Current Status of Thermal Ablation Treatments for Lung Malignancies

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ABSTRACT

About 75% of lung cancer patients are not surgical candidates, either due to advanced disease or medical comorbidities. Furthermore, conventional treatments that can be offered to these patients are beneficial only to a small percentage of them. Thermal ablation is a minimally invasive treatment that is commonly used in this group of patients, and which has shown promising results. Currently, the most widely used ablation techniques in the treatment of lung malignancies are radiofrequency ablation (RFA), microwave ablation, and cryoablation. Although the most studied technique is RFA, recent studies with microwave ablation and cryoablation have shown some advantages over RFA. This article reviews the application of thermal ablation in the thorax, including patient selection, basic aspects of procedure technique, imaging follow-up, treatment outcomes, and comparison of ablation techniques.

KEYWORDS: Lung cancer, thermal ablation, radiofrequency ablation, cryoablation, microwave ablation

Objectives: Upon completion of this article, the reader should be able to illustrate the basics of percutaneous thermal ablation in the thorax, including patient selection, basic aspects of procedure technique, imaging follow-up, treatment outcomes, and comparison of ablation techniques.

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Lung cancer is the second most common cancer and leading cause of cancer death in both men and women in the United States. An estimated 215,000 new cases of lung cancer were diagnosed in 2008, accounting for ~15% of cancer diagnoses.¹ An estimated 161,840 deaths, accounting for ~29% of all cancer deaths, were estimated to occur in 2008.¹ Complete resection of lung cancer with surgical lobectomy and complete lymph node dissection remains standard of care procedure and offers patients the best chance of a long-

term disease-free survival.² However, only about one-third of patients are surgical candidates.³ Other patients can be offered only conventional treatments, such as external beam radiation therapy with or without systemic chemotherapy. These treatments are beneficial only to a small percentage of patients, and can offer little chance for high quality, prolonged survival.⁴

Image-guided tumor ablation is a technique of controlled, direct thermal (heating or cooling) destruction of cells and tissue in a known manner. Because the

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technique is minimally invasive, it allows for reduced morbidity and mortality, conservation of normal lung tissue, and lower procedural cost. Thermal ablation is suitable for real-time imaging guidance, and can be performed in an outpatient setting. In addition, thermo-coagulation causes cytoreduction, which allows external beam therapy and chemotherapy to be more effective.⁵ Furthermore, there is evidence that combined therapy may result in improved survival as compared with either conventional radiation therapy or percutaneous ablation alone.^{6,7} It is becoming clearer that thermal ablation is a safe and technically feasible procedure for treatment of unresectable pulmonary malignancies. The goal of thermoablative therapy is to prolong disease-free survival with a reasonable quality of life. At the current time, the most widely used lung tumor ablation techniques include percutaneous radiofrequency ablation (RFA), microwave ablation, and cryoablation. This article reviews the application of thermal ablation in the thorax, including patient selection, basic aspects of procedure technique, imaging follow-up, treatment outcomes, and comparison of ablation techniques.

PATIENT SELECTION

Currently, image-guided thermal ablation procedures are best suited for medically inoperable, high-risk patients with early-stage lung cancers. These patients could qualify for surgical resection but are medically not operable due to comorbid cardiopulmonary disease, particularly severe chronic obstructive pulmonary disease, or inability to tolerate lung loss. Patients with small, oligonodular, and favorably located pulmonary metastatic lesions without hilar or mediastinal nodal and extrathoracic involvement,⁸ and patients who seek palliative measures for tumor-related symptoms or chest recurrences within treatment fields are also suited for this procedure. Patients who are stable enough to undergo computed tomography- (CT-) guided needle biopsy are good candidates for lung tumor ablation. Patients with severe pulmonary fibrosis and patients with severe emphysema with limited life expectancy (<1 year) should be considered poor candidates.⁴

PROCEDURE

Patients are initially evaluated clinically (history, physical examination, laboratory analysis), and explained the benefits and risks (such as bleeding and serious cardiopulmonary incapacitation) of the procedure. Side effects of the procedure may include postablation syndrome, a systemic response to circulating factors (such as tumor necrosis factor) that results in fever, malaise, and anorexia. Other complications include mild to moderate intraprocedural pain (usually controlled with adequate analgesics), mild pyrexia (usually self-

limited and lasting up to several weeks), pneumothorax, hemorrhage, hemoptysis, bronchopleural fistula, acute respiratory distress syndrome, reactive pleural effusion (usually self-limited), damage to adjacent anatomic structures, skin burns (secondary to inappropriate grounding pad placement in RFA), and infection or abscess formation.

