Available online at www.sciencedirect.com

SciVerse ScienceDirect

Journal of the Chinese Medical Association 76 (2013) 303−311

www.jcma-online.com

Review Article

Image-guided lung tumor ablation: Principle, technique, and current status

Chun-Ku Chen [a,b], Hsiao-Ping Chou [a], Ming-Huei Sheu [a,b,*]

[a] *Department of Radiology, Taipei Veterans General Hospital, Taipei, Taiwan, ROC*
[b] *National Yang-Ming University School of Medicine, Taipei, Taiwan, ROC*

Received July 11, 2012; accepted October 1, 2012

Abstract

Image-guided tumor ablation for lung malignancies has emerged as a treatment modality for medically inoperable patients. Overall, image-guided lung tumor ablation is a minimally invasive procedure that has an acceptable safety profile and less impact on lung function. This is important for patients with poor pulmonary and/or cardiac functions or with multiple comorbidities, which prevent them from undergoing surgery, chemotherapy, and radiation therapy. Herein, we review the principle, techniques, clinical application, and patient outcomes of image-guided lung tumor ablation.

Keywords: ablation; cryoablation; lung; microwave; radiofrequency; tumor

1. Introduction

The lungs are a common site where malignancy occurs frequently. Lung cancer is the primary cancer, with the highest mortality rate being reported in Taiwan; it accounted for 20% of all cancer deaths in 2010.[1] Although the 1-year survival rate for lung cancer has increased, the overall lung cancer survival rate remains low with the existing treatment methods; a 17% overall 5-year relative survival rate has been reported for all stages combined, a 52% survival rate for localized disease, a 25% survival rate for regional disease, and a 4% survival rate for distant disease.[2] The lungs are also a common site for the spread of metastatic tumor that originates from other parts of the body. Approximately 20−50% of patients who die from tumor malignancies are found to have pulmonary metastases.[3]

Surgical resection is the first-line treatment for early-stage non-small-cell lung cancer (NSCLC), and pulmonary metastasectomy is performed for certain primary tumors such as hepatocellular carcinoma; in general, metastasectomy is associated with prolonged survival.[4] However, only 15% of lung cancer patients have localized disease for which surgery is a treatment of option. This is further complicated by a decrease in lung function after surgery, which results in a mean change in forced expiratory volume in 1 second (FEV_1) in 11−25% of patients after lobectomy, in 11−13% of patients after segmentectomy, and in 9% of patients after wedge resection.[5,6] A proportion of individuals with low pulmonary reserve do not meet the criteria for a lung operation, as defined by the American College of Surgeons Oncology Group/National Institutes of Health (NIH) Inoperability Criteria for Lung Surgery.[7]

Medically inoperable patients account for 85% of all lung cancer patients, and may need systemic chemotherapy or external-beam radiation therapy. Radiation therapy has traditionally been used for patients with medically inoperable lung cancer at clinical stage I and clinical stage II. Despite the development of modern radiotherapy techniques such as intensity-modulated radiation therapy, radiation to the lung tissue, which has a low dose tolerance, may still be damaging. Pneumonitis induced by radiation therapy occurs in more than 16% of patients when the V20 exceeds 22%, which may cause serious respiratory distress, requiring hospitalization and intubation, and can be fatal.[8] Moreover, lung function may

---

* Corresponding author. Dr. Ming-Huei Sheu, Department of Radiology, Taipei Veterans General Hospital, 201, Section 2, Shih-Pai Road, Taipei 112, Taiwan, ROC.

E-mail address: mhsheu@vghtpe.gov.tw (M.-H. Sheu).

http://dx.doi.org/10.1016/j.jcma.2013.03.004

deteriorate after irradiation of the lung; for example, the FEV_1 may decline by 10% after 12−18 months of radiation therapy.[9] These midterm complications and long-term sequelae limit the use of radiation therapy in patients who have poor cardiopulmonary function. Additionally, approximately 43% of patients with lung cancer have a poor performance status of 2−4, which prevents them from receiving surgical, radiation, or chemotherapy treatment, resulting in a bleak 5-year survival rate. Therefore, development of less invasive treatment modalities for patients with localized primary disease is important.

Tumor ablation is a minimally invasive and relatively safe procedure that can be a treatment option for patients who are medically inoperable due to their poor pulmonary reserve. Ablation refers to direct application of chemical or thermal therapies to a specific focal tumor (or tumors) to achieve eradication of the tumor or its substantial destruction.[10] The most contemporary tumor ablation technique is thermoablation; the subtypes are radiofrequency ablation (RFA), microwave ablation (MWA), and cryoablation, which are named according to their energy sources. Ablation techniques used for lung tumors are of two types: image-guided (percutaneous) and thoracoscopic lung tumor ablation. Image-guided lung tumor ablation techniques share the common feature of an energy generator in that it transfers the energy source to the tumor by an image-guided, inserted, needle-like energy "applicator" for a certain period of time, which results in tumor destruction. Ablation has several advantages, including selective damage, minimal morbidity and mortality, decreased loss of lung function (because much of the normal lung tissue is spared), repeatability, lower cost, excellent monitoring during treatment, increased quality of life with less pain, and shorter hospital stays.[7] The present review article covers the clinical application, mechanism, techniques, and outcomes of image-guided ablation of lung tumor.

