Radiofrequency Ablation of Lung Metastasis Not Suitable for Surgery: Experience in Siriraj Hospital

Trongtum Tongdee MD*,
Pattama Tantigate MD*, Ranista Tongdee MD*

** Department of Diagnostic Radiology, Faculty of Medicine Siriraj Hospital, Mahidol University, Bangkok, Thailand*

Background: *Percutaneous image-guided radiofrequency ablation (RFA) is being promoted as a novel technique with low morbidity rate in treatment of inoperable lung tumor either primary lung tumor or metastatic disease.*
Objective: *To report our experiences of RFA treated for lung metastasis in Siriraj Hospital and to evaluate the efficacy and complication of RFA.*
Material and Method: *All patients who underwent RFA for lung metastasis at Siriraj Hospital, between January 2007 and December 2013, were included in the present study. Clinical data, pre-procedure image findings including lesion size, location, post-procedure image findings, complications, and outcome were retrospectively reviewed.*
Results: *Fourteen patients (10 male, 4 female) with 27 lung metastasis were treated with RFA. The ablated lung nodules consist of metastasis from hepatocellular carcinoma (n = 13), colorectal adenocarcinoma (n = 9), insular cell thyroid carcinoma (n = 3), and adenocarcinoma of prostate gland (n = 2). Mean patient age was 50 years (age range 28-67 years). Size of the ablated nodules range from 0.5 to 5.0 cm (median = 1.3 cm). The most common complication was pneumothorax, occurring in 71% (10 of 14 patients). Other complications included surgical site infection, atelectasis, loculated hemothorax, loculated empyema, and bronchopleural fistula, occurred in one patient each. Post-procedure image findings showed complete ablations without local tumor recurrence in 81% (22 of 27 nodules). Local tumor recurrences were seen in 19% (5 of 27 nodules).*
Conclusion: *Radiofrequency ablation for lung metastasis can be considered as a relatively safe, effective alternative treatment for lung metastasis. Risk factors that may associate with local recurrence include large size nodules and subpleural location.*

Keywords: *RFA, Radiofrequency ablation, Lung metastasis*

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Percutaneous radiofrequency ablation (RFA) is considered an alternative locoregional treatment for nonsurgical candidate lung metastasis patient. The predominant mechanism of action of RFA is thermal injury. A high-frequency alternating current emitted from the exposed non-insulated portion of the electrode generates frictional heat, agitating ions in the tissue surrounding the tip of the needle. The heat causes coagulative necrosis, driving extracellular and intracellular water out of the tissue, thereby denaturing proteins[1-3]. These effects are achieved in a predictable manner at predictable temperatures and in a relatively predictable volume[4]. A number of studies have reported the efficacy of RFA for treatment lung tumors either primary or metastatic disease. The purpose of the present study was to report our experience of RFA for treating lung metastasis and to demonstrate the efficacy and complication of RFA.

Correspondence to:
Tongdee R, Department of Radiology, Siriraj Hospital, Mahidol University, 2 Prannok Road, Bangkoknoi, Bangkok 10700, Thailand.
Phone: +66-2-4197086
E-mail: ranista@gmail.com

Material and Method

Patient selection

We retrospective reviewed all patients treated with pulmonary RFA at the Siriraj Hospital, between January 2007 and December 2013. Fourteen patients with 27 lung nodules were enrolled in the present study, including one patient who had repeated RFA procedure due to tumor recurrence. The study was approved by the Hospital Ethics Committee, and a waiver for individual patient consent for this retrospective review was obtained. The patient characteristics were listed in Table 1.

Radiofrequency ablation technique

Before the procedure, all patients underwent chest computed tomography (CT) to assess the tumor size and location to facilitate the procedure planning. Positron emission tomography-computed tomography

(PET-CT) was obtained in two selected patients who had equivocal findings on prior conventional chest CT scan. All RFA procedures were performed by 4 to 10 year-experienced interventional radiologists, using aseptic technique. First, RFA probes were advanced to the tumor under CT-guidance. The size and length of needle electrode (LeVeen® needle electrode, Radiotherapeutics, Sunnyvale, Calif) were selected according to the depth and diameter of the target lesions. After confirming successful central placement of a finder needle under CT guidance, inside of which the multiple tines are deployed to maximize the treatment area. The tines were covered around tumors in all cases. Multiple cycles of radiofrequency ablations were performed until the impedance was reaches. Tract ablations were routinely performed to prevent tumor seeding.

