

NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

Interventional procedure overview of percutaneous radiofrequency ablation for primary and secondary lung cancers

Lay description of the procedure:

This procedure involves the insertion of a needle-electrode (a special type of needle) through the chest into one or more areas of the lung that are affected by cancer. Once the needle-electrode is in the correct position, it releases heat to destroy ("ablate") the cancer. Heat is produced by electromagnetic ("radiofrequency") waves.

Introduction

This overview has been prepared to assist members of the Interventional Procedures Advisory Committee (IPAC) in making recommendations about the safety and efficacy of an interventional procedure. It is based on a rapid review of the medical literature and specialist opinion. It should not be regarded as a definitive assessment of the procedure.

Date prepared

This overview was prepared in January 2006.

Procedure names

- Percutaneous radiofrequency ablation for primary and secondary lung cancers
- Radiofrequency thermal ablation for primary and secondary lung cancers

Specialty societies

- British Thoracic Society
- British Society of Interventional Radiology
- Royal College of Radiologists
- Society of Cardiothoracic Surgeons of Great Britain and Ireland

Description

Indications:

Lung cancers (primary and secondary)

Lung cancer is the one of the most common types of cancer in the UK and the main cause is tobacco smoking. There are two main types of lung cancers: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). NSCLC is further divided histologically into three main subtypes: squamous cell carcinoma, adenocarcinoma and large cell carcinoma.

Symptoms and signs of lung cancer may include cough, shortness of breath, wheezing, haemoptysis, pneumonia, atelectasis (collapsed lung), pleural effusion and chest pain.

The stage (or extent) of the disease is the most important prognostic factor in lung cancer. The overall prognosis of patients with lung cancer is poor, particularly for SCLC. In patients with NSCLC tumours, prognosis is comparatively better for squamous cell tumours.

The lung is also a common site for deposition of tumours that originate from other parts of the body, including primary tumours in another part of the lung (known as lung metastases or secondary lung cancer). The prognosis of metastatic disease of the lung is usually poor.

Current treatment and alternatives

The treatment of lung cancer depends mainly on the histology of the tumour and stage of the disease, and may include surgical resection of the tumour, chemotherapy, radiotherapy, or a combination of these treatment modalities.

SCLC is usually inoperable and treated with chemotherapy and/or radiotherapy because the tumour has often spread by the time it is diagnosed. NSCLC may be detected while it is still localised, and for these patients surgery can provide a good chance of long-term disease free survival in patients with very early stage disease. Standard surgical approaches include thoracotomy (opening of the chest wall) and median sternotomy (cutting through the breastbone). Tumours may be resected by lobectomy (removal of a lobe of the lung), or by wedge resection (for peripheral lung tumours), with or without regional lymphadenectomy (removal of one or more lymph nodes).

Video-assisted thoracic surgery (VATS) is a less invasive surgical procedure that requires a smaller incision than those needed for thoracotomy or sternotomy. The technique uses a video camera to visualise and operate on the lung within the chest cavity and may be performed under computed tomography (CT) guidance. A further development is percutaneous (through the skin) insertion of wires under CT guidance, which may be used to identify lung tumour nodules and assist VATS, particularly in cases requiring wedge resection.

Interventional bronchoscopic treatments for the management of malignant endotracheal or endobronchial obstructions include diathermy, laser therapy, cryotherapy, brachytherapy, and photodynamic therapy.

What the procedure involves:

Percutaneous radiofrequency ablation (RFA) for lung cancer is usually performed under local anaesthesia with conscious sedation. Less frequently, either regional or general anaesthesia may be used. The procedure involves inserting a small needle electrode through the skin directly into the tumour, usually under CT guidance. Radiofrequency energy, consisting of an alternating electrical current in the frequency of radiowaves, is passed through the electrode producing heat at the tip of the needle electrode which coagulates and destroys the tumour tissue in the target area. A small margin of normal tissue next to the tumour is also destroyed to reduce the chance of any tumour cells remaining.

The procedure can be repeated and used alone or in combination with surgery, radiotherapy or chemotherapy. Patients usually go home on the same day or the day after the procedure.

Percutaneous RFA may be useful in patients with small, early-stage lung cancer who are not suitable for surgery or who do not wish to undergo conventional surgery, or for patients with a small number of lung metastases.

Efficacy:

Efficacy of the procedure is based on 8 case series involving 263 patients and an international survey including 493 percutaneous RFA procedures. Most of the evidence relates to patients with metastatic tumours.

Tumour response

In six case series^{1-5,7}, complete tumour response rates varied between 38% (12/32) and 98% (44/45) of primary or metastatic lung tumours. In general, tumour response rates were greater for small tumours (usually defined as those ≤ 3 cm in diameter)^{3,4}.

In a case series³ of 31 patients with 54 tumours (13 primary, 41 metastatic), no significant difference in complete tumour response rates was found between primary (46%) and metastatic (63%) tumours.

Survival

One-year survival was 85% in a series³ of 31 patients with 54 tumours. In this study, survival by tumour type was 89% for primary tumours and 84% for metastatic tumours, and by tumour size was 94% for tumours 3 cm or less and 74% for tumours more than 3cm in diameter. Mean survival in this cohort was 8.6 months.

In another case series⁷, 40% (12/30) of patients with various stages of non-small cell lung cancer survived at a mean follow-up of 15 months. Mean survival of patients by tumour response was significantly different between patients who had complete tumour necrosis (19.7 months) and patients with partial tumour necrosis (8.7 months). No difference in mean survival was found between patients with tumour size of less than 3 cm and those with tumour size of more than 3 cm.

Quality of life

Quality of life (as assessed by SF-36 v2) was found to be significantly reduced at 1 month after RFA treatment compared to pre-treatment values (physical summary scores, $P < 0.001$; mental summary scores, $P = 0.047$) in a study⁵ of 20 patients with lung metastases from colorectal cancer. However, quality of life was not found to be significantly different to pre-treatment values in subsequent follow-up (up to 1 year), except on the physical functioning subscale ($P=0.008$ at 1 year).

International survey

In an international survey of 7 centres⁹, the procedure was found to be predominantly performed under local anaesthesia with conscious sedation. General anaesthesia was used for ablation of multiple or large lesions. In terms of inpatient observation after the procedure, 4 centres reported that they routinely observed their patients for a few hours and treat them on an outpatient basis, while 2 centres routinely observed their patients overnight and 1 centre observed their patients for more than 24 hours.

Specialist advisor comments

The specialist advisors stated that long-term efficacy of the procedure is unknown. Relevant efficacy outcomes include post-procedure mortality, long-term survival, respiratory morbidity, need for repeat interventions, and local control of pulmonary metastatic disease.

Safety:

Complications

Pneumothorax was the most commonly reported complication and ranged between 9% (3/33) to 65% (13/20) of patients based on 8 case series¹⁻⁸. In 6 of these studies^{1-3, 5,6,8}, the proportion of patients who had pneumothoraces requiring chest tube insertion ranged between 3% (1/30) to 16% (5/31) of patients. In one case series⁷, subcutaneous emphysema was reported in 10% (3/30) of patients.

In one case series¹, haemothorax was reported in 2% (1/54) of treatment sessions, while another study⁸ reported haemothorax in 2% (1/50) of patients. Pleural effusion with reported pain was reported in 4% (2/54) of treatment sessions in one study¹, while asymptomatic pleural effusion was reported in 9% (3/33) of patients to 27% (12/45) of treatment sessions in 4 case series^{2,4,5,7}.

Other reported complications include:

- Haemoptysis (3% to 13% of patients)
- Fever (2% to 30% of patients)
- Chest pain (10% of patients to 24% of treatment sessions)
- Cough /haemoptysis /expectoration of necrotic lung tissue (4% to 33% of patients)
- Pneumonia (7% to 12% of patients)
- Lung abscess formation (2% of treatment sessions to 6% of patients)
- Skin burn at probe insertion site (3% of patients)
- Hoarseness of voice (3% of patients)
- Myalgia (3% of patients)
- Dyspnoea (reported to occur occasionally after the procedure)

There were no reports of procedure-related deaths in the 8 case series reviewed.

International survey

In an international survey of 7 centres⁹, minor complications (including small pneumothoraces, small pleural effusions, small intraparenchymal haemorrhages) not requiring further intervention, and large pneumothoraces requiring chest tube insertion were both reported to occur in up to 30% of procedures. Pleural effusions requiring aspiration was generally reported in less than 10% of procedures. There were 2 deaths (0.4%) among the 493 procedures reported, although the causes of death were not stated.

Specialist advisor comments

The specialist advisors stated that the procedure is relatively safe. Pneumothorax is common, but often does not require intervention. Theoretical adverse events include bronchopulmonary fistulae, arteriovenous fistulae and seeding of the tumour.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous radiofrequency ablation for primary and secondary lung cancers. Searches were conducted via the following databases, covering the period from their commencement to January 2006. Medline, PreMedline, EMBASE, Cochrane Library and other databases. Trial registries and the Internet were also searched. No language restriction was applied to the searches. (See Appendix C for details of search strategy.)

The following selection criteria (Table 1) were applied to the abstracts identified by the literature search. Where these criteria could not be determined from the abstracts the full paper was retrieved

Table 1 Inclusion criteria for identification of relevant studies

Characteristic	Criteria
Publication type	Clinical studies were included. Emphasis was placed on identifying good quality studies. Abstracts were excluded where no clinical outcomes were reported, or where the paper was a review, editorial, laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising methodology.
Patient	Patients with primary and secondary lung cancers
Intervention/test	Percutaneous radiofrequency ablation
Outcome	Articles were retrieved if the abstract contained information relevant to the safety and/or efficacy.
Language	Non-English-language articles were excluded unless they were thought to add substantively to the English-language evidence base.

List of studies included in the overview

This overview is based on 8 uncontrolled case series and an international survey.

