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Safety and efficacy of a novel transbronchial radiofrequency ablation system for lung tumours: One year follow-up from the first multi-centre large-scale clinical trial (BRONC-RFII)

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Abstract

Background and Objective: Radiofrequency ablation (RFA) is an emerging treatment of lung cancer, yet it is accompanied by certain safety concerns and operational limitations. This first multi-centre, large-scale clinical trial aimed to investigate the technical performance, efficacy and safety of an innovative transbronchial RFA system for lung tumours.

Methods: The study enrolled patients with malignant lung tumours who underwent transbronchial RFA using an automatic saline microperfusion system between January 2021 and December 2021 across 16 medical centres. The primary endpoint was the

Changhao Zhong and Enguo Chen contributed equally to this study.

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complete ablation rate. The performance and safety of the technique, along with the 1-year survival rates, were evaluated.

Results: This study included 126 patients (age range: 23–85 years) with 130 lung tumours (mean size: 18.77 × 14.15 mm) who had undergone 153 transbronchial RFA sessions, with a technique success rate of 99.35% and an average ablation zone size of 32.47 mm. At the 12-month follow-up, the complete ablation rate and intrapulmonary progression-free survival rates were 90.48% and 88.89%, respectively. The results of patients with ground-glass nodules (GGNs) were superior to those of the patients with solid nodules (12-month complete ablation rates: solid vs. pure GGN vs. mixed GGN: 82.14% vs. 100% vs. 96.08%, $p = 0.007$). No device defects were reported. Complications such as pneumothorax, haemoptysis, pleural effusion, pulmonary infection and pleural pain were observed in 3.97%, 6.35%, 8.73%, 11.11% and 10.32% of patients, respectively. Two subjects died during the follow-up period.

Conclusion: Transbronchial RFA utilizing an automatic saline microperfusion system is a viable, safe and efficacious approach for the treatment for lung tumours, particularly for patients with GGNs.

KEYWORDS

bronchoscopy, ground-glass nodule, lung tumour, radiofrequency ablation

INTRODUCTION

Lung cancer, a malignancy associated with significant mortality, has witnessed a rising incidence in recent years.[1] Surgical resection is the preferred radical treatment of pulmonary malignancies; however, it is contraindicated in certain patients with surgically resectable lung cancer due to the presence of cardiopulmonary comorbidities.[2] Targeted ablation techniques, such as radiofrequency ablation (RFA), have been employed to treat patients with peripheral lung tumours deemed unsuitable for surgery.[3]

The RFA catheter induces local coagulation necrosis by heating tissue above 60°C based on the electric current-based technique.[4] The efficacy of RFA in the treatment of lung tumours has been demonstrated in previous studies.[5] However, the relatively high incidence of procedure-related complications, such as pneumothorax, haemoptysis and haemothorax, has limited the clinical application of RFA, particularly the percutaneous approach.[6] Additionally, the elevated lung impedance can lead to tissue carbonization and disrupt electrical conduction, thereby restricting the ablation range even with increased power and prolonged duration of ablation.[7,8]

Transbronchial RFA, performed through a bronchoscopic path, is a theoretically safe approach as it facilitates avoiding injury to the neurovascular structures and pleura. Advances in bronchial navigation techniques has enabled the precise positioning of the bronchoscope.[9] Our previous study developed a novel RFA system with automatic saline microperfusion, which reduces tissue impedance by infusing saline into the lung tissue to diminish air content. This technique also facilitates real-time monitoring of lesion temperature and dynamic adjustment of the saline infusion rates and power output.[10] The safety and feasibility of this system have been preliminarily validated through preclinical animal experiments. However, the clinical efficacy and safety of this system remain to be established. Therefore, this prospective clinical trial aims to evaluate the efficacy and safety of transbronchial RFA for the treatment of peripheral lung tumours.

SUMMARY AT A GLANCE

The current prospective large-scale, multi-centre clinical trial has demonstrated transbronchial RFA with saline microperfusion as a safe and effective method for treating lung tumours.

METHODS

Study design

This prospective, multi-centre, open-label, single-group, target-value study aimed to evaluate the safety and efficacy of transbronchial RFA for the treatment of lung tumours (Table S1 in the Supporting Information). The study protocol was approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University (EC-2020-066-(QX)-02). Written informed consent was obtained from all participants prior to participation. The study was registered at ClinicalTrials.gov (NCT04619472).

Patients

Patients with lung tumours aged ≥18 years who declined or were deemed unsuitable to undergo surgery or receive radio- or chemotherapy were recruited from 16 medical centres in China. Lesions <3 cm in size that were accessible through the bronchus path using a bronchoscope and radial

endobronchial ultrasound (EBUS) probe were defined as target pulmonary lesions. Patients who had received radiotherapy within the preceding 6 months were excluded from the study. Table S2 in the Supporting Information presents the detailed inclusion criteria.

