NATIONAL INSTITUTE FOR HEALTH AND CLINICAL EXCELLENCE

INTERVENTIONAL PROCEDURES PROGRAMME

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

Percutaneous radiofrequency ablation of cancer in the lung involves inserting one or more electrodes (needle-like probes) through the chest into the lung. The electrodes are placed within the tumour and connected to a source of electrical current, producing heat with the aim of destroying ('ablating') the cancer cells.

Introduction

The National Institute for Health and Clinical Excellence (NICE) has prepared this overview to help members of the Interventional Procedures Advisory Committee (IPAC) make 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 April 2010.

Procedure name

- Percutaneous radiofrequency ablation for primary or secondary lung cancers

Specialty societies

- British Society of Interventional Radiology
- British Thoracic Society
- The Royal College of Radiologists
- Society for Cardiothoracic Surgery in Great Britain and Ireland.

Description

Indications and current treatment

Lung cancers (primary and secondary)

Lung cancer is one of the most common cancers in the UK. There are two main types of primary lung cancer: small cell lung cancer (SCLC) and non-small cell lung cancer (NSCLC). The lung is also a common site of secondary cancer via metastasis from other primary cancers elsewhere in the body such as the breast or colon. The overall prognosis of patients with primary lung cancer or lung metastases is poor.

The treatment of primary and secondary lung cancer depends mainly on tumour histology and stage, and may include surgical resection (open or thoracoscopic), external beam radiotherapy, chemotherapy, or a combination of these treatments.

If the tumour protrudes into the major airways, interventional bronchoscopic treatments including diathermy, laser therapy, cryotherapy, brachytherapy and photodynamic therapy may be used.

Percutaneous radiofrequency ablation (RFA) may be useful in patients with small, early-stage lung cancers or small numbers of lung metastases who are not suitable for (or are unwilling to undergo) surgery. It may also have a place in the multi-modality treatment of more advanced primary lung cancers.

What the procedure involves

Percutaneous RFA for lung cancer is usually performed under local anaesthesia with conscious sedation, although tumour size and anatomy may dictate the use of general anaesthesia. The procedure involves inserting a small needle electrode through the skin directly into the tumour, usually under computed tomography (CT) guidance. Radiofrequency energy, in the form of an alternating electrical current, is passed through the electrode causing heating of the tissues around the tip of the needle. The tumour tissue in the target area is coagulated and a small margin of normal tissue around the tumour is also destroyed to reduce the risk of local recurrence.

The procedure can be applied to more than one tumour during a single treatment session, or repeated in subsequent sessions. It can be used alone or in combination with surgery, radiotherapy or chemotherapy.

Literature review

Rapid review of literature

The medical literature was searched to identify studies and reviews relevant to percutaneous RFA for primary or secondary lung cancers. Searches were

conducted of the following databases, covering the period from their commencement to 30 March 2010: 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). Relevant published studies identified during consultation or resolution that are published after this date may also be considered for inclusion.

The following selection criteria (table 1) were applied to the abstracts identified by the literature search. Where selection 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, or a laboratory or animal study. Conference abstracts were also excluded because of the difficulty of appraising study methodology, unless they reported specific adverse events that were not available in the published literature.
Patient	Patients with primary or secondary lung cancer.
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 a case series of 493 procedures (patient numbers not reported) and approximately 789 patients from 7 case series and 5 case reports[1–13]. A further 3 studies were added after consultation: 1 review including 1584 patients, a case series of 100 patients and a case report describing 4 patients[14–16].

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.

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

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Steinke K (2004)[1]

Case series

Australia, USA, Italy, Germany, Switzerland

Recruitment period: not reported

Study population: patients with primary or metastatic lung cancer

n = 493 procedures

Age: not reported
Sex: not reported

Patient selection criteria: not reported

Technique: conscious sedation was predominantly used although 2 centres used general anaesthesia only. Two centres ablate lesions in both lungs at the same time while the other 5 only ablate lesions in 1 lung per session. All 7 centres used CT guidance.

Follow-up: not reported

Conflict of interest/source of funding: not reported</td>
<td>No efficacy outcomes were reported.</td>
<td>Complications were classified as small or large, defined as:
• 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.

• Deaths = 2 patients (0.4%) (it was not stated whether these were considered to be related to the procedure)

<table>
<tr><th>Centre</th><th>Rate of small complic-ations</th><th>Rate of large pneumo-thoraces</th><th>Rate of pleural effusion requiring tapping</th><th>Death</th></tr>
<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>
</table>

*related to aggressive draining to prevent pneumonia, bronchitis, etc. in a patient population with diminished pulmonary function
The rate of small complications requiring no further intervention ranged from <10% in 4 centres to 10–30% in 3 centres.</td>
<td>This study was included in the original overview.

This study was included in the review by Chan et al, 2010

Study design issues:
• Multicentre, retrospective study.
• The number of procedures performed per centre ranged from 2–297.
• 3 of the 7 centres (centres 1 to 3) performed 94% of the procedures.

Other issues:
• The authors note that the procedure was only palliative as the long-term results were not known.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Simon CJ (2007)[2] **Case series** USA Recruitment period: 1998–2005 Study population: patients with primary or metastatic lung cancer who refused or who were not candidates for surgery **n = 153 patients (116 primary NSCLCs, 73 metastatic lung cancers).** The primary goal of treatment was local control for 86% (132/153) of patients and palliation for 14% (21/153) of patients. Mean age (years): local control group = 69, palliation group = 64. Sex: local control = 57% male, palliation = 52% male Patient selection criteria: symptomatic patients with advanced-stage disease were considered to be the symptom palliation group. Symptoms included chest pain, haemoptysis, and cough, all of which were refractory to medical treatment. The remaining patients had stage I NSCLC and stage IV metastatic lung cancer. All patients refused surgery or were considered not to be candidates for surgery on the basis of age, disease extent, underlying lung disease or other medical comorbidities. Patients with stage II or III NSCLC were referred for other local control treatment options.	Number of patients analysed: **153** ***Local control group*** Initial technical success (no detectable residual tumour at initial postablation CT) = 98.1% (159/162) of tumours Median time to death for all patients with stage I NSCLC (n = 75) = 29 months (95% CI: 20 to 38 months). Survival rate estimates for patients with stage I NSCLC: • 1 year = 78% • 2 years = 57% • 3 years = 36% • 4 years = 27% • 5 years = 27% Median time to death for all patients with stage IV primary or metastatic lung cancer who were treated for local control (n = 57) = 31 months (95% CI: 19 to 43 months). Survival rate estimates for 57 patients with stage IV primary or metastatic lung cancer who were treated for local control: • 1 year = 70% • 2 years = 54% • 3 years = 44% • 4 years = 44% • 5 years = 44% Survival rate estimates for 18 patients with stage IV colorectal metastatic lung cancer who were treated for local control: • 1 year = 87% • 2 years = 78%	**Complications (183 ablation sessions):** • Mild pneumothorax (grade 1, asymptomatic) = 18.6% (34/183) • Moderate or severe pneumothorax (grade 2, symptomatic, requiring chest tube) = 9.8% (18/183) • Haemoptysis (grade 1, mild, <100 ml, intervention not required) = 2.7% (5/183) • Infection (grade 3, intravenous antibiotic therapy required) = 2.2% (4/183) • Complication requiring admission = 10.4% (19/183) Overall 30-day mortality = 3.9% (6/153) of patients 4 deaths were thought to be procedure-related, while 2 were caused by a combination of systemic cancer progression and medical comorbidities. ***Procedure-related deaths*** Case 1 – 50-year old man who had previously undergone a total left pneumonectomy had RFA of 2 right lower lobe metastases. After 1 day, the patient returned to hospital with increasing pain. Postmortem analysis revealed 1.5 l of fresh haemorrhage in the pleural space that was believed to be the cause of death. Case 2 – 74-year-old man admitted with acute respiratory failure 1 day after RFA. He was intubated and treated for congestive heart failure and cardiac arrhythmia. Death was attributed to exacerbation of his underlying pulmonary fibrosis. Case 3 – 80-year-old man who had previously undergone a total right pneumonectomy underwent RFA complicated by pneumothorax. He was readmitted 6 days after RFA with increasing respiratory distress and eventually required intubation. The cause of death was believed to be related to congestive heart failure. Case 4 – 79-year-old man with history of coronary	**This study was included in the review by Chan et al, 2010** **Follow-up issues**: • Follow-up CT was performed within 4 weeks after ablation, then 3, 6–12, and 18–24 months after RFA. Three-dimensional PET scan was generally done at 3–6 month intervals after RFA when local control and/or progression needed to be evaluated.. After 2001, patients received intravenous contrast for CT scans unless contraindicated. **Study design issues**: • Biopsies were not routinely performed during follow-up. • The Kaplan-Meier method was used to

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Technique: All ablations were performed by using CT fluoroscopic guidance. In general, tumours > 2 cm were treated with a cluster electrode rather than a single electrode. Some patients were treated concomitantly with systemic chemotherapy and/or external beam radiation therapy.

