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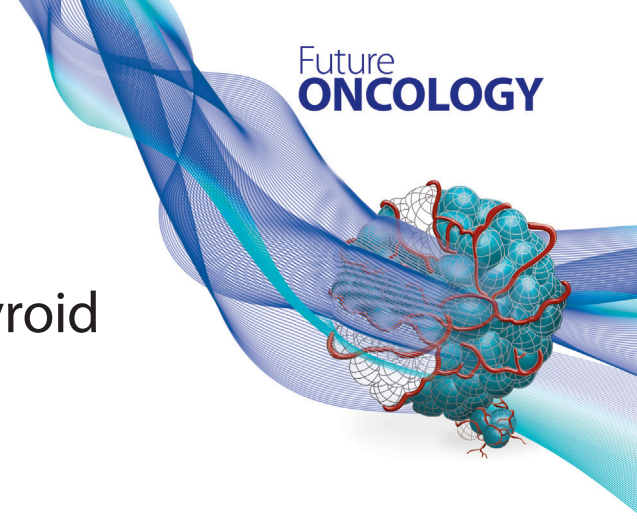

Microwave ablation of benign thyroid nodules

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ABSTRACT: Microwave ablation (MWA) has become increasingly popular as a minimally invasive treatment for benign and malignant tumors of the liver, lung and kidney. Recently, two studies have attempted to apply the technique to debulk benign thyroid nodules and gained positive results. MWA of benign nodules demonstrated significant volume reductions, while solving nodule-related clinical problems. This article reviews the basic physics, therapeutic indications, patient preparation, devices, procedures, clinical results and complications of thyroid MWA.

KEYWORDS

• laser ablation • microwave • radiofrequency ablation • thermal ablation • thyroid nodule • thyroid ultrasound

Thyroid nodules are common and found in 20–76% of the general population by means of ultrasound scan (US) scan [1]. The number, size and symptoms relating to thyroid nodules tend to increase and spoil quality of life as years go on [2]. Most thyroid nodules are benign, but some benign nodules may require treatment for cosmetic reasons, subjective symptoms or anxiety about a growth potential or a malignant change [3,4]. Both surgical and conservative approaches have drawbacks. Although surgery is curative, it can cause some problems such as long hospitalization, upper airway obstruction, nonesthetic scars, recurrent laryngeal nerve palsy, iatrogenic hypothyroidism and difficulty in reoperation [5]. Moreover, the thyroid hormone-suppressive therapy achieves very limited goiter shrinkage and results in the adverse effects of subnormal serum thyroid-stimulating hormone (TSH) levels [6]. Therefore, nonsurgical and minimally invasive treatment modalities, such as ethanol ablation, percutaneous laser ablation (LA), radiofrequency ablation (RFA), have been used to treat thyroid nodules and yielding good results [7–13].

Microwave ablation (MWA) is a minimally invasive technique that has been used to treat benign and malignant tumors of the liver, lung and kidney. Its use in thyroid nodules has been reported by Feng *et al.* and Yue *et al.* [14,15]. This article provides information regarding the basic principles, therapeutic indications, devices and techniques that have been specially modified to optimize thyroid MWA, as well as the clinical results and complications.

Basic principles of MWA

MWA uses the heat generated from the rotation of molecular dipoles following the alternating electric field component of the ultra-high-speed (2450 MHz) microwave. The microwaves pass through the tissue around the exposed antenna of the electrode, causing the water molecules in the tissue to vibrate and rotate, then heat is generated and results in thermal coagulation of the target tissue [16]. Therefore, this process of thermal injury secondary to heat generated from rotation

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of water molecules in thyroid tissue is the basic mechanism of MWA.

The nature of thermal damage caused by MWA is dependent on both the achieved tissue temperature and the duration of heating. In Feng *et al.*'s *ex vivo* experimental study, a power of 30 W for 12 min tended to form scope and spherical shape of the ablation lesion with the mean long axis of 2.5 cm and short-axis diameter of 0.7 cm. The mean temperature at the 5-mm site from the electrode was driven rapidly high to 60°C, in which nearly immediate tissue coagulation was induced with irreversible damage caused to tumor tissue. However, the maximum temperatures at 10 and 15 mm were low, which can guarantee the safety of surrounding tissue [14]. Compared with RFA, MWA may have advantages in the treatment of liver tumors: It has a larger ablation zone, less treatment time and more complete tumor kill [17]; it is less affected by the perfusion mediated heat sink effect, which may be helpful for treating tumors with a rich blood supply [18]; and multiple antennae can be used simultaneously to ablate larger tumors [19,20].

