Microwave Ablation of Lung Tumours – Clinical Update

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Abstract

Thermal ablation offers an intriguing therapeutic option to improve local tumour control and survival in patients with early-stage non-small cell lung cancer or patients with limited metastatic disease from non-lung primaries who are not candidates for surgery, either because of poor cardiopulmonary reserve, anatomic constraints limiting resection, failure of traditional therapies, or refusal of operative approaches. The new field of interventional oncology needs adequate knowledge of the therapeutic tools, advantages and limitations of each method, when and how to apply them, as well as of the new integrative protocols that improve their efficacy. This article provides a clinical review of the role of microwave ablation therapy of primary and metastatic tumours.

Keywords

Microwave, ablation, therapy, lung tumour, metastases

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Lung cancer remains the leading cause of cancer death in the US, accounting for an estimated 29 % of cancer deaths in 2009. Pneumonectomy or lobectomy with hilar and mediastinal lymph node sampling is the gold standard treatment and offers the best option for curing stage 1/2 non-small cell lung cancer (NSCLC),[1–5] Unfortunately, only 15 % of patients present with stage 1/2 disease, and many of these do not meet the pulmonary physiologic criteria for lobar resection. In addition to lung cancer, pulmonary metastases are present in 25–30 % of patients dying from all types of cancer. For some patients with oligometastatic pulmonary disease, metastectomy is associated with an improvement in survival. External beam radiation traditionally has been offered as the alternative to surgical resection for NSCLC or pulmonary metastatic disease. Unfortunately, the five-year survival following radiation for stage 1 and 2 NSCLC remains low at 15–20 %, with local recurrence being the most common type of failure.[1–5]

Thermal ablation offers an intriguing therapeutic option to improve local tumour control and survival in patients with early-stage NSCLC or with limited metastatic disease from non-lung primaries who are not candidates for surgical intervention, either because of poor cardiopulmonary reserve, anatomic constraints limiting resection, failure of traditional therapies or refusal of operative approaches. Thermal ablation has been shown to be effective in treating tumours in bone, kidney and liver. This article offers a clinical update on performing thermal ablation in lung tissue and reviews the current literature regarding microwave (MW) ablation therapy in the lung.

The evolving field of pulmonary interventional oncology can only be considered as a small integrative part in the complex area of oncology. The new field of interventional oncology needs adequate knowledge of the therapeutic tools, advantages and limitations of each method, when and how to apply them, as well as of the new integrative protocols that improve their efficacy. In recent years, several new minimally invasive techniques for the non-surgical treatment of lung malignancies, including percutaneous image-guided ablation therapy, have been developed and refined. Since the first reported use of thermal ablation for lung cancer in 2000, there has been a huge increase in the use of the procedure.[6–9]

'Tumour ablation' is defined as the direct application of thermal or chemical therapies to a specific focal tumour (or tumours) in order to achieve either eradication or substantial destruction. The expression 'image-guided' is added to the term 'tumour ablation' because most of the therapies are performed using imaging modalities such as fluoroscopy, ultrasound, computed tomography (CT) or magnetic resonance imaging (MRI). Tumour ablation can be divided into two main categories: chemical and thermal ablation. Classification in the 'chemical ablation' category is based on the agent used – for example, ethanol or acetic acid. By definition, chemical ablation induces coagulation necrosis and tumour ablation. The 'thermal ablation' category includes all energy sources that destroy a tumour with thermal energy, either by heat (radiofrequency [RF], laser-induced thermotherapy [LITT], MW, etc.) or by cold (cryoablation).[8]

Objectives of Ablation Therapy

The main objectives of ablation therapy of pulmonary tumours (and other malignancies) are:

- to eradicate all viable malignant cells in the target volume, with a safety margin to ensure complete eradication; and
- to minimise the damage to a certain targeted volume in order to provide a good functioning reserve of the rest of the lung; this is particularly important in patients with limited pulmonary function due to extensive underlying emphysema and fibrosis.[10,11]

The potential advantages of local tumour ablation therapy over surgical resection include:

- selective damage;
- minimal treatment morbidity and mortality;
- less breathing impairment in patients with borderline lung function through sparing healthy lung tissue;
- repeatability;
- fairly low cost;
- excellent imaging during the procedure and for follow-up; and last but not least
- gain in quality of life with less pain, much shorter hospitalisation (whether the intervention is performed on an outpatient basis or with overnight stay) and thus quicker re-access to social life.[11,12]