Median follow-up: 20.5 months (range 3–74)

Conflict of interest/source of funding: 1 author is a consultant for 3 manufacturers and was supported by Valleylab and Endocare, another author was supported by GE Healthcare.</td>
<td>• 3 years = 57%
• 4 years = 57%
• 5 years = 57%

Local tumour progression rates (assessed by CT and PET scans) were significantly lower in patients with smaller index tumours (≤3 vs >3 cm, p < 0.002).

Progression-free rates for tumours ≤3 cm:
• 1 year = 83%
• 2 years = 64%
• 3 years = 57%
• 4 years = 47%
• 5 years = 47%
Median time to progression = 45 months

Progression-free rates for tumours >3 cm:
• 1 year = 45%
• 2 years = 25%
• 3 years = 25%
• 4 years = 25%
• 5 years = 25%
Median time to progression = 12 months

Symptom palliation group (n = 21)
<table>
<tr><th>Symptom</th><th>No. of lesions treated</th><th>No. of lesions with symptom improve-ment</th><th>No. of lesions with symptom recurrence</th></tr>
<tr><td>Pain</td><td>20</td><td>19</td><td>7 (37%)</td></tr>
<tr><td>Haemoptysis</td><td>3</td><td>3</td><td>2 (67%)</td></tr>
<tr><td>Cough</td><td>4</td><td>4</td><td>1 (25%)</td></tr>
</table>
Estimated median survival = 6 months (95% CI: 2 to 10 months).Survival rate estimates:
• 1 year = 27.8%
• 2 years = 5.5%</td>
<td>artery disease, chronic obstructive pulmonary disease, and sleep apnoea suffered respiratory arrest while undergoing conscious sedation during RFA.</td>
<td>estimate survival functions for patient mortality and local tumour progression rates.

Study population issues:
• The authors note that ‘A proportion of patients were treated concomitantly with systemic chemotherapy and/or external beam radiation therapy’.
• Many patients had already been followed up for up to a year after diagnosis before RFA was performed.
• Same study centre as Beland et al. (2010), so there may be some duplicate reporting.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Sano Y (2007)[3] **Case series** Japan Recruitment period: 2001–4 Study population: patients with intrathoracic malignancies (primary or metastatic, 97% parenchymal) **n =137 patients, 366 tumours (30 primary lung cancer, 336 metastases).** Mean age: 62.9 years (range 34–88) Sex: 64% male (88/137) Patient selection criteria: all patients were nonsurgical candidates because they were medically unable to tolerate surgery or had refused surgery, or because of the extent of their disease. Technique: CT fluoroscopic guidance was used. Only 2 of 211 (0.9%) treatments were done under general anaesthesia. Cool-tipRF system (internally cooled electrode; Radionics/Valleylab) or a LeVeen Needle electrode (multitined expandable electrode; Boston Scientific) were used. **Follow-up: not reported** Conflict of interest/source of funding: not reported	Technical success rate = 100%	**Complications (211 ablation sessions)** • Mortality = 0.9% (2/211) (1 at 53 days after RFA due to intractable pneumothorax and pneumonia in a patient who had undergone right pneumonectomy 12 months previously and 1 at 28 days after RFA due to massive haemoptysis after ablation of hilar lymph nodes). **Major complications** (defined as an event that leads to substantial morbidity and disability, increased level of care, or results in hospital admission or substantially lengthened hospital stay): • Pneumothorax requiring chest tube drainage = 11.8% (25/211) • Pleuritis = 2.8% (6/211) • Pleural effusion requiring chest tube drainage = 1.9% (4/211) • Lung abscess = 0.5% (1/211) **Minor complications** • Pneumothorax (no drainage) = 40.3% (85/211) • Pleural effusion (no drainage) = 16.1% (34/211) • Haemoptysis = 4.3% (9/211) • Nausea and/or vomiting = 1.4% (3/211) • Subcutaneous emphysema = 1.4% (3/211) • Cough = 0.9% (2/211) • Skin burn = 0.9% (2/211) • Atelectasis = 0.5% (1/211) • Subileus = 0.5% (1/211) The only statistically significant risk factor for a major complication was older age (univariate analysis).	**This study was included in the review by Chan et al, 2010** **Study design issues**: • Retrospective study.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Nomura M (2008)[4] **Case series** Japan Recruitment period: 2002–6 Study population: Patients with primary or metastatic lung cancer **n = 130 patients (17 primary lung cancer, 21 lung cancer recurrence, 43 colorectal metastasis, 49 other metastasis)** Mean age: 65 years (range 12–88) Sex: 64% (83/130) male Patient selection criteria: no inclusion and exclusion criteria were listed. In 66% (217/327) of sessions, previous treatments had failed to control the lung tumours. Technique: A maximum of 3 tumours were treated on the same day. Any remaining tumours were treated by RFA the following week. Follow-up: not reported Conflict of interest/source of funding: not reported	No efficacy data were reported.	**Major complications in 327 ablation sessions** (defined as those resulting in admission to hospital for treatment, an unplanned increase in the level of care, prolonged hospitalisation or permanent adverse sequelae): • Death = 0.6% (2/327) (both due to interstitial pneumonia, which was judged to be radiation pneumonia. Both patients had undergone external beam radiotherapy and lung resection before RFA). • Pneumothorax = 15.3% (50/327) • Aseptic pleuritis = 0.6% (2/327) • Tumour dissemination = 0.3% (1/327) • Pyothorax = 1.5% (5/327) **Minor complications** • Pneumothorax = 29% (95/327) Large tumour size (≥ 2 cm) and previous external-beam radiotherapy were identified as significant risk factors associated with an increased C-reactive protein value in both univariate and multivariate analyses.	Same study centre as Yamakodo et al (2009), so there may be some duplicate reporting.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Lencioni R (2008)[5] **Case series** Italy, USA, Australia, Germany, UK Recruitment period: 2001–5 Study population: patients with lung tumours 3.5 cm in diameter or smaller **n = 106 patients (33 NSCLC, 53 colorectal metastases, 20 metastasis from other primary sites [6 breast, 3 ovary, 3 sarcoma, 2 melanoma, 2 renal cell carcinoma, 1 bladder, 1 gallbladder, 1 stomach, 1 oesophagus]), 183 tumours** Median tumour size = 1.5 cm Mean age: 64.9 years (range 29–85) Sex: 66% male (70/106) Patient selection criteria: age > 18 years; biopsy-proven NSCLC or lung metastasis; patients rejected for surgery and considered unfit for radiotherapy or chemotherapy; up to 3 tumours per lung, each 3.5 cm or smaller in diameter, detected by CT; tumours located at least 1 cm from trachea, main bronchi, oesophagus, aorta, aortic arch branches, main, right, or left pulmonary artery, and heart; tumours accessible by percutaneous route; Eastern Cooperative Oncology Group (ECOG) performance status of 0, 1 or 2; platelet count >100x10^9/l; international normalized ratio of 1.5 or less. Exclusion criteria included previous pneumonectomy; major comorbid medical conditions.	Number of patients analysed: **106** Technical success = 99% (105/106) (one patient could not be treated because of an inability to place the ablation device in to the tumour). **Confirmed complete response of all treated tumours lasting at least a year after treatment = 88% (75/85).** In the remaining 10 patients, there was evidence of local progression in at least 1 treated tumour (based on CT analysis). No differences were noted in tumour response between patients with NSCLC and those with lung metastases. At the end of the study, 68.9% (73/106) of patients were alive. **Overall survival for patients with NSCLC**: • 1 year = 70% (95% CI: 51 to 83%) • 2 years = 48% (95% CI: 30 to 65%) **Overall survival for patients with colorectal metastases:** • 1 year = 89% (95% CI: 76 to 95%) • 2 years = 66% (95% CI: 53 to 79%) **Overall survival for patients with other metastases:** • 1 year = 92% (95% CI: 65 to 99%) • 2 years = 64% (95% CI: 43 to 82%) **Cancer-specific survival for patients with NSCLC**: • 1 year = 92% (95% CI: 78 to 98%) • 2 years = 73% (95% CI: 54 to 86%) **Cancer-specific survival for patients with**	**Major complications (137 treatment sessions)** • Large or symptomatic pneumothorax requiring drainage = 19.7% (27/137) • Pleural effusion needing drainage = 2.9% (4/137) There were no procedure-related deaths. **Minor complications** • Pneumothorax not requiring treatment = 20.4% (28/137) • Pleural effusion not requiring treatment = 8.0% (11/137) • Self-limiting intrapulmonary haemorrhage = 2.2% (3/137)	**This study was included in the review by Chan et al, 2010** **Follow-up issues**: • 80% (85/106) of patients were assessed for the primary endpoint of confirmed complete response of the target tumour. The remaining patients were excluded from the analysis because of shorter follow-up (<12 months, n = 5), discontinuation of follow-up at the study centre (n = 6) or death in the absence of any evidence of progression of the target tumour (n = 10). • Follow-up visits were scheduled at 3-month intervals for 2 years and each included a CT scan. **Study design**

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

<table>
<tr><th>Study details</th><th>Key efficacy findings</th><th>Key safety findings</th><th>Comments</th></tr>
<tr>
<td>Technique: RFA system - RITA medical system Starburst XL; Angiodynamics.