Treatment indications & patient preparation

At present, indications for the MWA of benign thyroid nodules are local compressive symptom, neck discomfort or pain, foreign body sensation, cosmetic concern, ineligibility or refusal to undergo surgery or anxiety about a malignancy.

To exclude malignant thyroid nodules and follicular neoplasm, at least two separate US-guided fine-needle aspirations and/or core needle biopsies are recommended to confirm the benign nature of a nodule before ablation [6,21,22]. Like other thermal ablations, US examination is essential for characterizing a nodule and evaluating the surrounding anatomical structures [23]. Even if there are benign results seen on fine-needle aspiration or core needle biopsy, caution should be taken when performing MWA of nodules with malignant US features [24]. The shape, diameters, margin, echogenicity, calcification, vascularity and composition of nodules on US examination, laboratory data and clinical symptoms should be examined in all patients before treatment. An appropriate puncture route should be chosen on US. Three orthogonal diameters of thyroid nodules (the largest diameter and the two other perpendicular ones) should be measured by US before MWA. The nodular volume could be obtained by multiplying the three diameters of the nodules by 0.525 (ellipsoid volume) [15].

Laboratory tests usually include thyroid function (triiodothyronine, free thyroxine [fT4] and TSH), complete blood count, blood electrolytes, blood coagulation tests (prothrombin time and activated partial thromboplastin time) and calcitonin. Fiber laryngoscopy should be performed on all patients before MWA if possible and on patients who complained of hoarseness after MWA.

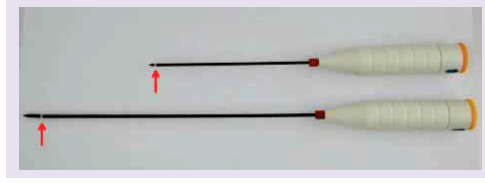

Figure 1. Microwave antenna. Top: the antenna used for thyroid nodules has a diameter of 16 G, a 10-cm shaft, and the narrow radiating segment (arrow) is 3 mm away from the top of the antenna. Bottom: the antenna used for abdominal tumors has a diameter of 15 G, an 18-cm shaft, and the narrow radiating segment (arrow) is 11 mm away from the tip of the antenna.
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MWA devices & procedures

• Devices for thyroid MWA

The microwave unit consists of a microwave generator, a flexible low-loss coaxial cable and an internally cooled shaft antenna. Taking into account the relative small size of the thyroid gland and the vital structures adjacent to it in a small region such as the neck, the MW antennas have been developed in China to debulk safely thyroid nodules. The internally cooled needle antenna is modified specially to treat superficial neck organ diseases (16 G, a 10 cm shaft, 3 mm between the narrow radiating segment and the tip of antenna), in contrast to the antenna used for abdominal tumors (15 G, an 18 cm shaft, 11 mm between the narrow radiating segment and the tip of antenna; **Figure 1**). The shaft is coated with polytetrafluoroethylene to prevent tissue adhesion, which can be easily seen on US. The generator is capable of producing 1–100 W of power at 2450 MHz, in the form of pulse or continuous. To prevent shaft overheating, distilled water is circulated through dual channels inside the antenna shaft, continuously cooling the shaft.