Post-radiofrequency ablation monitoring

All patients were monitored in hospital at least overnight, and chest radiography was performed after RFA procedure and before discharge to exclude pneumothorax and pleural effusion. Patients with small asymptomatic pneumothorax were observed. Symptomatic patients or those with large pneumothorax or effusions were managed with chest drain insertion and repeat radiograph until the pneumothorax had resolved. Contrast-enhanced CT scan of chest was performed to evaluate treatment response and divided into three phases at early (immediate after procedure to one week), intermediate (one week to two months), and late (after two months). Six patients underwent surgery after RFA due to tumor size reduction and improving patient's condition. The tumor characteristics were described in the Table 1.

Residual or recurrent tumors after RFA were determined based on imaging criteria[5]. CT and PET/CT imaging suggestive of residual or recurrence tumor after RFA included: Early Phase (≤1 week after RFA):- Incomplete envelopment of ablated tumor by ground-glass opacity, lack of enlargement of ablation zone beyond preablation size, enhancement more than preablation tumor, central or nodular enhancement >10 mm, and enhancement >15 HU at densitometry. Intermediate Phase (>1 week to 2 months after RFA):- Change from ground-glass opacity (GGO) to solid opacity, growth of ablation zone beyond early phase, enhancement more than preablation tumor, central or nodular enhancement >10 mm, enhancement >15 HU at densitometry, less than 60% reduction of uptake at two months, and relative to preablation baseline on PET/CT. Late Phase (>2 months after RFA):- Change from GGO to solid opacity, development of nodule along electrode tract or tines, growth of ablation zone after three months, growth of ablation zone beyond preablation size by six months, enhancement more than preablation tumor, central or nodular enhancement >10 mm, enhancement >15 HU at densitometry, persistent uptake centrally or at region of ablated tumor, increased activity after two months, and development of nodular activity at site or original tumor nodule on PET/CT.

Data collection

The patient's demographic, clinical data and treatment-related variables were retrieved from the computerized database, including sex, age, and the patient's known primary cancer. Tumor variables were recorded, including tumor size, number, location, length of aerated lung traversed by the electrode probe, and adjacent structures. Tumor size was the diameter measured along the longest axis of the lesion. Tumor location was divided into pleural, subpleural, and pulmonary location. Tumor located within 1 cm of pulmonary vessels or visceral structures was defined

Table 1. Patient and tumor characteristics

Baseline characteristic	n (%)
Age, mean ± SD	49.57±11.05
Sex	
Male	10 (71.4)
Female	4 (28.6)
Types of primary cancer	
HCC	9 (64.3)
Thyroid	1 (7.1)
Rectum	2 (14.3)
Sigmoid	1 (7.1)
Prostate and rectum	1 (7.1)
Location of tumor	
Pulmonary	17 (63.0)
Pleural	2 (7.4)
Subpleural	8 (29.6)
Tumor size, median (range)	1.3 (0.5-5.0)
Distance, mean ± SD	3.28±1.80
Adjacent organ involvement	
Liver	2 (7.1)
Pulmonary	1 (3.6)
Renal	1 (3.6)
Vascular	1 (3.6)
No adjacent organ involvement	23 (82.1)

HCC = hepatocellular carcinoma

as in close proximity to such structures. Diameter of pulmonary vessel larger than diameter of tumor was defined as enlarged pulmonary vessel. The length of the electrode trajectory through the aerated lung to each lesion was measured on CT images and defined as the distance from the site of pleural puncture to the edge of the tumor along the electrode trajectory. Moreover, post-procedure images were reviewed and postablation findings, size, and ablated margin were recorded. The postablation size was the diameter measured along the longest axis of the postablation zone. The ablation margin was the average length of ground-glass opacity surrounding the lung nodule.

