



**Australian Government**  
**Department of Health**

**MEDICAL SERVICES ADVISORY COMMITTEE**

Protocol to guide the assessment of microwave  
tissue ablation for primary and secondary lung  
cancer

**MSAC Application 1403**

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## List of Terms

AHRQ	Agency for Healthcare and Research Quality
ANZCTR	Australian and New Zealand Clinical Trials Registry
CHART	Continuous hyperfractionated accelerated radiotherapy
CMA	Canadian Medical Association
CRD	Centre for Reviews and Dissemination
CT	Computed tomography
DLCO	Diffusing capacity of the lungs for carbon monoxide
ECOG	Eastern Cooperative Oncology Group
FEV1	Forced expiratory volume
FRANZCR	Fellowship of the Royal Australian and New Zealand College of Radiologists
IGRT	Image-guided radiation therapy
IMRT	Intensity-modulated radiation therapy
IRSA	Interventional Radiology Society of Australasia
MBS	Medicare Benefits Schedule
MTA	Microwave tissue ablation
NICE	National Institute for Health and Care Excellence
NHMRC	National Health and Medical Research Council
NSCLC	Non-small cell lung cancer
PET	Positron emission tomography
RANZCR	Royal Australian and New Zealand College of Radiologists
RFA	Radiofrequency ablation
SBRT	Stereotactic body radiation therapy
SCLC	Small cell lung cancer
SEER	Surveillance Epidemiology End Results (SEER) Summary Staging
SIGN	Scottish Intercollegiate Guidelines Network
US	Ultrasound

## 1 Title of application

Microwave tissue ablation (MTA) for primary and secondary lung cancer

## 2 Purpose of application

MTA delivers electromagnetic radiation percutaneously in order to produce cell death via coagulative necrosis. MTA can be used to provide potentially curative tumour ablation in patients with early stage non-small cell lung cancers (NSCLC) who are not candidates for surgical resection (Dupuy 2013). While less developed in the literature, MTA may also be used as a potentially curative treatment in specific secondary lung tumours, and for symptom relief in palliative care.

Surgical resection is currently the best treatment for survival and local control of early stage NSCLC. However, Dupuy (2013) reported that over 15 per cent of all patients and 30 per cent of patients aged over 75 years, with technically resectable lung cancer, were not candidates for surgical resection, which limits their therapeutic management options (Dupuy 2013). This may be due to poor cardiopulmonary function, cardiovascular limitations, advanced age and other comorbidities (Dupuy 2013). Some patients, although operable, elect not to have major invasive surgery associated with lengthy hospital stays and protracted recovery. The primary treatment options in these patients include radiotherapy, chemoradiotherapy, and tissue ablation.

Radiofrequency soft tissue ablation (RFA) of the lung has been available for patients with unresectable lung cancer since 1998 with promising mid-and long-term survival data, (Ambrogio et al 2011; Simon et al 2007) mainly for tumours smaller than 3cm in longest diameter and located in the outer third of the lungs. This technique utilises ~480kHz wavelength in the radiofrequency spectrum. In contrast, MTA uses a higher frequency and shorter wavelength electromagnetic energy (up to 2.45GHz). Owing to these technical advantages, MTA offers shorter ablation times, larger and more predictable ablation zones, higher and more homogenous temperatures during ablation, and heat dissipation that is not limited by desiccated or charred tissue (Swan et al 2012). Furthermore, MTA is less susceptible to any heat sink effect – circulating blood causing an undesired local tissue cooling – thus carrying a lower risk of local tumour recurrence as compared to RFA.

Compared to conventional radiotherapy, where the total radiation dose is administered over usually 25-30 sessions, MWA is a single treatment event where patients are usually observed overnight and discharged the day after the procedure.

The applicant has advised that MTA is currently used in both the public and private settings as a replacement for RFA; however, there is no current Medicare Benefits Schedule (MBS) service for either MTA or RFA in the proposed populations. As such, patients in the private setting must meet the full cost of treatment. As the service is predominantly performed in public hospitals, a listing on the MBS could lead to cost shifts from States and Territories to the Commonwealth without additional benefits.

There are currently no systematic reviews of MTA for lung ablation available. The narrative review by Dupuy et al (2013) provides background context to the use of MTA in treating lung tumours. MTA for lung lesions has not previously been considered by MSAC.

### 3 Intervention – proposed medical service

#### 3.1 Description of the proposed medical service

MTA is a thermo-ablative technique that uses high frequency electromagnetic energy to produce large ablation volumes in short procedure times (up to ten minutes per ablation cycle), with high accuracy and predictability (Dupuy 2009). Microwaves are the part of the electromagnetic spectrum with frequencies ranging from 900 to 2450 MHz, lying between infrared radiation and radio waves (Banik et al 2003). Microwave is a non-ionising radiation and therefore does not contain sufficient energy per quantum to ionise (or completely remove an electron from) atoms or molecules. Consequently, microwave does not induce DNA damage in individual cells (Banik et al 2003; Ong et al 2009). When microwave radiation hits water molecules in tissue, they oscillate between two to five billion times per second, generating heat from the friction and subsequently leading to cell death through coagulation necrosis (Lu et al 2001; Ong et al 2009; Simon et al 2005).

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 antenna 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 then emits electromagnetic waves at a frequency of up to 2.45 GHz, with powers ranging from 20W to 140W through the non-insulated portion of the antenna to surrounding tissue (Dong et al 2003; Seki et al 2000). 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. Tumours in this field are treated to over 60°C to achieve coagulation necrosis (Swan et al 2012). The average ablation duration ranges between 60 and 300 seconds (Kuang et al 2007). Lower frequency microwave radiation at 0.915 GHz can theoretically be applied at a power of 45W, requiring longer duration of ablation (Simon et al 2005; Yu et al 2006).

In the context of pulmonary lesions, MTA is administered percutaneously with computed tomography (CT). US guidance is suitable for chest wall tumours, or tumours with broad pleural contact (He et al 2006). However, it is rarely used and for the purposes of this application MTA is considered to be administered with CT. Within Australia, available MTA systems are either 902 – 928 MHz or 2400 – 2500 MHz. Independent clinical feedback has indicated that both systems have the same indication profile, but that high powered systems are considered superior owing to their ability to conduct larger ablations in shorter times.

Clinical input suggests that MTA of lung tumours is ideally suited to tumours that do not exceed 4.5 to 5.0 cm, which accounts for a 0.5 cm circumferential safety margin. In terms of the maximum number of lesions suitable for MTA per-procedure, a soft rule of maximally 5 lesions per hemithorax has been widely adopted;(Gillams et al 2013; Smith and Jennings 2015) however, the best long-term survival rates are achieved in patients with up to 2 pulmonary metastases no larger than 3cm in diameter (de Baere et al 2015).

### 3.2 Registered trademark

The application for the proposed service is not limited to a registered trademark, but encompasses the technique of MTA more broadly. There are currently four MTA systems available in Australia, including:

- Acculis MTA system, sponsored by N Stenning and Co Pty Ltd.
- AVecure Microwave Ablation/Coagulation System, sponsored by Aurora BioScience Pty Ltd.
- Emprint™ Ablation System with Thermosphere™ Technology, sponsored by Covidien Pty Ltd.
- Amica microwave hyperthermia system, sponsored by Culpan Medical Pty Ltd.

Further details of the regulatory status and technical specifications of these devices are provided in section 12.

### 3.3 Proposed clinical setting

#### **Inpatient or outpatient, tertiary centres**

Major complications are a rare but severe consequence of MTA procedures. In order to effectively manage major complications, vascular interventional radiology, cardiothoracic surgery and intensive care units should be accessible. These services are typically only available in specialised tertiary centres, and are not accessible in stand-alone private radiology clinics. Therefore, MTA is provided in radiology departments within larger public or private hospitals, with patients either being kept overnight or in a day surgery setting. A chest X-ray is required within 3-4 hours after the procedure to monitor complications. If no complications are observed patients may be discharged on the same day. Patients may be admitted as inpatients for overnight observation to monitor perioperative complications. If patients remain stable they can be discharged the following day.

### 3.4 Service delivery

Percutaneous MTA is provided by interventional radiologists familiar with pulmonary interventions. Interventional radiology is a clinical subspecialty of radiology, which involves the conduct of minimally invasive procedures under image guidance. Radiologists completing the Fellowship of the Royal Australian and New Zealand College of Radiologists (FRANZCR) qualification are considered competent to perform interventional radiology procedures. The Interventional Radiology Society of Australia (IRSA) defines two tiers of intervention radiology competence (IRSA 2015):

- Tier A: includes basic diagnostic angiography and interventional techniques including angiography, nephrostomy, abscess drainage and biopsy. Tier A falls within the scope of requirements of RANZCR Fellowship training and any individual with FRANZCR may perform them.
- Tier B: includes a number of more complex interventional procedures such as neuro-interventional procedures and oesophageal and duodenal stent placement etc. For these procedures accreditation is based on proof of a certain number of procedures performed at IRSA/RANZCR accredited sites.

No formal requirements beyond FRANZCR are currently required to perform MTA procedures. However hospitals may apply their own credentialling standards to determine that the radiologist is competent and permitted to perform procedures. It is preferable, but not formally required, that interventional radiologists wishing to conduct MTA procedures conduct prior bench work or observation of procedures.

The pre-procedure patient preparation is similar to that for a CT-guided lung biopsy, added by the requirement of booking an overnight bed. Patients may be contraindicated for MTA if they have tumours abutting the hilum, large blood vessels or bronchi, severe coagulation disorders, or recently used anticoagulants (Schneider et al 2013; Simon and Dupuy 2005).

MTA is administered percutaneously, under CT image guidance to localise and position a thin microwave antenna into the centre of the target tumour (Simon et al 2005). A microwave generator emits electromagnetic waves at 915 MHz or 2.45 GHz through the non-insulated portion of the antenna to the surrounding tissue. This results in the surrounding dipole water molecules needing to constantly realign with the electric field, thus generating heat into the targeted tumour, inducing cellular death (Simon et al 2005; Swan et al 2013). During the procedure patients may receive conscious sedation or general anaesthesia.

The size, shape, location and vascular supply of the target lesion have an influence on the power and time required to complete an ablation. A single ablation is usually performed in less than 8 minutes, while overlapping ablations required in larger target lesions may add up to a total ablation time of 15-20 minutes. The procedure as a whole – including patient positioning and anaesthesia – typically takes between 1-1.5 hours.

