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The use of PTC and RFA as treatment alternatives with low procedural morbidity in non-small cell lung cancer

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ABSTRACT

Minimally invasive percutaneous ablative therapies for treating lung cancers are currently being studied as treatment alternatives. This present study investigated the efficacies of percutaneous thoracic cryotherapy (PTC) and radiofrequency ablation (RFA) on clinical courses of pulmonary malignant tumours, especially in the setting of non-surgical candidates. Sixty-five patients with lung malignancy underwent sixty-seven sessions of RFA and nine sessions of PTC. We evaluated the results of RFA and PTC including efficacies, local progression rate, survival rate, and complications. Twenty-nine patients (43.3%) treated with RFA and six patients (66.7%) with PTC attained complete ablation. In small-sized lung mass ($\leqslant$3 cm), complete ablation rate of RFA and PTC was increased to 76.2% and 85.7%, respectively. Additionally, we have found that the complete ablation group had significantly higher survival duration and progression free survival duration compared with the partial ablation group. Moreover, the complication profile was acceptable and the pain associated with the procedures disappeared within 1 day; 42 patients (62.7%) after RFA and all patients after PTC. This study provides evidence for the use of PTC and RFA as treatment alternatives with low procedural morbidity in the management of inoperable pulmonary malignant tumours, although the current study is limited by the small sample size and the short follow-up period.

1. Introduction

Lung cancer is one of the most commonly occurring malignancies in the world and ranks first for people aged 60 years and older. In spite of multiplicity in lung cancer treatment, lung cancer still accounts for the most fatal cancer with an estimated 5-year survival rate of 14%.[1] Until recently, therapeutic modalities for pulmonary malignant diseases have included surgical resection, chemotherapy, and/or external beam radiation therapy. Surgical resection remains the mainstay of therapy for early stage non-small cell lung cancer (NSCLC) and is also beneficial for selected patients with limited pulmonary metastases from extrathoracic originated tumours.[1,2] Even though surgical resection is regarded as the best treatment option for patients with localised disease, only small portions of tumours are suitable for potentially curative resection.[1,3] There are two main reasons that account for the unsuitability of surgery as the prime treatment modality: comorbid medical conditions and advanced stage of the disease.[4] In these conditions, non-invasive therapy such as chemotherapy, radiation therapy, or both may be considered for cure or expectant palliative treatment and even in cases

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of regional disease, a combination therapeutic strategy prevails as the standard treatment.[1,5,6] Although these modalities produce a modest improvement in survival, some patients suffer from substantial toxicity, especially in patients who already have other co-morbidities.[6]

With a need for the development and use of alternative treatment modalities, evidence has been accumulated which reports that less invasive therapies capable of tumour destruction or complete eradication may complement, improve, or even replace existing therapies. Recently, several less invasive therapies such as stereotactic radiotherapy, brachytherapy, bronchial arterial infusion of chemotherapy, photodynamic therapy and thermal ablation have been employed to treat lung cancer.[4]

Previous studies have shown that radiofrequency ablation (RFA), as an alternative management for lung malignancies, has advantages over traditional radiation therapy and systemic chemotherapy.[7] In addition, we have recently demonstrated that computed tomography (CT)-guided RFA appears to be a promising modality for the treatment of inoperable NSCLC, which composes the majority of pulmonary malignancies.[8] A more recently introduced thermal ablative modality is cryotherapy which is considered a new promising treatment option for various tumours of the prostate, kidney, liver and breast.[9–12] For treatment of lung cancer, bronchoscopic cryotherapy has been applied to the superficial endobronchial carcinoma with safety and effectiveness.[13,14] Very recently, some studies have demonstrated that percutaneous thoracic cryotherapy (PTC) is associated with low procedural morbidity and also appears to treat lung mass.[15,16] However, there are little data on the therapeutic efficacy for lung malignancies treated with thermal ablations such as PTC or RFA and the role of local tumour destruction in clinical outcome.

Based on these considerations, we have evaluated the therapeutic efficacies, local progression free duration, survival duration, and complications in patients with primary lung malignancies treated with RFA or PTC.