Other studies that were considered to be relevant to the procedure but were not included in the main extraction table (Table 2) have been listed in Appendix A.

Existing reviews on this procedure

No published systematic reviews on percutaneous RFA for the treatment of lung cancer were identified at the time of the literature search.

Related NICE Guidance:

Below is a list of NICE guidance related to this procedure. Appendix B details the recommendations made in each piece of guidance listed below.

Interventional Procedures:

Interventional procedures guidance no. IPG087 has been issued in August 2004 on “photodynamic therapy for advanced bronchial carcinoma” and covers the treatment of inoperable non-small cell lung cancer.

Interventional procedures guidance no. IPG142 has been issued in November 2005 on “cryosurgery for malignant endobronchial obstruction”, mainly for the palliative treatment of advanced lung cancer.

Technology Appraisals:

None applicable

Clinical Guidelines:

Clinical Guideline no. CG24 entitled “Lung cancer: the diagnosis and treatment of lung cancer” has been issued in February 2005. This guideline covers adults older than 18 years of age, who are suspected of having, or are diagnosed with, lung cancer. It does not cover the diagnosis and treatment of lung metastases.

Public Health:

None applicable

Table 2 Summary of key efficacy and safety findings on percutaneous radiofrequency ablation for primary and secondary lung cancers

Abbreviations used: CT, computed tomography; Ctr, centre; FDG, fluorodeoxyglucose; NSCLC, non small cell lung cancer; PET, positron emission tomography; RFA, radiofrequency ablation																																																		
Study Details			Key efficacy findings	Key safety findings	Comments																																													
<p>Yasui K et al. (2004)¹</p> <p>Prospective case series (Jun 2001 to Nov 2002) Japan</p> <p>35 patients with unresectable malignant thoracic tumours (95 lung, 4 pleural) 99 tumours (3 primary and 96 secondary) Mean age 65 (range 34-83) years</p> <table border="1"> <thead> <tr> <th>Tumour type</th> <th>Based on tumours (n=99)</th> <th>Based on patients (n=35)</th> </tr> </thead> <tbody> <tr> <td>Primary</td> <td>3</td> <td>3</td> </tr> <tr> <td>Secondary</td> <td>96</td> <td>32</td> </tr> <tr> <td>- lung cancer</td> <td>19</td> <td>10</td> </tr> <tr> <td>- colorectal cancer</td> <td>23</td> <td>6</td> </tr> <tr> <td>- renal cancer</td> <td>21</td> <td>4</td> </tr> <tr> <td>- synovial sarcoma</td> <td>10</td> <td>1</td> </tr> <tr> <td>- hepatocellular carcinoma</td> <td>6</td> <td>2</td> </tr> <tr> <td>- osteosarcoma</td> <td>3</td> <td>1</td> </tr> <tr> <td>- maxillary cancer</td> <td>3</td> <td>1</td> </tr> <tr> <td>- parathyroid cancer</td> <td>4</td> <td>1</td> </tr> <tr> <td>- oesophageal cancer</td> <td>3</td> <td>3</td> </tr> <tr> <td>- urachal cancer of the bladder</td> <td>1</td> <td>1</td> </tr> <tr> <td>- adenoid cystic carcinoma of external auditory canal</td> <td>1</td> <td>1</td> </tr> <tr> <td>- peritoneal carcinoma</td> <td>2</td> <td>1</td> </tr> </tbody> </table> <p>Mean tumour size = 19.5 ± 12.6 (range 3-80) mm Previous treatments (based on patients): surgical resection of primary tumours (n=26), radiotherapy for primary tumour (n=2), chemotherapy (n=1). Mean follow-up = 7.1 (range 1-17) months Disclosure of interest: not specified.</p>			Tumour type	Based on tumours (n=99)	Based on patients (n=35)	Primary	3	3	Secondary	96	32	- lung cancer	19	10	- colorectal cancer	23	6	- renal cancer	21	4	- synovial sarcoma	10	1	- hepatocellular carcinoma	6	2	- osteosarcoma	3	1	- maxillary cancer	3	1	- parathyroid cancer	4	1	- oesophageal cancer	3	3	- urachal cancer of the bladder	1	1	- adenoid cystic carcinoma of external auditory canal	1	1	- peritoneal carcinoma	2	1	<p>Technical success of procedure (appearance of ground-glass attenuation of the surrounding normal lung parenchyma on CT scan immediately after percutaneous RFA):</p> <ul style="list-style-type: none"> 100% of tumours <p>54 treatment sessions (visits to the interventional CT suite) were performed in 35 patients. Multiple sessions performed in 15 patients for multiple tumours and/or local recurrence.</p> <p>Tumour response after first procedure (assessed by CT):</p> <ul style="list-style-type: none"> Complete necrosis = 91% (90/99) tumours in 29 patients; mean pre-treatment tumour size 19.5 ± 13 mm Residual tumour/ local recurrence = 9% (9/99) tumours in 6 patients with lung metastases; mean pre-treatment tumour size 19.6 ± 7.7 mm (Retreatment was performed on 8 of the 9 residual tumours in 5 patients at 1-7 months after the first percutaneous RFA treatment.) <p>Tumour response at 2 months (assessed by needle biopsy on 33 tumours in 21 patients):</p> <ul style="list-style-type: none"> No viable tumour cells = 20/33 tumours Local tumour recurrence observed on CT scan in 1 tumour at 4 months (with retreatment), and 2 tumours at 4 and 6 months. Residual tumour cells = 13/33 tumours (however, 5 were considered "ghost cells" by pathologist) Second procedure was performed in 6 of the 13 residual tumours (4 patients). Retreatment was not performed in the other 7 tumours due to decrease in sustainability of the nuclei of the tumour cells. <p>Biopsies were performed in a total of 36 tumours in 21 patients including those at 2 months: (4 tumours in 4 patients at 4 months; 3 tumours in 3 patients at 6 months; 3 tumours in 1 patient at 7 months; 1 tumour in 1 patient at 9 months. 5 patients had repeat biopsies.</p>	<p>During the procedure:</p> <ul style="list-style-type: none"> All patients tolerated the procedure well except for 1 patient with right apical subpleural tumour treated under local anaesthesia who had severe pain during the procedure Pain = 29% (29/99) of tumours <p>Overall complication rate (based on treatment sessions):</p> <ul style="list-style-type: none"> 76% (41 of 54 sessions) <p>Complications (based on sessions):</p> <ul style="list-style-type: none"> Pneumothorax (mild) = 35% (19/54) Pneumothorax (requiring chest tube) = 7% (4/54) Fever higher than 37.5°C = 22% (12/54) Haemoptysis = 11% (6/54) Cough = 4% (2/54) Pleural effusion with pain = 4% (2/54) Lung abscess formation = 2% (1/54) Haemothorax = 2% (1/54) <p>Deaths No patient died of progression of thoracic lesions.</p> <p>6 patients died (3 - extrapulmonary causes, 1 - brain metastases from hepatocellular carcinoma, 1 - brain metastases from sigmoid colon cancer, 1 - suddenly during haemodialysis)</p>	<p>Patients were selected by consensus between interventional radiologists and thoracic surgeons.</p> <p>Epidural anaesthesia was used in the early period of the study due to severe pain experienced by a patient treated for right apical subpleural tumour under local anaesthesia. Subsequently, local anaesthesia with conscious sedation was found to be generally adequate for tumours that were not immediately beneath the pleura.</p>
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Abbreviations used: CT, computed tomography; Ctr, centre; FDG, fluorodeoxyglucose; NSCLC, non small cell lung cancer; PET, positron emission tomography; RFA, radiofrequency ablation			
Study Details	Key efficacy findings	Key safety findings	Comments
<p>Gadaleta C et al. (2004)²</p> <p>Prospective case series (Feb 2002 to May 2004)</p> <p>Italy</p> <p>34 patients with lung cancers 69 tumours (7 primary NSCLC, 62 secondary)</p> <p>Total 45 treatment sessions performed in 34 patients (1 session = 74% (25/34); 2 sessions= 21% (7/34); 3 sessions =6% (2/34))</p> <p>Median number of treated lesions per patient = 1 (range 1 -7)</p> <p>Gender: 22 male, 12 female Median age: 67 (range 26-81) years</p> <p>Tumour type (based on patients)</p> <ul style="list-style-type: none"> • Primary (NSCLC): 6 • Secondary 28 <ul style="list-style-type: none"> colorectal cancer 14 bladder cancer 2 breast cancer 2 malignant melanoma 2 Other 8 <p>Tumour size (maximum diameter)</p> <ul style="list-style-type: none"> • 0.5-3 cm = 77% (53/59) • 3-5 cm = 17% (12/59) • 5 cm = 6% (4/69) <p>Median tumour size = 2.7 (range 0.5-11) cm</p> <p>Previous treatment Surgery for lung cancer (3 patient), chemotherapy (32 patient), hormonal therapy (1 patient).</p> <p>Median follow-up: 9 (range 3-25) months</p> <p>Declaration of interest: not specified</p>	<p>Overall tumour response (assessed by contrast-enhanced CT and NMR)</p> <p>Note: the first 8 patients were assessed by CT only, while the following 26 patients were assessed by CT and NMR. There were 30 evaluable patients with 63 tumours</p> <ul style="list-style-type: none"> • Complete response = 92% (58/63) of tumours • Tumour relapse = 8% (5/63) of tumours (2 local recurrence, 3 local recurrence plus in distant sites; 3 tumours were > 3.5 cm) <p>Retreatment: 1 patient with NSCLC and early local recurrence was successfully retreated with 10 months progression-free interval. The patient died 18 months after the second treatment of metastatic disease in other distant sites.</p> <p>Survival at follow-up</p> <ul style="list-style-type: none"> • Disease-free = 9 patients • Progressive disease = 15 patients • Died = 10 patients <p>Median hospitalisation time after the procedure = 6 (range 3-13) days</p>	<p>Complications of the procedure (based on treatment sessions):</p> <ul style="list-style-type: none"> • Pneumothorax requiring pleural drainage = 16% (7/45) • Cough with rust-coloured spitting = 33% (15/45) • Asymptomatic pleural effusion = 27% (12/45) • Thoracic pain = 24% (11/45) • Moderate-grade fever = 18% (8/45) <p>There were no treatment-related deaths</p>	<p>The study mainly included patients with lung metastases.</p> <p>All patients had treatment for malignancies prior to percutaneous RFA.</p> <p>Tumour responses for primary and secondary tumours were not reported separately.</p> <p>General anaesthesia was used and was considered by the authors to facilitate the procedure by reducing movement of the patients and allowing the control of airway flow in the event of a massive pneumothorax or serious haemorrhage.</p>

