Artery-first microwave ablation in the treatment of benign thyroid nodules

Gulşah Yildirim^{A-F}, Hakki Muammer Karakas^{A,C,E,F}

Department of Radiology, Istanbul Fatih Sultan Mehmet Training and Research Hospital, Turkey

- A research concept and design; B collection and/or assembly of data; C data analysis and interpretation;
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Address for correspondence

Gulşah Yildirim E-mail: dr.gulsah.yildirim@gmail.com

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Abstract

Background. Microwave ablation (MWA) is a safe and effective procedure for the treatment of benign thyroid nodules. The MWA causes progressive nodule shrinkage as well as the improvement of the symptoms and cosmesis. Some basic techniques have been described to further increase the efficacy and safety of this procedure.

Objectives. To evaluate the efficacy of artery–first MWA as an advanced technique in the treatment of benign thyroid nodules.

Materials and methods. A total of 40 patients treated with MWA were enrolled in the study. Nineteen patients who underwent artery-first MWA were selected for the study group and 21 patients who underwent MWA alone were included in the control group. Nodular vascularization was assessed using a new Doppler technique (Superb Microvascular Imaging (SMI)) and characterized using a 3-point scale. All patients were evaluated in terms of volume, symptoms, cosmetic scores, and laboratory findings before the procedure as well as 3 months (early-term follow-up) and 6 months (intermediate-term follow-up) after the procedure.

Results. Both groups were comparable with respect to the baseline volume (p = 0.135). Nevertheless, the nodular volume reduction rate was significantly different at 3-month follow-up (study group: $56.97 \pm 11.39\%$, control group: $47.07 \pm 7.93\%$; p = 0.003) and 6-month follow-up (study group: $78.38 \pm 8.91\%$, control group: $69.54 \pm 9.41\%$; p = 0.004). In both groups, cosmetic and symptom scores decreased progressively (p < 0.005) and there were no major complications. Thyroid hormones and antibodies were within normal limits before the procedure, and no significant change was observed during follow-up after the ablation.

Conclusions. The artery-first MWA technique can be used in the treatment of benign thyroid nodules as a method of increasing the effectiveness of MWA.

Key words: thyroid nodule, microwave/therapeutic use, ablation techniques, ultrasonography/interventional

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Background

Thyroid nodules are common in the adult population and their prevalence depends on the diagnostic method used (ultrasound (US): 20-70%, physical examination: 4–7%, autopsy: 8–65%). A widespread use of imaging techniques has revealed an epidemic of incidental nonpalpable thyroid nodules. Most nodules are cytologically benign and do not warrant treatment. However, the nodules may grow, leading to symptoms by compressing the surrounding anatomical structures as well as causing cosmetic problems. Previously, the standard treatments of choice for benign thyroid nodules were total thyroidectomy and levothyroxine therapy. However, for patients with benign nodules that cause pressure symptoms and/or cosmetic concerns, current guidelines recommend thermal ablation as a cost- and risk-effective alternative to surgery or observation alone, without causing hypothyroidism or surgical complications.²

Among thermal ablation methods, microwave ablation (MWA) has been proven to be a safe and effective option for the treatment of thyroid nodules.³ It uses electromagnetic radiation to heat the tissue and dielectric hysterics to produce the heat. The MWA provides several advantages in comparison to the other heat-based modalities. It is less susceptible to local differences in impedance and vascular cooling by the heat sink effect, and produces faster heating and higher temperatures, resulting in a larger ablation volume in contrast to radiofrequency ablation (RFA).⁴

Several studies compare MWA with other methods; there are also studies comparing different MWA devices (i.e., cooled, uncooled). $^{2-4}$ In these studies, the efficacy was determined by a reduction in nodular volume after treatment. There are many predictive factors that affect volume reduction rates (VRRs), such as initial nodule volume, functional autonomy, components of the nodules, and energy delivery. In order to increase the efficacy and safety of the ablation procedure, some basic techniques have been proven to be efficacious, including the trans-isthmic approach, the moving shot technique and the overlapping technique. In addition, the artery-first nodular ablation technique, which was developed for RFA and has had efficacy studies conducted, is used as an advanced technique in the treatment of benign thyroid nodules. However, to our knowledge, there have not been any reports validating the efficacy of this technique in MWA.

Objectives

The objective of this study was to investigate the effects of intra-arterial MWA before nodular ablation on volume reduction and clinical improvement in the treatment of benign thyroid nodules.

Materials and methods

Patients

The study was approved by the Institutional Review Board of the Istanbul Fatih Sultan Mehmet Training and Research Hospital, Turkey (approval No. 17073117_050.06_050.06). Informed consent was obtained prior to the study and all patients were informed about the procedure.

