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ORIGINAL ARTICLE

Radiofrequency ablation vs. microwave ablation for patients with benign thyroid nodules: a propensity score matching study

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Abstract
Purpose To compare the efficacy and the safety of radiofrequency ablation and microwave ablation for treatment of benign thyroid nodules using a propensity score matching study design.
Methods Two hundred and sixty patients with benign thyroid nodules were studied retrospectively, including 102 patients treated with radiofrequency ablation and 158 treated with microwave ablation. To reduce confounding bias due to retrospective assignment, propensity score matching was performed to balance the preablation data of the two groups. After matching, a total of 102 patient pairs (1:1) were created. The volume reduction ratio, therapeutic success rate, symptom and cosmetic score, and major complication were compared between the two groups at 1, 3, 6, and 12 months after treatment.
Results Between the well-matched groups, no significant differences were found in all nodule volume-related end points at 6 months (volume reduction ratio: 79.4 vs. 77.2 %, $P = 0.108$; symptom score: 2.1 vs. 1.9, $P = 0.456$; cosmetic score: 2.1 vs. 2.3, $P = 0.119$; therapeutic success rate: 99 vs. 97 %, $P = 0.621$) and 12 months (volume reduction ratio: 83.6 vs. 81.6 %, $P = 0.144$; symptom score: 1.5 vs. 1.5, $P = 0.869$; cosmetic score: 1.6 vs. 1.7, $P = 0.409$; therapeutic success rate: 100 vs. 100 %, $P > 0.99$) after treatment. No major complications occurred in either group ($P > 0.99$).
Conclusions With well-matched groups and consistent procedure design, our results demonstrated that the volume reduction ratio, therapeutic success rate, symptom and cosmetic score, and complications related to treatment for the two techniques are equivalent. Radiofrequency ablation and microwave ablation are both effective and safe methods in treating benign thyroid nodules.

Keywords Radiofrequency ablation · Microwave ablation · Thermal ablation · Benign thyroid nodule · Ultrasound

Introduction

Thyroid nodule (TN) is a common clinical problem [1]. Current guidelines suggest that asymptomatically benign nodules demonstrating modest growth (less than a 50 % change in volume) should be followed without intervention, however, some patients require treatment for compressive symptoms, cosmetic concerns or concern of a malignant change [2, 3]. Surgery is a well-established and effective treatment method for TNs [2, 4], but the associated complications such as bleeding, post-operation infection, and permanent recurrent laryngeal nerve palsy are found in 2–10 % candidates [5]. To reduce the invasiveness and improve the safety, minimally invasive non-surgical

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percutaneous ablation modalities including ethanol ablation (EA), radiofrequency ablation (RFA), microwave ablation (MWA), and laser ablation (LA) have gained increasing attention in recent years [6–12].

Although EA has been shown to be effective for predominantly cystic (cystic component >90 %) TNs with excellent volume reduction ratio (VRR) of 84–98.5 % [10, 11], its utility in solid nodules is limited due to seepage of ethanol causing serious complications such as Horner syndrome, recurrent nerve palsy, and neck hematoma [13]. On the other hand, thermal ablations, such as RFA and MWA, have been proven to be effective in inducing sufficient necrosis and subsequent nodule shrinkage in both cystic and solid TNs after one treatment session and had VRRs of 50.7–84 % [14, 15] and 46–88 % [9, 16], respectively.

With RFA and MWA applied worldwidely for benign thyroid nodule (BTN) treatment, whether one of them is superior to the other and can be the optimal option becomes a hot spot. However, no groups have accumulated sufficient clinical experiences using these two devices, and practice guidelines regarding the preferred ablation method are not available yet. We therefore carried out the first comparison study involving two tertiary centers to compare RFA with MWA for treating BTNs, in terms of effectiveness and complications related to treatment. The aim was to provide evidence to select a better and more appropriate device for ablation of BTNs for clinicians or patients under specific conditions.

Materials and methods

This study was conducted as a retrospective analysis in two tertiary centers and was approved by the institutional review boards of the hospitals. The requirement to obtain informed consent was waived because of the retrospective nature of the study, but a written informed consent was obtained from each subject before RFA or MWA after full explanation of the purpose and nature of the procedure used.

Patients

All patients were selected with the following inclusion criteria: (a) maximum diameter of the TN ≥2 cm; (b) mainly solid nodule (solid portion >50 %); (c) reports of compressive symptoms or cosmetic problems; (d) patient underwent one single treatment session of RFA or MWA; (e) cytologic confirmation of benign nature of the nodule with ultrasound (US)-guided fine needle aspiration cytology (FNAC) examination according to the American Bethesda System for Reporting Thyroid Cytopathology [17] and nodule without change on US at least 12 months; (f) serum levels of thyrotropin, thyroid hormone, and calcitonin within normal limits. The exclusion criteria were: (a) patient underwent a medication treatment or others for TNs after ablation; (b) patients with incomplete imaging data or follow-up time shorter than 6 months were also excluded.