Device and technique

An RFA system (BroncAblate; Hangzhou Broncus Medical Co., Ltd., China) that incorporated a saline microperfusion setting was used in the current study to facilitate real-time monitoring of the local temperature and impedance at the distal end of the catheter (Figure S1 in the Supporting Information). Saline pre-infusion was initiated within the target pulmonary tumour prior to the RFA procedure to reduce the local impedance within the tumour to 100–350 Ohms and create an optimal environment for electrical conduction.

Treatment

During the screening period, all patients will undergo positron emission tomography-computed tomography (PET-CT) scans for tumour restaging. The bronchoscopic pathway was planned prior to RFA using the virtual navigation bronchoscopy system (LungPro, Broncus Medical, Inc., San Jose, CA, USA). All patients underwent induction of general anaesthesia with muscle relaxation and mechanical ventilation. An RFA catheter (diameter 1.85 mm) was used in conjunction with a bronchoscope (BF-P290 and BF-1TQ290; Olympus). Saline infusion was continuous during the RFA procedure, and the infusion rate was dynamically adjusted according to the real-time temperature, aimed at maintaining the temperature of the ablation zone at 60–90°C. The target bronchus was accessed under the guidance of the LungPro navigation system. The accessibility of the target lesion was re-confirmed using cone-beam computed tomography (CT) imaging (Cios Spin®, Siemens Healthcare GmbH, Erlangen, Germany). Ablation was initiated after confirming that the RFA catheter was precisely positioned within the pulmonary lesion on cross-sectional, coronal and sagittal views (Figure 2). Transbronchial RFA was recommended to be performed with 20 Watts of power for 10 min to achieve an ablation zone size of 2.5–3.0 cm.[10] In clinical practice, the bronchoscopist can modify the ablation parameters according to the lesion's characteristics. Under cone-beam CT, successful ablation is identified when the Post-Ablation Target Zone (PTZ)—an opaque, high-density area adjacent to the tumour after ablation—surrounds the Gross Tumour Region (GTR) and is encompasses the GTR of 5-10 mm. If the PTZ does not fully encompass the target lesion after the initial procedure, the catheter route can be adjusted to perform additional ablations. Follow-up data (clinical assessments, laboratory tests, lung function, contrast-enhanced CT or PET-CT) were collected and analysed at the following time points: preoperatively; 24 h postoperatively; before discharge/7 days postoperatively (whichever occurred first); and 1, 3, 6, 9 and 12 months after RFA treatment. Patients diagnosed with multiple pulmonary malignancies (≥2 lesions) underwent a second RFA within 2 weeks. For patients undergoing anticancer therapy (chemotherapy, targeted therapy or immunotherapy) but experiencing tumour progression or requiring ongoing treatment due to tumour metastasis or metastatic tumours, their original anticancer regimen was maintained during the follow-up period.

Complementary ablation is an essential and scheduled component of the RFA regimen. The patients were followed up as planned after the completion of transbronchial RFA. The ablation effect was first evaluated at the 3-month follow-up visit. A comprehensive assessment involving radiologists, pulmonologists and investigators was performed to determine the efficacy of the initial ablation. A complementary RFA was recommended if the effects were insufficient. The procedure was completed within 2 weeks of the originally planned follow-up, and the subsequent 6-month post-procedure follow-up was extended by 2 weeks. All other initially scheduled follow-up timeframes remained unchanged.

Efficacy evaluation

The complete ablation rate of the pulmonary lesions at 6 months was defined as the primary endpoint. Complete ablation was defined as the presence of the following findings on the enhanced computed tomography (CT) or positron emission tomography (PET)/CT images, as evaluated by a third-party: (1) unenhanced or non-metabolic solid nodules; (2) unenhanced pulmonary cavities; (3) post-ablation fibrosis and (4) unenhanced or non-metabolic atelectasis.[11] Twelve months complete ablation rate, overall survival (OS, the proportion of surviving subjects at 1 year from enrollment) and the intrapulmonary progression-free survival (PFS, at 12 months after overall ablation procedure, the proportion that subjects whose all ablation lesions maintain completely ablated account for all evaluable subjects) rates were the secondary endpoints. The EORCT QLQ C30 questionnaire was used to evaluate the quality of life (QoL). A change of 10 points in either direction between the baseline and 12 months post-RFA evaluations was deemed clinically significant.[12] The success rate of RFA catheter deployment, defined as the successful placement of the catheter at the target lesion area (either at the centre of the lesion or adjacent to it), PTZ encompasses the GTR of 5–10 mm and successful withdrawal of the catheter, was used to define the technical feasibility of transbronchial RFA.

Safety evaluation

The incidence of adverse events were recorded during RFA and at the follow-up visit. For RFA procedure-related adverse events, including definitely related, possibly related, definitely unrelated and possibly unrelated events, was evaluated by the investigators. Severe adverse events were

defined as any adverse event that resulted in death, life-threatening complications, hospitalization (initial or prolonged), disability or permanent damage, congenital anomaly/birth defect (defined as any structural or functional anomalies that occur during intrauterine life and can be identified prenatally, at birth or later in life.) or requirement of an intervention to prevent permanent impairment or damage.