A routine follow-up chest X-ray is performed 3-4 hours after the procedure, generally followed by a limited CT scan of the ablated area the morning after the procedure. The limited CT scan aims to assess the final thermal damage at the ablation site and potential salient complications (described in section 8.2); this scan is the baseline scan for comparison of future. Without complications requiring further action, the patient can be discharged after this CT scan.

Clinical feedback recommends routine CT imaging follow-up be performed at three, six and 12 months after ablation and yearly thereafter (Liu and Steinke 2013). However, a recent literature review conducted by Cancer Australia concluded that optimal post-operative follow-up remain contentious (Cancer Australia 2013).

#### **4 Co-dependent information**

There are no co-dependant services. MTA requires image guidance to locate the lesions to be ablated. The current wording of the proposed item indicates that this imaging is to be included in the proposed items (wording states “including any associated imaging services”).

## 5 Population eligible for the proposed medical service

### 5.1 Medical condition relevant to the service

Lung cancer is a major contributor to cancer-related mortality and burden of disease in Australia. It was the leading cause of cancer-related mortality in 2014 – accounting for 18.3 per cent of all cancer deaths (8,630 deaths) – and was the fifth most common primary cancer in Australia (excluding non-melanoma skin cancers) (AIHW 2014). Lung cancer was responsible for 9.4 per cent of new cancer diagnoses in 2014 (11,580 cases), with an estimated age-standardised (Australia 2001) incidence rate of 54.8 cases per 100,000 men and 33.2 cases per 100,000 women (AIHW 2014).

The high mortality rate associated with lung cancer is reflected in the current estimates of 5-year relative survival. In 2007-2011, the 5-year relative survival at diagnosis was 14.3 per cent (AIHW 2014). There is a strong correlation between age and relative survival, with a sharp decline in 5-year relative survival between patients aged 15-24 (76%) and 25-44 (29%), followed by a more gradual decline towards patients aged 75+ (8.7%) (AIHW 2014). However, the relative survival of lung cancer depends on the aetiology of the lesion.

#### Primary lung cancer

There are two broad categories of primary lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). SCLCs accounted for 12.3 per cent (1,140 cases) of all lung cancers in 2007, and are derived from neuroendocrine precursor cells in the bronchi and bronchioles. They are characterised by aggressive progression and spread throughout the body (AIHW 2011). Due to the manner in which SCLC progresses, patients with this form of cancer may not be suitable candidates for surgical resection and are often managed with palliative care. As a result, patients with SCLC are not considered to be appropriate candidates for MTA and are not included in the eligible patient populations.

In contrast, NSCLC accounted for 62.6 per cent (6,095 cases) of lung cancers in 2007, and may be derived from a range of bronchial epithelial progenitor cells. The main forms of NSCLC include squamous cell carcinoma, adenocarcinoma, and large cell carcinoma (AIHW 2011). They are characterised by slower growth and metastatic spread compared to SCLC (AIHW 2011). Due to their slower rate of progression, NSCLC may be amenable to curative treatments, including surgical resection, radiotherapy, and chemoradiotherapy. Based on data from the United States, it is estimated that 16.1 per cent of NSCLC in males and 19.6 per cent of NSCLC in females remains localised at the time of diagnosis (AIHW 2011).

#### Secondary lung cancer

Secondary lung cancers are metastases from primary malignancies elsewhere in the body. The lungs are the second most common site of metastases. Breast, colorectal, lung, kidney, head and neck, and uterine cancers are the most common primary tumours with lung metastasis at autopsy (Seo et al 2001). Colorectal cancer, which accounts for 10 per cent of all cancers, accounts for 15 per cent of all cases of pulmonary metastases (Hirakata et al 1993). In total, 20 per cent of metastatic disease is isolated to the lungs.

The presence of pulmonary metastases tends to indicate advanced, disseminated disease; however, it can occasionally be an isolated event. The patients' prognosis depends on the primary tumour and whether it is under control as well as whether the pulmonary metastatic spread is an isolated event or part of disseminated disease. The applicant has suggested that sarcomas, thyroid, renal, head & neck cancers tend to metastasise predominantly or exclusively to the lung. In the setting of metastases confined to the lung with the primary tumour under control, the patient may be eligible for curative therapy.

## 5.2 Proposed patient population(s)

There are three proposed population groups eligible for MTA of primary or secondary lung cancers. These groups include:

1. Patients with early stage NSCLC who are not eligible for surgical resection, and who are receiving treatment with curative intent.
2. Patients with pulmonary metastases, in whom the primary tumour is under control, and who are receiving treatment with curative intent (oligometastatic disease).
3. Patients with NSCLC or pulmonary metastases, who are receiving palliative treatment.

PASC feedback suggests that Population Two should be stratified into two groups at the assessment phase with respect to their primary tumours: those with sarcoma (bone and soft tissue) and those with non-sarcoma primaries.

MTA is primarily intended to be used in patients with early stage NSCLC who are not candidates for surgical resection. This group includes 15 per cent of all NSCLC patients, and 30 per cent of NSCLC patients over the age of 75 (Dupuy 2013). As lung cancer patient demographics are changing, with increasing age at time of diagnosis, invasive and costly therapies are becoming less attractive (Dupuy 2013). Factors that influence whether a patient is a candidate for surgery are discussed in Section 5.3.

MTA may also be used in patients with pulmonary metastases where the number and site of metastases, or previous lung surgery, precludes them from further surgery (Hiraki and Kanazawa 2012).

It is necessary to specify different clinical management algorithms and PICO criteria for each of these populations as the appropriate comparator for each group differs according to disease stage and treatment intent. This has flow on effects for the expected health outcomes of each patient group.

### 5.3 Defining surgical operability

Factors that influence whether a patient is a candidate for surgical resection include (Dupuy 2009; Lanuti et al 2012; Lee et al 2013):

- Anatomical suitability
- Fitness for surgery
- Local recurrence after previous surgery, radiotherapy or thermal ablation
- Patient willingness to undergo surgery.

An assessment of surgical resectability involves determining the anatomical suitability of the lesion, as well as the ability of the patient to withstand surgery and the loss of the resected lung. In some instances a patient may be deemed unresectable due to unwillingness to undergo surgery. Some considerations around the anatomical characteristics of disease that are not amenable to surgery, as well as the major considerations of the patient's ability to withstand surgery, are described below.

#### **Anatomical suitability**

An unresectable tumour is one that cannot be removed completely through surgery. The decision about the anatomic suitability of a primary tumour for curative resection depends upon the absence of significant mediastinal or distant spread as identified by CT, positron emission tomography (PET), bronchoscopy or mediastinoscopy (Gould 2006). Generally, patients with stage I and II disease, and some patients with stage IIIA disease, are considered to have surgically curable disease (British Thoracic Society 2001). The presence of distant metastases, stage IIIB disease and stage IV disease are usually indicative of unresectability. However, at any stage there are particular characteristics of the primary tumour that affect the ability of surgery to achieve complete resection. Features of the primary tumour that can indicate unresectability include (Quint 2004):

- significant mediastinal fat invasion
- invasion of a vital mediastinal structure
- combination invasion of the chest wall and mediastinal lymph node metastases
- proven ipsilateral mediastinal lymph node metastases with bulky lymph nodes or extracapsular nodal tumours
- patients with metastases in contralateral hilar, contralateral mediastinal, ipsilateral or contralateral scalene or supraclavicular lymph.

### **Fitness for surgery**

Postoperative complications and morbidity related to pulmonary resections can be significant, necessitating a thorough investigation of a patient's ability to withstand both surgery and the loss of the resected lung. In the context of thermal ablation of pulmonary lesions, expert advice suggests that comorbidities most often preclude patients from having surgery in the setting of primary early stage NSCLC. The number and distribution of metastases, which may leave the patient with too little functional lung if resected, are also considered. Overall suitability for surgery depends on the presence of risk factors and the extent of the planned surgery. The management of patients and the assessment of operative suitability will be based on clinical judgement of the risks and benefits informed by the patient age, pulmonary function, cardiovascular fitness, weight loss, performance status and nutrition.

### **Age**

Age alone is not a contradiction to lobectomy or wedge resection, particularly in early disease (Gould 2006). Guidelines from the British Thoracic Society state that surgery for stage I and stage II disease can be as effective in patients over 70 years as in younger patients, but note that pneumonectomy is associated with a higher mortality risk in the elderly (age >70) (British Thoracic Society 2001). Age may be considered a factor in deciding suitability for pneumonectomy, especially in octogenarians with more than one adverse prognostic comorbidity (Tammemagi et al 2004).

### **Pulmonary function**

Poor respiratory function can be indicative of increased risk of perioperative morbidity and mortality (Datta and Lahiri 2003). It can also indicate the possibility of postoperative poor quality of life secondary to respiratory insufficiency. Risks are related to the pre-existing pulmonary function of the patient and to the extent of the planned surgery. Pulmonary function is evaluated by reviewing the predicted postoperative values for Forced Expiratory Volume (FEV1) and diffusing capacity of the lung for carbon monoxide (DLCO); in patients with predicted postoperative values for FEV1 and DLCO less than 40 per cent of normal for age, further testing is required. A maximal oxygen uptake (VO<sub>2</sub> max) of less than 15 ml/kg is considered a contraindication for surgery (Datta and Lahiri 2003). These may vary according to the extent of the planned surgery.

### **Cardiovascular fitness**

The risk of myocardial infarction or death within 30 days of non-cardiac surgery is increased by the presence of pre-existing coronary artery disease. Major cardiovascular risk factors include: acute or recent myocardial infarction with evidence of important ischaemic risk by clinical symptoms or non-invasive study; unstable or severe angina; decompensated heart failure; significant arrhythmia; and severe valvular disease (British Thoracic Society 2001; Gould 2006). Guidelines on the evaluation of perioperative cardiovascular risk in non-cardiac surgery are available (Fleisher et al 2015).

### ***Weight loss, performance status and nutrition***

In patients with a history of recent weight loss, poor nutritional status and poor performance status on the Eastern Cooperative Oncology Group (ECOG) scale the prognosis is poor (Oken et al 1982). These factors are associated with advanced disease and poor overall outlook. These factors may be taken into account in considering a patient's fitness for surgery (British Thoracic Society 2001).