Methods

Preablation assessment

Before ablation, conventional US (Figs. 1a and 2a), contrast enhanced ultrasound (CEUS), US-guided FNAC, and laboratory examinations were carried out, and the clinical status was evaluated. Four radiologists (W.S.R., Z.Y.L., L. F. and S.L.P., with thyroid US experience of 15, 10, 10, and 12 years, respectively) performed US and US-guided FNAC using a ML6-15 liner transducer (frequency range: 6–15 MHz) and a real-time US system (GE Logiq E9, GE Healthcare, WI, USA). TNs were carefully evaluated according to a uniform standard on size, US features, and solid portion (%). Three orthogonal diameters (the largest diameter and two other perpendicular ones) of TNs were measured. TN volume and VRR (%) were calculated according to the following formulas: TN volume $= \pi * a * b * c/6$ (where a is the largest diameter, b and c are the other two perpendicular diameters) and VRR (%) = [(baseline volume − final volume) * 100]/baseline volume. Laboratory tests included thyroid function test (i.e., serum concentrations of thyroid stimulating hormone, triiodothyronine, free thyroxine, and thyroglobulin), complete blood count, and blood coagulation test (activated partial thromboplastin time, prothrombin time).

Before ablation, every patient was asked to rate symptom on a 10 cm visual analog scale, and the physician recorded the cosmetic grade score (score 1, no palpable mass; score 2, nocosmetic problem but a palpable mass; score 3, cosmetic problem on swallowing only; and score 4, a readily observable cosmetic problem) [10].

Ablation procedures

Ablations were carried out by W.S.R. (with 6 years of experience in thyroid MWA) and L.F. (with 5 years of experience in thyroid RFA) in the two tertiary centers. Before the study, they were all trained for MWA or RFA with 10 cases. With patient placed in supine position, local anesthesia with 2 % lidocaine was performed on the puncture site. After a small incision (<2 mm in length) was made, under US guidance, a mixture of 2 % lidocaine and 0.9 % normal saline was infused into the surrounding thyroid capsule, a so-called "hydrodissection technique"

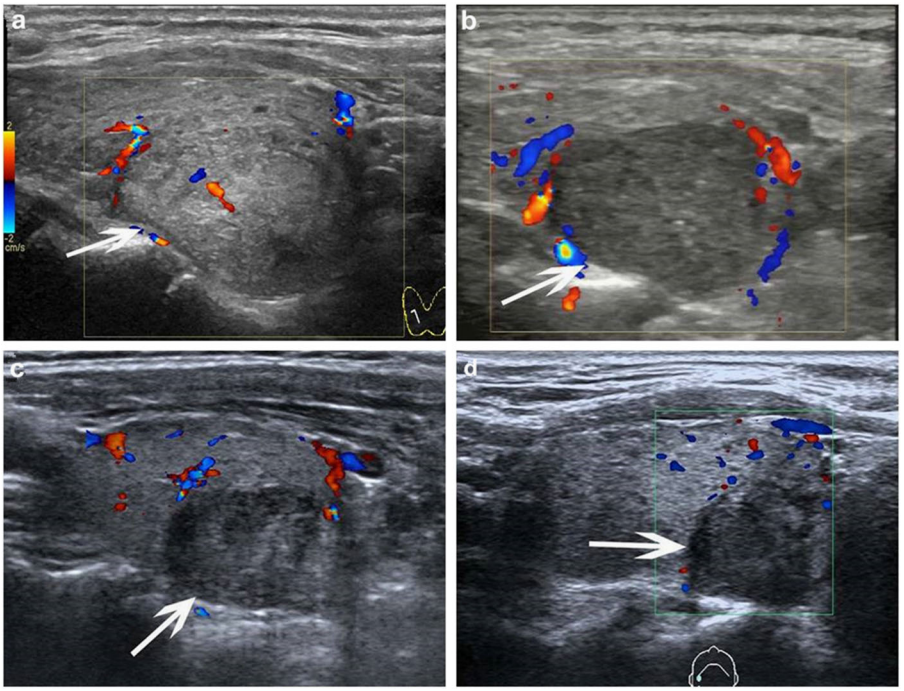

Fig. 1 Longitudinal ultrasound scans in a 53-year-old woman. **a** Ultrasound examination reveals a solid nodule (6.8 ml in volume) in the right thyroid gland before RFA. **b** One month after the ablation, the volume of the nodule decreases to 4.1 ml with a VRR of 39.7 % and the echogenicity of the nodule usually presents lower than that observed before ablation on the follow-up ultrasound examination. **c** Six month after the ablation, the volume of the nodule decreases to 1.8 ml with a VRR of 73.5 %. **d** Twelve month after the ablation, the volume of the nodule decreases to 1.6 ml with a VRR of 76.5 %

(Figs. 2b and 3), to provide a safe barrier for thermal damage to adjacent structures (carotid artery, trachea, esophagus, nerve) [9]. Then the MWA antenna or RFA electrode was inserted into the nodule along its short axis and positioned in the designated place (Fig. 2c). For patients with multiple nodules, only the largest nodule was subject to RFA or MWA treatment. Those patients formed the two treatment groups.

For RFA, a bipolar RFA instrument (Celon AG Medical Instruments, Teltow, Germany), consisting of an RF generator with a frequency of 470 KHz and maximum power output of 250 W was used. The bipolar RFA system is designed technically overcoming the disadvantages of use of grounding pads with monopolar RFA electrode such as skin burn or sweating during the procedure. According to the design specifications, bipolar RFA electrode can be classified into two types, 150-T09 (length of the conducting part: 9 mm, 18 gauge, 15-cm long, output power: 3–5 W) and 150-T20 (length of the conducting part: 20 mm, 15.5 gauge, 15-cm long, output power: 20–25 W). For 150-T20, an internally cooled electrode is provided with a peristaltic pump perfusing 0.9 % NaCl solution at 30 ml/min. The RFA system continuously measures the tissue resistance and power output stops automatically if resistance exceeds a specific limit (700 Ω) (Fig. 4). Both electrodes are the same in energy transmission: the high-frequency current flows between the two exposed portions of the tip of the bipolar electrode and the exposed portions are separated by an insulator at the tip. Then, the tissue surrounding the electrodes is heated up and the heat is conducted to the distant tissues. We used the electrode type of 150-T20 in all the RFA procedures in this study.