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<p>Akeboshi M et al. (2004)³</p> <p>Case series (Jan 2002 to March 2003)</p> <p>Japan</p> <p>31 patients with unresectable lung cancers 54 tumours (13 primary or 41 secondary)</p> <p>Gender: male 23, female 8 Mean age: 69 ± 11 years</p> <p>Previous treatment</p> <ul style="list-style-type: none"> • Surgery = 52% (16/31) • Chemotherapy = 90% (28/31) • Chemotherapy + radiotherapy = 23% (7/31) <table border="1"> <thead> <tr> <th>Tumour type</th> <th>Based on tumours (n=54)</th> <th>Based on patients (n=31)</th> </tr> </thead> <tbody> <tr> <td>Primary (NSCLC)</td> <td>13 (24%)</td> <td>10 (32%)</td> </tr> <tr> <td>Secondary</td> <td>41 (76%)</td> <td>21 (68%)</td> </tr> <tr> <td>- colorectal</td> <td>25 (46%)</td> <td>13 (42%)</td> </tr> <tr> <td>- hepatocellular carcinoma</td> <td>2 (4%)</td> <td>2 (6%)</td> </tr> <tr> <td>- renal cell carcinoma</td> <td>3 (6%)</td> <td>2 (6%)</td> </tr> <tr> <td>- bladder cancer</td> <td>1 (2%)</td> <td>1 (3%)</td> </tr> <tr> <td>- pancreatic cancer</td> <td>4 (7%)</td> <td>1 (3%)</td> </tr> <tr> <td>- pharyngeal cancer</td> <td>3 (6%)</td> <td>1 (3%)</td> </tr> <tr> <td>- retroperitoneal leiomyosarcoma</td> <td>3 (6%)</td> <td>1 (3%)</td> </tr> </tbody> </table> <p>Distant metastases other than the lung present in 23% (7/31) of patients</p> <table border="1"> <thead> <tr> <th>Tumour size</th> <th>Based on tumours (n=54)</th> <th>Based on patients (n=31)</th> </tr> </thead> <tbody> <tr> <td>Mean tumour size = 2.7 ± 1.3 (range 0.7-6) cm</td> <td></td> <td></td> </tr> <tr> <td>≤ 3 cm</td> <td>36 (67%)</td> <td>17 (55%)</td> </tr> <tr> <td>> 3 cm</td> <td>18 (33%)</td> <td>14 (45%)</td> </tr> </tbody> </table> <p>Mean follow-up = 9.2 (range 5-18) months</p> <ul style="list-style-type: none"> • 3 to 6 months = 26% (8/31) • > 6 months to 1 year = 45% (14/31) • > 1 year = 29% (9/31) <p>No conflict of interest was declared by authors.</p>	Tumour type	Based on tumours (n=54)	Based on patients (n=31)	Primary (NSCLC)	13 (24%)	10 (32%)	Secondary	41 (76%)	21 (68%)	- colorectal	25 (46%)	13 (42%)	- hepatocellular carcinoma	2 (4%)	2 (6%)	- renal cell carcinoma	3 (6%)	2 (6%)	- bladder cancer	1 (2%)	1 (3%)	- pancreatic cancer	4 (7%)	1 (3%)	- pharyngeal cancer	3 (6%)	1 (3%)	- retroperitoneal leiomyosarcoma	3 (6%)	1 (3%)	Tumour size	Based on tumours (n=54)	Based on patients (n=31)	Mean tumour size = 2.7 ± 1.3 (range 0.7-6) cm			≤ 3 cm	36 (67%)	17 (55%)	> 3 cm	18 (33%)	14 (45%)	<p>Technical success of the procedure (defined as achievement of break at least one time at each location):</p> <ul style="list-style-type: none"> • Achieved in all tumours <p>Tumour response (assessed by FDG-PET & contrast-enhanced CT):</p> <p>Complete response Initial response after first treatment:</p> <ul style="list-style-type: none"> • 59% (32/54) of tumours, or 61% (19/31) of patients <p>By tumour type (based on tumours):</p> <ul style="list-style-type: none"> • Primary = 46%; • Secondary = 63% (no significant difference, P=0.34) <p>By tumour size (based on tumours):</p> <ul style="list-style-type: none"> • ≤ 3 cm = 69% • > 3 cm = 39% (significant difference, P=0.04) <p>10 tumours (31%) reduced in size at follow-up.</p> <table border="1"> <thead> <tr> <th>Time</th> <th>Mean tumour size</th> <th>Change from pre-treatment</th> </tr> </thead> <tbody> <tr> <td>Before RFA</td> <td>2.3 ± 1.2 cm</td> <td></td> </tr> <tr> <td>At 1 week</td> <td>3.6 ± 1.5 cm</td> <td>P <0.01</td> </tr> <tr> <td>At 1 month</td> <td>3.6 ± 1.4 cm</td> <td>P <0.05</td> </tr> <tr> <td>At 3 months</td> <td>2.6 ± 1.2 cm</td> <td></td> </tr> </tbody> </table> <p>At the end of follow-up after re-treatment:</p> <ul style="list-style-type: none"> • 69% (37/54) of tumours <p>This includes 5 of 13 tumours that responded to retreatment at 3-6 months (mean 4.5 months)</p> <p>Partial response (residual tumours) Initial residual tumours:</p> <ul style="list-style-type: none"> • 41% (22/54) of tumours <p>2 residual tumours (9%) reduced in size at follow-up.</p> <table border="1"> <thead> <tr> <th>Time</th> <th>Mean tumour size</th> <th>Change from pre-treatment</th> </tr> </thead> <tbody> <tr> <td>Before RFA</td> <td>3.2 ± 1.3 cm</td> <td></td> </tr> <tr> <td>At 1 week</td> <td>4.7 ± 1.5 cm</td> <td><0.01</td> </tr> <tr> <td>At 1 month</td> <td>4.1 ± 1.7 cm</td> <td></td> </tr> <tr> <td>At 3 months</td> <td>4.0 ± 1.7 cm</td> <td></td> </tr> </tbody> </table> <p>At the end of follow-up after re-treatment:</p> <ul style="list-style-type: none"> • 31% (17/54) of tumours <p>Survival rate - see "Key safety findings" column</p>	Time	Mean tumour size	Change from pre-treatment	Before RFA	2.3 ± 1.2 cm		At 1 week	3.6 ± 1.5 cm	P <0.01	At 1 month	3.6 ± 1.4 cm	P <0.05	At 3 months	2.6 ± 1.2 cm		Time	Mean tumour size	Change from pre-treatment	Before RFA	3.2 ± 1.3 cm		At 1 week	4.7 ± 1.5 cm	<0.01	At 1 month	4.1 ± 1.7 cm		At 3 months	4.0 ± 1.7 cm		<p>Continued from "Key efficacy findings":</p> <p>Survival rate</p> <ul style="list-style-type: none"> • 3 patients died due to pneumonia (1), ileus (1), brain metastases (1) • Mean survival = 8.6 months • 1-year survival rate = 85% <p>1-year survival rate by tumour type, size, number and response:</p> <table border="1"> <thead> <tr> <th></th> <th>n (%)</th> <th>1-year survival rate (%)</th> <th>P-value</th> </tr> </thead> <tbody> <tr> <td>Tumour type:</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Primary</td> <td>10(32)</td> <td>89</td> <td>0.76</td> </tr> <tr> <td>Secondary</td> <td>21(68)</td> <td>84</td> <td></td> </tr> <tr> <td>Tumour size</td> <td></td> <td></td> <td></td> </tr> <tr> <td>≤ 3 cm</td> <td>17(55)</td> <td>94</td> <td>0.43</td> </tr> <tr> <td>> 3 cm</td> <td>14(45)</td> <td>74</td> <td></td> </tr> <tr> <td>Tumour no.</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Single</td> <td>16(52)</td> <td>91</td> <td>0.67</td> </tr> <tr> <td>Multiple</td> <td>15(48)</td> <td>93</td> <td></td> </tr> <tr> <td>Tumour response</td> <td></td> <td></td> <td></td> </tr> <tr> <td>Complete</td> <td>19(61)</td> <td>81</td> <td>0.92</td> </tr> <tr> <td>Residual</td> <td>12(39)</td> <td>91</td> <td></td> </tr> </tbody> </table> <p>Complications of the procedure (based on patients):</p> <p>Pneumothorax = 29% (9/31), of these patients</p> <ul style="list-style-type: none"> • 5 (56%) required chest drainage • 2 (22%) patients with large tumours greater than 5 cm developed lung abscess <p>No other complications were reported in the article.</p>		n (%)	1-year survival rate (%)	P-value	Tumour type:				Primary	10(32)	89	0.76	Secondary	21(68)	84		Tumour size				≤ 3 cm	17(55)	94	0.43	> 3 cm	14(45)	74		Tumour no.				Single	16(52)	91	0.67	Multiple	15(48)	93		Tumour response				Complete	19(61)	81	0.92	Residual	12(39)	91		<p>The study includes primary and secondary lung cancers.</p> <p>The procedure was performed under local anaesthesia.</p> <p>All patients were discharged within 10 days after the procedure, except for the 2 patients who had lung abscess.</p> <p>Tumour size was found to be an important factor in achieving complete tumour necrosis with a significantly higher percentage of complete tumour necrosis in tumours 3 cm or less.</p> <p>The authors suggest that tumour type (primary or secondary) did not influence complete necrosis rates.</p>
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IP overview: percutaneous radiofrequency ablation for primary and secondary lung cancers (February 2005)

