

# Radiofrequency Ablation of Cervical Thyroid Cancer Metastases—Experience of Endocrinology Practices in the United States

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## Abstract

**Context:** Radiofrequency ablation (RFA) is used in the United States to treat benign thyroid nodules; however, experience with treating cervical recurrence/persistence of papillary thyroid cancer (PTC) is limited.

**Objective:** To evaluate the efficacy RFA for the treatment of cervical recurrence/persistence of PTC in the United States.

**Methods:** This is a retrospective, multicenter study of 8 patients who underwent RFA of 11 cervical metastatic PTC lesions between July 2020 and December 2021. The volume reduction (VR) of the lesions, thyroglobulin (Tg) levels and complications following RFA were assessed. Energy applied per unit volume (E/V) during RFA was also determined.

**Results:** Nine out of 11 (81.8%) lesions had initial volume under 0.5 mL and showed a complete (n = 8) or near-complete (n = 1) response. The 2 lesions with initial volume over 1.1 mL had a partial response, 1 of which had regrowth. There was a median VR of 100% (range 56.3–100%) after a median follow-up period of 453 days (range 162–570 days), with corresponding decline in Tg levels from a median of 0.7 ng/mL (range 0–15.2 ng/mL) to a median of 0.3 ng/mL (range 0–1.3 ng/mL). All patients with an E/V of at least 4483 J/mL or higher had a complete or near-complete response. There were no complications.

**Conclusion:** RFA performed in an endocrinology practice is an efficacious treatment option for selected patients with cervical metastases of PTC, particularly those who cannot or do not want to undergo further surgery.

**Key Words:** radiofrequency ablation, thyroid cancer, recurrence, persistent disease

**Abbreviations:** E/V, energy applied per unit volume; PTC, papillary thyroid cancer; RFA, radiofrequency ablation; Tg, thyroglobulin; VR, volume reduction.

Well-differentiated thyroid cancer generally has a favorable prognosis; however, depending on risk factors, the incidence of structural recurrence ranges from 1% to 55% [1–3]. More than 90% of recurrences of papillary thyroid cancer (PTC) are in the neck and cervical lymph nodes [3, 4]. The conventional treatment options for metastatic thyroid cancer include surgery and radioiodine therapy. Repeated surgeries in the neck can lead to complications such as fibrosis, hypoparathyroidism, vocal cord paralysis, and alteration of normal tissue architecture [5, 6].

In cases of recurrent thyroid cancer in the neck where the patient is not a surgical candidate, the current American Thyroid Association (ATA) guidelines suggest the use of radiofrequency ablation (RFA) [7]. RFA is a minimally invasive procedure that has been used to treat benign thyroid lesions and recurrent thyroid neoplasms [8–12]. RFA has been shown to be safe and effective in the management of metastatic

cervical lymph nodes secondary to PTC in literature from South Korea and China [4, 10, 11].

Despite the increasing popularity of thermal ablation techniques being used to treat thyroid nodules and recurrent thyroid cancer in the United States, clinical data on efficacy and safety of RFA in the management of metastatic thyroid carcinoma to cervical lymph nodes remain extremely limited.

The first reported use of RFA in the United States for cervical recurrence of thyroid carcinoma was in 2001 at Brown Medical School, Rhode Island Hospital, Providence, where 8 patients (7 with PTC, and 1 with follicular thyroid carcinoma) were treated, with long-term follow-up reported in 2006 with 16 patients (15 with PTC, and 1 with medullary thyroid cancer), and in 2013 with 21 patients; after which only case reports have been published [13–17]. Table 1 summarizes the international studies on RFA used to treat cervical metastases from PTC [10, 11, 18–24]. A limited number of

**Table 1. International studies reporting radiofrequency ablation used in cervical metastases from papillary thyroid carcinoma**