Pathophysiology of Hyperthermic Ablation

Raising the tissue temperature to 45 °C for several hours results in irreversible cell damage. This cytotoxic effect can be drastically shortened down to a few minutes by increasing the temperature to up to 50–60 °C. At temperatures between 60 °C and 100 °C, almost instant coagulation of tissue is induced and manifests as irreversible damage to mitochondrial and cytosolic enzymes of the cells and to DNA. At more than 100–110 °C, tissue will vaporise and carbonise.[13] This thermobiological effect is at the core of hyperthermic ablation. The lung has a complex structure of ventilated alveoli and bronchi in addition to blood vessels. The air-filled cavities work as heat insulators, while the enclosing capillary beds function as heat dissipaters. Air in the bronchial system is continually exchanged by ventilation and, similarly, the high blood circulation carries away heat. The location-dependent variability of these structures can lead to a variation in thermal parameters.[14]

Indications for Pulmonary Ablation Therapy

The indications for local ablation of primary and metastatic lung neoplasms are similar to those established for resection, although with some modifications (see *Table 1*). It is usually applied when the number of lesions per hemithorax is five or less and the diameter of the largest lesion is less than 5 cm – however, there is institutional variability regarding these criteria. Ideally, tumours should be smaller than 3.5 cm in diameter and completely surrounded by non-tumourous lung.[6,11,15]

Most authors think that the treatment should be offered only to patients with no evidence of extrapulmonary disease; however, there is a role for thermal ablation in pain palliation. Ablation therapy can also be applied in patients who are refractory or not amenable to conventional therapies (surgery, chemotherapy and radiation therapy) as a result of coexistent morbidity (for example, pulmonary emphysema, liver cirrhosis, haemodialysis or another tumour). Contraindications for ablation therapy include bleeding coagulopathy (international normalised ratio (INR) greater than 1.5 and platelet count less than 75 x 10^3/µl).[6,9,11,15]

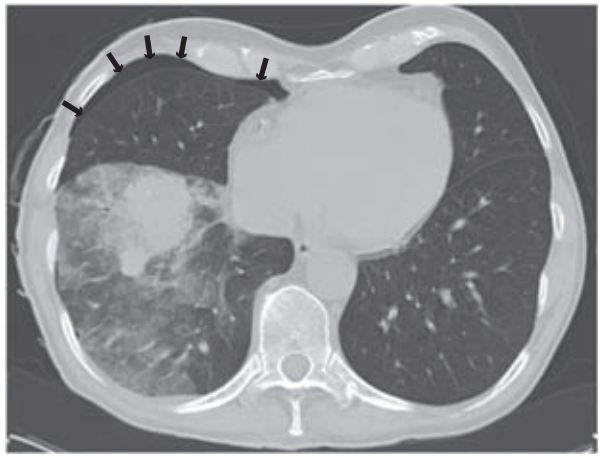
Complications of Pulmonary Ablation Therapy

From a procedural and technical point of view, pulmonary ablation therapy has been considered as a safe and minimally invasive method. Complications associated with it are outlined below.

Pneumothorax

In most large studies, the incidence of pneumothorax ranges from 15–25 %, which is similar to the incidence of pneumothorax after lung biopsy as reported in the literature. According to the literature, the most important risk factors include old age, chronic obstructive pulmonary disease, and deep basal and small lesions and long intrapulmonary ablation track (see *Figure 1*).[9,10,16]

Figure 1: Pneumothorax after Microwave Ablation in a 47-year-old Male Patient with Basal Pulmonary Metastasis from Colorectal Cancer



A 47-year-old male patient with basal pulmonary metastasis from colorectal cancer underwent microwave ablation. The computed tomography scan 24 hours post-ablation revealed the development of pneumothorax (black arrows). This is an example of the risk of pneumothorax associated with basal pulmonary lesions. The image also shows diffuse ground glass opacification in the right lower lobe surrounding the ablated lesion, which cleared within three weeks.