Statistical analysis

Repeated RFA sessions were considered to be independent events, and analysis was performed by using both the total number of patients and total number of ablation session as the sampling unit (total of 14 patients and 27 sessions). Patient demographics, tumor characteristic, and outcome were defined by descriptive statistical analysis. The tumor size and width of GGO margin were compared between controlled group and recurrence group using Student paired t-test analysis. Furthermore, student paired t-test analysis was performed to determine the effect of tumor size and distance of lung traversing by electrical probe on pneumothorax. Statistical analyses were performed using a commercially available software program (SPSS for Windows, version 18.0, SPSS Inc., Chicago, IL). A p-value of ≤ 0.05 was considered statistically significant.

Results

Patient demographics

Twenty-seven metastatic lung nodules in 14 patients (10 male, 4 female) were treated with computed tomography-guided percutaneous RFA under intravenous and local anesthesia. Mean patient age was 50 years (range 28-67 years). Five patients had one metastatic lung nodule, six patients had two metastatic lung nodules, two patients had three metastatic lung nodules, and one patient had four metastatic lung nodules. The median number of ablated tumors per patient was two (range 1 to 4 nodules) with four patients had bilateral disease.

Primary tumors consist of hepatocellular carcinoma (15 nodules in nine patients), colorectal adenocarcinoma (seven nodules in three patients), and insular cell thyroid carcinoma (three nodules in one patient). One patient who had two metastatic lung nodules had two known primary cancers including adenocarcinoma of rectum and adenocarcinoma of prostate gland, thus, the pathology of metastatic lung nodule is uncertain. The treated tumor were intrapulmonary in 17/27 (63%), subpleural in 8/27 tumors (30%), and pleural in 2/27 tumors (7%). The mean (± SD) size of ablated lung nodules was 1.5±1.0 cm (range, 0.5 to 5.0 cm). One nodule was adjacent to enlarged pulmonary vessel, two were adjacent to right diaphragm and liver, and another nodule was adjacent to right diaphragm and right kidney.

Mean (± SD) patient follow-up was 335±332 days, range from 22 days to 1,012 days.

Efficacy and associated factors

Two patients with three treated nodules had no available intermediate CT scans. However, late CT scans of both patients showed well-controlled tumors by imaging criteria. Late CT scans were not obtained in four patients with six post-RFA treated nodules. Two of these patients had undergone surgery after intermediate CT scan showing rim-enhancing cavitary lesion suspicious for tumor recurrence. One patient had rapid progression of primary disease and developed multiple distant metastasis. Another patient had been follow-up with chest X-ray.

Twenty-two post-RFA treated nodules (81%) were considered to be well-controlled, according to the patient's clinically stable and the absence of CT imaging criteria for recurrent tumor in the follow-up images.

Five post-RFA treated nodules had local recurrent tumors (19%). Four of which were diagnosed based on post-procedure CT findings and the remaining one was pathologically confirmed after surgery.

Of 14 patients, two patients with two metastatic nodules each had one well-controlled tumor and one recurrent tumor after RFA treatment.

Post-procedure CT findings of five recurrent tumors included focal enhancing nodules at intermediate CT scan (n = 1) and at late CT scan (n = 3), cavitary lesions with rim enhancement at both intermediate and late CT scan with increase F-18 FDG uptake in PET-CT study (n = 1). Of these five lesions, three (60%) located at subpleural location, two (40%) were intrapulmonary. None was close to any visceral organ or enlarged pulmonary vessel. Out of 22 well-controlled lung nodules, 15 nodules (68%) were intrapulmonary, five (23%) nodules were subpleural, and two (9%) were pleural nodules.