Mean follow-up: 15 months
Conflict of interest/source of funding: Funded by Angiodynamics.</td>
<td>colorectal metastases:
• 1 year = 91% (95% CI: 78 to 96%)
• 2 years = 68% (95% CI: 54 to 80%)

Cancer-specific survival for patients with other metastases:
• 1 year = 93% (95% CI: 67 to 99%)
• 2 years = 67% (95% CI: 48 to 84%)

Patients with stage I NSCLC had a 2-year overall survival of 75% (95% CI: 45 to 92%) and a 2-year cancer-specific survival of 92% (95% CI: 66 to 99%).

Quality of life scores (mean scores)
<table>
<tr><td></td><td>Baseline</td><td>12 months</td></tr>
<tr><td colspan="3">FACT-L</td></tr>
<tr><td colspan="3">NSCLC (n = 22)</td></tr>
<tr><td>FACT-G</td><td>80.5</td><td>82.2</td></tr>
<tr><td>LCS</td><td>22.5</td><td>23.6</td></tr>
<tr><td>TOI</td><td>64.2</td><td>67.5</td></tr>
<tr><td colspan="3">Colorectal metastases (n = 41)</td></tr>
<tr><td>FACT-G</td><td>87.2</td><td>83.0</td></tr>
<tr><td>LCS</td><td>25.1</td><td>24.0</td></tr>
<tr><td>TOI</td><td>72.6</td><td>68.2</td></tr>
<tr><td colspan="3">SF-12</td></tr>
<tr><td colspan="3">NSCLC (n = 22)</td></tr>
<tr><td>PCS</td><td>44.4</td><td>46.0</td></tr>
<tr><td>MCS</td><td>47.6</td><td>49.6</td></tr>
<tr><td colspan="3">Colorectal metastases (n = 41)</td></tr>
<tr><td>PCS</td><td>48.1</td><td>46.4</td></tr>
<tr><td>MCS</td><td>52.1</td><td>50.1</td></tr>
</table>
Differences were not statistically significant.

No significant worsening of pulmonary function was noted.</td>
<td></td>
<td>issues:
• Prospective, multicentre study
• Intention-to-treat analysis
• Quality of life was assessed by use of the validated FACT-G and SF-12 questionnaires (both scales 0 to 100, with higher scores indicating better quality of life).
• The paper did not state how many symptoms were included in the LCS (scored 0 to 4 for each symptom, with lower scores indicating fewer symptoms).
• The TOI combines the FACT-G scores on physical well-being, functional well-being and the lung cancer subscale.</td>
</tr>
</table>

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Yamakodo K (2009)[6] **Case series** Japan Recruitment period: 2002–8 Study population: patients with colorectal lung metastases. **n = 78 patients (198 tumours)** Mean maximum tumour diameter = 2.0 cm Mean age: 66.1 years Sex: 68% male (53/78) Patient selection criteria: not listed. 90% (70/78) of patients had tumours ≤ 3 cm in diameter. The diagnosis of lung metastasis was based on serial CT images. Technique: CT fluoroscopy and an internally cooled electrode were used (Cool-Tip, Valleylab). At most, 3 tumours were treated in a single day. 95% (74/78) of patients received systemic chemotherapy after RFA. **Mean follow-up: 24.6 months (range 6–84)** Conflict of interest/source of funding: not reported.	Number of patients analysed: **78 patients (140 sessions)** Technical success rate = 100% (140/140) **Local tumour progression = 14.1% (11/78)** (based on CT scan images) **Overall local tumour progression rates:** • 1-year = 10.1% (95% CI: 2.9 to 17.3) • 3-year = 20.6% (95% CI: 8.9 to 22.2) • 5-year = 20.6% (95% CI: 8.9 to 22.2) Local tumour progression rates for small tumours (≤ 3 cm): • 1-year = 5.1% (95% CI: 0.0 to 10.8) • 3-year = 13.8% (95% CI: 2.9 to 14.6) • 5-year = 13.8% (95% CI: 2.9 to 14.6) Local tumour progression rates for tumours > 3 cm: • 1-year = 53.1% (95% CI: 16.6 to 89.7) • 3-year = 68.8% (95% CI: 33.8 to 100) • 5-year = 68.8% (95% CI: 33.8 to 100) **Overall survival rates:** • 1-year = 83.9% (95% CI: 75.2 to 92.7) • 3-year = 56.1% (95% CI: 41.7 to 70.5) • 5-year = 34.9% (95% CI: 18.0 to 51.9) Median survival = 38.0 months 28 patients died because of cancer progression and 1 because of cerebral infarction. Lack of extrapulmonary metastases and a normal carcinoembryonic antigen level were significant independent factors for a better prognosis.	**Major complications (140 sessions)** • Pneumothorax requiring chest tube placement = 12.9% (18/140) • Aseptic pleuritis requiring chest tube placement = 1.4% (2/140) No procedure-related deaths were reported. **Minor complications** • Pneumothorax not requiring chest tube placement = 9.3% (13/140)	**Follow-up issues**: • An additional 3 patients were treated during the study period but were lost to follow-up. • Follow-up CT scans were done every 3–4 months. **Study design issues**: • Retrospective **Other issues**: • 95% (74/78) of patients received systemic chemotherapy after RFA. • Same study centre as Nomura et al. (2008), so there may be some duplicate reporting.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Beland MD (2010)[7] **Case series** USA Recruitment period: 1998–2008 Study population: patients with primary NSCLC **n = 79 patients (79 tumours)** Mean tumour size = 2.5 cm Mean age: 75 years Sex: 46% males (36/79) Patient selection criteria: patients who refused surgery or who were considered not to be candidates for surgery on the basis of age, disease extent, underlying lung disease or other medical comorbidities. Technique: RFA was performed with either a single or cluster Cool-tip electrode (Covidien). 24% (19/79) of patients underwent adjuvant external beam radiation and 11% (9/79) underwent concomitant brachytherapy. **Mean follow-up: 16 months (range 1–72)** Conflict of interest/source of funding: one of the authors was a consultant for Covidien.	Number of patients analysed: **79** **No evidence of residual or recurrent tumour at mean follow-up of 17 months = 57% (45/79)** Of the 34 recurrent tumours, 13 (38%) were local, 6 (18%) were intrapulmonary, 6 (18%) were nodal, 2 (6%) were mixed and 7(21%) were distant metastases. **Median disease-free survival = 23 months** (Kaplan-Meier) Increasing tumour size and stage had a statistically significant relationship to risk of recurrence (p = 0.02 and p = 0.007 respectively). Sex, tumour location and radiation therapy were not statistically significantly associated with risk of recurrence.	No safety outcomes were reported.	**Follow-up issues**: • An additional 10 patients with no post-treatment imaging results were excluded from the study. • Follow-up CT was performed within 4 weeks after ablation, then 3, 6–12, and 18–24 months after RFA. Three-dimensional PET scan was generally done at 3–6 month intervals after RFA. **Study design issues**: • Retrospective • Follow-up imaging was not the same for all patients. • Same study centre as Simon CJ et al. (2007), so there may be some duplicate reporting.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Pennathur A (2009)[8] **Case series** USA Recruitment period: 2000–7 Study population: patients with inoperable lung cancer (primary or metastatic) **n = 100 patients (46 primary, 25 recurrent, 29 metastatic [13 colorectal, 2 breast, 3 renal cell, 5 sarcoma, 2 cervical, 1 tongue, 1 testicular, 1 pheochromocytoma, 1 oesophageal])** Median age: 73.5 years (range 26–95) Sex: 40% male (40/100) Patient selection criteria: patients who were considered inoperable owing to poor pulmonary function or high cardiac risk; failure of previous therapies; patients who refused surgical resection. Exclusion criteria included central tumours (within 3 cm of the hilum). Technique: the majority of procedures were done under general anaesthesia. **Mean follow-up: 17 months** Conflict of interest/source of funding: none stated	Number of patients analysed: **100** **Response to treatment (assessed by CT scan and PET scan):** The response could not be evaluated in 9 patients. For the remaining patients: • Initial complete response = 21% • Partial response = 41% • Stable disease = 20% • Progressive disease = 18% **Local progression during follow-up = 35% (35/100)** **Median time to local progression = 15 months (95% CI: 8 to 27)** **Overall progression (all sites) = 60% (60/100)** **Median time to overall progression = 7 months (95% CI: 6 to 11)** **Median overall survival = 23 months (95% CI: 18 to 37)** **Median overall survival by type of neoplasm:** • Primary (all stages) = 27 months (95% CI: 18 to 47) • Recurrent = 33 months (95% CI: 11 to 45) • Metastatic disease = 18 months (95% CI: 7 months to not reached) **Estimated 2-year survival:** • Overall = 49% (95% CI: 37 to 60) • Primary lung neoplasm = 50% (95% CI: 33 to 65) • Recurrent lung neoplasm = 55% (95% CI: 25 to 77) • Metastatic disease = 41% (95% CI: 19 to 62)	**Complications** • Pneumothorax requiring a pigtail catheter = 59% (59/100) • Prolonged air leak (>5 days) = 7% (7/100) • Bleeding requiring bronchoscopy = 1% (1/100) • Myocardial infarction, cerebrovascular accident, deep vein thrombosis and respiratory failure = 1% (1/100) • Pleural effusion requiring drainage = 3% (3/100) • Arrhythmia = 6% (6/100) There was 1 death within 30 days of the procedure (at 2 weeks) (no further information supplied).	**Follow-up issues**: • No losses to follow-up were described. • Patients were followed up at 4-monthly intervals with CT scans. Some patients were also given PET scans. **Study design issues**: • Retrospective study • Consecutive patients • All the procedures were performed by thoracic surgeons. **Study population issues**: • The authors note that many patients had had failure of previous therapies. • The authors note that the patients had had significant associated comorbidities.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Hiraki T (2009)[9] **Case reports** Japan **n = 2** Conflict of interest/source of funding: none	**Needle-tract seeding after percutaneous RFA for lung cancer** Case 1: 70-year old man who had previously undergone left upper lobectomy, external beam radiation and systemic chemotherapy. Metastases were diagnosed in both lungs 17 months after surgery and treated with RFA. Immediately before RFA, a needle biopsy was done, which caused bleeding around the tumour. The electrode tract was not cauterized. 4 months after RFA, CT scans showed a small nodule that was considered to be along the path of the electrode or the biopsy needle. It was suggested to be needle-tract seeding but this was not histologically confirmed. The nodule was treated by RFA. The patient died of acute pneumonia at 27 months, which was not related to the cancer or RFA. Case 2: 79-year old woman who had previously undergone right upper lobectomy. A second tumour was diagnosed in the right lower lobe 22 months after surgery and treated with RFA. The electrode tract was not cauterized. CT scans at 7 months showed a small nodule, which was identified to be along the electrode tract. It was determined to be a needle-tract seeding although this was not histologically confirmed. RFA was performed and CT scans at 12 months showed complete ablation.		The authors note that after the experience of these 2 cases, they now cauterize the electrode tract while removing the electrode.
Burgoyne LL (2008)[10] **Case report** USA **n = 1** Conflict of interest/source of funding: none stated	**Massive haemoptysis and air embolism in a child undergoing RFA for metastatic lung cancer** 4-year old male child who had undergone multiple prior surgeries for stage IV metastatic hepatoblastoma. During RFA procedure, there was sudden onset of tachycardia and both limbs of the anaesthesia breathing circuit were seen to be filled with blood. A CT scan showed air in the left atrium and ventricle. Repeat CT scans showed no remaining air in the heart but a small amount of air in the cerebral blood vessels. Recovery from the event was unremarkable, however the patient died 21 days later of progressive disease. The authors note that the most likely mechanism for air entry was intrabronchial air passing from a bronchus to a blood vessel, with the track surrounding the needle acting as a conduit (‘bronchovenous fistula’).		