Table 1: Inclusion and Exclusion Criteria for Ablation Therapy of Pulmonary Neoplasms

Prerequisites	• Adequate assessment of the overall tumour situation • Incorporation of thermal therapy into a comprehensive treatment concept • Balance of advantages and disadvantages of a minimally invasive therapy by an interdisciplinary oncological team
Indications	• Exclusion of resectability • Medical reasons • Number of lesions <4–5* • Lesion diameter <3.5–5 cm*
Contraindications	• Progressive systemic disease • Lesions >5, diameter >5 cm • Septicaemia and coagulopathy
Relative contraindication	• Vicinity to critical structures

** There is variability between centres regarding these criteria.*

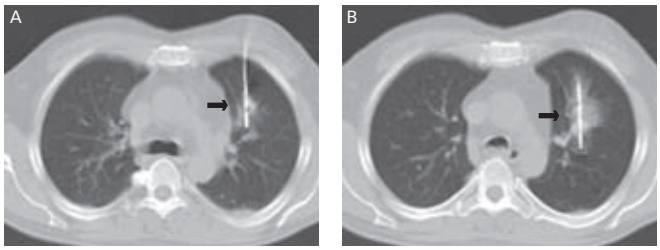
Pulmonary Haemorrhage

Haemorrhage is a known complication in lung ablation and results from the positioning of the ablation device rather than from the ablation process. The reported incidence of haemorrhage is <1 %, but it seems to be underestimated (see *Figure 2*).[12]

Pleural Effusion

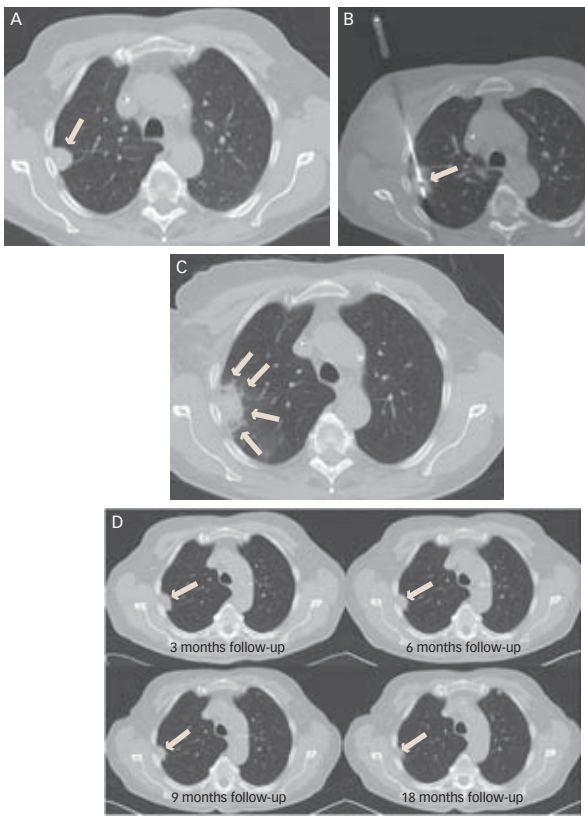
A small amount of pleural effusion is usually seen during the ablation procedure, increasing in size with ablation duration and number of lesions treated. On the control erect chest radiograph post-intervention, the lateral costophrenic angle is obliterated. These effusions, sympathetic in character, do not require tapping. They usually resolve within a couple of days and are asymptomatic.[9,17,18]

Figure 2: Pulmonary Haemorrhage Developing during Microwave Ablation in a 51-year-old Female Patient with Pulmonary Metastasis from Breast Cancer



A: Computed tomography scan during microwave ablation in a 51-year-old female patient with left upper lobe pulmonary metastasis from breast cancer. B: Notice the development of pulmonary haemorrhage (black arrow) in the track of ablation due to the applied microwave antenna traversing pulmonary vessels.

Figure 3: Successful Microwave Ablation of a Metastasis from Renal Cell Carcinoma in a 58-Year-Old Male Patient



A 58-year-old male patient had a history of left-sided renal cell carcinoma (RCC). He was treated by left nephrectomy. A: Computed tomography (CT) scan showing a right pleural based rounded pulmonary lesion (arrow). The lesion was histopathologically proven to be an RCC metastasis. B: CT scan during microwave (MW) ablation of the lesion (arrow). C: CT scan 24 hours post-MW ablation of the lesion, revealing ground glass opacification surrounding the lesion and veiling of its margin (arrows). D: Serial follow-up CT scans of the metastasis at three, six, nine and 18 months after MW ablation, revealing progressive scaring and reticulation of the ablated area (arrows) as well as reduction of its size denoting complete response.