For MWA, a microwave system (KY-2000, Kangyou Medical Instruments, Nanjing, China) including a microwave generator, a flexible low-loss coaxial cable and an internally cooled shaft antenna, was used. The generator is designed with a frequency of 2450 MHz and a maximum output power of 100 W. The MWA antenna is 16-gauge. The antenna type (10 cm in total length, 1.6 mm in diameter, 3 mm in length of the active tip) is especially suitable for superficial organs. The internally cooled feature is provided with distilled water circulating through dual channels inside.

Compared with liver ablation, thyroid gland is relatively small, whereas TNs are usually large and spherical in shape and no safety margin is needed. The benign natures of the TNs also make the safety margin not necessary. Therefore, a"moving shot technique"method [14] was used consistently in the two centers. Each nodule was divided into multiple small conceptual units and was treated in a unit-by-unit manner by moving the antenna or electrode [14]. The conceptual units were made smaller on the periphery and much larger in the central portion of the nodule. The tip of the antenna or electrode was initially positioned in the deepest portion of the nodule, which enabled easy monitoring of the tip without disturbance caused by hyperechoic cloud from the gas generated during the ablation procedures. According to the manufacturer's suggestion and previous studies [7, 9, 16], ablation power was set at 20–35 W for MWA, and 20–25 W (150-T20) for RFA.

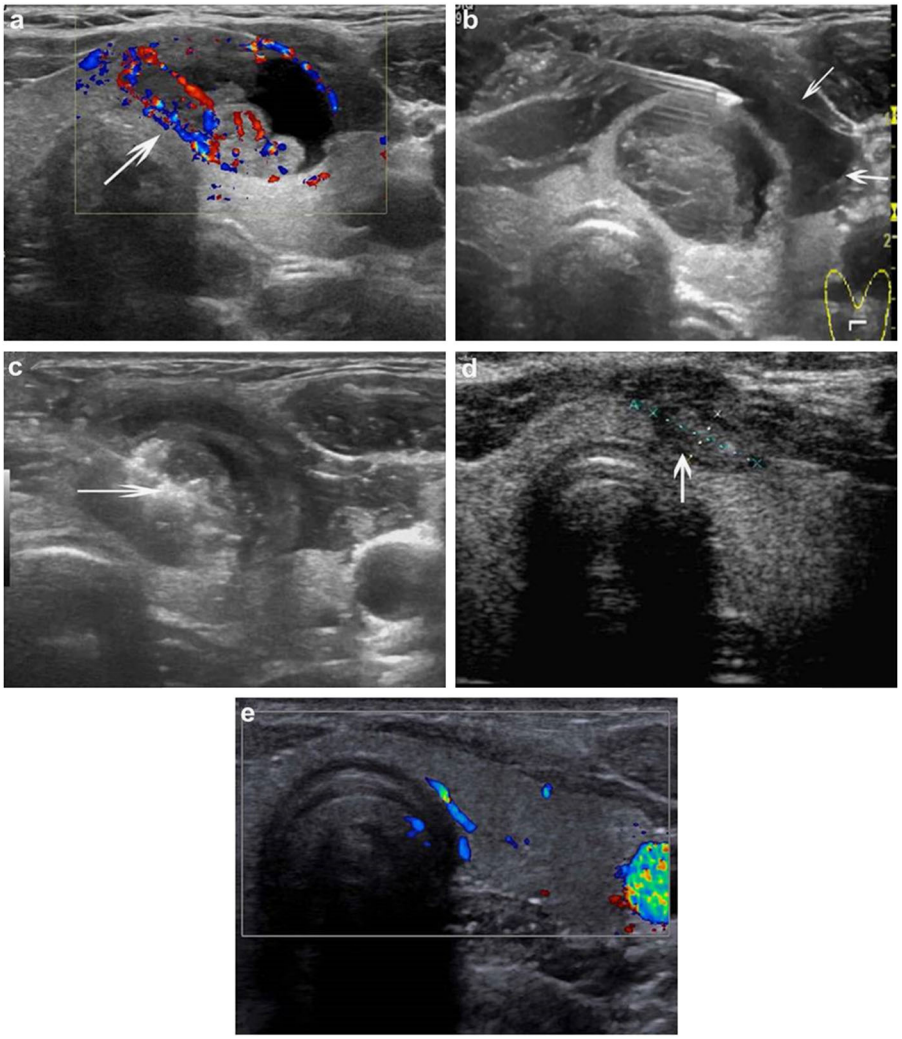

Fig. 2 Transverse ultrasound scans in a 56-year-old woman. **a** Ultrasound examination reveals a cyst-solid mixed nodule (solid portion: 81.7 %; volume: 3.9 ml) in the left thyroid gland before MWA. **b** The "hydrodissection technique" (*arrow*) method is applied in the MWA procedure. **c** During MWA, the MWA antenna could always be clearly visualized with real-time ultrasound as a hyperechoic line. Ultrasound obtained during treatment shows typical hyperechoic region (*arrow*) surrounding microwave antenna (16G). **d** TN (*arrow*) shows marked decrease in size (0.3 ml in volume, 7.7 % of original) at 6-month follow-up. **e** At another follow-up of this patient approximately 16 months later, we cannot find any evidence of tumor with no scar at the previous tumor site

