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Microwave ablation of benign thyroid nodules: 3-year follow-up outcomes

Fangqiong Luo MD[1,2] | Lei Huang MD[1,3] | Xiuqun Gong MD[1,4] | Zhiyu Han MD[1] | Fangyi Liu MD[1] | Zhigang Cheng MD[1] | Jianping Dou MD[1] | Xiaoling Yu MD[1] | Ping Liang MD, PhD[1] | Jie Yu MD, PhD[1]

[1]Department of Interventional Ultrasound, Chinese PLA General Hospital, Beijing, China

[2]Department of Ultrasound, Shandong Provincial Qianfoshan Hospital, The First Hospital affiliated with Shandong First Medical University, Shandong University, Jinan, China

[3]Department of Ultrasound, The First Affiliated Hospital of Anhui University of Science and Technology, Huainan First People's Hospital, Huainan, China

[4]Department of Neurology, The First Affiliated Hospital of Anhui University of Science and Technology, Huainan First People's Hospital, Huainan, China

Correspondence
Ping Liang, MD, PhD and Jie Yu, MD, PhD, Department of Interventional Ultrasound, Chinese PLA General Hospital, 28 Fuxing Road, Beijing, 100853, China.
Email: liangping301@hotmail.com (P.L.) and jiemi301@163.com (J.Y.)

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[Correction added on 04 September 2021, after first online publication: The co-corresponding author "Jie Yu" has been included in correspondence section in this version.]

Abstract

Purpose: To evaluate the effectiveness of microwave ablation (MWA) for the treatment of thyroid nodules according to nodule composition.

Materials and methods: This study evaluated 171 patients with 180 benign thyroid nodules (BTNs) that had been treated with ultrasound-guided MWA. The volume reduction rate (VRR) of thyroid nodules and factors, which had an influence on the VRR, were assessed. Therapeutic success was defined as a >50% volume reduction at the 12-month follow-up. Multivariate regression analysis was used to identify independent predictors of VRR for BTNs after MWA treatment.

Results: The mean diameter and volume of the nodules were 4.3 ± 1.3 cm and 18.9 ± 2.1 ml, respectively. The VRRs at the 1-, 3-, 6-, 12-, 24-, and 36-month follow-ups were 47.1%, 68.2%, 79.7%, 87.4%, 90.1%, and 93.2%, respectively. Of the 180 BTNs, there were 87 solid, 74 predominantly solid, and 19 predominantly cystic nodules. Solid nodules showed significantly lower VRRs compared with the predominantly solid and predominantly cystic nodules at the 1-, 3-, and 6-month follow-ups. For the multivariate regression analysis, the cyst component was an active prognostic factor for the VRR at the 1-, 3-, and 6-month follow-ups; the cyst component was not significantly associated with the VRR at the 12-, 24-, and 36-month follow-ups.

Conclusion: Our study suggested that ultrasound-guided MWA is an effective and safe procedure for the treatment of BTNs. Solid nodules indicate a lower VRR and less efficient than predominant solid nodules and predominant cystic nodules after MWA.

Abbreviations: BTN, benign thyroid nodule; CDFI, color Doppler flow imaging; HIFU, high-intensity focused ultrasound; MWA, microwave ablation; RFA, radiofrequency ablation; VRR, volume reduction rate.

Fangqiong Luo, Lei Huang, and Xiuqun Gong contributed equally to this study.

KEYWORDS
ablation benign, microwave, thyroid nodules

1 | INTRODUCTION

Thyroid nodules commonly occur and can be discovered with clinical palpation in 5% of healthy individuals.[1,2] High-resolution ultrasound imaging shows that 19%–68% of randomly selected individuals (higher frequencies among women and the elderly) have evidence of benign thyroid nodules (BTNs).[1,2] However, since most nodules are benign and do not grow rapidly, surgical resection is only indicated when they become large or are causing symptoms including dysphagia, neck pressure, shortness of breath (especially when in the supine position), a globus sensation, dyspnea upon exertion, or pain.[1–6] However, surgical resection is limited by the cost of surgery, the need for general anesthesia, the frequent need for life-long substitution therapy, the risk of complications, and the cosmetic impact of the operation. Thus, in recent years, there has been a growing interest in developing nonsurgical, minimally invasive techniques for the treatment of symptomatic benign BTNs, especially in elderly or fragile patients and those who decline surgery.[3,7] These minimally invasive techniques include percutaneous ethanol injection (PEI), laser ablation, radiofrequency ablation (RFA), microwave ablation (MWA), and high-intensity focused ultrasound (HIFU), which have been used increasingly in recent years with good clinical outcomes.[4–7]

MWA is a promising thermal ablation technique, which has several advantages over other ablation techniques in producing consistently higher intratumor temperatures, larger ablation volumes, less ablation time, and less dependence on the electrical conductivity of tissue.[8,9] Therefore, MWA may have a greater potential for the complete destruction of large BTNs.

Previous studies have shown that several factors determining the efficacy of LA or RFA for BTNs, including nodule composition,[10,11] the energy delivered per mL of nodule tissue,[12] and nodule volume.[11,13] However, evaluations of factors associated with efficiency of MWA in BTNs are limited. In particular, the influence of BTNs-related factors, such as nodule composition, growth location, shape, capsule, CDFI grading, ring-shape peripheral vascularity, and so on, needs further study. We aimed to evaluate the safety and efficacy of MWA therapy for the treatment of BTNs and to investigate the associations between BTNs clinical characteristics and the efficiency after WMA treatment.