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.			
Study details	**Key efficacy findings**	**Key safety findings**	**Comments**
Hiraki T (2009)[11] **Case report** Japan **n = 1** Conflict of interest/source of funding: none	**Aspergilloma in a cavity formed after percutaneous RFA for lung cancer** 66-year old woman with intrapulmonary metastasis in the left upper lobe was treated with 3 sessions of RFA. After the third ablation, the ablation zone was transformed into a cavity which was totally replaced by consolidation at 8 months after RFA. The consolidation was deemed to be a local progression but needle biopsy showed *Aspergillus* and no viable cancer tissue. The patient was treated with voriconazole and the latest follow-up scan (5 months after initiation of therapy for aspergilloma) showed shrinkage of consolidation.		
Le TX (2008)[12] **Case report** USA **n = 1** Conflict of interest/source of funding: none	**Thermal osteonecrosis of the rib after RFA in the thorax** 48-year old man underwent RFA of a pleural-based pulmonary metastasis from treated hepatocellular carcinoma. The procedure was uneventful and the patient had no pain immediately afterwards. 10 months after RFA, tumour recurrence with invasion of the chest wall was suspected and a thoracotomy with resection was performed. Pathologic evaluation demonstrated osteonecrosis of the rib but no malignancy.		
Thornton RH (2008)[13] **Case report** USA **n = 1** Conflict of interest/source of funding: 1 author is a member of the Scientific Advisory board of Angiodynamics, another receives support from a number of manufacturers.	**Phrenic nerve injury** Case 1: 69-year old man with stage IA NSCLC. Medical history was significant for chronic obstructive pulmonary disease, sleep apnoea, diabetes and hypertension. Radiograph after RFA showed new elevation of the right hemidiaphragm. Subsequently, the patient required 2l of oxygen by nasal cannula to maintain saturations above 92%.		Two additional cases of phrenic nerve injury after microwave ablation were also described.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Chan VO (2010)[14] **Review** Search date: June 2009 Ireland **n = 1584 patients (2905 ablations)** 46 studies (all case series) were appraised in detail (8 evaluated primary lung cancers alone, 11 evaluated pulmonary metastases alone, 25 evaluated both, and 2 did not specify the histology) Mean lesion size = 2.8 ± 1.0 cm Technique: sedation technique evolved from using general or epidural anaesthesia to conscious sedation (7 studies used general anaesthesia, 21 used conscious sedation, 1 used epidural anaesthesia alone and 6 used a combination). The needle type evolved from a single-tip probe in 2002 to a 4 to 9 multitined probe in 2009. **Mean follow-up: varied from 3 to 68.1 months (reported in 36 studies)** Conflict of interest/source of funding: none stated	Number of patients analysed: **1584** Local recurrence rates ranged from 0% to 64.7% (24 studies). Local recurrence rate for primary lung cancer = 22.2% Local recurrence rate for metastases = 18.1% Mean time to recurrence = 13 months (range 3–45) (19 studies) Mean overall survival = 59.4% (range 25–100%) over a mean follow-up period of 17.7 ± 12.4 months (21 studies) Mean cancer-specific survival rate = 82.6% (range 55–100%) over a mean follow-up period of 17.4 ± 14.1 months (24 studies) ***Primary cancer alone (8 studies)*** Overall survival rate = 58.3% over a mean follow-up period of 40.4 ± 40.3 months Cancer-specific survival rate = 82.1% (range 58–100%) over a mean follow-up period of 89.8 ± 8.6 months ***Metastatic pulmonary disease alone (10 studies)*** Overall survival rate = 65.5% over a mean follow-up period of 25.4 ± 19.4 months Cancer-specific survival rate = 75.2% (range 55–90%) over a mean follow-up period of 72.3 ± 13.4 months	Mean morbidity = 24.6% (range 0–100%) **Complications (2245 ablations)** • Minor pneumothorax = 28.3% (range 0–90%) • Pneumothorax requiring chest drain = 14.4% (range 0–63.2%) • Pleural effusions = 14.8% (range 0–86.7%) • Pneumonia = 1.5% (range 0–22.2%) • Abscess = 0.4% (range 0–6.5%) • Pain = 14.1% (range 0–100%) • Haemoptysis = 4.3% (range 0–37.5%) • Pyrexia = 4.4% (range 0–65.2%) • Bronchopleural fistula = 0.4% (range 0–33%) • Subcutaneous emphysema = 0.2% (range 0–2.2%) • Procedure-related death = 0.2% (range 0–5.6%) There were 6 procedure-related deaths: 2 occurred in the presence of concomitant pneumonia, with the development of adult respiratory distress syndrome, and 2 occurred secondary to haemothorax. One occurred secondary to massive haemoptysis post repeat-RFA of a central lesion.	**Follow-up issues**: The method of follow-up changed from a predominantly CT approach to a combined approach using CT and PET. **Study design issues**: Case reports or series with fewer than 5 cases were omitted from the analysis.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Chua TC (2010)[15] **Case series** Australia Recruitment period: 2000 onwards Study population: patients with inoperable pulmonary metastases from colorectal cancer **n = 100 patients** Mean age: 65 years Sex: 61% male (61/100) Patient selection criteria: aged between 18 and 85 years, not surgical candidates (previously treated lung or liver metastases, presence of more than 3 lesions identified in either lung, bilateral pulmonary disease or multiple lobar metastases, and those patients who refused surgery), patients with complete resection of primary colorectal tumour and any other sites of metastases. Exclusion criteria included >6 lesions per haemothorax, tumour diameter >5 cm, lesions immediately adjacent to major bronchi, significant coagulopathies and poor lung function. Technique: all procedures were done under local anaesthesia with sedation. **Follow-up: 23 months (median)** Conflict of interest/source of funding: none stated	Number of patients analysed: **100** Survival rate (at median follow-up of 23 months) = 51% (51/100) At end of follow-up, 27 patients had no evidence of any sites of metastatic disease, 24 patients were alive with disease, and 49 patients had died (39 had pulmonary metastases at the time of death). Median overall survival after RFA treatment = 36 months (95% CI 30–43) **Overall survival** • 1 year = 87% • 2 years = 66% • 3 years = 50% • 5 years = 30% Median overall survival from time of first diagnosis of colorectal cancer = 79 months; 5-year survival = 65%; 10-year survival = 17% Independent predictors for survival identified by multivariate analysis included response to RFA treatment (hazard ratio [HR] 3.8, 95% CI 2.2 to 6.5, p < 0.001), repeat RFA treatment (HR 0.2, 95% CI 0.1 to 0.6; p = 0.002), presence of extrapulmonary metastases at RFA (HR 3.0, 95% CI 1.34 to 6.64; p = 0.008), and adjunct systemic chemotherapy (HR 0.3, 95% CI 0.1 to 1.0; p = 0.05).	Complications • Pneumothorax or pleural effusions requiring chest tube = 23% (23/100) • Empyema = 1% (1/100) (required pleurectomy and decortication) Patients with ≥3 lesions were more likely to develop a complication that required chest tube drainage (p < 0.001). There was no treatment-related mortality.	**Follow-up issues:** Patients were followed up at 3-monthly intervals with CT scans every 6 months. **Study design issues:** Prospective study **Study population issues:** 4% of patients had no systemic chemotherapy treatment throughout their clinical course. The remaining patients had at least 1 line of chemotherapy.