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<p>Belfiore G et al. (2004)⁴</p> <p>Case series (beginning in March 2002)</p> <p>Italy</p> <p>33 patients with 35 unresectable primary lung cancers</p> <p>Gender: 26 male, 7 female Mean age: 66 (range 44-75) years</p> <p>Tumour type (all primary)</p> <ul style="list-style-type: none"> Adenocarcinoma = 21 patients Squamous cell carcinoma = 11 patients Small cell carcinoma = 1 patient <p>Patients were grouped on the basis of tumour size</p> <ul style="list-style-type: none"> Group 1 (< 3 cm) = 12 patients Group 2 (3-5 cm) = 19 patients Group 3 (> 5 cm) = 2 patients <p>Patients were also stratified using a clinical scoring system developed ad hoc to measure pain, coughing and dyspnoea.</p> <p>Clinical or radiological signs of active disease after chemotherapy or radiotherapy found in 15 of 33 patients.</p> <p>Inclusion criteria Patients with unresectable primary lung tumours at any disease stage and any thoracic location.</p> <p>Patients were not candidates for surgery due to the disease stage, comorbid medical or pulmonary dysfunction, or patient refused surgery.</p> <p>Exclusion criteria Patients with coagulation disorders, distant metastases, involvement of thoracic wall or massive invasion of mediastinum.</p> <p>Follow-up to 1 year Disclosure of interest: not specified</p>	<p>Technical success of procedure (defined as treatment performed according to protocol)</p> <ul style="list-style-type: none"> Achieved in all 35 tumours <p>Tumour response (assessed by contrast-enhanced CT) One patient had re-treatment of a lesion at 3 and 6 months after the initial ablation.</p> <p>At 6 months (assessed in 29 patients):</p> <table border="1"> <thead> <tr> <th></th> <th>Reduced tumour size, n=17 (59%)</th> <th>Unchanged tumour size, n=11 (38%)</th> <th>Increased tumour size, n=1 (3%)</th> </tr> </thead> <tbody> <tr> <td>Group 1 (n=12)</td> <td>9 (75%)</td> <td>3 (25%)</td> <td>0</td> </tr> <tr> <td>Group 2 (n=16)</td> <td>7 (44%)</td> <td>8 (50%)</td> <td>1 (6%)</td> </tr> <tr> <td>Group 3 (n=1)</td> <td>1 (100%)</td> <td>0</td> <td>0</td> </tr> <tr> <td>Complete necrosis</td> <td>4 (23.5%)</td> <td></td> <td></td> </tr> <tr> <td>Partial necrosis</td> <td>13 (76.5%)</td> <td></td> <td></td> </tr> </tbody> </table> <p>At 1 year (assessed in 10 patients) compared to CT scan at 6 months:</p> <table border="1"> <thead> <tr> <th></th> <th>Reduced tumour size (n=4)</th> <th>Unchanged tumour size (n=6)</th> </tr> </thead> <tbody> <tr> <td>Group 1 (n=5)</td> <td>3 (60%)</td> <td>2 (40%)</td> </tr> <tr> <td>Group 2 (n=4)</td> <td>1 (25%)</td> <td>3 (75%)</td> </tr> <tr> <td>Group 3 (n=1)</td> <td>0</td> <td>1 (100%)</td> </tr> </tbody> </table> <p>Tumour response (assessed by fine needle aspiration biopsy or core biopsy)</p> <p>At 6 months, assessed in 19 of 29 patients:</p> <ul style="list-style-type: none"> Complete necrosis = 7 (37%) [note: article states 36%] <ul style="list-style-type: none"> Group 1 (5 patients); Group 2 (2 patients) Partial necrosis = 12 (63%) <ul style="list-style-type: none"> Group 2 (11 patients); Group 3 (1 patient) <p>Clinical improvement in pre-treatment symptoms</p> <ul style="list-style-type: none"> At 6 months, observed in 12 of 29 patients <p>Survival rate (see "Key safety findings" column)</p>		Reduced tumour size, n=17 (59%)	Unchanged tumour size, n=11 (38%)	Increased tumour size, n=1 (3%)	Group 1 (n=12)	9 (75%)	3 (25%)	0	Group 2 (n=16)	7 (44%)	8 (50%)	1 (6%)	Group 3 (n=1)	1 (100%)	0	0	Complete necrosis	4 (23.5%)			Partial necrosis	13 (76.5%)				Reduced tumour size (n=4)	Unchanged tumour size (n=6)	Group 1 (n=5)	3 (60%)	2 (40%)	Group 2 (n=4)	1 (25%)	3 (75%)	Group 3 (n=1)	0	1 (100%)	<p>Continued from "Key efficacy findings":</p> <p>Survival rate</p> <p>At 6 months: 4 patients died (Group 2 = 3; Group 3 = 1) due to hepatic failure (2), heart failure (1), and massive extrathoracic tumour growth (1)</p> <p>More than 6 months to 1 year: 4 patients died due to hepatic failure (1), heart failure (1), and massive extrathoracic tumour growth (2)</p> <p>Overall: 8 patients died within 1 year of non-RFA-related causes</p> <p>Complications during procedure:</p> <ul style="list-style-type: none"> Sputum cruentum = 14% (5 patients) Pneumothorax = 9% (3 patients) Pleural effusion (asymptomatic) = 9% (3 patients) 	<p>The study presents preliminary assessment of CT-guided percutaneous RFA for the palliative treatment of unresectable primary lung cancers.</p> <p>The procedure was performed under local anaesthesia.</p> <p>A clinical scoring system was used to measure pain</p>
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<p>King J et al. (2004)⁵</p> <p>Prospective case series (Nov 2000 to Sep 2002)</p> <p>Australia</p> <p>20 patients with 45 colorectal cancer lung metastases</p> <p>Gender: 13 male, 7 female Median age: 65 (range 29-77) years</p> <p>17 patients had liver metastases that had been surgically resected or treated successfully with regional chemotherapy.</p> <p>Exclusion criteria Patients with > 10 lesions, tumour diameter > 3.5 cm, coagulopathy emphysematous bullae, lesions close to the hilum of the lung and/or large vessels, previous surgery or radiotherapy to the affected lung, excepted survival 3 months or less, age less than 18 or more than 85 years, and significant compromised lung function.</p> <p>Protocol violations 2 patients (one patient with previous pneumonectomy and one treated with radiotherapy for lung metastases in the lung contralateral to that treated by percutaneous RFA)</p> <p>Median follow-up = 730 (range 148-924) days (includes 14 patients at 9 months, 11 patients at 12 months)</p> <p>Disclosure of interest: equipment and partial financial support was provided by the manufacturer of the RFA device.</p>	<p>During the procedure:</p> <ul style="list-style-type: none"> • Mean number of lung metastases visible on CT = 2.7 ± 2.2 (range 1-7) • Mean number of lung metastases treated = 1.8 ± 1.0 <p>The difference was due to uncertainty early in the study regarding safety of treating multiple metastases in patients who had only the largest metastases ablated for palliation.</p> <p>Success of procedure (definition not specified):</p> <ul style="list-style-type: none"> • Successfully treated = 98% (44/45) of tumours in 95% (19/20) of patients at a total of 25 sessions 4 of the 19 successfully treated patients received IV chemotherapy at the time of the procedure. • Unsuccessful = 2% (1/45) of tumour in 5% (1/20) of patients at a total of 25 sessions The 1 unsuccessfully treated patient underwent surgical resection and died 412 days after RFA. <p>Tumour response (assessed by CT)</p> <p>At 6 months (39 tumours):</p> <ul style="list-style-type: none"> • Tumour not visible = 11 • Tumour stable or smaller = 25 • Tumour progression = 3 <p>At 12 months (25 tumours):</p> <ul style="list-style-type: none"> • Tumour not visible = 9 • Tumour stable or smaller = 11 • Tumour progression = 5 <p>Retreatment for recurrence: 2 patients at 12 and 22 months</p> <p>Retreatment for new lesions: 5 of 19 patients at 3, 6, 6, 12 and 13 months</p> <p>Serum carcinoembryonic antigen (CEA) concentration in 19 successfully treated patients: Proportion of patients with reduction in serum CEA was 38% (5/13) at 1 month, 53% (10/19) at 3 months, 39% (7/18) at 6 months, 36% (5/14) at 12 months.</p> <p>Quality of life (see "Key safety findings" column)</p>	<p>Continued from "Key efficacy findings":</p> <p>Quality of life (assessed by SF-36 v2) (data for second treatments were excluded)</p> <p>Of the 8 quality of life subscales, only physical functioning demonstrated a mean reduction from baseline at 1, 9 and 12 months.</p> <p>At 1 month, quality of life was significantly reduced for all subscales and for physical (P < 0.001) and mental (P=0.047) summary scores compared to pre-treatment.</p> <p>At 3 months, there were no significant changes from pre-treatment findings.</p> <p>At 1 year, only physical functioning subscale was significantly different from pre-treatment (P = 0.008)</p> <p>Key safety findings</p> <p>Treatment tolerability: 95% (19/20) patients tolerated the procedure well.</p> <p>Pleuritic pain developed in 1 patient with peripheral metastasis involving the pleura who was initially treated with only local anaesthetic and required IV sedation during treatment.</p> <p>Complications:</p> <ul style="list-style-type: none"> • Pneumothorax = 65% (13/20) of patients - 6 (46%) patients required chest tube insertion • Pleural effusion = 20% (4/20) of patients • Chest pain = 10% (2/20) of patients • Dyspnoea = in some patients, occasionally for few days after RFA (numbers not specified) • Fever = 30% (6/20) of patients • Expectorate small amounts of dessicated tissue = 10% (2/20) of patients at 1 month • Malignant pleural effusion = 5% (1/20) of patient at 6 months (patient died of lung, bone and cerebral disseminated disease) <p>Deaths: 9 patients died from disseminated disease at median 360 (range 148-730) days after RFA.</p>	<p>Patients received local anaesthetic alone (n=3) or with intravenous sedation and analgesia (n=17), and stayed in hospital for at least 24 hours after treatment.</p> <p>Patients with tumour recurrence or disseminated disease elsewhere were treated by surgery, chemotherapy or radiotherapy as required.</p> <p>Sedated patients who had lesions near the pleural surface required higher doses of IV pethidine-midazolam for pain relief.</p>