In this retrospective study, 40 patients who underwent 1 session of nodular MWA or artery-first nodular MWA from September 2019 to June 2021 were included, and a total of 40 benign thyroid nodules were evaluated. The cohort was divided into 2 groups: a study group, which consisted of 19 patients who were treated with artery-first MWA, and a control group of 21 patients who underwent MWA alone. The artery-first MWA technique was performed on hypervascularized nodules when the feeding artery could be clearly identified. The baseline characteristics of the patients in both groups are summarized in Table 1.

Table 1. Comparison of demographic and clinical characteristics of patients

Parameter	Control group (n = 21)	Study group (n = 19)	p-value	
Age, mean ±SD	46.05 ±10.43	43.47 ±10.24	0.437ª	
Male	9 (42.9)	9 (47.4)	0.774 ^b	
Female	12 (57.1)	10 (52.6)		
Right	9 (42.9)	8 (42.1)	0.621b	
Left	10 (47.6)	7 (36.8)	0.631 ^b	
Istmus	2 (9.5)	4 (21.1)		
Solid	18 (85.7)	17 (89.5)	1.000 ^b	
Mainly solid	3 (14.3)	2 (10.5)		

^a t-test for independent samples; ^b Fisher's exact test; SD – standard deviation.

The inclusion criteria included: 1) over 18 years of age and not pregnant; 2) benign thyroid nodules proven after 2 different US-guided fine-needle aspiration biopsies (according to the American Bethesda System for Reporting Thyroid Cytopathology); 3) solid or mainly solid nodules (solid component >80%) on US; 4) presence of subjective compressive symptoms (dysphagia, dysphonia, dyspnea, foreign body sensation, etc.) or cosmetic concerns; and 5) normal thyroid function. The exclusion criteria were: 1) retrosternal excessive growth; 2) presence of US findings indicating a malignant nodule despite benign results of biopsies; 3) incomplete US or laboratory data; and 4) follow-up time shorter than 6 months.

Equipment and pre-ablative assessment

Sonograms of all nodules were performed using the Aplio 500 ultrasound system (Toshiba Medical Systems, Tokyo, Japan) with a broad bandwidth linear array transducer (imaging frequency: 14 MHz). First, a grayscale US was performed to evaluate the size, volume, composition, and characteristics (echogenicity, shape, margin, etc.) of the nodules. The maximum diameter (A) and 2 vertical diameters (B and C) were measured and the nodular volume was calculated using the following equation:

volume =
$$(A \times B \times C)/2$$

Next, color Doppler (CD), power Doppler (PD), and monochrome and color Superb Microvascular Imaging (SMI) were performed to evaluate the vascularity of the nodules. Monochrome and color SMI were included in the pre-procedural vascular examination because the microvascular flow was provided in greater detail compared to CD and PD.5 This new Doppler technique has recently been developed to improve microvascular flow imaging. Intranodular blood flow was assessed subjectively using SMI and identified using a 3-point scale (1 - novascularization, 2 - slight vascularization, 3 - marked vascularization) in all patients.⁵ If the nodules were demonstrated to have slight or marked intranodular vascularization, the arterial flow was evaluated to determine which ablation procedure should be used. The artery-first MWA technique was performed in patients where the feeding artery could be clearly identified using SMI and whose intranodular vascularity index was 2 or 3. All examinations were performed by the same interventional radiologist who also performed the ablation procedure.

The MWA system used in this study was a 2.45 GHz microwave generator (TATO; Terumo, Rome, Italy) and an uncooled 18 G antenna. The indicated probe used during thyroid ablation had 8 cm in length and 50 g in weight.

It had a teflon (PTTFE) coating to prevent adhesions and a metal tip for soft and precise targeting of thyroid nodules.

Before the ablation, all patients underwent laboratory examination. Laboratory tests included a complete blood count, blood coagulation test and complete thyroid function tests (triiodothyronine (T3), free thyroxine (T4), and thyroid-stimulating hormone (TSH) levels). In addition, anti-thyroid peroxidase (anti-TPO) and anti-thyroglobulin (anti-TG) antibody levels were evaluated. Clinical examination was performed using symptom and cosmetic scores. Clinical symptoms were scored using a 10-cm visual analog scale, and a 4-point subjective scale (I – no palpable mass, II – an invisible but palpable mass, III – a visible mass during neck extension or swallowing, and IV – easily visible mass) was used for cosmetic scoring.