First author, year, country	N/n	%VR	%Efficacy	Follow-up (m)	Complications <sup>a</sup>
Chung, 2021, S. Korea	119/172	81.2	72.1	47.9	21.4%
Chung, 2019, S. Korea	29/46	99.5	91.3	80	10.3%
Guang, 2017, China	33/54	94.9	61.1	21	NR
Kim, 2016, S. Korea	129	NR	NR	NR	10.1%
Kim, 2015, S. Korea	27/36	NR	86.1	36	7.3%
Lim, 2015, S. Korea	39/61	95.1	82	26.4	7.7%
Long, 2015, China	12/12	NR	NR	6	NR
Lee, 2014, S. Korea	32/35	96.4	88.6	30	17%
Wang, 2014, China	8/20	76.9	25	9.4	0%
Guenette, 2013, Ireland	14/21	NR	NR	61.3	7.1%
Park, 2011, S. Korea	11/16	50.9	NR	6	9%
Baek, 2011, S. Korea	10/12	93	50	23	10%

Abbreviations: %VR, percentage volume reduction; %Efficacy, the percentage of nodes that completely disappeared after radiofrequency ablation; m, months; N, number of patients; n, number of nodes; NR, not reported.

<sup>a</sup>Complications, major and minor, as defined by the Society of Interventional Radiology criteria.

case reports with successful outcomes have also been published [25, 26].

This retrospective study was undertaken to evaluate the efficacy and safety of RFA as a treatment modality for PTC metastatic to cervical lymph nodes in adult patients in the United States performed in the private outpatient endocrinology practice setting.

## Materials and Methods

The study was carried out at The Thyroid Clinic at Salt Lake City, Utah, and the Southern California Thyroid Institute, Newport Beach, California. A retrospective chart review was conducted between July 1, 2020, and December 1, 2021, to identify all patients with recurrent PTC in the neck who were treated with radiofrequency ablation.

The electronic medical record was reviewed to extract the following data: demographics, laboratory and imaging findings, pathology results, complications, and a review of treatments provided with regards to the patients' thyroid cancer.

The protocol of this study was reviewed and approved by the University of Texas Southwestern Institutional Review Board.

## Inclusion Criteria

Patients who had a personal history of classic PTC with persistent disease or the development of recurrence in cervical lymph nodes or thyroid bed following initial surgical treatment with or without radioactive iodine, who were subsequently treated with RFA were included in the study.

Recurrence of thyroid malignancy was defined as a detectable thyroglobulin (Tg) level along with structural identification of cervical lymph node disease on imaging in a patient after surgical treatment. Cancer recurrence was confirmed with ultrasound-guided fine-needle aspiration cytology and measurement of the washout Tg concentration.

Local recurrence of malignant disease in the thyroid bed (diffuse appearance on ultrasonography) vs regional nodal recurrence (clearly identified borders on ultrasonography) of the central or lateral compartments of the neck was defined

utilizing the ATA working group paper on this subject [17]. Patients with 1 or 2 regional cervical nodal recurrences and no distant metastatic disease were considered candidates for treatment with RFA.

One patient was treated with palliative intent. Pt 3 had radioactive iodine refractory metastatic disease (BRAF-V600E mutation) with 2 recurrences in the neck. Her case was reviewed at the local head and neck tumor board; however, because of the critical location of 1 of her neck recurrences, she was deemed to not be a surgical candidate (invasion into tracheal invasion/thyroid and hyoid cartilage). Systemic therapy was planned; however, her other neck recurrence was in the tracheoesophageal groove with concern for impending invasion into the trachea and/or recurrent laryngeal nerve, so urgent intervention was recommended while she was being evaluated for chemotherapy.

## Exclusion Criteria

Patients with 3 or more metastatic cervical lymph nodes were excluded. Patients with evidence of distant metastatic disease were also excluded (except for Pt 3, as she was treated with palliative rather than curative intent). Absence of distant recurrence was confirmed by computed tomography of the neck and chest as well as iodine-131 whole body imaging. Patients with anaplastic thyroid carcinoma were not considered to be candidates for RFA. Patients who underwent RFA for medullary thyroid carcinoma and follicular thyroid carcinoma were also excluded from the study. Pregnant patients were excluded.

