Australian Government

Department of Health

MEDICAL SERVICES ADVISORY COMMITTEE

Final protocol to guide the assessment of microwave tissue ablation for primary and secondary liver cancer

MSAC Application 1402

January 2016

Table of Contents

List of Terms

BCLC	Barcelona Clinic Liver Cancer
CPG	clinical practice guideline
CRC	colorectal cancer
CECT	contrast enhanced computed tomography
CT	computed tomography
GHz	GigaHertz
HCC	hepatocellular carcinoma
HIFU	high-intensity focused ultrasound
LAPS	Ligation for Staged Hepatectomy
LTP	local tumour progression
MBS	Medicare Benefits Schedule
MHz	MegaHertZ
MTA	microwave tissue ablation
MSAC	medical services advisory committee
MWA	microwave ablation
NA	not applicable
NR	not reported
PEI	percutaneous ethanol injection
PET	Positron emission tomography
PET-MRI	Positron emission tomography–magnetic resonance imaging
RANZCR	Royal College of Australian and New Zealand Radiologist
RCT	randomised controlled trial
RFA	radiofrequency ablation
US	ultrasound
USA	United States of America
W	watts

1 Title of application

Microwave Tissue Ablation (MTA) for primary and secondary liver cancer

2 Purpose of application

MTA uses radiation in the electromagnetic spectrum to produce cell death via coagulative necrosis radial to a needle inserted into a liver tumour. MTA can be used to provide potentially curative tumour ablation to a proportion of patients with primary liver lesions or with liver metastases from extra-hepatic primary cancers who are not considered to be candidates for surgical resection. Resection of a tumour may be contraindicated due to tumour location or extent, poor physiological hepatic reserve due to diffuse liver disease, and the presence of prohibitive co-morbidities (Bhardwaj et al. 2010; Swan et al. 2012).

A multi-modality treatment approach may also be undertaken for patients with primary liver tumours or metastases in the liver, using MTA in conjunction with liver resection, chemoembolisation, radiotherapy or other regional or systemic cancer treatments (Swan et al. 2012).

Current clinical treatment for these patients is radiofrequency ablation (RFA). For patients with unresectable HCC MBS items 50950 and 50952 can be claimed for RFA procedures. The applicant claims that MTA offers faster and more predictable tumour ablation zones, which reach higher temperatures during ablation and are less susceptible to the heat sink effect. It is also claimed that there is a lower risk of tumour recurrences compared to RFA (Bhardwaj et al. 2010).

The applicant has advised that MTA is currently used in both the public and private settings; however, as there is no current Medicare Benefits Schedule (MBS) service for MTA, patients in the private setting must meet the full cost of treatment. There are four microwave ablation devices registered on the Australian register of therapeutic goods (ARTG) which are used in Australia for ablation of the liver and other soft tissue organs.

There are 11 systematic reviews that provide background on MTA. The most recent is Loveman et al. (2014) on the use of MTA to treat liver metastases, which includes an economic assessment. A thorough description of MTA treatment of unresectable HCC and CRC in a worldwide context is given in Boutros et al. (2010). Liang et al. (2013) summarizes the first clinical practice guideline for ultrasound-guided percutaneous MTA from the Society of Chinese Interventional Ultrasound.

MTA for liver tumours has not previously been considered by MSAC.

3 Intervention – proposed medical service

3.1 Description of the proposed medical service

Microwaves are the part of the electromagnetic spectrum with frequencies ranging from 900 to 2450MHz. Microwave wavelengths lie between those of infrared radiation and radio waves (Banik et al. 2003). When microwave radiation hits water molecules in tissue, they oscillate between 2–5 billion times per second, generating heat from the friction and subsequently

leading to cell death through coagulative necrosis (Lu et al. 2001; Ong et al. 2009; Simon et al. 2005). Microwave is a nonionising radiation and consequently does not induce DNA damage in individual cells (Banik et al. 2003; Ong et al. 2009).

In clinical application of MTA, a thin microwave antenna is positioned in the centre of the tumour (Ong et al. 2009). These antennas are straight applicators with active tips ranging in length from 0.6 to 4.0 cm, they can be single, dual or triple antennae which are simultaneously activated, and have either a straight or looped configuration affecting ablation volume (Meredith et al. 2005; Yu et al. 2006).

A microwave generator emits electromagnetic waves at a frequency of 2450MHz with powers ranging from 60 to 80W through the non-insulated portion of the antenna to surrounding tissue (Dong et al. 2003; Seki et al. 2000). Lower frequency microwave radiation at 915MHz can theoretically be applied at a power of 45W, requiring longer duration of ablation (Simon et al. 2005; Yu et al. 2006); however use of a higher frequency microwave results in a more uniform shape and size of ablation volume. The applicant has advised that 2450MHz ablation systems are used in almost every hospital in Australia. The microwave field allows for direct and uniform deposition of energy into tissue several centimetres from the antenna, rather than relying upon current flow and resistive heating. Multiple pulses can be applied and tumours in this field are heated to over 60°C to achieve coagulative necrosis (Swan et al. 2013).

MTA can be used to ablate tumours up to 6 cm in diameter. Multiple lesions can be ablated in one session and a lesion may undergo multiple ablation procedures if required (expert advice). The average ablation duration ranges between 60 and 300 seconds (Kuang et al. 2007).

The applicant has advised that follow-up cross-sectional imaging is performed approximately six weeks post-MTA. Expert advice is that follow-up imaging may be performed as early as three weeks following the MTA procedure.

3.2 Registered trademark

The application for the proposed items does not limit use to any registered trademark.

There are four MTA systems available in Australia including:

- The Acculis system, including a device and an applicator, is registered to be used in Australia with N Stenning and Co Pty Ltd as the sponsor and uses a frequency of 2450MHz and a power of 140W.
- Avecure Microwave Ablation/Coagulation System - microwave hyperthermia system, sponsored by Aurora BioScience Pty Ltd. For tumours in bone, kidney, liver, lung and pancreas. This device uses 902-928MHz and 32W.
- Emprint™ Ablation System with Thermosphere™ Technology - microwave hyperthermia system (226598), an intracorporeal microwave hyperthermia applicator (178369), and two hyperthermia microwave systems (152044; 178699) sponsored by Covidien Pty Ltd. For non-resectable liver tumours. This device uses 1400-1500MHz and 100W.

- Amica microwave hyperthermia system (212509), and an intracorporeal microwave hyperthermia applicator (212510) sponsored by Culpan Medical Pty Ltd. For soft tissue pathologies such as solid tumours or hyperplasia of the liver, kidney, lung, bone, breast, prostate, etc. This device uses 2450MHz and 20-140W.

3.3 Proposed clinical setting

The applicant has advised that both percutaneous and intra-operative MTA are conducted as in-patient procedures in both private and public hospitals within Australia. MTA usually requires an overnight stay. Percutaneous MTA is delivered in radiology departments by an interventional radiologist. Intra-operative MTA is performed in conjunction with liver surgery by the surgeon or an interventional radiologist in the operating theatre. Expert advice is that MTA is usually provided in tertiary hospitals and is highly unlikely to be performed in regional centres; however, PASC noted the applicant's advice that if Medicare funding were approved, there may be some extension of services in the private sector.

3.4 Service delivery

The applicant has advised that patients with primary and secondary liver tumours are all reviewed at a multidisciplinary liver meeting consisting of hepatologists, gastroenterologists, hepatobiliary surgeons, medical and radiation oncologists, interventional radiologists, nursing co-ordinators, and the clinical care team. At this meeting, decisions regarding patient management are discussed. The decision to perform MTA is a consensus based on the condition of the patient, the disease status and generally on international guidelines (Llovet et al. 2004).

MTA procedures are carried out under general anaesthesia and require the involvement of a qualified anaesthetist. For percutaneous MTA, a specialist interventional radiologist who is a qualified Fellow under the Royal College of Australian and New Zealand Radiologist (RANZCR) performs the ablative procedure. Interventional radiologists have generally performed subspecialist fellowship training to perform minimally invasive image guided interventions; however, this is not currently a requirement. The procedure is performed in the Radiology Department as imaging guidance with ultrasound and/or CT is routinely necessary.

For intra-operative MTA, the procedure is undertaken in the operating theatre and is performed by the surgeon or an interventional radiologist at the same time as the resection procedure.

The procedure involves accurate placement of the microwave antenna into the centre of the tumour under image guidance. Once placement is confirmed, the ablation is performed. Expert advice is that intra-operative US is used to guide open and laparoscopic MTA, while percutaneous US and/or CT may be used for percutaneous MTA procedures depending on a patient's clinical presentation.

Post procedure, patients are monitored by dedicated nursing staff for any immediate complications from the MTA procedure or anaesthesia. Follow up by the patient's treating specialist is performed with cross-sectional imaging between three and six weeks after the MTA.

The most common adverse events associated with MTA are bleeding, damage to adjacent structures and infection. Advice from the applicant is that these would occur in less than five per cent of patients.

Contraindications to MTA include patients who have (1) clinical evidence of liver failure, such as massive ascites or hepatic encephalopathy; (2) severe blood coagulation disorders (coagulopathy); (3) high intrahepatic tumor burden or high extrahepatic tumor burden; (4) acute or active inflammatory and infectious lesions in any organ; (5) acute or severe chronic renal failure, pulmonary insufficiency or heart dysfunction; (6) tumours located in close proximity to the gallbladder, diaphragm, gastrointestinal tract, pancreas, hepatic hilum or major bile duct or blood vessels; (7) and post-intervention hepatic reserve is likely to be too low due to the size and number of lesions (Liang et al. 2013). Any contraindications to RFA are also contraindications to MTA (expert advice).

4 Co-dependent information

4.1 Service

There are no co-dependant services. MTA requires image guidance to locate the lesions to be ablated (US and/or CT). Advice from PASC is that imaging should be considered part of the intervention in line with MBS items for RFA and the current wording of the proposed items reflects this advice.