Procedure

All MWA treatment procedures were performed as outpatient procedures. Local anesthesia (2% prilocaine) was injected subcutaneously into the puncture site in a supine cervical extension position. Ultrasound-guided hydrodissection procedures were performed around the capsule using a 1:1 concentration of 0.5% bupivacaine and 0.9% isotonic NaCl in order to protect neighbor structures from thermal damage and subcapsular anesthesia (Fig. 1). Then, the feeding artery was imaged with monochrome (Fig. 2A) and color SMI (Fig. 2B) and the antennas were inserted into the center of the feeding artery in the study group (Fig. 2C,D). After ablation of the artery, the following nodular ablation steps were performed in the same manner in both groups. The MWA antenna was placed into the nodule along its short axis using a trans-isthmic approach, which is preferred to minimize the risk of injury to vital structures and allow visualization of the entire length of the antenna on the transverse US. During the session, 15-Watt power output was used and the procedures were conducted using

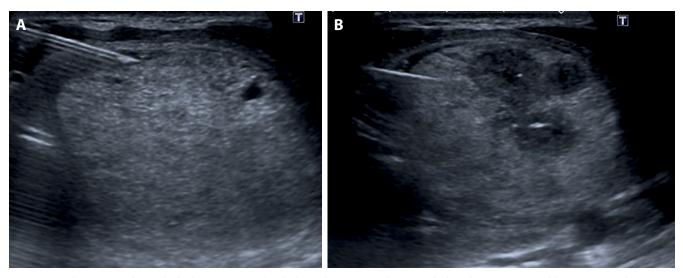


Fig. 1. Trans-isthmic approach (A,B), hydrodissection (A) and multiple overlapping (B) techniques, which are basic microwave ablation (MWA) techniques

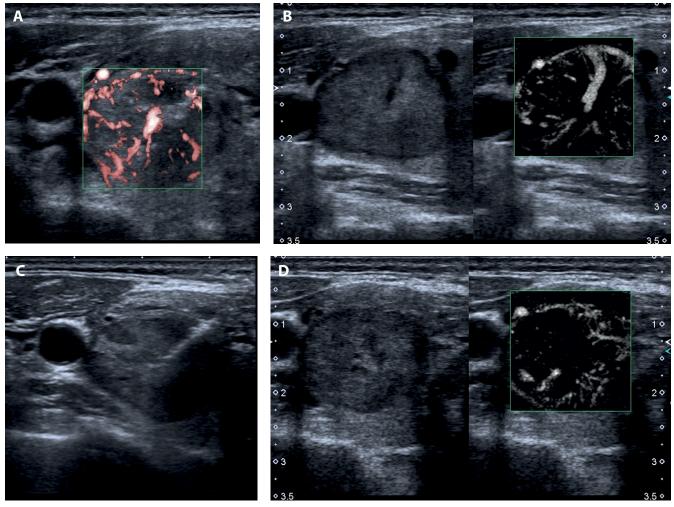


Fig. 2. A 52-year-old female patient who underwent artery-first microwave ablation (MWA). The feeding artery was detected with the color (A) and monocrome (B) Superb Microvascular Imaging (SMI) methods. Prior to nodular ablation, the probe was localized into the feeding artery (C). No flow was observed after artery ablation (D)

the multiple overlapping technique. Each overlapping ablation area was visualized with real-time US and satisfactory volume coverage was obtained. If the patient could not tolerate the pain and discomfort during the session, the procedure was interrupted for a short period. The extent of ablation was estimated taking into account the echogenic changes around the MWA probe, and the session was terminated when the hyper-echo area covered the entire nodule. Phonatory control was performed during and after the ablation procedure in order to exclude a recurrent laryngeal nerve injury. The complete procedure was performed under aseptic conditions. At the end of the procedure, mild cold compression was applied to the neck, and patients were observed in the hospital for 2 h. Before discharge, US was performed to exclude any possible complications.

Follow-up

Both groups were evaluated in terms of US examination, clinical symptoms and laboratory data 3 months (early-term follow-up) and 6 months (intermediate-term

follow-up) after the procedure. The US examination was performed to assess the characteristics of the nodule. We determined the VRRs as a primary outcome. Other efficacy outcomes included improvements in a patient's symptoms and cosmetic scores in the early- and intermediate-term follow-up. The percentage of volume reduction was calculated using the following formula:

 $VRR = [(Pre-procedural volume - follow-up volume) \times 100]/$ (Pre-procedural volume)

Statistical analyses

Nominal and ordinal parameters were described with frequencies. Mean and standard deviation (SD) were used for the description of scale parameters. Median and interquartile range (IQR) were used for skewed parameters. The Kolmogorov–Smirnov test was used to test for the normality distribution of scale parameters. For normally distributed parameters, independent samples t-tests were used. For non-normally distributed parameters, Mann–Whitney U tests were used.

