Microwave ablation for thyroid nodules: a new string to the bow for percutaneous treatments?

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Contributions: (I) Conception and design: All authors; (II) Administrative support: None; (III) Provision of study materials or patients: All authors; (IV) Collection and assembly of data: All authors; (V) Data analysis and interpretation: F Morelli; A Borelli, S Panella, A Sacrini, G Pompili, G Carrafiello; (VI) Manuscript writing: All authors; (VII) Final approval of manuscript: All authors.
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Background: Thyroid nodules are a fairly common finding in general population and, even if most of them are benign, a treatment can be however necessary. In the last years, non surgical minimally invasive techniques have been developed to treat this pathology, starting from percutaneous ethanol injection (PEI), to laser ablation (LA), radiofrequency ablation (RFA) and, most recently, microwave ablation (MWA).

Methods: We reviewed all medical literature searching in pubmed.gov the terms "microwave" & "thyroid". We found three original studies concerning MWA treatment, for a total of 263 patients (mean age 51.0 years; range, 15–80 years; male to female ratio 2.55) and 522 nodules.

Results: A total of 522 nodules (338 solid, 22 cystic, 162 mixed) in 263 patients were treated. Studies have shown a mean reduction in volume of thyroid nodules ranging from 45.9% to 65%. No study reported a significant and definitive change in laboratory parameters, except for one case (Heck *et al.*). No studies have reported major complications after procedure.

Conclusions: MWA is a new, promising technique among the minimally invasive treatments of thyroid nodules. Actually, the larger diameter of MW antenna seems to be the major limiting factor in the use of this technique. More studies are necessary to evaluate feasibility, safety and efficacy of the procedure.

Keywords: Ablation techniques; microwaves; thyroid nodule

Introduction

Nodular thyroid disease is detected in 3–75% of the general population, and in 20–76% at ultrasound (US) scan, especially in the context of multinodular goiter (1). Even if most of the thyroid nodules are benign, a treatment can be however necessary, in particular for subjective symptoms, cosmetic concerns, patient's fear for malignant transformation (2). If a therapy is necessary, total/partial thyroidectomy is actually the standard of care, while iodine therapy has been used with poor results (3). Many studies suggest total thyroidectomy in case of multinodular goiter, because of the risk of nodular recurrence in the thyroid remnant, with the need of reintervention, which carries out a higher risk of complications (4). Surgery has in fact some limitations, like a 2–10% complication rate, hiatrogenic hypothyroidism, hospitalization, general anesthesia and scar formation (5). In the last years, non surgical minimally invasive techniques have been developed to treat this pathology, starting from percutaneous ethanol injection (PEI), to laser ablation (LA) and radiofrequency ablation (RFA) (6-8). Most recently, microwave ablation (MWA) has been proposed to treat thyroid nodules, taking experience from its use in other organs like liver, kidney and lung in particular (9). MWA has the following advantages respect to RFA: reduction in treatment time, larger ablation zone,

Figure 1 US view of the MW antenna in a thyroid nodule. US, ultrasound; MW, microwave.

Figure 2 MW ablation of the nodule under US-guidance; note the hyperechoic area created by ablation. MW, microwave; US, ultrasound.

less heat sink effect (10). Aim of this review article was to evaluate all the studies concerning thyroid MWA, with a particular focus on safety and efficacy of the procedure and on results compared to RFA.

Methods

We reviewed all medical literature searching in pubmed. gov the terms "microwave" & "thyroid". We found three original studies concerning MWA treatment, for a total of 263 patients (mean age 51.0 years; range, 15–80 years; male to female ratio 2.55) and 522 nodules (11-13).

Preablation assessment

Nodule size and composition were recorded with US scan: nodule size was obtained by multiplying three orthogonal measures by 0.525 (resulted from ellipsoid volume equation); composition of the nodules was divided in: mainly solid (>80% solid), mainly cystic (>80% liquid) or mixed type. Laboratory tests were: thyroid function [thyroid stimulating hormone (TSH), triiodothyronine (fT3), free thyroxine (fT4)], thyroid antibodies, blood count, coagulation tests. Inclusion and exclusion criteria were quite similar among the studies. Inclusion criteria were: benign thyroid nodule proven with at least one recent fine needle aspiration biopsy (FNAB); subjective symptoms (compressive symptoms, neck discomfort, foreign body sensation); cosmetic concerns; refusal or contraindications to undergo surgery. Exclusion criterium was only FNAB evidence of malignancy, but caution should be exercised for retrosternal growth and for nodules with US aspect of malignancy.