#### **5.4 Expected utilisation**

Depending on a centre's catchment area, the applicant estimates that 20-35 pulmonary ablations would be expected to be performed per site, per year. This estimate is based on data from large tertiary hospitals currently conducting pulmonary RFA, including the Royal Perth Hospital and the Royal Brisbane and Women's Hospital. However, it is currently unclear how many sites would need to be considered in estimates of overall utilisation if the proposed service received MBS funding.

Beyond the above estimate of 20-35 ablations per site, it is difficult to substantiate the likely number of patients that may be eligible for MTA. In 2007, there were 6,095 cases new cases of NSCLC in Australia (AIHW 2011). Data from New South Wales, collected between 1995 and 2004, suggests that 29.6 per cent of staged lung cancers are localised (AIHW 2011). Based on these data, it may be *assumed* that up to 1500 cases of primary NSCLC may be technically eligible for MTA per year; however, these staging data are reported using the Surveillance Epidemiology End Results (SEER) Summary Staging system, which does not account for tumour size or additional factors that affect surgical resectability. This estimate also assumes that all candidates for MTA based on stage will receive MTA instead of existing treatment modalities, which may not be intended or likely.

It is unclear how often either MTA or RFA are used in current clinical practice. There is no current MBS item for RFA of the lung, and we are not aware of any specific data points for either RFA or MTA of the lung in the AIHW hospital procedures data cubes. We have identified AIHW hospital procedures data for RFA of the liver in the following section:

- Chapter 10, Procedures on digestive system
  - Subchapter 951–956, Liver
    - Block 956, Other procedures on liver
      - Procedure 50950–00: Radiofrequency ablation of the liver

We did not identify a similar procedure for the lung. The closest description of a procedure that may be related to RFA or MTA of the lung appears to be procedure 90181-00: destruction procedures on lung. Destruction procedures of the lung from 2011-12 and 2012-13 are reported in

Table 1.

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**Table 1 Number of Australian hospital procedures for the destruction of lung tissue, 2011-12 and 2012-13**

Chapter	Subchapter	Block	Procedure	Procedures 2011-12	Procedures 2012-13
7. Procedures on Respiratory System	548-558 Lung and Pleura	558 Other procedures on lung or pleura	90181-00 Destruction procedures on lung	127	135

## 5.5 Evidence for the population that would benefit from this service

A scoping search of PubMed, Cochrane Library, York CRD, and clinical guidelines databases (AHRQ, NICE, NHMRC, SIGN, CMA, Trip) was conducted, with no limit on publication date. Search terms included: (ablation OR ablative OR coag\*) AND microwave AND (lung OR pulmonary). A summary of the identified primary literature is presented in Table 2.

**Table 2 Summary of available literature on MTA of primary and secondary pulmonary lesions**

Population	Number of studies	Sample size range	Date range
Primary lung cancer	1 Comparative study (Wei et al 2015a) 7 Case series (Acksteiner and Steinke 2015; Grieco et al 2006; Liu and Steinke 2013; Palussiere et al 2015; Skonieczki et al 2011; Wei et al 2015b; Yang et al 2014)	74 participants 5-87 participants	2015 2006-2015
Secondary lung cancer	4 Case series (Little et al 2013; Lu et al 2012; Vogl et al 2011; Wolf et al 2008)	23-80 participants	2008-2013
Primary and secondary lung cancer*	9 Case series (Alexander et al 2013; Belfiore et al 2013; Carrafiello et al 2010; Carrafiello et al 2014; Feng et al 2002; He et al 2006; Vogl et al 2013; Wolf et al 2012; Zheng et al 2014)	9-184 participants	2002-2014

\*Studies combined primary and secondary cases.

Based on the results of the scoping search, MTA of primary and secondary lung tumours appears to have an emerging evidence base. No comparative evidence was identified for secondary lung cancer. Only one retrospective, comparative trial was identified for advanced stage primary NSCLC (Wei et al 2015a).

The comparative trial, conducted by Wei et al (2015), evaluated treatment outcomes for chemotherapy (n=28) compared to chemotherapy combined with MTA (n=46) in patients with advanced stage (IIIB and IV) NSCLC. Patients who had prior therapies, including radiotherapy, chemotherapy, surgery, or thermal ablation were excluded. The study found that patients treated with both MTA and chemotherapy had a median total time to local progression of 27.0 months (95% CI 22.2-31.7) compared to 4.8 months (95% CI 3.9-5.8) for chemotherapy alone (P=0.001). Patients who underwent chemotherapy have worse progression-free survival (4.8

months, 95% CI 3.9-5.8) compared to chemotherapy/MTA (10.9 months, 95% CI 5.1-16.7) ( $P=0.001$ ). The median overall survival within the follow-up period (mean follow up 21 months, range 5.1-39.2) was not significantly different between the chemotherapy (17.3 months, 95% CI 15.2-19.3) and chemotherapy/MTA (23.9 months, 95% CI 15.2-32.6) ( $P=0.14$ ).

The limited comparative evidence also appears to be an issue for other potential treatment options. A systematic review of local therapies for stage I and II lung cancers was conducted by the Agency for Healthcare Research and Quality (AHRQ) in 2013 (Ratko et al 2013). The review did not identify any comparative studies investigating the use RFA or and radiotherapy in this population.

Only one ongoing clinical trial investigating the use of MTA for lung cancer was identified on [clinicaltrials.gov](http://clinicaltrials.gov) and the Australian and New Zealand Clinical Trials Registry (ANZCTR):

- NCT01746810: IR-guided ablation (IRGA) combined with stereotactic ablative radiation (SABR) for large lung tumours.

## 6 Comparator

The applicant has suggested that RFA is the appropriate comparator; however, this technology is not widely diffused in the Australian healthcare system and is not currently associated with an MBS item. Therefore, in addition to RFA there are several other treatments for patients with primary and secondary lung cancer that can be considered comparators to MTA. These comparators are first described broadly below with the specific comparators for each patient population detailed at the end of this section.

### ***Radiofrequency ablation (RFA)***

RFA involves creating a closed circuit electrical current through the patient using grounding pads. Ablation can occur at any point along the closed circuit resulting in unpredictable ablation zones (Lloyd et al 2011). Unlike RFA, MTA produces localised, predictable ablation volume shapes and sizes (Bhardwaj et al 2010). The unpredictable ablative nature of RFA may potentially compromise healthy surrounding lung parenchyma. Further, as RFA requires an electrical circuit, it is less effective in low electrical conductivity and high baseline impedance areas such as lung parenchyma (Lee et al 2013). Brace and colleagues demonstrated in a swine model that microwave energy is a more effective energy source compared with radiofrequency for use in the lungs (Dupuy and Shulman 2010).

MTA has a steeper temperature gradient, with tissue temperatures reaching > 200 degrees Celsius, and faster conduction than RFA (Simo et al 2013). This allows for larger ablation volumes in faster times of 4-6 minutes in contrast to 12-20 minutes for single ablations required for RFA (Swan et al 2013). Brace et al. found that MTA ablation zones were 25 per cent larger in mean diameter, 50 per cent larger in cross sectional area and 133 per cent larger in volume compared to RFA (Brace et al 2009).

MTA has a favourable safety profile compared to RFA as it does not involve electricity or grounding pads. This eliminates the risk of pad site burns and potential malfunction of implanted cardiac devices (Lee et al 2013; Schutt et al 2009). MTA is also less susceptible to the “heat sink” effect due to its ability to reach high ablation temperatures in fast times

(Dupuy and Shulman 2010). These properties provide an indication in clinical settings, especially in pulmonary lesions, to move from RFA towards MTA.

### **Current best practice radiotherapy**

The intent of radiotherapy is to achieve a cytotoxic dose of ionising radiation to the tumour volume whilst attempting to minimize adverse effects of radiation on adjacent normal lung tissue and thoracic structures. Radiotherapy modalities used in the treatment of NSCLC include radical radiotherapy delivered in commonly employed regimens as well as continuous hyperfractionated accelerated radiotherapy (CHART). Radical radiotherapy is an intensive course of radiotherapy that may be used with curative intent. The course of treatment is usually given for five days a week in sessions of 10-15 minutes with course between four and seven weeks. CHART is an alternative method of delivering radical radiotherapy. CHART is given three times a day for 12 consecutive days ([NHS choices](#)).

Stereotactic body radiation therapy (SBRT) may also be used in the treatment of NSCLC; it uses advanced imaging techniques to deliver highly targeted radiation resulting in less damage to healthy tissue. Currently, there are no items for SBRT listed on the MBS, and no available evidence to suggest that SBRT would be superior to conventional radiation therapy for these treatment populations. SBRT can be used to give single high dose radiation or several fractionated radiation doses. One potential advantage of SBRT is that can be used to deliver higher doses of radiation than is possible with other radiotherapy techniques. SBRT treatments have the advantage of reducing the risk of damage to normal tissue. Guidelines from the Alberta health services define a role for SBRT in stage I NSCLC who cannot undergo surgery. These guidelines recommend SBRT for tumours five or less cm in size. Cancer Australia guidelines do not cover the use of SBRT for this indication.

Cancer Australia guidelines state that (Cancer Council Australia Lung Cancer Guidelines Working Party 2015):

For Stage I inoperable NSCLC,

*“In patients with inoperable stage I NSCLC and good performance status, high dose radiotherapy is an appropriate treatment option (Grade C). In patients with inoperable stage I NSCLC, high dose radiotherapy to a total of 60 Gy (gray) in 30 fractions over six weeks is a reasonable option. CHART may be used as an alternative to radical conventionally fractionated RT, provided the appropriate resources are available.”*

For Stage II inoperable NSCLC,

*“Patients with inoperable stage II disease could be offered radiotherapy with curative intent.”*

For stage III inoperable NSCLC

*“For patients with good performance status and inoperable stage III NSCLC, the concurrent administration of chemotherapy and radiotherapy is recommended (Grade A). It is recommended that for patients with inoperable stage III NSCLC undergoing curative therapy once daily thoracic radiotherapy to at least 60Gy in 2Gy/f plus chemotherapy is administered (Grade B). For patients with stage III NSCLC who are suitable for curative therapy, but where*

*chemotherapy is contra-indicated or refused, CHART may be used as an alternative to radical conventionally fractionated radiotherapy (Grade B)."*

Two additional forms of radiotherapy that may be applied are image-guided radiation therapy (IGRT) and intensity-modulated radiation therapy (IMRT). In IGRT frequent imaging is used during the course of radiation to improve the precision and accuracy of treatment. CT, MRI, US and x-ray imaging may all be used for IGRT (Radiological Society of North America 2014). In IMRT radiation is delivered in multiple small volumes; this allows the delivery of higher radiation doses to focused regions of known malignancy whilst minimising radiation to adjacent tissues. Treatment planning is conducted using 3D CT or MRI imaging (Radiological Society of North America 2015).