The Fisher's exact test and χ^2 likelihood ratio tests were used for differences in nominal and ordinal parameters. Repeated measures analysis of variance (ANOVA) tests were performed to evaluate the group and time effects on variables. The SPSS v. 17.0 for Windows (SPSS Inc., Chicago, USA) software was used with a 95% confidence interval (95% CI) and a p-value of 0.05 as the significance level.

Results

Both groups were compared regarding age, gender, location, and nodule composition (difference between the solid and mainly solid structure percentage), and the differences between the groups were not statistically significant (p > 0.05) (Table 1). Baseline nodular blood flow scores were 2.08 ± 0.51 in the study group compared to 1.30 ± 0.63 in the control group (p = 0.03). The SMI allowed for choosing the artery-first MWA technique for nodules demonstrating high nodular blood flow.

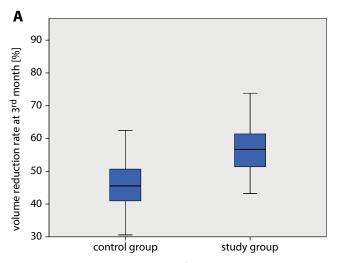
The mean baseline volume was 20.94 ±15.38 mL in the whole cohort and did not significantly differ between groups (p = 0.135). Volumes decreased progressively after ablation in the whole cohort and were found to be $10.13 \pm 8.39 \text{ mL}$ (p = 0.001) and $5.41 \pm 4.41 \text{ mL}$ (p = 0.001) at 3-month and 6-month follow-up, respectively. When the 2 groups were evaluated separately, the mean baseline volume of the study group was 17.10 ±14.65 mL, and it decreased to 5.90 ±4.4 mL at the 3-month follow-up and to 3.72 ± 3.92 mL at the 6-month follow-up. The mean nodular volume of control group was 24.23 ±15.55 mL at baseline, and decreased to 11.30 ±5.4 mL at the 3-month follow-up and 6.94 ±4.34 mL at the 6-month follow-up (Table 2). In addition, the longest baseline diameter was 37.41 ± 11.26 mm in the study group and 43.94 ± 9.10 mm in the control group (p = 0.053). In the study group, it decreased to 27.63 ±8.37 mm and 22.25 ±7.87 mm, and in the control group it decreased to 36.68 ±7.87 mm and 31.75 ±7.90 mm at 3-month and 6-month followup, respectively. Although the pre-procedural volumes (p = 0.135) and longest diameters (p = 0.053) were statistically similar in both groups, both parameters were significantly higher in the control group at 3-month and 6-month follow-up (p < 0.05) (Table 2).

As a primary endpoint, VRR in the cohort was $52.53\pm10.56\%$ at the 3-month follow-up and $73.91\pm10.11\%$ at the 6-month follow-up. The mean VRRs were higher in the study group at the 3-month follow-up (study group: $56.97\pm11.39\%$, control group: $47.07\pm7.93\%$, p = 0.003). This significant difference between the groups remained unchanged at the 6-month follow-up, registering a greater volume reduction percentage in patients treated with artery-first MWA than in patients treated with MWA only (study group: $78.38\pm8.91\%$, control group: $69.54\pm9.41\%$; p = 0.004) (Fig. 3A,B).

Table 2. Clinical and physical examination properties and difference analysis results of patient groups (study and control groups)