2 | MATERIALS AND METHODS

The applications for ultrasound-guided MWA treatment were owned by our institution. The authors had complete access of the data and the information for publication. This retrospective trial was approved by the local Institutional Review Board. All consecutive patients who underwent MWA for BTNs at the authors' institution from July 2014 to July 2017 were analyzed. For the present study, 171 patients with at least 36 months of follow-up after ablation were included. After treatment, the treated nodule was measured by ultrasound at 1, 3, 6, 12, 24, and 36 months.

To be eligible for MWA, the following inclusion criteria were applied: (a) BTNs confirmed via core-needle (18 Gauge) biopsy, (b) nodules with a largest diameter larger than 3 cm, (c) BTNs with a fluid component <80%, as seen with an ultrasound assessment, (d) a normal serum free thyroxine (fT4) level and a corresponding normal or low thyrotropin (TSH) level, and (e) no vocal cord immobility, as confirmed via a laryngoscope. The patients were retrospectively evaluated through medical record review to assess the efficacy and safety profile of MWA. All ultrasound assessments (baseline and subsequent visits) were conducted by an independent, experienced radiologist who was not directly involved in the study.

2.1 | Pretreatment evaluation

All BTN dimensions were measured using the LOGIQ e (GE Healthcare, Milwaukee, WI) scanner equipped with a 10–14 MHz linear matrix transducer. Three orthogonal diameters of the index nodule (its longest diameter and two other perpendicular diameters) were measured. In general, the longest diameter was the cranio-caudal dimension (length) of the nodule, while the other two perpendicular diameters were the medio-lateral (width) and antero-posterior (depth) dimensions of the nodule. All measurements were made to the nearest 0.1 mm. To estimate nodule volume, the formula for volume $(\text{ml} = (\text{width [cm]} \times \text{length [cm]} \times \text{depth [cm]}) \times (\pi/6)$ was used, where π was considered to be 3.1416.

According to the ultrasound presentation of the nodules on color Doppler flow imaging (CDFI), the nodular vascular scores were classified into four grades: Grade 0 with no color signal in the nodule; Grade 1 with color signals in <25% of the nodule; Grade 2 with color signals in 25%–50% of the nodule; and Grade 3 with color signals in >50% of the nodule.[14] Other parameters including the nodule's growth location, cyst component, tumor capsule, shape, and ring-shape peripheral vascularity were also evaluated before MWA treatment.

2.2 | Microwave ablation

All procedures were performed with ultrasound guidance. The microwave unit (KY-2000, Kangyou Medical, Nanjing, China) is capable of producing 100 W of power at 2450 MHz. The internal cooled antenna has a diameter of 1.6 mm (16 Gauge) and a length of 10 cm.

For the microwave procedure, a power output ranged from 20 to 30 W, depending on the tissue reaction, as monitored by ultrasound. If the nodule had a cystic portion, we first aspirated the fluid as much as possible, and then MWA was performed for the remaining solid portion. The hydrodissection technique was applied and 0.9% normal saline was injected into the surrounding thyroid capsule, which can provide a safe thermal barrier to ablation energy and avoid damage to critical adjacent structures.[15] Under ultrasound guidance, the cyst liquid was aspired before ablation; then, we performed MWA by using the moving-shot technique which has been shown to be effective in the ablation of BTNs.[16,17] We divided the BTNs into small ablation elements within our imaginations and performed MWA one-by-one for 5–10 s per element by moving the electrode following the reported procedure.

After the ablation, contrast enhanced ultrasound was performed immediately to evaluate whether the ablation was complete; if there was any residue left (enhanced zone), the ablation was continued. For nodules with a diameter ≤5 cm, MWA was performed in one session, while for nodules with a diameter >5 cm, MWA was performed in two or three sessions.

2.3 | Follow-up and outcome assessment

Outcomes were assessed by experienced radiologists (thyroid ultrasound experience of 6 and 15 years: Yu J, Cheng ZG, Han ZY, Liu FY, Luo FQ, Huang L) other than the operators who were blind to the treatment group allocation and study design. Ultrasound examination was performed in all patients at the time of the 1-, 3-, 6-, 12-, 24-, and 36-month follow-up examinations by two radiologists. Upon ultrasound examination, the changes in the volume of the nodules were evaluated. The volume, therapeutic success rate, and the improvement of symptomatic and cosmetic problems were checked. Therapeutic success was defined as a volume reduction rate (VRR) > 50% at the 12-month follow-up.[12] Technical efficiency was defined a VRR ≥50% of the initial nodule volume at each follow-up time point.[12] Recurrence was defined as a nodule volume increase >50% over the smallest recorded volume.[18] Any adverse events that occurred during the 36-month follow-up period were also recorded.

2.4 | Statistical analysis

Continuous variables are expressed as means ± standard deviations and as medians and interquartile ranges (IQR) as appropriate. The IQR was defined as the distance between the first and third quartile. Groups were compared using the Mann–Whitney *U* test. Chi-square tests were used to compare categorical variables. For correlations between continuous variables, Spearman's rho correlation test was performed. Both the univariate and multivariate analyses were performed using logistic regression analysis. Any parameters that were significantly associated with the VRR in the univariate analysis were entered into the multivariate analysis. All statistical analyses were conducted using SPSS version 19.0 or R version 2.14.0 software (SPSS, Chicago, Ill; R Foundation for Statistical Computing, Vienna, Austria). *p*-values less than or equal to 0.05 were considered to indicate a statistically significant difference.