### **Chemotherapy**

Chemotherapy is a systemic treatment for cancer that is taken by mouth or injected into a vein. It can be given as a combination of drugs (most often two). The National Institute for Health and Care Excellence (NICE) recommends that chemotherapy should be offered to patients with stage III NSCLC and good performance status with the aim of improving survival, disease control and quality of life (NICE 2011). Chemotherapy can also be delivered before or after radiotherapy as an adjuvant therapy. No recommendations about the role of chemotherapy delivered before or after radiotherapy were identified for NSCLC. When chemotherapy is delivered concurrently with radiotherapy it is called chemoradiotherapy. The rationale for combining chemotherapy and radiotherapy is to combine the benefits of locoregional control from radiotherapy with the benefits of chemotherapy in reducing the risks of metastatic disease. With concurrent chemoradiation there is the potential for chemotherapy, given during a course of radiotherapy, to enhance the effectiveness of radiotherapy. NICE recommends the consideration of chemoradiotherapy for patients with stage II or III NSCLC who are not suitable for surgery (NICE 2011). Cancer Australia guidelines state that there is insufficient evidence to recommend routine use of chemotherapy along with radiation for the treatment of patients with inoperable stage II NSCLC; however, the guidelines also state that patients with inoperable stage II disease who have good performance status and organ function may be considered for definitive concurrent chemoradiation with a platin-based regimen (this is based on data extrapolated from studies mainly including inoperable stage III disease). For patients with inoperable stage III disease, the guidelines state that the concurrent administration of chemotherapy and radiotherapy is recommended for those with good performance status (Cancer Council Australia Lung Cancer Guidelines Working Party 2015).

#### **Pulmonary Metastasectomy**

Lung metastases from a primary extrapulmonary malignancy are often a manifestation of widespread disease; however, some patients have metastases exclusive to the lung. In these patients surgical resection of the pulmonary metastases can substantially prolong survival and cure some patients. Surgical resection of secondary lung cancer is generally performed in patients who:

- have their primary tumour site controlled
- have no uncontrollable extra-pulmonary disease

- all visible lung metastases, including bilateral disease, are resectable while leaving the patient with adequate pulmonary reserve (Villeneuve and Sundaresan 2009).

A variety of surgical approaches for pulmonary metastasectomy have been described including video-assisted thoracic surgery (VATS), posterolateral thoracotomy, median sternotomy, clamshell (bilateral anterior thoracotomies with transverse sternotomy) and staged procedures (Nichols 2014). The applicant has indicated that MTA should be considered in selected patients with pulmonary metastases who are eligible for surgical resection.

FINAL

### **Comparators to MTA in early stage inoperable NSCLC with curative intent (Population One)**

The applicant has indicated that MTA is indicated in the treatment of early stage NSCLC with curative intent. The applicant has specified that this includes NSCLC T1a-T2b, N0, M0 (up to and including stage IIa). For patients with unresectable NSCLC treatment options are dependent upon the stage of cancer and patient characteristics such as performance status. Treatments can be stand alone or multimodal and generally comprise radiotherapy alone or in combination with chemotherapy. Comparators to MTA in this group include the following:

- RFA
- Current best practice radiotherapy with or without chemotherapy

### **Comparators to MTA for patients with lung metastases, in whom the primary tumour is under control and who are receiving treatment with curative intent (oligometastatic disease) (Population Two)**

The applicant has indicated that MTA has a role in the definitive treatment of patients with lung metastase(s) in whom the primary tumour is under control. In this patient group comparators include the following:

- RFA
- Surgical resection (any technique)
- Current best practice radiotherapy with or without chemotherapy

The applicant has indicated that thermal ablation can be considered in selected operable patients with uni- or bi-lateral disease because it is less invasive, more tissue-sparing, repeatable and can be performed in an outpatient setting or with an overnight stay, having the least negative impact on quality of life.

### **Comparators to MTA for patients with NSCLC who are not eligible for surgical resection and patients with pulmonary metastases who are receiving treatment with palliative intent (Population Three)**

MTA may have a role in treating patients with NSCLC with palliative intent. In this group, MTA may assist with symptom control and decrease tumour burden in metastatic disease. In this group the comparators to MTA include the following:

- Conventional palliative therapy without MTA

## 7 Clinical management algorithm

### 7.1 Current and proposed clinical practice

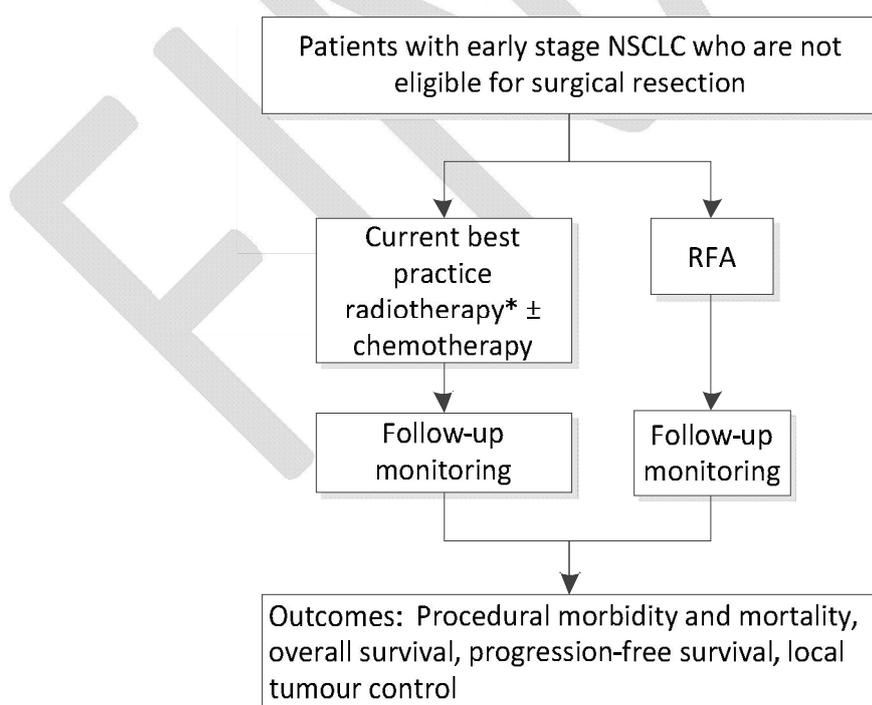
The following algorithm, Figure 1, shows the current management of unresectable, early stage NSCLC. MTA is shown as an alternative to RFA and current best practice radiotherapy with or without chemotherapy. In the proposed algorithm, Figure 2, MTA is shown as an alternative to current best practice radiotherapy with or without chemotherapy.

Figure 3 shows the current clinical management algorithm for the management of pulmonary metastases in patients with the primary cancer under control. In this algorithm MTA is an alternative to RFA and radiotherapy with or without platinum-based chemotherapy in patients who are not eligible for surgical resection. Figure 4, the proposed algorithm shows MTA as a comparator both to radiotherapy with or without chemotherapy and as a comparator to surgery in both bilateral and unilateral disease.

Figure 5 and Figure 6 show the current and proposed clinical management algorithms for the palliative management of NSCLC and pulmonary metastases respectively. MTA is shown as an additional treatment option to conventional palliative treatments for NSCLC and pulmonary metastases.

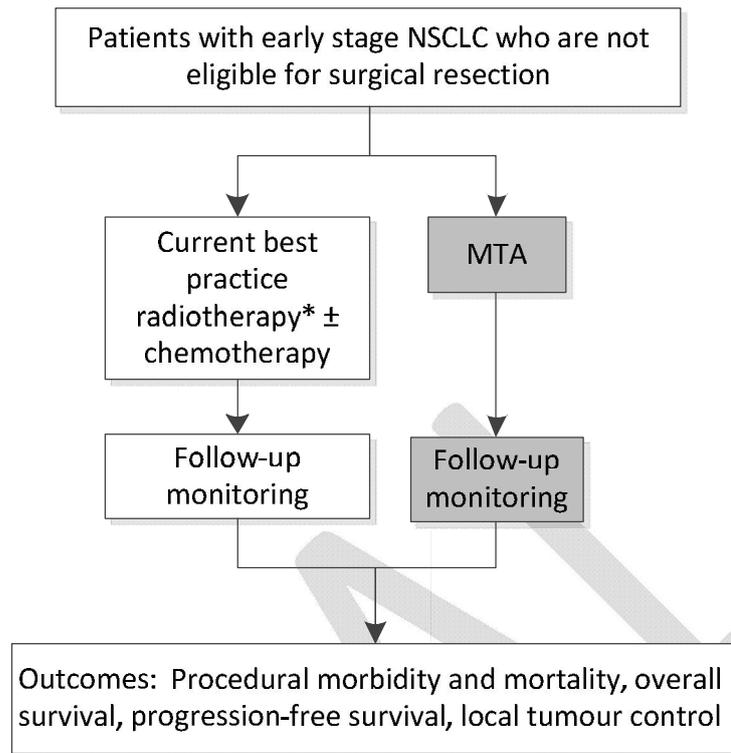
In each of the proposed algorithms MTA is replacing RFA.