Statistical analysis

The sample size was calculated based on the complete ablation rate. The 6-month complete ablation rate was assumed to be >80% based on the findings of previous studies, whereas the expected complete ablation rate was expected to be >90%. Thus, 126 patients had to be enrolled to achieve a power of 80% and an alpha level of 0.025 (one-sided), assuming a dropout rate of 15%.

All statistical analyses were performed using SPSS version 24 (SPSS Statistics version 24, IBM, New York, USA). The complete ablation and technical success rates were documented as absolute numbers and percentages, respectively. Subgroup analysis of the complete ablation rate was performed using the Chi-square test. Kaplan–Meier curves were used to analyse the survival data encompassing intrapulmonary PFS and OS, and differences in the survival curves were compared using the log-rank test. QoL was analysed using a paired *t*-test between baseline and 12-month follow-up in terms of the symptom scale and global health status. For adverse event, the investigators responsible for determining adverse events were clinically involved physicians, their assessments were conducted under third-party supervision to ensure objectivity and accuracy.

RESULTS

Demographic characteristics

Among the 134 participants who underwent transbronchial RFA for the treatment of primary lung cancer or pulmonary metastasis between January 2021 and December 2021, 126 were included in the study (113 patients were diagnosed with lung tumours through pathological analysis. The remaining 13 patients, who had a history of previous tumours, were diagnosed based on multidisciplinary team discussions and observed tumour growth during imaging follow-ups; Figure 1).

The median age of the enrolled participants was 68 years (range: 23–85 years). Chronic obstructive pulmonary disease (COPD) is the most frequent respiratory comorbidity (26.19%, 33/126). The Charlson Comorbidity Index results indicate that the majority of patients have moderate (point 3–4, 40.48%) or severe (point 5–6, 44.44%) comorbid conditions. In sum, 81.75% of enrolled subjects had stage I lung

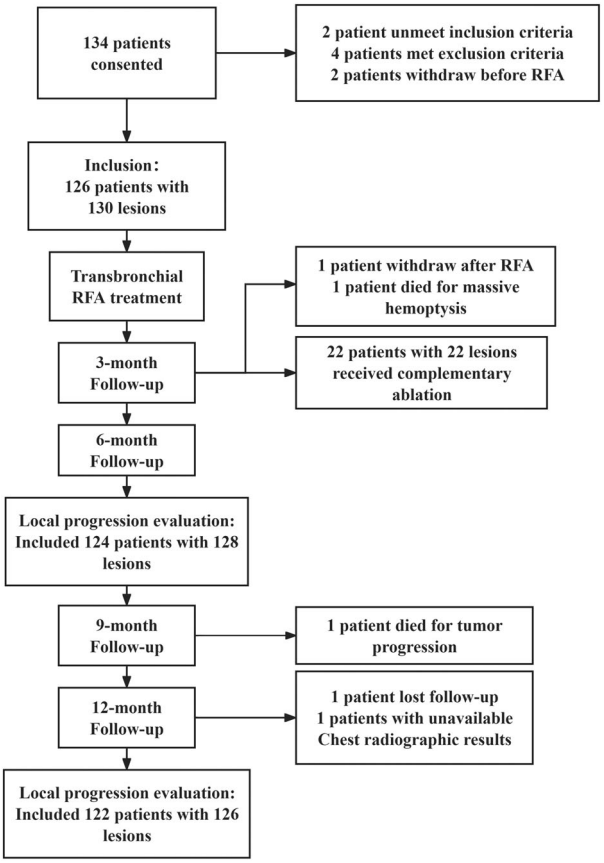

FIGURE 1 The flowchart of patient enrollment and follow-up process.

cancer (103/126). The majority of enrollees were deemed unsuitable candidates for surgery (73.81%). Other 11.90% of patients with unresectable tumours, and rest 14.29% of patients declined surgery. 76.98% patients were diagnosed of adenocarcinoma (97/126) and 13.49% of squamous cell carcinoma (17/126), while 5.56% were defined as lung metastasis (7/126). During the follow-up period, 16 patients continued with their original anticancer treatment regimens, comprising 2 receiving chemotherapy, 2 undergoing immunotherapy and 12 receiving targeted therapy. (Table 1).

Among the 126 patients (130 pulmonary lesions) who underwent transbronchial RFA, 45.38% (59/130) had solid nodules (Lesions that appear completely solid on imaging with no ground-glass opacity (GGO) component.), 14.62% (19/130) had pure ground-glass nodules (GGN, Lesions that appear as ground-glass opacity without any solid components on imaging.) and 40.00% (52/130) had mixed GGN (Lesions that have both solid and ground-glass opacity components on imaging.). The average tumour size was 18.77 ± 6.28 mm and 14.15 ± 4.65 mm in the long- and short-axes, respectively. The lesion size was <1, 1–2 and 2–3 cm in 6.15%, 51.54% and 42.31% of patients, respectively. The detailed location of Lesions was shown in Table S3 in the Supporting Information. The average distance from the lesions to the pleura was 1.90 ± 1.31 cm. Ten lesions were contact with the pleura, and 22 lesions were <1.0 cm away

TABLE 1 Characteristic of included patients and target lung lesion.

