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ORIGINAL RESEARCH

Role of Repeated Radiofrequency Ablation for Patients with Lung Metastases of Head and Neck Adenoid Cystic Carcinoma: Long-term Single-center Study in 16 Patients with 289 Tumors

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Abstract:
Purpose: To retrospectively assess the clinical outcomes of repeated radiofrequency ablation for lung metastases of head and neck adenoid cystic carcinoma.
Material and Methods: Consecutive 16 patients (mean age, 55.3 years) who were treated with radiofrequency ablation for 289 lung metastases were included. A 17-gauge electrode was used in all radiofrequency ablation procedures and placed under computed tomography fluoroscopic guidance. Evaluated were safety, technical success, local tumor control, and survival.
Results: In total, 143 radiofrequency ablation sessions were performed for 289 lung metastases. One session of radiofrequency ablation was not completed due to pleural hemorrhage during the procedure, resulting in a technical success rate of 99.3% (142/143). Major complications (pneumothorax and hemorrhage) occurred in 40 sessions (27.9%, 40/143). During the mean follow-up period of 5.5 ± 3.6 years (range, 0.4-13.4 years), local tumor progression was observed in 16 tumors (5.5%, 16/289) and repeated radiofrequency ablation (93.8%, 15/16) or metastasectomy (6.2%, 1/16) was performed for all locally progressed lung metastases. The local tumor control rates were 97.1% (95% confidence interval, 95.1%-99.2%) and 89.5% (95% confidence interval, 84.0%-95.0%) at 1- and 5-year. Median survival time after initial lung radiofrequency ablation was 9.8 years and 1-, 3-, 5-, and 10-year overall survival rates were 100% (95% confidence interval, 100%), 91.7% (95% confidence interval, 76.0%-100%), 64.3% (95% confidence interval, 35.7%-92.9%), and 35.7% (95% confidence interval, 0%-70.8%), respectively.
Conclusions: Repeated radiofrequency ablation for multiple lung metastases of adenoid cystic carcinoma was feasible and safe and may allow survival with good local control of lung metastases.

Keywords:
lung metastasis, radiofrequency ablation, adenoid cystic carcinoma

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Introduction

Adenoid cystic carcinoma (AdCC) is one of the rare cancers occurring in the head and neck region. It is reported to account for 1% of all head and neck cancers [1] and is characterized by a high rate of systemic metastasis but slow growth [2]. The lung is the most frequently involved organ for distant metastasis, and following that are the bone and liver [3]. However, systemic chemotherapy for lung metastases of AdCC is limited [4, 5], and surgical treatment is effective only in selected cases [6, 7]. Therefore, no standard treatment protocol for lung metastases of this disease has been established. RFA has been used as a local treatment for primary or metastatic lung tumors, mainly in patients who are unsuitable for surgery [8]. The advantages of RFA are that it is minimally invasive and repeatable, and studies of RFA for lung metastases of colorectal cancer and nasopharyngeal cancer have reported good results [9-11]. The aim of this retrospective study was to assess the clinical outcomes of repeated RFA for multiple lung metastases of AdCC.

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Table 1. Patient and Tumor Characteristics.

Patient characteristics	
No. of patients	n = 16
Sex	
Male	6 (37.5)
Female	10 (62.5)
Age (years)	
Mean ± SD	55.3 ± 12.5
<55	8 (50)
≥55	8 (50)
Primary sites	
Salivary gland	12 (75)
Others	4 (25)
Bronchus	1 (6.3)
Nasal cavity	1 (6.3)
External auditory canal	1 (6.3)
Paranasal cavity	1 (6.3)
Treatment of primary tumors	
Surgical resection	14 (87.5)
Proton beam therapy + intra-arterial infusion chemotherapy	1 (6.3)
Particle beam therapy	1 (6.3)
Histopathology of primary tumors	
with solid pattern	6 (37.5)
without solid pattern	10 (62.5)
Local tumor progression of primary site	
Yes	6 (37.5)
No	10 (62.5)
History of previous lung resection	
Yes	6 (37.5)
No	10 (62.5)
History of previous chemotherapy	
Yes	4 (25)
No	12 (75)
Lung mets at the time of primary tumor treatment	
Yes	5 (31.3)
No	11 (68.7)
No. of lung mets at the time of initial ablation	
Mean ± SD	12.7 ± 13.8
5 or less	9 (56.2)
6 or more	7 (43.8)
Mean tumor diameter of all tumors (cm)	
Mean ± SD	1.0 ± 0.6
Range	0.2–3.5
Maximum tumor diameter in each patient (cm)	
Mean ± SD	1.8 ± 1.0
Range	0.5–3.5
No. of the tumors <2 cm	9 (56.2)
No. of the tumors ≥2 cm	7 (43.8)
Extra-lung mets at the time of initial ablation	
Yes	5 (31.3)
Liver	2 (12.5)
Bone	2 (12.5)
Brain	1 (6.3)
No	11 (68.7)

Data are number of patients or tumors, with percentages in parentheses. No, number; SD, standard deviation; and mets, metastasis

Material and Methods

Study design and patients

This retrospective study was approved by the institutional review board (H2021-072), and informed consent was obtained from the patients to perform RFA for lung metastases and for inclusion in this retrospective study. An opt-out opportunity to withdraw consent for research collaboration was also guaranteed.