2. Clinical application

Currently, lung tumor ablation is applied to primary lung cancer and metastatic lung malignancies for curative, symptom relieving, and cytoreduction purposes.[11] Interdisciplinary coordination plays a major role in the selection of patients. Curative ablation is indicated for stage I primary lung cancer patients who are medically inoperable due to their poor pulmonary functional reserve or cardiac comorbidities. Ablation is also performed in patients with lung metastases generated from colorectal and renal cell carcinoma, melanoma, hepatocellular carcinoma, and sarcoma primary tumors. A tumor size of 3.5 cm and the tumor number of 5 are generally considered to be the upper limits for ablation.[12] Patients with symptoms such as chest wall pain due to tumor invasion, hemoptysis, and coughing can also be relieved completely or partially by tumor ablation.[13] A combination of ablation therapies for advanced lung cancer and metastatic lung malignancies may also provide cytoreduction.[14,15]

The absolute contraindication for image-guided lung tumor ablation is the presence of uncorrectable coagulopathies. An international normalized ratio of >1.5, an activated partial thromboplastin time of >1.5 times the normal value, or a platelet count of $<50{,}000/\mu L$ should all be considered for correction. Plavix and aspirin should be withheld for 5 days.[16] Relative contraindications include a poor patient performance status of 3 or more and very limited life expectancy in the Eastern Cooperative Oncology Group.[12] Although ablation has a limited effect on pulmonary function, a low FEV_1 of less than 0.6 L is considered a relative contraindication.[17]

3. Radiofrequency ablation

3.1. Principle

Radiofrequency is the frequency of oscillation in the range of 3 kHz−300 GHz. The RFA applicator serves as an active electrode, and the reference electrode is the grounding pad. In modern RFA, electric fields are established between electrodes oscillate within the radiofrequency range (375−500 MHz). Ions in the tissue then oscillate with the oscillating electric fields, and their friction generates heat. The heat is then dispersed gradually through the tissue by conduction. Additionally, coagulation necrosis occurs after a period of RFA application. At the tumor site, if the tissue temperature remains at approximately 45°C for several hours, irreversible cell damage occurs; at 50°C permanent damage occurs within a few minutes; at 60°C coagulation is induced almost instantly; and at more than 100°C the tissue will vaporize and carbonize. Because carbonizing, also called charring, impedes heat conduction, which plays a major role in heat dispersion throughout the entire lesion, the ideal therapeutic temperature range for RFA is 60−100°C.[5,18] The extent of tissue destruction by ablation is called the ablation zone.

3.2. Equipment and techniques

Currently, there are three major types of equipment systems for RFA: a multitine electrode with temperature control, a multitine electrode with impedance control, and an internally cooled straight electrode. Each type of device consists of an electrical generator, a needle electrode, and a ground pad. The electrode diameter ranges from 14 gauge to 17 gauge. The maximal output of the generator is approximately 200 W (Fig. 1).

Prior to ablation surgery, patients fast overnight and have intravenous access established. The grounding pads are attached to their thighs, and the skin of the planned insertion site is then prepped. Under local anesthesia with or without conscious sedation, the electrode is placed under the guidance of computed tomography (CT). In some institutions, CT-fluoroscopy is utilized to achieve fast and precise electrode insertion. The generator is then turned on to produce the RF electric fields, and heat is generated at the target lesion. After a period of ablation, the patient is transferred to the recovery room for observation, and chest radiography is performed a few hours after the procedure. If no pneumothorax or

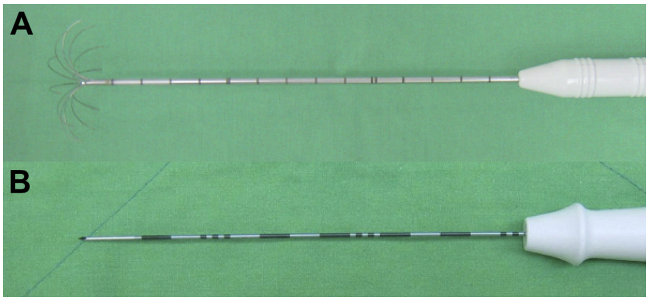

Fig. 1. Tip of the electrodes for radiofrequency ablation. (A) The multitines of the 14-gauge retractable multitine electrodes with an umbrella diameter of 4.0 cm (LeVeen Needle Electrode; Boston Scientific, Natick, MA, USA). (B) The tip of the 17-gauge straight electrode with a 2-cm active tip with an internally cooled system (Cool-tip ACT electrode; Covidien, Boulder, CO, USA).

hemothorax is observed, the patient is discharged on the same day or after overnight observation.

In a study, an observation of the microscopic infiltration of tumor cells surrounding the main tumor revealed that the mean value of microscopic extension was 2.69 mm for lung adenocarcinoma and 1.48 mm for lung squamous cell carcinoma. Thus, an ablation zone covering a margin of 5−10 mm beyond the visualizable tumor border is suggested.[19] The actual ablation zone may be estimated by the extent of ground glass opacity surrounding the lesion during RFA (Fig. 2). A 5-mm ground glass rim covering the lesion in the immediate postprocedural CT images suggests a good chance of complete treatment.[13] For large tumors, multiple overlapping ablations are used to achieve an adequate ablation zone. Precise electrode placement is critical for achieving the planned overlapping zone accurately, which can sometimes be difficult; therefore, a detailed preprocedural planning and monitoring during the procedure are important.

Several factors affect the ablation zone in lung tumor RFA. Vessels with flowing blood have a heat sink effect, removing heat from the region adjacent to the ablated site, which decreases the size of the ablation zone. This effect appears to be related to the vessel size and was observed consistently in vessels with diameters larger than 4 mm.[20] The air in the pulmonary parenchyma acts as an insulator to both heat and electric current conductions. Moreover, the ventilated bronchus removes the applied heat in a way similar to that of an air-cooled radiator. Thus, inserting the electrode precisely into the center of the planned ablation zone is important to obtain an optimal result.

3.3. Patient outcome

A meta-analysis study by Zhu et al[21] describes the complications of RFA for lung tumors, which include