2. Patients and methods

2.1. Study populations

From May 2000 to March 2007, sixty-five patients with primary lung malignancies were treated with RFA or PTC with CT guidance at Chonbuk National University Hospital. Indications for these thermal ablative therapies were pulmonary malignant tumours in patients with medical comorbidities, pulmonary compromise, or refusal of surgery. All tumours were primary lung malignancies proven histologically by percutaneous transthoracic needle biopsy or bronchoscopic biopsy. The PTC system was introduced to our institute in January 2006. Since then, all candidates for image-guided ablation were treated with either RFA or PTC. When the size (<10 cm) and location of tumour were appropriate for use of an ablation procedure, one of two thermal ablative modalities, RFA or PTC, was selected. None of the patients had any coagulation disorder or other bleeding diathesis. Anticoagulants or antiplatelet agents were stopped before procedure. This study was performed with the approval of the institutional ethics committee, and written informed consent had been obtained from every patient before the initiation of treatment.

2.2. Procedures

One radiologist performed all procedures on inpatients who had fasted for 12 h. The patients' vital signs were continuously monitored throughout the procedure. The RFA and PTC were always performed under CT guidance. All of the patients underwent chest CT (Somatom Plus 4 or Sensation 16, Siemens, Erlangen, Germany) before performing procedures, and selected scans were obtained within the area of interest with a 5- to 10-mm slice thickness depending on the size of the lesion.

The RFA was performed with 17-gauge, single or clustered internally cooled radiofrequency electrodes. To minimise the incidence of pneumothorax, we attempted to limit the number of electrode passes through the pleura to a single insertion. If an additional ablation was required, we changed the position of the needle within the tumour by withdrawing it into superficial tissue, changing the angle, and then reinserting it into the target without a complete withdrawal of the electrode out of the pleura. Once proper electrode positioning was confirmed, we attached the electrode to a 500-kHz monopolar radiofrequency generator (CC-1, Radionics, Burlington, Massachusetts, USA) that produces an output of 150–200 W. Tissue impedance was continuously monitored using the circuitry incorporated in the generator. At the end of each treatment, the perfusion was stopped and the maximal temperature was recorded. If the temperature exceeded 60 °C, the electrode was withdrawn in increments of 1 cm up to the length of the active tip; at the same time, the intratumoural temperature was measured. If, after the first treatment, the maximal intratumoural temperature did not exceed 60 °C, an additional treatment was performed at the same site. Based on descriptions of tumour ablation performed in other organ systems, we chose to apply radiofrequency for 12 min during the initial ablation and for 6–12 min during subsequent ablations, with a maximum peak current of 1000–2000 mA and 80–150 W. After the ablation procedure, the electrode was withdrawn without cauterising the probe tract.

To perform PTC, we used an argon: helium-based system and 17-gauge cryoneedle (IceRod™, Oncura, Plymouth Meeting, PA). This instrument was used for freezing the high-pressure argon gas and thawing helium gas by means of the Joule–Thompson principal. After identification of tumour location, the treatment area was prepared and draped in sterile manner. According to the size of the tumour, one or two cryoprobes were inserted at the centre of the tumour and the cryoablation cycle proceeded, consisting of freezing and thawing.

2.3. Follow-up CT examination

All patients underwent unenhanced and contrast-enhanced helical CT within 1 week before ablation, immediately (within 30 min) after RFA or PTC, and 1 month later. Treatment efficacy was assessed on the basis of the post-treatment contrast-enhanced CT scans obtained immediately after the procedure. One experienced chest radiologist quantified the

degree of enhancement for each examination. All of the areas that did not display contrast enhancement within the boundaries of the treated area after the contrast agent administration were defined as complete ablation. Ablated tissue and the tumour regions that showed enhancement were defined as partial ablation. Our bases for this protocol were the data extrapolated from the radiologic–pathologic correlation in liver tumours performed by Goldberg and colleagues.[17] Repeated unenhanced and contrast-enhanced helical CT examinations were performed at 3-month intervals.

2.4. Statistical analysis

We used SPSS statistical software (version 13.0, SPSS, Chicago, IL). The Kaplan–Meier curve was used to estimate survival function for survival rate and local tumour progression rate. Comparisons of survival functions were performed by using the log-rank test. To assess differences of the rate of complete ablation according to tumour size, we used chi-square test analysis. Cox proportional hazard regression was also used to examine interactions among potential covariates. For all statistical analyses, a p value less than 0.05 was considered to indicate a statistically significant difference.