From October 2004 to December 2023, all patients with lung metastases of AdCC who underwent RFA under CT guidance were included in this retrospective study. The patient demographics and tumor characteristics are listed in **Table 1**. Sixteen patients (6 men, 10 women), with a mean age of 55.3 ± 12.5 years (mean ± standard deviation [SD]; range, 37-78 years) were included. The patients were followed for ≥6 months. One patient (6.3%, 1/16) with a short follow-up of 0.4 years was also included due to the rarity of AdCC. The primary sites of lung metastases were the following; salivary glands in 12 patients (75%, 12/16), trachea, nasal cavity, external auditory canal, and paranasal cavity in one each (6.3%, 1/16). Surgical resection of primary tumors was performed in 14 patients (87.5%, 14/16) before lung RFA. One patient each received particle-beam therapy (6.3%, 1/16) and a combination of proton-beam therapy with intra-arterial infusion chemotherapy (6.3%, 1/16), respectively, before lung RFA. During follow-up, local tumor progression at the primary site was observed in 6 patients, resulting in an additional resection in 3 patients, proton-beam therapy in 2, and systemic chemotherapy in 1 patient.

The total number of lung metastases was 12.7 ± 13.8 tumors (mean ± SD; range, 1-41 tumors) at the time of initial lung RFA. New lung metastases developed during the mean follow-up period of 5.5 ± 3.6 years (mean ± SD; range, 0.4-13.4 years) after initial lung RFA in 15 patients (93.8%, 15/16), and these tumors were also repeatedly treated with lung RFA. In total, 289 lung metastases were treated with RFA.

At the time of initial RFA, 5 patients (31.3%, 5/16 patients) had a history of extra-lung metastasis to the liver (12.5%, 2/16), bone (12.5%, 2/16), and brain (6.3%, 1/16). These tumors were treated as follows: liver metastasectomy and gamma-knife surgery for a brain tumor in 1 patient each before initial lung RFA. Liver RFA and surgical resection of mandibular tumor were performed 2 and 5 months after initial lung RFA, respectively, in 1 patient each. A slow-growing rib metastasis in 1 patient was followed without treatment.

Before initial lung RFA, 6 patients (37.5%, 6/16) had undergone partial resection of the lung for the treatment of lung metastases. Systemic chemotherapy had been performed in 5 patients (31.3%, 5/16); specifically, cisplatin and fluorouracil were administered to 2 patients, tegafur-gimeracil-oteracil potassium to another 2, and cisplatin + navelbine to the remaining patient.

Table 2. Complications.

No. of RF Ablation sessions	n=143
Treatment-related death	0 (0%)
Major complications	40 (27.9%)
Pneumothorax	37 (25.9%)
Pleural hemorrhage	3 (2.1%)
Minor complications	40 (27.9%)
Pneumothorax	38 (26.6%)
Pleural hemorrhage	1 (0.7%)
Mediastinal hemorrhage	1 (0.7%)

Data are numbers of patients or tumors, with percentages in parentheses. No, number; and RF, radiofrequency

Lung RFA

Diagnosis of lung metastasis was based on CT images. Newly detected or enlarged lung nodules were diagnosed as lung metastasis without histopathological confirmation. The decision on the indication for RFA for lung metastases was made in a multidisciplinary discussion among thoracic surgeons, interventional radiologists, medical oncologists, and radiation oncologists. RFA was performed in patients who declined to receive surgical treatment or those who were not surgical candidates. For multiple lung metastases, larger lung lesions with relatively rapid enlargement were selected for sequential RFA. Lung RFA was discontinued under the following conditions: (i) the appearance of a new extra-lung metastasis, which was considered to be a prognostic factor and difficult to treat, or (ii) a rapid increase in the number of new lung metastases beyond the therapeutic pace of RFA (3 lung metastases/month in our clinical practice of RFA).

All thermal ablation procedures were performed by 2 interventional radiologists, each with >10 years of experience. All RFA procedures were performed under conscious sedation conditions. Real-time CT fluoroscopy (X-Vigor, Asterion, or Aquilion, Canon Medical Systems Corporation, Otawara, Japan) was used for image guidance. Lidocaine and fentanyl were used as a local anesthetic and analgesia. In all cases, a 17-gauge internally cooled radiofrequency electrode (Cool-Tip RFA System, Medtronic, Minneapolis, MN, USA) was used, and the RF electrode exposure length was selected according to the sizes of the lung tumors. After connecting the electrode to the generator (Cool-Tip RF Generator, Medtronic, Minneapolis, MN, USA), an impedance-control algorithm was applied to ablate the lung metastasis. Tract ablation was routinely performed when the electrode was removed.

The mean follow-up period of the patients was 5.5 ± 3.6 years (range, 0.4-13.4 years). Usually, chest CT images were obtained within a week after the treatment and then every 3-4 months on an outpatient basis. Two diagnostic radiologists evaluated the obtained images.

