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# Repeat thermal ablation for local progression of lung tumours: how safe and efficacious is it?

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## Abstract

**Aim:** To retrospectively evaluate the safety and efficacy of repeat thermal ablation for local progression of lung tumours after prior ablation(s).

**Methods:** From December 2009 to March 2017, 13 patients underwent repeat ablation [11 repeat microwave ablations and 2 repeat radiofrequency ablations] of a lung tumour [9 non-small cell lung carcinomas, 3 metastatic colorectal adenocarcinomas, 1 metastatic pelvic sarcoma] for local progression after prior ablation(s). Safety of the procedure was assessed by presence or absence of adverse events. Efficacy of the procedure was assessed by local tumour response to ablation and survival time.

**Results:** Repeat ablation procedures were safe, without major adverse events. Median length of hospital stay was 2 days (interquartile range 1-2). Pneumothorax was the most common complication [5 (38%) of 13 repeat ablation procedures]. There was one death within 30 days of ablation, but the cause of death and its relation to the procedure were unknown. Of the 12 patients with imaging follow-up [median follow-up 26 months (range 3-62)], 10 (83%) had complete ablation and 2 (17%) had local progression. Of all 13 patients, 8 (62%) were alive and 5 (38%) had died with a median overall survival of 43 months (95% confidence interval 36-49 months).

**Conclusion:** Repeat ablation in locally progressing tumours after prior ablation attempt(s) is a safe therapeutic option and often achieves local tumour control.

**Keywords:** Local progression, lung tumours, microwave ablation, radiofrequency ablation, repeat ablation



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## INTRODUCTION

CT-guided thermal ablation has developed in the last 20 years as a minimally invasive management option for pulmonary malignancies, both primary and secondary, in patients who are non-surgical candidates<sup>[1]</sup>. Radiofrequency ablation (RFA), an electric current-based heating technique, has been the most evaluated method<sup>[2]</sup>. Microwave ablation (MWA), which uses an electromagnetic field around the ablation device to create heat, is a more updated technique with theoretical advantages in terms of lesser susceptibility to heat-sink effect, larger ablations, more uniform ablation zones, and shorter procedural times<sup>[2,3]</sup>. Ablation failure and subsequent local tumour progression remain an issue for both methods, with tumour diameter greater than 3 cm, proximity to a large vessel and insufficient ablative margin being risk factors for failure<sup>[2,4]</sup>. There are limited data on the role of repeat ablation for local progression of lung tumours after prior ablation, and with most data on repeat RFA<sup>[5-7]</sup>. This retrospective cross-sectional study aimed to evaluate the safety and efficacy of repeat MWA and RFA, in locally progressing lung tumours after prior ablation(s) at a large tertiary hospital.

## METHODS

### Patients

Ethics approval for this study was obtained from the Hospital Institutional Review Board (HREC/14/QRBW/553). Patients were identified using the radiology thermal ablation database at our large tertiary hospital. Data were collected retrospectively through systematic review of patient charts and imaging. Inclusion criteria were consecutive patients who underwent repeat percutaneous CT-guided thermal ablation of a lung tumour for local progression after prior ablation(s) between December 2009 and March 2017. There were no exclusion criteria for this study. Repeat ablation was defined as the most recent ablation procedure, after prior ablation(s). All lesions were referred for ablation if patients are medically inoperable or refuse surgery. Patients were informed of the risks and benefits of ablation, and all provided written informed consent for the procedure.