Characteristic			$N = 126$ (130 lesions)	Proportion
Median age (years)			68 (range: 23–85)	
Male/Female			73/53	
Mean BMI			22.21 ± 3.26	
Charlson Comorbidity Index	2		17	13.49%
	3–4		51	40.48%
	5–6		56	44.44%
	7		2	1.59%
Comorbidity	COPD		33	26.19%
	ILD		0	0%
Lung function	FEV1% predict		84.56 ± 24.81	
	FEV1 (L)		2.08 ± 0.74	
	DLCO% predict		74.55 ± 24.06	
	DLCO (mL/min/mm Hg)		16.40 ± 6.10	
Pre-RFA tumour stage[a]	I		103	81.75%
	II		1	0.79%
	III		7	5.56%
	IV		9	6.35%
	Lung metastasis		6	4.76%
Histopathology	Adenocarcinoma		97	76.98%
	Squamous cell carcinoma		23	18.25%
	Lung metastasis	Colorectal cancer	4	4.17%
		Breast cancer	1	0.79%
		Kidney cancer	1	0.79%
Tumour size	0–1 cm		8	6.15%
	1–2 cm		67	51.54%
	2–3 cm		55	42.31%
	Long axis (mm)		18.77 ± 6.28	
	Short axis (mm)		14.15 ± 4.65	
Lesion properties	Solid nodule		59	45.38%
	Mixed GGN		52	40.00%
	Pure GGN		19	14.62%
Lesion location	Right upper lobe		44	33.85%
	Right middle lobe		11	8.46%
	Right lower lobe		33	25.38%
	Left upper lobe		30	23.08%
	Left lower lobe		12	9.23%
Vascular permeation lesion[b]			52	40.00%
Lesion-to-pleura distance (cm)			1.90 ± 1.31	
	Contact to pleura (0 cm)		10	7.69%
	<1 cm		22	15.38%
	≥1 cm		98	76.92%

Abbreviations: COPD, chronic obstructive pulmonary disease; GGN, ground-glass nodule.
[a]Based on the CT or PET-CT imaging in screening period.
[b]The vessel that diameter was greater than 3.0 mm within their target ablation zone.

from the pleura. Lesion with accompanying vessels (the presence of vessels with a diameter greater than 3 mm within the ablation zone on CT imaging) was observed in 40.00% of lesions (Table 1).

Transbronchial RFA performance

In total, 126 patients with pulmonary lesions underwent 153 RFA sessions, including 23 complementary ablations, in

the present study. One session of complementary ablation could not be completed owing to unsuccessful catheter placement. Hence, the overall technical success rate of RFA was 99.35% (152/153). Transbronchial RFA procedures were performed with a median ablation power of 20 watts (range: 10–20 watts) for a median duration of 19.40 min (range: 10–96 min), with a median of 1 ablation per session (range 1–6). This achieved an average ablation zone size of 32.47 mm at the 1-month follow-up visit. However, the ablation zone size gradually decreased over time (Table S4 in the Supporting Information).

A slight increase in the ablation time compared with that of the other lesions was observed among the 47 lesions with accompanying vessels (median: 23.5 vs. 18.0 min, Mann–Whitney test, $p = 0.025$). However, no statistically significant difference was observed in the ablation power (median: 18 vs. 24 Watts, Mann–Whitney test, $p = 0.10$). The lesions with accompanying vessels demonstrated an ablation zone size similar to that of the other lesions (32.44 ± 12.21 vs. 32.48 ± 11.84 mm, $p = 0.98$).

Post-procedure radiographic changes

CT imaging was performed at baseline; 24 h; and 1, 3, 6, 9 and 12 months after RFA to evaluate the ablation effect. The target lesion zone exhibited significant enlargement and a typical fried egg sign (characterized by a solid, honeycomb-like structure and GGO), and a clear outer reaction area 24 h after the procedure.[11] GGO resolved within 3 months after RFA; however, the area of the target lesion zone remained larger than that of the gross tumour. Complete resolution of the GGO was observed within the subsequent 3 months, and a continued reduction in the size of the treated area was observed. The lesion had transformed into a solid nodule, occasionally accompanied by cavities or involuting fibrosis, at the 6-month to 12-month follow-up visits (Figure 2 and Figure S2 in the Supporting Information).

Efficacy of transbronchial RFA

The complete ablation rate was 93.75% (120/128) at 6 months, whereas it was 90.48% (114/126) at 12 months. Survival analysis demonstrated that the 1-year OS and intrapulmonary PFS rates were 96.83% and 88.89%, respectively (Table 2).