Assessment

Evaluated were technical success, complications, change in pulmonary function, local tumor progression (LTP), overall survival (OS), and recurrence-free survival (RFS). Technical success was defined as the puncture of the electrode needle as planned on preoperative CT and covering the lung tumor with ground-glass opacity on CT images obtained immediately after RFA [12]. According to the Society of Interventional Radiology (SIR) grading [13], complications were evaluated on a session basis. Pulmonary function was assessed by percentage of vital capacity to predicted value (%VC) and percentage of forced expiratory volume in 1 second to forced vital capacity (FEV1%). Paired t-test was used to compare the results of the test performed before the initial lung RFA and the last test. The time from initial RFA to last observation or death was defined as OS. The development of tumor lesions at the edge of the ablated zone despite technical success, as evidenced by follow-up CT images, was defined as LTP, and assessed on a tumor basis. The period from lung RFA to the development of LTP, new lung tumor, or extra-lung tumor was defined as RFS. OS and progression-free survival (PFS) were assessed on a patient basis.

Statistical analysis

Continuous variables were expressed as means ± SD and categorical variables as percentages. To assess LTP, OS, and RFS rates, the Kaplan-Meier method was applied. Univariate logistic regression analysis was applied to assess the potential factors that affected the LTP, OS, and RFS rates. Multivariate analysis was not performed due to the small sample size. All statistical analyses were performed with GraphPad Prism 10 (GraphPad Software Inc., Boston, MA, USA). Differences with values of $p < 0.05$ were regarded as significant.

Results

Technical success

In total, 143 sessions of RFA (8.9 sessions per patient, 143/16) were performed for 289 lung tumors with a mean tumor diameter of 1.0 ± 0.6 cm (range, 0.2-3.5 cm). One session of ablation was not completed according to the planned protocol due to pleural hemorrhage during the insertion of an RF electrode, resulting in a technical success rate of 99.3% (142/143).

Complications

There were no treatment-related deaths (**Table 2**). According to SIR grading, the most frequent major complication was pneumothorax requiring chest tube placement (25.9%, 37/143) followed by pleural hemorrhage (2.1%, 3/143). Minor complications were asymptomatic pneumothorax (26.6%, 38/143), pulmonary hemorrhage (0.7%, 1/143), and mediastinal hemorrhage (0.7%, 1/143).

Change in pulmonary function

Pulmonary function test results were available for 11 patients (68.8%, 11/16) with data obtained before the initial

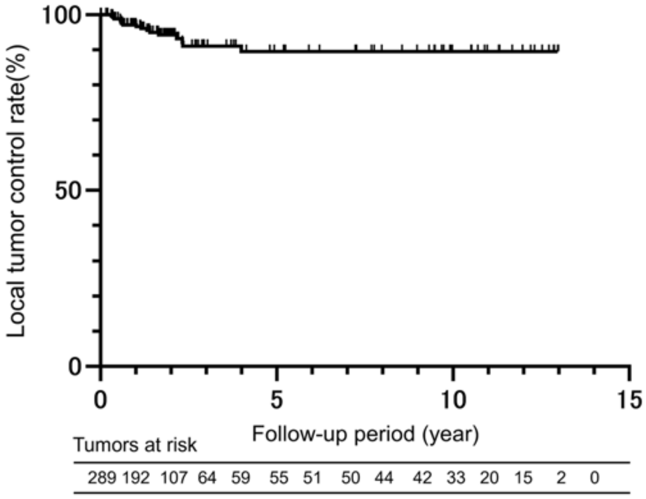

Figure 1. Kaplan–Meier curve of local tumor control rates after radiofrequency (RF) ablation for lung metastasis. Local tumor control rates at 1-, 3-, 5-, and 10-year after lung RFA were, respectively, 97.1% (95% CI, 95.1%-99.2%), 91.0% (95% CI, 86.3%-95.8%), 89.5% (95% CI, 84.0%-95.0%), and 89.5% (95% CI, 84.0%-95.0%).

lung RFA and the latest test (mean interval period; 3.0 years, range, 0.3-9.6 years). In 8 of 11 patients (72.7%, 8/11), Pulmonary function test after RFA was not performed after the most recent lung ablation because of preserved performance status, no symptoms of suspected respiratory dysfunction, and limited availability of pulmonary function testing due to the COVID-19 pandemic.

In the 11 patients, the mean reduction in %VC and FEV 1% was 7.7 (range, −35.4 to 7.6, p = 0.045) and 4.9 (range, −11.0 to 1.7, p = 0.004) after 1-46 sessions of RFA (mean, 15.1 sessions/patient), respectively. Four of these patients (36.4%, 4/11) had undergone metastasectomy during this period. In 7 patients who had not received metastasectomy (43.8%, 7/16), the mean reduction in %VC and FEV1% were 3.3 (range, −10.5 to 7.6, p = 0.2) and 5.4 (range, −11.0 to 1.7, p = 0.02) after 1-36 sessions of RFA (mean, 13.4 sessions/patient), respectively. No patient developed symptomatic respiratory dysfunction during the follow-up period.