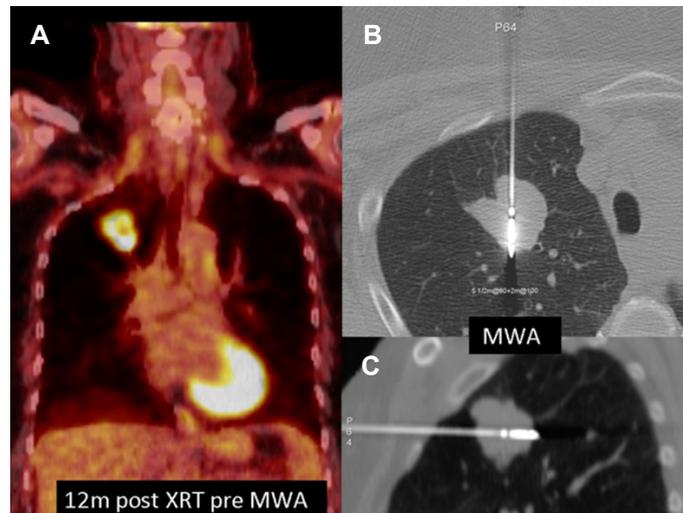
### Ablation procedure and imaging follow-up

Ablations were performed percutaneously under CT guidance (Philips Brilliance 64, Eindhoven, The Netherlands, replaced in 2015 by Aquilion ONE, Toshiba Medical Systems, Otawara, Tochigi, Japan). Both RFA and MWA modalities were used (with MWA having replaced RFA at our institution by mid-2010). All ablations were performed by the same interventional radiologist who had more than 15 years' experience in image-guided ablation. No prophylactic antibiotic treatment was administered. The ablation applicator was inserted under sterile conditions under CT guidance, with analgesia and sedation administered by the anaesthetic team. Parameters such as the type of applicator, number of overlapping ablations, ablation duration, and amount of energy delivered were based on individual tumour size, location and tumour characteristics. Patients received a chest X-ray 3 h post-procedure to assess for post-procedural complications, and in all MWA cases, a limited non-contrast CT scan of the ablated site was performed 24 h post-procedure. Technically successful ablation was defined as completed planned ablation cycle(s) and circumferential perilesional ground-glass opacity. Patients were requested to have serial repeat CT scanning at 3, 6 and 12 months post-ablation and 6 monthly scans thereafter to evaluate treatment outcome. An FDG-PET scan was also requested at 6 months post-ablation.

### Outcomes

Safety of the procedure was assessed by presence or absence of adverse events. Adverse events were recorded and classified in accordance with the Common Terminology Criteria for Adverse Events version 4.03<sup>[8]</sup>.

Efficacy of the procedure was assessed by local tumour response to ablation and survival time. For MWA, the limited CT scan of the ablated site 24 h post-ablation served as the baseline scan that all subsequent follow-up scans were compared against; for RFA, the immediate post-ablation scan was used. Local progres-



**Figure 1.** 57-year-old female with RUL SCC. A: Coronal FDG-PET scan 12 months post definitive radiotherapy (58 Gy) RUL T2N0 SCC; B, C: microwave antenna (Acculis standard pMTA) centrally within the tumour; a total of 7 min 30 s ablation time-5 min 30 s at 80 W followed by 2 min at 100 W. RUL: right upper lobe; SCC: squamous cell carcinoma

sion after initial ablation was defined as an increase in the size (maximum axial diameter) of the ablation zone on CT. Stability or decrease in size of the ablation zone on CT was considered complete ablation<sup>[9]</sup>. Patients were followed up until 30 Jun 2017. Patients were either alive, evidenced by a documented visit to an outpatient clinic, general practitioner or scan appointment after this date, or deceased, as recorded on the state health database. Follow-up periods were calculated from date of repeat ablation.

### Statistical methods

The characteristics of patients and treatment outcomes were summarised using frequencies and percent for categorical variables and mean [standard deviation (SD)] or median [interquartile range (IQR) and range] for continuous variables. Kaplan-Meier survival estimates were produced for overall survival. STATA 15<sup>[10]</sup> was used for analyses.