Abbreviations used: CT, computed tomography; Ctr, centre; FDG, fluorodeoxyglucose; NSCLC, non small cell lung cancer; PET, positron emission tomography; RFA, radiofrequency ablation			
Study Details	Key efficacy findings	Key safety findings	Comments
<p>vanSonnenberg E et al. (2005)⁶</p> <p>Case series</p> <p>USA</p> <p>30 patients with malignant thoracic lesions 36 lesions (18 primary, 11 secondary, 1 mesothelioma of pleura and 5 secondarily eroded, painful ribs who underwent ablation; 1 patient had 2 ablations)</p> <p>Gender: 17 male, 13 female Mean age: 64.5 (range 29-89) years</p> <p>Primary cancers: 13 patients with NSCLC, 5 patients with squamous cell carcinoma.</p> <p>Secondary cancers: 1 patient each with adenoid cystic carcinoma of parotid gland, the tongue, and lacrimal gland; squamous cell carcinoma of tongue; hepatocellular carcinoma; renal cell carcinoma; prostate carcinoma; cystosarcoma phylloides of the uterus; pleomorphic sarcoma and adenocarcinoma of colon (n=2).</p> <p>Selection criteria: Patients were non-surgical candidates, or had exhausted chemotherapy and radiotherapy options, or had refused surgery, or undergone unsuccessful surgery.</p> <p>Main indications for RFA were pain (n=11) and tumour cure or palliation (n=19).</p> <p>Previous treatment: surgery (n=15), chemotherapy (n=21), radiotherapy (n=13). Two patients had undergone attempted resection of their lesions without success.</p> <p>Adjunctive procedures: A variety was often used with percutaneous RFA.</p> <p>Follow-up = 2 to 26 months Disclosure of interest: not specified</p>	<p>Technical success of procedure: 100%</p> <p>Imaging technique: All patients had contrast-enhanced CT before and after treatment. 24 patients had PET before treatment, and 10 patients after treatment. 14 patients had MRI before treatment and 12 patients after treatment.</p> <p>Tumour response assessed by contrast-enhanced CT, PET and/or MRI</p> <p>After first procedure:</p> <ul style="list-style-type: none"> • Tumour necrosis of > 90% = 90% (26/29) of patients with lung lesions <p>A second procedure was performed in 18 of 24 patients in whom "roll off" was achieved.</p> <p>Tumour response was also assessed by needle biopsy in 28 patients.</p> <p>At 3 months in 19 patients assessed by contrast-enhanced CT (based on patients):</p> <ul style="list-style-type: none"> • Persistent necrosis = 68% (13/19) • Tumour shrinkage = 37% (7/19) • Cavitation = 32% (6/19) • Tumour recurrence = 5% (1/19) <p>The above findings were not reported in terms of tumours.</p> <p>Pain relief in patients treated for pain (n=11):</p> <ul style="list-style-type: none"> • Complete relief = 36% (4/11) patients • Partial relief = 64% (7/11) patients <p>Hospital stay Mean duration 1.8 (1 to 12) days; 87% (26/30) patients discharged 1 or 2 days after procedure</p>	<p>Complications:</p> <ul style="list-style-type: none"> • Pneumothorax = 8 patients (1 patient (12.5%) required chest tube placement) • Local skin burn (3rd degree) = 1 patient • Haemoptysis (self limiting) = 4 patients • Transient atrial fibrillation = 1 patient • Hoarseness = 1 patient (mild hoarseness persisted for 2 months) • Transient re-intubation (after extubation) = 2 patients (both patients had severe emphysema) <p>Deaths There were no procedure-related deaths</p> <p>4 patients died within 1 year of the procedure from extrathoracic spread of tumour (at 3, 4, 6, and 9.5 months)</p>	<p>Patient selection was determined by consensus among members consisting of an interventional radiologist, oncologist, thoracic surgeon and anaesthesiologist.</p> <p>Pain (n=11) and tumour cure or control (n=19) were the main indications for percutaneous RFA.</p> <p>As adjunctive procedures were often used with percutaneous RFA, it is difficult to differentiate efficacy and safety findings that are specifically related to percutaneous RFA.</p> <p>CT guidance and general anaesthesia were used in all patients except for one. Sonographic guidance and IV conscious sedation was used in the first patient.</p> <p>General anaesthesia was used routinely by the authors – reasons cited include lack of intraprocedural pain or movement by patients, and full respiratory control.</p>