Tumor progression and survival

During the mean follow-up period of 5.5 ± 3.6 years (range, 0.4-13.4 years), LTP was observed in 16 tumors (5.5%, 16/289) and repeated RFA (93.8%, 15/16) or metastasectomy (6.2%, 1/16) was performed for all locally progressed lung metastases. The local tumor control rates at 1-, 3-, 5-, and 10-year after RFA were, respectively, 97.1% (95% CI, 95.1%-99.2%), 91.0% (95% CI, 86.3%-95.8%), 89.5% (95% CI, 84.0%-95.0%), and 89.5% (95% CI, 84.0%-95.0%) (**Fig. 1**).

During follow-up, 1 female patient (6.3%, 1/16) developed bilateral breast cancer after she received 26 sessions of lung RFA for 46 tumors. Other patients (93.8%, 15/16) did not develop secondary cancers. Nine of 16 patients (56.3%, 9/16) stopped sequential lung RFA because of tumor progression beyond our treatment indication criteria (**Fig. 2**). Four patients (25%, 4/16) underwent pulmonary metastasectomy for tumors which were unsuitable for RFA after initial lung RFA as a hybrid therapy. Of 6 patients (37.5%, 6/16) who died during follow-up, all causes of death were tumor progression (100%, 6/6). The OS rates at 1-, 3-, 5-, and 10-years after initial RFA were, respectively, 100% (95% CI, 100%), 91.7% (95% CI, 76.0%-100%), 64.3% (95% CI, 35.7%-92.9%), and 35.7% (95% CI, 0.6%-70.8%) with a median survival time of 9.8 years (**Fig. 3**). The RFS rates at 1-, 3-, 5-, and 10-year after initial RFA were, respectively, 56.3% (95% CI, 31.9%-80.6%), 8.0% (95% CI, 0%-23.0%), and 8.0% (95% CI, 0%-23.0%), 0% (95% CI, 0%) (**Fig. 4**).

The presence of lung metastases at the time of primary tumor treatment was detected as the only significant prognostic factor for worse OS (p = 0.0002) in univariate analysis of patients and tumor demographics (**Fig. 5** and **Table 3**). No factors affecting LTP or PFS were found.

Discussion

The results of this retrospective analysis showed RFA for lung metastases was a feasible and safe treatment option which provided a promising local tumor control. In AdCC, distant metastases are very common, occurring in >50% of cases, and lungs are the most commonly metastasized organ, present in 75% of cases of metastasis [14]. Patients with lung metastases are often treated with chemotherapy or surgery [2]. However, chemotherapy is less effective, and the treatment protocols have not been established [2, 14-16]. Although the effect of pulmonary metastasectomy on OS in patients with head and neck AdCC is uncertain [7, 16, 17], some studies have suggested that pulmonary metastasectomy should be considered if complete resection is possible [6, 18].

The recently reported survival rates of 109 AdCC patients who underwent lung metastasectomy were 66.8% and 40.5% at 5- and 10-year, respectively, which are comparable to the results of our study (64.3% at 5 years and 35.7% at 10 years) (**Fig. 3**) [6]. Iguchi et al. [2] reported the clinical outcomes of RFA for 45 metastatic lung tumors from AdCC in 9 patients. Although the reported OS of 83.3% at 5 years was higher than our result, factors affected survival were not detected. In our study, lung metastasis at the time of primary tumor treatment was a significant factor for a worse prognosis. Among patients without lung metastases at the time of primary tumor treatment, the survival rates at 5- and 10-years after initial RFA were as high as 85.7% and 47.6%, respectively (**Fig. 5**). Given that patients with a higher number of lung metastases were included in our study, local treatment with repeated RFA can be a useful treatment option for AdCC patients who did not have lung metastases at the time of treatment of primary tumor. Patients with a limited tumor burden of oligometastases can benefit from local treatment [19, 20], however, the number of lung metastases (5 or less/6 or more) was not a signifi-