analysis results of patient groups (study and control groups)								
Mean ±SD	Control group (n = 21)	Study group (n = 19)	p-value					
Volume								
Preprocedural	24.41 ±15.55	17.10 ±14.65	0.135ª					
3 rd month, median (IQR)	11.30 (5.4)	5.90 (4.4)	0.000 ^b					
6 th month	6.94 ±4.34	3.72 ±3.92	0.019ª					
Volume reduction ratio								
3 rd month	47.07 ±7.93	56.97 ±11.39	0.003ª					
6 th month	69.54 ±9.41	78.38 ±8.91	0.004ª					
Longest diameter								
Preprocedural	43.94 ±9.10	37.41 ±11.26	0.053ª					
3 rd month	36.68 ±7.87	27.63 ±8.37	0.001a					
6 th month	31.75 ±7.90	22.25 ±7.87	0.001a					
C	osmetic store							
Preprocedural, median (IQR)	4.00 (0)	3.00 (1)	0.006 ^b					
3 rd month, median (IQR)	3.00 (2)	2.00 (1)	0.069 ^b					
6 th month, median (IQR)	2.00 (1)	2.00 (1)	0.153 ^b					
Sy	mptom score							
Preprocedural, median (IQR)	6.00 (1)	6.00 (1)	0.668 ^b					
3 rd month	2.71 ±1.06	2.16 ±1.30	0.144ª					
6 th month, median (IQR)	1.00 (2)	1.00 (2)	0.830 ^b					
	TSH							
Preprocedural	1.33 ±0.58	1.21 ±0.57	0.543ª					
3 rd month	1.55 ±0.84	1.47 ±0.90	0.783ª					
6 th month	1.63 ±1.02	1.34 ±0.77	0.309ª					
	fT4							
Preprocedural, median (IQR)	1.02 (0.12)	1.02 (0.23)	0.979 ^b					
3 rd month	1.11 ±0.20	1.03 ±0.19	0.214ª					
6 th month	1.21 ±0.26	1.08 ±0.17	0.081ª					
	T3							
Preprocedural	3.18 ±0.31	3.23 ±0.42	0.726ª					
3 rd month	3.29 ±0.32	3.23 ±0.48	0.658ª					
6 th month	3.32 ±0.43	3.16 ±0.29	0.197ª					
	Anti-TG							
Preprocedural	4.55 ±7.68	9.30 ±12.55	0.294 ^b					
3 rd month	11.16 ±19.68	6.98 ±6.17	0.999 ^b					
6 th month	9.84 ±9.98	9.22 ±7.47	0.828ª					
Anti-TPO Anti-TPO								
Preprocedural	9.00 ±19.72	6.97 ±7.94	0.573 ^b					
3 rd month	10.60 ±20.69	7.01 ±7.63	0.768 ^b					
6 th month	8.82 ±5.09	8.19 ±6.87	0.520 ^b					

^a independent samples t-test; ^b Mann–Whitney U test. Data are presented as mean ± standard devation (SD). Median and interquartile range (IQR) were added for skewed parameters. TSH – thyroid-stimulating hormone; fT4 – free thyroxine; T3 – triiodothyronine; anti-TG – anti-thyroglobulin; anti-TPO – anti-thyroid peroxidase antibody.



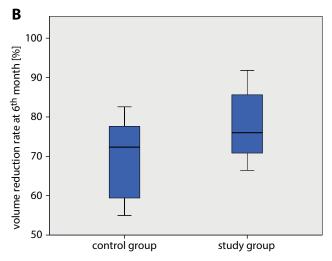


Fig. 3. Box-plot (ranges, 1st quartile (Q1), 3rd quartile (Q3), medians) of the volume reduction rate (VRR) compression at 3-month (A) and 6-month (B) follow-up in respective groups

In the study group, symptom scores decreased from 6.00 ± 1 at baseline to 2.16 ± 1.30 at the 3-month follow-up and 1.00 ± 2 at the 6-month follow-up. In the control group, symptom scores decreased from 6.00 ± 1 at baseline to 2.71 ± 1.06 at the 3-month follow-up and 1.00 ± 2 at the 6-month follow-up. Thus, we observed that these scores decreased rapidly at 3-month follow-up in both groups. There were no significant differences between the groups in terms of symptom scores before ablation (p = 0.668) and at 3-month (p = 0.144) and 6-month (p = 0.830) follow-up.

In addition, cosmetic score decreased from 3.00 ± 1 to 2.00 ± 1 , 2.00 ± 1 in the study group and from 4.00 ± 0 to 3.00 ± 2 and to 2.00 ± 1 in the control group at 3- and 6-month follow-up, respectively. Pre-procedural cosmetic scores were significantly higher in the control group (p = 0.006) (Table 2).

Patients had normal thyroid laboratory values at baseline and 3-month and 6-month follow-up. There were no significant differences between groups in terms of thyroid hormone levels (TSH, fT4, T3) and thyroid antibodies (anti-TG, anti-TPO) at baseline and both follow-up assessments (Table 2).

The results of repeated measures ANOVA showed that the differences in volume, longest diameter and cosmetic scores between the groups were statistically significant (p < 0.05). However, time (3-month and 6-month follow-up) and group effect among subjects did not reach statistical significance (p > 0.05) (Table 3).

Although the treatment was well-tolerated, mild pain was reported by 2 patients during the ablation and was easily managed by reducing the energy. One patient in the study group developed first-degree burns to the skin at the puncture site, which did not require any specific treatment and resolved within days. There were no major complications in either group during the session and at post-procedural follow-up assessments.