4.2 Pharmaceutical

There is no co-dependent pharmaceutical medicine. General anaesthetic may be required and the item descriptor reflects the need to claim for this service.

4.3 Medical device or prosthesis

There are no co-dependent devices or prostheses.

5 Population eligible for the proposed medical service

5.1 Medical condition relevant to the service

5.1.1 Primary liver cancer

There are four main types of primary malignant liver lesions: HCC, cholangiocarcinoma (cancer of the bile ducts, CCA), angiosarcoma and hepatoblastoma. Of these, the most common is HCC, accounting for approximately 80 per cent of all primary liver cancers. Intrahepatic CCA accounts for between 10 and 20 per cent of primary liver cancers. Angiosarcoma and hepatoblastoma are very rare (each accounting for approximately one per cent of primary liver cancers) (ASCO 2014)..

HCC is the sixth most common cancer worldwide and the third most common cause of cancer-related death (Forner et al. 2012; Lau 2000). In the majority of cases, HCC is caused by liver damage from infection (hepatitis C, B or D), toxins (primarily alcohol and aflatoxins) or metabolic disorders (diabetes and fatty liver disease) (Forner et al. 2012; Parikh and Hyman 2007).

The incidence of HCC in Australia has more than doubled over the last 20 years, with an Australian age standardised incidence rate of 9.1 per 100,00 population in 2010 compared with 3.9 per 100,000 in 1990 (AIHW 2014).

The wording of the proposed items allow for the treatment of any type of unresectable primary liver lesions

5.1.2 Secondary liver cancer

Metastases in the liver are common to many types of primary cancer due to the liver's dual blood supply and the presence of humoral factors which support cell growth (Khan and Karani 2011). Liver metastases are reported to be 20 to 50 times more common than primary liver cancers (Bree et al. 2000). Colorectal cancer (CRC) is the leading cause of malignancy in western countries, and the primary cause of hepatic metastases (Ismaili 2011; Sheth and Clary 2005). In Australia and New Zealand, the age-adjusted annual incidence rate of CRC is 39.0 per 100,000 of the population (Bala et al. 2013). During the course of colorectal cancer up to 70 per cent of patients will develop hepatic metastases, and 20 to 25 per cent will present with metastases at the time of diagnosis (Niekel et al. 2010; Tsoulfas and Pramateftakis 2012). After CRC, the most common source of secondary liver tumours are neuroendocrine tumours which comprise almost 10 per cent of all liver metastases (Lee et al. 2012). Hepatic metastases occur in more than half of patients with primary neuroendocrine tumours (Chamberlain et al. 2000).

Non-neuroendocrine tumours, including breast carcinoma, renal carcinoma, gynaecological tumours, gastrointestinal stromal tumours, oesophageal carcinoma, gastric carcinoma, exocrine pancreatic carcinoma, lung cancer, melanoma and testicular tumours can also metastasise in the liver (Bala et al. 2013; Treska et al. 2011). Of these, secondary breast cancer is the most common, with approximately 50 per cent of all patients with metastatic breast cancer developing secondary tumours in the liver.. Australian data on the exact number of each type of metastasis could not be obtained as these are recorded with the primary tumour. In an American autopsy study, lung, colon, pancreas, breast, and stomach were the most frequent sources of metastases to the liver, accounting for 24.8, 15.7, 10.9 , 10.1 and 6.1 per cent, respectively, of all patients with metastatic liver disease. Ovarian, endometrial, prostate, and urothelial carcinomas were less frequent sources of liver metastases, each accounting for 4% or less (Centeno 2006).

The proposed item wording for MTA of secondary liver tumours does not limit service provision to any type/s of primary tumour. Expert feedback is that ablative technologies are primarily used to treat CRC liver metastases. While ablation can hypothetically be used to treat other types of liver metastases, it is not routinely considered in the treatment algorithm due to the fact that; once liver metastases develop, disease is usually widely disseminated (Feedback from PASC).

5.2 Proposed patient population and expected utilisation

There are three population groups proposed to be veligible for MTA treatment of liver lesions

1. Patients with unresectable primary liver lesions where MTA is used with curative intent.
2. Patients with unresectable secondary liver lesions, without extra-hepatic spread, where MTA is used with curative intent.
3. Patients with unresectable neuroendocrine liver metastases with or without extrahepatic spread who are refractory to somatostatin analogue therapy where MTA is used for palliative treatment of secretory syndromes.

The applicant has suggested MTA is conducted in the following circumstances:

- When surgical resection is not possible due to the presence of liver malignancy in unresectable locations, the number and anatomical distribution of tumour lesions, and/or the presence of extrahepatic disease (metastatic neuroendocrine tumours only) or poor liver function (Hemming and Gallinger 2001; Orloff 1981). Other contraindications to resection may include: patients whose hepatic metastases are unresectable due to medical comorbidities, such as low hepatic reserve, cardiac insufficiency, or poor performance status; patients with no or minimal extrahepatic disease; patients who have synchronous hepatic metastases; and patients whose hepatic metastases have recurred after resection (Belinson et al. 2012; Belinson et al. 2013).

If the proposed items are listed, advice from PASC is that MTA is expected to fully replace RFA. The most recent MBS data show that services for RFA (both percutaneous and intra-operative) were claimed 85 times in Australia in the 2013/14 financial year. The annual number of RFA services claimed has remained approximately stable since the 2009/10 financial year. Other potential ablative comparators are cryotherapy and percutaneous ethanol injection (PEI). MBS services for cryotherapy were claimed 11 times in 2013/14 financial year. PEI is not listed for use on the MBS and expert advice is that cryotherapy and PEI are rarely used in Australia.

It is unclear how many RFA procedures were undertaken for patients with liver metastases in the private hospital sector as there is no MBS item for that service. The most recent AIHW hospital data show that RFA of the liver was performed 325 times in Australia in the 2012/13 financial year. 'Other destruction of liver' was used 72 times which could include MTA procedures being performed in public hospitals. This number has consistently increased since 2006 when 186 ablative procedures were performed (AIHW National Hospital Morbidity Database 2014a). For patients with liver metastases MTA may be delivered with or without adjuvant chemotherapy.

5.3 Evidence for the population that would benefit from this service

In order to identify whether there is evidence for populations 1-3 described in this protocol; a literature search was conducted in PubMed. The search identified evidence relevant to patients with HCC and CRC metastases. Evidence may not be available for patients with other types of liver tumour that are included in the populations outlined in this protocol. Identified evidence is presented in Table 1 to Table 6.

Table 1 Included systematic reviews on primary and secondary liver cancer

Study ID Study type Location	Included studies	Interventions	Population	Key outcomes
Lahat et al. 2014 **SR** **Israel**	1 level II study, 2 level III-3 studies on primary and secondary tumours	RFA, MTA and Nano knife	Primary and secondary tumours	A systematic review of complications after ablation reported on one observational study comparing RFA to MTA and two studies using MTA only. Major complication rates were found to be 4.1% and 4.6% for RFA and MTA, respectively. Meanwhile the minor complication rates were 5.9% and 5.7% for RFA and MTA. Overall, there was no statistically significant difference in the mortality rates, major complications, and minor complications between the RFA and MTA groups (P>0.05).
Bhardwaj et al. 2010 **SR** **UK**	9 primary studies on HCC and CRC	RFA, cryoablation, MTA; not all were comparative studies	HCC and CRC tumours	Nine studies on MTA. Results suggest that survival in patients undergoing resection and ablation is similar to those patients undergoing hepatic resection only.
Bertot et al. 2011 **SR** **Japan**	1 level II study and 1 level III study on primary and secondary tumours	RFA, PEI and MTA	Primary and secondary tumours	Results indicated that MTA is a safe technique in terms of mortality and major complication rate. However the results should be interpreted with caution because of being based on one large study.
Boutros et al. 2010 **SR** **USA**	17 primary studies on HCC and CRC	MTA v resection, other ablation or PEI	HCC and CRC tumours	The use of MTA with a 915MHz device with triple antennas is recommended over RFA for hepatic tumour ablation. Recurrence rates for lesions <3 cm, 3-year survival rates and major and minor complication are comparable between MTA and the current RFA literature, however data regarding tumours >3 cm and in close approximation to large vascular structures favoured MTA.
Ong et al. 2009 **SR** **UK**	25 primary studies on primary and secondary tumours	RFA, resection; not all were comparative studies	Primary and secondary tumours	Survival rates comparable to surgical resection, however recurrence are rates higher than resection. Suitable in situations where resection is implausible, which is increasing. A useful addition to the currently available treatment options.

Study ID Study type Location	Included studies	Interventions	Population	Key outcomes
Erce & Parks 2003 **SR** **UK**	8 primary studies on HCC and secondary tumours	Cryoablation, RFA, MTA, ILP, ethanol ablation, other injections	HCC and CRC tumours	At this time, MTA of liver had primarily been used to treat HCC. Complete necrosis is possible in tumours <2cm. Recurrence was low.
Garcea et al. 2003 **SR** **UK**	2 primary studies on primary and secondary tumours	Ten types of ablation	Primary and secondary tumours	Studies on treatment of secondary and primary cancer with PEI, percutaneous acetic acid injection, other percutaneous injections, RFA, high-intensity focused ultrasound (HIFU), interstitial laser photocoagulation (ILP), MTA, electrolysis and cryotherapy. Two studies reported on MTA use in the liver. Fair therapeutic results were achieved with MTA in lesions of 30 mm or less, and in well differentiated HCCs.