Abbreviations used: CI, confidence interval; CT, computed tomography; FACT-G, Functional Assessment of Cancer Therapy – General; FACT-L, Functional Assessment of Cancer Therapy – Lung; NSCLC, non-small cell lung cancer; OR, odds ratio; SF-12, Short-Form-12; LCS, Lung Cancer Subscale; MCS, mental component summary; PCS, physical component summary; PET, positron-emission tomography; RFA, radiofrequency ablation; TOI, trial outcome index.

Study details	Key efficacy findings	Key safety findings	Comments
Hiraki T (2010)[16] **Case report** Japan **n = 4** Conflict of interest/source of funding: none	**Brachial nerve injury** Case 1: 76-year old man with primary NSCLC, located in the apex of the left lung. RFA was performed under epidural anaesthesia with a multitined expandable electrode. After the radiofrequency energy was initiated, the patient reported sensory discomfort in the fifth finger of the left hand, which indicated a possible brachial nerve injury. An artificial pneumothorax was created to separate the tines away from the apical and medial pleura. After the procedure, symptoms improved and only slight numbness of the upper arm persisted at the latest follow-up (17 months). Case 2: 49-year old man with lung metastasis, in contact with the right apical pleura. The procedure was considered to pose a high risk of brachial nerve injury as the T1 nerve root was located immediately above the tumour. RFA was performed under epidural anaesthesia. Three hours after the procedure, the patient described numbness and pain along the medial side of the upper arm. Numbness and hypoaesthesia (grade 2) persisted at the latest follow-up (1 month). Case 3: 73-year old man with lung metastasis, located in the apex of the left lung. RFA was performed under epidural anaesthesia with a multitined expandable electrode. Three days after the procedure, the patient experienced paraesthesia along the medial side of the left upper arm and forearm as well as hypoaesthesia and motor dysfunction of the fourth and fifth fingers of the left hand. The patient underwent rehabilitation therapy and symptoms improved but persistent motor dysfunction of the fingers was noted 18 months after RFA. Case 4: 42-year old woman with lung metastasis, located in the apex of the left lung. RFA was performed under epidural anaesthesia. After the radiofrequency energy was initiated, the patient reported numbness along the medial side of the left upper arm. Subsequently, a sensory and motor disturbance (grade 2) developed along the medial side of the left upper arm. The patient underwent rehabilitation therapy and symptoms improved; only slight numbness persisted on the side of the upper arm.		The authors note that these 4 cases occurred during their 8-year experience of 733 sessions of RFA of lung tumours. The authors note that the indications of RFA in patients with apical lung cancer should be carefully determined because of the risk of brachial nerve injury.

Efficacy

Survival

A review of 46 studies including 1584 patients reported a mean overall survival of 59% over a mean follow-up period of 18 months[14]. The mean cancer-specific survival rate was 83% over a mean follow-up period of 17 months.

In a case series of 153 patients, the 1-, 3- and 5-year survival rates after RFA for 75 patients with stage 1 NSCLC were 78%, 36% and 27% respectively[2]. Survival rate estimates for 57 patients with stage IV primary or metastatic lung cancer were 70% at 1 year, 44% at 3 years and 44% at 5 years. In the same study, 21 patients with advanced disease were treated for symptom palliation and the 1- and 2-year survival rates in this group were 28% and 6% respectively. A case series of 106 patients reported overall 1- and 2-year survival rates of 70% and 48% for 33 patients with NSCLC, and 89% and 66% for 53 patients with colorectal lung metastases[5]. In a case series of 78 patients with colorectal lung metastases, overall 1-, 3- and 5-year survival rates were 84%, 56% and 35% respectively[6]. The median overall survival was 38 months. A case series of 100 patients with colorectal lung metastases reported median overall survival after RFA treatment of 36 months and overall 5-year survival rate of 30% [15].

A case series of 100 patients reported a median overall survival of 27 months for patients with primary lung cancer, 33 months for patients with recurrent lung cancer and 18 months for patients with metastatic disease[8]. The estimated 2-year survival rates were 50%, 55% and 41%, respectively.

Tumour progression

The case series of 153 patients reported the median time to progression (assessed by follow-up CT scans and also positron-emission tomography (PET) scans in selected patients) for tumours 3 cm or smaller was 45 months, with 1-, 3- and 5-year progression-free rates of 83%, 57% and 47%, respectively[2]. Median time to progression for larger tumours was 12 months, with 1-, 3- and 5-year progression-free rates of 45%, 25% and 25%, respectively. The case series of 78 patients with colorectal lung metastases reported 1-, 3- and 5-year overall tumour progression rates of 10%, 21% and 21%, respectively (assessed by follow-up CT scans)[6]. Again, the rates of progression were higher for larger tumours. The case series of 100 patients reported local progression (assessed by CT scans and also PET scans in selected patients) in 35% (35/100) of patients after a mean follow-up of 17 months; the median time to local progression was 15 months[8].

The case series of 106 patients reported a confirmed complete response of all treated tumours (assessed by CT scans) lasting at least a year after RFA for 88% (75/85) of patients[5].

Quality of life

In the case series of 106 patients, there were no statistically significant differences between the quality of life at baseline and at 12 months after RFA, using the Functional Assessment of Cancer Therapy – Lung (FACT-L) and the Short-Form-12 (SF-12) questionnaires[5].

Safety

Mortality

A review of 46 studies including 1584 patients reported that procedure-related mortality ranged from 0% to 6%, with an overall procedure-related mortality rate of 0.2%[14].

A case series of 153 patients treated by 183 sessions of RFA reported 4 deaths that were considered to be procedure-related[2]. One death was due to haemorrhage in the pleural space, 1 was due to exacerbation of underlying pulmonary fibrosis, 1 was related to congestive heart failure (RFA was complicated by pneumothorax) and 1 patient had a respiratory arrest while undergoing conscious sedation during RFA. Two of these patients had previously undergone a total pneumonectomy. A case series of 137 patients and 211 RFA sessions reported 2 deaths: 1 due to intractable pneumothorax and pneumonia, and the other due to massive haemoptysis after RFA[3]. A case series of 130 patients and 327 RFA sessions reported 2 deaths, both due to interstitial pneumonia[4].