All patients were clinically assessed to determine their suitability for this treatment option. Written and verbal informed consent was obtained from all patients. It was explained to the patients by the treating endocrinologists and surgeons that the current standard of care for cervical metastasis of thyroid cancer is surgery and that high-resolution ultrasonography may miss metastatic lesions in the central and lateral compartment of the neck. Patients were informed that RFA is not a substitute for a compartment dissection in these cases. Active surveillance was also offered as an option for low-risk patients,

and patients who preferred active surveillance rather than intervention were excluded.

All RFA procedures were performed by 3 endocrinologists (S.A., J.A., S.N.) who are experts at ultrasound-guided thyroid RFA, having performed a cumulative total of over 400 office-based RFA procedures on thyroid nodules in the United States.

### Preablation Assessment

Thyroid function tests and tumor markers including thyroid-stimulating hormone, free thyroxine and Tg panels were recorded for all patients. All patients underwent diagnostic ultrasonography, with either the MyLab Gamma ultrasound system (Esaote North America) with linear probe operating at a frequency of 4 to 14 MHz at the Thyroid Clinic, Utah, or the GE LOGIQ P9 ultrasound system with linear probe operating at a frequency of 4.5 to 14 MHz at the Southern California Thyroid Institute, California. Each lymph node was measured in 3 dimensions and the nodules volume was calculated using the ellipsoid volume formula [27]:

$$\text{Volume (mL)} = [\text{length (sagittal) in cm} \\ \times \text{depth (anteroposterior) in cm} \\ \times \text{width (transverse) in cm}] \times 0.524$$

### Radiofrequency Ablation

RFA was performed in the outpatient clinic for 7 patients and in the operating room for 1 patient. Standard aseptic techniques and a combination of local anesthesia with lidocaine and mild conscious sedation using intravenous midazolam administered by an anesthesiologist or certified registered nurse anesthetist.

Patients were placed in supine position with the neck hyperextended. The target lesion and vital anatomic structures were visualized with ultrasonography in real time. RFA was performed with an 18-gauge internally cooled electrode (STARMed, Seoul, South Korea) that was 7 cm in length with a 0.5-cm active tip and was powered by a VIVA RF generator (STARMed). The procedure was performed using a limited hydrodissection and fixed RFA technique with a medial to lateral approach when possible. For all patients, an initial power between 20 and 30 W was used for the ablation. This was increased in increments of 5 to 10 W every 10 seconds, if needed, up to a maximum of 80 W.

An estimate of the energy applied per unit volume (E/V) was calculated using the following equation:

$$E/V(\text{J/mL}) = [\text{Power (watts)} \times \text{Active ablation time (seconds)}] / \\ \text{Volume of lymph node(s) (ml)}$$

In cases where the power was changed during the procedure, the maximum power was used. In cases where 2 lymph nodes were ablated in the same session and only the total energy applied for the session was available, the volume of the treated lymph nodes was added together to estimate the average energy applied per unit volume for each node.

### Hydrodissection

Hydrodissection was performed for all patients in this study to protect vital structures, specifically the recurrent laryngeal in central compartment and vagus nerve in lateral compartment. A safety margin was created by injecting cold (0-4 °C)

dextrose 5% in water (D5W) between the metastatic lesion and the adjacent vulnerable structures, such as the recurrent laryngeal nerve and neurovascular bundle, effectively protecting these structures from thermal injury [28].

### Voice Evaluation

Voice evaluation was carried out every 1 to 2 minutes by asking the patient to verbalize every 1 to 2 minutes to assess voice quality. A change in voice indicates thermal injury to the recurrent laryngeal nerve, which is more at risk when ablating central neck recurrences. In case of any changes in voice, our practice protocol is to stop ablation and inject cold D5W in the trachea–esophageal groove in 5 to 10 mL boluses until the voice recovers [28, 29]. None of the patients in this study had any change in phonation so rescue hydrodissection was not required.