The energy in the radiofrequency and microwave spectrum (10^9 to 10^{11} Hz) can potentially interfere with cardiac devices. Therefore, coordination with the patient's cardiac electrophysiologist and careful positioning of the grounding pads should be made. External pacing and defibrillation should be available for emergency use.

Most procedures may be performed under midazolam and fentanyl sedation, although in certain situations, when procedural pain is problematic and in pediatric patients, a general anesthetic or monitored anesthesia care may be required. Van Sonnenberg et al report using intercostal and paravertebral nerve blocks with a long-acting local anesthetic to prevent postprocedural discomfort and pain.⁹ There are also reports of cryoanalgesia effect in the intercostals nerves during cryoablation procedures.¹⁰ During ablation procedures, patients undergo monitoring with continuous pulse oximetry, electrocardiography, and measurement of blood pressure every 5 minutes.

To reduce potential complications of intravenous moderate sedation, patients are treated after an overnight fast. On the day of the procedure, patients with hypertension and cardiac disease are recommended to take their medications as usual. Insulin-dependent diabetic patients are asked to administer only half of their usual morning insulin dose. A short physical examination is performed and an intravenous line is placed right before the procedure.

The skin entry site for ablation is determined using preprocedure CT images. The area is then prepared in a sterile fashion, and local and deeper extrapleural lidocaine anesthesia is administered.

RADIOFREQUENCY ABLATION

In RFA, an electrode connected to an RFA generator is placed directly into the target tissue. A reference electrode (grounding pad) is placed directly on the patient's skin, in an area with good electrical conductivity (usually thigh or opposite chest wall). When an electric current (in the frequency of radio waves 460–480 kHz) is applied, tissue heating results from resistive energy loss (frictional heating) as electrons agitate ionic molecules in tissue as they move toward the reference electrodes. The goal is to heat tissue to 60 to 100°C. This temperature is considered lethal to target tissue.⁴ Energy generated during the RFA procedure is accumulated within the lung mass because the normal lung parenchyma acts as

an insulator and therefore concentrates the RF energy in the target tissue.¹¹ There is also a “heat-sink” effect from medium to large blood vessels and airways, which dissipates heat away from the normal adjacent tissue and concentrates the energy within the solid component of the target lesion.¹² This same effect may limit successful RFA of larger lesions.

CT fluoroscopy is used to assess placement of the needle and to plan the trajectory of the RF electrode. The choice of electrode length and the active tip is made according to the size and depth of the lesion. The electrode has an internal thermocouple that measures temperature in the tissue. It may also be coupled to an infusion pump with ice water to internally cool the electrode tip. Treatment times are typically between 4 to 12 minutes in one position. Electrodes used in RFA may be a single tip or a cluster electrode (three closely spaced electrodes), the latter of which can obtain a thermocoagulation diameter of up to 3 to 5 cm.¹³

Once the target lesion is treated, the RF electrodes are removed and a postprocedure CT scan is performed to evaluate for and treat pneumothorax, if needed. All patients are observed for 2 to 4 hours postprocedure, and a repeat chest radiograph is obtained to confirm the absence of pneumothorax.

MICROWAVE ABLATION

Microwave ablation can be performed percutaneously, laparoscopically, or through open surgical access. Electromagnetic microwaves traveling at 9.2×10^8 Hz produce friction and heat by agitating water molecules within the surrounding tissues and causing the molecules to flip.¹⁴ This procedure induces heat and coagulation necrosis and cell death. To maximize the interaction of the water molecules, microwave radiation can specifically be tuned to the natural frequency of water molecules. Temperature is used to measure the amount of heat generated depending on how fast the water molecules oscillate within the target lesion.

Microwave ablation has been successfully utilized in the treatment of hepatic malignancies by several groups.^{15–17} Tumors larger than 2 cm use three microwave applicators to create a large enough area of thermocoagulation. Internally cooled (to reduce conductive heating and prevent skin damage) single microwave antennas may be used individually or may be combined to give a triple cluster configuration to achieve greater ablation volumes.