3. Results

3.1. Subjects characteristics

The characteristics of sixty-five patients with lung malignancies are described in Table 1. We performed sixty-seven sessions of RFA and nine sessions of PTC. The mean follow-up period was 20.5 months (range 2.6–74.3; median 20.8 ± 4.7). Eight patients received re-treatment (a total of eleven sessions: nine sessions of RFA and two sessions of PTC) because of local tumour progression; Six patients received two sessions of RFA. One patient received three sessions of RFA and one session of PTC. One patient received two sessions of RFA and one session of PTC.

3.2. Complete and partial ablation in pulmonary tumours by PTC and RFA

Of all the procedural sessions, complete ablation was attained in twenty-nine patients (43.3%) treated with RFA and six patients (66.7%) treated with PTC. The results of RFA and PTC were analysed according to tumour size (⩽3.0 cm versus >3.0 cm). The complete ablation rate for the target lesions by RFA or PTC was significantly higher in smaller sized tumours than those in tumours larger than 3.0 cm (Fig. 1A). The rate of complete ablation by RFA was 76.2% for tumours smaller than 3.0 cm and 28.3% for tumours larger than 3.0 cm (Fig. 1B). In the PTC group, six of seven tumours smaller than 3.0 cm (85.7%) were ablated completely, while all of two tumours larger than 3.0 cm were partially ablated (Fig. 1C). Representative CT of thermal ablation therapy is shown in Fig. 2.

In addition, a subgroup analysis of the re-treatment group (11 sessions) showed that the size of the completely ablated tumours after re-treatment with RFA or PTC was small (four of eleven sessions; mean size, 2.8 ± 0.7 cm) compared with the partially ablated lesions (seven of eleven sessions; mean size, 5.3±2.1 cm) after re-treatment.

Table 1 – Characteristics of patients and tumours.

	Patients (n=65)	Procedure	
		RFA (n = 67)	PTC (n = 9)
Age, years, mean	68.4 ± 10.1	69.2 ± 9.8	66.8 ± 9.3
Sex, n (%)			
Male	53 (81.5)	54 (80.6)	6 (66.7)
Female	12 (18.5)	13 (19.4)	3 (33.3)
Stage, n (%)			
I		20 (29.9)	3 (33.3)
II		7 (10.4)	1 (11.1)
III		22 (32.8)	2 (22.2)
IV		18 (26.9)	3 (33.3)
Tumour location (lobe), n (%)			
Right upper		22 (32.8)	2 (22.2)
Right middle		1 (1.5)	1 (11.1)
Right lower		16 (23.9)	2 (22.2)
Left upper		15 (22.4)	3 (33.3)
Left lower		13 (19.4)	1 (11.1)
ECOG performance status, n (%)			
0 or 1		51 (86.4)	16 (94.1)
2 or 3		8 (13.6)	1 (5.9)
Tumour histology, n (%)			
Adenocarcinoma	32 (49.2)	32 (47.8)	6 (66.7)
Squamous cell carcinoma	33 (50.8)	35 (52.4)	3 (33.3)
Tumour size, cm, mean	4.1±2.2	4.4±2.2	2.1±1.2

Data are presented as n (%) or mean ± SD.