### Postablation Assessment

All patients were evaluated for 15 to 20 minutes postprocedure for any compressive symptoms, difficulty breathing, hoarseness, or bleeding. They were contacted 1 to 2 days after the RFA procedure to evaluate for complications including pain, fever, hematoma or swelling, voice change (both immediate and after 24 hours), and onset of dysphagia.

Complications were defined by the criteria outlined in Mauri et al, and classified into minor and major complications [27].

Patients were evaluated with repeat ultrasonography, and measurement of tumor markers and thyroid function tests 6 to 12 weeks after the RFA procedure, with subsequent follow-up visits planned at 6 and 12 months. The volume reduction (VR) for each nodule was expressed as a percentage and calculated using the following equation:

$$\text{VR} = \{[\text{baseline volume (mL)} - \text{final volume (mL)}] / \\ \text{baseline volume (mL)}\} \times 100$$

The response to treatment was defined as follows:

1. Complete response: The treated metastatic lymph node/lesion had a volume reduction of 100% and was no longer visible on ultrasonography.
2. Near-complete response: a volume reduction of more than 90% in the treated metastatic lymph node/lesion, with the node/lesion still visible on ultrasonography.
3. Partial response: a volume reduction of 50% to 90% in the treated metastatic lymph/lesion node.
4. Inadequate response: a volume reduction of less than 50% in 6 months in the treated metastatic lymph node/lesion.
5. Treatment failure: the treated metastatic lymph node/lesion has an increase in volume of 50% or more due to regrowth after initial volume reduction.

Based on clinical picture and clinician discretion, metastatic lesions were considered for a second RFA if they had a partial or inadequate response.

### Results

A total number of 8 patients (4 male, 4 female) with 11 metastatic lesions meeting the inclusion criteria were treated with

RFA from July 2020 to November 2021. All treatment options, including surgery and/or active surveillance were discussed with the patients. In the case of 3 patients, after surgical consultation, it was determined that further surgery would be too high risk and they were told that they were not surgical candidates.

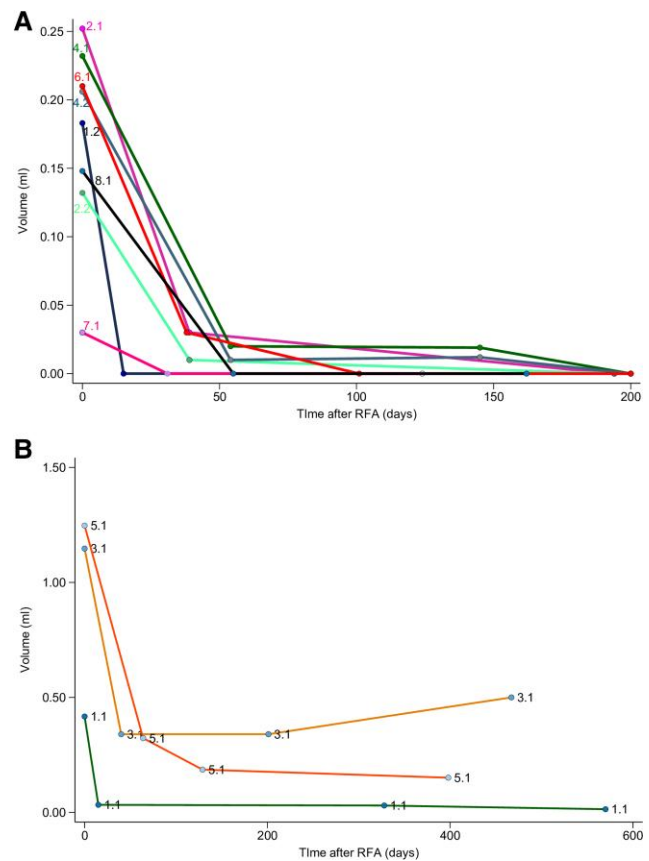
Active surveillance was offered to patients with small lymph nodes in noncritical locations; however, all patients who participated in the study wanted intervention. Four patients were surgical candidates; however they refused surgery and preferred nonsurgical intervention such as RFA.