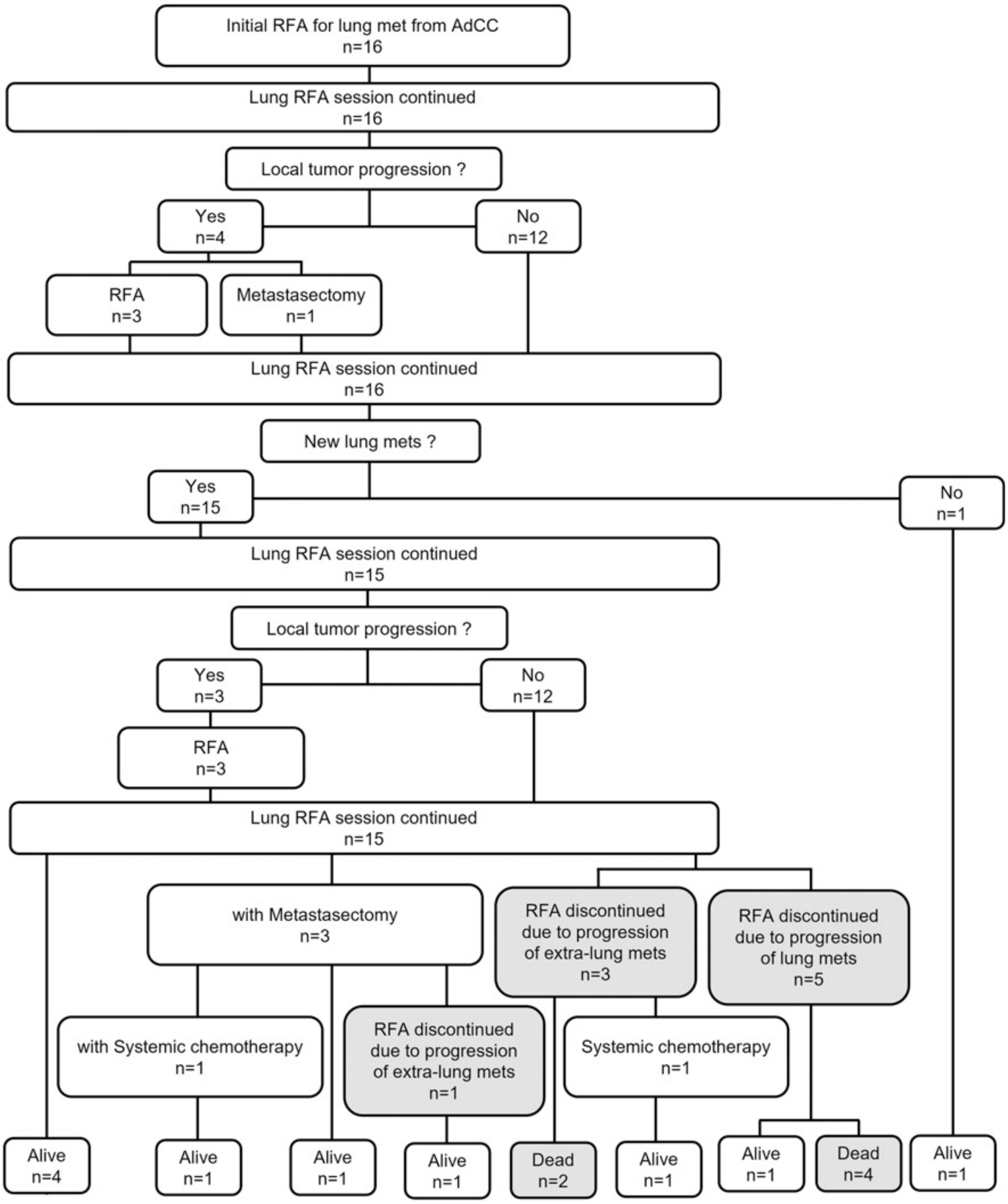

Figure 2. Flowchart of the clinical course of included patients with lung metastases from adenoid cystic carcinoma.
met; metastasis, AdCC; adenoid cystic carcinoma

cant factor for OS in this study. This result may, in part, be inconsistent with the concept of oligometastases. This might be because repeated lung RFA was effective even in patients beyond-oligometastases because of the slow growth of AdCC. Presence of the solid tumor component reportedly is a poor prognostic factor [21, 22]. However, no significant difference was found in OS between solid and non-solid types in our study. For the local treatment of multiple lung metastases, RFA was selected after multidisciplinary discussion because of its advantages over pulmonary metastasectomy in being less invasive and repeatable. Even for patients in whom local treatment for all lung metastases appeared to be difficult due to the number or location of lung tumors, treatment with sequential lung RFA was applied. In such cases, larger lung lesions or lesions with relatively rapid enlargement were preferentially selected for sequential RFA. Such sequential ablation strategy was previously reported in slow-growing lung metastases of parathyroid carcinoma [23]. Lung metastases of AdCC are also slow-growing and repeated lung RFA can be an option for local treatment. However, we experienced lung tumor progression resulting in discontinuation of additional ablation sessions in 5 patients (31.3%, 5/16) (**Fig. 2**). It is uncertain that such tumor progression was due to unfavorable immune-related systemic effect after thermal ablation [24-26] or natural history of AdCC, further investigation for immune response in a pa-

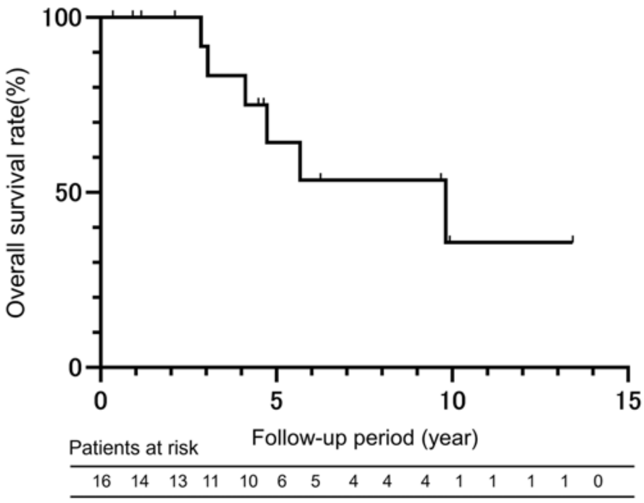

Figure 3. Kaplan–Meier curve of overall survival rates after initial radiofrequency (RF) ablation for lung metastasis. The median and mean survival time were 9.8 and 5.5 years. Overall survival rates at 1-, 3-, 5-, and 10-year after initial lung RFA were, respectively, 100% (95% CI, 100%), 91.7% (95% CI, 76.0%-100%), 64.3% (95% CI, 35.7%-92.9%), and 35.7% (95% CI, 0%-70.8%).