HCC = hepatocellular carcinoma; HIFU = high-intensity focused ultrasound; ILP = interstitial laser photocoagulation; MHz = Megahertz; MTA = microwave tissue ablation; PEI = percutaneous ethanol injection; RFA = radiofrequency ablation; SR = systematic review; UK = United Kingdom; USA = United States of America

Table 2 Included systematic reviews on primary liver cancer

Study ID Study type Location	Evidence level of included studies	Interventions	Population	Key outcomes
Weiss et al. 2013 SR Germany	1 level II study on HCC	RFA, resection*, PEI, laser ablation and MTA	HCC	Included one RCT on RFA versus microwave ablation (one trial, 72 participants). No significant difference was found between RFA and percutaneous MTA regarding local progression. Rate of complications in both groups was low.

*Included Shibata et al. 2002 only; HCC = hepatocellular carcinoma; ILP = interstitial laser photocoagulation; MTA = microwave tissue ablation; PEI = percutaneous ethanol injection; RCT = randomised controlled trial; RFA = radiofrequency ablation; SR = systematic review

Table 3 Included systematic reviews on secondary liver cancer

Study ID Study type Location	Evidence level of included studies	Interventions	Population	Key outcomes
Loveman et al. 2014 SR UK	1 Level II study, 1 level IV study on secondary tumours	Resection*, MTA	Secondary tumours	There is currently limited high-quality research evidence upon which to base any firm decisions regarding ablative therapies for liver metastases. One RCT of microwave ablation versus surgical resection was identified and showed no improvement in outcomes compared with resection.

Study ID Study type Location	Evidence level of included studies	Interventions	Population	Key outcomes
Bala et al. 2013 Cochrane SR Europe	1 Level 1 study on secondary tumours	Resection*, MTA	Secondary tumours	On the basis of one RCT, which had methodological limitations, evidence is insufficient to show whether MTA brings any significant benefit in terms of survival or recurrence compared with conventional surgery for patients with liver metastases from CRC. The number of adverse events, except for the requirement for blood transfusion, which was more common in the liver resection group, was similar in both groups. At present, microwave therapy cannot be recommended outside randomised clinical trials.
Pathak et al. 2011 SR UK	1 level I, 1 level II, 11 level III-2 on CRC	Cryotherapy, chemotherapy and MTA; not all were comparative studies	CRC	This systematic review on treatments for CRC found thirteen studies on MTA. Concluded ablative therapies (cryotherapy and MTA) offer significantly improved survival compared with palliative chemotherapy alone. Complication rates are low. For MTA 1-, 3- and 5-year survival rates were 40–91.4%, 0–57% and 14–32%. The major complication rate was 0–19%. Median survival was 20.5–43 months, with a local recurrence rate of 2–12.5%.

*Included Shibata et al. 2000 primarily in analysis; CRC = colorectal cancer; MTA = microwave tissue ablation; RCT = randomised controlled trial; RFA = radiofrequency ablation; SR = systematic review; UK = United Kingdom

Table 4 Included randomised controlled trials on primary liver cancer

Study ID Study type Location	population	Intervention Comparator	Key outcomes	Method
Shibata et al 2002. RCT	72 patients with 94 HCC nodules	RFA	No statistically significant differences between the treatments for therapeutic effect, major complications or rates of residual foci of untreated disease. The number of treatment sessions per nodule was significantly lower for the RFA group.	percutaneous

HCC = hepatocellular carcinoma; RCT = randomised controlled trial; RF A= radiofrequency ablation;

Table 5 Included randomised controlled trial on secondary liver cancer

Study ID Study type Location	population	Intervention Comparator	Key outcomes	Method
Shibata et al. 2000 RCT	30 patients with multiple metastatic CRC	resection	No statistically significant difference in 1-, 2- and 3-year survival rates between treatments. Statistically significant lower level of blood loss in MTA treatment.	laparoscopic

CRC = colorectal cancer; MTA = microwave tissue ablation; RCT = randomised controlled trial

Table 6 Other studies of interest

Study ID Study type Location	Included studies Population	Intervention Comparator	Key outcomes
Blue Cross Blue Shield 2013 Review USA	2 level I, 1 level II, 2 level III-2 and 4 level IV (9 studies in total) including patients with HCC only	For the 1 level II and the 2 level III-2 studies the comparator was RFA	The RCT comparing RFA to MTA reported no significant differences between the techniques in the rate of untreated disease during follow-up or major complication rate. The number of treatment sessions required per nodule was significantly lower in the RFA group; however the treatment time per session was significantly higher than for MTA. One of the non-randomised comparative studies (MTA versus RFA) reported no significant differences between MTA and RFA for complete ablation, local tumour recurrence, major complications or disease-free survival at 1, 2 and 3 years. The other reported no significant differences in tumour ablation volumes between MTA and RFA but that operative times were shorter in the MTA group. One of the level IV studies reported that a significantly higher rate of major complications and more ablation sessions were experienced when a non-cooled shaft antenna was used than when newer technology involving cooled-shaft antennas were used.

Study ID **Study type** **Location**	**Included studies** Population	**Intervention** **Comparator**	**Key outcomes**
Liang et al. 2013 Guidelines China	NR	NR	This article outlines the first CPG ultrasound-guided percutaneous microwave ablation therapy for liver cancer. Describes MTA mechanism, techniques, equipment, indications, contraindications, patient preparation and aftercare, combined treatment with other modalities, follow-up and assessment of therapeutic efficacy.
Blue Cross Blue Shield 2012 Review USA	6 level I, II and IV studies on patients with CRC only	MTA v RFA	One of the three systematic reviews reported results for liver metastases separately. This review, which included 13 studies with a total of 406 patients, reported mean survival rate of 73%, 30% and 16% at 1-, 3- and 5- years respectively. The authors of this systematic review recognized the limitations in the available evidence base but felt survival rates following MTA were favourable in comparison to palliative chemotherapy alone. The RCT* found non-significant differences in survival rates and mean disease-free survival. Intra-operative blood loss and the need for blood transfusion were significantly lower in the MTA group compared with the resection group where 6 patients required blood transfusion. Two case series studies, one retrospective (n=39) the other prospective (n=100), reported high rates of complete ablation and low rates of major complications.
NICE 2011 Guidelines UK	8 studies on secondary tumours	MTA v resection	Survival and tumour response were measured. In the one RCT, disease-free survival was 11.3 months and 13.3 months in the MTA and resection groups, respectively (p=0.47).Tumour response, measured by mean ablation diameter was significantly greater following MTA than RFA.

*Shibata et al. 2000; CPG = clinical practice guidelines; CRC = colorectal cancer; HCC = hepatocellular carcinoma; MTA = microwave tissue ablation; NR = not reported; RCT = randomised controlled trial; RFA = radiofrequency ablation; UK = United Kingdom; USA = United States of America

Eleven systematic reviews were retrieved on primary, secondary or primary and secondary liver cancer (Bala et al. 2013; Bertot et al. 2011; Bhardwaj et al. 2010; Boutros et al. 2010; Erce and Parks 2003; Garcea et al. 2003; Lahat et al. 2014; Loveman et al. 2014; Ong et al. 2009; Pathak et al. 2011; Weis et al. 2013). There is significant overlap between the systematic reviews and most of the included studies were level III studies (NHMRC 2009).

A total of two RCTs were identified. One included patients with HCC and compared MTA to RFA (Shibata et al. 2002).The second RCT included patients with CRC liver metastases and compared MTA to liver resection (Shibata et al. 2000).

In addition to the controlled trials, the search identified 33 potentially relevant non-randomised comparative studies with patient numbers between 18 and 879 patients and 44 potentially relevant single arm studies. These are listed in Appendix A: potentially relevant literature.

Other studies of interest include NICE (2011), a UK clinical practice guideline and an article by Liang et al. (2013) which summarizes the first clinical practice guideline for ultrasound-guided percutaneous MTA from the Society of Chinese Interventional Ultrasound.

As far as generalisability of the trials to the Australian context, there is no difference in the techniques used. There is; however, a difference in the machines used in Asia and the USA. In a recent Australian multicentre trial (Chinnaratha et al. 2015), 2450MHz of radiation is used at a maximum power output of 140W. This is in conformance with what is used in Asian studies, with microwave devices in the 2GHz range. Machines with both ranges are available in Australia. It is unknown whether these different machines results in different clinical outcomes.

Clinical Trials

There are nine clinical trials reported to be currently underway (Clinical trials website). Two relevant publications have come from them, a non-randomized trial on MTA of secondary liver cancer, and a prospective cohort study on using PET-MRI after ablation. Most other current trials are single arm. They concern primary (3), secondary (3) and both primary and secondary (3) liver cancers. Completion dates range from Apr 2009 to Dec 2017. Table 7 displays key information on current clinical trials.

Table 7 Current clinical trials

Clinical trial	Status	Study type	Completion date	Published articles
Single-probe Microwave Ablation (MWA) of Metastatic Liver Cancer - secondary	Completed	Non-randomized trial	Apr 2009	Hompes et al. 2010
Laparoscopic Microwave Ablation and Portal Vein Ligation for Staged Hepatectomy (LAPS) - both	Recruiting	Single arm trial	June 2016	10 – not MTA related
Freehand Ultrasound Elasticity Imaging in Liver Surgery - both	Unknown	Single arm trial	Sept 2011	None
Advanced Image Guidance Utilized in Liver Surgery - Primary	Completed	Single arm trial	Sept 2013	None

Clinical trial	Status	Study type	Completion date	Published articles
Single-probe Microwave Ablation (MWA) of Metastatic Liver Cancer - secondary	Completed	Non-randomized trial	Apr 2009	Hompes et al. 2010
Laparoscopic Microwave Ablation and Portal Vein Ligation for Staged Hepatectomy (LAPS) - both	Recruiting	Single arm trial	June 2016	10 – not MTA related
PET-MRI After Radiofrequency Ablation (RFA) or Microwave Ablation (MWA) – Secondary	Recruiting	Prospective cohort study	Jan 2015	Nielsen et al 2014
Microwave Ablation of Resectable Liver Tumours - Primary	Unknown	Prospective observational study	Apr 2015	None
Effectiveness of Microwave Ablation of Hepatocellular Carcinoma as Compared to Radiofrequency Ablation - Primary	Recruiting	Phase 3 randomized controlled trial	Oct 2015	None
Fusion Guided Thermal Ablation Combined With External Beam Radiation for Hepatic Neoplasms - both	Recruiting	Single arm trial	Jan 2016	3 – not MTA related
LOTCOL Study: Local Treatment of Colo-rectal Liver Met - Secondary	Recruiting	Single arm trial	Dec 2017	None

RFA = radiofrequency ablation; MTA = microwave tissue ablation; MWA = microwave ablation; LAPS = Ligation for Staged Hepatectomy

6 Comparator

6.1 Comparator for population 1

Current clinical management of patients with unresectable primary liver lesions is treatment by radiofrequency ablation (RFA). MBS item descriptors for RFA of unresectable HCC lesions are presented in Table 8 and Table 9. There are no MBS items to cover RFA of other primary liver lesions. Advice from the applicant and PASC is that MTA is expected to fully replace RFA if the proposed items are listed.