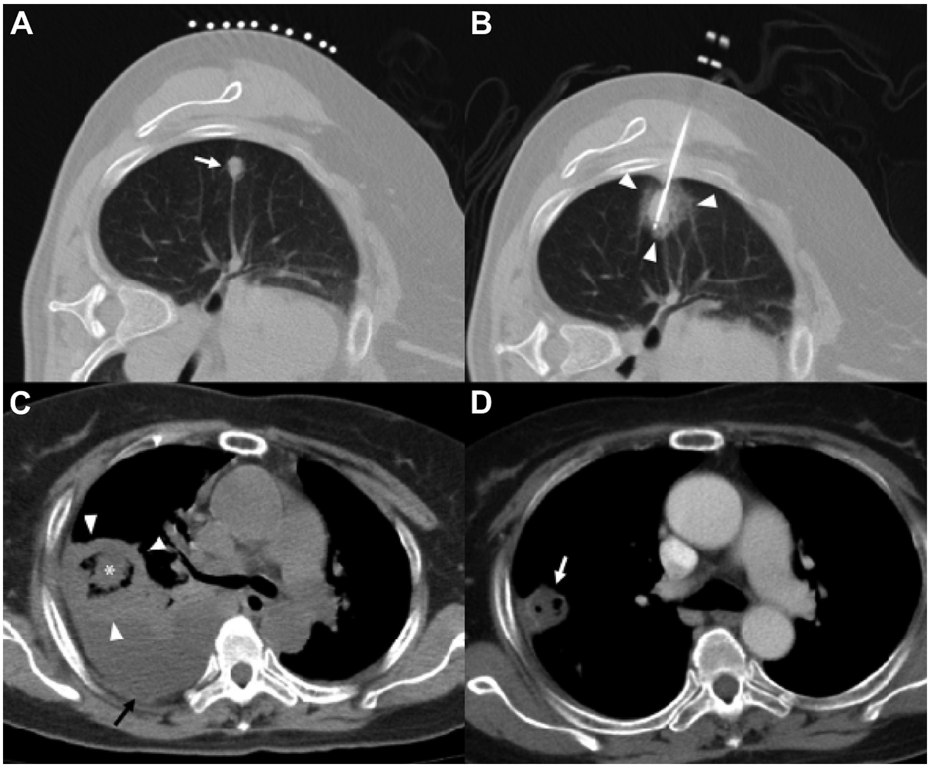

Fig. 2. Serial images of the radiofrequency ablation for a 76-year-old female who had colorectal cancer with lung metastasis. (A) A preprocedural image showing the lesion (arrow). (B) An electrode in the lesion with perilesional ground glass opacity (arrowheads), which provides an estimate of the ablation zone. (C) A computed tomography (CT) image 1 week after ablation showed cavitation of ablation zone (arrowheads) covering the original tumor (asterisk). Pleural effusion is noted (arrow). (D) A CT image 1 month after the procedure showed that the ablation zone is of low density, lacks nodular enhancement, and contains small gas bubbles (arrow).

pneumothorax in 32% (range, 4.5–61.1%) of the procedures, pneumothorax requiring drainage in 9.5% (range, 3.3–38.9%), pneumonia in 2.2% (range, 6–12%), pulmonary abscess in 0.6% (range, 0–6.6%), pleural effusion in 14%, pleural effusion requiring chest drainage in 0.1%, hydropneumothorax in 0.2%, hemothorax in 0.7% (range 0–16.7%), intrapulmonary bleeding in 1.6% (range, 0–11%), hemoptysis in 3.4% (range, 0–18.2%), pleuritis chest pain in 2.9% (range, 0–24%), cough in 2.1% (range, 0–33%), fever in 4.3% (range, 0–22%), and acute respiratory distress syndrome in 0.1% of the procedures. Additionally, two cases of tumor seeding have been reported,[18] with pulmonary embolus being noted in 0.1% of patients. Procedure-related complications, with an adverse event grade of higher than 3, occurred in approximately 6% of the cases.[22] Overall complication rates of RFA for lung tumor are similar to those of percutaneous lung biopsy.

Rare complications of RFA for lung tumor include bronchiolitis obliterans and organizing pneumonia, which are reported to have an incidence of 0.4%; the treatment involves pulse steroid therapy if the symptoms are severe.[23] Unintentional burns are rare, and burns of the skin and of organs adjacent to the lesion are considered as two different types of burns. Attachment of the ground pad away from the metallic prosthesis prevents concentration of the energy, and avoiding excessive hair and sweating at the grounding pad attachment site decreases the adhesion of the ground pad, which may help decrease the chance of skin burns.[11,24] Special caution is needed when the ablation is prolonged or has a high current. Burns to nontargeted organs are more likely when they are within 1 cm of the target lesion[11]; hollow organs and diaphragms are the vulnerable organs.[25]

Few cases of mortality have been reported. Herrera and colleagues[26] reported a death as a result of fatal hemoptysis after ablation of a central pulmonary nodule in a patient who had received brachytherapy recently. Vaughn and colleagues[27] described a case report of an elective intraoperative RFA of primary lung cancer in a patient who suffered a massive intraparenchymal and an extrapleural pulmonary hemorrhage; the patient died from aspiration pneumonia. Previous radiation therapy was reported to be a risk factor for the development of fatal interstitial pneumonia after radiofrequency.[28] The procedure-related mortality was reported to be 0.6%.[29]

Ambrogi et al[30] studied the change in lung function after RFA for lung tumors and found that lung function was slightly decreased at 1 month after the procedure and returned to almost normal at 3 months after RFA. Similar findings were reported in other studies, and this result is especially important for patients with poor pulmonary reserve.[31]

CT is used to monitor response to therapy. A decrease in tumor size and a lack of contrast medium enhancement in the ablation zone indicate no local tumor progression. It is worth noting that the appearance of the ablation zone changed with time. The ablation zone was commonly found to be enlarged in the immediate and 1-month follow-up CT images, and reported to decrease in size at 3 months, 6 months, 9 months, and 12 months by 6%, 11%, 14%, and 40%, respectively.[32] It is better to judge the treatment response between 1 month and 3 months after ablation than at 1 month. Cavitation and tiny gas bubbles were commonly found at the ablation zone and could be observed up to 1 year after ablation.[33] In the mid- and long-term follow-ups, no enhancement or thin rim enhancement was noted in the lesion that was completely ablated, whereas focal nodular enhancements of more than 15 Hounsfield units (HU) were considered to have local tumor progression. Local tumor progression occurred in 31% of tumors after ablation.[22] The frequency of local tumor progression was found to be correlated significantly with size; recurrence tended to be close to the ablated tumor site and more frequent in larger tumors (>4 cm in diameter) and at higher disease stages.[34] Simon et al[29] reported improved local tumor progression-free rates for tumors <3 cm in diameter. Proximity to vessels larger than 3 mm in diameter has also been found to be associated with an increased risk of local tumor progression.[35] Tumors that are in contact with a bronchus larger than 2 mm in size have a reportedly poorer response to RFA.[36]

The survival rates of stage I lung cancer patients is 78–94% at 1 year, 57–86% at 2 years, 36–74% at 3 years, 67% at 4 years, and 61% at 5 years.[22,29,37] The cancer-specific survival rates are 100%, 93%, 80%, 80%, and 74% at 1 year, 2 years, 3 years, 4 years, and 5 years, respectively. The disease-free survival percentages are 82%, 64%, 53%, 46%, and 46% at 1 year, 2 years, 3 years, 4 years, and 5 years, respectively. With respect to survival of a patient receiving radiotherapy, a meta-analysis showed that the 3-year overall survival rate of stage I NSCLC patients receiving conventional external beam radiation therapy is 34%.[38] Patients receiving stereotactic radiotherapy, a novel radiotherapy technique, have been reported to have a survival rate of 81% or higher at 1 year and a survival rate of 60% at 2 years.[39] Essentially, RFA may offer a benefit comparable to that of radiation therapy for patients with inoperable stage I lung cancer.