Procedure

Feng *et al*. and Yue *et al*. performed MWA on an inpatient basis, while Heck *et al*. on an outpatient basis. Patients were put in a supine position with mild hyperextended neck, in aseptic conditions. Feng *et al*. and Heck *et al*. performed a 1–2 mm incision after local anesthesia. Only Feng *et al*. spoke about unconscious i.v. anesthesia by an anesthesiologist but, according to literature on RFA, a bland systemic sedation is routinely performed and perhaps not described in the other two studies. A fine needle aspiration was conducted in mainly cystic nodules before ablation. Then, an internally cooled antenna with various diameters (from 16 to 14 Gauge) was positioned in the thyroid nodules (*Figure 1*). All the authors used the "moving-shot" technique with trans-isthmic approach, as possible (14). This approach allows to see the entire length of the antenna on US view; furthermore, the danger triangle, which includes recurrent laryngeal nerve, trachea and esophagus, is more easily avoided. Multiple areas of the nodule are treated unit-by-unit by moving the electrode tip, until an echoic area in the unit is developed (*Figure 2*). The procedure is terminated when hyperechoic changes are present in the entire nodule, even if undertreated areas are recommended if the nodule is nearby the danger triangle. Mean power and treatment time were recorded by Heck *et al*. and Feng *et al*. Yue *et al*. injected a mixture of 0.9% lidocaine and physiological saline under the thyroid capsule to achieve a "liquid isolating region" protecting the surrounding structures of the neck (carotid artery, nerves, trachea, esophagus) from thermal injury.

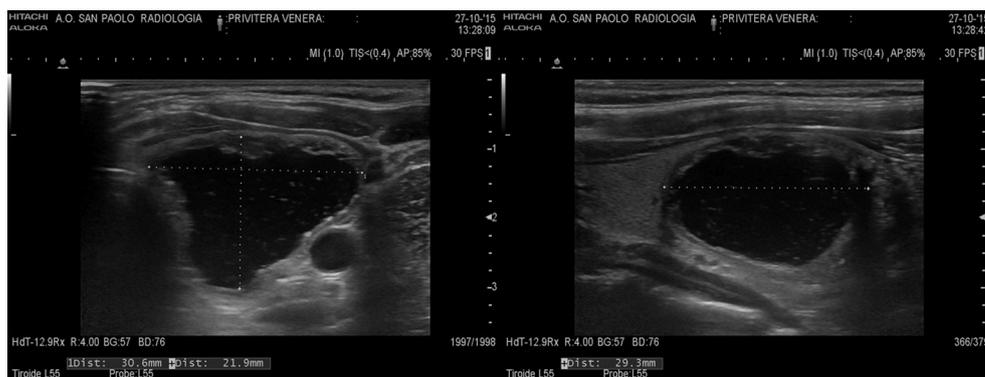Yue *et al*. and Feng *et al*. kept patients under observation,

Figure 3 Pre-ablation measurement of a mostly cystic thyroid nodule (volume: 9.8 cc).
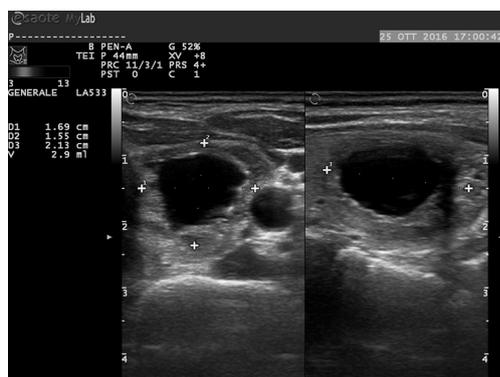

Figure 4 US control at 1 year after MW ablation of the thyroid nodule, showing reduction of 71.4% of the volume. US, ultrasound; MW, microwave.

with compression of the neck lasting for 15–30 minutes. Follow up was quite different among the authors. However, all performed a 3- and 6-month US control of nodule volume (*Figures 3,4*), assessing also symptom score (visual analog scale of subjective symptoms, from 0 to 10) and cosmetic score (1: no palpable mass; 2: invisible but palpable mass; 3: mass visible only swallowing; 4: easily visible mass). Thyroid laboratory tests were also examined by all.