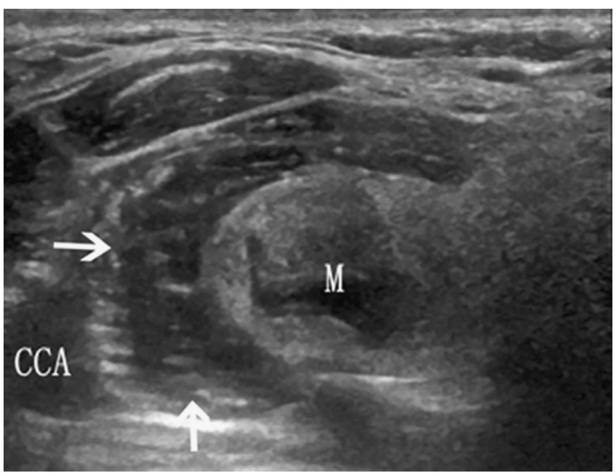

Fig. 3 Under ultrasound guidance, a mixture of 2 % lidocaine and 0.9 % normal saline is infused into the surrounding thyroid capsule—a so-called "hydrodissection technique" to provide a safe thermal barrier to ablation energy (*arrow*). CCA, common carotid artery; M, tumor

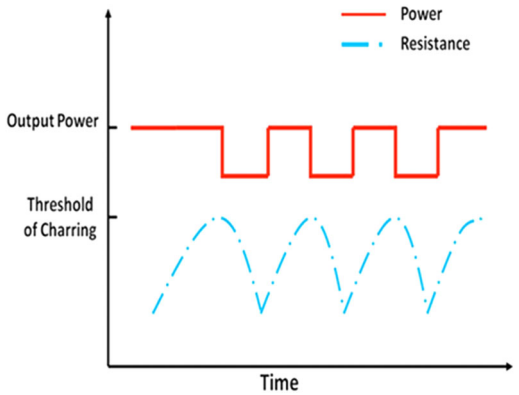

Fig. 4 Schematic illustrates the automatic power control design feature of the bipolar RFA device used in this study. As tissue dehydrates during RFA with an output power of an fixed value, its resistance increases continuously. Once the resistance reaches the threshold of charring, power output will be stopped automatically and the coagulation process will be ended which may induce a precise controllable effect in the tissue

The ablation procedures were monitored by real-time US, and ablations were not terminated until the transient hyperechoic cloud caused by the gas covered all units of the nodule. Procedure-related pain was graded into four categories (grade 0, no pain experienced during ablation; grade 1, mild tolerable pain with no need to turn off the power output; grade 2, ablation power was turned off one or more times because of pain; and grade 3, ablation was incompletely terminated because of severe pain). All patients were closely observed for 20–30 min after treatments.

Postprocedural follow-up

US assessments including gray scale US and color Doppler US were performed in the same manner as before at 1, 3, 6, and 12 months after treatment and every 6 months thereafter (Figs. 1b–d, 2d, e). Also the cosmetic and symptoms scores and thyroid function test (i.e., serum concentrations of thyroid stimulating hormone, triiodothyronine, free thyroxine, and thyroglobulin) were evaluated at each follow-up visit. Furthermore, local therapeutic efficacy was assessed with CEUS at 1 month, and complete ablation was defined as absence of contrast enhancement by CEUS in the ablated area. Additional ablations were applied for unsuccessfully treated nodules. Therapeutic success was defined as a VRR greater than 50 % [10]. Any adverse event (i.e., voice change, skin burn, fever, hyperthyroidism, hypothyroidism, etc.) that occurred during follow-up period was also addressed. Minor and major complications were recorded based on those specified by the Society of Interventional Radiology [18].

Statistical analysis

The primary end point of this study was the VRR (%) at 1, 3, 6, and 12 months after treatment; the secondary end points consisted of therapeutic success rate, improvement of cosmetic and symptom score, and major complication. To reduce confounding bias due to nonrandomized retrospective assignment, propensity score matching was performed to balance the preablation data of the two groups. The propensity score is the conditional probability of receiving an exposure given a vector of the measured covariates [19]. In our study, propensity scores for all the patients were estimated by multiple logistic-regression models using the following baseline characteristics as covariates: sex, age, nodule solid portion (%), macrocalcification, nodule diameter, volume, follow-up period, symptom, and cosmetic score. Before matching, the mean propensity score was 0.535 for patients in the RFA group ($n = 102$) and 0.655 for patients in the MWA group ($n = 158$), with a standardized difference of 11.9 % ($P < 0.001$). We matched all 102 patients in the RFA group with 102 patients (1:1) in the MWA group using the nearest neighbor method. After matching, the mean propensity score was 0.535 for patients in the RFA group ($n = 102$) and 0.591 for patients of the MWA group ($n = 102$), with a standardized difference of 5.6 % ($P = 0.101$). Standardized difference was used to evaluate the balance of all baseline covariates between the two groups before and after the propensity score matching. Our propensity score model was discriminated effectively and well calibrated between patients who underwent RFA and MWA at baseline. Before and after the 1:1 matching, qualitative variables were analyzed using χ^2 test or Fisher's exact test. Normal distribution quantitative data were compared by means of one-way analysis of variance. Skew distributional data were analyzed using Mann–Whitney U test. Bivariate correlation test was used to examine relationship between VRR and baseline volume. Power analysis, with a one-sided $\boldsymbol{\alpha}$ level set at 0.05 and an acceptable difference set as 8 % for the VRR [10, 20], was performed to evaluate whether our resultant sample size had the sufficient magnitude to show an equivalence of MWA to RFA. Statistical analyses were performed by using the SPSS software (version18.0; SPSS, Chicago, IL, USA), SPSS Sample Power (version3.0; IBM, USA), and PASS (version 11.0; NCSS, USA). The significance level was defined as P value of less than 0.05.