3 | RESULTS

3.1 | Baseline characteristics

From July 2014 to July 2017, a total of 659 BTNs patients were treated with MWA; of them, 189 patients met the inclusion criteria. Additionally, at 12, 24, and 36 months of follow-up, the number of people lost to follow-up was 18, 38, and 49, respectively. Finally, the study included 180 nodules in 171 patients (39 males and 132 females) with a mean age of 47.0 ± 14.2 years, while the number of patients studied was 151 and 140 at 24 and 36 months of follow-up. The baseline characteristics of the BTNs and the treatment characteristics are presented in Table 1.

The mean diameter of these nodules was 4.3 ± 1.3 cm, and the mean volume was 21.2 ± 18.9 ml. Of the nodules, 58 (32.2%), 85 (47.2%), and 37 (20.6%) had volumes ≤10, 10.0–30, and ≥ 30 ml, respectively.

For the fluid component assessment, 87 (48.3%) were solid (≤10% fluid component), 74 (41.1%) were

TABLE 1 The clinical features of patients and nodules

Variable	Datum
No. of patients	171
Mean age (years)[a]	47.0 ± 14.2 (15–76)
Sex	
Female	132 (77.2%)
Male	39 (22.8%)
No. of nodules	180
≤ 10 ml	58 (32.2%)
10–30 ml	85 (47.2%)
≥ 30 ml	37 (20.6%)
Mean nodules diameters (cm)[a]	4.3 ± 1.3 (3.0–11.1)
Mean nodules volume (ml)[b]	18.9 ± 2.1 (3.1–107.8)
Growth locations of nodules	
Left lobe	89 (49.4%)
Right lobe	89 (49.4%)
Isthmus	2 (1.0%)
Adjacent to tissue	
Trachea	162 (90.0%)
Esophagus	87 (26.1%)
Recurrent laryngeal nerve	98(54.4%)
Carotid artery and jugular vein	150(83.3%)
None of above	9 (5.0%)
Mean fluid component (%)[a]	16.1 ± 19.0 (0–79)
Solid(≤10% of fluid component)	87 (48.3%)
Predominantly solid (11%–50% of cyst component)	74 (41.1%)
Predominantly cystic (51%–90% of cyst component)	19 (10.6%)
Cystic (>90% of cyst component)	0
Shape	
Regular	162 (90.0%)
Irregular	18 (10.0%)
Tumor capsule	
Yes	171 (95.0%)
No	9 (5.0%)
CDFI grading	
0	0 (0)
1	73 (40.6%)
2	85 (47.2%)
3	22 (12.2%)
Ring-shape peripheral vascularity	
Yes	109 (60.6%)
No	71 (39.4%)

Note: CDFI grading: color Doppler flow imaging (CDFI), the nodular vascular scores were classified into four grades: (0) no color signal in the nodule; (1) color signals in <25% of the nodule; (2) color signals in 25%–50% of the nodule; and (3) color signals in >50% of the nodule.
[a]Data are means ± standard deviation; data in parentheses are ranges.
[b]Data are median; data in parentheses are interquartile range.

predominantly solid (11%–50% fluid component), and 19 (10.6%) were predominantly cystic nodules (51%–90% fluid component); none of the nodules were cystic (>90% fluid component).

3.2 | Technical success

Contrast-enhanced ultrasound was used to evaluate complete nodule ablation immediately and 1 day after ablation.[19] The total complete ablation ratio was 60.0% (118/180). Therapeutic success in 180 nodules was 97.8%. In our study, the total technical efficiencies were 35.6%, 75.6%, 92.8%, and 97.8% at the 1-, 3-, 6-, and 12-month follow-ups, respectively. One representative case is shown in Figure 1. Forty-two patients with a nodule diameter > 5 cm underwent MWA for two sessions, and other nodules were treated by a single session. In the 171 patients, four had nodule recurrence at 12 months after MWA and two had another MWA treatment due to unsatisfactory results. The initial mean nodule size in the four patients who had recurrence ranged from 3.0 to 5.4 cm. In the patients who experienced recurrence, all of the nodules were adjacent to important tissues and CDFI grades were 3 or 4; one nodule had a 35.0% cyst component, and three nodules were full solid nodules. The patient with the nodule with a 35.0% cyst component underwent an ultrasound scan 24 months after MWA and the ablated BTN showed the heterogeneously hypoechoic ablation area with peripheral and intranodular vascularity, the largest diameter was 2.2 cm (Figure 2).

3.3 | Volume reduction in different size

The changes in the volume of the masses before MWA and at each follow-up time point are summarized in Table 2.

For small nodules with a volume ≤ 10 ml, the VRR at the 1-, 3-, 6-, and 12-month follow-ups were 40.6 ± 23.2%, 61.1 ± 20.8%, 74.6 ± 19.1%, and 84.7 ± 13.0%, respectively. For medium nodules with a size of 10–30 m, the VRR at the 1-, 3-, 6-, and 12-month follow-ups were 45.9 ± 20.9%, 62.6 ± 22.0%, 77.2 ± 17.5%, and 85.7 ± 15.3%, respectively. And for large nodules with a size of ≥30 ml, the VRR at the 1-, 3-, 6-, and 12- follow-ups were 42.2 ± 24.5%, 58.8 ± 32.9%, 74.0 ± 32.9%, and 86.6 ± 14.7%, respectively. The VRR in different nodule size groups showed a significant increase at each follow-up time point compared with 1- versus 3-month (all the $p < 0.001$) follow-up and compared between 3- versus 6-month (all the $p < 0.001$) and 6- versus 12-month follow-up (all the $p < 0.001$). However, the VRR at