**Figure 1 Current clinical management algorithm for the management of unresectable, early stage NSCLC with curative intent (Population One)**



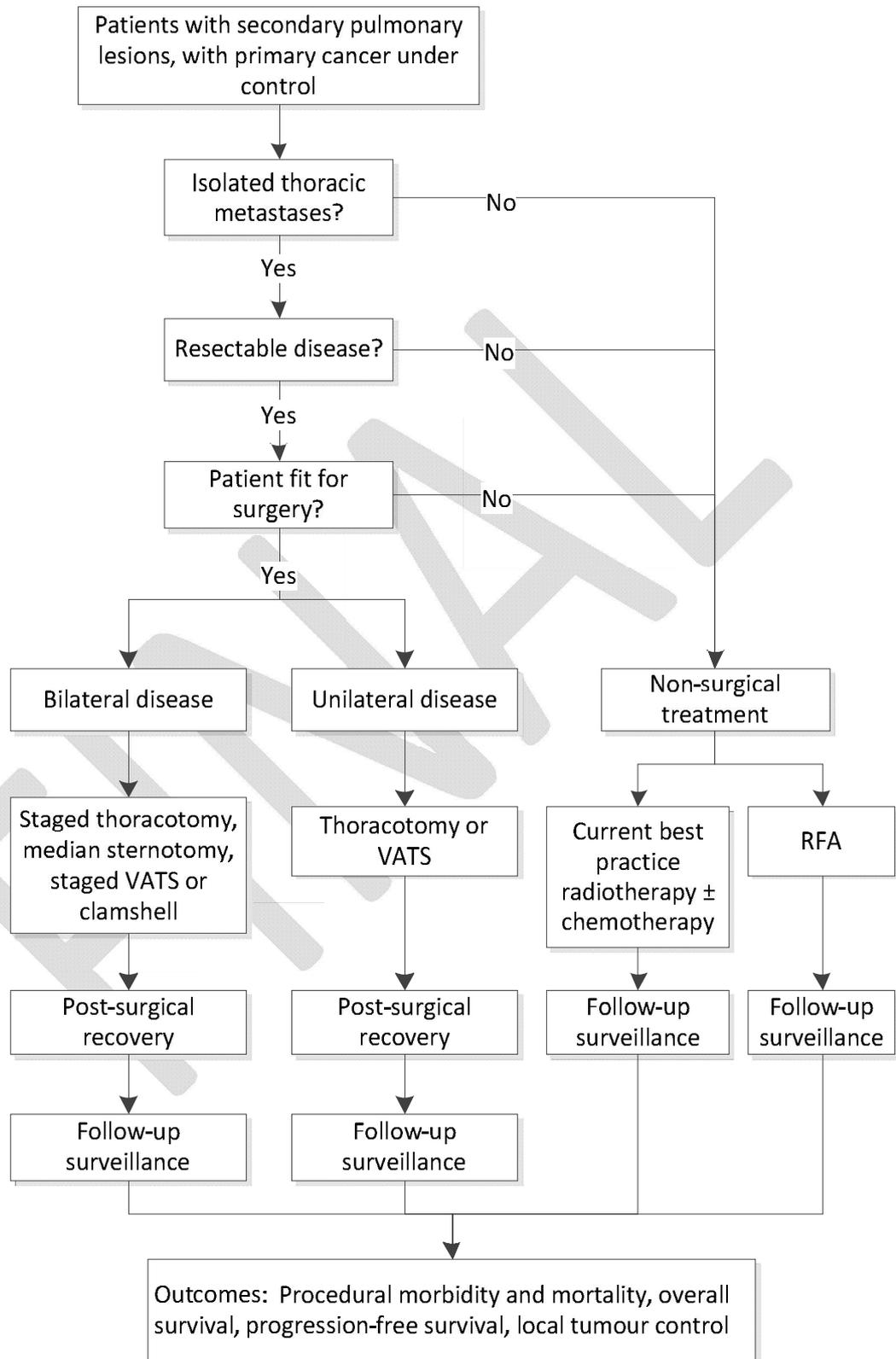
\*Stage IIA patients are considered to be unsuitable for SBRT. NSCLC = non-small cell lung cancer. RFA = radiofrequency ablation. SBRT = stereotactic body radiotherapy

**Figure 2 Proposed clinical management algorithm for the management of unresectable, early stage NSCLC with curative intent (Population One)**



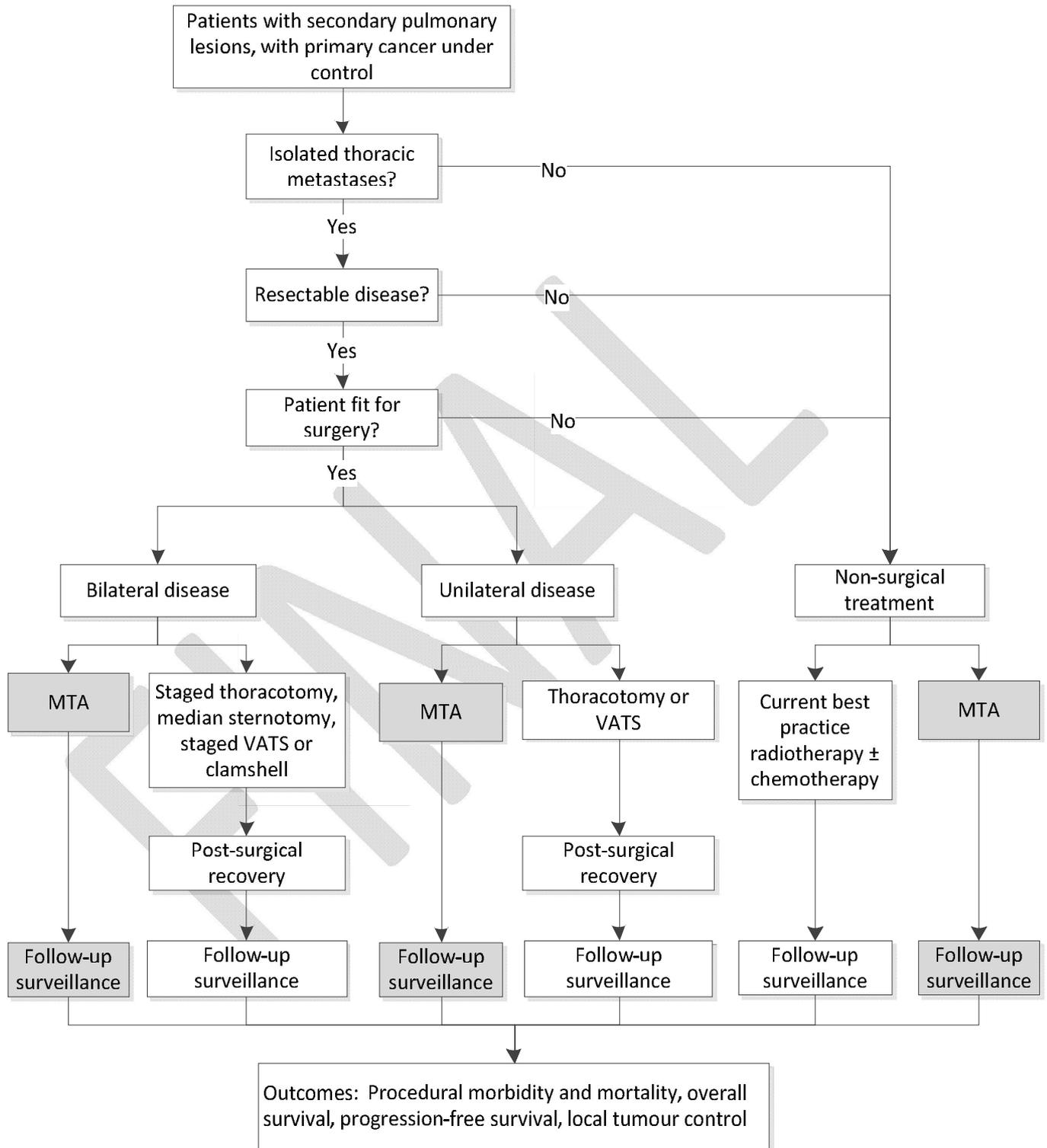
\*Stage IIA patients are considered to be unsuitable for SBRT. MTA = microwave tissue ablation. NSCLC = non-small cell lung cancer. SBRT = stereotactic body radiotherapy

**Figure 3 Current clinical management algorithm for the management of pulmonary metastases with curative intent in patients with the primary cancer under control (Population Two)**



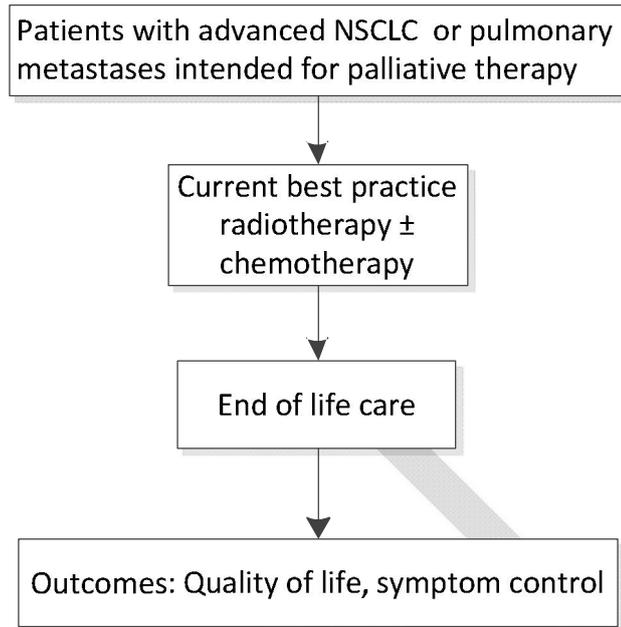
RFA = radiofrequency ablation. VATS = Video-assisted thoracoscopic surgery.

**Figure 4 Proposed clinical management algorithm for the management of pulmonary metastases with curative intent in patients with the primary cancer under control (Population Two)**



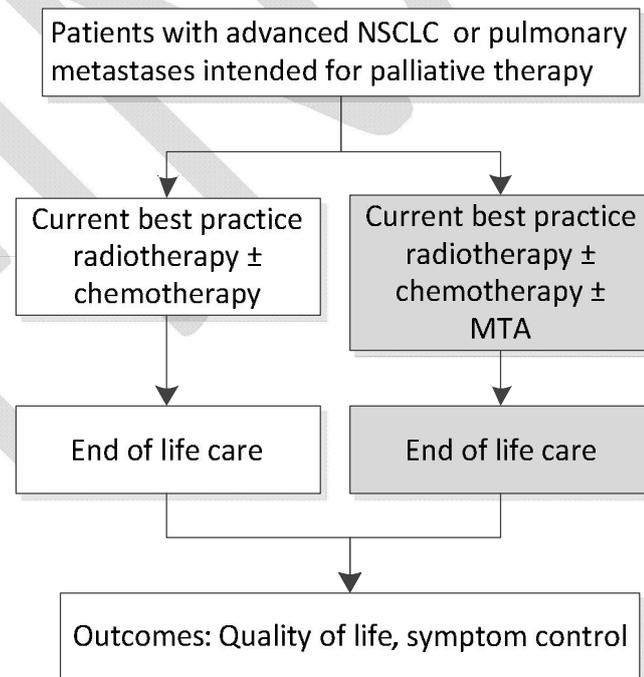
MTA = microwave tissue ablation. VATS = video-assisted thorascopic surgery.