Results

Baseline characteristics

From June 2012 to October 2015, 372 patients with BTNs were treated with percutaneous thermal ablations in the two tertiary centers (Fig. 5). Among them, 260 patients who had undergone percutaneous thermal ablations were included and were classified into RFA group ($n = 102$) or MWA group ($n = 158$) according to the initial treatment strategy. Baseline clinical and demographic parameters are shown in Table 1. Due to the inevitable selection bias, compared with patients in the MWA group, those in the RFA group had a higher prevalence of solid portion (%) nodules, lower age, less calcification, larger tumor diameter, higher cosmetic, and symptoms scores. After performing propensity score matching for the entire population, a total of 102 matched patient pairs were created (Table 1). The RFA group consisted of 75 women (mean age, 46.7 years; age range, 19–69 years) and 27 men (mean age, 44.8 years; age range, 24–68 years). The MWA group consisted of 74 women (mean age, 49.3 years; age range, 21–66 years) and 28 men (mean age, 47.7 years; age range, 23–70 years). At enrollment, clinical or TN characteristics did not differ significantly between the propensity-matched groups.

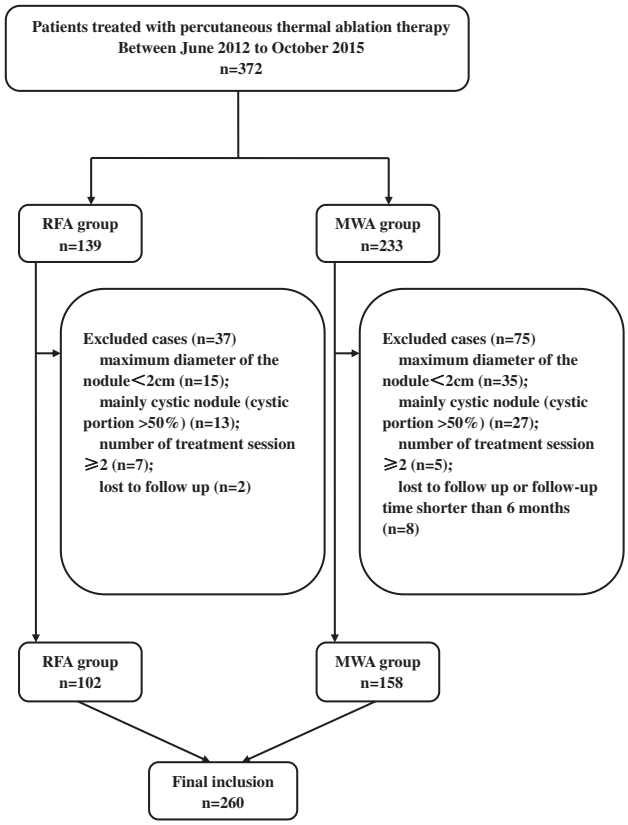

Fig. 5 Flowchart summarizes patient inclusion. RFA Group, patients treated with radiofrequency ablation, MWA Group, patients treated with microwave ablation

Treatment outcomes

The average follow-up was 10.7 months for the RFA group and 10.6 months for the MWA, 41 (40.2 %) and 45 (44.1 %) patients were followed up for more than 1 year in the RFA and MWA groups, respectively. Treatment results of the two groups are summarized in Table 2. In regard to the primary end point, VRRs of the RFA group were 79.4 ± 8.6 % at 6 months (Fig. 1c) and 83.6 ± 5.2 % at 12 months (Fig. 1d), and those of the MWA group were 77.2 ± 10.8 % at 6 months (Fig. 2d) and 81.6 ± 8.8 % at 12 months. There were no significant differences between two groups ($P = 0.108$ and $P = 0.144$, respectively) with power of 99.7 and 89 %, respectively.

In regard to the secondary end points, at 6 months after treatment, the therapeutic success rate of the RFA group was 99 % (101/102) and that of the MWA group was 97 % (99/102) ($P = 0.621$). While at 12 months, all patients studied in both groups achieved therapeutic success in which there was no significant difference ($P > 0.99$). In the RFA group, the symptom score decreased significantly from 4.5 ± 1.4 to 2.1 ± 1.3 at 6-month follow-up and to 1.5 ± 1.0 at 12-month follow-up (both $P < 0.001$) (Fig. 6a), and in the MWA group it decreased from 4.3 ± 1.3 to 1.9 ± 1.5 and to 1.5 ± 0.9 at 6-month and 12-month follow-up, respectively (both $P < 0.001$) (Fig. 6b). In the RFA group, cosmetic score decreased from 3.1 ± 0.8 to 2.1 ± 1.1 at 6-month follow-up and to 1.6 ± 0.9 at 12-month follow-up (both $P < 0.001$), and in the MWA group it decreased from