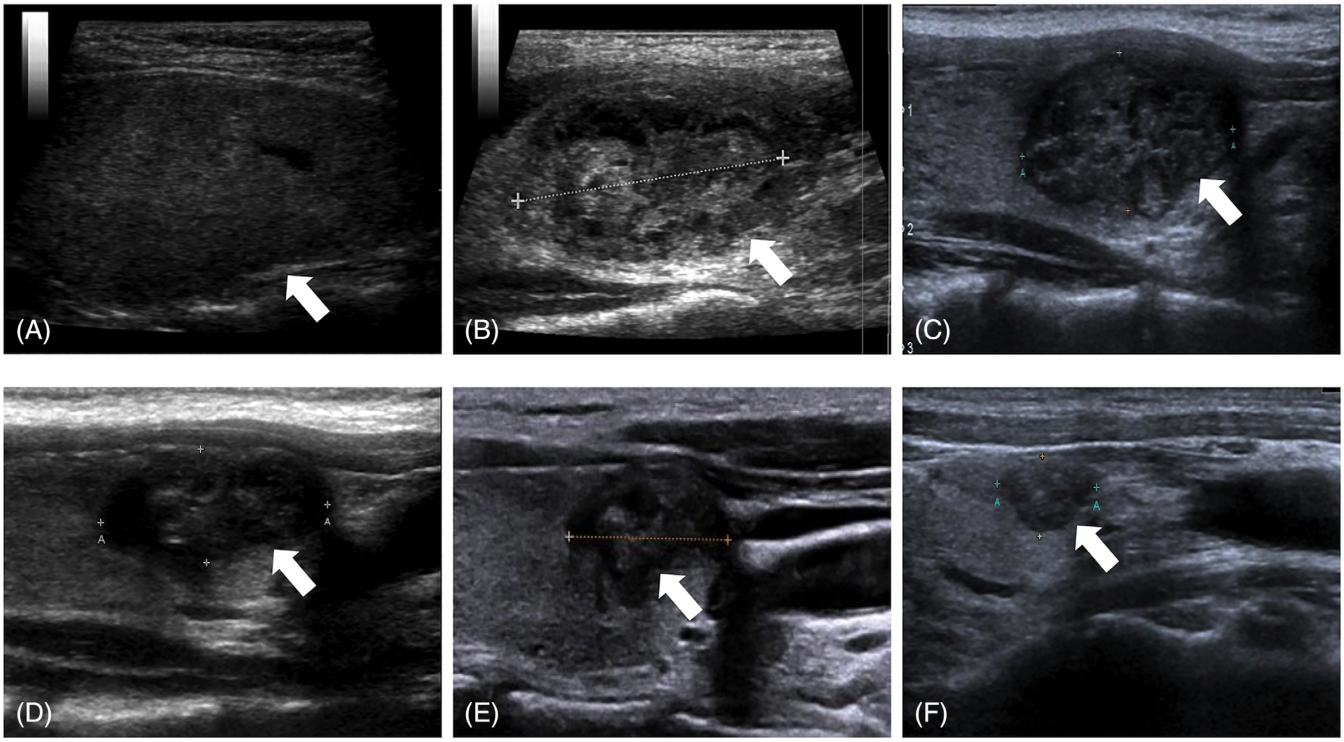

FIGURE 1 Ultrasound images of longitudinal scan in a 57-year-old woman show a benign thyroid nodule with the size of $6.4 \times 4.9 \times 3.6$ cm^3. (A) image acquired before MWA treatment. (B–F) Ultrasound variance of the thyroid benign nodules after MWA during follow-up at 1, 3, 6, 12, and 24 months, respectively. Tumor size decreased gradually during the process and disappeared on the US image at the end [Color figure can be viewed at wileyonlinelibrary.com]

different follow-up times showed no significant difference at each size subgroup compared with small versus medium size (all the $p > 0.05$) and compared between small versus large size (all the $p > 0.05$) and medium versus large size (all the $p > 0.05$).

3.4 | Volume reduction in different composition

Table 3 shows that for solid nodules, the VRR at the 1-, 3-, 6-, and 12-month follow-ups were 31.1 ± 26.9%, 56.4 ± 22.2%, 72.6 ± 19.6%, and 83.3 ± 15.8%, respectively. The VRR in different nodule size groups showed a significant increase at each follow-up time point compared with 1-month versus 3-month (all the $P < 0.001$) follow-up and compared between 3- versus 6-month (all the $p < 0.001$) and 6- versus 12-month follow-up (all the $p < 0.001$). The VRR in solid nodules was significantly lower than in predominantly solid or cystic nodules (all $p < 0.05$) at the 1-, 3-, and 6-month follow-ups. At the 12-month follow-up, the VRR of solid nodules was lower than that in predominantly solid nodules with no significant difference ($p = 0.08$). Meanwhile, there was no significant difference in the VRR between the solid nodules and the predominantly cystic nodules at the 12-month follow-up ($p = 0.13$). Solid nodules achieved lower technical efficiency than predominantly solid and cystic nodules at each follow-up time point.

3.5 | Univariate and multivariate quantitative correlation analysis

Univariate analysis revealed that being female ($p = 0.034$), the nodule diameter ($p = 0.011$), and nodule volume ($P = 0.019$) were prognostic factors for poor VRR at the 1-month follow-up. Ring-shaped peripheral vascularity was a prognostic factor for poor VRR at the 3-month follow-up. Importantly, the cyst component is a prognostic factor for poor VRR at the 1-, 3-, and 6-month follow-up, and it showed no significant relationship with VRR at the 12-month follow-up ($p = 0.095$) (Table 4).

