

NORTH AMERICAN SOCIETY OF INTERVENTIONAL ENDOCRINOLOGISTS**Consensus Statement on Thermal and Chemical Ablation of Thyroid Nodules and Neck Lesions**

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INTRODUCTION

Thermal and chemical ablation techniques for the non-surgical treatment of thyroid nodules and neck lesions have been used internationally for decades, with only relatively recent interest and acceptance in the United States of America. This statement is intended to be an evolving document that provides a framework for the safe and effective practice of chemical and thermal ablation techniques for the management of thyroid nodules in the outpatient setting in the United States.

There is a wealth of international data on outcomes of thyroid ablation on benign thyroid nodules available, however, North American data is limited to the studies in Table 1. The reported literature, both international and from the United States supports the notion that thermal and chemical ablation is a viable alternative to traditional surgical management.

Chemical ablation causes coagulative necrosis via cell dehydration and ischemic necrosis by small vessel thrombus formation. Ethanol is the most common agent used for this and has been used to treat both benign thyroid nodules and recurrent thyroid cancer in the United States.

Thermal ablation involves raising the cell temperature to over 50 – 60 °C (122 – 140 °F) resulting in coagulative necrosis using various techniques. Radiofrequency ablation (RFA) uses a high frequency alternating current to generate heat via ionic friction, followed by conduction through the tissue. Laser ablation (LA) uses optical fibers to deliver a focused beam of light energy of near infrared wavelength, which then generates heat. Microwave ablation (MWA) uses microwaves to create an electromagnetic field resulting in oscillation of polar water molecules generating frictional heat.

Of the thermal ablation techniques, RFA has gained the most traction in the United States, and LA is also being used. MWA has only recently become available in the United States, whereas High Intensity Focused Ultrasound (HIFU) for thyroid nodules is not yet available.

Thermal and chemical ablative techniques have the advantage of being amenable to being performed in an office setting; and should be part of the treatment options offered by practices who see patients with nodular thyroid disease. They have negligible risk of hypothyroidism, no scarring, and lower complication rates compared with surgery.

Table 1 Outcomes of Chemical and Thermal Ablative Therapies in North America

First Author, Year	Study Design	n	% VR	Vol.	Follow-up (m)	Comp.* (%)
RFA						
Kandil, 2022	PC	70	76	4.17	12	2.5
Hussain, 2021	RC	47	70.8	8	3.5	4.2
Kuo, 2021	RC	24	50.7	8.52	1.1	5
Sinclair, 2021	PC	20	46.3, 57.7**	NR	12	NR
Hamidi, 2018	RC	14	44.6	24.2	8.6	NR
EA						
Abdelgawad, 2022	RC	34	28.6	2.32	6	4.55
Steinl, 2022	RC	17	66 – 78	21.3	1 – 12	NR
Sharma, 2020,	RC	18	56.1	5.7	3	NR
Iniguez-Ariza, 2018	RC	20	75.64	19.6	24	20

Abbreviations: RFA, radiofrequency ablation; EA, ethanol ablation; n, number of nodules; % VR, percentage volume reduction; Vol., median volume of nodules being treated; m, months; Comp., complications; %, percentage; RC, retrospective cohort; PC, prospective cohort; RCT, randomized controlled trial; NR, not reported. *Complications, major and minor, as defined by the Society of Interventional Radiology criteria. **Initial percentage volume reduction only reported for the two nodules that underwent regrowth.

RATIONALE AND SCOPE

This statement mainly focuses on benign thyroid nodules, with brief mention of parathyroid adenomas, primary thyroid malignancies and recurrent thyroid cancer in the neck. Ablation of thyroid malignancies, both primary and recurrent will be covered in more detail in a separate consensus statement.

The target audience is primarily endocrinologists who see nodular thyroid disease; however, it can be used by other medical practitioners such as surgeons or interventional radiologists who co-manage these patients. The recommendations contained herein are intended as a helpful guide to the decision-making process when considering ablative techniques; and are not in any way meant to restrict or limit care based on assessment of individual patients by the clinician.

METHODOLOGY

The author panel consists of endocrinologists who have personally performed chemical and/or thermal ablation of thyroid nodules in the United States for more than 3 years. An outline covering the scope of the statement was created, the sections were discussed as a group, and then authors were assigned a section and invited to give recommendations and statements based on literature review and expert opinion.

After all statements were received, they were collated, and a modified Delphi method was applied to assess whether each statement met consensus as described. The series of best practice statements were distributed to the author panel, and a 9-point Likert scale was used to measure agreement using the following anchor points: 1 (strongly disagree), 3 (disagree), 5 (neutral), 7 (agree), and 9 (strongly agree). Each author was blinded to the other panelists selections. Statements were defined as achieving consensus if there was a mean score of 7 or greater, with no outlier value lower than 5. If consensus was not initially achieved, then modifications were made with further rounds of scoring until consensus was achieved. Where the panel was not able to agree, it is noted that consensus was not achieved. The final document was distributed to NASOIE members for comments and modifications will continually be made keeping these comments in mind.