Table 1 Baseline characteristics of patients with TNs treated with radiofrequency and MWA before and after matching

Characteristics	Before matching			After matching		
	RFA group $n = 102$	MWA group $n = 158$	P value	RFA group $n = 102$	MWA group $n = 102$	P value
Age (y)	46.4 ± 13.3	50.8 ± 10.1	0.002	46.4 ± 13.3	49.5 ± 10.2	0.061
Sex			>0.99			>0.99
Male	27 (26.5)	42 (26.6)		27 (26.5)	28 (27.5)	
Female	75 (73.5)	116 (73.4)		75 (73.5)	74 (72.5)	
Solid portion (%)	86.5 ± 15.3	82.1 ± 14.6	0.019	86.5 ± 15.3	84.9 ± 14.5	0.433
Macrocalcification			0.003			>0.99
Yes	15 (14.7)	49 (31.0)		15 (14.7)	17 (16.7)	0.848
No	87 (85.3)	109 (69.0)		87 (85.3)	85 (83.3)	
Nodule diameter(mm)[a]	28.1 (24.0–35.2)	26.0 (23.0–32.0)	0.014	28.1 (24.0–35.2)	28.0 (24–34.9)	0.52
Nodule volume (ml)[a]	5.7 (3.8–10.3)	4.6 (3.4–8.5)	0.067	5.7 (3.8–10.3)	5.5 (3.5–9.6)	0.527
Symptoms score	4.5 ± 1.4	4.1 ± 1.3	0.011	4.5 ± 1.4	4.3 ± 1.3	0.419
Cosmetic score	3.1 ± 0.8	2.9 ± 0.8	0.004	3.1 ± 0.8	3.0 ± 0.8	0.376
Follow-up period (mo)	10.7 ± 5.1	10.5 ± 2.8	0.684	10.7 ± 5.1	10.6 ± 2.8	0.85

Note: RFA group, patients treated with radiofrequency ablation; MWA group, patients treated with microwave ablation; Except for nodule diameter, nodule volume and P values, data are reported as No. (%) or mean ± standard deviations

[a] Data are with skewed distribution and are reported as median with the inter-quartile range in parentheses and analyzed using Mann-Whitney U test

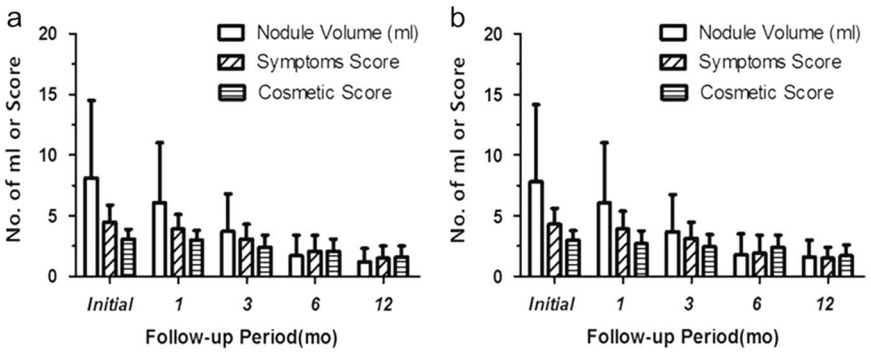

Fig. 6 **a** Efficacy of RFA. Graph shows the volume of TN, symptom and cosmetic scores before ablation and at the 1-month, 3-months, 6-months, and 12-months follow-up. Significant decreases in nodule volume, symptom and cosmetic scores (all $P < 0.001$) were observed at the 12-months follow-up visit. **b** Efficacy of MWA. Graph shows the volume of TN, symptom and cosmetic scores before ablation and at the 1-month, 3-months, 6-months, and 12-months follow-up. Significant decreases in nodule volume, symptom and cosmetic scores (all $P < 0.001$) were observed at the 12-months follow-up visit

3.0 ± 0.8 to 2.3 ± 1.0 and to 1.7 ± 0.9 at 6-month and 12-month follow-up, respectively (both $P < 0.001$). There were no significant between-group differences in symptom or cosmetic score at 6-month or 12-month follow-up ($P = 0.456$, $P = 0.119$, $P = 0.869$, and $P = 0.409$, respectively). Energy deposition per milliliter (EDPM) during RFA or MWA was calculated with the following equation: EDPM (J/ml) = OP * AT/V, where OP is output power in watts, AT is ablation time in seconds, and V is the baseline volume in milliliter (ml). For the RFA and MWA groups, the EDPM were 6444.2 and 6708.1 J/ml ($P = 0.216$), respectively.

During and after ablation, the degree of pain was grade 1 ($n = 101$) and grade 2 ($n = 1$) in RFA group and grade 1 ($n = 100$) and grade 2 ($n = 2$) in MWA group. Four (3.9 %) patients of the RFA group and 5 (5.9 %) patients of the MWA group complained of hoarseness, all recovering within 3 months spontaneously. A mild sensation pain was experienced by most patients, whereas no one asked to stop the procedure and no procedure-related major complications occurred in either group ($P > 0.99$). Results of laboratory studies were normal in all patients at 6-month follow-up.