• Procedures for thyroid MWA

The patient is placed in the supine position with hyper extended neck and a venous catheter is inserted in a forearm vein. After localization of the best puncture site, local anesthesia with 2% lidocaine is performed subcutaneously. The 'liquid-isolating region' technique has recently been introduced [15]. A mixture of 0.9% lidocaine and physiological saline is infused into the surrounding thyroid capsule to achieve a liquid-isolating region, protecting the vital structures of the neck (carotid artery, trachea, esophagus and nerve) from the thermal injury **(Figure 2)**. With US guidance, the tumor is localized and optimal approach is determined. In the thyroid, a trans-isthmic approach has been routinely used for thermal ablation [4,25]. With this method, the antenna is inserted from the isthmus to the lateral aspect of a targeted nodule along its short axis. This route of approach has several advantages. Firstly, the entire length of the antenna can be visualized on a transverse US view. The second advantage is minimal exposure to the heat of the danger triangle [26], which includes the recurrent laryngeal nerve, esophagus and trachea. Finally, the antenna passes through a sufficient amount of thyroid parenchyma, which prevents a change in the position of the electrode tip during swallowing or talking. If large numbers of vessels are located in the isthmus, the lateral approach can be used to prevent hemorrhage **(Figure 3)**. Operators usually apply a power of 2–50 W with a duration of 5–15 min depending on the size and the heterogeneous nature of the nodules. The extent of ablation area is presumed by variations in the echo from the nodule, which is monitored by real-time US. The ablation power and the antenna location are regulated according to the echogenic change. If the heat-generated hyperechoic water vapor does not completely encompass the entire nodule at one site, the tip of the antenna should be moved backward. If a hyperechoic zone does not form surrounding the antenna within 5–10 s, MW power is increased in 5 W increments. For mixed/mainly cystic nodules, MWAs should be performed only after aspiration of internal fluid. When a patient cannot tolerate the pain associated with ablation, the power should be reduced or turned off for several seconds. The therapy is terminated when the hyperecho covered the whole nodule. However, some regions of thyroid nodules that are close to critical structures such as the recurrent laryngeal nerve and esophagus may remain undertreated. At the end of the procedure, all patients should remain under observation for 30 min with compression on the neck to prevent bleeding or hematoma formation.

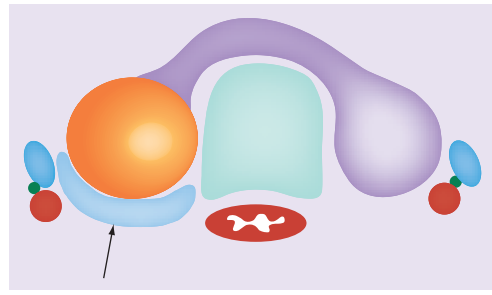

Figure 2. Liquid-isolating region. A mixture of 0.9% lidocaine and physiological saline is infused into the surrounding thyroid capsule to achieve a 'liquid-isolating region' (arrow), protecting the vital structures of the neck (carotid artery, trachea, esophagus and nerve) from the thermal injury.

• Follow-up evaluation

US examinations and the clinical symptoms are routinely evaluated at 1, 3, 6 and 12 months after the procedure. The US examination is performed to assess the changes of MW-induced lesions, including the size, echogenicity and vascularity. The reduction in volume is determined by US imaging and calculated by the following equation: volume reduction ratio (%) = ([initial volume - final volume] × 100)/initial volume. Laboratory tests should be performed immediately on patients who complain of symptoms indicating any thyroid function abnormality. Side effects and complications of MWA are evaluated at the end of ablation as well as 24 h and 1 month after the procedure by analysis of clinical signs and symptoms.

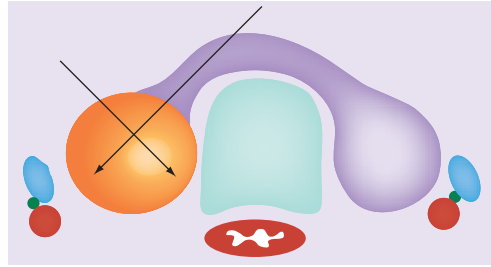

Figure 3. Puncture route of thyroid microwave ablation. The internally cooled microwave antenna (arrow) is positioned into the thyroid nodule utilizing the transisthmic approach or the lateral approach.