Pneumothorax requiring chest tube drainage

A review of 46 studies including 1584 patients reported pneumothorax requiring chest tube drainage in 14% of patients [14].

In a case series of 493 RFA procedures performed in 7 different centres, the rate of pneumothorax requiring the insertion of a chest tube was <10% in 4 centres and 10–30% in 3 centres[1]. In 5 further case series, the rate of pneumothorax requiring chest tube drainage ranged from 10% (18/183) to 20% (27/137)[2–6] .

Pleural effusion/pleuritis

In a case series of 493 RFA procedures performed in 7 different centres, the rate of pleural effusion requiring drainage was <10% in 6 centres and >30% in 1 centre[1]. In 3 case series, the rates of pleural effusion requiring drainage were 2% (4/211), 3% (4/137) and 3% (3/100)[3,5,8].

Three case series reported rates of pleuritis of 1% (2/140), less than 1% (2/327) and 3% (6/211)[6,4,3]. A case series of 130 patients reported pyothorax after 2% (5/327) of procedures[4]. Another case series reported infection requiring intravenous antibiotics after 2% (4/183) of RFA procedures[2].

Other complications

A review of 46 studies including 1584 patients reported pain in 14% of patients, haemoptysis in 4% of patients, pneumonia in 1.5% of patients, and abscess, bronchopleural fistula and subcutaneous emphysema each in <1% of patients[14].

Among the 9 case series, there was 1 case of tumour dissemination and 1 patient who experienced myocardial infarction, cerebrovascular accident, deep vein thrombosis and respiratory failure[3,4,8].

In addition 6 case reports described needle-tract seeding, massive haemoptysis and air embolism, aspergilloma, thermal osteonecrosis of the rib, phrenic and brachial nerve injury after RFA[9-13,16] .

Validity and generalisability of the studies

- There was significant heterogeneity in the patient population (and tumour types) both within and between different studies. One study only included patients with primary tumours and one only included patients with colorectal metastases[7,6]. The remaining studies included a mixture of primary and secondary tumours (mainly colorectal metastases).
- One study stated that the procedure was only palliative[1]. Another study reported results separately for patients treated for symptom palliation[2]. The other studies did not specify whether the treatment intent was palliative or curative.
- One study excluded patients with central lung tumours (within 3 cm of the hilum)[8].
- One study only included patients with small lung tumours (<3.5 cm in diameter)[5].
- 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. For example, some studies followed-up patients by CT scans only, whereas others also

used PET scans. This may need to be taken into consideration when interpreting the results.

- Two studies reported from the same study centre in Japan and there may be some patients included in both [4,6]. Two other studies reported from the same study centre in the USA and there may be some duplicate reporting[2,7].
- Some studies reported that patients were given additional treatments such as systemic chemotherapy, adjuvant external beam radiation and concomitant brachytherapy.

Existing assessments of this procedure

There were no published assessments from other organisations identified at the time of the literature search.

Related NICE guidance

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

Interventional procedures

- Percutaneous radiofrequency ablation for primary and secondary lung cancers. NICE interventional procedures guidance 185 (2006). Available from www.nice.org.uk/guidance/IPG185. This guidance is currently under review.
- Photodynamic therapy for advanced bronchial carcinoma. NICE interventional procedures guidance 87 (2004). Available from www.nice.org.uk/guidance/IPG87.
- Photodynamic therapy for localised inoperable endobronchial cancer. NICE interventional procedures guidance 137 (2005). Available from www.nice.org.uk/guidance/IPG137.
- Cryotherapy for malignant endobronchial obstruction. NICE interventional procedures guidance 142 (2005). Available from www.nice.org.uk/guidance/IPG142.

Clinical guidelines

- Lung cancer: diagnosis and treatment. NICE clinical guideline 24 (2005). Available from www.nice.org.uk/guidance/CG24.

Specialist Advisers' opinions

Specialist advice was sought from consultants who have been nominated or ratified by their Specialist Society or Royal College. The advice received is their individual opinion and does not represent the view of the society.

Dr J Cockburn, Dr F Miller (British Society of Interventional Radiology), Mr S Padley (British Thoracic Society), Dr P Gaines, Dr A Gillams (The Royal College of Radiologists), Mr R Page (Society for Cardiothoracic Surgery in Great Britain and Ireland).

- Three Advisers described the procedure as established practice and 2 described it as definitely novel with uncertain safety and efficacy. The other commented that the safety and efficacy are well understood but the procedure is not yet widely practiced.
- It is only suitable for a small proportion of patients.
- One Adviser stated that appropriate comparators would be limited lung resection of metastases via open thoracotomy or video-assisted thoracic surgery, or palliative chemotherapy for unresectable lesions. Another Adviser stated that comparators would be radiotherapy, chemotherapy or palliative care for inoperable primary lung tumours; currently all cases are non-surgical.
- Theoretical adverse events include pneumothorax, haemorrhage, abscess, infection, pleural effusion, pulmonary embolism, pain, damage to other intrathoracic structures, and death from interstitial pneumonitis.
- Key efficacy outcomes include postprocedure mortality, symptomatic improvement, quality of life, local tumour control, progression-free survival, overall survival, respiratory morbidity, and the need for repeat interventions.
- The procedure is more efficacious for smaller tumours.
- Training and experience are required in CT fluoroscopy, image-guided needle placement for biopsy and image-guided pneumothorax drainage, the theory of ablation, patient selection, radiofrequency devices, factors influencing necrosis, expected appearances post ablation, recognition of complications and recurrence.

- Two Advisers thought that the procedure is likely to have a major impact on the NHS. The others thought that the impact is likely to be minor.

Patient Commentators' opinions

NICE's Patient and Public Involvement Programme sent 60 questionnaires to 1 trust for distribution to patients who had the procedure (or their carers). NICE received 29 completed questionnaires.

The Patient Commentators' views on the procedure were consistent with the published evidence and the opinions of the Specialist Advisers.

Issues for consideration by IPAC

- None other than those discussed above.

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14. Chan VO, McDermott S, Malone DE et al. (2010) Percutaneous radiofrequency ablation of lung tumors. Evaluation of the literature using evidence-based techniques. Journal Thoracic Imaging (in press).

15. Chua TC, Thornbury K, Saxena A et al. (2010) Radiofrequency ablation as an adjunct to systemic chemotherapy for colorectal pulmonary metastases. Cancer 116: 2106–14.

16. Hiraki T, Gobara H, Mimura H et al. (2010) Brachial nerve injury caused by percutaneous radiofrequency ablation of apical lung cancer: a report of four cases. Journal of Vascular & Interventional Radiology 21: 1129–33.

Appendix A: Additional papers on percutaneous radiofrequency ablation for primary or secondary lung cancers