**Figure 5** Current clinical management algorithm for the palliative management of NSCLC and pulmonary metastases (Population Three)



NSCLC = non-small cell lung cancer

**Figure 6** Proposed clinical management algorithm for the palliative management of NSCLC and pulmonary metastases (Population Three)



MTA = microwave tissue ablation. NSCLC = non-small cell lung cancer.

## 8 Expected health outcomes

### 8.1 Expected patient-relevant health outcomes

The clinical literature suggests that the primary health outcome of relevance to patients treated with curative intent is overall and disease-free survival. Secondary outcomes of relevance to patients include disease control, recurrence and the need for re-ablation. If RFA is an appropriate comparator, a further secondary outcome may include patient discomfort and total treatment time. This is because the applicant states that MTA minimises patient discomfort and enables considerably faster treatment times than RFA.

#### ***Primary effectiveness outcomes***

The patient population is restricted to patients who are not candidates for surgical resection. The treatment intent of MTA in this patient group is to extend patient life through destruction of primary tumours or through local control of pulmonary metastases. Measures of survival relevant to the patient population include: mortality rates from NSCLC or pulmonary metastatic tumour at 1-,2-,3- and 5-years; overall survival; the survival rates at 1-,2-,3- and 5-years; and, the recurrence free survival period and recurrence free survival rates.

In patients treated with palliative intent the primary outcomes are symptom control/relief and median survival time.

#### ***Secondary effectiveness outcomes***

Secondary effectiveness outcomes include measures of disease control and recurrence including: local recurrence rates, 1-year local control rate, mean time to first recurrence, distal metastases and tumour progression. There are a range of measures associated with quantifying local control that would be relevant to this patient population and should be included at the assessment phase. Other secondary effectiveness outcomes may include procedural discomfort, total procedure time and length of patient hospital stays. Quality of life measures should also be considered.

In patients treated with palliative intent the secondary outcomes include relative survival rates.

### 8.2 Potential risks to patients

The primary safety concern with the proposed service is procedure-related mortality and morbidity due to peri-operative complications. The applicant states that the complication rate for MTA varies. Percutaneous MTA requires general anaesthesia or conscious sedation and may therefore be associated with anaesthesia related adverse events. The procedure may also involve exposure to CT, which carries an associated risk of ionising radiation exposure. Potential adverse events that may arise as a result of MTA of the lung identified in the literature include (Acksteiner and Steinke 2015; Alexander et al 2013; Belfiore et al 2013; Carrafiello et al 2010; Carrafiello et al 2014; Feng et al 2002; Grieco et al 2006; He et al 2006; Little et al 2013; Liu and Steinke 2013; Lu et al 2012; Palussiere et al 2015; Skonieczki et al 2011; Vogl et al 2011; Vogl et al 2013; Wei et al 2015a; Wei et al 2015b; Wolf et al 2012; Wolf et al 2008; Yang et al 2014; Zheng et al 2014):

- Pneumothorax
- Needle track implantation
- Haemoptysis
- Haemothorax
- Skin burns
- Broncho-pleural fistula
- Rib fracture
- Pneumonitis
- Infection
- Chest pain
- Pain
- Other adverse events
- Post-ablation syndrome

## 9 Clinical claim for the proposed intervention

### 9.1 Clinical claim

The clinical claim associated with this application depends upon the intended use of, and available treatment alternatives to MTA.

#### **Clinical claim in patients with early stage inoperable NSCLC who are receiving treatment with curative intent (Population One)**

The applicant has indicated that MTA has a role in the definitive treatment of early stage inoperable NSCLC. In these patients, guidelines recommend the use of radiotherapy including SBRT or radical radiotherapy and chemoradiotherapy. MTA is intended to be offered as an alternative to these therapies in selected patients. It is understood that the clinical claim associated with the application for this patient group is that MTA offers equivalent effectiveness outcomes to radiotherapy or chemoradiotherapy with an acceptable safety profile.

#### **Clinical claim in patients with lung metastase(s), in whom the primary tumour is under control and who are receiving treatment with curative intent (Population Two)**

In these patients the potential treatments for lung metastases depends on whether the patient is suitable for surgical resection. In patients who are not suitable for surgical resection the clinical claim is that MTA offers equivalent effectiveness to radiotherapy or chemoradiotherapy with an acceptable safety profile.

In patients who are eligible for surgical resection the applicant has indicated that MTA can be considered in selected operable patients with unilateral or bilateral disease, as it is much less invasive, more tissue-sparing, repeatable and can be performed in an outpatient setting or with an overnight stay, having the least negative impact on quality of life. Hence, the clinical claim associated with patients in this group eligible for surgical resection is that MTA demonstrates equivalent effectiveness to surgical resection with an acceptable safety profile. Further to this the applicant claims that MTA offers certain benefits over surgical resection in terms of invasiveness, repeatability and quality of life.

### **Clinical claim in patients with NSCLC who are not eligible for surgical resection and patients with pulmonary metastases who are receiving treatment with palliative intent (Population Three)**

MTA may have a role in treating patients with NSCLC with palliative intent. In these patients chemotherapy and radiotherapy are the main treatment options. MTA may be offered as an adjunct to radiotherapy and/or chemotherapy in these patients, as a means of de-bulking prominent tumours for symptom relief. In this population, MTA may improve symptom relief as opposed to conventional palliative therapies without MTA.

### **Clinical claim with respect to RFA in all patient groups**

The applicant suggests there are significant treatment advantages of MTA over RFA, especially in the setting of lung tumour ablation. MTA is arguably more controllable and considered a safer procedure. MTA also offers larger, faster, more predictable ablation zones and higher temperatures during ablation. This may result in lower local recurrence rates and better patient-relevant health outcomes. Hence, in all the patient groups the applicant has suggested that RFA is a treatment option and that MTA is superior to RFA in terms of effectiveness for all patient groups and is associated with an acceptable safety profile.

## **9.2 Economic evaluation**

The economic evaluation for the proposed service is informed by the following clinical claims:

- Superior safety and effectiveness compared to RFA (Population One and Two).
- Non-inferior effectiveness compared to surgery (Population Two) and current best practice radiotherapy with or without chemotherapy (Population One and Two).
- Superior safety compared to surgery (Population Two) and current best practice radiotherapy with or without chemotherapy (Population One and Two).

In this context, the economic evaluation of the proposed service will be a cost-effectiveness analysis/cost-utility analysis.

## 10 Decision analytic

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

PICO Criteria	Comments
<b>Patients</b>	Patients with early stage non-small cell lung cancer who are not eligible for surgical resection, and who are receiving treatment with curative intent.
<b>Intervention</b>	Percutaneous microwave tissue ablation
<b>Comparator</b>	<ol style="list-style-type: none"> <li>1. Radiofrequency ablation</li> <li>2. Current best practice radiotherapy including, but not limited to SBRT, with or without chemotherapy</li> </ol>
<b>Outcomes</b>	<p><b>Primary Effectiveness</b></p> <ul style="list-style-type: none"> <li>NSCLC or pulmonary metastatic tumour mortality at 1-,2-,3- and 5-years</li> <li>Overall survival</li> <li>Relative survival rates at 1-,2-,3- and 5-years</li> <li>Recurrence free survival period</li> <li>Recurrence free survival rates</li> </ul> <p><b>Secondary Effectiveness</b></p> <ul style="list-style-type: none"> <li>Local recurrence rates</li> <li>1-year local control rate</li> <li>Mean time to first recurrence</li> <li>Distant metastases</li> <li>Tumour progression</li> <li>Procedure time</li> <li>Length of hospital stay</li> <li>Recovery time</li> <li>Patient discomfort</li> <li>Quality of life</li> </ul> <p><b>Safety</b></p> <ul style="list-style-type: none"> <li>Procedure-related mortality</li> <li>30 day mortality</li> <li>Adverse events</li> </ul> <p><b>Cost Effectiveness</b></p>
<b>Prior tests</b>	<p>Depending on patient and disease characteristics, prior imaging may include:</p> <ol style="list-style-type: none"> <li>1. Chest X-ray</li> <li>2. Computed tomography (CT) – usually contrast-enhanced</li> <li>3. PET-CT (prior to treatment with curative intent)</li> </ol>

**Research question for assessment:** In patients with early stage NSCLC who are not eligible for surgical resection and who are receiving treatment with curative intent, what is the safety, effectiveness and cost effectiveness of percutaneous MTA compared to RFA and current best practice radiotherapy with or without chemotherapy?