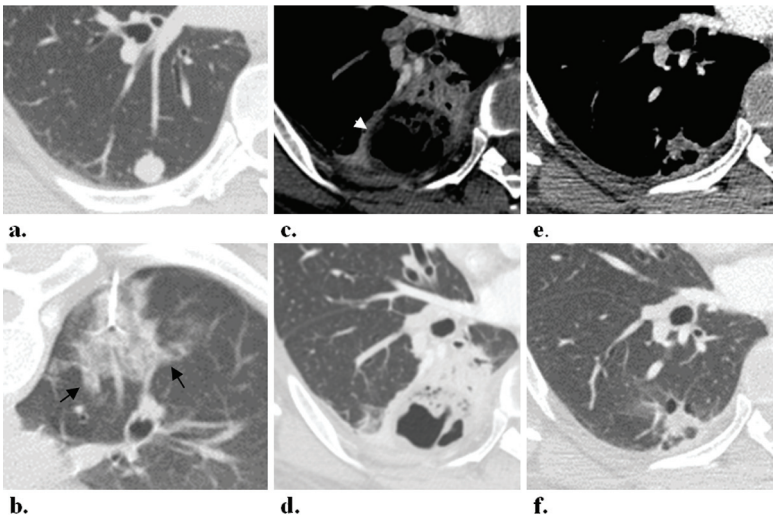

Fig. 1 Metastatic pulmonary nodule from hepatocellular carcinoma in a 55-year-old man undergoing RFA. (a) Pre-procedure contrast-enhanced CT image showed a rounded pulmonary nodule at posterior basal segment of right lower lobe. (b) CT image obtained during RFA in prone position showed electrical needle within the ablated nodule with surrounding ground-glass opacification (arrow). (c, d) Soft tissue-window CT images (c) and lung-window CT images (d) at 2 weeks after RFA showed faint thin rim enhancement without central nodularity (arrowhead) (e, f) Soft tissue-window CT images (e) and lung-window CT images (f) at 7 months after RFA showed a residual fibrotic scar. No residual enhancement was observed. This tumor was considered to be well-controlled after RFA.

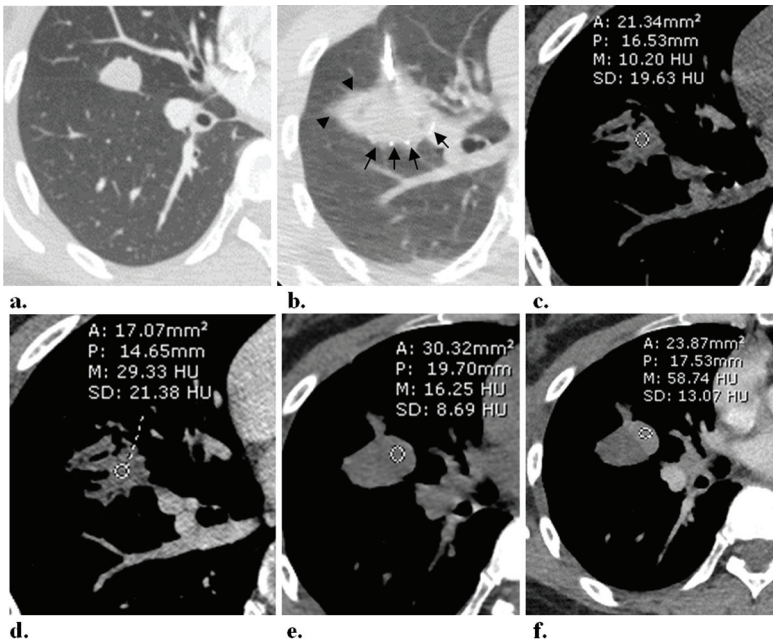

Fig. 2 Recurrent metastatic subpleural nodule after RFA in a 38-year-old woman with underlying hepatocellular carcinoma. (a) Pre-procedure contrast-enhanced CT image showed a rounded solid subpleural nodule abutting right major fissure. (b) Lung window CT image obtained during RFA showed the electrical probe covering the nodule (arrows). Surrounding ground-glass opacification was observed (arrowhead). (c, d) Pre contrasted CT images (c) and post-contrast CT images (d) at 1 month after RFA demonstrated contrast enhancement of the nodule more than 15 HU. (e, f) Pre-contrast CT images (e) and post-contrast CT images (f) at 3 months after RFA showed increased size of nodule with enhancement more than 15 HU, suggestive of tumor recurrence.

In recurrent group, the mean (± SD) initial size of ablated nodules was 2.2±1.6 cm (range, 1.1 to 5.0 cm), whereas those of well-controlled group was 1.4±0.8 cm (range, 0.5 to 4.2 cm), $p = 0.08$.

Ground-glass opacities surrounding the ablated tumors were observed in all lesions except one pleural nodule. In recurrent group, the mean (± SD) width of ground-glass opacity margin was 1.0±0.3 cm (range, 0.7 to 1.3 cm), whereas those of well-controlled group was 1.1±0.5 cm (range, 0 to 2.4 cm), $p = 0.79$.