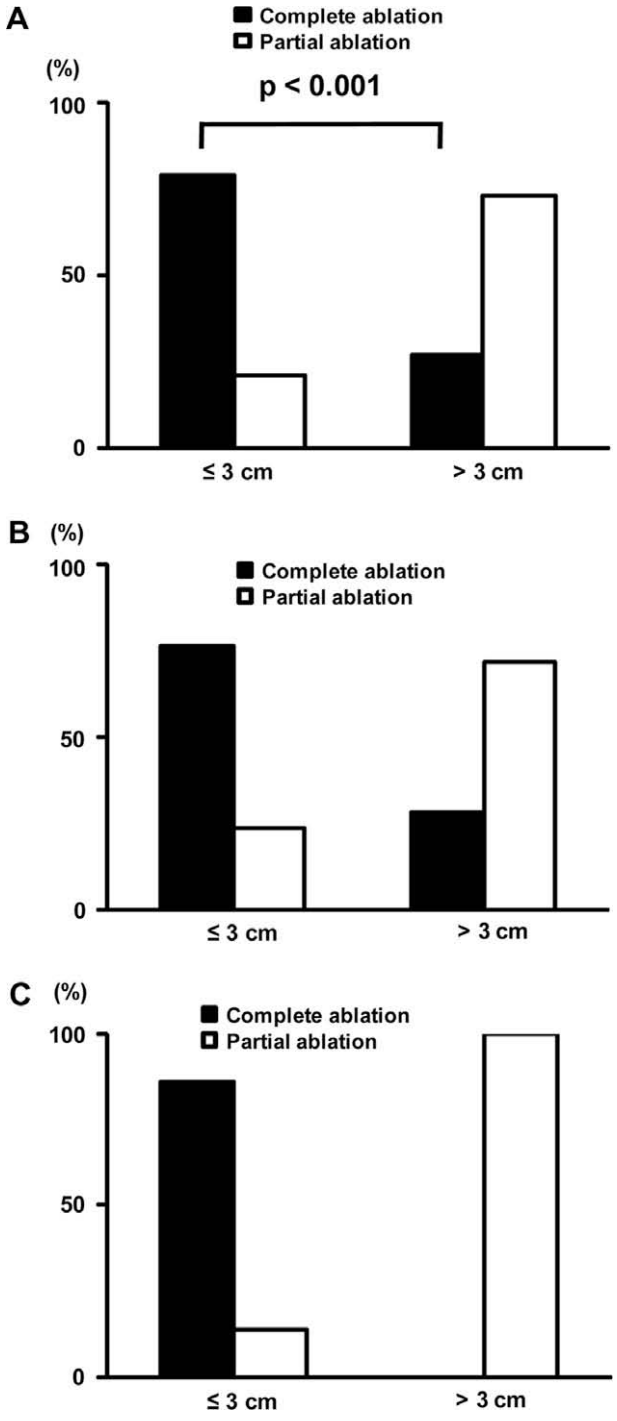

Fig. 1 – Proportion of complete and partial ablation in (A) overall procedure, (B) RFA, and (C) PTC according to the tumour size.

3.3. *Survival analysis and local tumour progression*

During the observed period, forty-two (64.6%) patients expired. The overall median survival duration was 20.8±4.7 months with 1-, 2-, and 3-year survival rates of all patients being 67%, 46% and 27%, respectively. Log-rank analysis showed that both median survival duration and progression free duration of patients with complete ablation were substantially longer than those of patients with partial ablation (Fig. 3). Median survival durations of patients with complete ablation and with partial ablation were 34.6 ± 6.8 months and 14.4 ± 2.3 months ($p = 0.002$), respectively. Median local progression free duration was 14.8 ± 4.5 months in the complete ablation group and 7.8 ± 0.7 months in the partial ablation group ($p = 0.002$). In addition, Kaplan–Meier analysis revealed that 1-, 2- and 3-year survival rates were 79%, 62% and 47%, respectively, in patients with complete ablation, and 57%, 32% and 9% in patients with partial ablation. Estimated 1- and 2-year progression free survival rates were 72% and 39% in patients with complete ablation, whereas they were 31% and 16% in patients with partial ablation. In the re-treatment patients, the patients with complete ablation also had longer recurrence-free survival than patients with partial ablation (mean 16.0 ± 11.4 versus 5.5 ± 3.9 months). In the multivariate Cox regression model, we found that the extent of ablation (i.e. complete ablation versus partial ablation) was closely related to all-cause mortality (HR = 0.38, $p < 0.05$, Table 2).

3.4. *Side effects and complications*

Complications after RFA and PTC are summarised in Table 3. The majority of patients had mild pain during the procedures. However, the pain was controlled simply by analgesic and disappeared within 1 day after the thermal ablations (Fig. 4). There were seventeen cases of haemoptysis. Of those, one patient was controlled by bronchial arterial embolisation and the others were spontaneously recovered without specific intervention. Eight patients suffered from pneumothorax of which two patients were treated with tube thoracostomy. One patient suffered from bronchopleural fistula after RFA and was treated with thoracoscopic surgery. A more serious complication included one case of acute respiratory distress syndrome which occurred at 7 days after RFA.