**Table 4: Summary of PICO to define the research question(s) for Population Two**

PICO Criteria	Comments
<b>Patients</b>	<p>Patients with lung metastases in who the primary tumour is under control, and who are receiving treatment with curative intent (oligometastatic disease).</p> <p><i>At the assessment phase Population Two should be stratified into two groups with respect to their primary tumours: those with sarcoma (bone and soft tissue) and those with non-sarcoma primaries.</i></p>
<b>Intervention</b>	Percutaneous microwave tissue ablation
<b>Comparator</b>	<ol style="list-style-type: none"> <li>1. Radiofrequency ablation</li> <li>2. Surgical resection (any technique)</li> <li>3. Current best practice radiotherapy including, but not limited to, SBRT with or without chemotherapy</li> </ol>
<b>Outcomes</b>	<p><b>Primary Effectiveness</b></p> <ul style="list-style-type: none"> <li>Overall survival</li> <li>Relative survival rates at 1-,2-,3- and 5-years</li> <li>Recurrence free survival period</li> <li>Recurrence free survival rates</li> </ul> <p><b>Secondary Effectiveness</b></p> <ul style="list-style-type: none"> <li>Local recurrence rates</li> <li>1-year local control rate</li> <li>Mean time to first recurrence</li> <li>Distant metastases</li> <li>Tumour progression</li> <li>Procedure time</li> <li>Length of hospital stay</li> <li>Recovery time</li> <li>Patient discomfort</li> <li>Quality of life</li> </ul> <p><b>Safety</b></p> <ul style="list-style-type: none"> <li>Procedure-related mortality</li> <li>30 day mortality</li> <li>Adverse events</li> </ul> <p><b>Cost Effectiveness</b></p>
<b>Prior tests</b>	<p>Depending on patient and disease characteristics, prior imaging may include:</p> <ol style="list-style-type: none"> <li>1. Chest X-ray</li> <li>2. Computed tomography (CT) – usually contrast-enhanced</li> <li>3. PET-CT (prior to treatment with curative intent)</li> </ol>

**Research question for assessment:** In patients with lung metastases, in whom the primary tumour is under control and who are receiving treatment with curative intent, what is the safety, effectiveness and cost effectiveness of percutaneous MTA compared to RFA, surgical resection and current best practice radiotherapy with or without chemotherapy?

**Table 5: Summary of PICO to define the research question(s) for Population Three**

PICO Criteria	Comments
<b>Patients</b>	Patients with non-small cell lung cancer or pulmonary metastases, who are receiving palliative treatment.
<b>Intervention</b>	Conventional palliative therapy with percutaneous microwave tissue ablation
<b>Comparator</b>	Conventional palliative therapy without percutaneous microwave tissue ablation
<b>Outcomes</b>	<p><b>Primary Effectiveness</b></p> <ul style="list-style-type: none"> <li>Symptom relief/control</li> <li>Quality of life</li> <li>Median survival times</li> </ul> <p><b>Secondary Effectiveness</b></p> <ul style="list-style-type: none"> <li>Relative survival rates at 1-,2-,3- and 5-years</li> <li>Procedure time</li> <li>Length of hospital stay</li> <li>Recovery time</li> <li>Patient discomfort</li> </ul> <p><b>Safety</b></p> <ul style="list-style-type: none"> <li>Procedure-related mortality</li> <li>30 day mortality</li> <li>Adverse events</li> </ul> <p><b>Cost effectiveness</b></p>
<b>Prior tests</b>	Depending on patient and disease characteristics, prior imaging may include: <ul style="list-style-type: none"> <li>1. Chest X-ray</li> <li>2. Computed tomography (CT)</li> <li>3. Contrast-enhanced CT (contrast preferable, but not mandatory)</li> </ul>

**Research question for assessment:** In patients receiving palliative treatment for NSCLC or pulmonary metastases, what is the safety, effectiveness and cost effectiveness of conventional palliative therapy with percutaneous MTA compared to conventional palliative therapy without percutaneous MTA?

## 11 Fee for the proposed medical service

### 11.1 Type of funding proposed for this service

The current application requests the listing of six new ‘Category 3 – Therapeutic Procedures’ items on the MBS (Table 6-11). The proposed items are graduated based on the number of ablated lesions, and are intended to cover the cost of pre-, intra- and post-operative imaging. This includes a limited planning scan, intra-operative image guidance, and a post ablation control scan.

**Table 6: Proposed MBS item for microwave tissue ablation of up to three pulmonary lesions (curative intent)**

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS [item number TBD]</p> <p>NONRESECTABLE PRIMARY LUNG CANCER OR PULMONARY METASTATIC DISEASE, destruction of up to three lesions, by percutaneous microwave tissue ablation (MTA) with curative intent, including any associated imaging services.</p> <p>(Anaes)</p> <p>Fee: \$1300 <b>Benefit:</b> 75% = \$975.00 85% = \$1105.00</p>

**Table 7: Proposed MBS item for microwave tissue ablation of four or five pulmonary lesions (curative intent)**

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS [item number TBD]</p> <p>NONRESECTABLE PRIMARY LUNG CANCER OR PULMONARY METASTATIC DISEASE, destruction of four or five lesions, by percutaneous microwave tissue ablation (MTA) with curative intent, including any associated imaging services.</p> <p>(Anaes)</p> <p>Fee: \$1600 <b>Benefit:</b> 75% = \$1200.00 85% = \$1360.00</p>

**Table 8: Proposed MBS item for microwave tissue ablation of more than five pulmonary lesions (curative intent)**

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS [item number TBD]</p> <p>NONRESECTABLE PRIMARY LUNG CANCER OR PULMONARY METASTATIC DISEASE, destruction of more than five lesions, by percutaneous microwave tissue ablation (MTA) with curative intent, including any associated imaging services.</p> <p>(Anaes)</p> <p>Fee: \$2000 <b>Benefit:</b> 75% = \$1500.00 85% = \$1700.00</p>

**Table 9: Proposed MBS item for microwave tissue ablation of up to three pulmonary lesions (palliative intent)**

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS [item number TBD]</p> <p>NONRESECTABLE PRIMARY LUNG CANCER OR PULMONARY METASTATIC DISEASE, destruction of up to three lesions, by percutaneous microwave tissue ablation (MTA) with palliative intent, including any associated imaging services.</p> <p>(Anaes)</p> <p>Fee: \$1300 <b>Benefit:</b> 75% = \$975.00 85% = \$1105.00</p>

**Table 10: Proposed MBS item for microwave tissue ablation of four or five pulmonary lesions (palliative intent)**

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS [item number TBD]</p> <p>NONRESECTABLE PRIMARY LUNG CANCER OR PULMONARY METASTATIC DISEASE, destruction of four or five lesions, by percutaneous microwave tissue ablation (MTA) with palliative intent, including any associated imaging services.</p> <p>(Anaes)</p> <p>Fee: \$1600 <b>Benefit:</b> 75% = \$1200.00 85% = \$1360.00</p>

**Table 11: Proposed MBS item for microwave tissue ablation of more than five pulmonary lesions (palliative intent)**

Category 3 – THERAPEUTIC PROCEDURES
<p>MBS [item number TBD]</p> <p>NONRESECTABLE PRIMARY LUNG CANCER OR PULMONARY METASTATIC DISEASE, destruction of more than five lesions, by percutaneous microwave tissue ablation (MTA) with palliative intent, including any associated imaging services.</p> <p>(Anaes)</p> <p>Fee: \$2000 <b>Benefit:</b> 75% = \$1500.00 85% = \$1700.00</p>

### 11.2 Direct costs associated with the proposed service

Clinical feedback suggests RFA is cheaper than MTA. The costs associated with RFA range between \$1,500 and \$2,000 for consumables, as opposed to \$2,200 and \$2,900 for MTA. Private health insurance usually covers the cost of the consumables; however, it is currently understood that gap payments are charged on top of the cost of consumables. Many of the following costs associated with MTA will need to be identified during the assessment phase:

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

### 11.3 Proposed fee

As the applicant has not suggested a proposed fee for MTA of pulmonary lesions, the proposed fee has been adopted from Application 1402 (MTA of liver tumours). Application 1402 states:

*“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 physician to ensure better patient outcomes”*

According to the applicant the number of tumours treated alters the complexity of the procedure. A graduated fee structure for the number of tumours treated should be supported by evidence of increased complexity and increased clinical benefits. To determine the value of a graduated fee, PASC has advised that the assessment phase should include a stratified survival analysis based on the number of ablated lesions.

As there is no Medicare number for lung RFA, the maximum rebate that can be received in private practice is \$470.00 (MBS item 57341 for CT-guided interventions). The fee for RFA services for liver [both percutaneous and open/laparoscopic (50952)] is \$817.10. It should be noted, the application claims MTA has a faster ablation time which would result in less time overall spent in the radiology suite, and may impact on the cost of the procedure.

## 12 Regulatory information and registered trademark

The application refers to the Acculis MTA System with a single use microwave applicator, which is registered to be used in Australia with N Stenning and Co Pty Ltd as the sponsor. In addition to the Acculis MTA system, there are three additional MTA systems currently available in Australia. Other devices registered in Australia include:

- The Avecure Microwave Ablation / Coagulation System sponsored by Aurora BioScience Pty Ltd (ARTG ID 200325) is listed on the ARTG for ablation/coagulation of soft tissue. This device uses 902-928 MHz microwaves, and 32W.
- The Emprint™ Ablation System with Thermosphere™ Technology - microwave hyperthermia system (ARTG ID 226598), an intracorporeal microwave hyperthermia applicator (ARTG ID 178369), and two hyperthermia microwave systems (ARTG IDs 152044, 178699) sponsored by Covidien Pty Ltd. The system is intended to be used for percutaneous, laparoscopic, and intraoperative coagulation (ablation) of soft tissue. This system uses 1.4-1.5 GHz and 100Watts.
- The Amica microwave hyperthermia system (ARTG ID 212509), and an intracorporeal microwave hyperthermia applicator (ARTG ID 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. The system uses 2.45 GHz and 20-140W of power.

The Acculis MTA system involves thermal coagulation of soft tissue using 2.45GHz microwave energy. The system consists of the Sulis VpMTA Generator, Acculis Local Control Station (LCS),

Acculis MTA Applicators and optional MTA Temperature Probes. The ARTG listing or registration number:

- Temperature Probes (ARTG ID 174513): 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 (ARTG ID 195697): 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 (ARTG ID 174514): The Single Use Microwave Applicator is intended to be used with the Acculis MTA System for intraoperative coagulation of soft tissue.
- Microwave Generator System (ARTG ID 157722): Treat lesions using microwave hyperthermia

### 13 Healthcare resources

The healthcare resources related to the proposed service and comparator interventions are outlined in Table 12.