A 14-gauge microwave antenna is placed within the tumor after standard preparation. The exposed noninsulated portion of the antenna, which emits the electromagnetic microwave, is placed at the distal margin of the lesion. Each microwave generator is capable of producing 45 W of power at a frequency of

915 MHz.¹⁴ Grounding is not necessary with microwave ablation. Intratumoral temperatures are measured with separately placed thermocouple devices. Unlike RFA, tissue charring is not a significant limitation of electromagnetic wave propagation used in microwave ablation.

CRYOABLATION

Percutaneous cryoablation is based on the Joule-Thomson effect, in which gas in a region of high pressure travels through a porous plug into an area of lower pressure, thereby allowing the gas to expand and become cooler. Argon gas allows expansion from high pressure to low pressure through a constricted orifice (J-T port) within the cryoprobe at ultracold temperatures (approximately -160°C) and forms an “ice ball” as a marker for identifying the ablative margins. At the end of the procedure, helium gas is used to warm the probe and facilitate removal. Each cryoablation treatment typically consists of consecutive freeze (10 minutes), thaw (8 minutes), and freeze (10 minutes) cycles. Faster ablation schemes using a 3-minute freeze, 3-minute thaw, 7-minute freeze, 7-minute thaw, and a final 5-minute freeze have been proposed to improve the zone of ablation and slightly shortening the ablation time to 25 minutes compared with 28 minutes.

The cryoablation procedure is based on the freeze, thaw, freeze technique, with osmotic shifts causing cellular membrane rupture and eventual cell death. The resulting endothelial damage leads to platelet aggregation and microthrombosis.

FOLLOW-UP

Imaging studies immediately after the procedure and during follow-up are necessary to measure the success or failure of the initial procedure, interval tumor growth, need for repeat ablation, and metachronous tumor development.⁴ Unfortunately, at the current time, there is no proven imaging modality or time interval for immediate postablation and subsequent imaging to accurately depict success or failure of the initial ablation.

During and immediately after RFA, CT can be used to identify and analyze the “ground glass opacity” that occurs in the lung around the ablated mass (Fig. 1). This imaging appearance is a rough approximation of margin of tissue necrosis. There may be wrinkling of edges, vaporization, and “cockade phenomenon,” which demonstrates concentric rings of varying attenuation.¹⁸ The tumor diameter may decrease or may not change during treatment depending upon tumor type. At 1-month follow-up, the lesion may appear as an area of consolidation and nodularity and the diameter will be larger than before ablation (Fig. 1). There may also

Figure 1 An 81-year-old man with right upper lobe nonsmall cell lung cancer felt to be poor candidate for lobectomy due to underlying heart disease. Axial positron emission tomography-computed tomography (PET-CT) image (A) shows intense avidity in right upper lobe mass (arrow) without evidence of regional or distant spread of disease. Axial CT (B) shows 2.2-cm mass (arrow) to have speculated margins and small pleural tail consistent with biopsy diagnosis of adenocarcinoma, stage T1b, N0, M0 (stage IA). Axial CT image (C) with patient prone during radiofrequency ablation (RFA) shows ground glass halo sign (arrows) after application of RF energy. Halo gives rough indication of energy penetration into aerated lung around mass. Axial contrast-enhanced CT images (D) in mediastinal (top) and lung (bottom) windows 3 months post-RFA shows lesion consolidation with peripheral and pleural reactive enhancement and central nonenhancement consistent with adequate treatment. Axial PET-CT image (E) shows intense uptake in mass (arrow), which is unusual given size and technical success of treatment. Therefore, repeat biopsy performed (F), which confirmed activity was due to underlying inflammatory reaction and not due to residual tumor. This is an example of false-positive PET examination due to reactionary inflammation, which is seen commonly along a pleural surface. Axial contrast-enhanced CT images (G) 9 months after RFA show contraction of mass (arrow) consistent with involution of thermal scar.

be cavitations and “bubbly lucencies.”¹² Successfully treated lung tumor also shows decreased contrast enhancement. Positron emission tomography (PET) is also useful in the follow-up evaluation. A decrease or

complete absence of PET activity (photopenia) is suggestive of necrosis with no residual tumor. If there is residual or recurrent tumor, there is increased PET uptake within the periphery of the lesion.