Table 8 MBS item for percutaneous radiofrequency ablation

Category 3 - THERAPEUTIC PROCEDURES
MBS 50950 NONRESECTABLE HEPATOCELLULAR CARCINOMA, destruction of, by percutaneous radiofrequency ablation, including any associated imaging services, not being a service associated with a service to which item 30419 or 50952 applies Fee: $817.10 [Relevant explanatory notes]

Table 9 MBS item for open or laparoscopic radiofrequency ablation

Category 3 - THERAPEUTIC PROCEDURES
MBS 50952 NON RESECTABLE HEPATOCELLULAR CARCINOMA, destruction of, by open or laparoscopic radiofrequency ablation, where a multi-disciplinary team has assessed that percutaneous radiofrequency ablation cannot be performed or is not practical because of one or more of the following clinical circumstances: - percutaneous access cannot be achieved; - vital organs/tissues are at risk of damage from the percutaneous RFA procedure; or - resection of one part of the liver is possible however there is at least one primary liver tumour in a non-resectable region of the liver which is suitable for radiofrequency ablation, including any associated imaging services, not being a service associated with a service to which item 30419 or 50950 applies Fee: $817.10 [Relevant explanatory notes]

The RFA procedure involves placing a monopolar electrode into target tissue, using the 375-480 kHz frequency of current which will follow the path of lowest impedance through the circuit. Ablation can occur at any point along the closed circuit through the patient (Lloyd et al. 2011).

Resources used in the delivery of RFA will be similar to those needed for MTA. Imaging is required to diagnose and locate the liver tumours. Hospital admission, radiology suite, general anaesthesia, other consumables and the time of the interventional radiologist are used.

RFA is performed as an inpatient procedure requiring an overnight stay for open or laparoscopic RFA. For percutaneous service delivery; the procedure may be a day-surgery procedure or require an overnight stay depending on the patient's age, time of day at which the procedure is undertaken, anaesthetic type, procedure duration and comorbidities.

Expert advice is that cryotherapy (MBS item no. 30419) and PEI (not listed on the MBS) are rarely used in Australia and are therefore are not considered as comparators.

6.2 Comparator for population 2

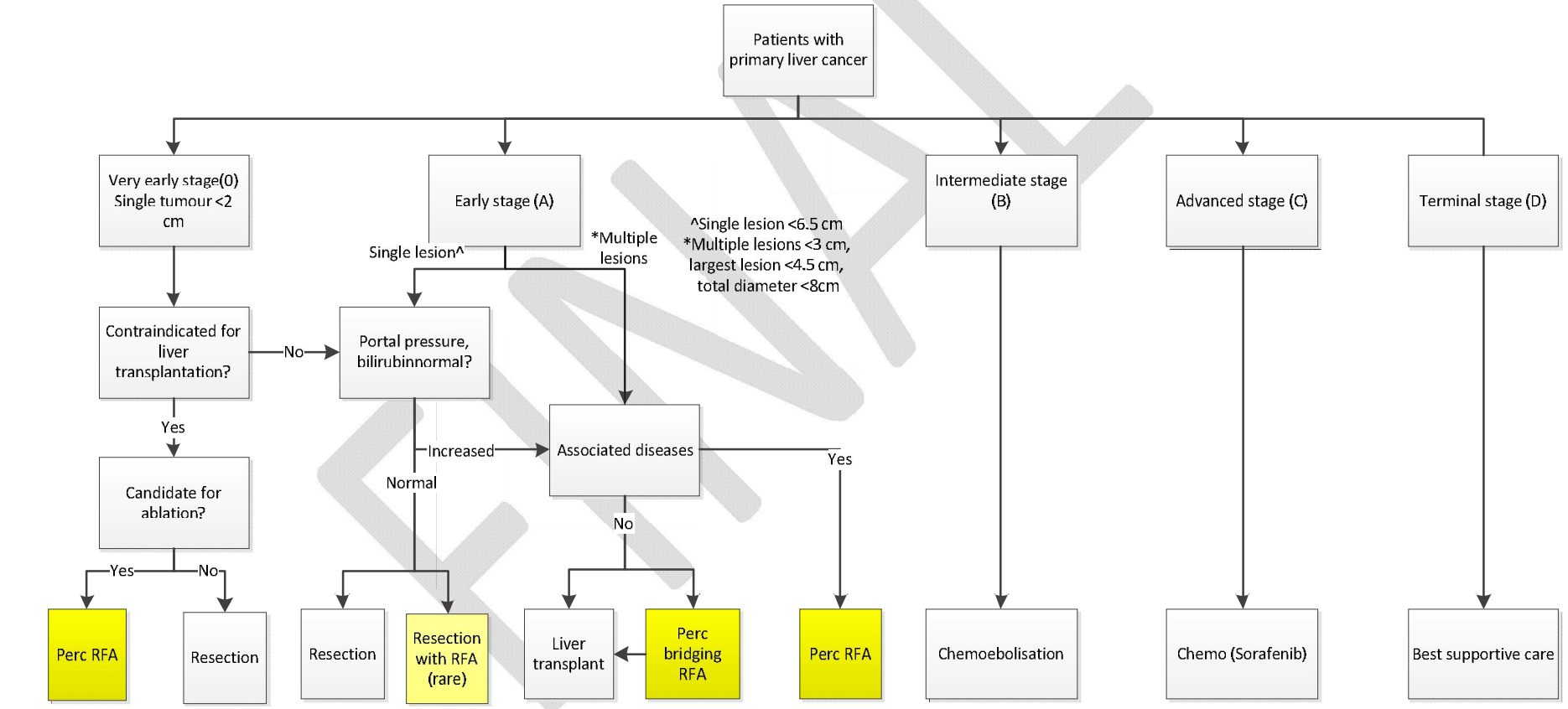
Advice from the applicant and PASC is that the comparators for population 2 are RFA (with or without adjuvant chemotherapy) and chemotherapy. RFA is not currently listed on the MBS for use in this population.

6.3 Comparator for population 3

Advice from the applicant and PASC is that the comparators for population 3 are RFA (with or without adjuvant chemotherapy), chemotherapy, chemoembolisation, radioembolisation, radiolabelled somatostatin analogue therapy, or resection (rarely). RFA is not currently listed on the MBS for use in this population.