RFA and sublobar resection have comparable efficacy. Lee et al[14] retrospectively compared survival in elderly patients with primary NSCLC between those receiving surgical treatment and those receiving RFA, and found that surgical treatment alone yields a median survival time of 34 months, whereas RFA alone yields a survival time of 28 months. The difference is not statistically significant.

The combination of RFA with radiation therapy, brachytherapy, and systemic chemotherapy results in an increased survival and local control of the lung malignancies.[14,40,41]

4. Microwave ablation

4.1. Principle

Microwave frequencies refer to the region of the electromagnetic spectrum with frequencies ranging from 300 MHz to 300 GHz. Modern MWA utilizes devices that generate electromagnetic waves that have electric charge flipping in the range of microwave frequencies, between 900 MHz and 2450 MHz.[42,43] The electromagnetic wave has an electric charge that flips between positive and negative. For a microwave frequency oscillating at 915 MHz, the charge changes signs nearly 2 billion times per second. Water molecules (H_2O) are polar; the hydrogen side of the molecule has a positive charge and the oxygen side has a negative charge. When it interacts with a microwave, the molecule flips. The fast movement of water molecules raises the temperature in tissue and induces cellular death via coagulation necrosis.[42]

Due to the inherent properties of the microwave (no electrical current being produced), the device does not need to be grounded, abolishing the problem of grounding pad burns. Additionally, microwave energy may be less likely to be affected by charring and may thus provide better heating around soft tissue nodules compared with RF energy. The heat sink effect that is prominent in RFA is not only less likely in MWA, but selective tracking of the ablation zone along the blood vessel may actually increase the ablation zone.[44]

4.2. Equipment and techniques

Currently, two microwave tumor ablation systems are available in Taiwan (Evident; Covidien, Mansfield, MA, USA, and AveCure; MedWaves, San Diego, CA, USA): one uses a generator with a fixed frequency of 915 MHz and the other uses one with variable frequencies in the range 908−920 MHz. The microwave energy applicator is called the antenna, and the size of microwave antennas ranges from 12 gauge to 16 gauge. The active tip length is from 2 cm to 4 cm. Through the exposed, noninsulated active tip, a microwave generator emits an electromagnetic wave via the image-guided inserted antenna to achieve ablation.[42]

4.3. Patient outcome

After MWA, the ablated foci undergo a cavitary change of 43−50% in which the air−fluid level is 14%. Pleural thickening is observed in 44% of patients. Initially, the ablation zones are enlarged, up to a diameter of 0.65 cm, and then decrease gradually by consolidation.[45]

In current studies, no cases with 30-day mortality were reported. Approximately 33−39% of sessions resulted in pneumothorax. Approximately 0−12% of procedures required chest tube insertion [Common Terminology Criteria for Adverse Events (CTCAE) grade 2]. A skin burn was observed in 3% of the patients attending all sessions, and one patient required debridement (CTCAE grade 3). A total of 2% of patients had postablation syndrome, while 2% of individuals developed respiratory distress (CTCAE grade 4) and recovered after 1 week.[45,46] Mild pleural effusion without the need for thoracocentesis was noted in 20−30% of patients.

The median time of first distant metastases is 16 months. When the tumor size is larger than 3 cm, patients are more likely to have recurrent tumor at follow-ups. The local control rate is 67% at 1 year.[45] In a series of nine patients with a mean follow-up time of 3.6 months, Carrafiello et al[46] reported a local recurrence at 3 months after MWA in one patient.

Wolf et al[45] ablated 82 masses in 50 patients with a median follow-up period of 10 months. The overall survival percentages were 65%, 55%, and 45% at 1 year, 2 years, and 3 years, respectively. The cancer-specific survival rates were 83%, 73%, and 61% at 1 year, 2 years, and 3 years, respectively. A Kaplan−Meier analysis of all-cause mortality revealed a median time to death of 19 months.

5. Cryoablation

5.1. Principle

Cryoablation is a thermoablation technique in which a freezing temperature is used to destroy tissue. Modern cryoablation techniques consist of alternative cycles of decreasing temperature (freezing) and increasing temperature (thawing), which cause direct cell and vascular injury. As the temperature is lowered in the freezing range, water in the tissue is crystallized. The ice crystals are first formed in the extracellular spaces, increasing the extracellular osmolarity; as a consequence, the water diffuses from the intracellular space into the extracellular space. The cell then shrinks, and the cell membranes are damaged. If the cooling is fast, intracellular ice is formed in most of the cells at a temperature of −40°C. The shear force during ice formation disrupts the organelles and cell membranes, resulting in cell death almost definitely.[47] During thawing, when the temperature is between −20°C and −40°C, the maximum direct cell injury, caused by the process of fusing small ice crystals into a larger ice ball, results in abrasion and possible injury of the cell membrane. As the temperature continues to rise, the ice at the extracellular space will melt and cause a hypotonic condition, followed by water entering the cell through the already injured cell membrane. The cell will rupture eventually. Vascular injury begins during the freezing phase at which the circulation ceases. After thawing the tissue to a temperature of more than 0°C, vasodilatation with a hyperemic response damages the cell membrane and causes edema. Then, aggregation of platelets and thrombosis of the circulation occur, resulting in uniform necrosis of the tissue.[48]