All patients had previously undergone a total thyroidectomy: 2 had previously had a central neck dissection, and 3 had a central and lateral neck dissection. Of these patients, 7 had nodal recurrence/persistence of PTC in the neck and 1 patient (Pt 3) was treated with palliative intent for a locally recurrent PTC mass in the tracheoesophageal groove.

All patients underwent a single session of RFA, except for Pt 5 who underwent 2 sessions, the first in Salt Lake City, Utah, and the second, 65 days later, in Islamabad, Pakistan. Pt 1 had previously documented contralateral vocal cord paralysis due to her prior thyroidectomy; therefore, RFA was performed in the operating room with an otolaryngologist available in case of thermal damage to the ipsilateral recurrent laryngeal nerve, which could potentially result in need for tracheostomy. All other procedures were performed in the outpatient clinic.

The median age of the patients was 38 years (range: 33-51 years), and they were predominantly Caucasian (only Pt 5 was South Asian). The characteristics and clinical features of the patients are described in Table 2.

The initial median volume was 0.21 mL (range 0.148-1.247 mL); after treatment with RFA the median volume was 0 mL (range 0-0.15 mL). Each patient had at least 2 follow-up visits, with a median volume reduction of 92.1% (range 70.3-100%) after the first median follow-up period of 40 days (range 15-55 days), and an overall median volume reduction of 100% (range 56.3-100%) after a median follow-up period of 453 days (range 162-570 days) (Fig. 1).



**Figure 1.** Change of volume over time in metastatic cervical lymph nodes/lesions after radiofrequency ablation (RFA). Time 0 days of the RFA procedure, with the length of the line indicating the duration of follow-up. Each circle represents a point in time where the volume of the treated lesion was measured by ultrasonography, and the points are connected by lines to indicate an approximate rate of volume reduction. (A) Change in volume of lymph nodes/lesions with initial volume of less than 0.3 mL (line not extended beyond 200 days as most nodules had disappeared by that time). (B) Change in volume of lymph nodes/lesions with initial volume of more than 0.3 mL.

**Table 2. Characteristics and baseline clinical features of patients included in the study**

Patients (age/sex)	TNM	ATA/MACIS	Time (y)	Location	Num	Surg	RAI	Sys	Reason
Pt 1 (35/F)	T1b,N1a,M0	L/<4	2.5	L level VI	2	1	N	N	NSC: prior RLN injury
Pt 2 (43/M)	T1a,N1a,M0	I/<4	12	C level VI	2	4	Y	N	NSC: high risk
Pt 3 (44/F)	T3,Nx,M1	H/>4	4.3	L thyroid bed	1	1	Y	Y	Palliative
Pt 4 (51/M)	T2,N1a,M0	I/<4	9.5	R level VI	2	2	Y	N	Pt preference
Pt 5 (33/M)	T2,N1b,M0	I/<4	2.1	L thyroid bed	1	1	Y	N	NSC: high risk
Pt 6 (37/F)	T1,N1a,M0	L/<4	2	L level IV	1	1	Y	N	Pt preference
Pt 7 (37/F)	T2,N1a,M0	I/>4	5.7	R level III	1	1	Y	N	Pt preference
Pt 8 (39/M)	NA	NA	10.6	L level III	1	2	Y	N	Pt preference

Age is given in years.

Time refers to the time between the patients' initial thyroid surgery and the radiofrequency ablation procedure. Location refers to the surgical level of the neck the recurrence occurred. Reason refers to the reason patient underwent radiofrequency ablation rather than surgery.

MACIS score <4 indicates low-risk disease and >4 indicates higher risk disease.