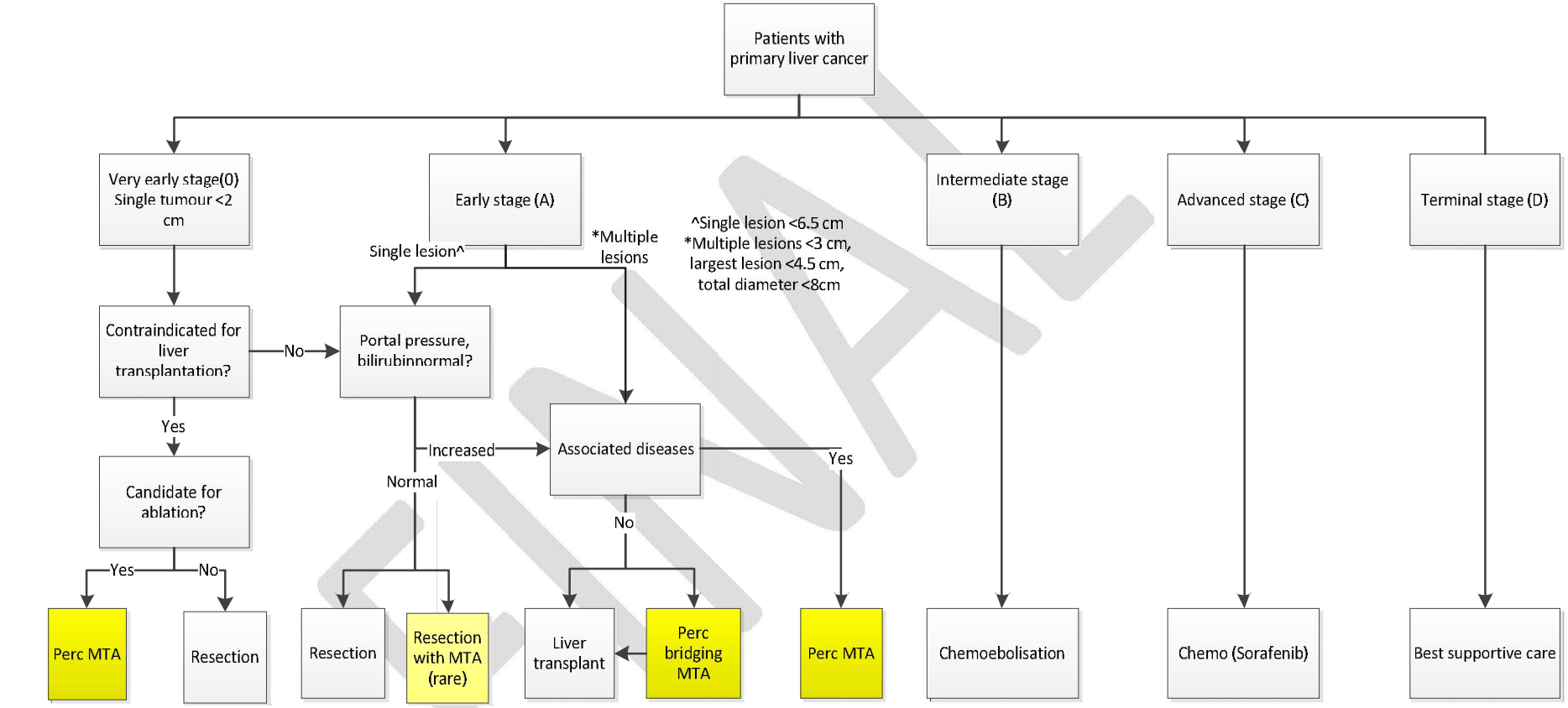
7 Clinical management algorithm

7.1 Current clinical practice – Population 1



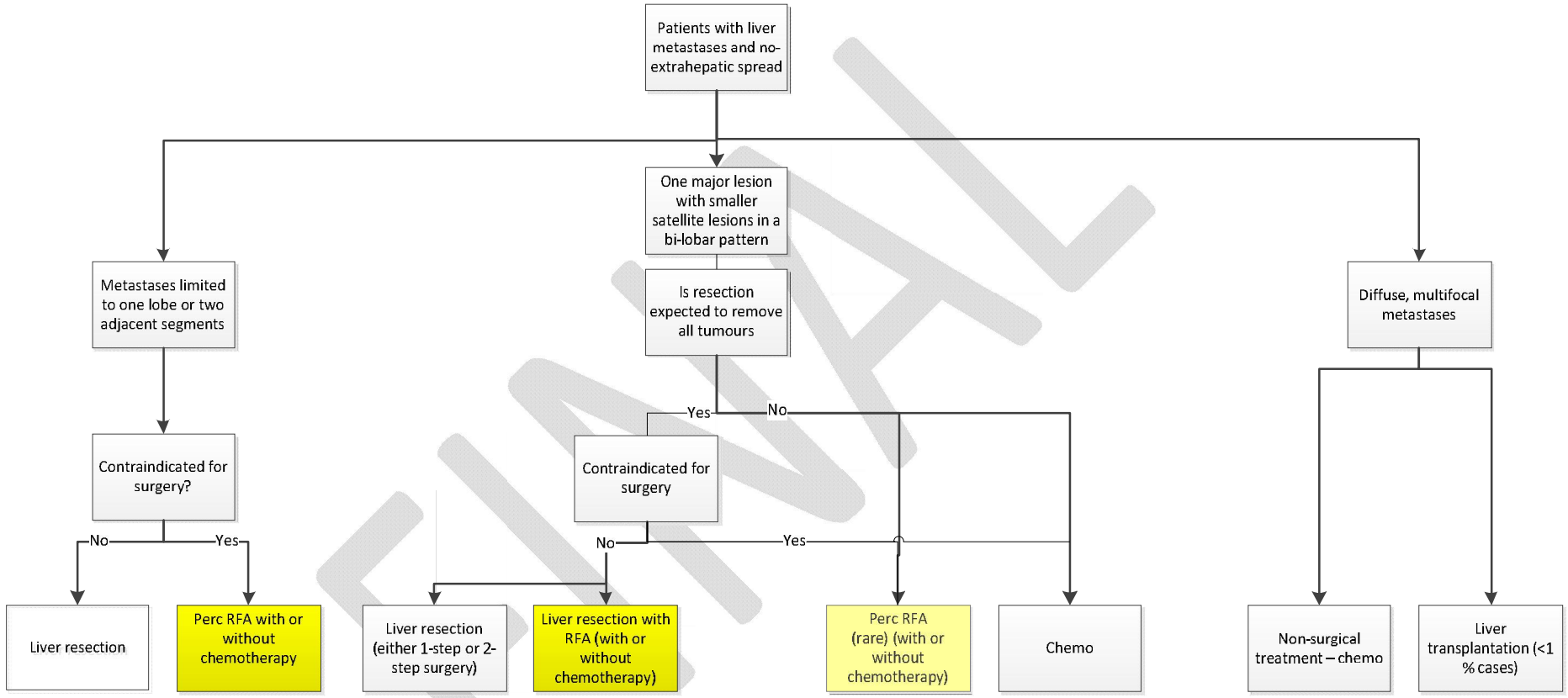
Chemo = chemotherapy; HCC = hepatocellular carcinoma; Perc = percutaneous; RFA = radiofrequency ablation

7.2 Proposed clinical practice – Population 1



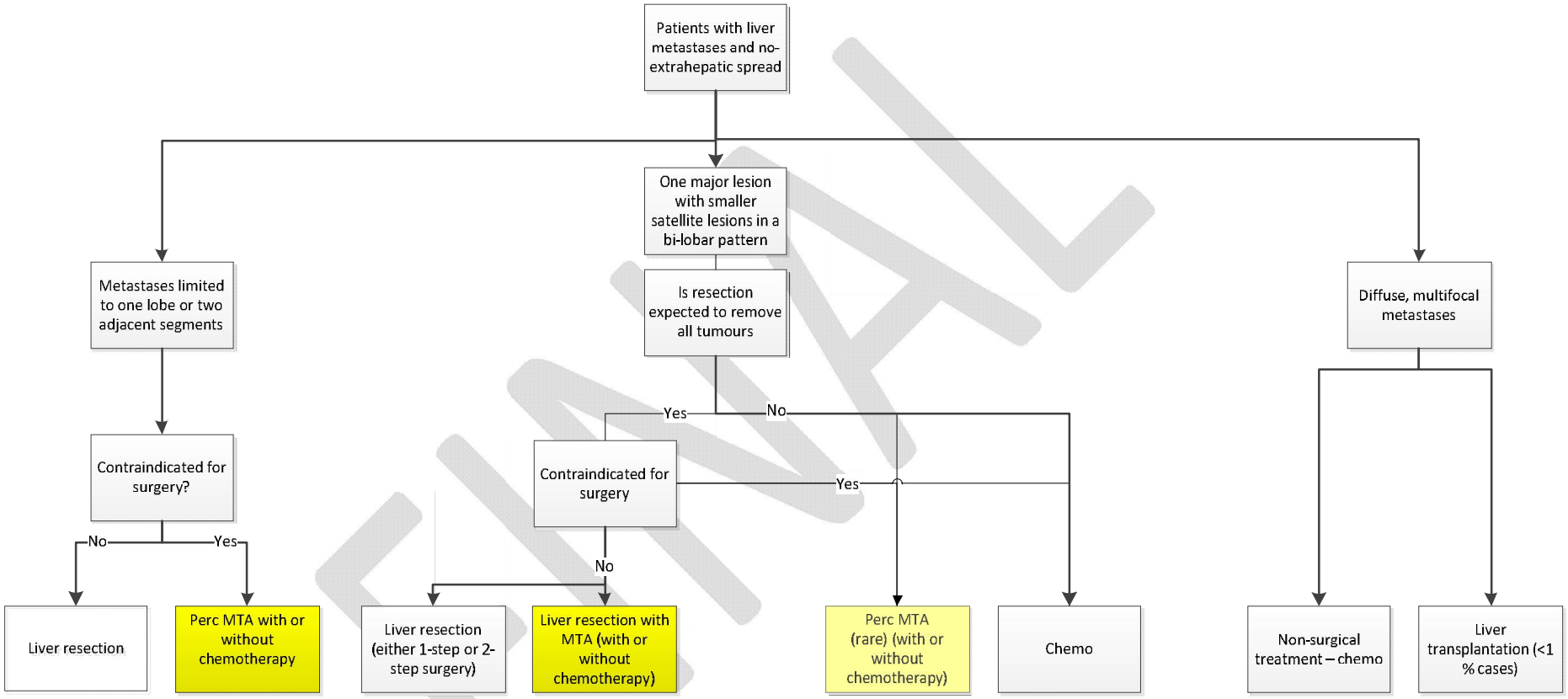
Chemo = chemotherapy; HCC = hepatocellular carcinoma; Perc = percutaneous; MTA = microwave tissue ablation; RFA = radiofrequency ablation