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Study Details	Key efficacy findings	Key safety findings	Comments																																																																														
<p>Lee JM et al. (2004)⁷</p> <p>Prospective case series (May 2000 to Jun 2002) Korea</p> <p>30 patients with unresectable lung cancers 32 tumours (27 primary NSCLC in 26 patients, 5 metastases in 4 patients)</p> <p>Gender: 25 male, 5 female Mean age 65.2 (range 27-78) years</p> <p>7 patients had multiple courses of chemotherapy alone or with radiotherapy before RFA (metastatic (1), unresectable stage III or IV (6))</p> <p>Tumour type/stage (based on patients)</p> <ul style="list-style-type: none"> Primary (NSCLC) = 87% (26/30) <ul style="list-style-type: none"> Stage IA or IB = 33% (10/30) Stage IIB = 3% (1/30) Stage IIIA = 7% (2/30) Stage IIIB or IV = 43% (13/30) Metastases = 13% (4/30) <p>Primary tumours of metastases were colorectal cancer, choriocarcinoma, bile duct cancer, hepatocellular carcinoma. Primary tumours were resected 6-12 months prior to RFA in all patients.</p> <p>Tumour size Mean tumour size = 5.2 ± 2.4 (range 0.5-12) cm ≤ 3 cm: 19% (6/32) tumours > 3 cm: 81% (26/32) tumours</p> <p>Tumour location Periphery = 44% (14/32) tumours Central = 56% (18/32) tumours</p> <p>Inclusion criteria: Patients ineligible for surgery with histologically proven NSCLC or metastases (confirmed by biopsy); no coagulation disorders.</p> <p>Mean follow-up = 12.5 (1-24) months</p> <p>Disclosure of interest: not specified</p>	<p>Group 1 = Intent to cure: 10 (33%) patients with stage I tumours treated with intent to cure Group 2 = Palliative therapy: 20 (67%) patients (all other NSCLC and metastases)</p> <p>Tumour response (assessed by contrast-enhanced CT): Overall response in all lesions:</p> <ul style="list-style-type: none"> Complete necrosis = 38% (12/32) of lesions Partial (>50%) necrosis = 62% (20/32) of lesions <p>Response by treatment group:</p> <ul style="list-style-type: none"> Group 1 (n=10): <ul style="list-style-type: none"> Complete necrosis = 60% of lesions Partial necrosis = 40% of lesions Group 2 (n=20): <ul style="list-style-type: none"> Complete necrosis = 27% (6/22) of lesions Partial necrosis = 73% (16/22) of lesions <p>Response by tumour size at 6 months:</p> <table border="1"> <thead> <tr> <th>Tumour size</th> <th>Complete necrosis</th> <th>Partial (50-90%) necrosis</th> </tr> </thead> <tbody> <tr> <td>< 3 cm</td> <td>6 (100%)</td> <td>0</td> </tr> <tr> <td>3.1-5.0 cm</td> <td>5 (38%)</td> <td>8 (62%)</td> </tr> <tr> <td>> 5 cm</td> <td>1 (8%)</td> <td>12 (92%)</td> </tr> <tr> <td>Total</td> <td>12 (38%)</td> <td>20 (62%)</td> </tr> </tbody> </table> <p>Survival rate</p> <ul style="list-style-type: none"> Patients survived = 40% (12/30) patients at follow-up (mean 15.2 ± 5.1 (range 11-24) months) Patients died = 60% (18/30) patients during follow-up (mean 6.9 ± 5.8 (range 1-21) months) <p>Mean survival of patients by tumour response:</p> <ul style="list-style-type: none"> Complete necrosis = 19.7 ± 2 months Partial necrosis = 8.7 ± 1.8 months <p>Difference statistically significant, P<0.01</p> <p>Mean survival of patients by tumour size:</p> <ul style="list-style-type: none"> < 3 cm = 18.6 ± 2.2 months > 3 cm = 11.3 ± 1.8 months <p>Not significantly different, P=0.09.</p>	Tumour size	Complete necrosis	Partial (50-90%) necrosis	< 3 cm	6 (100%)	0	3.1-5.0 cm	5 (38%)	8 (62%)	> 5 cm	1 (8%)	12 (92%)	Total	12 (38%)	20 (62%)	<p>Continued from "Key efficacy findings":</p> <p>Survival rate</p> <p>Mean survival of patients by treatment group:</p> <ul style="list-style-type: none"> Group 1 = 80% patients alive at mean follow-up 14.8 ± 5 months Group 2 = 20% patients alive at mean follow-up 16.3 ± 5.8 months <p>Difference statistically significant, P<0.01</p> <p>Remaining 16 patients died (mean 5.6 ± 4.4 months)</p> <p>Complications of RFA (based on patients):</p> <table border="1"> <thead> <tr> <th rowspan="2"></th> <th colspan="2">Tumour location</th> <th rowspan="2">Total n (%)</th> <th rowspan="2">P</th> </tr> <tr> <th>C n=14 (%)</th> <th>P n=16 (%)</th> </tr> </thead> <tbody> <tr> <td>Major complications</td> <td></td> <td></td> <td>3(10)</td> <td></td> </tr> <tr> <td>Severe pneumothorax</td> <td>2(14)</td> <td>0</td> <td>2(7)</td> <td>.21</td> </tr> <tr> <td>Acute respiratory distress syndrome</td> <td>1(7)</td> <td>0</td> <td>1(3)</td> <td>.47</td> </tr> <tr> <td>Minor complications</td> <td></td> <td></td> <td>18(60)</td> <td></td> </tr> <tr> <td>Small pneumothorax</td> <td>5(36)</td> <td>2(13)</td> <td>7(23)</td> <td>.20</td> </tr> <tr> <td>Subcutaneous emphysema</td> <td>0</td> <td>3(19)</td> <td>3(10)</td> <td>.23</td> </tr> <tr> <td>Obstructive pneumonia</td> <td>0</td> <td>2(13)</td> <td>2(7)</td> <td>.21</td> </tr> <tr> <td>Fever</td> <td>1(7)</td> <td>1(6)</td> <td>2(7)</td> <td>.72</td> </tr> <tr> <td>Pleural effusion</td> <td>0</td> <td>2(13)</td> <td>2(7)</td> <td>.49</td> </tr> <tr> <td>Haemoptysis</td> <td>1(7)</td> <td>0</td> <td>1(3)</td> <td>.47</td> </tr> <tr> <td>Myalgia</td> <td>1(7)</td> <td>0</td> <td>1(3)</td> <td>.47</td> </tr> </tbody> </table> <p>Tumour location: C, central; P, peripheral.</p>		Tumour location		Total n (%)	P	C n=14 (%)	P n=16 (%)	Major complications			3(10)		Severe pneumothorax	2(14)	0	2(7)	.21	Acute respiratory distress syndrome	1(7)	0	1(3)	.47	Minor complications			18(60)		Small pneumothorax	5(36)	2(13)	7(23)	.20	Subcutaneous emphysema	0	3(19)	3(10)	.23	Obstructive pneumonia	0	2(13)	2(7)	.21	Fever	1(7)	1(6)	2(7)	.72	Pleural effusion	0	2(13)	2(7)	.49	Haemoptysis	1(7)	0	1(3)	.47	Myalgia	1(7)	0	1(3)	.47	<p>The study included mainly patients with primary lung cancers (NSCLC) (87%) with tumour size > 3 cm (81%).</p> <p>The procedure was performed with conscious sedation and analgesia in all patients.</p>	
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Study Details	Key efficacy findings	Key safety findings	Comments
<p>Kang S et al (2004)⁸</p> <p>Prospective case series (Nov 1999 to May 2002)</p> <p>China</p> <p>50 patients with primary or secondary lung cancers (number of tumours was not specified)</p> <p>Gender: male 32, female 18 Median age: 51 (range 35-74) years</p> <p>Tumour type (based on patients)</p> <ul style="list-style-type: none"> • Primary = 46% (23/50) • Secondary = 54% (27/50) <ul style="list-style-type: none"> ○ breast = 26% (13/50) ○ colon = 18% (9/50) ○ other sites = 10% (5/50) <p>Tumour number (based on patients)</p> <ul style="list-style-type: none"> • Single = 34% (17/50) • Multiple = 66% (33/50) <p>RFA procedure</p> <ul style="list-style-type: none"> • Maximum of 4 lesions or 6 target areas were treated during one operating procedure • All patients were given general anaesthesia. • Tumours < 3.5 cm given single RFA • Tumours > 3.5 cm given multiple RFA <p>Inclusion criteria</p> <ul style="list-style-type: none"> • Patients with primary or metastatic lung tumours <p>Exclusion criteria</p> <ul style="list-style-type: none"> • Patients with bleeding tendency or serious heart, liver and renal failure <p>Follow-up: 1-2 weeks</p> <p>Disclosure of interest: no conflict of interest declared by authors.</p>	<p>Tumour response at 1-2 weeks after RFA</p> <p>Appearance of tumour:</p> <ul style="list-style-type: none"> • PET: <ul style="list-style-type: none"> • Tumours < 3.5 cm: Complete necrosis seen (numbers not specified) • Tumours > 3.5 cm: The area within 3.5 cm diameter was destroyed, while the area beyond 3.5 cm remained (numbers not specified) • CT & chest X-ray: tumour image appears larger <p>Detection of tumour destruction:</p> <ul style="list-style-type: none"> • PET = 70% (35/50) • CT = 38% (19/50) • chest X-ray = 26% (13/50) 	<p>Complications of RFA (based on patients):</p> <ul style="list-style-type: none"> • Fever = 20% (10/50) • Pneumothorax = 18% (9/50) (5 patients did not require treatment) • Congested pneumonia = 12% (6/50) • Haemothorax requiring chest drainage = 2% (1/50) 	<p>The study focuses on evaluating the feasibility of RFA and the usefulness of FDG-PET scan in assessing tumour response after RFA.</p> <p>The study shows that PET is more effective in detecting tumour destruction than CT or chest X-ray shortly after RFA treatment.</p> <p>The study suggests that tumours < 3.5 cm in diameter can be effectively destroyed by a single RFA procedure. Whereas, tumour destruction may not be effective beyond this area with the current RFA instrumentation used.</p>

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<p>Steinke K et al. (2004)⁹</p> <p>International retrospective survey</p> <p>Australia, Europe, USA (7 centres)</p> <p>493 RFAs for primary and secondary lung cancers</p> <p>7 of 15 centres responded to a questionnaire survey sent to radiologists (USA = 3, Europe = 3, Australia = 1)</p> <p>Number of procedures by centre</p> <ul style="list-style-type: none"> 3 centres performed 463 (94%) of RFAs <table border="1"> <thead> <tr> <th>Ctr</th> <th>Number of procedures</th> <th>Type of tumours ablated*</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>297</td> <td>P+S</td> </tr> <tr> <td>2</td> <td>90</td> <td>P+S</td> </tr> <tr> <td>3</td> <td>76</td> <td>P+S</td> </tr> <tr> <td>4</td> <td>14</td> <td>P+S</td> </tr> <tr> <td>5</td> <td>10</td> <td>S</td> </tr> <tr> <td>6</td> <td>4</td> <td>P+S</td> </tr> <tr> <td>7</td> <td>2</td> <td>S</td> </tr> </tbody> </table> <p>* P, primary tumours, S, secondary tumours</p> <p>Location of tumours ablated</p> <ul style="list-style-type: none"> near heart, main bronchi, aorta: 2 centres as above, plus large vessels: 1 centre near large vessels: 2 centres not near any structures: 2 centres <p>Sedation/anaesthesia</p> <ul style="list-style-type: none"> Conscious sedation predominantly used: 5 centres General anaesthesia only was performed in 2 centres <p>Follow-up: not specified Disclosure of interest: not specified</p>	Ctr	Number of procedures	Type of tumours ablated*	1	297	P+S	2	90	P+S	3	76	P+S	4	14	P+S	5	10	S	6	4	P+S	7	2	S	<p>Observation time after the procedure:</p> <table border="1"> <thead> <tr> <th>Ctr</th> <th>Routine observation time after procedure</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>Few hours on outpatient basis or > 24 hours</td> </tr> <tr> <td>2</td> <td>Few hours on outpatient basis</td> </tr> <tr> <td>3</td> <td>Overnight hospitalisation</td> </tr> <tr> <td>4</td> <td>Overnight hospitalisation</td> </tr> <tr> <td>5</td> <td>> 24 hours</td> </tr> <tr> <td>6</td> <td>Few hours on outpatient basis</td> </tr> <tr> <td>7</td> <td>Few hours on outpatient basis</td> </tr> </tbody> </table>	Ctr	Routine observation time after procedure	1	Few hours on outpatient basis or > 24 hours	2	Few hours on outpatient basis	3	Overnight hospitalisation	4	Overnight hospitalisation	5	> 24 hours	6	Few hours on outpatient basis	7	Few hours on outpatient basis	<p>Complications were classified as small or large, defined as:</p> <ul style="list-style-type: none"> Small complications include small pneumothoraces, small pleural effusions, small intraparenchymal haemorrhages that do not require further interventions. Large pneumothoraces are those that require insertion of a chest tube. <p>Complications:</p> <ul style="list-style-type: none"> Small complications = mainly 10-30% of patients Pneumothorax = up to 30% of patients Pleural effusion requiring aspiration = less than 10% of patients Deaths = 2 (0.4%) of patients (it was not stated whether these were considered to be related to the procedure) <table border="1"> <thead> <tr> <th>Ctr</th> <th>Rate of small complications</th> <th>Rate of large pneumothoraces</th> <th>Rate of pleural effusion requiring tapping</th> <th>Death</th> </tr> </thead> <tbody> <tr> <td>1</td> <td>10-30%</td> <td>10-30%</td> <td>>30%*</td> <td>1</td> </tr> <tr> <td>2</td> <td><10%</td> <td><10%</td> <td><10%</td> <td>1</td> </tr> <tr> <td>3</td> <td>10-30%</td> <td>10-30%</td> <td><10%</td> <td>0</td> </tr> <tr> <td>4</td> <td>10-30%</td> <td>10-30%</td> <td><10%</td> <td>0</td> </tr> <tr> <td>5</td> <td><10%</td> <td><10%</td> <td><10%</td> <td>0</td> </tr> <tr> <td>6</td> <td><10%</td> <td><10%</td> <td><10%</td> <td>0</td> </tr> <tr> <td>7</td> <td><10%</td> <td><10%</td> <td><10%</td> <td>0</td> </tr> </tbody> </table> <p>*related to aggressive draining to prevent pneumonia, bronchitis, etc. in a patient population with diminished pulmonary function</p>	Ctr	Rate of small complications	Rate of large pneumothoraces	Rate of pleural effusion requiring tapping	Death	1	10-30%	10-30%	>30%*	1	2	<10%	<10%	<10%	1	3	10-30%	10-30%	<10%	0	4	10-30%	10-30%	<10%	0	5	<10%	<10%	<10%	0	6	<10%	<10%	<10%	0	7	<10%	<10%	<10%	0	<p>The study is a retrospective survey of the international experience with RFA for lung cancers.</p> <p>No efficacy data or long-term safety data were collected.</p> <p>3 of 7 centres (centres 1 to 3) performed 94% of the procedures. The other centres performed relatively few procedures, thus may not provide representative complication rates.</p>	
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Validity and generalisability of the studies