Factors related to the treatment outcomes

Bivariate correlation analyses between 6 months VRR and baseline volume in the MWA and RFA groups showed that the correlation coefficient were 0.076 ($P = 0.498$) and 0.060 ($P = 0.593$), respectively. Thus VRR was not associated with the baseline volume statistically in either group. According to the location of nodules and the preference of radiologists, ablations can be conducted through lateral cervical approach (LCA) or median line approach (MLA) (Fig. 7). The RFA group consisted of 53 patients using LCA and 49 patients using MLA. The MWA group consisted of 67 patients using LCA and 35 patients using MLA ($P = 0.064$). For the 120 nodules treated with LCA, the mean VRR was 78.7 ± 9.7 % at 6 months, and that of the 84 nodules treated with MLA was 77.7 ± 10.0 % ($P = 0.496$). However, in the MWA group 4 patients who complained of transient hoarseness were treated with the MLA ablation method and another 1 patient was LCA ($P = 0.046$).

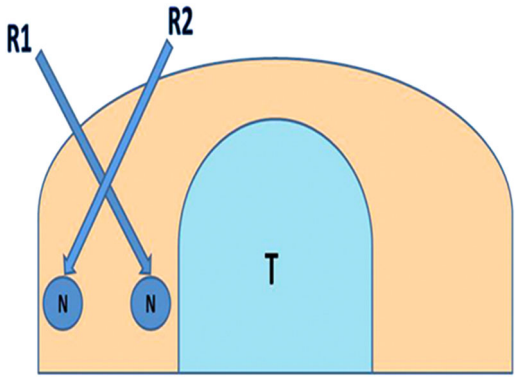

Fig. 7 On transverse scan, the thyroid gland can be divided into four quadrants. For nodules located in the lower-inner quadrant, ablations are conducted through the LCA (R1), but for nodules located in the lower-outer quadrant, the MLA ablation therapies are used (R2). For nodules located in the other two quadrants, either approach was acceptable. The core principle of the puncture route we adopted is not only that the RF electrode or MW antenna could be percutaneously inserted into the nodule and positioned in the designated place, but that injury of major structures (i.e., carotid artery, trachea, esophagus) could also be avoided. T, trachea; N, thyroid nodule

Discussion

Our study showed that RFA and MWA were both effective and safe techniques in treating BTNs. There were no significant differences in VRR, therapeutic success rate or cosmetic and symptom score improvement between two techniques, and neither procedure was associated with major complications.

Bipolar RFA device is shown to be associated with a feature of automatic power control. As tissue dehydrates during RFA with an output power of an fixed value, its resistance increases continuously, and once the resistance reaches the threshold of charring, power output will stop automatically and the coagulation process will end, which

Table 2 Treatment results in the RFA and MWA groups in a propensity-matched population of patients with TNs

Parameter	RFA group	MWA group	*P* value
Primary end point			
VRR at 1 month (%)	24.0 ± 5.9	22.3 ± 9.1	0.121
VRR at 3 months (%)	55.0 ± 6.4	52.7 ± 10.1	0.065
VRR at 6 months (%)	79.4 ± 8.6	77.2 ± 10.8	0.108
VRR at 12 months (%)	83.6 ± 5.2	81.6 ± 8.8	0.144
Secondary end points			
Symptom score at 6 months	2.1 ± 1.3	1.9 ± 1.5	0.456
Cosmetic score at 6 months	2.1 ± 1.1	2.3 ± 1.0	0.119
Therapeutic success rates at 6 months (%)[a]	99	97	0.621
Symptom score at 12 months	1.5 ± 1.0	1.5 ± 0.9	0.869
Cosmetic score at 12 months	1.6 ± 0.9	1.7 ± 0.9	0.409
Therapeutic success rates at 12 months (%)[a]	100	100	>0.99
Major complications	None	None	>0.99

Note: RFA group, patients treated with radiofrequency ablation; MWA group, patients treated with microwave ablation; Except for therapeutic success rates, major complications, and *P* values, data are reported as mean ± standard deviations

[a] Therapeutic success is defined as volume reduction greater than 50 %

may induce a precise controllable effect in the tissue. Compared with MWA, RFA has significant superiority in design, making it possible to improve the efficacy and reduce the complications. On the other hand, MWA device can be an attractive alternative to RFA device because of the less "heat sink"effect (local cooling of thermal process) [21]. Actually, the "heat sink" effect during liver ablation is caused by major intrahepatic vessels including portal vein and hepatic veins [22, 23], and because there are few major vessels in and around the thyroid gland, TN ablation is thus less susceptible to "heat sink" effect. This was confirmed by Jeong et al. and Yue et al. and they even suggest that RFA might be superior to MWA regarding VRR (91.06 vs. 82.3 %) [9, 14] in their studies with more than 200 patients. However, these previous studies were somewhat limited by the different baseline characteristics and inconsistent therapeutic process, and thus direct comparison of these results is not available yet. Given that usually the output power used in the MWA procedure is higher than that in the RFA procedure and thus the tissue surrounding the MW antenna will be heated up more quickly. In addition, thyroid gland is relatively small, whereas TNs are usually large and spherical in shape and no safety margin is needed. The benign natures of the TNs also make the safety margin not necessary. Compared with "multiple fixed shot", the moving shot technique would be more controllable and safer since it reduces the heat deposition and thus reduces the possible damage to adjacent critical structures. Therefore, in our study, a consistent procedure design—"hydrodissection technique" and "moving shot technique" [9] was applied, and the results showed that VRR of RFA group did not differ significantly from that of MWA group (79.4 vs. 77.2 % and 83.6 vs. 81.6 % at 6-month and 12-month follow-up) in a propensity-matched population. In this study, one single session of RFA or MWA did not only achieved nodule volume reduction, but was also therapeutically successful, as it achieved a volume reduction greater than 50 % in most of the patients (99 vs. 97 %) at 6-month follow-up, but there were no significant between-group differences. This was unexpected, and whether this equivalent result is directly associated with the technique itself or whether it is effected by other factors that affect treatment response remains unknown. However, this finding highlighted an equal role of RFA and MWA when giving medical care to patients with BTNs.