Cavitation and Infection

Cavitation at the ablation site can develop, but it usually resolves uneventfully. Cavitation is seen significantly more frequently when the size of the lesion at one week after treatment exceeds the size of the pre-treatment lesion by 200 % or more. Some centres performing ablation therapy apply prophylactic intravenous antibiotics prior to the ablation on the day of the intervention; others even cover the day before and the day after the ablation.[12]

Tumour Seeding

Tumour seeding by the carrying of tumour cells along the probe's pathway(s) is typically detected three to 12 months after the procedure and is basically an issue of inappropriate technique. The risk of tumour seeding can be almost eliminated if the probe is properly positioned on the first pass and does not cross the tumour primarily; otherwise, tumour cells can be pushed out of the tumour in its periphery. A sufficient safety margin around the tumour and removing the probe by additional ablation of the needle tract will further lower the risk of tumour cell spread.[12,19]

Common Minor Side Effects

Common minor side effects include pain in the puncture site area, pleuritic pain, nausea, vomiting, moderate fever, tiredness and headache. Fever, nausea, tiredness and vomiting are the main elements of post-ablation syndrome, which is seen in about two-thirds of patients and might last for one to two weeks. In general, supportive therapy, including mild analgesics and non-steroidals, is sufficient in such cases.[9,12,18]

Physics of Microwave Heating

Microwaves belong to the electromagnetic waves with wavelengths in the range of 30 cm (frequency = 1 GHz) to 1 mm (300 GHz). For medical uses, specific frequencies between 915 mHz and 2.4 GHz are employed. As the water molecule exhibits an electric dipole moment, the electric field of the MW excites harmonic oscillations in the water as they try to align themselves with the alternating electric field, resulting in warming. Other molecules are heated by convection due to the fact that macromolecules are not directly affected by microwaves. The lowest resonance frequency of the water molecule is at 22.2 GHz. However, even at MW frequencies in the range of 1–2 GHz, the electromagnetic energy is effectively absorbed with a typical efficiency factor of 50–60 %.[20,21]

Microwave Ablation – Literature and Clinical Considerations

Compared with RF ablation, which deposits thermal energy in the tissue by resistive heating using alternating current at 365–480 kHz, MW ablation uses a different principle theoretically providing several advantages. The MW antenna emits electromagnetic radiation into the tissue without the necessity of an electrical current. The resulting coagulation necrosis, however, is similar at histopathological examination with both modalities (see *Figure 3*).[20,21] As no electrical current is applied, carbonisation, tissue boiling and steam bubbles surrounding the applicator do not hamper the energy deposition. Compared with RF ablation, much higher tumour temperatures of up to 150 °C may therefore be reached. As there is an exponential dependence between tissue temperature and induced cell death, complete coagulation of malignant tissue may be achieved in much shorter time. No electric current is passing through the patient's body, therefore there is no need for the use of grounding pads. The danger of tissue heating in unwanted areas, which may occur in RF ablation (especially at transitions of anatomical structures with relatively high electrical resistance, such as vessel walls and skin next to grounding pads) is strongly reduced.

Both RF and MW ablation are reported to show comparable ablation diameters. RF ablation typically creates ablation diameters of 2–4 cm depending on the system applied (multi-tined, internally cooled single or cluster).[22] The MW devices used in clinical practice show varying sizes of coagulation volume depending on their geometry: applicators

Table 2: Literature on Microwave Ablation of Lung Tumours

Study	Number of Patients; Tumour Data	Indication	Local Control Rate	Survival
Feng et al., 2002[28]	20; 28 lesions: 8 primary, 12 metastatic	Local control	Local response rate of 57 %	Not reported
Wolf et al., 2008[25]	50; 30 primary lung cancers, 20 metastatic	Local control	Primary local control in 74 % of patients at a median follow-up of 10 months, with additional secondary local control in 6 % of patients for a total local control rate of 80 %	1-, 2-, and 3-year actuarial survival rate of 65 %, 55 % and 45 %, respectively
Vogl et al., 2011[27]	80 patients; 130 metastatic lesions	Local tumour control	Primary local control in 73.1 % of patients at a median follow-up of 16 months	1- and 2-year actuarial survival rate of 91.3 % and 75 %, respectively

of straight geometry are reported to achieve coagulation of up to 2.5 cm in diameter, whereas single loop-antenna applicators have been reported to result in coagulation of up to 3.5 cm in diameter.[21,23,24]