- This overview is based on 8 case series and an international survey. Most of these studies were based on limited patient numbers with short follow-up. In addition, the efficacy and safety outcomes were not always well described.
- There was significant heterogeneity in the patient population (and tumour types) both within and between different studies.
- Tumour response rates for primary and secondary lung cancers were usually reported together in the studies making it impossible to assess the outcomes of the two types of lung cancers separately.
- In studies that treated primary lung cancers, the type and stage of the disease were often not stated.
- Efficacy and safety outcomes reported in the literature may relate to patients, tumours or treatment sessions.
- The criteria for assessing tumour response and the imaging techniques used to detect and measure tumour size may vary between studies. This may need to be taken into consideration when interpreting the results.
- Where survival rates have been reported, these may be influenced by disease stage, tumour size, location and numbers, age and performance status of the patient, and treatments given prior to and after RFA.
- Similarly, survival rates, particularly for patients with lung metastases, may be influenced by the type of primary cancer and the extent of disseminated disease to other sites in addition to the lung.
- None of the studies were conducted in the UK.
- The treatment protocol may vary between studies (and tumour types) including the number of ablation for each tumour (including re-treatment for local recurrence and multiple tumours), the duration of ablation and the length of the exposed portion of the RFA needle-electrode. These may need to be taken into consideration when comparing between studies.

Specialist advisors' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College.

Prof A Adam, Dr. A Gillams, Mr. R Page, Dr. C Peebles

- The procedure is currently performed in patients who are not suitable candidates for surgery and is particularly suitable for small tumours, preferably located peripherally.
- Early studies suggest the procedure to be relatively safe with acceptable morbidity.

- Pneumothorax is common but often does not require intervention. Patients with primary lung cancer often have associated chronic obstructive pulmonary disease and are therefore more likely to require intervention than patients with secondary lung cancer in the event of a pneumothorax.
- The long-term efficacy of the procedure is unknown.
- There is uncertainty about appropriate patient selection and outcomes.
- There is uncertainty as to whether the procedure produces equivalent results to standard surgery for resectable lesions and to palliative chemotherapy for unresectable lesions.
- The use of RFA in conjunction with radiotherapy and/or chemotherapy has not been evaluated and is being explored.

Issues for consideration by IPAC

None

References

- 1 Yasui K, Kanazawa S, Sano Y et al. (2004) Thoracic tumors treated with CT-guided radiofrequency ablation: Initial experience. *Radiology* 231(3):850-857.
- 2 Gadaleta C, Catino A, Ranieri G et al. (2004) Radiofrequency thermal ablation of 69 lung neoplasms. *Journal of Chemotherapy* 16(SUPPL 5):86-89.
- 3 Akeboshi M, Yamakado K, Nakatsuka A et al. (2004) Percutaneous radiofrequency ablation of lung neoplasms: initial therapeutic response. *Journal of Vascular & Interventional Radiology* 15(5): 463-470.
- 4 Belfiore G, Moggio G, Tedeschi E et al. (2004) CT-guided radiofrequency ablation: a potential complementary therapy for patients with unresectable primary lung cancer--a preliminary report of 33 patients. *American Journal of Roentgenology* 183(4):1003-11.
- 5 King J, Glenn D, Clark W et al. (2004) Percutaneous radiofrequency ablation of pulmonary metastases in patients with colorectal cancer. *British Journal of Surgery* 91(2):217-223.
- 6 vanSonnenberg E, Shankar S, Morrison PR et al. (2005) Radiofrequency ablation of thoracic lesions: part 2, initial clinical experience--technical and multidisciplinary considerations in 30 patients. *American Journal of Roentgenology* 184(2):381-90.
- 7 Lee JM, Jin GY, Goldberg SN et al. (2004) Percutaneous radiofrequency ablation for inoperable non-small cell lung cancer and metastases: preliminary report. *Radiology* 230(1):125-134.
- 8 Kang S, Luo R, Liao W et al. (2004) Single group study to evaluate the feasibility and complications of radiofrequency ablation and usefulness of post treatment position emission tomography in lung tumours. *World Journal of Surgical Oncology* 2:6p.
- 9 Steinke K, Sewell PE, Dupuy D et al. (2004) Pulmonary radiofrequency ablation--an international study survey. *Anticancer Research* 24(1):339-43.

Appendix A: Additional papers on percutaneous radiofrequency ablation for primary and secondary lung cancers not included in summary Table 2

The following table outlines the studies that are considered potentially relevant to the overview but were not included in the main data extraction table (Table 2). It is by no means an exhaustive list of potentially relevant studies.

Article title	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in Table 2
Bojarski JD, Dupuy DE and Mayo-Smith WW. (2005) CT imaging findings of pulmonary neoplasms after treatment with radiofrequency ablation: results in 32 tumors. <i>American Journal of Roentgenology</i> 185(2): 466-471.	Case series 26 patients with 32 thoracic cancers (14 primary, 18 metastases) Mean follow-up 10.1 (range 1-30) months	Many treated tumours increase in size from baseline on follow-up CT scans at 1-3 months and then remain stable thereafter. Enlargement of a treated tumour after 6 months is considered to represent local recurrence.	Small series
Fernando HC, De Hoyos A, Landreneau RJ, et al. (2005) Radiofrequency ablation for the treatment of non-small cell lung cancer in marginal surgical candidates. <i>Journal of Thoracic & Cardiovascular Surgery</i> 129(3): 639-644.	Case series 18 patients with 21 peripheral primary NSCLC tumours (stage I (n=9), II (n=2), III (n=3) and IV (n=4)) RFA treatment (16 percutaneous, 2 minithoracotomy) Median follow-up 14 months	One post-operative death from pneumonia after open RFA. 39% pneumothorax requiring chest tube or pigtail catheter. Median hospital stay = 2.5 days 15 (83.3%) patients alive at median follow-up. Progression-free interval (mean 16.8 months, median 18 months)	Small series

<p>Gadaleta C, Mattioli V, Colucci G et al. (2004) Radiofrequency ablation of 40 lung neoplasms: preliminary results. <i>American Journal of Roentgenology</i> 183:381-386.</p>	<p>Case series 18 patients with lung cancers (40 nodules: 4 primary, 16 metastases) treated in 24 sessions</p> <p>Median follow-up 8 (range 2-14) months)</p>	<p>No evidence of tumour relapse in 94.4% patients at median follow-up.</p> <p>Complications were moderate pneumothorax requiring pleural drainage, cough, fever, slight dyspnoea, pain.</p>	<p>Small series.</p> <p>Later follow-up reported in Gadaleta C et al (2004)²</p>
<p>Hataji O, Yamakado K, Nakatsuka A et al. (2005) Radiological and pathological correlation of lung malignant tumors treated with percutaneous radiofrequency ablation. <i>Internal Medicine</i> 44(8): 865-869.</p>	<p>Two case reports 2 of 11 patients with lung cancers (1 primary squamous cell carcinoma, 1 metastasis from colon cancer)</p> <p>Follow-up: 3 months (primary tumour), and 4 months (metastatic tumour)</p>	<p>Although RFA is effective in causing coagulative tumour necrosis, some viable cells may persist in the peripheral areas of the tumour.</p>	<p>Small series</p>
<p>Herrera LJ, Fernando HC, Perry Y et al. (2003) Radiofrequency ablation of pulmonary malignant tumors in nonsurgical candidates. <i>Journal of Thoracic & Cardiovascular Surgery</i> 125(4): 929-937.</p>	<p>Case series 18 patients with 33 malignant lung tumours (5 lung cancer, 8 metastatic carcinoma, 5 sarcoma)</p> <p>RFA treatment (13 percutaneous, 5 minithoracotomy)</p> <p>Mean follow-up 6 months (range 1-14 months)</p>	<p>RFA is feasible for small peripheral lung tumours. Larger tumours responded poorly.</p> <p>One death due to haemoptysis 19 days after RFA ablation of a central nodule. Patient had also recently received brachytherapy.</p> <p>53.8% (7/13) pneumothorax in percutaneously-treated patients.</p>	<p>Small series</p>
<p>Inoue Y, Miki C, Hiro J et al. (2005) Improved survival using multi-modality therapy in patients with lung metastases from colorectal cancer: A preliminary study. <i>Oncology Reports</i> 14(6): 1571-1576.</p>	<p>Retrospective case series 21 patients with lung metastases from colorectal cancer. (12 patients had >5 lesions)</p> <p>All patients treated with modified pharmacokinetic modulating chemotherapy (PMC) and 11 patients also treated with RFA and/or radiotherapy (Multimodality)</p> <p>Median follow-up 25.1 months</p>	<p>Cumulative 3-year survival rate of patients in PMC group 33.3% and multimodality group 87.5% (p=0.004)</p> <p>Pneumothorax occurred in 36.4% (4/11) of patients treated with RFA. All required chest drainage.</p>	<p>Small series</p>
<p>Jin GY, Lee JM, Lee YC et al. (2004) Primary and secondary lung malignancies treated with percutaneous radiofrequency ablation: evaluation with follow-up helical CT. <i>American Journal of Roentgenology</i> 183(4):1013-20.</p>	<p>Case series 21 patients with lung cancers (17 patients had primary, 4 patients had metastases)</p> <p>Follow-up not specified in abstract (at least up to 15 months)</p>	<p>9 complete ablation, 12 partial ablation.</p> <p>The enhancement pattern and size of the change in the ablated lesion are the most important CT findings for determining whether complete ablation has been achieved.</p>	<p>Small series</p>