Clinical results

The efficacy of MWA is evaluated by change in nodule volume and improvement in clinical problems, including pressure symptoms and cosmetic issues. The first study on the use of MWA reported by Feng *et al.* demonstrated a reduction of nodule volume and improvement of nodule-related symptoms. The mean volume reduction ratio of MWA was 45.9% at the last follow-up [14]. The result of this study was confirmed by Yue *et al.* in a large series study, which found that the mean nodule volume reduction ratio is 65% in whole group (58% in mainly solid nodules, 83% in mixed nodules and 88% in mainly cystic nodules) at the 6-month follow-up with 30.7% index nodules disappearing **(Table 1)** [15]. The other thermal ablations with variable nodule volume reduction were also reported. The mean volume reduction ratio of laser, radiofrequency in mainly solid nodules was 42.7–82% [8,10,27–30], 50.7–84.9% [13,31–33], respectively **(Table 2)**. Regarding the mixed/mainly cystic nodules, a study of RFA showed a volume reduction of 90% at 6–8.9 months follow-up [33]. What's more, studies of combined RFA/ethanol ablation treatment of cystic nodules were reported with a volume reduction of 91–92% at the 6-month follow-up [34,35]. In treatment with LA, Dossing *et al.* reported that the mixed nodule got an overall median volume reduction of 73% [9]. Pacella *et al.* reported that mixed nodules got a volume reduction of 64% without aspiration the cystic component, which is not different from the mainly solid nodules [29]. It seems that mixed/mainly cystic nodules showed a better treatment response than the mainly solid tumors. However, the superior outcome might be due to the removal of the cystic component that accounts for big proportion of the nodules.

Thyroid functions are considered to be merely minimally influenced by MWA, as with the other thermal ablations. In Feng *et al.*'s clinical study, Serum TSH levels decreased, fT4 levels increases and serum triiodothyronine did not change 1 day after MWA, which recovered in the following days [14]. Kim *et al.* reported serum fT4 levels were abnormal in three patients and Jeong *et al.* reported the TSH had decreased in three patients 1 day after RFA. But, they were normalized at follow-up in all cases [4,33]. Thyroid function was also unaltered after LA [8,9]. It is likely that ablation-induced fT4 release from intraglandular stores and serum TSH level decreases due to feedback regulation.

Complications

US-guided percutaneous MWA is similar to LA and RFA in terms of side effects and complications **(Table 3)**. Even though its side effects seem to be mild, it is important to know the possible complications and suggested technical tips for safe ablation and proper management.

Nerve injury is the most serious complication in thyroid MWA. Yue *et al.* reported that 3.6% (eight out of 222) of patients complained of voice change could recover within 3 months spontaneously [15]. In Feng *et al.*'s study, one out of 11 (9.1%) patient complained of voice change and recovered within 2 months after using of corticosteroids, physical therapy and vocal exercises [14]. The incidence of transient (and never permanent) voice change in previous studies of RFA or LA is described to be 0–8.3% [4,8,10,29,32,37]. Voice change is likely due to thermal injury directly to the recurrent laryngeal nerve or nerve compression caused by perinodular edema. In RFA with the internally cooled needle, Baek *et al.* suggested nerve injury may be prevented by using the moving shot technique and undertreating the conceptual ablation units adjacent to the nerve [4,25,36]. What's more, the incidence of nerve injury could be decreased by separated therapy sessions if nodules are located in both lobes of thyroid and temperature monitoring via a thermocouple needle, which can be percutaneously placed at a designated location to monitor temperature in real time, or infusion of saline into the surrounding thyroid capsule called the liquid-isolating region technique [15].

Table 1. Treatment results of microwave ablation for benign thyroid nodules.

Nodule type	Nodules (n)	VR (mean)				
		V init. (ml)	*V last (ml)*	*VR1 (%)*	*VR6 (%)*	*VR last (%)*
Mainly solid	320	1.07	0.50	82	58	25
Mixed	136	4.23	1.50	37	83	65
Mainly cystic	21	4.64	0.46	49	88	72

V init.: Initial volume before microwave ablation; V last: Volume on the last follow-up; VR: Volume reduction; VR1, VR6 and VR last: Volume reduction at 1, 6 months and on the last follow-up, respectively.
Data taken from [15].

However, most patients usually experienced slight pain or sensation of heat in the neck at the ablated site during MWA. They can tolerate the symptoms well without analgesics [14,15]. The uncomfortable sensation is usually self-limited. Whereas, in a large series study of RFA, 5.5% of patients required analgesics for more than 2 days after ablation [4]. In LA, persistent pain occurred in 8–40% of patients that may require additional medication [9,10,27–29]. If severe pain in the neck occurs during the procedure, the power should be reduced or turned off immediately. Oral painkillers can be selectively used after ablation.