## RESULTS

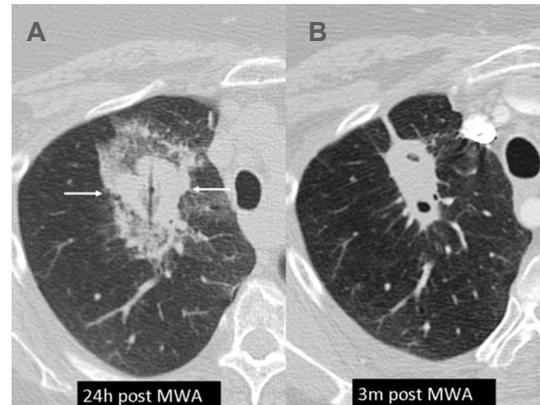
### Patient and tumour characteristics

From December 2009 to March 2017, 13 patients (6 male, 7 female) underwent repeat ablation of a lung tumour due to local progression after prior ablation(s) [Figures 1-5]. All prior ablations had been technically successful. Mean age at repeat ablation was 72 years (SD 11, range 53-88) [Table 1].

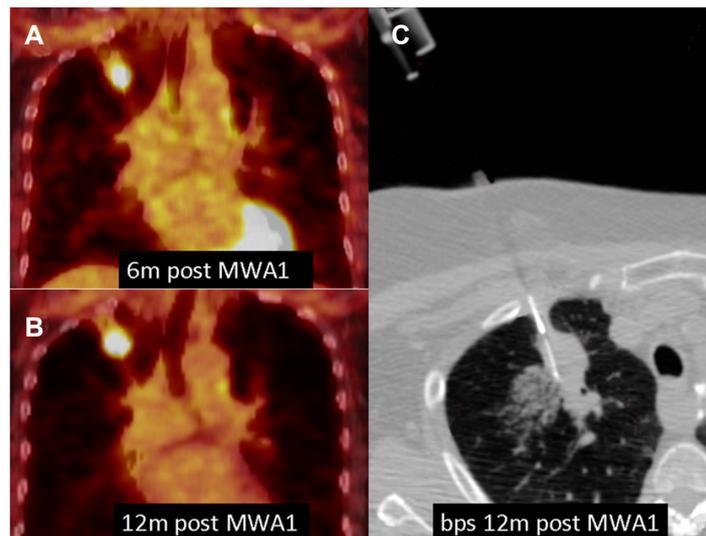
The ablated lung tumours consisted of: non-small cell lung carcinoma (NSCLC) (8 stage 1 NSCLCs, and 1 multifocal bronchioloalveolar carcinoma with bilateral lung involvement), metastatic colorectal adenocarcinoma (3) and metastatic pelvic sarcoma (1). Four of the NSCLC lesions had locally progressed post-radiotherapy and were subsequently referred for ablation.

### Thermal ablation characteristics

Eleven of the 13 patients had repeat MWA; 7 patients after 1 prior MWA procedure, 2 patients after 2 prior MWA procedures, and 2 patients after 1 prior RFA treatment. The remaining 2 patients had repeat RFA after 1 prior RFA treatment. Nine of the 11 repeat MWAs were performed with the Acculis Microwave Tissue Ablation system (Angiodynamics, Latham, New York, USA), which operates at 2.45 GHz with a maximum power output of 140 watts; a standard antenna with a 16 mm active tip was used in these 9 cases. The remaining 2 repeat MWAs were performed with the HS Amica microwave system (HS Amica, HS Hospital



**Figure 2.** 57-year-old female with right upper lobe squamous cell carcinoma. Axial CT scan lung windows. A: 24 h post microwave ablation showing surrounding GGO, most narrow GGO zone medially and laterally (arrows); B: 3 months post microwave ablation showing satisfactory shrinking of ablation zone, small central cavities. GGO: ground-glass opacity