7.3 Current clinical practice – Population 2



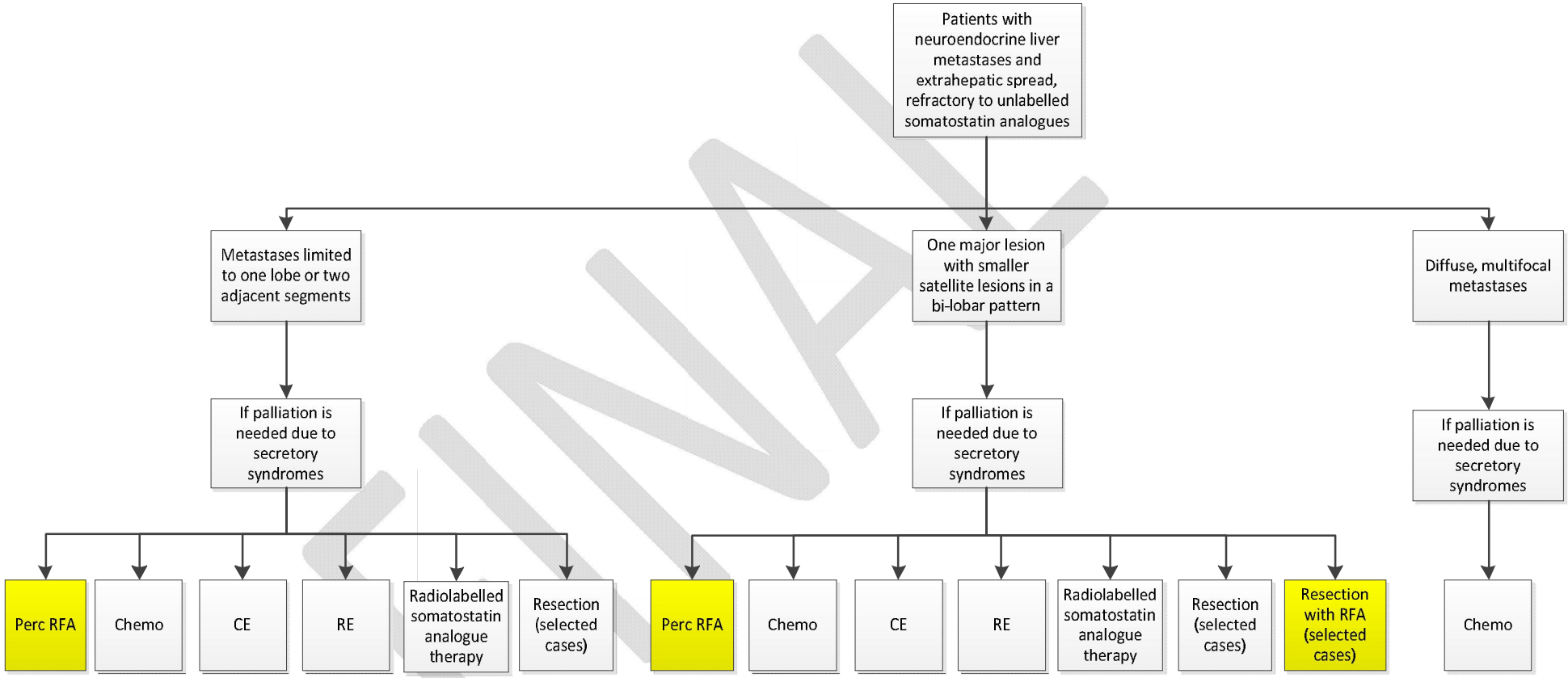
Chemo = chemotherapy; Perc = percutaneous; RFA = radiofrequency ablation

7.4 Proposed clinical practice – Population 2



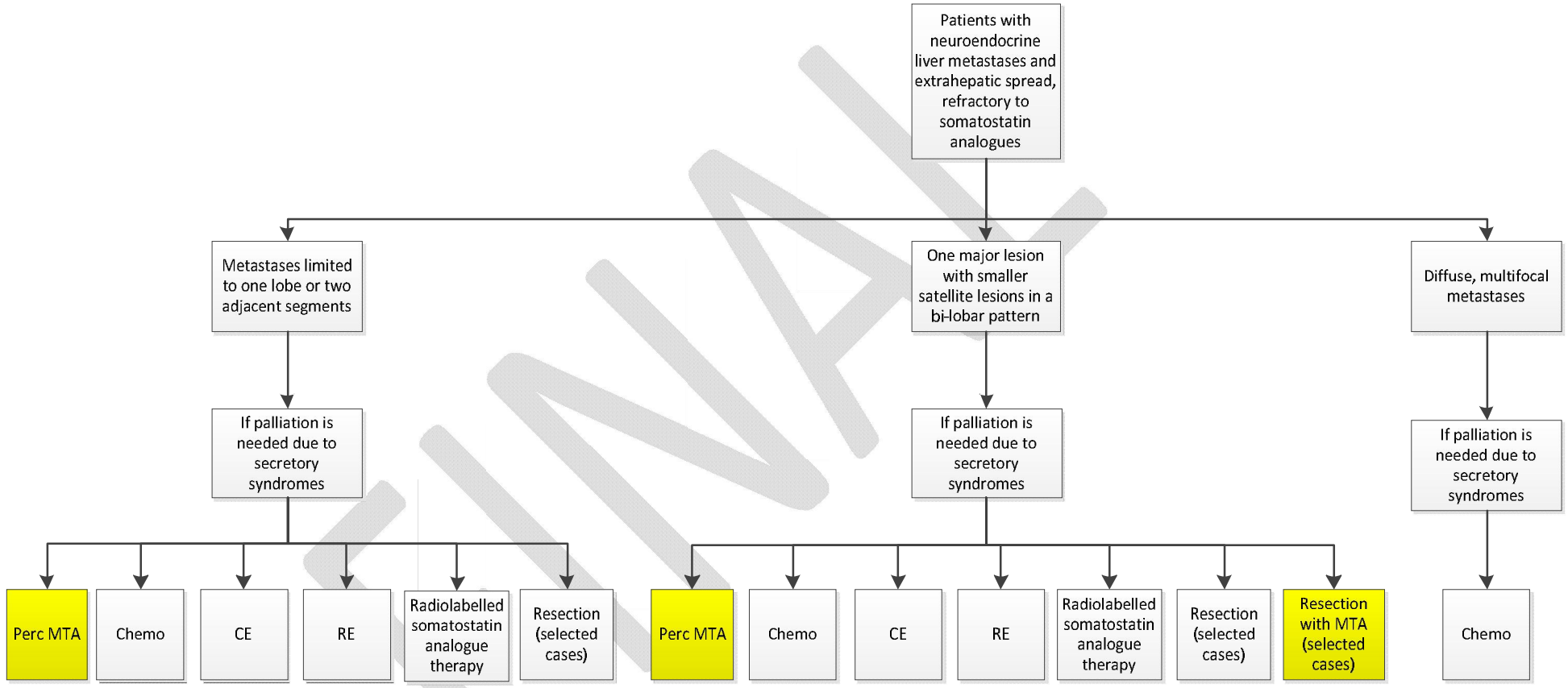
Chemo = chemotherapy; Perc = percutaneous; MTA = microwave tissue ablation; RFA = radiofrequency ablation

7.5 Current clinical practice – Population 3



CE = chemoembolization, Chemo = chemotherapy; Perc = percutaneous; RE = radioembolization, RFA = radiofrequency ablation

7.6 Proposed clinical practice – Population 3



CE = chemoembolization, Chemo = chemotherapy; Perc = percutaneous; RE = radioembolization, RFA = radiofrequency ablation

In the above clinical practice algorithms, MTA is introduced as a replacement for RFA (either percutaneous or intra-operative). It is proposed that the same patients would be eligible for both types of ablation and that no additional patients would be treated under the proposed pathways. A total of 2,834 patients were diagnosed with HCC in the 2012/13 financial year (AIHW National Hospital Morbidity Database 2014b). Data from an epidemiology study in the Northern Territory showed that of 80 cases diagnosed between 2000 and 2011, 42 patients (53%) received palliative care. Of the remaining 38 patients, three (8%) underwent liver transplantation, 12 (32%) had liver resection, seven (18%) had RFA, eight (21%) had TACE and 10 (26%) received chemotherapy with sorafenib. Two patients received more than one intervention (Parker et al. 2014). The Applicant has advised that this is broadly representative of the Australian population.

Expert advice is that percutaneous tumour ablation is rarely performed in patients with liver metastases. For patients with liver metastases and extra-hepatic spread, expert advice is that tumour ablation would only rarely be performed in patients with neuroendocrine tumours as a palliative procedure to reduce symptoms associated with secretory syndromes. The main treatment option for patients with liver metastases and extra-hepatic spread is management by chemotherapy.

8 Expected health outcomes

8.1 Expected patient-relevant health outcomes

For patients who have MTA as a 'curative' procedure, the following outcomes are relevant (NICE 2007; NICE 2011):

Primary effectiveness:

- Tumour recurrence
- Percentage of lesions with complete ablation
- Overall survival (short term and long-term)
- Recurrence free survival (short term and long-term)
- Need for repeat ablation
- Accuracy of ablation margins

Secondary effectiveness:

- Procedure time
- Length of hospital stay
- Recovery time
- Patient discomfort
- Quality of life

Primary safety

- Rates of adverse events associated with the intervention and comparator potential risks are discussed in the following section)

For patients who have MTA as a 'palliative' procedure the following primary effectiveness outcomes are relevant:

- Symptom reduction
- Quality of life measures
- Median survival time

8.2 Potential risks to patients

Complications associated with MTA and RFA include (NICE 2007; NICE 2011):

- Bleeding (intra-abdominal and gastrointestinal)
- Bile duct injury or stenosis
- Wound dehiscence
- Pain
- Post-operative ascites

- Skin burns
- Vagovagal reflex
- Liver abscess
- Hepatic infarction
- Colonic perforation
- Deterioration in liver function
- Damage to adjacent organs (kidney, lung, heart)
- Pneumothorax
- Pleural effusion
- Fever
- Tumour tract seeding (risk may be reduced by tract ablation)

Advice from the applicant is that the most common adverse events associated with MTA are bleeding, damage to surrounding tissue and infection.

9 Clinical claim for the proposed intervention

9.1 Clinical claim

The applicant has advised that MTA is superior to RFA in both safety and effectiveness.

Specifically; the applicant claims that, in contrast to RFA, MTA produces more predictable ablation volume shapes and sizes reducing the potential for compromise of healthy liver tissue and extrahepatic tissue injury (Bhardwaj et al. 2010).

In addition, MTA is claimed to have a steeper temperature gradient, with tissue temperatures reaching > 200 degrees Celsius, and faster conduction than RFA (Simo et al. 2012). This allows for larger ablation volumes in faster times of 4-6 minutes in contrast to 10-20 minutes (Swan et al. 2012).