### 14 Questions for public funding

None

**Table 12: 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, FDG PET etc.)	Radiologists	Radiology clinic or radiology department (hospital)	100%							
Resources provided to deliver proposed intervention (MTA)										
Machine cost (\$50,000)	Hospital	Radiology clinic or radiology department	100%							
Disposable probe (\$2,960)	Hospital	Radiology clinic or radiology department	100%							
Time to perform procedure (ablation time of 4-6 minutes per lesion, also time for patient positioning, anaesthetic administration)	Interventional radiologist	Radiology clinic or radiology department	100%							
Image-guidance (CT or US)	Interventional radiologist	Radiology clinic or radiology department	100%							
Anaesthetic	Anaesthetist	Radiology clinic or radiology department	100%							

	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 in association with proposed intervention (MTA)										
Aftercare	Dedicated nursing staff	Radiology clinic or radiology department	100%							
Follow-up imaging (cross-sectional) 6 weeks post-procedure	Radiologist/radiographer	Radiology clinic or radiology department	100%							
Resources provided to deliver comparator 1 (RFA)										
Machine cost (\$40,000-\$65,000**)	Hospital	Out-patient	100%							
Disposable probe (\$1,700-\$2,700)**	Hospital	Out-patient	100%							
Time to perform ablation (10-20 minutes)	Interventional radiologist or surgeon	Radiology clinic or radiology department	100%							
Imaging (CT or US)	Interventional radiologist or surgeon	Radiology clinic or radiology department	100%							
Anaesthetic	Anaesthetist	Radiology clinic or radiology department	100%							
Resources provided in association with comparator 1 (RFA)										

	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
Aftercare	Dedicated nursing staff	Radiology clinic or radiology department	100%							
Follow-up imaging	Radiologist/radiographer	Radiology clinic or radiology department	100%	24 hrs post procedure						
Resources provided to deliver comparator 2 (Radiotherapy)										
Simulation	Radiation oncologist	Outpatient	100%		15550 (\$658.60), 15553, 15600, 15500					
Dosimetry	Radiation oncologist	Outpatient	100%		15518, 15521, 15524, 15527, 15530, 15533					
Treatment	Radiation oncologist	Outpatient	100%		15000, 15006, 15100, 15106, 15112					
Verification	Radiation oncologist	Outpatient	100%		15700, 15705, 15710					
Resources provided in association with comparator 2 (Radiotherapy)										
Aftercare			100%							
Follow-up imaging	Radiologist/radiographer	Outpatient	100%							

	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 deliver chemotherapy (potential adjunct to the intervention and comparators 1 and 2)										
Initial specialist consult	specialist		100%							
Chemotherapy planning	Specialist/multi-disciplinary team		100%							
Pathology monitoring			100%							
Administering chemotherapy	Nurse/specialist oncologist/haematologist	Outpatient or hospital	100%							
Chemotherapy drug(s)	Nurse/specialist oncologist/haematologist	Outpatient or hospital	100%			Cisplatin, max safety net: \$37.70	PBS, Dispensed price per maximum amount: \$126.72		Max price to consumer: \$37.70	
Resources provided in association with chemotherapy (potential adjunct to the intervention and comparators 1 and 2)										
Aftercare	Dedicated nursing staff	Outpatient or hospital	100%	6-weekly follow-up intervals						
Resources used to manage patients successfully treated with the proposed intervention										
Follow-up imaging to confirm no tumour recurrence			100% of patient successfully treated							
Follow-up treatment as 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										
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			100% of patients unsuccessfully treated							
Re-staging of disease and treatment as determined according to current disease status			100% of patients unsuccessfully treated							
Resources used to manage patients successfully treated with comparator 1										
Follow-up imaging to confirm no tumour recurrence			100% of patient successfully treated							
Follow-up treatment as required										
Follow-up palliative care as required										
Resources used to manage patients who are unsuccessfully treated with comparator 1										
Follow-up imaging to confirm incomplete ablation of tumour and/or tumour recurrence			100% of patients unsuccessfully treated	at 3, 6 and 12 months and yearly thereafter						

	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
Re-staging of disease and treatment as determined according to current disease status			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.



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FINAL

## Appendix A – current MBS items for treatment of lung cancer

**Table 13 Radiotherapy treatments for lung cancer currently listed on the MBS**

Category 3 – Therapeutic Procedures
<p><b>MBS item 15215</b>            RADIATION ONCOLOGY TREATMENT, using a single photon energy linear accelerator with or without electron facilities - each attendance at which treatment is given - 1 field - treatment delivered to primary site (lung).            Fee: \$57.40; Benefit: 75% = \$43.05; 85% = \$48.80</p>
<p><b>MBS item 15230</b>            RADIATION ONCOLOGY TREATMENT, using a single photon energy linear accelerator with or without electron facilities - each attendance at which treatment is given - 2 or more fields up to a maximum of 5 additional fields (rotational therapy being 3 fields) - treatment delivered to primary site (lung).            The fee for item 15215 plus for each field in excess of 1, an amount of \$36.50.</p>

**Table 14 Stereotactic radiosurgery treatments for lung cancer currently listed on the MBS**

Category 3 – Therapeutic Procedures
<p><b>MBS item 15215</b>            RADIATION ONCOLOGY TREATMENT, using a single photon energy linear accelerator with or without electron facilities - each attendance at which treatment is given - 1 field - treatment delivered to primary site (lung).            Fee: \$57.40; Benefit: 75% = \$43.05; 85% = \$48.80</p>

**Table 15 Surgical treatments for lung cancer currently listed on the MBS**

Category 3 – Therapeutic Procedures
<p><b>MBS item 38418</b>            THORACOTOMY, exploratory, with or without biopsy            Multiple Services Rule            (Anaes.) (Assist.)            Fee: \$922.10</p>
<p><b>MBS item 38421</b>            THORACOTOMY, with pulmonary decortication            Multiple Services Rule            (Anaes.) (Assist.)            Fee: \$1,473.95</p>
<p><b>MBS item 38438</b>            PNEUMONECTOMY or LOBECTOMY or SEGMENTECTOMY not being a service associated with a service to which Item 38418 applies            Multiple Services Rule            (Anaes.) (Assist.)            Fee: \$1,473.95 Benefit: 75% = \$1,149.00</p>
<p><b>MBS item 38440</b>            LUNG, wedge resection of            Multiple Services Rule</p>

(Anaes.) (Assist.)

**Fee:** \$1,103.75 **Benefit:** 75% =

**MBS item 38441**

RADICAL LOBECTOMY or PNEUMONECTOMY including resection of chest wall, diaphragm, pericardium, or formal mediastinal node dissection

Multiple Services Rule

(Anaes.) (Assist.)

**Fee:** \$1,746.40 **Benefit:** 75% = \$1,361.40

**Multiple Services Rule: Note T8.3.**

Procedure Performed with Local Infiltration or Digital Block

It is to be noted that where a procedure is carried out with local infiltration or digital block as the means of anaesthesia, that anaesthesia is considered to be part of the procedure and an additional benefit is therefore not payable.

FINAL

**Appendix B – Summary TNM staging system for lung cancer from the American Joint Committee on Cancer (AJCC). (American Joint Committee on Cancer 2009)**

Anatomic stage	Prognostic groups		
	Tumour classification (T)	Regional lymph node involvement (N)	Distant metastatic spread (M)
<b>Occult carcinoma</b>	TX	N0	M0
<b>Stage 0</b>	Tis	N0	M0
<b>Stage IA</b>	T1a	N0	M0
	T1b	N0	M0
<b>Stage IB</b>	T2a	N0	M0
<b>Stage IIA</b>	T2b	N0	M0
	T1a	N1	M0
	T1b	N1	M0
	T2a	N1	M0
<b>Stage IIB</b>	T2b	N1	M0
	T3	N0	M0
<b>Stage IIIA</b>	T1a	N2	M0
	T1b	N2	M0
	T2a	N2	M0
	T2b	N2	M0
	T3	N1	M0
	T3	N2	M0
	T4	N0	M0
	T4	N1	M0
<b>Stage IIIB</b>	T1a	N3	M0
	T1b	N3	M0
	T2a	N3	M0
	T2b	N3	M0
	T3	N3	M0
	T4	N2	M0
	T4	N3	M0
<b>Stage IV</b>	Any T	Any N	M1a
	Any T	Any N	M1b

**Primary Tumour (T) Classification**

**TX** Primary tumour cannot be assessed, or tumour proven by the presence of malignant cells in sputum or bronchial washings but not visualized by imaging or bronchoscopy

**T0** No evidence of primary tumour

**Tis** Carcinoma in situ

**T1** Tumour 3 cm or less in greatest dimension, surrounded by lung or visceral pleura, without bronchoscopic evidence of invasion more proximal than the lobar bronchus

**T1a** Tumour 2 cm or less in greatest dimension

**T1b** Tumour more than 2 cm but 3 cm or less in greatest dimension

**T2** Tumour more than 3 cm but 7 cm or less or tumour with any of the following features (T2 tumours with these features are classified T2a if 5 cm or less): involves main bronchus, 2 cm or more distal to the carina; invades visceral pleura (PL1 or PL2); associated with atelectasis or obstructive pneumonitis that extends to the hilar region but does not involve the entire lung

**T2a** Tumour more than 3 cm but 5 cm or less in greatest dimension

**T2b** Tumour more than 5 cm but 7 cm or less in greatest dimension

**T3** Tumour more than 7 cm or one that directly invades any of the following: parietal pleural (PL3), chest wall (including superior sulcus tumours), diaphragm, phrenic nerve, mediastinal pleura, parietal pericardium; or tumour in the main bronchus less than 2 cm distal to the carina<sup>1</sup> but without involvement of the carina; or associated atelectasis or obstructive pneumonitis of the entire lung or separate tumour nodule(s) in the same lobe

**T4** Tumour of any size that invades any of the following: mediastinum, heart, great vessels, trachea, recurrent laryngeal nerve, oesophagus, vertebral body, carina, separate tumour nodule(s) in a different ipsilateral lobe

#### **Regional Lymph Node (N) Classification**

**NX** Regional lymph nodes cannot be assessed

**N0** No regional lymph node metastases

**N1** Metastasis in ipsilateral peribronchial and/or ipsilateral hilar lymph nodes and intrapulmonary nodes, including involvement by direct extension

**N2** Metastasis in ipsilateral mediastinal and/or subcarinal lymph node(s)

**N3** Metastasis in contralateral mediastinal, contralateral hilar, ipsilateral or contralateral scalene, or supraclavicular lymph node(s)

#### **Distant Metastasis (M) Classification**

**M0** No distant metastasis

**M1** Distant metastasis

**M1a** Separate tumour nodule(s) in a contralateral lobe, tumour with pleural nodules or malignant pleural (or pericardial) effusion

**M1b** Distant metastasis (in extrathoracic organs)