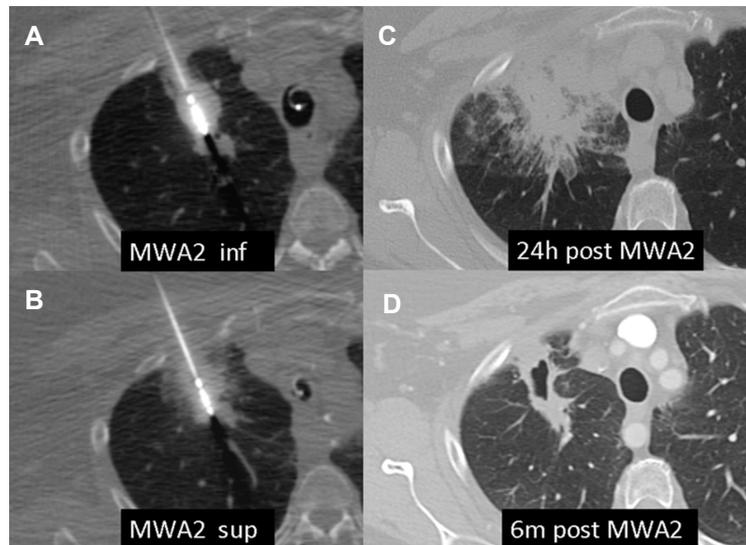


**Figure 3.** 57-year-old female with right upper lobe SCC. A, B: Coronal FDG-PET/CT scans 6 months and 12 months post microwave ablation showing residual FDG avidity increasing; C: CT guided core biopsy demonstrated local recurrence of SCC. CT guided core biopsy demonstrated local recurrence of SCC. SCC: squamous cell carcinoma

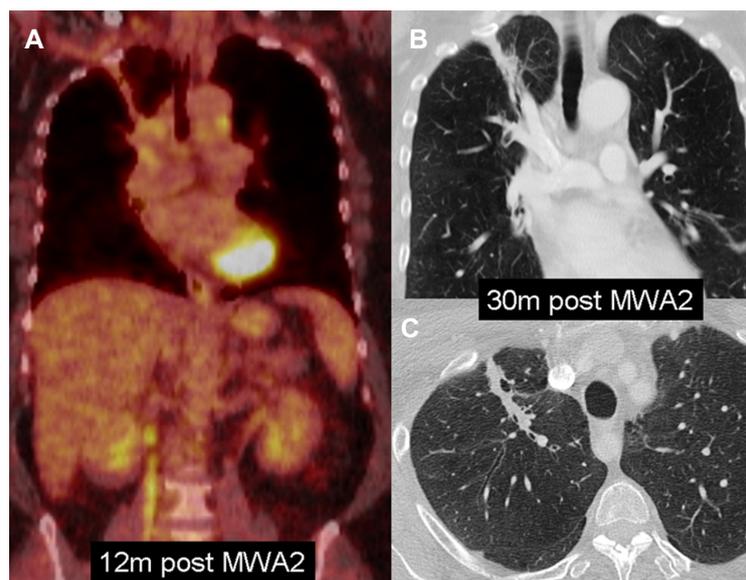
Service, Rome, Italy), which operates at 2.45 GHz with a maximum power output of 140 watts; a 16 gauge 15 cm probe was used in both cases. Of the 2 patients treated with repeat RFA, the Cool-tip internally cooled electrode system (Cool-tip, Valleylab, Boulder, Colorado, USA) with a 3 cm active tip was used for one patient, and the Rita Starbust XL Electrosurgical device (Rita Medical Systems, Mountain View, California, USA, now Angiodynamics) was used for the other patient.

### Procedure tolerability and complications

Repeat ablation procedures were generally safe, without major adverse events [Table 2]. Median length of hospital stay was 2 days (IQR 1-2, range 1-7) [Table 2]. All but 1 (8%) of the repeat ablation procedures were technically successful. One procedure was complicated by intraprocedural pneumothorax, which enlarged during the procedure, prompting a request from the anaesthetic team to abort the procedure given the patient's comorbidities of chronic obstructive pulmonary disease on home oxygen, obstructive sleep apnoea and morbid obesity. The pneumothorax was aspirated twice during the procedure, and required chest tube