<p>Lee JM, Jin GY, Goldberg SN et al. (2004) Percutaneous radiofrequency ablation for inoperable non-small cell lung cancer and metastases: preliminary report. <i>Radiology</i> 230(1):125-34.</p>	<p>Case series 10 patients with stage I NSCLC</p> <p>Median follow-up 13 months</p>	<p>Complete necrosis in 6 tumours (all ≤ 4 cm) and partial necrosis on 4 tumours.</p> <p>2 patients died at median follow-up (of non-cancer-related pulmonary causes)</p>	<p>Small series</p>
<p>Liu Z, Zhou J and Li Q. (2002) CT-guided radiofrequency ablation in the treatment of lung cancer. [Chinese]. <i>Chinese Journal of Lung Cancer</i> 5(2): 136-138.</p>	<p>Case series 22 patients with locally advanced lung cancer</p> <p>Follow-up not specified in abstract</p>	<p>Out of 20 patients, 1 had complete response, 12 had partial response, 4 had minor response, 3 had stable disease.</p>	<p>Non-English</p>
<p>Nishida T, Inoue K, Kawata Y et al. (2002) Percutaneous radiofrequency ablation of lung neoplasms: a minimally invasive strategy for inoperable patients. <i>Journal of the American College of Surgeons</i> 195 (3):426-430.</p>	<p>Prospective case series 6 patients with 8 malignant lung tumours (2 metachronous primary, 4 metastatic)</p> <p>Mean tumour size 1.8 ± 0.94 cm (range 1-4.1 cm)</p> <p>Follow-up 6 to 21 months</p> <p>Local anaesthesia used</p>	<p>No tumour recurrence in all 5 patients, who were still alive at 6 to 21 months after RFA.</p> <p>1 patient died of progression of lung metastases other than treated lesion at 287 days after RFA.</p> <p>Pneumothorax in 67% (4/6) of patients.</p>	<p>Small series</p>
<p>Steinke K, King J, Glenn D et al. (2003) Pulmonary hemorrhage during percutaneous radiofrequency ablation: A more frequent complication than assumed? <i>Interactive Cardiovascular & Thoracic Surgery</i> 2(4): 462-465.</p>	<p>Case series 46 patients received 101 RFA; 81 were retrospectively assessed for periprocedural intrapulmonary bleeding.</p> <p>Follow-up not specified in abstract</p>	<p>Incidence of haemorrhage during percutaneous lung RFA = 5.9%</p> <p>Intraparenchymal lung haemorrhage during percutaneous RFA of primary and secondary lung malignancies is similar to reported lung haemorrhage for diagnostic core biopsies. The authors believe this complication to be under-reported in the literature.</p>	<p>Incidence of only one complication reported</p>
<p>Steinke K, King J, Glenn D et al. (2003) Radiologic appearance and complications of percutaneous computed tomography-guided radiofrequency-ablated pulmonary metastases from colorectal carcinoma. <i>Journal of Computer Assisted Tomography</i> 27(5): 750-757.</p>	<p>Case series 20 patients with 41 lung metastases</p>	<p>Ablated lesion size is usually larger than that of the initial tumour for the first 3 months after ablation and continuously shrinks thereafter.</p> <p>50% pneumothorax (chest tube required in 50% of affected patients). 7.5% intraparenchymal haemorrhage.</p>	<p>Small series</p>

<p>Steinke K, Glenn D, King J et al. (2004) Percutaneous imaging-guided radiofrequency ablation in patients with colorectal pulmonary metastases: 1-Year follow-up. <i>Annals of Surgical Oncology</i> 11(2): 207-212.</p>	<p>Case series 23 patients treated with RFA for 52 lung metastases from colorectal cancer</p> <p>Median follow-up 428 (range 173-829) days</p> <p>The paper reports data to 1 year.</p>	<p>At 1 year, 5 patients died. 18 patients have 40 lesions (17 disappeared, 5 decreased, 4 stable/same size, 14 increased)</p> <p>Median hospital stay 2 days (range 1-9 days)</p> <p>43% (10/23) pneumothorax (6 patients required chest tube placement)</p>	<p>Small series</p>
<p>Suh RD, Wallace AB, Sheehan RE et al. (2003) Unresectable Pulmonary Malignancies: CT-guided Percutaneous Radiofrequency Ablation - Preliminary Results. <i>Radiology</i> 229(3): 821-829.</p>	<p>Case series 12 patients with 19 lung tumours (6 adenocarcinoma, 1 large cell carcinoma, 2 bronchoalveolar, 4 colorectal carcinoma, 6 sarcoma)</p> <p>Mean follow-up 4.5 (range 1-12 months)</p>	<p>In 8 patients with 3 months follow-up, 2 lesion size increased, 6 remained stable.</p> <p>12 pneumothorax (2 patients required chest tube placement), 2 pleural effusion, 2 moderate pain.</p>	<p>Small series</p>
<p>Vogl TJ, Straub R, Lehnert T et al. (2004) Percutaneous thermoablation of pulmonary metastases. Experience with the application of laser-induced thermotherapy (LITT) and radiofrequency ablation (RFA), and a literature review. [German]. <i>ROFO-Fortschritte auf dem Gebiet der Rontgenstrahlen und der Bildgebenden</i> 176(11): 1658-1666.</p>	<p>Case series 20 patients with 32 lung metastases</p> <p>Follow-up not specified in abstract.</p>	<p>Complete "roll off" (increase in impedance) achieved in all RFA ablations.</p> <p>Local tumour control rate = 85% at 6 months follow-up.</p> <p>Pneumothorax in 15% (5/32) of procedures, without insertion of chest tube.</p>	<p>Non-English</p>
<p>Wang S, Chen J and Cao W. (2005) The observation of the clinical effect for combination therapy of RFA with GP on advanced stage lung cancer. [Chinese]. <i>Chinese Journal of Clinical Oncology</i> 32(11): 628-630.</p>	<p>Case series 34 patients with advanced NSCLC stage III and IV</p> <p>All patients were treated with RFA combined with Gemcitabine plus Cisplatin (GP)</p> <p>Follow-up not specified in abstract.</p>	<p>Results were compared with outcomes for patients who received GP chemotherapy alone.</p> <p>RFA/ GP group was superior to GP group in terms of therapeutic effect (P<0.01), "life quality marks" and survival time.</p>	<p>Non-English</p>
<p>Yamakado K, Akeboshi M, Nakatsuka A et al. (2005) Tumor seeding following lung radiofrequency ablation: A case report. <i>Cardiovascular & Interventional Radiology</i> 28(4): 530-532.</p>	<p>Case report 1 patient with primary lung adenocarcinoma</p> <p>Follow-up 5 months</p>	<p>A description of a patient with tumour seeding. A new tumour was found at 3 months after RFA in the chest wall at a location corresponding to the puncture route of the RFA electrode.</p>	<p>Small series</p>

Appendix B: Related published NICE guidance for percutaneous radiofrequency ablation for primary and secondary lung cancers

Guidance	Recommendation
Interventional Procedures	<p>IPG 087, photodynamic therapy for advanced bronchial carcinoma</p> <ul style="list-style-type: none"> • Current evidence on the safety and efficacy of photodynamic therapy for advanced bronchial carcinoma appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. • These recommendations apply only to the use of this technique to treat advanced bronchial carcinoma. The Institute will consider photodynamic therapy for early bronchial carcinoma separately. <p>IPG 142, cryosurgery for malignant endobronchial obstruction</p> <ul style="list-style-type: none"> • Current evidence on the safety and efficacy of cryotherapy for malignant endobronchial obstruction appears adequate to support the use of this procedure provided that the normal arrangements are in place for consent, audit and clinical governance. • Clinicians should ensure that patients fully understand that this is one of a variety of treatment options available. In addition, use of the Institute's <i>Information for the Public</i> is recommended.
Technology Appraisals	None applicable
Clinical Guidelines	<p>CG 24, lung cancer: the diagnosis and treatment of lung cancer</p> <p>The guideline did not include any ablation procedures for the treatment of lung cancers.</p>
Public Health	None applicable

Appendix C: Literature search for percutaneous radiofrequency ablation for primary and secondary lung cancers

Databases	Version searched (if applicable)	Date searched
The Cochrane Library	The Cochrane Library 2005, Issue 2	2/06/2005
CRD		2/06/2005
Embase	1980 to 2005 Week 21	05/01/2006
Medline	1966 to May Week 3 2005	05/01/2006
Premedline	May 25, 2005	05/01/2006
CINAHL	1982 to May Week 3 2005	05/01/2006
British Library Inside Conferences (limited to current year only)		05/01/2006
National Research Register	2005 Issue 2	2/06/2005
Controlled Trials Registry		2/06/2005

The following search strategy was used to identify papers in Medline. A similar strategy was used to identify papers in other databases.

1. catheter ablation/
2. (catheter adj5 ablat\$).tw.
3. rfa.tw.
4. (radiofrequen\$ adj3 ablat\$).tw.
5. or/1-4
6. *lung neoplasms/
7. ((lung\$ or pulmon\$) adj2 metastas\$).tw.
8. *carcinoma, non-small-cell lung/
9. or/6-8
10. 5 and 9
11. limit 10 to humans