Figure 2 An 80-year-old man with cavitary squamous cell carcinoma. Axial computed tomography (CT) (A) one week after biopsy shows residual pneumothorax and cavitary mass in left upper lobe (arrow). (B) Three microwave antennae placed after instillation of fluid into air filled cavity. Note ground glass halo (arrows) after a single 10-minute treatment. Axial CT (C) 3 months after microwave ablation shows enlargement of mass with central cavitation.

False-positive PET within 6 months can be seen with pleural reaction (Fig. 1). Akeboshi et al demonstrated that PET was more sensitive than contrast-enhanced CT to detect early tumor progression.¹⁹

On initial postablation contrast-enhanced CT scans, microwave-ablated tumors demonstrate the effects of thermally induced necrosis. A hazy ground-glass opacification is most commonly seen. At 1-, 3-, and 6-month intervals, ablation zones increase in size due to thermal changes in adjacent lung tissue, followed by a persistent reduction in diameter consistent with consolidation. Cavitary changes are also identified (Fig. 2). Ablated tumors abutting the visceral pleura result in pleural thickening in 34% of ablation zones or pleural retraction in 5% of ablation zones.²⁰

Kawamura et al reported imaging follow-up for patients that underwent cryoablation, reporting response according to the Response Evaluation Criteria in Solid Tumors (RECIST) protocol (based on objective measurements of lesion size before and after treatment). The response rate to cryoablation according to RECIST was 50% (Fig. 3).¹⁰

OUTCOMES AND COMPARISON OF THERMAL ABLATION TECHNIQUES

Presently, thermal ablation is best used for patients with early-stage lung cancer who are not surgical candidates, patients with small and favorably located pulmonary metastases, and patients in whom palliative care of tumor-related symptoms is the goal. Without this treatment, the majority of patients with lung cancer (86%) die of their disease.²¹ The overall 5-year survival rate for all clinical stages is dismal at 14%.²² The literature regarding the outcomes of thermal ablation is diverse because study groups are heterogeneous, and follow-up periods, reporting, and evaluation are different.⁴

Simon et al retrospectively reviewed 153 consecutive patients with 189 inoperable primary or metastatic lung cancers who received RFA and a median 20.5-month follow-up period.²³ The Kaplan-Meier 1-, 2-, 3-, 4-, and 5-year survival rates for stage I nonsmall cell lung cancer were 78%, 57%, 36%, 27%, and 27%, respectively, demonstrating a survival benefit in nonsurgical candidates. The corresponding survival rates for colorectal pulmonary metastases were 87%, 78%, 57%, 57%, and

Figure 3 A 75-year-old man with chest wall recurrence of nonsmall cell lung cancer after external beam radiotherapy presented with pain. Axial positron emission tomography-computed tomography (PET-CT) image (A) shows extensive metabolically active tumor invading chest wall. Axial CT image (B) after second freeze cycle from three cryoprobes shows expanding ice ball into chest wall (arrows). (C) 3-month follow-up (left) PET-CT shows cavitation and rim activity, which improved 6 months later (right).

57%. However, most of these patients received prior and/or adjuvant chemotherapy, therefore the sole effect of RFA is difficult to evaluate. The local tumor progression-free rates at 1-, 2-, 3-, 4-, and 5-years were 83%, 64%, 57%, 47%, and 47%, respectively. Tumor size was a statistically significant predictor of local tumor progression.

De Baere et al followed 60 patients with five or fewer tumors per patient, with a diameter of <4 cm.²⁴ Ninety-seven of 100 targeted tumors were treated and showed an overall survival rate at 71% and a lung disease-free survival at 18 months of 34%.²⁴ At 18 months, the overall survival rates were 76% for primary lung tumors and 71% for metastatic disease. This study also reports a 54% rate of pneumothorax, with chest tube placement in 9% of the procedures.

In a study with 50 patients that were treated with microwave ablation, Kaplan-Meier analysis yielded an actuarial survival of 65% at 1 year, 55% at 2 years, and 45% at 3 years from ablation.²⁰ Cancer-specific mortality yielded a 1-year survival of 83%, a 2-year survival of 73%, and a 3-year survival of 61%. These values were not significantly affected by index size of >3 cm, index size ≤ 3 cm, or presence of residual disease.