In the multivariate regression analysis, the cyst component showed significant correlations with VRR at the 1-, 3-, and 6-month follow-ups and no significant correlation with VRR at the 12-month follow-up after adjusting for sex, mean nodule diameter, mean nodule volume, CDFI grading, and ring-shaped peripheral vascularity.

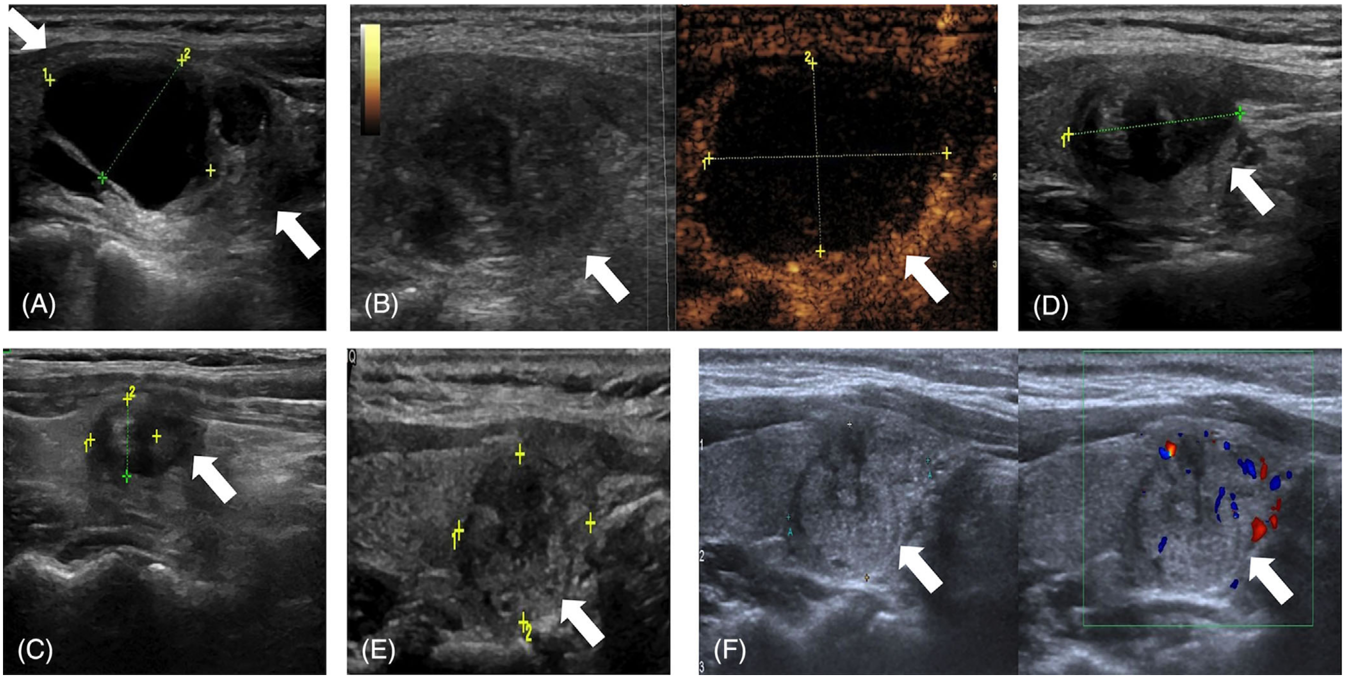

FIGURE 2 A 43-year-old woman with a benign thyroid nodule. (A). Ultrasound scan before MWA shows the nodules with the size is 3.8 × 2.9 × 2.8 cm^3. The size of cyst area is 2.5 × 2.4 × 1.8 cm^3. (B) contrast enhanced ultrasound on the second day after MWA showed the nodule is non-enhancement (arrow) in arterial phase. (C,D) Ultrasound obtained 3 and 6 months after MWA shows the heterogeneously hypoechoic ablation zone, respectively, tumor size decreased gradually during the process on the US image. (E) Ultrasound obtained 12 months after MWA shows the hypoechoic ablation zone, the size is 1.9 × 1.3 × 1.2 cm^3. (F) Ultrasound obtained 24 months after MWA shows the hypoechoic ablation zone, the size is 2.2 × 1.4 × 1.4 cm^3, and the heterogeneously hypoechoic ablation area with peripheral and intranodular vascularity [Color figure can be viewed at wileyonlinelibrary.com]

The cyst component is an active prognostic factor for VRR at the 1-, 3-, 6-month follow-ups, and there was no significant correlation with VRR at the 12-month follow-up (Table 5).

3.6 | Cosmesis and satisfaction

The BTN-related neck symptoms included pressure symptoms in the neck, difficulty with swallowing, growing nodule size, and esthetic complaints. In our study, nodule shrinkage was also accompanied by an improvement in cosmesis and symptoms. Prior to MWA, 40.9% (70/171)of the patients complained of discomfort, and this percentage decreased to 17.5% (30/171) 3 months post-MWA. For the other symptoms, 30.4% of the patients had esthetic complaints before MWA, which decreased to 15.2%; 13.5% of the patients complained of pressure in the neck, which decreased to 4.7%; the percentage of patients with difficulty swallowing decreased from 9.9% to 4.7%; and the percentage of patients with growing nodule size decreased from 5.2% to 1.8% 3 months after MWA. All of the symptoms and cosmetic problems above were completely resolved at the 12-month follow-up.