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. Case series with fewer than 50 patients have been excluded, unless they are describing specific safety outcomes.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Ambrogi MC, Lucchi M, Dini P et al. (2006) Percutaneous radiofrequency ablation of lung tumours: results in the mid-term. European Journal of Cardio-thoracic Surgery 30: 177–83.	Case series n = 54 Mean follow-up = 24 months	Complete response = 62% Mean overall survival = 17 months Mean local progression-free interval = 13 months	Small case series.
Casal RF, Tam AL, Eapen GA. (2010) Radiofrequency ablation of lung tumors. Clinics in Chest Medicine 31: 151-63.	Review	RFA may play a useful role in patients with medically inoperable lung cancer. Appropriate patient selection is critical, and it is fairly clear that lesions <3.5 cm have a much higher rate of response. Follow-up imaging for assessment of treatment response remains very challenging.	A review with analysis is already included (Chan et al, 2010) (study published after consultation)
Chen J-H, Cao W-H, Wang S-B et al. (2007) Prognosis and influencing factors on 80 patients with lung cancer after percutaneous radiofrequency ablation treatment. Technology in Cancer Research and Treatment 6: 507–10.	Case series n = 80 Follow-up = 4–68 months	Prognostic factors for survival: age, International Union Against Cancer (UICC) classification and systemic chemotherapy.	Larger case series are included.
Choe YH, Kim SR, Lee KS et al. (2009) The use of PTC and RFA as treatment alternatives with low procedural morbidity in non-small cell lung cancer. European Journal of Cancer 45: 1773–80.	Non-randomised comparative study n = 65 Mean follow-up = 21 months	43% (29/67) of RFA sessions and 6/9 percutaneous thoracic cryotherapy sessions attained complete ablation.	Small sample size.
Clasen S, Kettenbach J, Kosan B et al. (2009) Delayed development of pneumothorax after pulmonary radiofrequency ablation. Cardiovascular & Interventional Radiology 32: 484–90.	Case reports n = 3	**Delayed development of pneumothorax** 1 patient required chest drain placement 32 hours after RFA and 1 developed tension pneumothorax 5 days after RFA. The remaining patient did not require treatment.	Pneumothorax has already been mentioned as a complication.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Crocetti L, Lencioni R. (2010) Radiofrequency ablation of pulmonary tumors. European Journal of Radiology 75: 23-27.	Review	RFA is a safe modality for the local control of pulmonary tumours.	A review with analysis is already included (Chan et al, 2010) (study published after consultation)
De Baere T, Palussiere J, Auperin A et al. (2006) Midterm local efficacy and survival after radiofrequency ablation of lung tumors with minimum follow-up of 1 year: Prospective evaluation. Radiology 240: 587–96.	Case series n = 60 Follow-up = 12 months to 2 years	Incomplete local treatment at 18 months = 7% per tumour and 12% per patient. Overall survival at 18 months = 71% Lung disease-free survival = 34%	Small case series.
De Baère T. (2010) Lung tumour radiofrequency ablation: where do we stand? Cardiovascular and Interventional Radiology 29 Apr 2010 [epub ahead of print]	Review	RFA is a promising treatment, with high success rates of complete ablation in small primary and metastatic lung tumours.	A review with analysis is already included (Chan et al, 2010) (study published after consultation)
Fernando HC, Schuchert M, Landreneau R et al. (2010) Approaching the high-risk patient: sublobar resection, stereotactic body radiation therapy, or radiofrequency ablation. Annals of Thoracic Surgery 89: S2123–7.	Review	Non operative therapies should be reserved for medically inoperable patients. However, RFA may be clinically equivalent to resection because it may be associated with a lower complication profile and quicker return to normal function and quality of life.	A review with analysis is already included (Chan et al, 2010) (study published after consultation)
Gadaleta C, Catino A, Mattioli V (2006) Radiofrequency thermal ablation in the treatment of lung malignancies. In Vivo 20: 765–8.	Case series n = 54 Median follow-up = 18 months	Complete ablation = 95% (88/93) Local recurrence only in the treated area = 2% Recurrence in treated area and/or distant sites = 5%	Small case series.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Guihaire J, Verhoye J-P, de Latour B et al. (2010) Parietal tumor recurrence of lung metastasis after radiofrequency ablation. Interactive Cardiovascular and Thoracic Surgery 10: 650-1.	Case report n = 1	Iatrogenic parietal contamination after RFA.	Case report (study published after consultation)
Hiraki T, Tajiri N, Mimura H et al. (2006) Pneumothorax, pleural effusion, and chest tube placement after radiofrequency ablation of lung tumors: Incidence and risk factors. Radiology 241: 275–83.	Case series n = 142 Follow-up = not reported	Pneumothorax = 52% (117/224) Pleural effusion = 19% (42/224)	Another study from the same centre is included.
Hiraki T, Sakurai J, Tsuda T et al. (2006) Risk factors for local progression after percutaneous radiofrequency ablation of lung tumors: Evaluation based on a preliminary review of 342 tumors. Cancer 107: 2873–80.	Case series n = 128 Median follow-up = 12 months	Larger tumour size and the use of an internally cooled electrode were independent risk factors for local progression after RFA of lung tumours.	Studies with longer follow-up are included.
Hiraki T, Gobara H, Mimura H et al. (2010) Does tumor type affect local control by radiofrequency ablation in the lungs? European Journal of Radiology 74: 136-41.	Case series n = 105 patients Follow-up = 24 months	Overall local control rates: • 12 months = 86% • 18 months = 81% • 24 months = 76% Metastatic colorectal cancer showed significantly higher local control rates than other tumour types. However, multivariate analysis indicated that tumour type per se did not significantly influence local control.	Larger studies are included (study published after consultation)
Jeannin A, Saignac P, Palussiere J et al. (2009) Massive systemic air embolism during percutaneous radiofrequency ablation of a primary lung tumor. Anesthesia & Analgesia 109: 484–6.	Case report n = 1	**Massive systemic air embolism** Myocardial infarction and stroke responded to resuscitation measures, including hyperbaric oxygenation.	Another case report of air embolism is included.
Nachiappan AC, Sharma A, Shepard JA et al. (2010) Radiofrequency ablation in the lung complicated by positive airway pressure ventilation. Annals of Thoracic Surgery 89: 1665–7.	Case report n = 1	Bronchopleural fistula, exacerbated by detrimental effects of positive airway pressure on necrotic lung tissue after RFA.	Case report (complication already described) (study published after consultation)
Nour-Eldin N-E, Naguib NNN, Saeed A-S et al. (2009) Risk factors involved in the development of pneumothorax during radiofrequency ablation of lung neoplasms. American Journal of Roentgenology 193: W43–8.	Case series n = 82	Pneumothorax = 11% (14/124) of sessions. Risk factors for pneumothorax: age > 60 years, emphysema, tumour diameter ≤ 1.5 cm, lesions in lower part of lung, aerated lung parenchyma traversed by needle track for a distance ≥ 2.6 cm and traversal of a major pulmonary fissure.	Study focused on pneumothorax.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Okuma T, Matsuoka T, Yamamoto A et al. (2010) Determinants of local progression after computed tomography-guided percutaneous radiofrequency ablation for unresectable lung tumors: 9-year experience in a single institution. Cardiovascular & Interventional Radiology 33: 787–93.	Case series n = 72 patients Mean follow-up = 14 months	Local progression = 32% (44/138) Overall local control rates: • 1 year = 61% • 3 years = 57% • 5 years = 38% Significant risk factor for local progression was tumour size ≥2 cm.	Larger studies are included. (study published after consultation)
Okuma T, Matsuoka T, Yamamoto A et al. (2008) Frequency and risk factors of various complications after computed tomography-guided radiofrequency ablation of lung tumors. Cardiovascular and Interventional Radiology 31: 122–30.	Case series n = 57	Side effects = 17% Minor complications = 50% Major complications = 8% of sessions(fever >38.5°C [n=3], abscess [n=3], pneumothorax requiring chest tube [n=2], air embolism [n=1])	Small case series.
Okuma T, Matsuoka T, Yamamoto A et al. (2007) Factors Contributing to Cavitation after CT-guided Percutaneous Radiofrequency Ablation for Lung Tumors. Journal of Vascular and Interventional Radiology 18: 399–404.	Case series n = 48	Frequency of cavitation = 14% by CT performed on an average of 1.5 months. The majority were asymptomatic and resolved after 2.7 months.	Small case series.
Okuma T, Matsuoka T, Tutumi S et al. (2007) Air Embolism during Needle Placement for CT-guided Radiofrequency Ablation of an Unresectable Metastatic Lung Lesion. Journal of Vascular and Interventional Radiology 18: 1592–4.	Case report n = 1	**Air embolism** The patient became unresponsive; however, he recovered 10 minutes later and the air embolism disappeared spontaneously.	Another case report of air embolism is included.
Pua BB, Thornton RH, Solomon SB. (2010) Ablation of pulmonary malignancy: current status. Journal of Vascular and Interventional Radiology 21: S223–32.	Review	RFA is a viable option for those patients who cannot undergo surgery for technical factors based on tumour location, earlier radiation, or medical contraindications to surgery.	A review with analysis is already included (Chan et al, 2010) (study published after consultation)
Sakurai J, Hiraki T, Mukai T et al. (2007) Intractable Pneumothorax Due to Bronchopleural Fistula after Radiofrequency Ablation of Lung Tumors. Journal of Vascular and Interventional Radiology 18: 141–5.	Case report n = 2	**Intractable pneumothorax attributed to bronchopleural fistula** In 1 patient, air leakage persisted and the patient died of pneumonia 52 days after RFA.	Intractable pneumothorax is already reported by the same study centre.
Sakurai J, Mimura H, Gobara H et al. (2010) Pulmonary artery pseudoaneurysm related to radiofrequency ablation of lung tumor. Cardiovascular and Interventional Radiology 33: 413-16.	Case report n = 1	Haemoptysis from pulmonary artery pseudoaneurysm.	Case report (study published after consultation)

