tr>
<td>Cost of no metastases TN</td>
<td>$0.00</td>
<td>$0.00</td>
<td>$0.00</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>-</td>
<td>Assumption</td>
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<tr>
<td>Utility of metastases curative TP</td>
<td>0.78</td>
<td>0.27</td>
<td>1.00</td>
<td>0.26</td>
<td>Beta</td>
<td>1.19</td>
<td>0.34</td>
<td>[31]</td>
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<tr>
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<td>0.67</td>
<td>0.01</td>
<td>1.00</td>
<td>0.38</td>
<td>Beta</td>
<td>0.36</td>
<td>0.18</td>
<td>[28]</td>
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<tr>
<td>Disutility for delayed surgery FN</td>
<td>0.30</td>
<td>0.14</td>
<td>0.46</td>
<td>0.08</td>
<td>Gamma</td>
<td>14.06</td>
<td>46.88</td>
<td>[15, 28]</td>
</tr>
<tr>
<td>Disutility for delayed palliative care FN</td>
<td>0.20</td>
<td>0.04</td>
<td>0.36</td>
<td>0.08</td>
<td>Gamma</td>
<td>6.25</td>
<td>31.25</td>
<td>[15, 28]</td>
</tr>
<tr>
<td>Utility for unnecessary surgery for FP</td>
<td>0.74</td>
<td>0.47</td>
<td>1.00</td>
<td>0.14</td>
<td>Beta</td>
<td>6.52</td>
<td>2.29</td>
<td>[43]</td>
</tr>
<tr>
<td>Utility of unnecessary palliative care for FP</td>
<td>0.61</td>
<td>0.22</td>
<td>1.00</td>
<td>0.20</td>
<td>Beta</td>
<td>3.02</td>
<td>1.93</td>
<td>[44]</td>
</tr>
<tr>
<td>Utility of no metastases</td>
<td>0.85</td>
<td>0.58</td>
<td>1.00</td>
<td>0.14</td>
<td>Beta</td>
<td>4.68</td>
<td>0.83</td>
<td>[29]</td>
</tr>
<tr>
<td>Survival of curative metastasis</td>
<td>0.75</td>
<td>0.71</td>
<td>0.79</td>
<td>0.08</td>
<td>Beta</td>
<td>23.36</td>
<td>7.71</td>
<td>[15]</td>
</tr>
<tr>
<td>Survival of non-curative metastasis</td>
<td>0.57</td>
<td>0.40</td>
<td>0.67</td>
<td>0.28</td>
<td>Beta</td>
<td>1.20</td>
<td>0.91</td>
<td>[15]</td>
</tr>
<tr>
<td>Survival of no metastasis</td>
<td>0.97</td>
<td>0.96</td>
<td>0.97</td>
<td>0.01</td>
<td>Beta</td>
<td>359.98</td>
<td>11.89</td>
<td>[15]</td>
</tr>
</tbody>
</table>

β was calculated for Beta distribution; λ was calculated for Gamma distribution

Note: costs were measured in 2014/2015 Australian dollars
Table 2: Cost-effectiveness of MRI and CT

<table>
<thead>
<tr>
<th></th>
<th>Costs (AUD)</th>
<th>QALYs</th>
<th>ICER (cost per QALY gained)</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Base</strong></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>$3,740</td>
<td>0.66</td>
<td>-</td>
</tr>
<tr>
<td>CT</td>
<td>$3,311</td>
<td>0.65</td>
<td>-</td>
</tr>
<tr>
<td>Incremental outcomes</td>
<td>$429</td>
<td>0.01</td>
<td>$40,548</td>
</tr>
<tr>
<td><strong>Sensitivity analysis</strong></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>Assume all MRI receive contrast MultiHance®</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>$3,474</td>
<td>0.66</td>
<td>-</td>
</tr>
<tr>
<td>CT</td>
<td>$3,282</td>
<td>0.65</td>
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</tr>
<tr>
<td>Incremental outcomes</td>
<td>$192</td>
<td>0.01</td>
<td>$29,404</td>
</tr>
<tr>
<td>Assume no unnecessary surgical treatment (costs and utilities of FP same as TN)</td>
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<td></td>
<td></td>
</tr>
<tr>
<td>MRI</td>
<td>$3,604</td>
<td>0.66</td>
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</tr>
<tr>
<td>CT</td>
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<tr>
<td>Incremental outcomes</td>
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<td>$44,827</td>
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<tr>
<td>Assume that probability of curable metastasis same for TP and FN</td>
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<tr>
<td>MRI</td>
<td>$3,742</td>
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<tr>
<td>CT</td>
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<tr>
<td>Incremental outcomes</td>
<td>$421</td>
<td>0.01</td>
<td>$42,448</td>
</tr>
</tbody>
</table>

ICER = incremental cost-effectiveness ratio, QALY = quality adjusted life years
Figure 2: One-way sensitivity analysis for CE-MRI and CE-CT

Figure 3: Cost-effectiveness acceptability curve
Reference


[23] Medical Services Advisory Committee. 1372: Final protocol to guide the assessment of magnetic resonance imaging of liver lesions. 2014.