The applicant has also advised that there is a lower risk of complications with MTA compared to RFA as MTA does not involve electricity or grounding pads. This removes the risk of sustaining burns from the grounding pads (Schutt et al. 2009). MTA technology is less susceptible to the "heat sink" effect due to its ability to reach high ablation temperatures in fast times (Bhardwaj et al. 2010).

9.2 Economic evaluation

On the basis of the clinical claim, a cost-effectiveness/cost-utility analysis should be provided.

10 Decision analytic

Table 10 Summary of PICO to define the research question(s) for Population 1

PICO Criteria	Comments
Patients	Patients with unresectable primary liver lesions
Intervention	Microwave tissue ablation (MTA) of the liver (percutaneous OR laparoscopic/open)
Comparator	Radiofrequency ablation (RFA) of the liver (percutaneous OR laparoscopic/open)
Outcomes	Primary effectiveness: tumour recurrence, percentage of lesions with complete ablation, overall survival (short term and long-term), recurrence free survival (short term and long-term), need for repeat ablation, accuracy of ablation margins. Secondary effectiveness: procedure time, length of hospital stay, recovery time, patient discomfort, quality of life. Safety: rate of adverse events including (bleeding, bile duct injury or stenosis, wound dehiscence, pain, post-operative ascites, skin burns, liver abscess, hepatic infarction, colonic perforation, deterioration in liver function, damage to adjacent organs, pneumothorax, pleural effusion, and fever), procedure related mortality.

In patients with unresectable primary liver lesions, what are the safety, effectiveness and cost effectiveness of percutaneous MTA compared to RFA?

In patients with unresectable primary liver lesions, what are the safety, effectiveness and cost effectiveness of open or laparoscopic MTA compared to RFA?

Table 11: Summary of PICO to define the research question(s) for Population 2

PICO Criteria	Comments
Patients	Patients with unresectable metastatic liver disease without extrahepatic spread
Intervention	Microwave tissue ablation (MTA) of the liver (percutaneous OR laparoscopic/open) with curative intent, with or without adjuvant chemotherapy
Comparator	Radiofrequency ablation (RFA) of the liver (percutaneous OR laparoscopic/open) (with or without chemotherapy) Chemotherapy
Outcomes	Primary effectiveness: tumour recurrence, percentage of lesions with complete ablation, overall survival (short term and long-term), recurrence free survival (short term and long-term), need for repeat ablation, accuracy of ablation margins. Secondary effectiveness: procedure time, length of hospital stay, recovery time, patient discomfort, quality of life. Safety: rate of adverse events including (bleeding, bile duct injury or stenosis, wound dehiscence, pain, post-operative ascites, skin burns, liver abscess, hepatic infarction, colonic perforation, deterioration in liver function, damage to adjacent organs, pneumothorax, pleural effusion, and fever), procedure related mortality.

In patients with unresectable liver metastases without extrahepatic spread, what are the safety, effectiveness and cost effectiveness of percutaneous MTA with curative intent (with or without chemotherapy) of liver tumours compared to RFA, chemotherapy or both?

In patients with unresectable liver metastases without extrahepatic spread, what are the safety, effectiveness and cost effectiveness of open or laparoscopic MTA with curative intent (with or without chemotherapy) of liver tumours compared to RFA, chemotherapy or both?

Table 12: Summary of PICO to define the research question(s) for Population 3

PICO Criteria	Comments
Patients	Patients with unresectable neuroendocrine liver lesions, with extrahepatic spread, refractory to somatostatin analogues requiring palliative treatment for secretory syndromes.
Intervention	Microwave tissue ablation (MTA) of the liver (percutaneous OR laparoscopic/open)
Comparator	Radiofrequency ablation (RFA) of the liver (percutaneous OR laparoscopic/open) Chemotherapy Chemoembolization Radioembolization Radiolabelled somatostatin analogue therapy Resection (rare)
Outcomes	Primary effectiveness: symptom reduction, quality of life, median survival Safety: rate of adverse events including (bleeding, bile duct injury or stenosis, wound dehiscence, pain, post-operative ascites, skin burns, liver abscess, hepatic infarction, colonic perforation, deterioration in liver function, damage to adjacent organs, pneumothorax, pleural effusion, and fever)

In patients with unresectable neuroendocrine liver metastases (with or without extrahepatic spread) with secretory syndromes refractory to somatostatin analogues requiring palliative treatment , what is the safety, effectiveness and cost effectiveness of percutaneous MTA of liver tumours compared to RFA, chemotherapy, chemoembolisation, radioembolisation, radiolabelled somatostatin analogue therapy or resection?

In patients with unresectable neuroendocrine liver metastases (with or without extrahepatic spread) with secretory syndromes refractory to somatostatin analogues requiring palliative treatment , what is the safety, effectiveness and cost effectiveness of open or laparoscopic MTA of liver tumours compared to RFA, chemotherapy, chemoembolisation, radioembolisation, radiolabelled somatostatin analogue therapy or resection?

11 Fee for the proposed medical service

11.1 Type of funding proposed for this service

The following wording for the proposed MBS items for MTA has been suggested in line with the current items for RFA of the liver (50950 and 50952):

Table 13 Proposed MBS Item for percutaneous microwave tissue ablation, unresectable HCC

Category 3 - THERAPEUTIC PROCEDURES
MBS [item number] NONRESECTABLE PRIMARY LIVER LESIONS, destruction of, by percutaneous microwave tissue ablation, including any associated imaging services, not being a service associated with a service to which items 30419, 50950, 50952 or (other MTA items) applies Fee: $TBA [Relevant explanatory notes if required]

Table 14 Proposed MBS Item for open or laparoscopic microwave tissue ablation, unresectable HCC

Category 3 - THERAPEUTIC PROCEDURES
MBS [item number] NONRESECTABLE PRIMARY LIVER LESIONS, destruction of, by open or laparoscopic microwave tissue ablation, including any associated imaging services, where a multi-disciplinary team has assessed that percutaneous microwave ablation cannot be performed or is not practical because of one or more of the following clinical circumstances: - percutaneous access cannot be achieved; - vital organs/tissues are at risk of damage from the percutaneous MTA procedure; or - resection of one part of the liver is possible however there is at least one primary liver tumour in a non-resectable region of the liver which is suitable for microwave ablation, including any associated imaging services, not being a service associated with a service to which items 30419, 50950, 50952 or (other MTA items) applies Fee: $TBA [Relevant explanatory notes if required]

Table 15 Proposed MBS Item for percutaneous microwave tissue ablation, unresectable metastatic liver tumours

Category 3 - THERAPEUTIC PROCEDURES
MBS [item number] NONRESECTABLE METASTATIC LIVER LESIONS, destruction of, by percutaneous microwave tissue ablation, including any associated imaging services, not being a service associated with a service to which items 30419, 50950, 50952 or (other MTA items) applies Fee: $TBA [Relevant explanatory notes if required]

Table 16 Proposed MBS Item for open or laparoscopic microwave tissue ablation, unresectable metastatic liver tumours

Category 3 - THERAPEUTIC PROCEDURES
MBS [item number] NONRESECTABLE METASTATIC LIVER LESIONS, destruction of, by open or laparoscopic microwave tissue ablation, including any associated imaging services, where a multi-disciplinary team has assessed that percutaneous microwave ablation cannot be performed or is not practical because of one or more of the following clinical circumstances: - percutaneous access cannot be achieved; - vital organs/tissues are at risk of damage from the percutaneous MTA procedure; or - resection of one part of the liver is possible however there is at least one primary liver tumour in a non-resectable region of the liver which is suitable for microwave ablation, including any associated imaging services, not being a service associated with a service to which items 30419, 50950, 50952 or (other MTA items) applies Fee: $TBA [Relevant explanatory notes if required]

The applicant has advised that the phrase "including all associated imaging" would preclude the claiming of other imagining items in association with the proposed items for MTA. Advice from PASC is that imaging should be considered part of the intervention as with items for RFA and should not be claimed separately.

11.2 Direct costs associated with the proposed service

Many of the following costs will need to be identified during the assessment phase.

- MTA equipment – including: cost of machine $50,000 and applicator $2,960, other associated costs (trolley, temperature probe) (source: application documents)
- Interventional radiologist, time (percutaneous procedures)
- Surgeon, time (open or laparoscopic procedures)
- Radiology suite or operating theatre usage
- Other consumables, e.g. dressings
- Anaesthetic
- Anaesthetist, time
- Follow-up imaging
- Dedicated nursing staff for post-intervention care
- Overnight stay in hospital

11.3 Proposed fee

The applicant has proposed the following fee structure:

"A $1300 fee for ablation of 2-3 lesions, a $1600 fee for ablation of 4-5 lesions and a $2000 fee for ablation of >5 lesions. The higher fee for >5 lesions reflects the increased risk to the patients such as collateral damage as well as more skill, time and expertise required of the physican to ensure better patient outcomes"

The fee for RFA services (both percutaneous (50950) and open/laparoscopic (50952)) is $817.10. It should be noted, there are claims MTA has a faster ablation time (Swan et al. 2012) which would result in less time overall spent in the radiology suite, and may impact on the cost of the procedure.

PASC has agreed that graduated fees for up to five lesions should be considered in the assessment phase. PASC has advised that the assessment phase should include a stratified survival analysis based on the number of ablated lesions.

12 Regulatory information

The application does not specify the type of MTA device to be used. Under the wording of the proposed items any MTA machine listed on the ARTG could be used in conjunction with the procedure being claimed. MTA devices registered in Australia include:

The Acculis MTA system consists of the Sulis VpMTA Generator, Acculis Local Control Station (LCS), Accu2i pMTA Applicators and optional MTA Temperature Probes.

- Temperature Probes: 174513
- Trolley: 195697
- Applicator: 174514
- Microwave System: 157722

TGA-approved indication(s) or purpose(s):

Temperature Probes: The temperature probes used with the Acculis MTA System are intended to monitor the temperature of the probes at the point of delivery of the microwave energy (i.e.: at the point of tissue coagulation).