Discussion

Minimally invasive thermal ablation has been used to successfully treat benign thyroid nodules, with MWA being a more recently developed ablation technique. Microwaves create an ablation area with thermal and nonthermal effects. Coagulation necrosis is a thermal effect, while electroporation, ion acceleration, collision, and dipole rotation are nonthermal effects. 6-8 This explains the main mechanisms in which MWA causes significant volume reductions in thyroid nodules. 9 These 2 different mechanisms of ablation provide some advantages to MWA, as compared to RFA and percutaneous laser ablation (LA). Several reports have shown that MWA has a lower complication rate and similar efficacy when compared to RFA.^{10,11} Recent studies have recognized the efficacy and safety of MWA in the treatment of benign thyroid nodules. 12,13 However, the VRRs of nodules have wide variations of approx. 40-80% after 3 months, 48-86% after 6 months and 75–90% after 12 months. 12–17 As stated above, this situation may be due to certain factors and the type of system may be one of the important determinants. Uncooled systems that provide real-time temperature control may have a different effect on the nodular tissue surrounding the ablated area during the procedure, which may affect the success of the treatment.¹⁵ In this study, we performed the procedures with an uncooled system. Because the properties of the system are dedicated to the thyroid, it is 18 G in size and has an 8-cm shaft that provides safe and ergonomic use. Furthermore, literature studies and our recent study have shown that the tumor volume, clinical scores and symptom scores significantly improve after treatment with an uncooled MWA system with low complication rates. 14,16,17 In the present study, the findings in both groups were consistent with the literature and the overall mean VRR of the treated nodules reached 53% and 74% at 3 and 6 months after ablation, respectively.

Table 3. Repeated measures results for research parameters based on time and group

Parameter	F and p-value	Source			
		Intercept	Group	Time	Group * Time
Volume	F	6.923	20.956	58.489	0.414
	p-value	0.119	0.045	0.017	0.662
Longest diameter	F	69.683	82.416	74.945	0.329
	p-value	0.014	0.012	0.013	0.720
Cosmetic score	F	39.150	98.880	312.189	0.133
	p-value	0.025	0.010	0.003	0.876
Symptom score	F	4.520	2.883	414.366	0.745
	p-value	0.167	0.232	0.002	0.477
TSH	F	352.967	5.618	4.895	0.218
	p-value	0.003	0.141	0.170	0.804
fT4	F	1563.772	9.043	4.362	0.469
	p-value	0.001	0.095	0.187	0.627
ТЗ	F	37152.998	1.012	0.352	0.661
	p-value	0.000	0.420	0.740	0.518
Anti-TG	F	112.197	0.000	0.384	1.485
	p-value	0.009	0.996	0.723	0.231
Anti-TPO	F	1238.864	6.001	0.316	0.124
	p-value	0.001	0.134	0.760	0.883

Group * Time – effect of both group and time on the parameters; T3 – triiodothyronine; fT4 – free thyroxine; TSH – thyroid-stimulating hormone; anti-TG – anti-thyroglobulin; anti-TPO – anti-thyroid peroxidase antibody. The p-values in bold are statistically significant.

Thermoablative treatment was performed on an afferent artery of the nodule in the artery-first approach in order to obtain a better ablation of the nodular tissue and increase the volume of the induced necrosis. Intranodal prominent vascularity is less than 15% in small benign thyroid nodules, but can be more than 50% in large benign thyroid nodules.¹⁸ Artery-first MWA is an advanced technique and, to the best of our knowledge, no other studies have demonstrated a difference in the efficacy (VRRs) of artery-first MWA. In our study, the efficacy of arteryfirst ablation was demonstrated and the VRR showed a significant difference at the 3-month (p = 0.000) and 6-month (p = 0.003) follow-up. In our study, 3-month and 6-month follow-up were assessed because, as mentioned by Cui et al., the changes in VRR become evident with the removal of necrotic tissue during the 3rd to 6th month post-procedure, due to a delay in the immune system.¹⁹

Many benign thyroid nodules are hypervascularized and the artery-first ablation technique can be performed in hypervascularized nodules when a prominent feeding artery can be identified. The nodules in the upper pole of the thyroid are usually vascularized from the superior thyroid artery, while those in the lower pole are vascularized by the inferior thyroid artery. In recent studies, the feeding artery was detected using CD and PD. Land P

flow signals from large to small vessels and depicts this information at high-frame rates as a color overlay image or as a grayscale flow map.²² In recent studies, the arteryfirst technique was used to reduce the dispersion of generated heat in the RFA of thyroid nodules, and has increased the efficacy of the procedure during follow-up.²³ Offi et al. pointed out that the differences between RFA and artery-first RFA techniques were seen in nodular volume at follow-up. At the 3-month follow-up, the mean VRR was 72.7 ±8.99% in the study group and 56.28 ±14.55% in the control group (p = 0.003). Moreover, at the 6-month follow-up, the mean VRR was 83.01 ±5.04% in the study group and 70.0 $\pm 15.04\%$ in the control group (p = 0.013).²⁴ Similarly, in our study, a significant difference was found between the 2 techniques in VRR at the 3-month (p = 0.000) and 6-month (p = 0.012) follow-up. These data lead us to hypothesize that artery-first ablation may increase the efficacy of the procedure and allow a more rapid reduction in volume. Furthermore, this study detected a significant improvement in clinical findings between baseline and the 3-month and 6-month follow-up, but there was no significant difference between the 2 groups.