Hematoma and fever have been reported after MWA. Four patients were observed with subcapsular bleeding and no perithyroidal or intranodular bleeding was observed [14]. Jeong *et al.* found five patients (2.1%) developed perithyroidal hematoma in RFA [4], while in a report of LA, 2.5% of patients experienced thyroid pericapsular bleeding and 7.4% of patients experienced intranodular bleeding [10]. It can usually be controlled by compressing the neck for several minutes. Serious perithyroidal hemorrhage seldom occurs owing to examining the perithyroidal vessels before inserting the electrode and using small antenna of electrodes. Most hematomas completely disappear within half a month. There may be slight fever found in patients after ablation lasting 1 or 2 days and could disappear without management.

The other complications that occur during thermal ablation of laser and radiofrequency have been seldom observed in MWA, including skin burn, hypothyroidism and edema. It may be due to the insufficient cases compared to LA and RFA. Although fatal complications have not been observed, esophageal perforation, tracheal injury, infection, abscess formation and procedure-related deaths are possible complications. These complications could be minimized by improvements in knowledge and the study of complication-prevention techniques, such as the liquid-isolating region technique, the transisthmic approach method and the moving shot technique. In addition, swallowing of cold water during the procedure could prevent injury to the esophagus. MWA should be stopped to prevent tracheal injury when patients are coughing.

Conclusion

MWA is a newly developed minimally invasive technique for treating cytologically benign thyroid nodules. It may become a safe and effective

Table 2. Treatment results of patients undergoing microwave ablation, radiofrequency ablation and laser ablation of thyroid nodules.

	MWA		RFA							LA			
	Yue et al. *(2012)* [15]	*Feng* et al. *(2012)* [14]	*Faggiano* et al. *(2012)*† [13]	*Baek* et al. *(2010)* [36]	*Baek* et al. *(2009)* [25]	*Spiezia* et al. *(2009)* [32]	*Jeong* et al. *(2008)* [4]	*Deandrea* et al. *(2008)* [31]	*Kimet* et al. *(2006)* [33]	*Dossing* et al. *(2011)*† [8]	*Papini* et al. *(2007)*† [28]	*Dossing* et al. *(2005)*† [27]	*Valcavi* et al. *(2010)* [10]
Patients (n)	222	11	40	15	9	94	302	33	35	78	62	30	122
Nodules (n)	477	11	20	15	9	94	236	31	30	78	62	30	122
Nodule type	Cold	Cold	Cold plus AFTN	Cold	AFTN	Cold plus AFTN	Cold	Cold plus AFTN	Cold	Cold	Cold	Cold	Cold
Solid component (%)	0–100	0–100	>70	>50	60–100	>30	0–100	>30	0–100	100	>80	100	>80
Follow-up period (months)	1–24	1–9	1–12	6–8	6–17	12–24	1–41	6	1–18	12–114	12	6	36
V init. (ml)	2.13	5.30	13.3	7.5	15.0	24.5	6.13	27.7	6.3	8.2	6.2	8.2	23.1
VR1 (%)	41	–	36.5	49	36	54	58	33	47	–	–	26.5	6.2
VR6 (%)	65‡	–	76.5	80	71	–	85	51	64	–	–	44	47.5
VR last (%)	38	45.99	86.5	–	75	79	84	–	–	51	42.7	44	47.8

†Study is randomized trial.
‡In total, 254 out of 477 nodules remained in 6-months follow-up.
AFTN: Autonomously hyperfunctioning thyroid nodule; LA: Laser ablation; MWA: Microwave ablation; RFA: Radiofrequency ablation; V init.: Initial volume before MWA; VR1, VR6 and VR last: Volume reduction at 1, 6 months and on the last follow-up, respectively.

Table 3. Complications associated with microwave ablation, radiofrequency ablation and laser ablation of thyroid nodule.