To increase the coagulation volume, multi-applicator approaches may be used (multi-polar RF devices, multi-applicator MW devices). With increasing ablation power, however, the danger of tissue heating in unwanted areas significantly increases in RF ablation, whereas this is not an issue in MW ablation. In RF ablation, the pathway of the electrical current through the body is dependent on anatomical structures, and notable distortions of the spherical geometry of the ablation volume have been reported, decreasing the predictability of the outcome. Another drawback of RF ablation is the limited possibility of multi-applicator use with conventional monopolar techniques due to a shielding effect of the electric current among the multiple RF applicators, leading to unpredictable coagulation geometries for arbitrary placement of electrodes. No interference between different electrodes is found in MW ablation.

Three different modalities of energy disposition in a MW multi-applicator approach have been described. The conventionally applied technique is the coherent application of energy with one generator for each electrode. Another approach is the incoherent application of energy, in which one generator switches rapidly between the multiple applicators. To further improve the uniformity of power deposition, phase modulation between applicators has also been proposed. The last two modalities, however, have not yet been sufficiently investigated.

Vascular flow may cause a significant reduction in the effectiveness of RF ablation due to the cooling of the perivascular area, which is called the heat sink effect.[21,23,24] In several recent publications, the opposite effect was described for MW ablation, where a selective tracking of the ablation zone along blood vessels was discovered. Up to now, this effect has not been completely explained. It has been suggested that the presence of a vessel might cause a distortion or extension of the energy distribution pattern of the electromagnetic irradiation. It has also been suggested that the effect could possibly be due to thermally produced vapour travelling though the vessel. The increased performance of MW ablation close to vessels may reduce the local relapse rate close to liver veins, compared with RF ablation. However, it may carry an increased risk of complications associated with thrombosis of major vessels.[25,26,27]

Some of the studies of MW ablation of lung tumours are summarised in *Table 2*.

Conclusion

MW ablation therapy is a safe therapeutic tool for the treatment of primary and metastatic pulmonary neoplasms. The efficacy of treatment is determined mainly by pre-ablation tumour size and location in relation to the hilum. Successful MW ablation of pulmonary lesions is more likely for peripheral lesions of 3 cm or smaller. The pre-ablation tumour size (>3 cm) is the most significant independent predictor of ablation success. The careful selection of cases in which the benefit of ablation therapy will outweigh the potential complications is key to ensuring optimal patient outcomes. ■