Abbreviations: ATA, American Thyroid Association 2015 guidelines; C, central; F, female; H, high; I, intermediate; L, left; Lo, low; M, male; MACIS, distant metastasis, patient age, completeness of resection, local invasion, and tumor size; N, no; NA, not available; NSC, not a surgical candidate; Num, number: refers to the number of metastatic lymph nodes or lesions that were present; Pt, patient; R, right; RAI, radioactive iodine ablation; RLN, recurrent laryngeal nerve; Surg, surgeries: refers to the number of surgeries, including initial thyroidectomy the patient had prior to radiofrequency ablation; Sys, systemic therapies; TNM, tumor, node and metastases staging; Y, yes.

**Table 3. Outcomes of cervical metastatic lymph nodes treated with radiofrequency ablation**

Node	Pre-RFA vol (mL); d (cm); Tg (ng/mL)	Post-RFA vol (mL); d (cm); Tg (ng/mL)	E/V (J/mL)	Follow-up (days)	VR (%)	Response
1.1	0.417; 0.83; 0.7	0.014; 0.3; 0.4	1336	570	96.6	Near complete
1.2	0.183; 0.68; 0.7	0; 0; 0.4	1336	570	100	Complete
2.1	0.252; 1; 1.4	0; 0; 0.4	1367	494	100	Complete
2.2	0.132; 0.7; 1.4	0; 0; 0.4	1367	494	100	Complete
3.1	1.147; 1.4; 2	0.5; 0.6; 1.3	3979	467	56.3	Partial
4.1	0.232; 0.7; 0.8	0; 0; 1.3	4483	523	100	Complete
4.2	0.206; 0.8; 0.8	0; 0; 1.3	4483	523	100	Complete
5.1	1.247; 1.2; 15.2	0.15; 0.6; 0.2	2165	398	87.9	Partial
6.1	0.210; 1; 0.1	0; 0; 0.1	12 250	363	100	Complete
7.1	0.269; 0.38; <2	0; 0; <2	8333	438	100	Complete
8.1	0.148; 0.71; <0.4	0; 0; <0.4	30 405	162	100	Complete

Abbreviations: d, diameter: refers to the largest short-axis diameter of the lymph node/lesion; E/V, energy applied per unit volume; post-RFA vol, postradiofrequency ablation volume; pre-RFA vol, preradiofrequency ablation volume; Tg, thyroglobulin; VR, volume reduction.

Nine out of 11 lesions (81.8%) had a near-complete to complete response to RFA treatment; 8 of these had a complete response. All patients had at least a partial response to treatment. Both patients with an initial metastatic node volume of over 1.1 mL showed a partial response, whereas all the other patients with initial metastatic node volumes of less than 0.5 mL showed a near-complete or complete response. There was no regrowth noted for the duration of the study period in patients treated with curative intent. Pt 3 was treated with RFA because of the critical location of her recurrence, and although she had initial volume reduction, there was some regrowth later in the follow-up period despite additional treatment with lenvatinib.

All patients were treated with a power between 20 W and 35 W, except for Pt 3 with the left thyroid bed mass who was treated with a maximum power of 80 W. The median active ablation time was 32 seconds (range 10-180 seconds). The median estimated E/V was 3979 J/mL (range 1336-30 405 J/mL). All patients with a median estimated E/V of at least 4483 J/mL or higher had a near-complete or complete response (Table 3).

The serum Tg levels declined from a median of 0.7 ng/mL (range 0-15.2 ng/mL) to a median of 0.3 ng/mL (range 0-1.3 ng/mL) over the study period. None of the patients had elevated Tg antibody levels. No minor or major complications were noted. Outcomes of individual lymph nodes/lesions are detailed in Table 3.

## Discussion

Although it is well recognized that surgery is the treatment of choice for recurrent thyroid cancer in the neck, some patients are not surgical candidates, or may not want to undergo repeat surgeries after their initial resection. While active surveillance is an option for selected patients, many patients have anxiety with this approach and may choose intervention despite no progression in tumor kinetics or size [30, 31]. RFA is emerging as an alternative option for these patients.

RFA is minimally invasive and has a lower complication rate than surgery; however, use in recurrent cervical PTC recurrence is still limited in the United States [12-14, 17]. The

results of our study are illustrative of the real-world outpatient application and results using this technique.