Subgroup analyses were performed based on the size of the tumour and lesion properties. The complete ablation rate and intrapulmonary PFS rate were higher in lesions <2 cm in size; however, no significant differences were

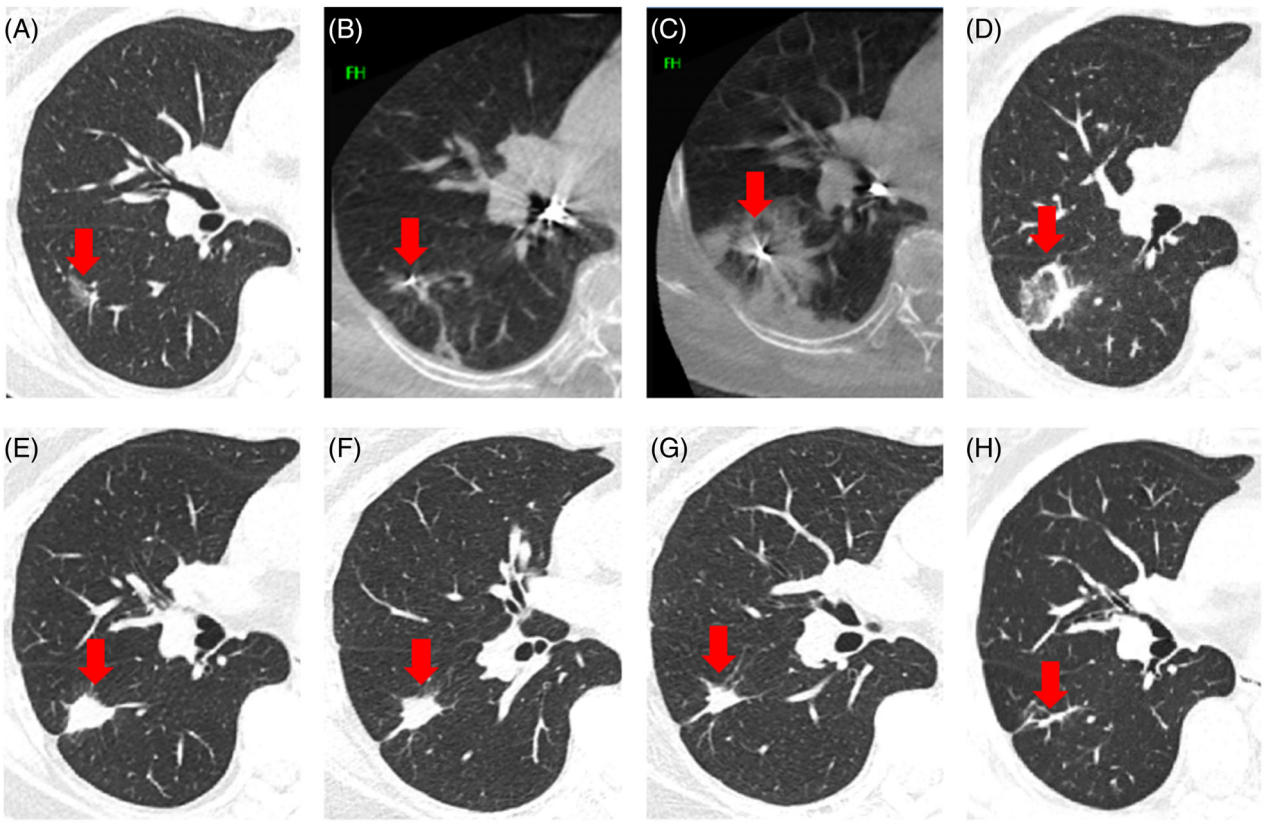

FIGURE 2 CT images acquired for preoperative evaluation and of the surgical procedure. (A): CT images acquired for preoperative evaluation. Red arrow: Target lesion. (B): Cone-beam CT images of intraoperative electrode positioning. Red arrow: Target lesion and RFA electrode. (C): Cone-beam CT images acquired immediately after ablation. Red arrow: Target ablation zone. (D–H): CT images acquired at 24 h, 1 month, 3 months, 6 months, 12 months. Red arrow: Target ablation zone.

TABLE 2 Efficacy of transbronchial RFA in the first 1-year follow-up.

Efficacy outcome		6 months complete ablation % (*N*)	12 months complete ablation % (*N*)	Intrapulmonary pregression-free-survival % (*N*)	Overall survival % (*N*)
Total		93.75% (120/128)	90.48% (114/126)	88.89% (112/126)	96.83% (122/126)
Tumour size	<2 cm	98.67% (74/75)	93.33% (70/75)	92.95% (66/71)	
	2–3 cm	86.79% (46/53)	86.27% (44/51)	83.63% (46/55)	
Lesion property	Solid nodule	85.96% (49/57)[a]	82.14% (46/56)[a]	78.95% (45/57)[a]	
	Pure GGN	100.00% (19/19)	100.00% (19/19)	100.00% (18/18)	
	Mixed GGN	100.00% (52/52)	96.08% (49/51)	96.08% (49/51)	

[a]In comparison to the other groups, $p < 0.05$.

observed (6-month complete ablation rate: $p = 0.081$, 12-month complete ablation rate: $p = 0.20$, intrapulmonary PFS rate: $p = 0.051$, survival curve: HR: 0.37 [0.12–1.08], $p = 0.067$). Furthermore, transbronchial RFA exhibited more favourable efficacy in patients with GGNs than in those with solid nodules, achieving superior complete ablation and tumour control (complete ablation and intrapulmonary PFS rate: $p < 0.05$, Survival curve: HR: 5.95 (2.04–17.33), $p < 0.001$) (Table 2 and Figure 3).