Trolley: A general-purpose trolley or conveyance designed for transporting/supplying any kind of devices, medical equipment or goods within a department or hospital. It may have one or more shelves

Applicator: The Single Use Microwave Applicator is intended to be used with the Acculis MTA System for intra-operative coagulation of soft tissue.

Microwave System: Treat lesions using microwave hyperthermia

The Avecure Microwave ablation system sponsored by Aurora BioScience Pty Ltd comprises of a microwave generator and disposable probes (that are supplied in two gauges, three antenna lengths and three antenna sizes). The system is designed to produce and control the delivery of high heat to the body (i.e. temperatures greater than 43°C) using microwave energy for the ablation/coagulation of soft tissue. Using temperature feedback, power feedback and an automatic tissue matching-frequency controller the generator controls the ablation process whilst the probes apply the microwave energy into the surrounding local area.

- Trolley: 191102
- Microwave System: 200325

TGA-approved indication(s) or purpose(s):

Trolley: A cart designed for transporting/storing medical equipment and supplies within a hospital/institutional.

Microwave System: The system is designed to produce and control the delivery of high heat to the body (i.e. temperatures greater than 43°C) using microwave energy for the ablation/coagulation of soft tissue.

The Emprint™ Ablation System with Thermosphere™ Technology sponsored by Covidien Pty Ltd involves antennas in three lengths to accommodate a variety of procedural applications, a generator, integrated cart, cooling pump, footswitch, remote temperature probe and reusable cable.

- Temperature Probes: 179391
- Trolley: 127266/178512
- Generator: 152044
- Applicator: 178369
- Microwave System: 226598

TGA-approved indication(s) or purpose(s):

Temperature Probes: This device along with various other accessories is used to monitor tissue temperature at or near the ablation site.

Trolley: A general-purpose trolley to store/transport medical devices and goods within the area of a hospital/healthcare institution.

Generator: Intended for the coagulation (ablation) of soft tissue. The generator delivers microwave output to a single antenna for the ablation of soft tissue.

Applicator: Intended for use with the microwave generator for the coagulation of soft tissue. This series of antennas work in conjunction with the microwave ablation pump and microwave pump tubing set to provide a cooled shaft suitable for use in percutaneous, laparoscopic and intra-operative ablation procedures.

Microwave System: Intended for use in percutaneous, laparoscopic, and intrao-perative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumours.

The Evident™ Microwave Ablation Generator Sponsored by Covidien Pty Ltd involves multiple surgical antennas, the generator, pump and cart and pump tubing for when used percutaneously.

- Temperature Probes: 179391
- Trolley: 127266/178512
- Generator: 152044
- Applicator: 178369
- Microwave System: 178699

TGA-approved indication(s) or purpose(s):

Temperature Probes: This device along with various other accessories is used to monitor tissue temperature at or near the ablation site.

Trolley: A general-purpose trolley to store/transport medical devices and goods within the area of a hospital/healthcare institution.

Generator: Intended for the coagulation (ablation) of soft tissue. The generator delivers microwave output to a single antenna for the ablation of soft tissue.

Applicator: Intended for use with the microwave generator for the coagulation of soft tissue. This series of antennas work in conjunction with the microwave ablation pump and microwave pump tubing set to provide a cooled shaft suitable for use in percutaneous, laparoscopic and intra-operative ablation procedures.

Microwave System: Intended for use in percutaneous, laparoscopic, and intra-operative coagulation (ablation) of soft tissue, including partial or complete ablation of non-resectable liver tumours.

The Amica microwave hyperthermia system sponsored by Culpan Medical Pty Ltd involves an electro-medical apparatus (generator) intended for thermoablation treatment of soft tissue pathologies, using microwave energy and/or radiofrequency energy.

- Temperature Probes: 230566
- Applicator: 212510
- Microwave System: 212509

TGA-approved indication(s) or purpose(s):

Temperature Probes: Thermocouple temperature sensor lodged in a closed interstitial needle, for percutaneous, intra-operative or laparoscopic use, for intra-tissue thermometric readings during ablation treatments.

Applicator: An interstitial microwave applicator for the thermoablation of soft tissues.

Microwave System: An electro-medical apparatus (generator) intended for thermoablation treatment of soft tissue pathologies (such as solid tumours or hyperplasia of the liver, kidney, lung, bone, breast, prostate, etc.), using microwave energy and/or radiofrequency energy.

13 Healthcare resources

14 Questions for public funding

None

Table 17 List of resources to be considered in the economic analysis

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS Item	Safety nets*	Other government budget	Private health insurer	Patient	Total cost
Resources provided to identify eligible population										
Diagnostic imaging (US, CT, CECT, MRI etc.)	Radiologists	Radiology clinic or radiology department (hospital)	100%		55036 (US abdomen), 56407, 56447 (CT abdomen)					
Liver function tests	Pathology	laboratory	unknown		66515					
Biopsy	Hepatologists or radiologists	Out-patient hospital	unknown		30409					
Resources provided to deliver proposed intervention (MTA)										
Machine cost ($50,000)	Hospital	In-patient	100%		NA					
Disposable probe ($2,960)	Hospital	In-patient	100%		NA					
Time to perform procedure (ablation time of 4-6 minutes per lesion, also time for patient positioning, anaesthetic administration)^	Interventional radiologist or surgeon	Radiology suite or operating theatre	100% (split between two services not known)		NA					
Imaging (CT or US)	Interventional radiologist or surgeon	Radiology suite or operating theatre	100% (split between two services not known)		55036 (US abdomen), 56407, 56447 (CT abdomen)					

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS Item	Safety nets*	Other government budget	Private health insurer	Patient	Total cost
Anaesthetic	Anaesthetist	Radiology suite or operating theatre	100%		17610- 17625 (initial consult) 21922 (anaesthesia management)					
Resources provided in association with proposed intervention (MTA)										
Aftercare	Dedicated nursing staff	In-patient	100%		NA					
Follow-up imaging (cross-sectional) 3 to 6 weeks post-procedure	Radiologist/radiographer	Radiology clinic or radiology department	100%		56407, 56447 (CT abdomen)					
Resources provided to deliver comparator 1 (RFA)										
Machine cost ($40,000-$65,000**)	Hospital	In-patient (laparoscopic or open). Out-patient (percutaneous)**	100%		NA					
Disposable probe ($1,700-$2,700)**	Hospital	In-patient (laparoscopic or open). Out-patient (percutaneous)**	100%		NA					
Time to perform ablation (10-20 minutes)	Interventional radiologist or surgeon	Radiology suite or operating theatre	100%^^		50950 (percutaneous) 50952 (open or laparoscopic)					

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS Item	Safety nets*	Other government budget	Private health insurer	Patient	Total cost
Imaging (CT or US)	Interventional radiologist or surgeon	Radiology suite or operating theatre	100%^^		55036 (US abdomen), 56407, 56447 (CT abdomen)					
Anaesthetic	Anaesthetist	Radiology suite or operating theatre	100%^^		17610- 17625 (initial consult) 21922 (anaesthesia management)					
Resources provided in association with comparator 1 (RFA)										
Aftercare	Dedicated nursing staff	In-patient (laparoscopic/open) or out-patient (percutaneous)	100%		NA					
Follow-up imaging	Radiologist/radiographer	Radiology clinic or radiology department	100%		56407, 56447 (CT abdomen)					
Resources used to manage patients successfully treated with the proposed intervention										
Follow-up imaging to confirm no tumour recurrence	Radiologist/radiographer	Radiology clinic or radiology department	100% of patient successfully treated							
Follow-up treatment as required	Multidisciplinary team as required	Dependant on type of treatment required								

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS Item	Safety nets*	Other government budget	Private health insurer	Patient	Total cost
Follow-up palliative care as required	Multidisciplinary team as required	Dependant on type of treatment required								
Resources used to manage patients who are unsuccessfully treated with the proposed intervention										
Follow-up imaging to confirm incomplete ablation of tumour and/or tumour recurrence	Radiologist/radiographer	Radiology clinic or radiology department	100% of patients unsuccessfully treated							
Re-staging of disease and treatment as determined according to current disease status	Multidisciplinary team as required	Dependant on type of treatment required	100% of patients unsuccessfully treated							
Resources used to manage patients successfully treated with comparator 1										
Follow-up imaging to confirm no tumour recurrence	Radiologist/radiographer	Radiology clinic or radiology department	100% of patient successfully treated							
Follow-up treatment as required	Multidisciplinary team as required	Dependant on type of treatment required								
Follow-up palliative care as required	Multidisciplinary team as required	Dependant on type of treatment required								
Resources used to manage patients who are unsuccessfully treated with comparator 1										

	Provider of resource	Setting in which resource is provided	Proportion of patients receiving resource	Number of units of resource per relevant time horizon per patient receiving resource	Disaggregated unit cost					
					MBS Item	Safety nets*	Other government budget	Private health insurer	Patient	Total cost
Follow-up imaging to confirm incomplete ablation of tumour and/or tumour recurrence	Radiologist/radiographer	Radiology clinic or radiology department	100% of patients unsuccessfully treated							
Re-staging of disease and treatment as determined according to current disease status	Multidisciplinary team as required	Dependant on type of treatment required	100% of patients unsuccessfully treated							

CECT – contrast enhanced CT. CT= computed tomography. MRI = magnetic resonance imaging. MBS = Medicare Benefits Scheme. MTA = microwave tissue ablation. NA = not applicable. RFA = radiofrequency ablation. US – ultrasound. *Includes costs relating to both the standard and extended safety net. ** Data from MSAC Application 1052: RFA of liver tumours (2003). ^ Data from Application. ^^ MBS data from 2013/14 suggests a 94:6 split between percutaneous and surgical procedures

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16 Appendix A: potentially relevant literature

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