4. Discussion

This present study has evaluated the clinical outcomes in patients pulmonary malignant tumours treated with CT-guided thermal ablation, focusing on therapeutic efficacy, survival duration and their complications. The rate of complete ablation was 76.2% of patients treated with RFA and 85.7% in patients treated with PTC for pulmonary tumours which were smaller than 3.0 cm in diameter. Survival duration and progression free survival duration were significantly longer in patients with completely ablative tumours than those in patients with partially ablative tumours. In addition, the extent of ablation for tumours appears to be an independent predictor for mortality of patients with lung malignancies. These findings indicate that RFA and PTC may potentially develop into treatment alternatives in the management of pulmonary malignant diseases, especially for non-surgical patients.

Since first being reported in 2000, lung RFA has become a promising treatment option in the management of non-surgical lung cancer patients. RFA brings to the table some important advantages over traditional standard therapies.[7] One of

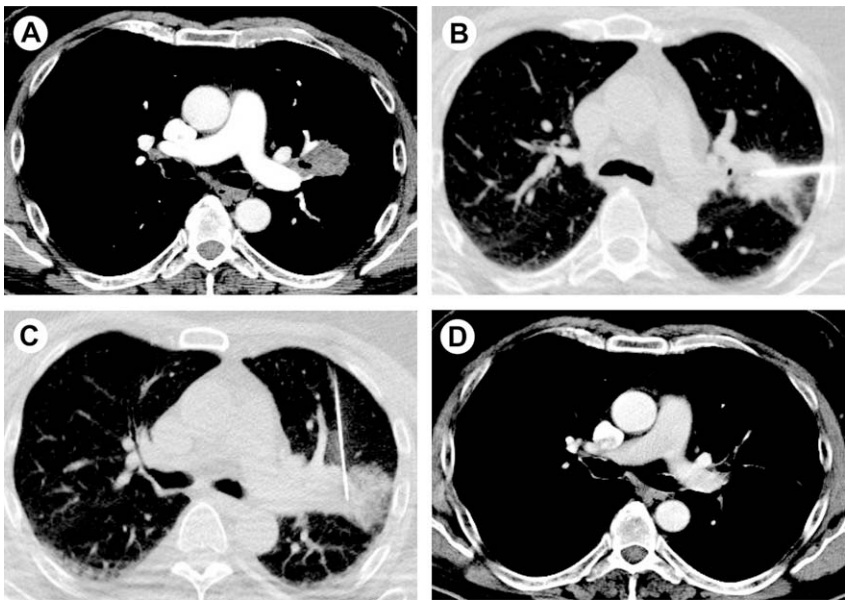

Fig. 2 – A 60-year-old man with 3.0 × 2.7 cm-sized mass on left upper lobe, which was confirmed pathologically as an adenocarcinoma. (A) Initial CT section of lung window shows the ill-defined mass adjacent to the left main pulmonary artery. (B–C) CT sections of lung window during PTC. Initially, cryoablation was performed by horizontally inserted cryoprobe. Another cryoprobe was then inserted vertically and remnant mass was ablated. (D) Follow-up CT at 10 months after PTC showing the disappearance of lung mass.