Moving MW antenna or RF electrode tip unit-by-unit allows the entire tumor to be treated safely, which is essential for preventing marginal regrowth and achieving a significant nodule volume reduction. Consistent with it, using the moving shot technique, a recent study showed that all nodules had VRRs of more than 50 % after 6 months of the RFA procedure [24] and that was in line with our results. The similar excellent results of our study may also be related to the similar modified internally cooled design of the two devices that could prevent tissue charring and improve radius of ablation energy deposition [25].

Overall, the factors that seem to affect treatment response include nodule volume [10], initial solidity, and functionality [26]. Among these factors, the EDPM has been advocated as the most important factor contributing to long-term shrinkage. In this study there were no significant differences between two groups in the type of EDPM of thyroid tissue. The majority of effect of energy transmission in tissue at RFA is caused by thermal conduction [27].

In comparison, MWA has a much larger area of active heating [28], with the zone of active heating being a function of the wave length of the applied energy. Although the effect of energy transmission in tissue between MWA and RFA is somewhat different [29], compared with MW antenna used in the treatment of abdominal tumors, the MW antenna used in this study has been improved: the total length has been shortened from 20 to 10 cm, and the radiating segment has been narrowed from 11 to 3 mm [9], which will reduce the zone of active heating and narrow the differences between MWA and RFA. Secondly, the ablation power was set at 20–35 W for MWA, and 20–25 W for RFA, so there is not much difference between MWA and RFA in terms of the ablation power that plays an important role in the velocity of heat generation and thus has essential effect on temperature field establishment, making differences in thermal effect between MWA and RFA in this study smaller. In addition, compared with the blood vessels such as hepatic vein and protal vein in the liver, those in the thyroid are much smaller, which will reduce the heat sink effect from the blood vessels on RFA. However, it may be worth noting that although MWA has less "heat sink" effect than RFA during treatment in patient with liver tumor, several studies have shown that there is no statistically significant difference in efficacy and safety between two procedures [30, 31]. Therefore, a consistent procedure design of "ablation power setting", "hydrodissection technique", and "moving shot technique" was applied in the well-matched treatment groups. These might be the possible reasons for why there is no difference in results between the two groups.

Previous studies have reported various complications (i.e., voice change, skin burn, fever, etc.) related to RFA and MWA [7, 9, 14, 15]. RFA studies showed 0–3.3 % cases were associated with recurrent laryngeal nerve injury [14, 15, 20], and the rates were 0–9.1 % for MWA [7, 9, 16]. In our study, all patients tolerated well and no major complications occurred. Four (3.9 %) patients of the RFA group and 5 (5.9 %) patients of the MWA group complained of voice changes, thus the incidence was not very different from other available data. Moreover, our study showed that LCA could lower the rate of complications when used in MWA procedure, but not for RFA. The difference was difficult to explain and it might rely on differences in mechanisms of the two devices. The mechanism of RFA is that the electrode transmits alternating current into tissue, causing significant ionic agitation and intratumoural hyperthermia [32]. In comparison, for MWA intratumoural hyperthermia depends directly on the high-speed motion of polar molecule under microwave field [33], acquiring a faster ablation time and consistently higher intratumoral temperature. Compared with RFA, the peculiarly thermogenic feature of MW technology makes it need hydrodissection more. And in fact, in the procedure of LCA ablation, in order to avoid injury of major structures (i.e., carotid artery, trachea, esophagus), a more fully "hydrodissection technique" was usually used than the MLA ablation therapy, and that might lead to the lower rate of complications. So this finding emphasized a higher priority of LCA, especially for MWA. However, our study showed that the adverse event rates of MWA were inconsistent with RFA and that may be due to the fully hydrodissection used in most of the MWA procedures. Or, our study suggest that if given full preparation MWA can work just as well as RFA.

This study had several limitations. First, the retrospective nature of this study could not avoid selection bias. Although propensity score-matched analysis was performed to adjust for potential confounding factors, it not only does not correct for unknown or unmeasured variables but also does not overcome initial selection bias. Second, the same sample size of 102 in each group might not be able to provide sufficient information about differences between the ablation technologies and this study involved two tertiary centers, one center focused on MWA, the other RFA, thus different doctors for the two techniques might affect the treatment efficacy. So a fair comparison would be needed basing on a prospective randomized controlled study additionally in long-term follow-up studies. Despite all of the above limitations, this study showed the first comparison result between both techniques and constituted available evidence for MWA and RFA treatment efficacy of BTNs. Also the study showed the first result about the effect of puncture route on treatment outcomes.

Theoretically, MWA has less heat sink effect and is more powerful in comparison with RFA. However, with well-matched treatment groups and consistent ablation procedure design, our results demonstrate the VRRs, therapeutic success rates, symptoms and cosmetic scores, and complications related to treatment for the two techniques are equivalent. MWA and RFA are both effective and safe methods in treating BTNs.

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Compliance with ethical standards

Conflict of interest The authors declare that they have no competing interests.

Informed consent For this type of study, formal consent is not required.

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