Kawamura et al performed cryoablation on metastatic pulmonary lesions accounting for 35 tumors in 20

patients.²⁵ The 1-year survival rate was 89.4%, with local recurrence of seven tumors in seven patients (20%).²⁵ Wang et al studied the feasibility and safety of the procedure for thoracic malignancy and demonstrated that tumor size and location were highly predictive of tumor ice coverage even when controlled for tumor stage and type.²⁶ A short-term follow-up showed palliative benefits of cryoablation in terms of general health status with increased dietary intake and weight gain.²⁶

The greatest advantage of RFA is experience. Most of the studies performed in the field of pulmonary thermal ablation are made with RFA. The main disadvantages of RFA are that the RFA systems are to be avoided in the mediastinum and high in the lung apex, as they can cause mechanical and thermal injury.⁴ Cavitation is a limitation of RFA as well. Jin et al reported one case of acute stroke in 200 patients treated.²⁷ Vaughn et al reported a case of massive hemorrhage in a 70-year-old man undergoing RFA of a lung malignancy due to concomitant clopidogrel.²⁸

The advantages of microwave ablation include consistently higher intratumoral temperatures, larger tumor ablation volumes, fast ablation times, use of multiple applicators, more effective heating in cystic masses, and improved convection profile.¹⁴ There is also increased affinity for water-based tissues and decreased “heat-sink”

effect. In addition, because microwave ablation does not rely on an electrical circuit as does RFA, multiple applicators can be applied simultaneously. It was demonstrated by Brace and colleagues in a swine model that microwave energy compared with RF energy is more effective energy source for use in the lung.²⁹

The advantages of cryoablation over RFA include larger tumor ablation volumes, ability to use multiple applicators, and less procedural pain. Cryoablation technique does not require the use of grounding pads, thereby eliminating the problem of grounding pad injuries. Other advantages are the ability to preserve collagenous and other structural cellular architecture in any frozen tissue, and the ability to see lower attenuation ice as it covers a soft tissue mass during the freeze cycles.⁴ Theoretical problems with cryoablation include bleeding, requiring additional maneuvers such as tract coagulation with fibrin glue.

CONCLUSION

Further research is being performed to identify the ideal tumor size, cell type, tumor morphology, and location for percutaneous ablation. In addition, the appropriate imaging follow-up criteria and timing to accurately determine the treatment success has yet to be completely defined. In the future, further delineation of which thermal ablation technique is best for the various clinical scenarios should be performed. Additionally, new advances and emerging technology should be focused on generating greater ablation volume in shorter time periods with real-time monitoring of treatment effects.