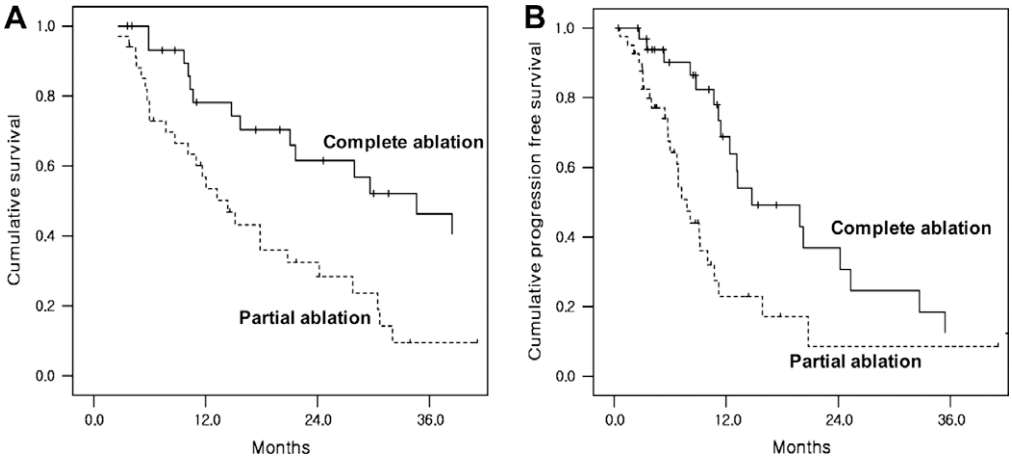

Fig. 3 – Kaplan–Meier curves showing the survival function. (A) Survival duration of completely ablative patients compared with partially ablative patients ($p = 0.002$). (B) Progression free duration of completely ablative patients compared with partially ablative patients ($p = 0.002$).

the major advantages of RFA is that it allows ablation of tumours without major damage to surrounding normal parenchyma.[18–20] In addition, this technique can be performed percutaneously, avoiding a thoracotomy for patients with severe comorbidities or those who refuse open resection. A recent report has demonstrated that RFA's safety profile is similar to that of percutaneous image-guided lung biopsy.[4] Therefore, RFA has been considered as an attractive treatment option for local control of pulmonary malignant tumours. In this study, the complete ablation of lung tumours by RFA was attained in 16 patients with masses less than or equal to 3.0 cm and in 13 patients with masses larger than 3.0 cm (76.2% versus 28.3%). The median survival duration and local progression free duration of patients with complete ablation were 34.6 ± 6.9 months and 13.2 ± 2.3 months, respectively. These durations were significantly longer than those of patients with partial ablation. These results suggest that successful local control of patients lung masses by RFA may effectively prolong their survival duration regardless of their medical comorbidities and severities.

Table 2 – Multivariate Cox proportional hazards model for independent predictors of recurrent-free survival and mortality.

Variables	Hazard ratio	95% CI	*p* Value
Disease-free survival			
Extent of ablation[a]	0.288	0.133–0.624	0.002
Survival			
Stage[b]	0.321	0.141–0.735	0.007
Extent of ablation	0.378	0.190–0.752	0.006

a Complete ablation versus partial ablation.
b Stage I versus stage II–IV.

Table 3 – Complications after RFA and PTC.

	RFA	PTC
Haemoptysis		
Self-limited	15 (22.4)	1 (11.1)
Treated with bronchial artery	1 (1.5)	0 (0.0)
Embolisation		
Pneumothorax	5 (7.5)	1 (11.1)
Self-limited	2 (3.0)	0 (0.0)
Treated with thoracostomy	1 (1.5)	0 (0.0)
Haemothorax	1 (1.5)	0 (0.0)
Bronchopleural fistula	1 (1.5)	0 (0.0)
Acute respiratory distress syndrome		

Data are presented as *n* (%).

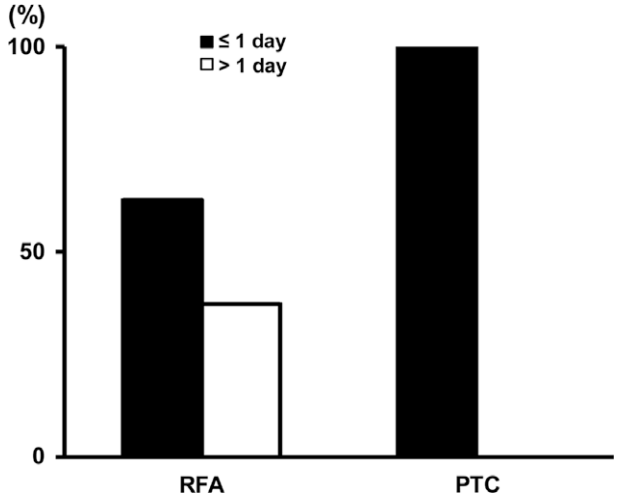

Fig. 4 – Comparison of pain duration associated with the procedures in patients treated with RFA and PTC.