	MWA; n (%)		RFA; n (%)	LA; n (%)
	Yue et al. *(2012)* [15]	*Feng* et al. *(2012)* [14]	*Baek* et al. *(2012)* [37]	*Valcavi et al.* *(2010)* [10]
Patients (n)	222	11	1459	122
Hematoma	–	4 (36.4)	15 (1.02)	12 (9.9)
Fever	–	3 (27.3)	–	5 (4.1)
Severe pain	–	–	38 (2.6)	9 (7.4)
Voice change	8 (3.6)	1 (9.1)	15 (1.02)	2 (1.6)
Skin burn	–	–	4 (0.27)	1 (0.8)
Edema	–	–	–	11 (9.0)
Hypothyroidism	–	–	1 (0.07)	–

LA: Laser ablation; MWA: Microwave ablation; RFA: Radiofrequency ablation.

alternative to surgery. It can achieve shrinkage of nodule size and relief of clinical symptoms. Though side effects and complications are few, the operators still should be aware of the significance and the available preventative techniques. Further studies are needed to define the role of the procedure and improve this technique.

Future perspective

MWA could be a minimally invasive technique with great promise for the treatment of benign thyroid nodules. Unfortunately, no head-to-head studies have been performed so far and the comparison of the results of laser with those of radiofrequency and MWA techniques is impossible. So far, the series of patients treated with these procedures have not been comparable, in terms of baseline volumes or in terms of the fluid content of the lesions undergoing LA. The studies about thyroid MWA are limited and most data on MWA are the results of single-center experiences, so further prospective randomized studies will be necessary. As RFA and LA have been reported to treat malignant thyroid [38], as well as autonomously functioning thyroid nodule [10,13,29,31–32,39], it should be further explored whether MWA could be used to treat those tumors. In addition, the technique is expecting to be improved to enhance efficacy and reduce complications of MWA.

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EXECUTIVE SUMMARY

- Nonsurgical and minimally invasive treatments have been used to treat benign thyroid nodules, of which microwave ablation (MWA) is newly developed.
- MWA is based on thermal injury secondary to heat generated from rotation of water molecules and have several advantages in tumor ablation.
- Patients with thyroid nodules should be evaluated by ultrasound (US), US-guided fine-needle aspirations and/or core needle biopsies, and laboratory tests before ablation.
- The internally cooled shaft antenna is modified specially for thyroid MWA.
- During the procedure, the 'liquid-isolating region' technique, as well as the trans-isthmic approach is used and the ablation is regulated according to the echogenic change under US guidance.
- Studies of thyroid MWA demonstrate significant volume reductions and improvement of clinical symptoms.
- Side effects and complications are few, mainly including nerve injury, pain, hematoma and fever, and it is important to be aware of the preventative techniques.

References

Papers of special note have been highlighted as:
• of interest; •• of considerable interest

1 Gharib H, Papini E, Paschke R *et al.* American Association of Clinical Endocrinologists, Associazione Medici Endocrinologi, and European Thyroid Association medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. *J. Endocrinol. Invest.* 33(5 Suppl.), 1–50 (2010).

2 Klubo-Gwiezdzinska J, Wartofsky L. Thyroid emergencies. *Med. Clin. North Am.* 96(2), 385–403 (2012).

3 Weiss RE, Lado-Abeal J. Thyroid nodules: diagnosis and therapy. *Curr. Opin. Oncol.* 14(1), 46–52 (2002).

4 Jeong WK, Baek JH, Rhim H *et al.* Radiofrequency ablation of benign thyroid nodules: safety and imaging follow-up in 236 patients. *Eur. Radiol.* 18(6), 1244–1250 (2008).

• **Demonstrates that thyroid nodule radiofrequency ablation is a safe and effective modality on reducing volume in benign thyroid nodules.**

5 Shemen LJ, Strong EW. Complications after total thyroidectomy. *Otolaryngol. Head Neck Surg.* 101(4), 472–475 (1989).

6 Gharib H, Papini E, Valcavi R *et al.* American Association of Clinical Endocrinologists and Associazione Medici Endocrinologi medical guidelines for clinical practice for the diagnosis and management of thyroid nodules. *Endocr. Pract.* 12(1), 63–102 (2006).

7 Bennedbaek FN, Karstrup S, Hegedus L. Percutaneous ethanol injection therapy in the treatment of thyroid and parathyroid diseases. *Eur. J. Endocrinol.* 136(3), 240–250 (1997).

8 Dossing H, Bennedbaek FN, Hegedus L. Long-term outcome following interstitial laser photocoagulation of benign cold thyroid nodules. *Eur. J. Endocrinol.* 165(1), 123–128 (2011).