Experiments have shown that performing two ablation cycles, each consisting of 10 minutes of freezing and 5 minutes of thawing, using a single 2.4-mm cryoprobe results in an ablation zone (with complete necrosis) with a mean diameter of 2.4 cm ± 0.2 cm. Because this diameter is most closely related to the −20°C isotherm, the critical temperature for inducing cellular death in the lung parenchyma is likely to be approximately −20°C.[49]

5.2. Equipment and techniques

In cryoablation, the cryogen generates a low temperature in the applicator (e.g., the cryoprobe) to destroy the tissue. The currently available, third-generation cryoablation model uses argon as the cryogen. The high-pressure argon gas from the control unit passes into the inner chamber of the cryoprobe prior to passing through a small nozzle into the larger outer

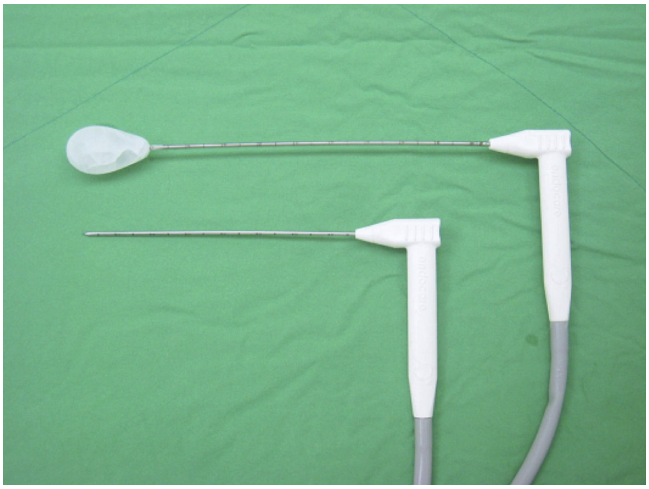

Fig. 3. Cryoprobes and ice ball. The upper applicator is a 20-cm-long cryoprobe with a diameter of 2.4 mm, and a preformed ice ball was formed after 7 minutes in water. The lower applicator is a 15-cm-long cryoprobe with a diameter of 2.4 mm (Cryocare System; Endocare, Inc., Irvine, CA, USA).

chamber of the cryoprobe. According to the Joule–Thomson effect, as the volume of argon expands, the temperature may decrease to −187°C. Helium gas acts as a heating source by increasing the temperature up to 67°C as volume is increased.[50] The diameter of the modern percutaneous cryoprobes ranges from 1.47 mm (17 gauge) to 2.4 mm, and each cryoprobe size has an ablation zone estimate. The control unit may connect up to 25 cryoprobes simultaneously (Fig. 3).

In the cryoablation procedure, the cryoprobe(s) is(are) inserted into the lesion under CT guidance. The crystals formed by freezing fuse as a well-demarcated volume of ice ball, with a density between 0 HU and −50 HU when the ice ball is in soft tissue or fat.[51] Because the cytotoxic isotherm curves (at −20°C) occur approximately 3–5 mm inside of the visualized ice margins, the zone of ablation can be estimated. In a large tumor, inserting multiple cryoprobes and freezing simultaneously produce a larger ablation zone.

5.3. Patient outcome

Complications from cryoablation for lung tumor were reported in three large series with 644 cases, 200 cases, and 193 cases, with pneumothorax occurring in 12–62%, and CTCAE grade 2 or more in 4%. Hemoptysis was noted in 37–62% of cases, and CTCAE grade 2 hemoptysis was noted in 0.6%. Pleural effusion occurred in 14–71%. Fever was noted in 3–42%, hypertension in 33%, and subcutaneous emphysema in 5% of cases. Skin injury was noted in 5% of cases, and the percentage of complications (CTCAE grade of more than 3) was approximately 1.5%. Lung infection occurred in 6.7% of cases. Brachial plexus injury and recurrent laryngeal nerve paralysis occurred in 1% and 0.5% of cases, respectively. The mortality rate was 0.6%.[52,53]

Cavitation is the most common postablation finding, which occurred in 77% of cases. In most cases of tumor ablation, the ablation zones were initially larger than the original tumor.