3.7 | Complications

After ablation, no life-threatening complications were observed in these patients. Further, no major complications were reported. These included voice changes that recovered after 1 month, permanent voice change, nodule rupture with abscess formation requiring drainage, Horner syndrome, and spinal accessory nerve injury.

Nodule ruptures were detected in three patients with BTN, at 2 and 3 weeks post-MWA. These patients complained of abrupt neck swelling and pain; however, symptoms improved within 1–2 weeks after treatment with nonsteroidal anti-inflammatory drugs such as ibuprofen for 1 or 2 weeks; in both cases, the lesions gradually regressed without further treatment. Slight pain at the ablative site was reported by most patients on the first day after WMA. Four patients complained of transient hoarseness, but all recovered within 1 month. No hematoma or hypertension treated with medication was

TABLE 2 nodule characteristics and the effect on ablation procedure in different size

		Nodule diameters		
	Total	≤10 ml	10–30 ml	≥30 ml
No. of nodules	180	58	85	37
Mean duration of ablation(min)	14.7 ± 8.2	14.9 ± 6.5	15.3 ± 9.0	15.8 ± 9.5
Technical success	97.8% (176/180)	96.6% (56/58)	97.6% (83/85)	100% (37/37)
Total energy (kJ)	19.9 ± 12.1	20.2 ± 9.0	21.5 ± 14.5	17.4 ± 9.5
Nodule volume (ml)				
Baseline	21.2 ± 18.9	11.5 ± 4.7	15.1 ± 8.5	22.8 ± 8.2
1 month	10.6 ± 9.5*	7.5 ± 1.9*	11.4 ± 8.1*	27.9 ± 13.1*
3 months	6.2 ± 6.0*#	4.5 ± 1.7*#	6.7 ± 5.6*#	14.8 ± 10.9*#
6 months	3.9 ± 5.1*◆	3.0 ± 1.6*#◆	4.1 ± 3.8*#◆	10.1 ± 12.4*#◆
12 months	2.4 ± 3.2*#◆✪	1.2 ± 1.1*#◆✪	2.5 ± 3.0*#◆✪	5.6 ± 6.3*#◆✪
VRR (%)				
1 month	47.1 ± 20.2	40.6 ± 23.2	45.9 ± 20.9	42.2 ± 24.5
3 months	68.2 ± 18.1	61.1 ± 20.8†††	62.6 ± 22.0†††	58.8 ± 32.9†††
6 months	79.7 ± 15.9	74.6 ± 19.1†††	77.2 ± 17.5†††	74.0 ± 32.9†††
12 months	87.4 ± 12.3	84.7 ± 13.0†††	85.7 ± 15.3†††	86.6 ± 14.7†††

Note: Data of Nodule volume are median(minimum, maximum), the other data are means ± standard deviation.
Abbreviation: VRR, volume reduction rate.
*$p < 0.001$ versus baseline values respectively, #$p < 0.001$ versus 1 month values respectively, ◆$p < 0.001$ versus 3 month values respectively, ✪$p < 0.05$ versus 6 month values respectively. †††$p < 0.001$ versus VRR(%) at 1-month follow-up after ablation, respectively.

TABLE 3 Nodule characteristics and the effect on ablation procedure in different component

		Nodule diameters		
	Total	Solid	Predominant solid	Predominant cystic
No. of nodules	180	87	74	19
Mean duration of ablation(min)	14.7 ± 8.2	14.8 ± 7.7	15.2 ± 8.5	10.7 ± 7.4
Technical success	97.8% (176/180)	96.6% (84/87)	98.6% (73/74)	100% (19/19)
Total energy (kJ)	19.9 ± 12.1	20.2 ± 11.4	20.5 ± 12.9	14.2 ± 12.5
Nodule volume (ml)				
Baseline	21.2 ± 18.9	17.3 ± 15.2	24.4 ± 20.5	26.5 ± 2.4
1 month	10.6 ± 9.5*	9.7 ± 7.9*	11.8 ± 10.7*	9.7 ± 9.6*
3 months	6.2 ± 6.0*#	5.8 ± 5.0*#	6.8 ± 5.5*#	5.5 ± 5.3*#
6 months	3.9 ± 5.1*#◆	3.6 ± 2.6*#◆	4.4 ± 3.3*#◆	3.7 ± 4.6*#◆
12 months	2.4 ± 3.2*#◆✪	2.2 ± 2.1*#◆✪	2.5 ± 3.1*#◆✪	2.8 ± 3.9*#◆✪
VRR (%)				
1 month	47.1 ± 20.2	31.1 ± 26.9	38.5 ± 31.8	35.0 ± 34.3
3 months	68.2 ± 18.1	56.4 ± 22.2†††	65.2 ± 22.6†††	73.3 ± 17.3†††
6 months	79.7 ± 15.9	72.6 ± 19.6†††	78.3 ± 20.6†††	83.9 ± 10.8†††
12 months	87.4 ± 12.3	83.3 ± 15.8†††	87.4 ± 13.5†††	88.9 ± 10.1†††

*$p < 0.001$ versus baseline values respectively, #$p < 0.001$ versus 1 month values respectively, ◆$p < 0.001$ versus 3 month values respectively, ✪$p < 0.05$ versus 6 month values respectively, †††$p < 0.001$ versus VRR(%) at 1-month follow-up after ablation respectively.