Results

Nodules treated were 338 solid, 22 cystic, 162 mixed. Feng *et al*. and Heck *et al*. recorded both mean power ablation and mean time of ablation (see *Table 1*). Heck *et al*. did not found significant changes in laboratory parameters at 3 and 6 months follow-up, except for one case of persistent suppressed TSH. Thyreoglobulin levels increased 1 day after MWA but were normal at 3 and 6 months follow up. Yue *et al*. did not report any new case of hypothyroidism after the treatment. Feng *et al*. found cases of decrease in TSH and increase in fT_4, but only in the day after MWA.

Reduction analysis

Volume reductions of the three studies and of other three studies concerning RFA, matched in number, were reported in the *Table 2* (2,15,16). The study conducted by Feng *et al*. demonstrated a mean reduction of nodule volume of 45.9% at the least follow up, with a volume decrease from 5.30 to 2.40 mL. Yue *et al*., in a large series study, confirmed these results showing a mean reduction of nodule volume of 65% at the 6 months follow up, with a volume decrease from 2.13 to 0.45 mL. Only 254 of 477 nodules reached a 6-month follow up: as a consequence, a high number of patients did not reach an adequate follow up, resulting in a poor volume reduction at last control (38%). Heck *et al*. in their study demonstrated a mean reduction of nodule volume of 51.4% at 3 months follow-up, which was attended by all 30 patients, and a mean reduction of 58.8% at 6 months follow-up, reached only by 11 patients. Yue *et al*. and Feng *et al*. observed that cystic nodules decrease more respect to mixed nodules, and that mixed nodules show better results than solid nodules. Furthermore, Yue *et al*. found an inverse correlation between baseline volume and volume reduction after ablation. Feng *et al*. recorded symptom score and cosmetic score: symptom score was reduced in all symptomatic patients (4/4); cosmetic score was reduced in 8/11 patients.

Side effects

After MWA, all studies reported that most patients

Table 1 Composition of nodules and technical aspects of microwave ablation in the three studies reported

Nodules and MWA characteristics	Feng *et al.* [2012]	Yue *et al.* [2012]	Heck *et al.* [2015]	Sum
Cystic nodules (n)	1	21	–	22
Mixed nodules (n)	5	136	21	162
Solid nodules (n)	5	320	13	338
MWA power (Watt), mean [range]	26.4 [20–30]	[30–50]	29.2 [24–40]	28.4 [20–50]
MWA time (min) , mean [range]	9.5 [4–16.5]	–	11.2 [5–25]	10.8 [4–25]

MWA, microwave ablation; n, number.

Table 2 Data report of microwave ablation compared to three studies on radiofrequency ablation matched for number of patients/nodules and initial volume

MWA and RFA results	MWA			RF		
	Feng *et al.* [2012]	Yue *et al.* [2012]	Heck *et al.* [2015]	Baek *et al.* [2010]	Jeong *et al.* [2008]	Spiezia *et al.* [2009]
Patients (n)	11	222	30	15	236	66
Nodules (n)	11	477	34	15	302	66
Follow-up period (months)	1–9	1–24	3–6	6–8	1–41	12–24
V. init (mL)	5.30	2.13	35.67(mean); 18.1 (median)	7.5	6.1	21.1
VR 1 (%)	–	41 (355/477[†])	–	49	58	43.7
VR 3 (%)	–	41 (318/477[†])	51.4 (30/30[‡])	–	–	–
VR 6 (%)	–	65 (254/477[†])	55.8 (11/30[‡])	–	–	–
VR last (%)	45.99	38 (477/477[†])	53.6	80	84	76.6

[†], number of nodules at follow up; [‡], number of patients at follow up. n, number; MWA, microwave ablation; RFA, radiofrequancy ablation; V. init, initial volume; VR, volume reduction.

complained of a sensation of heat in the neck and/or slight pain in the ablated site, whereas no one claimed the procedure to stop. Feng *et al.* and Yue *et al.* described choking and coughing at the end of treatment in some patients, which disappeared without any treatment or after corticosteroids physical therapy, water training, and vocal exercises. Only Heck *et al.* reported that two patients developed first-degree burns alongside the puncture channel, which did not require any therapy. In the study conducted by Heck *et al.* was described the formation of a cervical hematoma without active bleeding, with development of a mild Horner's syndrome that disappeared without any treatment. There were no major complications such as esophageal perforation and tracheal injury.