Of four patients who had recurrent tumor, three patients also had progressive primary cancer. One patient had local recurrent tumor at RFA treated area without progression of primary tumor. Of 10 patients without recurrent tumor, six patients had progressive primary disease, and four patients had well-controlled primary disease.

Morbidity and mortality

There was no procedure-related mortality. The mean and median hospital stay was 4.3 and three days, respectively (range 3 to 14 days). The most common adverse effect was pneumothorax, occurring in 10 of 14 patients (71%) or 15 of 27 tumors (56%). Of these, five nodules (33%) were subpleural, nine nodules (60%) were intrapulmonary, and one (7%) was a pleural nodule. The mean (± SD) distance of traversing lung parenchyma to the ablated nodule in pneumothorax group was 2.1±2.3 cm (range, 0 to 6.0 cm), whereas those without pneumothorax was 2.0±2.1 cm (range, 0 to 5.6 cm), $p = 0.91$.

In pneumothorax group, the mean (± SD) initial size of ablated tumors was 1.3±0.5 cm (range, 0.7 to 2.4 cm), whereas those without pneumothorax was 1.8±1.4 cm (range, 0.5 to 5 cm), $p = 0.18$.

In seven out of 10 patients (incidence of pneumothorax = 10), the degree of pneumothorax was mild and the patients were asymptomatic, requiring no further treatment. The remaining three patients (incidence of pneumothorax = 5) had symptomatic moderate pneumothoraces and required chest tube insertion. Of these three patients, one had pure pneumothorax, one patient had associated infected hemothorax, and another patient had loculated empyema with bronchopleural fistula. The latter patient subsequently underwent decortications with fistula repair and lung resection.

Other complications included atelectasis (n = 1/27, 4%), and surgical site infection (n = 1/27, 4%). The detail of patient's demographics, post-RFA CT findings, complications, and results of treatment were summarized in Table 1.

Mean (± SD) initial size of ablated nodule and width of ground-glass opacity margin in controlled group and recurrence group was showed in Table 2.

Mean (± SD) initial size of ablated nodule and distance of traversing lung parenchyma in pneumothorax group and non-pneumothorax group was demonstrated in Table 3.

Discussion

RFA destroys tissue with a thermal energy delivery system that emits a high-frequency alternating

Table 2. Initial size of ablated nodule and width of ground-glass opacity margin on post-procedure CT image in well-controlled group and recurrence group

Variable	Patient outcome		
	Well-controlled n (%), mean ± SD	Recurrence n (%), mean ± SD	*p*-value
Initial size of ablated nodule (cm)	21 (81), 1.4±0.8	5 (19), 2.2±1.6	0.08
Width of GGO margin on post-procedure CT image (cm)	21 (81), 1.1±0.5	5 (19), 1.0±0.3	0.79

GGO = ground-glass opacity

Table 3. Initial size of ablated nodule and distance of traversing lung parenchyma by electrical probe in pneumothorax group and non-pneumothorax group

Variable	Patient group		
	Pneumothorax n (%), mean ± SD	No pneumothorax n (%), mean ± SD	*p*-value
Initial size of ablated nodule (cm)	15 (56), 1.3±0.5	12 (44), 1.8±1.4	0.18
Distance of traversing lung parenchyma by electrical probe (cm)	15 (56), 2.1±2.3	12 (44), 2.0±2.1	0.91

current through an electrode needle to destroy tumor cells. The alternating current is widely used to treat pulmonary malignancies either primary or metastatic tumors. Many prior studies reported the feasibility and safety of RFA for treating lung cancer and demonstrated that it could improve survival and local control rate[6-16].

Many investigators reported rate of recurrence after RFA, varying from 7% to 55% between one and three years of follow-up[7-16]. In the present series, the local recurrence rate at the treated lung nodule was 19%. Previous literature suggested that the pre-procedural factors associated with decreased local recurrence rate after RFA included; tumor size less than 3 to 3.5 cm, tumor location more than 3 to 10 mm away from a vessel, and peripheral location of tumor[11-20]. In the present study, the authors found that the mean (± SD) size of nodule with local recurrence (2.2±0.8 cm) was larger than the size of nodule without local recurrence (1.4±0.7 cm). However, there was no statistical significant between two groups (p = 0.08), probably due to the small number of patient included in the present study.