1. Greene FL, American Joint Committee on Cancer, American Cancer Society, *AJCC Cancer Staging Handbook and AJCC Cancer Staging Manual,* 6th edn, New York: Springer, 2002.
2. Davidson RS, Nwogu CE, Brentjens MJ, Anderson TM, The surgical management of pulmonary metastasis: current concepts, *Surg Oncol,* 2001;10:35–42.
3. Labow DM, Buell JE, Yoshida A, et al., Isolated pulmonary recurrence after resection of colorectal hepatic metastases – is resection indicated? *Cancer J,* 2002;8:342–7.
4. Sibley GS, Jamieson TA, Marks LB, et al., Radiotherapy alone for medically inoperable stage I non-small-cell lung cancer: the Duke experience, *Int J Radiat Oncol Biol Phys,* 1998;40:149–54.
5. Sirzén F, Kjellén E, Sörenson S, et al., A systematic overview of radiation therapy effects in non-small cell lung cancer, *Acta Oncol,* 2003;42:493–515.
6. McTaggart RA, Dupuy DE, Thermal ablation of lung tumors, *Tech Vasc Interv Radiol,* 2007;10:102–13.
7. Vogl TJ, Naguib NN, Eichler K, et al., Volumetric evaluation of liver metastases after thermal ablation: long-term results following MR-guided laser-induced thermotherapy, *Radiology,* 2008;249:865–71.
8. Goldberg SN, Grassi CJ, Cardella JF, et al., Image-guided tumor ablation: standardization of terminology and reporting criteria, *J Vasc Interv Radiol,* 2009;20:377–90.
9. De Baère T, Lung tumor radiofrequency ablation: where do we stand? *Cardiovasc Intervent Radiol,* 2011;34:241–51.
10. Lencioni R, Crocetti L, Cioni R, et al., Response to radiofrequency ablation of pulmonary tumours: a prospective, intention-to-treat, multicentre clinical trial (the RAPTURE study), *Lancet Oncol,* 2008;9:621–8.
11. Hiraki T, Gobara H, Iishi T, Sano Y, Iguchi T, Fujiwara H, Tajiri N, Sakurai J, Date H, Mimura H, Kanazawa S, Percutaneous radiofrequency ablation for clinical stage I non-small cell lung cancer: results in 20 nonsurgical candidates, *J Thorac Cardiovasc Surg,* 2007;134:1306–12.
12. Steinke K, Radiofrequency ablation (RFA). In: Vogl TJ, Helmberger TK, Mack MG, Reiser MF (eds), *Percutaneous Tumor Ablation in Medical Radiology,* 1st edn, Berlin, Heidelberg: Springer, 2008;179–96.
13. Goldberg SN, Radiofrequency tumor ablation: principles and techniques, *Eur J Ultrasound,* 2001;13:129–47.
14. Helmberger T, Radiofrequency. In: Vogl TJ, Helmberger TK, Mack MG, Reiser MF (eds), *Percutaneous Tumor Ablation in Medical Radiology,* 1st edn, Berlin, Heidelberg: Springer, 2008;7–20.
15. Sharma A, Moore WH, Lanuti M, Shepard JA, How do I do it: radiofrequency ablation and cryoablation of lung tumors, *J Thorac Imaging,* 2011;26:162–74.
16. Hiraki T, Gobara H, Mimura H, et al., Does tumor type affect local control by radiofrequency ablation in the lungs? *Eur J Radiol,* 2010;74:136–41.
17. Simon CJ, Dupuy DE, DiPetrillo TA, et al., Pulmonary radiofrequency ablation: long-term safety and efficacy in 153 patients, *Radiology,* 2007;243:268–75.
18. Sonntag PD, Hinshaw JL, Lubner MG, et al., Thermal ablation of lung tumors, *Surg Oncol Clin N Am,* 2011;20:369–87.
19. Guihaire J, Verhoye JP, de Latour B, Leguerrier A. Parietal tumor recurrence of lung metastasis after radiofrequency ablation, *Interact Cardiovasc Thorac Surg,* 2010;10:650–1.
20. Simon CJ, Dupuy DE, Mayo-Smith WW, Microwave ablation: principles and applications, *Radiographics,* 2005; 25(Suppl. 1):S69–83.
21. Boss A, Dupuy D, Pereira PL, Microwave. In: Vogl TJ, Helmberger TK, Mack MG, Reiser MF (eds), *Percutaneous Tumor Ablation in Medical Radiology,* 1st edn, Berlin, Heidelberg: Springer, 2008;21–8.
22. Durick NA, Laeseke PF, Broderick LS, et al., Microwave ablation with triaxial antennas tuned for lung: results in an in vivo porcine model, *Radiology,* 2008;247:80–7.
23. Brace CL, Hinshaw JL, Laeseke PF, et al., Pulmonary thermal ablation: comparison of radiofrequency and microwave devices by using gross pathologic and CT findings in a swine model, *Radiology,* 2009;251:705–11.
24. Carrafiello G, Mangini M, De Bernardi I, et al., Microwave ablation therapy for treating primary and secondary lung tumours: technical note, *Radiol Med,* 2010;115:962–74.
25. Wolf FJ, Grand DJ, Machan JT, et al., Microwave ablation of lung malignancies: effectiveness, CT findings, and safety in 50 patients, *Radiology,* 2008;247:871–9.
26. Wright AS, Sampson LA, Warner TF, et al., Radiofrequency versus microwave ablation in a hepatic porcine model, *Radiology,* 2005;236:132–9.
27. Vogl TJ, Naguib NN, Gruber-Rouh T, et al., Microwave ablation therapy: clinical utility in treatment of pulmonary metastases, *Radiology,* 2011;261:643–51.
28. Feng W, Liu W, Li C, et al., Percutaneous microwave coagulation therapy for lung cancer, *Zhonghua Zhong Liu Za Zhi,* 2002;24:388–90.