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Wang S-B, Chen J-H, Xie X-Y et al. (2007) The technical study on the cluster electrode radio frequency therapy of liver cancer and lung cancer. Technology in Cancer Research and Treatment 6: 511–4.	Case series n = 134	Median survival time = 15 months	Report focused on technical issues.
Yamakado K, Hase S, Matsuoka T et al. (2007) Radiofrequency ablation for the treatment of unresectable lung metastases in patients with colorectal cancer: a multicenter study in Japan. Journal of Vascular and Interventional Radiology 18: 393–8.	Case series n = 71 Mean follow-up = 19 months	Pneumothorax = 37% Emphysema = 1% Intrapulmonary recurrence = 47% Estimated 3-year survival rate = 46%	Small case series.
Yamakado K, Takaki H, Takao M et al. (2010) Massive hemoptysis from pulmonary artery pseudoaneurysm caused by lung radiofrequency ablation: Successful treatment by coil embolization. Cardiovascular and Interventional Radiology 33: 410–2.	Case report n = 1	Massive haemoptysis from pulmonary artery pseudoaneurysm caused by lung RFA.	Case report (study published after consultation)
Yan TD, King J, Sjarif A et al. (2007) Treatment failure after percutaneous radiofrequency ablation for nonsurgical candidates with pulmonary metastases from colorectal carcinoma. Annals of Surgical Oncology 14: 1718–26.	Case series n = 55	Local recurrence rate = 38% Overall recurrence rate = 66% In multivariate analysis, a largest size of lung metastasis of >3 cm was independently associated with a reduced overall progression-free survival.	Small case series.
Yan TD, King J, Sjarif A et al. (2006) Percutaneous radiofrequency ablation of pulmonary metastases from colorectal carcinoma: Prognostic determinants for survival. Annals of Surgical Oncology 13: 1529–37.	Case series n = 55 Median follow-up = 24 months	Overall median survival = 33 months Actuarial survival: • 1 year = 85% • 2 year = 64% • 3 year = 46% Multivariate analysis showed that largest size of lung metastasis >3 cm was independently associated with reduced overall survival.	Small case series.
Yan TD, King J, Sjarif A et al. (2006) Learning curve for percutaneous radiofrequency ablation of pulmonary metastases from colorectal carcinoma: a prospective study of 70 consecutive cases. Annals of Surgical Oncology 13: 1588–95.	Case series n = 70	There was a significant decline in the incidence of overall morbidity, pneumothorax and chest drain requirement in the second group of 35 patients compared with the initial 35 patients.	Small case series.
Yoshimatsu R, Yamagami T, Terayama K et al. (2009) Delayed and recurrent pneumothorax after radiofrequency ablation of lung tumors. Chest 135: 1002–9.	Case series n = 68	Pneumothorax = 42% (82/194) of RFA sessions . Delayed or recurrent pneumothorax = 17% (33/194).	Pneumothorax is already described as a complication.

Article	Number of patients/ follow-up	Direction of conclusions	Reasons for non-inclusion in table 2
Zemlyak A, Moore WH, Bilfinger TV. (2010) Comparison of survival after sublobar resections and ablative therapies for stage I non-small cell lung cancer. Journal of the American College of Surgeons 211: 68–72.	Non-randomised comparative study n = 64 Follow-up = 3 years	3-year survival: • Sublobar resection = 87.1% • RFA = 87.5% • Percutaneous cryoablation = 77% 3-year cancer-free survival: • Sublobar resection = 60.8% • RFA = 50% • Percutaneous cryoablation = 45.6%	Small non-randomised comparative study. (study published after consultation)
Zhu JC, Yan TD, Glenn D et al. (2009) Radiofrequency ablation of lung tumors: feasibility and safety. Annals of Thoracic Surgery 87: 1023-8.	Case series n = 100	Overall morbidity rate = 43% (55/129) Pneumothorax = 32% (41/129) Pleuritic chest pain = 18% (23/129) Haemoptysis = 7% (9/129) Pleural effusion = 12% (15/129) Chest drain insertion = 20% (26/129)	Larger case series are included.
Zhu JC, Yan TD, Morris DL. (2008) A systematic review of radiofrequency ablation for lung tumors. Annals of Surgical Oncology 15: 1765-74.	Systematic review 17 studies (all case series)	Procedure-related morbidity ranged from 15% to 56% and mortality from 0% to 6%.Rate of pneumothorax ranged from 5% to 61%, with 3% to 39% requiring chest drain insertion. Local recurrence = 3–38% (median 11%) Median progression-free interval= 15–27 months (median 21 months) Survival rates: • 1 year = 63–85% • 2 year = 55–65% • 3 year = 15–46%	Search date: 2006 No meta-analysis.

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

Guidance	Recommendations
Interventional procedures	**Percutaneous radiofrequency ablation for primary and secondary lung cancers. NICE interventional procedures guidance 185 (2006).** ***This guidance is currently under review.*** 1.1 Current evidence on the safety and efficacy of percutaneous radiofrequency ablation for primary and secondary lung cancers shows that there are no major safety concerns with this procedure. There is evidence that the treatment can reduce tumour bulk; however, this evidence is limited and is based on heterogeneous indications for treatment. The procedure should therefore be used only with special arrangements for consent, audit and clinical governance. 1.2 Clinicians wishing to undertake percutaneous radiofrequency ablation for primary and secondary lung cancers should take the following actions. • Inform the clinical governance leads in their Trusts. • Ensure that patients understand the uncertainty about the procedure's safety and efficacy and provide them with clear written information. In addition, use of the Institute's information for patients ('Understanding NICE guidance') is recommended (available from www.nice.org.uk/IPG185publicinfo). • Audit and review clinical outcomes of all patients undergoing percutaneous radiofrequency ablation for primary and secondary lung cancers. 1.3 Patient selection should be carried out in the context of a multidisciplinary team, usually including a thoracic surgeon, an oncologist and a radiologist. This procedure should be used in patients for whom surgery is inappropriate or who are unwilling to undergo surgery. 1.4 Further research will be useful in relation to survival and quality-of-life outcomes, and in establishing the potential role of this procedure as either curative or palliative treatment.

	Photodynamic therapy for advanced bronchial carcinoma. NICE interventional procedures guidance 87 (2004). 1.1 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. 1.2 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. **Photodynamic therapy for localised inoperable endobronchial cancer. NICE interventional procedures guidance 137 (2005).** 1.1 Current evidence on the safety and efficacy of photodynamic therapy for localised inoperable endobronchial cancer appears adequate to support the use of this procedure provided that the normal arrangements are in place for audit and clinical governance. 1.2 This procedure is a treatment option for patients with localised endobronchial cancer that is unsuitable for surgical resection. Clinicians should ensure that patients understand the aim of the treatment, especially when its purpose is palliation. Patients should also be informed of the alternative treatment options available. Clinicians should provide them with clear written information and, in addition, use of the Institute's Information for the public is recommended. 1.3 Further research and audit will be useful in clarifying the indications and benefits of this procedure. **Cryotherapy for malignant endobronchial obstruction. NICE interventional procedures guidance 142 (2005).** 1.1 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. 1.2 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 Information for the public is recommended.

Clinical guidelines	**Lung cancer: diagnosis and treatment. NICE clinical guideline 24 (2005)** 1.9.6 Patients with endobronchial symptoms that are not palliated by other means may be considered for endobronchial therapy.

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

Databases	Date searched	Version/files
Cochrane Database of Systematic Reviews – CDSR (Cochrane Library)	30/03/2010	Issue 1, 2010
Database of Abstracts of Reviews of Effects – DARE (CRD website)	30/03/2010	-
HTA database (CRD website)	30/03/2010	-
Cochrane Central Database of Controlled Trials – CENTRAL (Cochrane Library)	30/03/2010	Issue 1, 2010
MEDLINE (Ovid)	30/03/2010	1950 to March Week 3 2010
MEDLINE In-Process (Ovid)	30/03/2010	March 29, 2010
EMBASE (Ovid)	30/03/2010	1980 to 2010 Week 09
CINAHL (NLH Search 2.0)	30/03/2010	-
Zetoc	30/03/2010	-

Trial sources searched on: 30/03/2010

- National Institute for Health Research Clinical Research Network Coordinating Centre (NIHR CRN CC) Portfolio Database
- Current Controlled Trials *meta*Register of Controlled Trials – *m*RCT
- Clinicaltrials.gov

Websites searched on: 30/03/2010

- National Institute for Health and Clinical Excellence (NICE)
- Food and Drug Administration (FDA) - MAUDE database

MEDLINE search strategy

The MEDLINE search strategy was adapted for use in the other sources.

1	exp Lung Neoplasms/
2	((lung* or pulmon* or thora*) adj3 (neoplasm* or cancer* or carcinoma* or adenocarcinom* or tumour* or tumor* or malignan* or metasta*)).tw.
3	or/1-2
4	Catheter Ablation/
5	(catheter adj3 ablat*).tw.
6	((needle* or electrode* or heat*) adj3 ablat*).tw.
7	(radiofrequen* adj3 ablat*).tw.
8	(radio frequen* adj3 ablat*).tw.
9	(radio-frequen* adj3 ablat*).tw.
10	(rf adj3 ablat*).tw.
11	rfa.tw.
12	or/4-11
13	3 and 12
14	Animals/ not Humans/
15	13 not 14
16	limit 15 to ed=20091106-20100331