REFERENCES

1. American Cancer Society. Cancer Facts and Figures 2008. Atlanta, GA: American Cancer Society; 2008
2. Robinson LA, Ruckdeschel JC, Wagner H Jr, Stevens CW; American College of Chest Physicians. Treatment of non-small cell lung cancer-stage IIIA: ACCP evidence-based clinical practice guidelines (2nd edition). *Chest* 2007;132(3, Suppl):243S–265S
3. Gandhi NS, Dupuy DE. Image-guided radiofrequency ablation as a new treatment option for patients with lung cancer. *Semin Roentgenol* 2005;40(2):171–181
4. McTaggart RA, Dupuy DE, DiPetrillo T. Image guided ablation in the thorax. In: Geschwind J-F H, Soulen MC, eds. *Interventional Oncology: Principles and Practice*. New York: Cambridge University Press; 2008:440–474
5. Jain SK, Dupuy DE, Cardarelli GA, Zheng Z, DiPetrillo TA. Percutaneous radiofrequency ablation of pulmonary malignancies: combined treatment with brachytherapy. *AJR Am J Roentgenol* 2003;181(3):711–715
6. Grieco CA, Simon CJ, Mayo-Smith WW, DiPetrillo TA, Ready NE, Dupuy DE. Percutaneous image-guided thermal ablation and radiation therapy: outcomes of combined treatment for 41 patients with inoperable stage I/II non-small-cell lung cancer. *J Vasc Interv Radiol* 2006;17(7):1117–1124
7. Hines-Peralta A, Goldberg SN. Image guided interventions: fundamentals of radiofrequency tumor ablation. In: Geschwind J-F H, Soulen MC, eds. *Interventional Oncology: Principles and Practice*. New York: Cambridge University Press; 2008: 55–63
8. Suh R, Reckamp K, Zeidler M, Cameron R. Radiofrequency ablation in lung cancer: promising results in safety and efficacy. *Oncology (Williston Park)* 2005;19(11, Suppl 4): 12–21
9. VanSonnenberg E, Shankar S, Morrison PR, et al. Radiofrequency ablation of thoracic lesions: part 2, initial clinical experience—technical and multidisciplinary considerations in 30 patients. *AJR Am J Roentgenol* 2005;184(2): 381–390
10. Kawamura M, Izumi Y, Tsukada N, et al. Percutaneous cryoablation of small pulmonary malignant tumors under computed tomographic guidance with local anesthesia for nonsurgical candidates. *J Thorac Cardiovasc Surg* 2006;131(5): 1007–1013
11. Dupuy DE, Mayo-Smith WW, Abbott GF, DiPetrillo T. Clinical applications of radio-frequency tumor ablation in the thorax. *Radiographics* 2002;22:S259–S269
12. Nahum Goldberg S, Dupuy DE. Image-guided radio-frequency tumor ablation: challenges and opportunities—part I. *J Vasc Interv Radiol* 2001;12(9):1021–1032
13. Beland MD, Dupuy DE. Current and future applications of percutaneous radiofrequency ablation in the treatment of lung neoplasms. *Appl Radiol* 2006;35(12):21–26
14. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. *Radiographics* 2005; 25(Suppl 1):S69–S83
15. Shibata T, Iimuro Y, Yamamoto Y, et al. Small hepatocellular carcinoma: comparison of radio-frequency ablation and percutaneous microwave coagulation therapy. *Radiology* 2002;223(2):331–337
16. Seki T, Tamai T, Nakagawa T, et al. Combination therapy with transcatheter arterial chemoembolization and percutaneous microwave coagulation therapy for hepatocellular carcinoma. *Cancer* 2000;89(6):1245–1251
17. Lu MD, Chen JW, Xie XY, et al. Hepatocellular carcinoma: US-guided percutaneous microwave coagulation therapy. *Radiology* 2001;221(1):167–172
18. Gadaleta C, Catino A, Ranieri G, et al. Radiofrequency thermal ablation of 69 lung neoplasms. *J Chemother* 2004; 16(Suppl 5):86–89
19. Akeboshi M, Yamakado K, Nakatsuka A, et al. Percutaneous radiofrequency ablation of lung neoplasms: initial therapeutic response. *J Vasc Interv Radiol* 2004;15(5):463–470
20. Wolf FJ, Grand DJ, Machan JT, DiPetrillo TA, Mayo-Smith WW, Dupuy DE. Microwave ablation of lung malignancies: effectiveness, CT findings, and safety in 50 patients. *Radiology* 2008;247(3):871–879
21. Kvale PA, Simoff M, Prakash UB. American College of Chest Physicians. Lung cancer. Palliative care. *Chest* 2003;123(1, Suppl):284S–311S
22. Munden RF, Swisher SS, Stevens CW, Stewart DJ. Imaging of the patient with non-small cell lung cancer. *Radiology* 2005; 237(3):803–818
23. Simon CJ, Dupuy DE, DiPetrillo TA, et al. Pulmonary radiofrequency ablation: long-term safety and efficacy in 153 patients. *Radiology* 2007;243(1):268–275
24. de Baère T, Palussière J, Aupérin A, et al. Midterm local efficacy and survival after radiofrequency ablation of lung

- tumors with minimum follow-up of 1 year: prospective evaluation. *Radiology* 2006;240(2):587-596
25. Kawamura M, Izumi Y, Tsukada N, et al. Percutaneous cryoablation of small pulmonary malignant tumors under computed tomographic guidance with local anesthesia for nonsurgical candidates. *J Thorac Cardiovasc Surg* 2006;131(5):1007-1013
26. Wang H, Littrup PJ, Duan Y, Zhang Y, Feng H, Nie Z. Thoracic masses treated with percutaneous cryotherapy: initial experience with more than 200 procedures. *Radiology* 2005;235(1):289-298
27. Jin GY, Lee JM, Lee YC, Han YM, Lim YS. Primary and secondary lung malignancies treated with percutaneous radiofrequency ablation: evaluation with follow-up helical CT. *AJR Am J Roentgenol* 2004;183(4):1013-1020
28. Vaughn C, Mychaskiw G II, Sewell P. Massive hemorrhage during radiofrequency ablation of a pulmonary neoplasm. *Anesth Analg* 2002;94(5):1149-1151
29. Dupuy DE. Microwave ablation compared with radiofrequency ablation in lung tissue-is microwave not just for popcorn anymore? *Radiology* 2009;251(3):617-618