9 Dossing H, Bennedbaek FN, Hegedus L. Interstitial laser photocoagulation (ILP) of benign cystic thyroid nodules – a prospective randomized trial. *J. Clin. Endocrinol. Metab.* 98(7), E1213–E1217 (2013).

10 Valcavi R, Riganti F, Bertani A, Formisano D, Pacella CM. Percutaneous laser ablation of cold benign thyroid nodules: a 3-year follow-up study in 122 patients. *Thyroid* 20(11), 1253–1261 (2010).

11 Hegedus L. Therapy: a new nonsurgical therapy option for benign thyroid nodules? *Nat. Rev. Endocrinol.* 5(9), 476–478 (2009).

12 Pacella CM, Bizzarri G, Guglielmi R *et al.* Thyroid tissue: US-guided percutaneous interstitial laser ablation-a feasibility study. *Radiology* 217(3), 673–677 (2000).

•• **Establishes the scientific foundation for the percutaneous treatment of benign thyroid nodules.**

13 Faggiano A, Ramundo V, Assanti AP *et al.* Thyroid nodules treated with percutaneous radiofrequency thermal ablation: a comparative study. *J. Clin. Endocrinol. Metab.* 97(12), 4439–4445 (2012).

14 Feng B, Liang P, Cheng Z *et al.* Ultrasound-guided percutaneous microwave ablation of benign thyroid nodules: experimental and clinical studies. *Eur. J. Endocrinol.* 166(6), 1031–1037 (2012).

• **One of two studies on microwave ablation of benign thyroid nodules with significant volume reductions and improvement of clinical symptoms.**

15 Yue W, Wang S, Wang B *et al.* Ultrasound guided percutaneous microwave ablation of benign thyroid nodules: safety and imaging follow-up in 222 patients. *Eur. J. Radiol.* 82(1), e11–e16 (2013).

• **One of two studies on microwave ablation of benign thyroid nodules with significant volume reductions and improvement of clinical symptoms.**

16 Dodd GD 3rd, Soulen MC, Kane RA *et al.* Minimally invasive treatment of malignant hepatic tumors: at the threshold of a major breakthrough. *Radiographics* 20(1), 9–27 (2000).

17 Simon CJ, Dupuy DE, Mayo-Smith WW. Microwave ablation: principles and applications. *Radiographics* 25(Suppl. 1), S69–S83 (2005).

18 Wright AS, Sampson LA, Warner TF, Mahvi DM, Lee FT Jr. Radiofrequency versus microwave ablation in a hepatic porcine model. *Radiology* 236(1), 132–139 (2005).

19 Kuang M, Lu MD, Xie XY *et al.* Liver cancer: increased microwave delivery to ablation zone with cooled-shaft antenna – experimental and clinical studies. *Radiology* 242(3), 914–924 (2007).

20 Dong BW, Liang P, Yu XL *et al.* Sonographically guided microwave coagulation treatment of liver cancer: an experimental and clinical study. *Am. J. Roentgenol.* 171(2), 449–454 (1998).

21 Sung JY, Na DG, Kim KS *et al.* Diagnostic accuracy of fine-needle aspiration versus core-needle biopsy for the diagnosis of thyroid malignancy in a clinical cohort. *Eur. Radiol.* 22(7), 1564–1572 (2012).

22 Na DG, Lee JH, Jung SL *et al.* Radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers: consensus statement and recommendations. *Korean J. Radiol.* 13(2), 117–125 (2012).

• **Guideline developed for the optimal use of radiofrequency ablation for thyroid nodules based on a comprehensive analysis of the multicenter studies and expert consensus.**

23 Moon WJ, Baek JH, Jung SL *et al.* Ultrasonography and the ultrasound-based management of thyroid nodules: consensus statement and recommendations. *Korean J. Radiol.* 12(1), 1–14 (2011).

24 Moon WJ, Jung SL, Lee JH *et al.* Benign and malignant thyroid nodules: US differentiation – multicenter retrospective study. *Radiology* 247(3), 762–770 (2008).