Technical success has traditionally been defined as a 50% volume reduction in the thermal ablation literature with regards to benign thyroid nodules; however, in case of malignancy, treatment should be with curative intent. Therefore, we have defined complete success as a 100% volume reduction that mimics the results after surgery, and have recognized that a near-complete response of 90% volume reduction is likely to be clinically similar to a complete response, as the remaining tissue may not be viable or may have only microscopic disease that can be monitored. This is further supported by the low postprocedure Tg levels in these patients.

It has been recognized that smaller nodules respond better to RFA [12], and in keeping with this our cohort shows that the larger lesions in the group (ie, over 1.1 mL) have a partial, though still significant, response, while the smaller ones (ie, less than 0.5 mL) have had near-complete or complete responses. It also noted that most of the volume reduction occurs between the date of procedure and first follow-up (within 4-8 weeks), with the target lesions remaining stable thereafter (Fig. 1). This would indicate that failure to respond would become evident within the first 2 months of RFA treatment.

There are some data to suggest applying more E/V can result in a higher volume reduction, with Deandrea et al reporting that 99% of patients should have a volume reduction of 50% or more of benign thyroid nodules if at least 2670 J/mL of energy is delivered [32]. Similar studies have not been done on malignant lesions; however, it would follow that for these lesions even more energy would need to be applied per unit volume as the aim would be to achieve a 90% to 100% volume reduction. In our study, we do note that all nodules receiving E/V of 4483 J/mL or higher had a near-complete or complete response. It should be recognized that our measurement of energy applied is an estimation, as the assumption was made that the maximum power setting was used for the duration of the active ablation time, whereas some portion of the active ablation would have been performed at a lower power setting. This means that the actual energy applied may be lower than our calculated values.



Complication rates for RFA of recurrent thyroid cancers are higher than for benign thyroid nodules but are still quite low compared with surgery and are generally operator dependent [33]. Fortunately, there were no complications in this study, although this may be attributed to the low sample size. Of note, the patient with contralateral recurrent nerve paralysis would have required a tracheostomy in case of injury to the remaining recurrent laryngeal nerve, therefore precautions were taken. We are of the view that if there is any risk of bilateral recurrent laryngeal nerve paralysis then this should be explained to the patient in detail, and if the decision is made to proceed then the procedure should be performed in an appropriate setting with airway management capability. Unilateral recurrent nerve injury during RFA can be managed in the outpatient setting with rescue hydrodissection [28, 29].

Regrowth after RFA remains a concern in those lesions who do not have a complete response, especially with the relatively short follow-up time in some of the patients. In any case, longer-term studies with 5 to 10 years of follow-up would be needed to determine what the regrowth rates of recurrent cervical PTC with partial response to RFA treatment are. We suggest that for future studies our definition of treatment failure be modified to an increase in volume of 50% or more due to regrowth after initial volume reduction within 5 years of the initial ablation with a repeat fine-needle aspiration to confirm or exclude malignancy suggesting local regrowth of ablated lesion. More than 1 session may be required in case of partial response or treatment failure, and treatment failure should prompt a re-evaluation of all the treatment options available to the patient, including local and systemic therapies.

The insurance coverage for RFA of recurrent cervical PTC is somewhat better than the coverage for benign thyroid nodules, although patients in the United States are still limited to the few centers that offer these procedures.

## Conclusion

RFA is a safe and effective treatment option for metastatic cervical lymph node recurrences of PTC in carefully selected patients with thyroid cancer. It is particularly suitable for those not deemed candidates for further surgery or who decline further surgical intervention.

## Acknowledgments

We would like to thank Sheraz Latif Malik for making the graphs for Fig. 1.

## Funding

None.

## Disclosures

The authors have no conflicts of interest to disclose.

## Data Availability

Some or all dataset generated and analyzed during the current study are not publicly available but are available from the corresponding author on reasonable request.

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