According to the EORCT QLQ C30 questionnaire, transbronchial RFA treatment resulted in no significant improvement in the global health status (−0.74 ± 24.01 points, paired *t*-test, $p = 0.74$). The scores of fatigue, pain and dyspnoea increased slightly (5.75 ± 16.54, 3.87 ± 17.18 and 4.76 ± 19.93, respectively; paired *t*-test, $p < 0.05$); however, the change was not significant (<10 points).

Safety of transbronchial RFA

The median hospital stay after RFA was 3 days (range: 1–12 days). During the 12-month follow-up period, 102 of the 126 patients (51.59%) experienced 377 adverse events. Among the 377 adverse events, 317 were mild and required no additional treatment. No device defects were reported during the RFA operation. Approximately 42.97% of adverse events were definitively unrelated to the RFA procedure, while 16.98% were clearly associated with the procedure. In terms of severe adverse events, eight cases were related to the RFA procedure. Apart from one patient who succumbed to haemoptysis (as detailed below), all other patients fully recovered following appropriate treatment. Respiratory disorders, such as pneumothorax (3.97%), haemoptysis (6.35%), pleural effusion (8.73%), pulmonary infection (11.11%) and pleural pain (10.32%), were the most frequently reported adverse events. No cases of haemothorax during the follow-up period. Apart from one patient who died due to massive haemoptysis, the remaining haemoptysis cases presented as blood-tinged sputum. For those patients experiencing fever and/or pleural effusion, nine were administered NSAIDs for symptom relief. Three patients developed pneumothorax, while another three presented with pleural effusion prior to discharge, necessitating additional chest drainage and prolonged hospital stays. (Table 3).

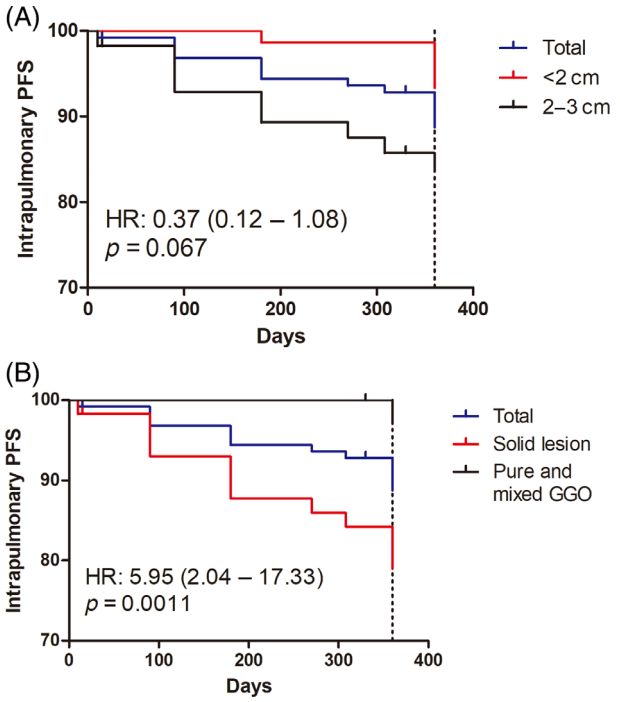

FIGURE 3 Kaplan–Meier survival curves of intrapulmonary progression-free survival. (A): Subgroup analysis of lesions <2 cm and 2–3 cm in size. (B): Subgroup analysis of solid nodules with ground-glass nodule.

The mortality rate at enrollment was 1.59% (2/126 patients). A 71-year-old male patient with compromised lung function was diagnosed with squamous cell carcinoma of the right upper lobe of the lung. The pulmonary lesion was a solid nodule (23.00 mm × 15.50 mm in size) positioned adjacent to a vessel and cavity. No anticoagulant medications was used prior to the procedure. The patient developed a fever, and pulmonary infection was confirmed 24 h post-ablation (22 Watts for 25 min) via CT imaging. The patient did not respond to anti-infectious treatment, and his condition deteriorated steadily. Haemoptysis was observed on the eighth day post-RFA, and multiple patchy shadows and ablation-related cavities in the lungs were observed on CT images (Figure S3 in the Supporting Information). The patient died of massive haemoptysis despite effective antibiotic and haemostatic treatment.

TABLE 3 Adverse events of the transbronchial RFA.