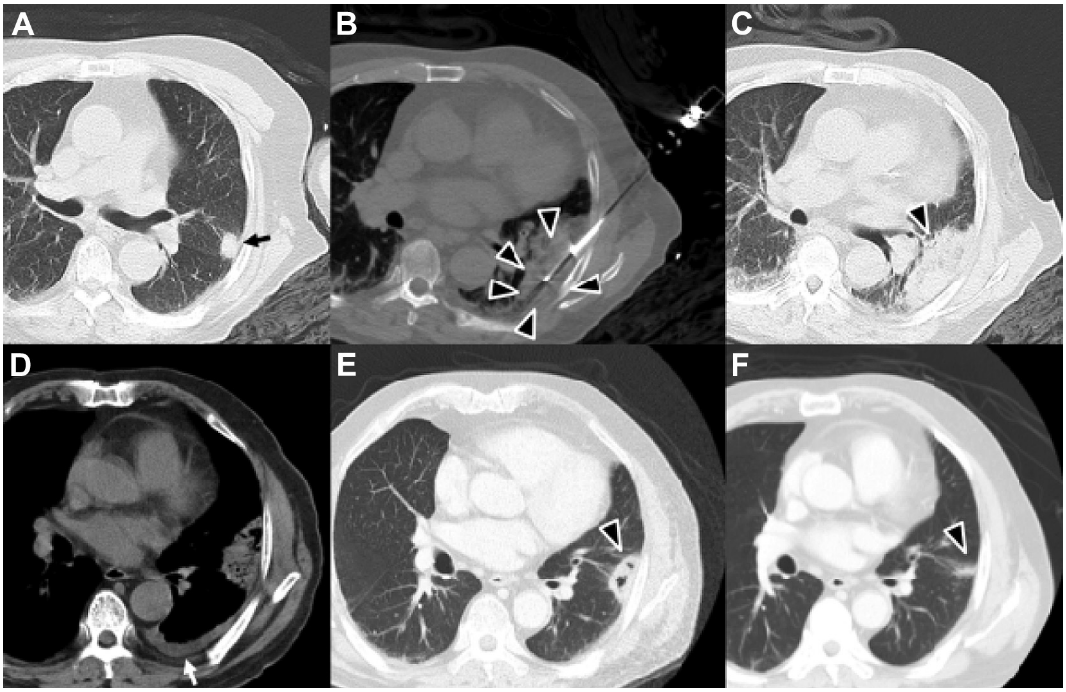

Fig. 4. Images of squamous cell carcinomas in an 83-year-old male. (A) A preprocedural axial chest computed tomography (CT) image showed a nodule at the left upper lobe (arrow). (B) An image during the freezing phase of the ablation cycle showed a low-density elliptical ice ball, which is unique to cryoablation (compared to other modalities), covering the lesion (arrowheads). (C) The ablation zone is estimated by the consolidation rather than the ground glass surrounding the lesion. (D) Three days after the procedure, pleural effusion (arrow) was observed, which is a common finding in cryoablation for subpleural lesions. (E) The ablation zone (arrowhead) showed involution with cavitation at 8 months after the procedure. (F) The CT at 12 months after the procedure showed further involution of the ablation zone (arrowhead).

Approximately 17% of the ablated lesions disappeared at 12 months. The remaining lesions without local recurrence might decrease in size or maintain a stable size (Fig. 4).[54]

CT is used to monitor the local tumor progression, usually with the same criteria as used in RFA. Immediate postprocedural positron emission tomography (PET)/CT is unable to monitor the immediate therapeutic effect.[55] The reported local control rates for the cryoablation for stage I lung cancer with an average tumor size of 1.4 cm are 97%, 97%, and 97% at 1 year, 2 years, and 3 years, respectively. The cause of local tumor progression was an insufficient margin of ablation. A total of 27% of the patients developed recurrence at a site other than the local site at a median follow-up period of 23 months.[56]

The overall survival rates were 95% at 1 year, 88% at 2 years, and 88% at 3 years. The disease-free survival percentages were 91%, 78%, and 67% at 1 year, 2 years, and 3 years, respectively.[56] According to recent reports, the efficacy of lung tumor cryoablation is comparable with RFA and sublobar resection. Zemlyak et al[7] retrospectively compared sublobar resection, RFA, and cryoablation for 64 patients with NSCLC. The survival percentages were 87%, 87%, and 77% for sublobar resection, RFA, and cryoablation, respectively. No significant difference was noted between the three groups. For surgical therapy, RFA, and cryoablation, respectively, the cancer-specific 3-year-survival percentages were 91%, 88%, and 90%, and the disease-free survival percentages were 61%, 50%, and 46%.

6. Comparison and limitations

6.1. Comparison according to the ablation modality

Unlike RFA, cryoablation does not result in substantial collagen damage and appears to be a better option for patients with extensive emphysema.[7] Cryoablation also has potential applications in the lesions that are adjacent to the diaphragm where use of other modalities may cause diaphragmatic rupture.[57] MWA has a larger ablation zone than RFA and a reduced heat sink effect, which makes it a better fit for patients who have larger tumors or tumors that are close to larger vessels because it can provide more complete ablation.[44,58] Radiofrequency has the advantages of a low cost and relatively round ablation zone, which may be effective for medium-sized tumors (1.0−2.5 cm) that can be covered with fewer electrodes.

6.2. Limitations of image-guided tumor ablation

Lung tumor ablation has several limitations. First, because local tumor ablation can destroy only the targeted tumor and does not affect lymph node metastases, it is important to perform local tumor ablation only on patients who lack lymph node metastases or have their lymph node metastases controlled by another modality, such as radiation therapy, if the aim of treatment is curative. Second, the application of ablation for lesions near the mediastinum and lateral aspect of the lung apex can be limited. When the lesions are near vital structures such as the phrenic nerve and brachial plexus, they can damage these structures, compromising their function.[59] Third, pulmonary hilar lesions are difficult to target; they usually have the same density as major vessels in the pulmonary hilum under CT guidance. Therefore, an appropriate positioning of the applicator for sufficient coverage of the tumor, without puncturing the hilar vessels and causing substantial bleeding, is challenging. Fourth, ablating a superficial lesion is challenging for cryoablation because the ice ball of the cryoablation in most cryoprobes is elliptical, as it is approximately 4−5 cm in the direction parallel to the cryoprobes. As a result, the skin can easily be included in the ice ball, causing skin injury, which may limit the application of ablation for superficial lesions. Fifth, MWA may damage nontarget tissue along the vessel as a result of the tracking of the ablation zone along blood vessels; this may limit the application of MWA. Sixth, in RFA, individual tines of multitine electrodes are sometimes difficult to monitor precisely, especially when used adjacent to vulnerable structures such as the mediastinum and diaphragms, and the individual tines can penetrate those structures and cause complications.[25]

In conclusion, image-guided tumor ablation is a minimally invasive treatment option for selected inoperable patients with lung malignancy. A prospective, randomized, controlled trial is needed to further compare the outcomes of limited resection, stereotactic body radiation therapy, and different ablation methods. However, the current evidence reveals a relatively safe profile and substantial efficacy of lung tumor ablation for tumor control and patient survival. These results are particularly relevant for treating patients with pulmonary comorbidities as well as localized or limited malignant lung disease (tumors being less than 3.5 cm in size and located in the peripheral two-thirds of the lungs) who otherwise have no treatment options.