Discussion

Thyroid nodules have a very high prevalence in the general population. Even if benign, they tend to increase over the years, in some cases causing symptoms or cosmetic concerns. The standard option has been so far surgical thyroidectomy, while other treatments (radioiodine therapy or levothyroxine) failed. Since the first study on PEI in 1990 (17), other mini-invasive treatments have been developed for this condition: LA, RFA and then MWA. They all have some advantages on surgery: no hiatrogenic hypothyroidism, no scar formation, lesser costs. Adverse events are comparable: the most common major adverse effect, recurrent laryngeal nerve palsy, is 11.8% (9.8% transient, 2% permanent) in surgery (18) and 0–8% (only

transient) in RFA and LA (6-8,17,19-23). PEI has revealed to be useful for cystic nodules: it can be used with fine needles (21G), and is quite inexpensive and shows good results (53–80% reduction in volume) (24). Because of this, PEI is still the percutaneous technique of choice in cystic/predominantly cystic lesions (25). LA consists on photons emission by excited atoms toward a target lesion. Energy is delivered with a thin needle (21G), through which a spherical area of necrosis is created. However, maximum diameter of coagulative necrosis is never bigger than 2 cm in diameter, so that multiple needles or multiple treatments are necessary to treat large nodules, thus increasing the risk of adverse effects (26). Mean volume reduction of both solid and cystic lesions is 44–73% (20). RFA is the most promising percutaneous technique for both solid and cystic lesions (27). Thermal injury induced by an 18G needle induces a coagulative necrosis of the nodule. Transisthmic approach and the moving-shot technique have improved efficacy and reduced adverse effects (14). Mean volume reduction is the higher among percutaneous techniques: 51–85% (2,15-28). One of the major limits is the heat sink effect, which impacts a lot on high vascularized structures like thyroid parenchyma and thyroid nodules (29). MWA is the more recent percutaneous technique developed. Original articles in literature show that, respect to RFA, MWA has a similar complication rate and a slightly lower efficacy (30). Rate of recurrent laryngeal nerve palsy was 3.4% in the three studies examined. Hematoma developed in more than one half of the patients, a data in harmony with the large needle of MWA (14–16G). Fortunately, there was only one deep and large hematoma (47×22), not requiring treatments. Other adverse events were rare and did not differ from those recorded in RFA studies. The mean reduction volume at 6 months, or at last follow-up, was 45.9–65%, which still overlaps with RFA results. The results may depend from the limited knowledge of this new technique, which is from learning curve effect. According to experimental studies and studies on other organs, MWA could be a further step in percutaneous techniques for thyroid nodules, giving the advantage to reduce treatment time, reduce the heat sink effect, create an ellipsoidal ablated zone which best fits with the shaping of thyroid nodules. In our opinion, these advantages are poor in thyroid ablation: treatment time depends much more from repositioning of the needle that from effective ablation time; heat sink effect could reduce the effective ablation volume, but in a benign condition like thyroid nodules the target is only the volume reduction, and not the ablation of the entire lesion; trans-isthmic approach does not allow to treat thyroid nodules through their main axes, which is the craniocaudal. On the other side, the use of a larger needle carries out a higher complication rate in MWA respect to RFA, in particular the development of neck hematomas, as seen before. In conclusion, MWA is a new, promising technique among the minimally invasive treatments of thyroid nodules. Actually, the larger diameter of MW antenna seems to be the major limiting factor in the use of this technique. More studies are necessary to evaluate feasibility, safety and efficacy of the procedure. In particular, randomized studies between MWA and RFA are necessary to define which should be the ablative treatment of choice for thyroid nodules.

Acknowledgements

Footnote

Conflicts of Interest: The authors have no conflicts of interest to declare.

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