Adverse events		$N = 126$	Proportion	Recovery	Related to procedure	Lesion-to-pleura distance <1 cm
Respiratory disorder		87	69.05%			
	Pneumothorax	5	3.97%	5/5	5/5	2/5
	Haemoptysis	8	6.35%	7/8	8/8	2/8
	Pleural effusion	11	8.73%	11/11	6/11	3/11
	Pulmonary infection	14	11.11%	13/14	8/14	0/14
	Pleural pain	13	10.32%	13/13	13/13	1/13
	Haemothorax	0	0%			
Systemic response		18	14.29%			
	Fever	7	5.56%	7/7	4/7	
	Fatigue	7	5.56%	7/7	0/7	
Digestive disorder		23	18.25%			
	Nausea and vomiting	7	5.56%	7/7	0/7	
	Constipation	5	3.97%	5/5	0/5	
	Diarrhoea	3	2.38%	3/3	0/3	
Other		71	56.35%			
	Metabolic disorder	19	26.76%			
	Nervous system disorder	15	21.13%			
	Kidney and urinary disorder	9	12.68%			
Death		2	1.59%		1/2	
	Massive haemoptysis	1	0.79%		1/1	
	Tumour progression	1	0.79%		0/1	

A 67-year-old female patient diagnosed with advanced lung cancer underwent RFA successfully; however, the patient died of tumour progression and multiple organ failure 9 months after ablation treatment.

Among the 126 eligible patients, pulmonary function data were available for all patients before treatment and 109 patients at 12 months. No significant deterioration in the forced expiratory volume in one second (FEV_1), forced expiratory volume in one second/forced vital capacity (FEV_1/FVC) ratio, or diffusing capacity of the lungs for carbon monoxide (DLCO) was observed at any follow-up visit. Slight decreases observed in these values were not statistically significant or clinically relevant. (Table S5 in the Supporting Information).

DISCUSSION

This is the first prospective, large-sample size, multi-centre clinical study to determine the efficacy of transbronchial RFA for the treatment of lung tumours. An RFA technical success rate of 99.3%, generating an initial ablation range of >3 cm along the long axis, was observed in the present study. The complete ablation rate at the 12-month follow-up visit was 90.3% for all lung tumours and 97.10% for pure or mixed GGNs. Transbronchial RFA displayed commendable safety. Moreover, most adverse events were mild. Pneumothorax and haemoptysis were observed in only 3.97% and 6.35% of patients, respectively.

RFA, a minimally invasive technique that was initially introduced in 2000, has been widely used in the treatment of pulmonary malignancies.[5] Previous studies have shown that percutaneous RFA is feasible and effective for the treatment of lung tumours.[13,14] However, the elevated lung impedance can result in tissue carbonization and disrupt electrical conduction, thereby limiting the ablation range even with increased power and prolonged duration of ablation.[8] Moreover, the potential risks of percutaneous RFA-related complications, such as pneumothorax and haemoptysis, must be highlighted.[15,16] A program-controlled saline microperfusion system was introduced to reduce the amount of air within the lung tissue and improve the conduction efficiency of the radiofrequency energy. The infusion rate and energy output were dynamically adjusted according to the real-time temperature such that the impedance at the distal end of the catheter remained relatively stable and the temperature was maintained between 60 and 90°C.[10] Thus, a larger ablation range and higher rate of complete ablation was observed during RFA treatment, which resulted in a reduction in the influence of the heat sink effect.

Efficacy of transbronchial RFA was preliminary evaluated in this 1-year follow-up. The 12-month local control rate of transbronchial RFA observed in the present study was superior to that reported in other small simple size transbronchial RFA studies (90.32% vs. 82.60%).[17] GGNs, which account for over 60% of primary lung cancer diagnoses,[18] usually occur when the lung alveoli are partially filled with fluid or cells that contain a certain amount of air,

thereby resulting in high tissue impedance.[19] The saline microperfusion system effectively reduced the air content in the local lung tissue via the perfusion of saline into the alveolar cavity. Moreover, this system aided in achieving a complete ablation rate of 100% and 96.0% in patients with pure GGN and mixed GGN, respectively. The findings of the present study are comparable with those of microwave ablation or SBRT for GGN (1 year local control rate, microwave ablation: 94.3%, SBRT: 100%); however, further follow-up is required.[20,21]

Previous studies have not reported any major adverse events related to transbronchial RFA.[17,22,23] Nevertheless, the safety profile of transbronchial RFA remains unclear owing to the limited sample size. Almost all transbronchial RFA procedures were completed without intraoperative complications in the present study. The majority of adverse events were mild and unrelated to the RFA procedure. Most severe adverse events were effectively managed through appropriate treatments. The nature of complications observed in the present study closely resembled those observed after percutaneous RFA. Transbronchial RFA resulted in reduced incidence of procedure-related complications compared with percutaneous RFA. Pneumothorax and haemoptysis were observed in 3.97% (vs. 28.4%) and 6.35% (vs. 12.0%) of patients, respectively.[24,25] COPD is a common comorbidity observed in 30%–70% of patients with lung cancer.[26–28] Poor lung function limits the efficacy of surgical treatment, and an increased risk of pneumothorax has been associated with pulmonary hyperinflation.[29] In this study, 21 of the total 126 patients with emphysema were treated with transbronchial RFA. The procedure did not affect lung function in these patients, and pneumothorax was observed in 2/21 of patients.