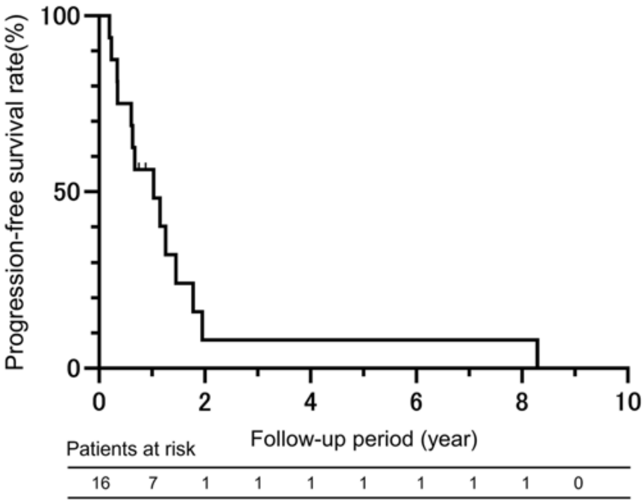

Figure 4. Kaplan–Meier curve of progression-free survival (PFS) rates after initial RFA for lung metastasis. The PFS rates at 1-, 3-, 5-, and 10-year after initial lung RFA were, respectively, 56.3% (95% CI, 31.9%-80.6%), 8.0% (95% CI, 0%-23.0%), and 8.0% (95% CI, 0%-23.0%), 0% (95% CI, 0%).

tient who was treated with repeated ablation during long-term is required.

Though the decrease in %VC and FEV1% were statistically significant after 15.1 sessions of lung RFA, no patient developed respiratory symptoms after multiple RFA sessions in this study. Tada et al. [27] assessed the change in pulmonary function after lung RFA in short-term follow-up and severe pleuritis and large ablation volume were significant factors related to decreased pulmonary function. In our study, no patient developed severe pleuritis and the decrease in %VC was not statistically significant in 7 patients who were treated without metastasectomy. Multiple lung RFA

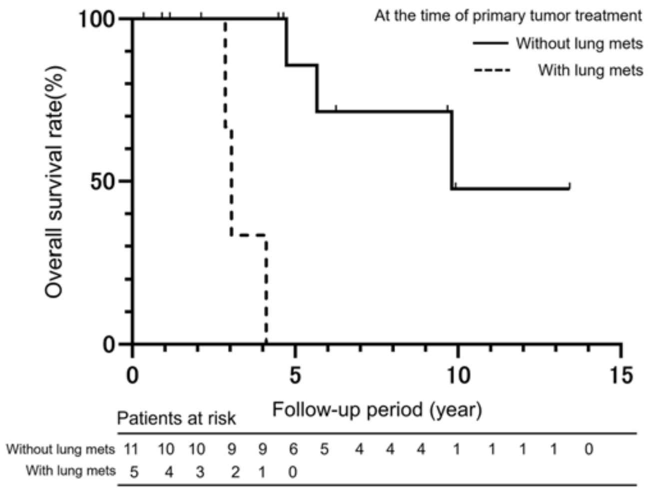

Figure 5. Kaplan–Meier curves of overall survival (OS) rates based on the presence of lung metastasis at the time of primary tumor treatment. The OS rates at 1-, 3-, 5-, and 10-year after initial lung RFA were, respectively, 100% (95% CI, 100%), 100% (95% CI, 100%), 85.7% (95% CI, 59.8%-100%), and 47.6% (95% CI, 3.5%-91.8%) in patients who did not have lung metastases at the time of treatment of primary tumor. Conversely, the OS rates at 1-, 3-, and 5-years were 100% (95% CI, 100%), 66.6% (95% CI, 13.3%-100%), and 0% in patients with lung metastases at the time of treatment of primary tumor (p = 0.0002).

over a long period in patients with multiple lung tumors can be feasible while maintaining pulmonary function.

In 1 female patient, bilateral breast cancer was found during follow-up. The risk of breast cancer reportedly increased after chest radiotherapy and frequent X-rays during childhood [28-30]. Doody et al. [31] and Koo et al. [32] reported that radiation exposure before age 40 was a risk factor for breast cancer. In our patient, lung RFA started at age 37 years, and after 26 sessions of lung RFA, bilateral breast cancer developed at age 47, so a relationship to repeated radiation exposure during RFA could not be ruled out. The cumulative total radiation exposure dose of included patients during lung RFA should be calculated. However, we moved to a new hospital in 2011, and DICOM Radiation Dose Structured Reports for CT scans performed in the previous hospital were not available and it was not possible to calculate the radiation exposure. Care must be taken to avoid unnecessary radiation exposure by carefully considering treatment indications and refining treatment techniques. This study had several limitations that should be considered. This was a single-center retrospective study, the results were not compared to those of other local therapeutic techniques of pulmonary metastasectomy or radiotherapy, pathological evaluation of lung tumors was lacking, radiation exposure could not be assessed, lung function was inadequately assessed, and our study cohort was small. However, the results of this study for a rare disease of AdCC may help to decide the indication of lung RFA in future AdCC patients with lung metastases.