References

1. Department of Health. *Deaths in Taiwan, 2011*. http://www.doh.gov.tw/ufile/doc/Deaths%20in%20Taiwan%202011.docx; 2012 [accessed 2.09.12].
2. National Cancer Institute. *Cancer of the lung and bronchus (invasive). Trends in SEER incidence and U.S. mortality.* SEER Website. http://seer.cancer.gov/csr/1975_2009_pops09/results_merged/sect_15_lung_bronchus.pdf; 2012 [accessed 2.09.12].
3. Quiros RM, Scott WJ. Surgical treatment of metastatic disease to the lung. *Semin Oncol* 2008;**35**:134−46.
4. Chen YJ, Hsu HS, Hsieh CC, Wu YC, Wang LS, Hsu WH, et al. Pulmonary metastasectomy for hepatocellular carcinoma. *J Chin Med Assoc* 2004;**67**:621−4.
5. Welter S, Cheufou D, Sommerwerck U, Maletzki F, Stamatis G. Changes in lung function parameters after wedge resections: a prospective evaluation of patients undergoing metastasectomy. *Chest* 2012;**141**:1482−9.
6. Rapicetta C, Tenconi S, Voltolini L, Luzzi L, Scala V, Gotti G. Impact of lobectomy for non-small cell lung cancer on respiratory function in octogenarian patients with mild to moderate chronic obstructive pulmonary disease. *Eur J Cardiothorac Surg* 2011;**39**:555−9.
7. Zemlyak A, Moore WH, Bilfinger TV. Comparison of survival after sublobar resections and ablative therapies for stage I non-small cell lung cancer. *J Am Coll Surg* 2010;**211**:68−72.
8. Graham MV, Purdy JA, Emami B, Harms W, Bosch W, Lockett MA, et al. Clinical dose-volume histogram analysis for pneumonitis after 3D treatment for non-small cell lung cancer (NSCLC). *Int J Radiat Oncol Biol Phys* 1999;**45**:323−9.

9. Rubenstein JH, Richter MP, Moldofsky PJ, Solin LJ. Prospective prediction of post-radiation therapy lung function using quantitative lung scans and pulmonary function testing. *Int J Radiat Oncol Biol Phys* 1988;**15**:83–7.
10. Goldberg SN, Grassi CJ, Cardella JF, Charboneau JW, Dodd 3rd GD, Dupuy DE, et al. Image-guided tumor ablation: standardization of terminology and reporting criteria. *J Vasc Interv Radiol* 2005;**16**:765–78.
11. Vogl TJ, Naguib NN, Lehnert T, Nour-Eldin NE. Radiofrequency, microwave and laser ablation of pulmonary neoplasms: clinical studies and technical considerations—review article. *Eur J Radiol* 2011;**77**:346–57.
12. Pereira PL, Masala S. Standards of practice: guidelines for thermal ablation of primary and secondary lung tumors. *Cardiovasc Intervent Radiol* 2012;**35**:247–54.
13. Lee JM, Jin GY, Goldberg SN, Lee YC, Chung GH, Han YM, et al. Percutaneous radiofrequency ablation for inoperable non-small cell lung cancer and metastases: preliminary report. *Radiology* 2004;**230**:125–34.
14. Lee H, Jin GY, Han YM, Chung GH, Lee YC, Kwon KS, et al. Comparison of survival rate in primary non-small cell lung cancer among elderly patients treated with radiofrequency ablation, surgery, or chemotherapy. *Cardiovasc Intervent Radiol* 2012;**35**:343–50.
15. Dupuy DE, DiPetrillo T, Gandhi S, Ready N, Ng T, Donat W, et al. Radiofrequency ablation followed by conventional radiotherapy for medically inoperable stage I non-small cell lung cancer. *Chest* 2006;**129**:738–45.
16. Malloy PC, Grassi CJ, Kundu S, Gervais DA, Miller DL, Osnis RB, et al. Consensus guidelines for periprocedural management of coagulation status and hemostasis risk in percutaneous image-guided interventions. *J Vasc Interv Radiol* 2009;**20**:S240–9.
17. Sharma A, Moore WH, Lanuti M, Shepard JA. How I do it: radiofrequency ablation and cryoablation of lung tumors. *J Thorac Imaging* 2011;**26**:162–74.
18. Hiraki T, Mimura H, Gobara H, Sano Y, Fujiwara H, Iguchi T, et al. Two cases of needle-tract seeding after percutaneous radiofrequency ablation for lung cancer. *J Vasc Interv Radiol* 2009;**20**:415–8.
19. Giraud P, Antoine M, Larrouy A, Milleron B, Callard P, De Rycke Y, et al. Evaluation of microscopic tumor extension in non-small-cell lung cancer for three-dimensional conformal radiotherapy planning. *Int J Radiat Oncol Biol Phys* 2000;**48**:1015–24.
20. Steinke K, Haghighi KS, Wulf S, Morris DL. Effect of vessel diameter on the creation of ovine lung radiofrequency lesions *in vivo*: preliminary results. *J Surg Res* 2005;**124**:85–91.
21. Zhu JC, Yan TD, Morris DL. A systematic review of radiofrequency ablation for lung tumors. *Ann Surg Oncol* 2008;**15**:1765–74.
22. Hiraki T, Gobara H, Mimura H, Matsui Y, Toyooka S, Kanazawa S. Percutaneous radiofrequency ablation of clinical stage I non-small cell lung cancer. *J Thorac Cardiovasc Surg* 2011;**142**:24–30.
23. Hiraki T, Gobara H, Kato K, Toyooka S, Mimura H, Kanazawa S. Bronchiolitis obliterans organizing pneumonia after radiofrequency ablation of lung cancer: report of three cases. *J Vasc Interv Radiol* 2012;**23**:126–30.
24. Livraghi T, Solbiati L, Meloni MF, Gazelle GS, Halpern EF, Goldberg SN. Treatment of focal liver tumors with percutaneous radio-frequency ablation: complications encountered in a multicenter study. *Radiology* 2003;**226**:441–51.
25. Hiraki T, Gobara H, Masaoka Y, Toyooka S, Kanazawa S. Diaphragmatic hernia after percutaneous radiofrequency ablation of lung tumor. *J Vasc Interv Radiol* 2011;**22**:1777–8.
26. Herrera LJ, Fernando HC, Perry Y, Gooding WE, Buenaventura PO, Christie NA, et al. Radiofrequency ablation of pulmonary malignant tumors in nonsurgical candidates. *J Thorac Cardiovasc Surg* 2003;**125**:929–37.
27. Vaughn C, Mychaskiw 2nd G, Sewell P. Massive hemorrhage during radiofrequency ablation of a pulmonary neoplasm. *Anesth Analg* 2002;**94**:1149–51.
28. Nomura M, Yamakado K, Nomoto Y, Nakatsuka A, Ii N, Takaki H, et al. Complications after lung radiofrequency ablation: risk factors for lung inflammation. *Br J Radiol* 2008;**81**:244–9.
29. Simon CJ, Dupuy DE, DiPetrillo TA, Safran HP, Grieco CA, Ng T, et al. Pulmonary radiofrequency ablation: long-term safety and efficacy in 153 patients. *Radiology* 2007;**243**:268–75.
30. Ambrogi MC, Lucchi M, Dini P, Melfi F, Fontanini G, Faviana P, et al. Percutaneous radiofrequency ablation of lung tumours: results in the mid-term. *Eur J Cardiothorac Surg* 2006;**30**:177–83.
31. Lencioni R, Crocetti L, Cioni R, Suh R, Glenn D, Regge D, 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.
32. 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**:1013–20.
33. Bojarski JD, Dupuy DE, Mayo-Smith WW. CT imaging findings of pulmonary neoplasms after treatment with radiofrequency ablation: results in 32 tumors. *AJR Am J Roentgenol* 2005;**185**:466–71.
34. Huang L, Han Y, Zhao J, Wang X, Cheng Q, Li X, et al. Is radiofrequency thermal ablation a safe and effective procedure in the treatment of pulmonary malignancies? *Eur J Cardiothorac Surg* 2011;**39**:348–51.
35. Gillams AR, Lees WR. Radiofrequency ablation of lung metastases: factors influencing success. *Eur Radiol* 2008;**18**:672–7.
36. Sakurai J, Hiraki T, Mimura H, Gobara H, Fujiwara H, Tajiri N, et al. Radiofrequency ablation of small lung metastases by a single application of a 2-cm expandable electrode: determination of favorable responders. *J Vasc Interv Radiol* 2010;**21**:231–6.
37. Pennathur A, Luketich JD, Abbas G, Chen M, Fernando HC, Gooding WE, et al. Radiofrequency ablation for the treatment of stage I non-small cell lung cancer in high-risk patients. *J Thorac Cardiovasc Surg* 2007;**134**:857–64.
38. Qiao X, Tullgren O, Lax I, Sirzen F, Lewensohn R. The role of radiotherapy in treatment of stage I non-small cell lung cancer. *Lung Cancer* 2003;**41**:1–11.
39. Pennathur A, Luketich JD, Heron DE, Abbas G, Burton S, Chen M, et al. Stereotactic radiosurgery for the treatment of stage I non-small cell lung cancer in high-risk patients. *J Thorac Cardiovasc Surg* 2009;**137**:597–604.
40. Chua TC, Thornbury K, Saxena A, Liauw W, Glenn D, Zhao J, et al. Radiofrequency ablation as an adjunct to systemic chemotherapy for colorectal pulmonary metastases. *Cancer* 2010;**116**:2106–14.
41. Chan MD, Dupuy DE, Mayo-Smith WW, Ng T, Dipetrillo TA. Combined radiofrequency ablation and high-dose rate brachytherapy for early-stage non-small cell lung cancer. *Brachytherapy* 2011;**10**:253–9.
42. Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. *Radiographics* 2005;**25**(Suppl 1):S69–83.
43. Carrafiello G, Lagana D, Mangini M, Fontana F, Dionigi G, Boni L, et al. Microwave tumors ablation: principles, clinical applications and review of preliminary experiences. *Int J Surg* 2008;**6**(Suppl 1):S65–9.
44. Brace CL. Radiofrequency and microwave ablation of the liver, lung, kidney, and bone: what are the differences? *Curr Probl Diagn Radiol* 2009;**38**:135–43.
45. 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**:871–9.
46. Carrafiello G, Mangini M, De Bernardi I, Fontana F, Dionigi G, Cuffari S, et al. Microwave ablation therapy for treating primary and secondary lung tumours: technical note. *Radiol Med* 2010;**115**:962–74.
47. Gage AA, Baust JM, Baust JG. Experimental cryosurgery investigations *in vivo*. *Cryobiology* 2009;**59**:229–43.
48. Hoffmann NE, Bischof JC. The cryobiology of cryosurgical injury. *Urology* 2002;**60**:40–9.
49. Hinshaw JL, Lee Jr FT, Laeseke PF, Sampson LA, Brace C. Temperature isotherms during pulmonary cryoablation and their correlation with the zone of ablation. *J Vasc Interv Radiol* 2010;**21**:1424–8.
50. Zisman A, Pantuck AJ, Cohen JK, Belldegrun AS. Prostate cryoablation using direct transperineal placement of ultrathin probes through a 17-gauge brachytherapy template-technique and preliminary results. *Urology* 2001;**58**:988–93.
51. Saliken JC, McKinnon JG, Gray R. CT for monitoring cryotherapy. *AJR Am J Roentgenol* 1996;**166**:853–5.
52. Inoue M, Nakatsuka S, Yashiro H, Ito N, Izumi Y, Yamauchi Y, et al. Percutaneous cryoablation of lung tumors: feasibility and safety. *J Vasc Interv Radiol* 2012;**23**:295–302.