Formation of a massive cavity following ablation is the primary cause of massive haemoptysis. Ablation-related cavitation has been observed in 14%–17% of patients within 3.1 ± 1.7 days post percutaneous RFA.[30] Most patients who develop cavitation remain asymptomatic; however, such a cavity can enlarge over time or rupture in some cases, leading to the incidence of pneumothorax and haemorrhage.[31] Clinicians need to be vigilant for the formation of cavitations in the lesion within 1 week after RFA. Assess the risk of haemoptysis using enhanced CT or angiography in patients with significantly enlarged cavities is essential.[32] It is crucial to promptly identify the source of bleeding; ensure airway patency; and intervene using methods, such as thrombin injection or pulmonary artery embolization, in patients with symptoms of haemoptysis.[33]

This study has several limitations. First, the follow-up duration of the present study was relatively short; therefore, further studies must be conducted to determine the long-term effects of transbronchial RFA. Similarly, the survival analysis for patients with different natures of lesions in this study requires further validation. The original medical treatments, such as chemotherapy, targeted therapy or immunotherapy, were continued during follow-up. Thus, evaluating the specific impact of these therapies on tumour progression was challenging. Lastly, this was a single-arm study that lacked a direct comparison with percutaneous RFA, microwave ablation, or radiotherapy. Further studies must be conducted to definitively demonstrate the advantages of transbronchial RFA.

In conclusion, the findings from this 12-month follow-up study provide preliminary evidence supporting the feasibility and safety of transbronchial RFA incorporating an automatic saline microperfusion system. Superior local tumour control was observed in patients with GGN. This pioneering large-scale, multi-centre clinical trial provides strong evidence for the development and integration of transbronchial ablation as a treatment modality for lung tumours. Long-term follow-up studies are currently underway to corroborate these promising results and to further elucidate the role of transbronchial RFA in the comprehensive management of lung cancer.

AUTHOR CONTRIBUTIONS

Changhao Zhong: Conceptualization (equal); data curation (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); supervision (equal); validation (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). **Enguo Chen:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); project administration (equal); writing – original draft (equal); writing – review and editing (equal). **Zhuquan Su:** Conceptualization (equal); data curation (equal); formal analysis (equal); funding acquisition (equal); investigation (equal); methodology (equal); project administration (equal); resources (equal); validation (equal); visualization (equal); writing – original draft (equal); writing – review and editing (equal). **Difei Chen:** Conceptualization (equal); data curation (equal); formal analysis (equal); investigation (equal); methodology (equal); writing – original draft (equal); writing – review and editing (equal). **Feng Wang:** Conceptualization (supporting); data curation (supporting); investigation (equal); methodology (equal); writing – review and editing (equal). **Xiaoping Wang:** Conceptualization (supporting); data curation (supporting); investigation (equal); writing – review and editing (equal). **Guangnan Liu:** Conceptualization (supporting); data curation (equal); investigation (equal); writing – review and editing (equal). **Xiaoju Zhang:** Conceptualization (supporting); data curation (supporting); investigation (equal); methodology (equal); writing – review and editing (equal). **Fengming Luo:** Conceptualization (supporting); data curation (equal); investigation (equal); methodology (equal); writing – review and editing (equal). **Nan Zhang:** Conceptualization (supporting); data curation (supporting); investigation (equal); methodology (equal); writing – review and editing (equal). **Hongwu Wang:** Conceptualization (supporting); data curation (equal); investigation (equal); methodology (equal); writing – review and editing (equal). **Longyu Jin:** Conceptualization (supporting); data curation (equal); investigation

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CONFLICT OF INTEREST STATEMENT

This trial is sponsored by Broncus Medical Co. The funders and sponsors of the study had no role in study design, data collection, data analysis, data interpretation, or writing of the report. The authors have no conflicts of interest to declare.

DATA AVAILABILITY STATEMENT

The study protocol is provided in Appendix S1 of the Supporting Information. The data utilized in this study will be made available upon request from the researchers post the clinical trial's completion. Access to de-identified individual participant data will be granted to researchers submitting scientifically sound proposals. Proposals must be directed to the corresponding author, Shiyue Li (lishiyue@188.com). Review and approval of proposals will be conducted by the sponsor, investigator and collaborators. Data requestors will need to sign a data access agreement to obtain access.

HUMAN ETHICS APPROVAL DECLARATION

This study was performed in accordance with the Declaration of Helsinki and approved by the Ethics Committee of the First Affiliated Hospital of Guangzhou Medical University—approval: EC-2020-066-(QX)-02. Participant registration took place from January 2021 to March 2023. All adult participants provided written informed consent to participate in this study.

Clinical trial registration: NCT04619472 at ClinicalTrials.gov.

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SUPPORTING INFORMATION

Additional supporting information can be found online in the Supporting Information section at the end of this article.

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