In conclusion, although it was not fully evaluated that RFA for multiple lung metastases contributed to prolonged

Table 3. Univariate Analysis of Variables Relevant to Overall Survival.

Variable	n (%)	Hazard ratio (95% CI)	MST (year)	P value
Sex				
Male	6 (37.5%)	1.23 (0.50–3.42)	5.7	0.64
Female	10 (62.5%)		9.8	
Age (years)				
<55	8 (50%)		9.8	0.95
≥55	8 (50%)	1.02 (0.44–2.43)	5.7	
Primary tumor sites				
Salivary glands	12 (75%)		9.8	0.89
Others	4 (25%)	1.06 (0.39–2.62)	5.7	
Histopathology of primary tumors				
with Solid pattern	6 (37.5%)	1.65 (0.72–4.45)	5.7	0.24
without Solid pattern	10 (62.5%)		—	
Local tumor progression of primary site				
Yes	6 (37.5%)		—	0.82
No	10 (62.5%)	1.14 (0.43–5.08)	7.7	
History of previous lung resection				
Yes	6 (37.5%)		7.7	0.98
No	10 (62.5%)	1.01 (0.41–2.80)	9.8	
History of previous chemotherapy				
Yes	5 (31.3%)		5.2	0.96
No	11 (68.7%)	1.02 (0.45–2.74)	9.8	
Lung mets at the time of primary tumor treatment				
Yes	5 (31.3%)	327.1 (16.3–6584.0)	3.0	0.0002
No	11 (68.7%)		9.8	
No. of lung mets at the time of initial ablation				
5 or less	9 (56.2%)		9.8	0.40
6 or more	7 (43.8%)	1.05 (0.39–2.39)	5.7	
Maximum tumor size (cm)				
<2	9 (56.2%)		9.9	0.17
≥2	7 (43.8%)	1.75 (0.78–4.74)	4.7	
Extra-lung mets at the time of initial ablation				
Yes	5 (31.3%)	2.1 (0.76–5.21)	4.3	0.08
No	11 (68.7%)		9.8	
Total number of patients	16			

Data are numbers of patients. MST, median survival time; CI, confidence interval; mets, metastasis; and No., number

survival in AdCC patients due to the small study cohort, repeated RFA for multiple lung metastases of AdCC was found to be feasible, safe, and may allow patients to survive with good local control of lung metastases.

Part of this study was presented in SIO2023 and JSIR 2023. This manuscript has not been published elsewhere and is not under consideration by another journal.

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Author Contribution: All authors contributed to the study conception and design. Material preparation and data collection were performed by Yuki Omori, Masashi Fujimori, Takashi Yamanaka, Ken Nakajima, and Naritaka Matsushita. Data analysis was performed by Yuki Omori, Masashi Fujimori, and Toru Ogura. The first draft of the manuscript was written by Yuki Omori, and all authors commented on previous versions of the manuscript. All authors read and approved the final manuscript.
Disclaimer: Masashi Fujimori is one of the Editorial Board members of Interventional Radiology. This author was not involved in the peer-review or decision-making process for this paper.
Clinical Registration Number: This retrospective study was approved by Institutional Review Board of Mie University Hospital (H2021-072). Opt-out consents were obtained for retrospective use of data.

References

1. Spiro RH, Huvos AG, Strong EW. Adenoid cystic carcinoma of salivary origin. A clinicopathologic study of 242 cases. Am J Surg. 1974; 128: 512-520.
2. Iguchi T, Hiraki T, Gobara H, et al. Radiofrequency ablation of