**Figure 4.** 57-year-old female with right upper lobe squamous cell carcinoma. A, B: Repeat microwave ablation, 2 overlapping ablation cycles; C: axial CT 24 h post re-ablation shows circumferential ground-glass opacity of at least 1 cm; D: axial CT 6 months post re-ablation shows significant shrinking of ablation site with central cavitation



**Figure 5.** 57-year-old female with RUL squamous cell carcinoma. A: Coronal FDG-PET/CT shows no residual FDG uptake at the RUL ablation site 12 months post re-ablation; B, C: coronal and axial CT scan lung windows 30 months post re-ablation shows band-like scarring/atelectasis at site of previous tumour. RUL: right upper lobe

insertion after the procedure, which resolved the pneumothorax. The patient subsequently had an uneventful recovery.

There were no intraprocedural deaths. Five (38%) patients experienced pneumothorax from the procedure, 3 (23%) of whom required chest tube insertion [Table 2]. There was 1 (8%) death within 30 days of the procedure (repeat ablation of metastatic pelvic sarcoma), although the cause of death and relation to the procedure were unknown. The patient had been discharged the day after an uneventful ablation procedure and died at home two days after the procedure of a sudden death during the night<sup>[11]</sup>. The presumed cause

**Table 1. Patient and lung tumour characteristics at repeat ablation**

	Total (n = 13)
Age (years), Mean (SD)	72 (11.0)
Sex	
Female	7 (54)
Male	6 (46)
Tumour type	
Non-small cell lung carcinoma	9 (69)
Colorectal adenocarcinoma	3 (23)
Pelvic sarcoma	1 (8)
Type of prior ablation/s	
MWA	9 (69)
RFA	4 (31)
Number of prior ablation/s	
1	11 (85)
2	2 (15)
Radiotherapy prior to ablations	
No	9 (69)
Yes	4 (31)
Lobe	
LLL	2 (15)
LUL	8 (62)
RLL	1 (8)
RUL	2 (15)
Repeat ablation modality	
MWA	11 (85)
RFA	2 (15)
Diameter (mm) <sup>†</sup> , median (IQR)	28.2 (22.0-40.0)
Number of ablation cycles	
1	1 (8)
2	8 (62)
3	4 (31)
Maximum power used (Watts) (MWA, n = 11)	
60-80	3 (27)
100-120	8 (73)
Total ablation duration (minutes) (MWA, n = 11), median (IQR)	4.5 (4.0-6.0)

<sup>†</sup>longest axial diameter in millimetres, immediately prior to repeat ablation. Data are presented as n (%) for categorical variables and as mean [standard deviation (SD)] or median [interquartile range (IQR)] for continuous variables. MWA: microwave ablation; RFA: radiofrequency ablation; LUL: left upper lobe; LLL: left lower lobe; RUL: right upper lobe; RLL: right lower lobe

of death was pulmonary embolism or myocardial infarction, however autopsy was declined and the cause of death was not definitively determined<sup>[11]</sup>.

### Response to treatment

Only 12 patients had follow-up imaging performed. The 1 patient without follow-up imaging had died 2 days after the procedure. Median length of CT follow-up was 26 months (range 3-62), and median length of FDG-PET follow-up was 6 months (range 0-26). Ten of twelve (83%) patients had complete ablation from their repeat ablation procedure. Two of twelve (17%) had local progression [Table 2], one of whom had the technically unsuccessful repeat ablation procedure. Time to first detection of local progression on imaging for the 2 patients with local progression were 8 and 27 months respectively.

Six of twelve (50%) patients had nodal or distant metastasis on follow-up imaging. Four of these patients had subsequent chemotherapy (the 2 patients in the local progression group, and 2 patients in the complete ablation group). Median time to first detection of metastasis on imaging was 20 months (range 11-36).