The MWA-associated complications are classified as major and minor. Major complications include transient or permanent voice change, hypoparathyroidism, esophageal injury, dysphagia, infection, and nodule rupture. Minor complications include severe pain requiring medication for relief, skin burns, hematoma, and vomiting. Thermal ablation procedures have significantly lower

complication rates, and recent studies have reported that the complications of MWA are mostly minor, although it was reported that both MWA methods (cooled and uncooled) had similar incidence of major complications (4.9% compared to 5.0%, p = 0.49). Pain and skin burns were reported as the most common minor complications and were significantly higher in the uncooled MWA group (p < 0.01).¹⁴ In our study, 2.5% of treated patients had minor complications and there were no major complications. The low complication rate achieved using the uncooled system compared to previous studies may be due to artificial liquid isolation-assisted ablation, real-time US guidance, phonatory control during the procedure, the overlapping technique, and the trans-isthmic approach. In addition, as an advanced technique, arterial ablation may have reduced the risk of procedure-related hemorrhage.²³

Limitations

This study has some limitations. First, it was a retrospective in design single-center study with a small sample size. Second, follow-up longer than 6 months may be necessary to further observe nodular behavior, since nodule regrowth may occur and the decision to undergo repeat thermal ablation or surgery may be needed. Some studies have suggested supplementary treatment 3–6 months after ablation. Regardless, in our study, we achieved a 79% VRR with a single session using artery-first MWA, and this result is consistent with the current literature. In addition, in this retrospective study, we did not collect any data on elastography for nodular stiffness. In the literature, some measurements with elastography have been found to positively correlate with better results in thermal ablation, but these were not clearly defined factors to predict success. 27

Conclusions

In conclusion, MWA devices and techniques continue to evolve amidst minimally invasive treatment of thyroid nodules. The use of basic and advanced technical strategies is critical to ensure treatment efficacy and patient safety. Therefore, additional prospective studies with large-scale and long-term follow-up are necessary to validate our findings.

ORCID iDs

References

- Efremidou EI, Papageorgiou MS, Liratzopoulos N, Manolas KJ.
 The efficacy and safety of total thyroidectomy in the management
 of benign thyroid disease: A review of 932 cases. Can J Surg. 2009;
 52(1):39–44. PMID:19234650. PMCID:PMC2637645.
- Papini E, Monpeyssen H, Frasoldati A, Hegedüs L. 2020 European Thyroid Association Clinical Practice Guideline for the Use of Image-Guided Ablation in Benign Thyroid Nodules. Eur Thyroid J. 2020;9(4): 172–185. doi:10.1159/000508484