53. Niu L, Wang J, Zhou L, Wu B, Mu F, Li H, et al. Complications of cryoablation in 644 lung cancer patients and its treatment. *Zhongguo Fei Ai Za Zhi* 2010;**13**:832−4 [in Chinese].
54. 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**:289−98.
55. Sainani NI, Shyn PB, Tatli S, Morrison PR, Tuncali K, Silverman SG. PET/CT-guided radiofrequency and cryoablation: is tumor fluorine-18 fluorodeoxyglucose activity dissipated by thermal ablation? *J Vasc Interv Radiol* 2011;**22**:354−60.
56. Yamauchi Y, Izumi Y, Hashimoto K, Yashiro H, Inoue M, Nakatsuka S, et al. Percutaneous cryoablation for the treatment of medically inoperable stage I non-small cell lung cancer. *PLoS ONE* 2012;**7**: e33223.
57. Chen CK, Chou TY, Chen CB, Hsu WH. Image-guided cryoablation for metastatic diaphragmatic thymoma. *J Vasc Interv Radiol* 2012;**23**:1097−9.
58. Brace CL, Hinshaw JL, Laeseke PF, Sampson LA, Lee Jr FT. 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.
59. Matsui Y, Hiraki T, Gobara H, Uka M, Masaoka Y, Tada A, et al. Phrenic nerve injury after radiofrequency ablation of lung tumors: retrospective evaluation of the incidence and risk factors. *J Vasc Interv Radiol* 2012;**23**:780−5.