25 Baek JH, Moon WJ, Kim YS, Lee JH, Lee D. Radiofrequency ablation for the treatment of autonomously functioning thyroid nodules. *World J. Surg.* 33(9), 1971–1977 (2009).

26 Baek JH, Lee JH, Valcavi R, Pacella CM, Rhim H, Na DG. Thermal ablation for benign thyroid nodules: radiofrequency and laser. *Korean J. Radiol.* 12(5), 525–540 (2011).

27 Dossing H, Bennedbaek FN, Hegedus L. Effect of ultrasound-guided interstitial laser photocoagulation on benign solitary solid cold thyroid nodules – a randomised study. *Eur. J. Endocrinol.* 152(3), 341–345 (2005).

28 Papini E, Guglielmi R, Bizzarri G *et al.* Treatment of benign cold thyroid nodules: a randomized clinical trial of percutaneous laser ablation versus levothyroxine therapy or follow-up. *Thyroid* 17(3), 229–235 (2007).

• **Prospective randomized trial demonstrates a single laser ablation induces significant volume reduction of benign large cold thyroid nodules and improvement of local symptoms.**

29 Pacella CM, Bizzarri G, Spiezia S *et al.* Thyroid tissue: US-guided percutaneous laser thermal ablation. *Radiology* 232(1), 272–280 (2004).

30 Cakir B, Topaloglu O, Gul K *et al.* Effects of percutaneous laser ablation treatment in benign solitary thyroid nodules on nodule volume, thyroglobulin and anti-thyroglobulin levels, and cytopathology of nodule in 1 yr follow-up. *J. Endocrinol. Invest.* 29(10), 876–884 (2006).

31 Deandrea M, Limone P, Basso E *et al.* US-guided percutaneous radiofrequency thermal ablation for the treatment of solid benign hyperfunctioning or compressive thyroid nodules. *Ultrasound Med. Biol.* 34(5), 784–791 (2008).

32 Spiezia S, Garberoglio R, Milone F *et al.* Thyroid nodules and related symptoms are stably controlled two years after radiofrequency thermal ablation. *Thyroid* 19(3), 219–225 (2009).

• **Excellent study investigates the long-term effectiveness of percutaneous radiofrequency ablation for treating solid benign thyroid nodules.**

33 Kim YS, Rhim H, Tae K, Park DW, Kim ST. Radiofrequency ablation of benign cold thyroid nodules: initial clinical experience. *Thyroid* 16(4), 361–367 (2006).

• **Initial experience of radiofrequency ablation for benign thyroid nodules.**

34 Jang SW, Baek JH, Kim JK *et al.* How to manage the patients with unsatisfactory results after ethanol ablation for thyroid nodules: role of radiofrequency ablation. *Eur. J. Radiol.* 81(5), 905–910 (2012).

• **Demonstrates that radiofrequency ablation is effective and safe treatment of benign thyroid nodules in patients whose clinical problems were incompletely resolved after ethanol ablation.**

35 Lee JH, Kim YS, Lee D, Choi H, Yoo H, Baek JH. Radiofrequency ablation (RFA) of benign thyroid nodules in patients with incompletely resolved clinical problems after ethanol ablation (EA). *World J. Surg.* 34(7), 1488–1493 (2010).

• **Demonstrates that radiofrequency ablation is effective and safe treatment of benign thyroid nodules in patients whose clinical problems were incompletely resolved after ethanol ablation.**

36 Baek JH, Kim YS, Lee D, Huh JY, Lee JH. Benign predominantly solid thyroid nodules: prospective study of efficacy of sonographically guided radiofrequency ablation versus control condition. *Am. J. Roentgenol.* 194(4), 1137–1142 (2010).

37 Baek JH, Lee JH, Sung JY *et al.* Complications encountered in the treatment of benign thyroid nodules with US-guided radiofrequency ablation: a multicenter study. *Radiology* 262(1), 335–342 (2012).

38 Pacella CM, Papini E. Image-guided percutaneous ablation therapies for local recurrences of thyroid tumors. *J. Endocrinol. Invest.* 36(1), 61–70 (2013).

39 Barbaro D, Orsini P, Lapi P *et al.* Percutaneous laser ablation in the treatment of toxic and pretoxic nodular goiter. *Endocr. Pract.* 13(1), 30–36 (2007).