lung metastases from adenoid cystic carcinoma of the head and neck: retrospective evaluation of nine patients. J Vasc Interv Radiol. 2015; 26: 703-708.
3. Chang CF, Hsieh MY, Chen MK, Chou MC. Adenoid cystic carcinoma of head and neck: a retrospective clinical analysis of a single institution. Auris Nasus Larynx. 2018; 45: 831-837.
4. Dodd RL, Slevin NJ. Salivary gland adenoid cystic carcinoma: a review of chemotherapy and molecular therapies. Oral Oncol. 2006; 42: 759-769.
5. Imamura Y, Kiyota N, Tahara M, et al. Systemic therapy for salivary gland malignancy: current status and future perspectives. Jpn J Clin Oncol. 2022; 52: 293-302.
6. Girelli L, Locati L, Galeone C, et al. Lung metastasectomy in adenoid cystic cancer: is it worth it? Oral Oncol. 2017; 65: 114-118.
7. Bobbio A, Copelli C, Ampollini L, et al. Lung metastasis resection of adenoid cystic carcinoma of salivary glands. Eur J Cardiothorac Surg. 2008; 33: 790-793.
8. Okuma T, Matsuoka T, Yamamoto A, et al. Determinants of local progression after computed tomography-guided percutaneous radiofrequency ablation for unresectable lung tumors: 9-year experience in a single institution. Cardiovasc Interv Radiol. 2010; 33: 787-793.
9. Petre EN, Jia X, Thornton RH, et al. Treatment of pulmonary colorectal metastases by radiofrequency ablation. Clin Colorectal Cancer. 2013; 12: 37-44.
10. Yamakado K, Inoue Y, Takao M, et al. Long-term results of radiofrequency ablation in colorectal lung metastases: single center experience. Oncol Rep. 2009; 22: 885-891.
11. Pan CC, Wu PH, Yu JR, et al. Comparative survival analysis in patients with pulmonary metastases from nasopharyngeal carcinoma treated with radiofrequency ablation. Eur J Radiol. 2012; 81: e473-e477.
12. Kodama H, Yamakado K, Taniguchi J, et al. Advances in percutaneous lung tumor therapy: 2019 update. Chin Clin Oncol. 2019; 8: 64.
13. Sacks D, McClenny TE, Cardella JF, Lewis CA. Society of Interventional Radiology clinical practice guidelines. J Vasc Interv Radiol. 2003; 14: S199-202.
14. Cavalieri S, Mariani L, Vander Poorten V, et al. Prognostic nomogram in patients with metastatic adenoid cystic carcinoma of the salivary glands. Eur J Cancer. 2020; 136: 35-42.
15. Argiris A, Ghebremichael M, Burtness B, Axelrod RS, Deconti RC, Forastiere AA. A phase 2 trial of bortezomib followed by the addition of doxorubicin at progression in patients with recurrent or metastatic adenoid cystic carcinoma of the head and neck: a trial of the Eastern Cooperative Oncology Group (E1303). Cancer. 2011; 117: 3374-3382.
16. van Herpen CM, Locati LD, Buter J, et al. Phase II study on gemcitabine in recurrent and/or metastatic adenoid cystic carcinoma of the head and neck (EORTC 24982). Eur J Cancer. 2008; 44: 2542-2545.
17. Liu D, Labow DM, Dang N, et al. Pulmonary metastasectomy for head and neck cancers. Ann Surg Oncol. 1999; 6: 572-578.
18. Locati LD, Guzzo M, Bossi P, et al. Lung metastasectomy in adenoid cystic carcinoma (ACC) of salivary gland. Oral Oncol. 2005; 41: 890-894.
19. Pfannschmidt J, Dienemann H. Surgical treatment of oligometastatic non-small cell lung cancer. Lung Cancer. 2010; 69: 251-258.
20. Yano T, Okamoto T, Haro A, et al. Local treatment of oligometastatic recurrence in patients with resected non-small cell lung cancer. Lung Cancer. 2013; 82: 431-435.
21. Ishida E, Ogawa T, Rokugo M, et al. Management of adenoid cystic carcinoma of the head and neck: a single-institute study with over 25-year follow-up. Head Face Med. 2020; 16: 14.
22. Morita N, Murase T, Ueda K, et al. Pathological evaluation of tumor grade for salivary adenoid cystic carcinoma: a proposal of an objective grading system. Cancer Sci. 2021; 112: 1184-1195.
23. Tochio M, Takaki H, Yamakado K, et al. A case report of 20 lung radiofrequency ablation sessions for 50 lung metastases from parathyroid carcinoma causing hyperparathyroidism. Cardiovasc Interv Radiol. 2010; 33: 657-659.
24. Erinjeri JP, Thomas CT, Samoilia A, et al. Image-guided thermal ablation of tumors increases the plasma level of interleukin-6 and interleukin-10. J Vasc Interv Radiol. 2013; 24: 1105-1112.
25. Iwahashi S, Shimada M, Utsunomiya T, et al. Epithelial-mesenchymal transition related genes are linked to aggressive local recurrence of hepatocellular carcinoma after radiofrequency ablation. Cancer Lett. 2016; 375: 47-50.
26. Takaki H, Cornelis F, Kako Y, Kobayashi K, Kamikonya N, Yamakado K. Thermal ablation and immunomodulation: from preclinical experiments to clinical trials. Diagn Interventional Imaging. 2017; 98: 651-659.
27. Tada A, Hiraki T, Iguchi T, et al. Influence of radiofrequency ablation of lung cancer on pulmonary function. Cardiovasc Intervent Radiol. 2012; 3: 860-867.
28. Schellong G, Riepenhausen M, Ehlert K, et al. Breast cancer in young women after treatment for Hodgkin's disease during childhood or adolescence—an observational study with up to 33-year follow-up. Dtsch Ärztebl Int. 2014; 111: 3-9.
29. Nemoto M, Chida K. Reducing the breast cancer risk and radiation dose of radiography for scoliosis in children: a phantom study. Diagnostics (Basel). 2020; 10: 753.
30. Ronckers CM, Doody MM, Lonstein JE, Stovall M, Land CE. Multiple diagnostic X-rays for spine deformities and risk of breast cancer. Cancer Epidemiol Biomarkers Prev. 2008; 17: 605-613.
31. Doody M, Lonstein J, Stovall M, Hacker DG, Luckyanov N, Land CE. Breast cancer mortality after diagnostic radiography findings from the U.S. scoliosis cohort study. Spine. 2000; 25: 2052-2063.
32. Koo E, Henderson MA, Dwyer M, Skandarajah AR. Management and prevention of breast cancer after radiation to the chest for childhood, adolescent, and young adulthood malignancy. Ann Surg Oncol. 2015; 22: S545-S551.