Cryoablation is regarded as an intraoperative modality used primarily in the ablation of prostate and hepatic mass.[10,21] In the treatment of lung cancer, bronchoscopic cryoablation has been performed.[13,14,22] Recently, Wang and colleagues have demonstrated that PTC for various thoracic masses yields palliative benefits with low procedural morbidity even when near the mediastinal structure.[15] A benefit of cryoablation over other heat-based thermal ablative modalities, such as RFA and microwave ablation, is the apparent ability to preserve collagenous and other structural cellular architecture in virtually any frozen tissues.[13,14,22] In our present study, six patients with lung masses less than or equal to 3.0 cm in diameter had complete ablation after PTC, while no patient with lung mass larger than 3.0 cm had complete ablation (85.7% versus 0%). Interestingly, a few complications during and after PTC were observed in patients with lung malignancies although cryoablation has been shown to accompany high complication rates as compared with RFA.[9] Moreover, the pain duration associated with the procedure was very short in our study. Notwithstanding its feasibility, this minimally invasive therapy has the limited ability of ablating large tumours. A number of previous reports have discussed tumour responses after RFA, and there is a general consensus that complete tumour ablation by RFA is achievable with a tumour being no more than 3.0 cm in diameter. In the previous studies, the percentage of complete ablation by RFA was 63–100% of tumours smaller than 3.0 cm in diameter, whereas it was only 23–39% of tumours larger than 3.0 cm.[8,23] However, the appropriate size criteria of tumours for PTC, for making substantial tumour ablation, is not elucidated. Several reports have shown that cryoablation could be considered as an effective method for local destruction of liver metastases up to 3 to 4 cm in diameter but it is also associated with a significant rate of complications.[24,25] In our population, we could not achieve complete ablation of any tumours greater than 3.0 cm in diameter using PTC: The sizes of two tumours were 3.4 and 3.8 cm. Although an ice ball cover after PTC was satisfactory in each case, the follow-up CT images showed enhanced rim at the ablated margin.

Recent studies have demonstrated that tumour stage, tumour size, and the extent of ablation are the influential factors for the survival duration of patients treated with RFA.[8,26] Our present analysis revealed that the extent of ablation was an independent predictor for recurrence-free survival and overall survival duration of patients with lung malignancies. Even in patients with masses greater than 3.0 cm in diameter, complete ablation provided a better survival rate and longer progression free duration than partial ablation did. These results suggest that the sufficient destruction of pulmonary malignant tumours using both thermal ablation, RFA and PTC, may allow the patients to expect a better prognosis, although the current study is limited by the small sample size and the short follow-up period. Thus, we expect that this study will be a cornerstone for future research related to the survival benefit of ablation treatment with a large-sized and prospective controlled design.

In conclusion, RFA and PTC are promising treatment modalities for pulmonary malignant tumours with satisfactory outcome of tumour destruction, especially for tumours less than or equal to 3.0 cm in diameter. Moreover, the extent of ablation can be an independent predictor for progression free survival of patients with lung malignancies. Most complications by both thermal ablative modalities are self-limited. This study indicates that RFA or PTC can be considered as one of the treatment options with low procedural morbidity for various pulmonary malignant tumours, especially for non-surgical candidates having small-sized masses.

Conflict of interest statement

None declared.