- 3. Wu W, Gong X, Zhou Q, Chen X, Chen X, Shi B. US-guided percutaneous microwave ablation for the treatment of benign thyroid nodules. Endocr J. 2017;64(11):1079–1085. doi:10.1507/endocrj.EJ17-0152
- Klein JA, Lee Jr FT, Hinshaw L, Lubner MG, Brace CL. Overview of thermal ablation devices: Microwave. In: Clark T, Sabharwal T, eds. Interventional Radiology Techniques in Ablation. London, UK: Springer; 2013:21–28. doi:10.1007/978-0-85729-094-6
- Cappelli C, Pirola I, Gandossi E, et al. Ultrasound microvascular blood flow evaluation: A new tool for the management of thyroid nodule? Int J Endocrinol. 2019;2019:1–6. doi:10.1155/2019/7874890
- Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: Principles and applications. *RadioGraphics*. 2005;25(Suppl 1):S69–S83. doi:10.1148/rg.25si055501
- Ward RC, Healey TT, Dupuy DE. Microwave ablation devices for interventional oncology. Exp Rev Med Devices. 2013;10(2):225–238. doi:10. 1586/erd.12.77
- Banik S, Bandyopadhyay S, Ganguly S. Bioeffects of microwave: A brief review. *Bioresour Technol*. 2003;87(2):155–159. doi:10.1016/ S0960-8524(02)00169-4
- Brace CL. Microwave ablation technology: What every user should know. Curr Probl Diagn Radiol. 2009;38(2):61–67. doi:10.1067/j.cpradiol. 2007.08.011
- 10. Yang YL, Chen CZ, Zhang XH. Microwave ablation of benign thyroid nodules. Future Oncol. 2014;10(6):1007–1014. doi:10.2217/fon.13.260
- Yue WW, Wang SR, Lu F, et al. Radiofrequency ablation vs. microwave ablation for patients with benign thyroid nodules: A propensity score matching study. *Endocrine*. 2017;55(2):485–495. doi:10.1007/s12020-016-1173-5
- Korkusuz H, Happel C, Heck K, Ackermann H, Grünwald F. Percutaneous thermal microwave ablation of thyroid nodules: Preparation, feasibility, efficiency. *Nuklearmedizin*. 2014;53(04):123–130. doi:10.3413/Nukmed-0631-13-10
- Feng B, Liang P, Cheng Z, et al. Ultrasound-guided percutaneous microwave ablation of benign thyroid nodules: Experimental and clinical studies. Eur J Endocrinol. 2012;166(6):1031–1037. doi:10.1530/ EJE-11-0966
- Zheng BW, Wang JF, Ju JX, Wu T, Tong G, Ren J. Efficacy and safety of cooled and uncooled microwave ablation for the treatment of benign thyroid nodules: A systematic review and meta-analysis. *Endocrine*. 2018;62(2):307–317. doi:10.1007/s12020-018-1693-2
- Mader OM, Tanha NF, Mader A, Happel C, Korkusuz Y, Grünwald F. Comparative study evaluating the efficiency of cooled and uncooled single-treatment MWA in thyroid nodules after a 3-month follow up. Eur J Radiol Open. 2017;4:4–8. doi:10.1016/j.ejro.2017.01.004
- Yıldırım G. Uncooled microwave ablation method for thyroid nodules: Our early-term results. Bosphorus Med J. 2021;8(1):13–20. doi:10.14744/ bmj.2020.62681
- 17. Korkusuz H, Nimsdorf F, Happel C, Ackermann H, Grünwald F. Percutaneous microwave ablation of benign thyroid nodules: Functional imaging in comparison to nodular volume reduction at a 3-month follow-up. *Nuklearmedizin*. 2015;54(01):13–19. doi:10.3413/Nukmed-0678-14-06
- Lyshchik A, Moses R, Barnes SL, et al. Quantitative analysis of tumor vascularity in benign and malignant solid thyroid nodules. J Ultrasound Med. 2007;26(6):837–846. doi:10.7863/jum.2007.26.6.837
- 19. Cui T, Jin C, Jiao D, Teng D, Sui G. Safety and efficacy of microwave ablation for benign thyroid nodules and papillary thyroid microcarcinomas: A systematic review and meta-analysis. *Eur J Radiol*. 2019; 118:58–64. doi:10.1016/j.ejrad.2019.06.027
- Shin JH, Baek JH, Chung J, et al. Ultrasonography diagnosis and imaging-based management of thyroid nodules: Revised Korean Society of Thyroid Radiology Consensus Statement and Recommendations. Korean J Radiol. 2016;17(3):370. doi:10.3348/kjr.2016.17.3.370
- 21. Kong J, Li JC, Wang HY, et al. Role of Superb Microvascular Imaging in the preoperative evaluation of thyroid nodules: Comparison with power Doppler flow imaging. *J Ultrasound Med*. 2017;36(7):1329–1337. doi:10.7863/ultra.16.07004
- Machado P, Segal S, Lyshchik A, Forsberg F. A novel microvascular flow technique: Initial results in thyroids. *Ultrasound Q*. 2016;32(1):67–74. doi:10.1097/RUQ.000000000000156
- 23. Park HS, Baek JH, Park AW, Chung SR, Choi YJ, Lee JH. Thyroid radio-frequency ablation: Updates on innovative devices and techniques. *Korean J Radiol*. 2017;18(4):615. doi:10.3348/kjr.2017.18.4.615

- 24. Offi C, Garberoglio S, Antonelli G, et al. The ablation of thyroid nodule's afferent arteries before radiofrequency ablation: Preliminary data. *Front Endocrinol.* 2021;11:565000. doi:10.3389/fendo.2020.565000
- 25. Jeong WK, Baek JH, Rhim H, et al. Radiofrequency ablation of benign thyroid nodules: Safety and imaging follow-up in 236 patients. *Eur Radiol*. 2008;18(6):1244–1250. doi:10.1007/s00330-008-0880-6
- 26. Liu YJ, Qian LX, Liu D, Zhao JF. Ultrasound-guided microwave ablation in the treatment of benign thyroid nodules in 435 patients. *Exp Biol Med (Maywood)*. 2017;242(15):1515–1523. doi:10.1177/1535370217727477
- Bisceglia A, Rossetto R, Garberoglio S, et al. Predictor analysis in radiofrequency ablation of benign thyroid nodules: A single center experience. Front Endocrinol. 2021;12:638880. doi:10.3389/fendo.2021. 638880