The presence of ground-glass opacity margin surrounding the ablated tumor has been used to determine the end point of procedure[21]. Anderson et al showed that a circumferential GGO margin of >5 mm is the minimal margin required to ensure complete tumor ablation[20]. Some investigators suggested that a 1-cm GGO margin should be ablated to reduce the risk of incomplete ablation[5]. In our institution, the authors performed multiple cycles of RFA until the impedance was reached, regardless of the presence or width of the ground-glass opacity margin. However, the immediate CT scans in our patients showed mean (± SD) width of GGO margin of 1.0±0.4 cm in recurrent group and 1.1±0.4 cm in locally-controlled group. There was no statistically significant difference between two groups (p = 0.79).

Another risk factor for local recurrence after RFA reported in previous studies was inadequate ablation zone due to "heat sink effect". The effect caused by the nearby circulating blood, resulting in lower temperature of the ablation zone. If the ablated zone is cooled below 60°C, the adequate ablation zone may not be achieved[20].

In the present study, only one ablated nodule located close to the enlarged pulmonary vessel. However, this nodule had no local recurrence in 4-month follow-up after RFA treatment.

Regarding to the location of nodule, the authors found that subpleural nodules tend to be recurrent more than the intrapulmonary or pleural location. Among five nodules with local recurrence, three located at peripheral or subpleural region, whereas two were intrapulmonary. Of all eight subpleural nodules, three (38%) nodules had local recurrence, and five (62%) nodules were well-controlled. Whereas 2/17 (12%) intrapulmonary nodules had local recurrence and 15/17 (88%) intrapulmonary nodules were well-controlled. No pleural nodule was recurrence after RFA.

Similar to prior studies[22-27], the most common adverse effect in the present study was pneumothorax, which tended to occur in nodules with intrapulmonary location. Most cases of pneumothorax were mild degree and did not require treatment. Of all 15 incidence of pneumothorax, five ablated nodules (33%) were subpleural, nine (60%) were intrapulmonary, and one (7%) was a pleural nodule. However, unlike the prior study by Zhu et al[28], the authors found no significant difference of the mean distance of traversing lung parenchyma to the ablated nodule in pneumothorax group and without pneumothorax group. Moreover, the authors did not find relationship between size of ablated nodule and incidence of pneumothorax.

Conclusion

Radiofrequency ablation for lung metastasis can be considered as a relatively safe, effective alternative treatment for lung metastasis. Risk factors that may associate with local recurrence include large size and subpleural location.

Limitations

The limitation in the present study included its retrospective design. Thus, the follow-up CT scan might not be performed or available to review in some patients. Relatively small number of patients and ablated nodules were another limitation of this single-site study. Moreover, the diagnosis of lung metastasis was based on presence of known primary cancer with newly developed pulmonary nodules. Most patients did not undergo surgery so that the histopathological diagnosis of the ablated nodules was not obtained.

What is already known on this topic?

RFA has been used to treat many primary and metastatic tumor, most frequently hepatic tumor. The usefulness of RFA has been well established as the alternative treatment for hepatocellular carcinoma and metastatic hepatic tumor, particularly from colorectal cancer. Recently, RFA has been introduced for

treatment of primary lung cancer and pulmonary metastasis in patients who are not suitable candidates for surgery. Its efficacy and outcome were reported in some prior literatures in which the studies were mostly conducted in western countries. In Thailand, the experience in using RFA for treatment of pulmonary metastasis is still limited, partly due to the limited healthcare providers familiar with this treatment method.

What this study adds?

To the best of our knowledge, we are the first to report experience in using RFA to treat lung metastasis in Thailand. Obtaining good efficacy and acceptable evidence of minor complications, comparable to the prior reports, RFA should be considered another alternative treatment method for treating lung metastasis in Thai population. Moreover, this published article aims to alert healthcare providers to the availability of this treatment method in Thailand.

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Potential conflicts of interest

None.