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REFERENCES

1. Jemal A, Siegel R, Ward E, Murray T, Xu J, Thun MJ. Cancer statistics, 2007. *CA Cancer J Clin* 2007;**57**:43–66.
2. Pastorino U, Buyse M, Friedel G, et al. Long-term results of lung metastasectomy: Prognostic analyses based on 5206 cases. The international registry of lung metastases. *J Thorac Cardiovasc Surg* 1997;**113**:37–49.
3. Rajdev L, Keller SM. Neoadjuvant and adjuvant therapy of non-small cell lung cancer. *Surg Oncol* 2002;**11**:243–53.
4. Simon CJ, Dupuy DE. Current role of image-guided ablative therapies in lung cancer. *Expert Rev Anticancer Ther* 2005;**5**:657–66.
5. Boring CC, Squires TS, Tong T, Montgomery S. Cancer statistics, 1994. *CA Cancer J Clin* 1994;**44**:7–26.
6. Mountain CF. Revisions in the international system for staging lung cancer. *Chest* 1997;**111**:1710–7.
7. Dupuy DE, Zagoria RJ, Akerley W, Mayo-Smith WW, Kavanagh PV, Safran H. Percutaneous radiofrequency ablation of malignancies in the lung. *AJR Am J Roentgenol* 2000;**174**:57–9.
8. Lee JM, Jin GY, Goldberg SN, et al. Percutaneous radiofrequency ablation for inoperable non-small cell lung cancer and metastases: Preliminary report. *Radiology* 2004;**230**:125–34.
9. Lee Jr FT, Chosy SG, Littrup PJ, Warner TF, Kuhlman JE, Mahvi DM. Ct-monitored percutaneous cryoablation in a pig liver model: Pilot study. *Radiology* 1999;**211**:687–92.
10. Bahn DK, Lee F, Badalament R, Kumar A, Greski J, Chernick M. Targeted cryoablation of the prostate: 7-year outcomes in the primary treatment of prostate cancer. *Urology* 2002;**60**:3–11.
11. Collyer WC, Landman J, Olweny EO, et al. Comparison of renal ablation with cryotherapy, dry radiofrequency, and saline augmented radiofrequency in a porcine model. *J Am Coll Surg* 2001;**193**:505–13.
12. Littrup PJ, Freeman-Gibb L, Andea A, et al. Cryotherapy for breast fibroadenomas. *Radiology* 2005;**234**:63–72.
13. Thurer RJ. Cryotherapy in early lung cancer. *Chest* 2001;**120**:3–5.
14. Deygas N, Froudarakis M, Ozenne G, Vergnon JM. Cryotherapy in early superficial bronchogenic carcinoma. *Chest* 2001;**120**:26–31.
15. 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.
16. Ahmed A, Littrup P. Percutaneous cryotherapy of the thorax: Safety considerations for complex cases. *AJR Am J Roentgenol* 2006;**186**:1703–6.
17. Goldberg SN, Gazelle GS, Compton CC, Mueller PR, Tanabe KK. Treatment of intrahepatic malignancy with radiofrequency ablation: Radiologic–pathologic correlation. *Cancer* 2000;**88**:2452–63.
18. Goldberg SN, Gazelle GS, Compton CC, Mueller PR, McLoud TC. Radio-frequency tissue ablation of vx2 tumor nodules in the rabbit lung. *Acad Radiol* 1996;**3**:929–35.
19. Miao Y, Ni Y, Bosmans H, et al. Radiofrequency ablation for eradication of pulmonary tumor in rabbits. *J Surg Res* 2001;**99**:265–71.
20. Putnam JB, Thomsen SL, Siegenthaler M. Therapeutic implications of heat-induced lung injury. In: Ryan TP, editor. *Matching the energy source to the clinical need. Proceedings of the SPIE, BiOS 2000, International Symposium on Biomedical Optics 2000 Jan 23–24, San Jose, CA*. Bellingham, WA: SPIE Press; 2000. p. 139–60.
21. Lee Jr FT, Mahvi DM, Chosy SG, et al. Hepatic cryosurgery with intraoperative us guidance. *Radiology* 1997;**202**:624–32.
22. Maiwand MO. The role of cryosurgery in palliation of tracheobronchial carcinoma. *Eur J Cardiothorac Surg* 1999;**15**:764–8.
23. Akeboshi M, Yamakado K, Nakatsuka A, et al. Percutaneous radiofrequency ablation of lung neoplasms: Initial therapeutic response. *J Vasc Interv Radiol* 2004;**15**:463–70.
24. Seifert JK, Morris DL. Prognostic factors after cryotherapy for hepatic metastases from colorectal cancer. *Ann Surg* 1998;**228**:201–8.
25. Niu R, Yan TD, Zhu JC, Black D, Chu F, Morris DL. Recurrence and survival outcomes after hepatic resection with or without cryotherapy for liver metastases from colorectal carcinoma. *Ann Surg Oncol* 2007;**14**:2078–87.
26. Simon CJ, Dupuy DE, DiPetrillo TA, et al. Pulmonary radiofrequency ablation: Long-term safety and efficacy in 153 patients. *Radiology* 2007;**243**:268–75.