### Survival

Of all 13 patients, 8 (62%) were alive [median follow-up 30 months (range 3-91)] and 5 (38%) had died (me-

**Table 2. Repeat ablation treatment outcomes and complications**

	Total (n = 13)
Technically successful	
No	1 (8)
Yes	12 (92)
Complications	
No	7 (54)
Yes	6 (46)
Pneumothorax (CTCAE grade 1)	1
Pneumothorax (CTCAE grade 1) and death within 30 days of procedure (CTCAE grade 5)	1
Pneumothorax (CTCAE grade 2)	2
Pneumothorax (CTCAE grade 2) and subcutaneous emphysema	1
Pleural effusion (CTCAE grade 1)	1
Length of hospital stay (days)	2 (1-2)
Post-ablation diameter (mm) <sup>†</sup>	54.0 (41.0-60.0)
Diameter on latest follow-up (mm) (n = 12)	38.5 (25.3-49.9)
Local tumour response to ablation (n = 12)	
Complete ablation	10 (83)
Local tumour progression	2 (17)
Nodal or distant metastasis on follow-up imaging (n = 12)	
No	6 (50)
Yes	6 (50)
Mortality	
Alive	8 (62)
Deceased	5 (38)

<sup>†</sup>For MWA, maximum axial diameter on 24 h post-ablation CT scan. For RFA, maximum axial diameter on immediate post-ablation CT scan. Data are presented as n (%) for categorical variables and as median [interquartile range (IQR)] for continuous variables. MWA: microwave ablation; RFA: radiofrequency ablation; CTCAE: Common Terminology Criteria for Adverse Events.

dian time to death 37 months (range 2 days-43 months). Median overall survival was 43 months (95% confidence interval 36-49).

In the 9 patients with NSCLC, 5 (56%) were alive [median follow-up 30 months (range 30-91)] and 4 (44%) had died [median time to death 38 months (range 27-43)]; all 4 had metastatic NSCLC at time of death. All were alive at 2 years.

All 3 patients with metastatic colorectal cancer were alive at the last date of follow-up [median follow-up 23 months (range 3-38)].

Local response to ablation and corresponding survival status at follow-up for all patients is summarised in [Table 3](#).

## DISCUSSION

We described the safety and efficacy of repeat ablation in a heterogeneous population of locally progressing lung tumours after prior ablation, including both primary and metastatic lesions. Repeat ablations were safe and well-tolerated, and often achieved local control despite local progression after prior technically successful ablation. Pneumothorax was the most common procedural complication, asymptomatic or manageable with chest tube insertion. Rate of pneumothorax requiring chest tube insertion (23% of procedures) was similar to that of other studies (11%-29%)<sup>[7,12-18]</sup>. Other reported complications of lung ablation include pain, post-ablation syndrome, pleural effusion, subcutaneous emphysema, pneumonia, bronchopleural fistula, pulmonary haemorrhage, haemoptysis, nerve injury and, rarely, death<sup>[7,11-18]</sup>. Our study had one 30-day post-procedural death, but the cause of death and relation to the procedure were unknown. Other studies have estimated the 30-day mortality rate after thermal ablation to be 0%-3%<sup>[12-15,19]</sup>.

**Table 3. Local tumour response to ablation and survival status at follow-up**

Local response	Survival status		Total
	Alive	Dead	
Complete ablation	7	3	10
Local progression	1	1	2
No imaging follow-up	0	1	1
Total	8	5	13

While surgery is the treatment of choice in early stage NSCLC, many patients are not candidates for surgery due to comorbidities<sup>[1]</sup>. Percutaneous thermal ablation is a minimally invasive alternative treatment option with minimal impact on the uninvolved lung parenchyma and overall pulmonary function<sup>[20]</sup>. Our results demonstrate that even after failed initial attempt(s) at ablation, repeat ablation can achieve local control. Only 2 of our patients experienced local progression on follow-up imaging after repeat ablation. Two-year overall survival in our NSCLC patients after repeat ablation was 100%. Yang *et al.*<sup>[7]</sup> recently reported repeat MWA to be a safe and effective treatment for local progression of medically inoperable stage 1 NSCLC after initial MWA, with 21 of 24 (87.5%) patients achieving local control after repeat MWA, and with median overall survival 41.5 months after first MWA, similar to those treated with single MWA and with no local progression (median overall survival 48 months) at their institution. Our results support these findings that repeat thermal ablation is a safe and effective treatment for local progression of stage 1 NSCLC after initial ablation.