TABLE 4 Univariate Relationship between preablation parameters and VRR

Variable	VRR (1 month)		VRR (3 months)		VRR (6 months)		VRR (12 months)	
	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value	OR (95% CI)	*p*-value
Sex								
Male	Reference							
Female	−0.2[a] (−0.3, 0.0)	0.0	−0.1 (−0.2, 0.0)	0.1	−0.1 (−0.2, 0.0)	0.1	−0.0 (−0.2, 0.1)	0.5
Age	0.1 (−0.1, 0.1)	1.0	0.1 (−0.2, 0.1)	0.5	0.1 (−0.2, 0.0)	0.3	0.1 (−0.2, 0.0)	0.1
Mean nodules diameters (cm)	−0.2[a] (−0.4, 0.0)	0.0	−0.1 (−0.2, 0.1)	0.2	−0.0 (−0.2, 0.1)	0.6	−0.0 (−0.2, 0.2)	1.0
Mean nodules volume (ml)	−0.2[a] (−0.4, 0.0)	0.0	−0.1 (−0.2, 0.1)	0.5	−0.0 (−0.1, 0.1)	0.9	0.0 (−0.1, 0.1)	0.7
Growth locations of nodules(right/left/isthmus)	0.1 (−0.1, 0.2)	0.3	0.1 (−0.1, 0.2)	0.4	0.1 (−0.1, 0.2)	0.4	0.1 (−0.0, 0.2)	0.2
Adjacent to tissue	0.0 (−0.1, 0.2)	1.0	0.1 (−0.2, 0.1)	0.4	−0.1 (−0.2, 0.1)	0.3	−0.1 (−0.2, 0.1)	0.4
Cyst component (%)	0.2[b] (0.1, 0.4)	0.0	0.3[b] (0.1, 0.4)	0.0	0.2[b] (0.1, 0.3)	0.0	0.1 (0.0, 0.2)	0.1
Solid	Reference							
Predominant solid	0.7[b] (0.6, 0.8)	0.0	0.5[b] (0.4, 0.8)	0.0	0.3[b] (0.2, 0.5)	0.0	0.2[b] (0.0, 0.3)	0.0
Predominant cystic	−0.3[b] (−0.5, −0.1)	0.0	−0.3[b] (−0.5,-0.1)	0.0	−0.3[b] (−0.5, −0.1)	0.0	−0.3[b] (−0.5, −0.0)	0.0
Shape								
Unregular	Reference							
Regular	0.0 (−0.1, 0.2)	0.6	0.1 (−0.1, 0.2)	0.5	0.1 (−0.1, 0.2)	0.4	0.0 (−0.1, 0.2)	0.7
Tumor capsule								
No	Reference							
Yes	−0.0 (−0.2, 0.1)	0.6	−0.0 (−0.2, 0.1)	0.7	−0.1 (−0.2, 0.1)	0.4	−0.1 (−0.2, 0.1)	0.3
CDFI grading	−0.0 (−0.2, 0.1)	0.8	−0.1 (−0.2, 0.1)	0.4	−0.1 (−0.2, 0.1)	0.3	−0.0 (−0.2, 0.0)	0.3
Ring-shape peripheral vascularity								
No	Reference							
Yes	−0.1 (−0.3, 0.0)	0.1	−0.2[a] (−0.3, 0.0)	0.0	−0.1 (−0.2, 0.1)	0.2	0.0 (−0.1, 0.2)	0.9
Ablation power(W)	−0.1 (−0.2, 0.1)	0.4	−0.1 (−0.2, 0.1)	0.2	−0.1 (−0.2, 0.0)	0.1	−0.0 (−0.3, 0.0)	0.8
Median duration of ablation(min)	−0.1 (−0.3, 0.0)	0.1	−0.1 (−0.2, 0.0)	0.2	−0.1 (−0.2, 0.1)	0.4	−0.0 (−0.2, 0.1)	0.7
Median ablation energy(kJ)	−0.1 (−0.2, 0.0)	0.2	−0.1 (−0.2, 0.0)	0.2	−0.1 (−0.2, 0.0)	0.3	−0.0 (−0.2, 0.1)	0.7
Ablation of ring-shape peripheral vascular								
No	Reference							
Yes	−0.0 (−0.3, 0.0)	0.1	−0.1 (−0.2, 0.0)	0.2	−0.1 (−0.2, 0.1)	0.3	0.0 (−0.1, 0.2)	0.9

[a]Correlation was significant at the 0.05 level.
[b]Correlation was significant at the 0.01 level.

TABLE 5 Multivariate Relationship between preablation parameters and VVR

Variable	VRR (1 month) OR (95% CI)	p-value	VRR (3 months) OR (95% CI)	p-value	VRR (6 months) OR (95% CI)	p-value	VRR (12 months) OR (95% CI)	p-value
Sex	0.0 (−0.1, 0.1)	1.0	−0.1 (−0.1, 0.0)	0.4	−0.1 (−0.1, 0.0)	0.3	0.1 (−0.1, 0.0)	0.2
Mean nodules diameters (cm)	0.1 (0.0, 0.1)	0.2	0.1 (0.0, 0.1)	0.5	−0.1 (−0.1, 0.0)	0.2	−0.1 (−0.1, 0.0)	0.3
Mean nodules volume (ml)	0.1 (0.0, 0.1)	0.3	−0.1 (−0.1, 0.0)	0.4	0.1 (0.2, 0.1)	0.3	0.0 (−0.4, 0.0)	0.5
Cyst component	0.2[a] (0.0, 0.0)	0.0	0.2[a] (0.1, 0.0)	0.0	0.2[a] (−0.1, 0.0)	0.0	0.1 (−0.1, 0.0)	0.2
CDFI grading	0.1 (0.0, 0.1)	0.2	0.1 (0.0, 0.1)	0.5	0.0 (−0.4, 0.0)	0.9	0.0 (−0.4, 0.0)	0.6
Ring-shape peripheral vascularity	−0.1 (−0.2, 0.0)	0.1	−0.1 (−0.1, 0.0)	0.4	0.0 (−0.4, 0.1)	0.9	0.0 (0.0, 0.1)	1.0