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การจี้ด้วยคลื่นวิทยุความถี่สูงเพื่อรักษามะเร็งปอดทุติยภูมิในผู้ป่วยที่ไม่เหมาะแก่การรักษาด้วยการผ่าตัดในโรงพยาบาลศิริราช

ตรงธรรม ทองดี, ปัทมา ตันติเกตุ, รณิษฐา ทองดี

วัตถุประสงค์: *เพื่อรายงานประสบการณ์ในการรักษามะเร็งปอดทุติยภูมิด้วยการจี้ด้วยคลื่นวิทยุความถี่สูงในโรงพยาบาลศิริราช และประเมินประสิทธิภาพการรักษาและภาวะแทรกซ้อนของการรักษาด้วยวิธีนี้*

วัสดุและวิธีการ: *เป็นการศึกษาในผู้ป่วยทั้งหมดที่ได้รับการรักษามะเร็งปอดทุติยภูมิด้วยการจี้ด้วยคลื่นวิทยุความถี่สูงในโรงพยาบาลศิริราช ในระหว่างเดือนมกราคม พ.ศ. 2550 ถึง ธันวาคม พ.ศ. 2556 โดยการบันทึกข้อมูลทางคลินิก ขนาด และตำแหน่งของรอยโรคที่เห็นจากภาพคอมพิวเตอร์สแกนก่อนรับการรักษา ตลอดจนภาวะแทรกซ้อนและผลการรักษาจากภาพคอมพิวเตอร์สแกนและการตรวจติดตาม เพื่อประเมินประสิทธิผลของการรักษา*

ผลการศึกษา: *มีผู้ป่วยทั้งหมดจำนวน 14 ราย (ชาย 10 ราย หญิง 4 ราย) อายุเฉลี่ย 50 ปี มีก้อนมะเร็งทุติยภูมิในปอดรวมกันทั้งหมด 27 ก้อน ได้เข้ารับการรักษาด้วยการจี้ด้วยคลื่นวิทยุความถี่สูงในโรงพยาบาลศิริราชในช่วงระหว่างเดือน มกราคม พ.ศ. 2550 ถึง ธันวาคม พ.ศ. 2556 ก้อนมะเร็งแพร่กระจายมาจากมะเร็งตับ 13 ก้อน มะเร็งลำไส้ 9 ก้อน มะเร็งต่อมไทรอยด์ชนิดอินซูลาเซลล์ 3 ก้อน และมะเร็งต่อมลูกหมาก 2 ก้อน ภาวะแทรกซ้อนหลังการรักษาที่พบได้บ่อยที่สุดคือ ภาวะลมในเยื่อหุ้มปอดประมาณร้อยละ 71 (10 ใน 14 ราย) ขนาดเฉลี่ยของก้อนที่ได้รับการรักษาอยู่ระหว่าง 0.5 ถึง 5 เซนติเมตร ภาวะแทรกซ้อนอื่นๆ เช่น การติดเชื้อในบริเวณที่เข็มผ่านผิวหนัง ภาวะปอดแฟบ เลือดคั่งในช่องเยื่อหุ้มปอด ฝีหนองในช่องเยื่อหุ้มปอด และการเกิดรูเชื่อมระหว่างช่องเยื่อหุ้มปอดและหลอดลม พบได้อย่างละ 1 ราย จากภาพคอมพิวเตอร์สแกนหลังการรักษาพบว่า ผู้ป่วยร้อยละ 81 มีการควบคุมโรคได้ดีและไม่เห็นลักษณะของมะเร็งที่เหลืออยู่หรือเกิดขึ้นใหม่ในบริเวณที่รับการรักษา ผู้ป่วยร้อยละ 19 มีลักษณะของมะเร็งที่เหลืออยู่หรือเกิดขึ้นใหม่ในบริเวณที่รับการรักษา*

สรุป: *จากการศึกษาพบว่าการรักษาด้วยคลื่นวิทยุความถี่สูงเป็นวิธีที่ค่อนข้างปลอดภัยและมีผลการรักษาดีสำหรับรักษาผู้ป่วยมะเร็งปอดทุติยภูมิ โดยก้อนขนาดใหญ่และอยู่บริเวณใต้ต่อเยื่อหุ้มปอดจะมีความเสี่ยงต่อการเหลือหรือการกลับเป็นซ้ำของมะเร็งในบริเวณที่ได้รับการรักษามากกว่าก้อนขนาดเล็กและอยู่ภายในเนื้อปอด*