Thermal ablation may also be used for local control of secondary lung metastases. The goal in such patients is to improve patient quality of life and prolong survival. In a series of 566 patients with 1037 lung metastases of various primary origin, RFA treatment resulted in a median overall survival of 62 months, and a 4-year local control rate of 44.1%, with patients re-treated with RFA safely up to four times<sup>[9]</sup>. Our small sample of metastatic colorectal cancer patients re-treated with MWA all achieved local control and were alive after a median follow-up time of 23 months. The minimally invasive nature and repeatability of ablation are of utility in local control of lung metastases.

Six out of 12 patients had nodal or distant metastasis on follow-up imaging, with 2 of these patients demonstrating local progression at the ablation site, suggesting systemic disease progression despite local control in the other four patients. We believe offering repeat ablation for local control is still of value, as it is a minimally invasive technique which may improve patient quality of life and prolong survival, without significant increase in morbidity.

In this study, we defined local tumour response to ablation as based on increase, stability or decrease in size of ablation zone on CT<sup>[9]</sup>. FDG-PET scan findings are more difficult to interpret, as local uptake may be due to post-treatment inflammatory changes rather than local tumour progression, and this effect may last up to 12 months after ablation<sup>[21-23]</sup>. Additionally, false positive FDG-PET scans have been reported greater than 12 months after ablation<sup>[23]</sup>. The optimal timing of FDG-PET scan after ablation is controversial and not yet defined<sup>[24]</sup>. FDG-PET is likely a useful adjunct to CT in assessing local response to ablation, as well as for diagnosis of nodal or distant metastasis. However, further research is needed in imaging criteria to determine treatment response to ablation.

This study was limited by small sample size, heterogeneity of tumour size and histology, difference of ablation systems used and retrospective assessment. Additionally, as some patients had to travel long distances for their procedure and were not followed up by the respective teams they had been admitted under for their ablations, follow-up CT and FDG-PET scans were occasionally not performed at the requested time, although local tumour response to ablation was still able to be determined based on the most recent follow-up CT. Furthermore, some patients who had nodal or distant metastasis on follow-up imaging subsequently had chemotherapy, which may have influenced local response to ablation. In the future, larger

studies should evaluate the effect of tumour type, and the use of other treatments such as chemotherapy, on response to repeat ablation.

In conclusion, despite these limitations, our study demonstrates that repeat MWA or RFA in locally progressing tumours after initial ablation attempt(s) may be generally safe, well tolerated, and often achieves local control. These findings should be validated in larger prospective studies.

## DECLARATIONS

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### Authors' contributions

Design, literature research, data acquisition, drafted manuscript: Zhao H, Steinke K

Data analysis: Zhao H, Okano S, Pelecanos A, Steinke K

Substantively revised manuscript: Zhao H, Okano S, Pelecanos A, Steinke K

### Availability of data and materials

Patients were identified using the radiology thermal ablation database at the Royal Brisbane and Women's Hospital. Data were collected retrospectively through systematic review of patient charts and imaging. The de-identified data is available by contacting the corresponding author Associate Professor Karin Steinke.

### Financial support and sponsorship

None.

### Conflicts of interest

All authors declared that there are no conflicts of interest.

### Ethical approval and consent to participate

Ethics approval for this study was obtained from the Royal Brisbane and Women's Hospital Human Research Ethics Committee (HREC/14/QRBW/553). All patients provided written informed consent.

### Consent for publication

All patients provided written, informed consent.

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