[a]Correlation was significant at the 0.05 level.
[b]Correlation was significant at the 0.01 level.

reported after ablation. No sedatives or antibiotics were given to any patients before or after ablation.

4 | DISCUSSION

Although most histologically benign BTNs do not require any intervention other than surveillance, some do become large and may cause obstructive and/or local pressure symptoms.[4–6] In that situation, surgery either in the form of lobectomy or total thyroidectomy as the most effective therapeutic option is recommended.[1,2] However, some patients do not wish to undergo surgery due to the risk of complications, the need for general anesthesia, high cost, and/or permanent loss of thyroid parenchyma.[3,7] Over the last few years, ultrasound (US)-guided minimally invasive treatment (MIT) (including chemical ablation and energy-based ablations) gained an increasing role in the management of BTNs.[20] Retrospective feasibility studies have focused on the effect of PEI in predominantly cystic nodules and thyroid cysts, in which PEI showed higher volume reduction in simple cystic nodules than predominant cystic nodules.[19] For solid, symptomatic, nonfunctioning, benign nodules, thermal ablation may be proposed as a first-line treatment(21).

To date, RFA, MWA, LA, and HIFU are mainly used for thermal ablation treatment for BTNs and have been yield effective results.[15,16,19,21,22] The effect of RFA on thyroid nodules has been reported in meta-analyses,[2,17] with statistically significant improvements in outcome (e.g., volume, symptoms, and cosmetic effects).[19] A comparison study between MWA and RFA in BTNs showed no significant difference in the duration of application, energy transmission, or volume reduction; however, MWA requires less shots to treat the whole nodule.[23]

In a multicenter study for LA treatment, four optical fibers were used for large volume nodules and the total energy delivery was increased according to the baseline size of the lesion to be ablated.[24]

Regarding HIFU, one single application is often less effective for causing shrinkage in larger-sized nodules[25]; two sequential applications were reported to have better treatment efficacy for large-sized nodules.[26]

Several studies have demonstrated that MWA showed good results in sufficient necrosis and subsequent nodule shrinkage in the treatment of BTNs with excellent VRRs of 82.5%–90.0% at 12-month follow-up and a low major complication rate of 6.6%.[23,27,28] In our study, we included a relatively large number of samples with 180 BTNs larger than 3 cm and performed a long-term observation with a median follow-up of 15.6 months. The MWA procedure with a single session (mean: 1.23 session) induced significant volume reduction with a safety outcome and favorable VRR (87.4%).

In our study, the method of aspiration of cyst liquid before MWA was used for BTNs. Aspirating the cyst liquid firstly may reduce the volume of nodules, which made the antenna fully contract the solid part of nodules and achieved more completion of tumor necrosis. In some cases, large nodules were close to one and/or two even several structures (trachea, esophagus, recurrent laryngeal nerve, carotid artery, and jugular vein). To overcome these limitations, the hydrodissection technique and real-time ultrasound guided ablation were the main protective measures. And the well experienced doctors with over 3–5 years of thermal ablation operation (Yu J, Cheng ZG, Han ZY, Liu FY, Liang P, Yu XL) guaranteed the good VRR effect and low complications. The ring-shaped vascular ablation method could lead to a similar effect with complete necrosis of the BTN capsule. In addition, MWA is known to cause increased tissue shrinkage compared with RF ablation; this may be an advantage when treating large tumors.[26,29]

From our research, we found that MWA is a safe and well-tolerated procedure. There was no significant morbidity and all patients underwent ablation successfully. According to our results, the initial BTN cyst component may serve as a predictor for the VRR effect of MWA for BTNs. Solid nodules indicate a lower VRR and less efficiency than predominantly solid and predominantly cystic nodules after MWA. As the cyst component percentage may decrease in proportion to the initial nodule volume, the efficacy of MWA ablation may be influenced by the initial volume of nodules.

This study had some limitations. Firstly, although the minimum 12-month follow-up period was achieved in all patients, a future study with a follow-up period of 3–5 years is warranted for BTNs. Second, this was only a single center study; thus, a multi-center randomized clinical trial with other techniques would be more convincing.

5 | CONCLUSION

In conclusion, we have shown that ultrasound-guided MWA is an effective and safe noninvasive treatment method for BTNs. However, prospective clinical trials with a longer follow-up period should be undertaken to evaluate the long-term effectiveness and safety and to define the spectrum of BTNs most suitable for this treatment.

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CONFLICT OF INTEREST

The authors declare that they have no conflict of interest.

ETHICS STATEMENT

This retrospective studies conducted on already available data or biological material, without any additional intervention (Medical Ethics Committee of The PLA General Hospital).

DATA AVAILABILITY STATEMENT

The data that support the findings of this study are available from the corresponding author upon reasonable request.

ORCID

Lei Huang https://orcid.org/0000-0003-4835-7909

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