CONSENSUS STATEMENT

Chemical and thermal ablative techniques are primarily indicated for benign, symptomatic nodules, both autonomously functioning and non-functioning, however, have also been used for malignant lesions and parathyroid adenomas. The choice of treatment will depend on the type of nodule, availability of method, and nodule characteristics.

Recommendation 1: Chemical ablation (ethanol ablation) is recommended for recurrent cystic nodules that are either symptomatic or cause cosmetic issues and is not recommended for solid or predominantly solid nodules.

Partially cystic nodules usually respond better to thermal ablation, or a combination of chemical and thermal ablation, however ethanol ablation alone may be considered in cases where thermal ablation is not available.

Recommendation 2: Thermal ablation is indicated for benign thyroid nodules that are either symptomatic or cause cosmetic issues; or those that are growing and are expected to eventually cause symptoms.

Recommendation 3: Thermal ablation is indicated in autonomously functioning thyroid nodules that cause thyroid dysfunction or symptoms, especially in those with volume less than 20 mL.

Larger autonomously functioning thyroid nodules may require repeated thermal ablation sessions to achieve adequate volume reduction to normalize thyroid function tests. Radioactive iodine uptake and scan should be performed in cases of toxic multinodular goiter to target the autonomously functioning nodules. There is no indication to perform a radioactive iodine uptake and scan in non-functioning thyroid nodules prior to ablation. Chemical or thermal ablation should not be used to treat thyroid dysfunction caused by Graves' disease.

Recommendation 4: Thyroid nodules should be confirmed to be benign by fine needle aspiration biopsy and absence of high-risk ultrasound features prior to ablation.

Recommend confirmation of benign nodules by two benign aspirations except for spongiform nodules or pure cystic lesions as they have extremely low risk of malignancy. Autonomously functioning thyroid nodules can be confirmed to be benign with one benign aspiration. Thermal ablation may be considered for indeterminate nodules (only Bethesda III) with benign molecular marker testing results; there is no consensus on whether it may be considered for Bethesda IV nodules with benign molecular markers. Thermal or chemical ablation is not recommended for nodules with high-risk ultrasound features, regardless of cytopathology results.

Recommendation 5: Thermal ablation is not recommended for treatment of primary thyroid malignancies except in certain patients.

Thermal ablation has shown some promise in treatment of thyroid microcarcinomas in carefully selected patients. In these cases, it is important to make sure there is no extrathyroidal extension or metastatic disease and the physician is confident that they can completely ablate the malignant nodule without damage to surrounding structures. In case of RFA and MWA, this means the microcarcinoma should be intra-thyroidal with a clear buffer of at least 2 mm of surrounding normal thyroid tissue. In case of LA, there needs to be a buffer of 1 cm or more between the lesion and critical structures, which can sometimes be achieved through

hydrodissection. Chemical ablation is not recommended for treatment of primary thyroid malignancies.

Recommendation 6: Thermal ablation may be considered as a palliative therapy for large thyroid cancer recurrences in patients who are not candidates for surgery.

Recommendation 7: Thermal ablation may be considered for treatment of recurrent thyroid cancer in the neck in selected patients.

Surgical resection is the standard of care for lymph node recurrence of thyroid cancer in the neck; however, in certain patients, thermal ablation may be considered. Chemical ablation has also been used to treat recurrent thyroid cancer in the neck in selected patients, and may be considered when thermal ablation is not available or financially feasible. In order to be effective, the physician should be confident they can completely ablate the lesion without damage to surrounding structures and there should not be more than 2 – 3 involved lesions/lymph nodes.

Recommendation 8: Radiofrequency ablation or microwave ablation may be considered for treatment of parathyroid adenomas causing primary hyperparathyroidism that meets criteria for surgery in selected patients who are not surgical candidates or who refuse surgery.

Parathyroidectomy is the standard of care for primary hyperparathyroidism; however, some patients may not be surgical candidates, or may refuse surgery despite meeting criteria for surgical treatment. RFA or MWA is a treatment option for parathyroid adenomas that would otherwise have to be removed surgically if the physician is confident that they would be able to achieve a complete ablation without damage to surrounding structures. Hydrodissection needs to be utilized to separate the adenoma from critical structures. RFA or MWA may be especially useful in cases of intra-thyroidal parathyroid adenomas as this would avoid the need for a hemi-thyroidectomy. Laser ablation is not recommended for parathyroid ablation because of insufficient data. There was no consensus reached on whether ethanol ablation should be used for ablation of parathyroid adenomas.

Recommendation 9: Familiarity with neck anatomy and ultrasonography, and proficiency in fine needle aspiration biopsies using the parallel technique and trans-isthmic approach is recommended prior to performed chemical or thermal ablation in the neck.

These skills are essential to learn prior to performing safe chemical and thermal ablation in the neck. In thyroid ablation, the electrode (RFA), antenna (MWA), fiber (LA) or needle (ethanol ablation) used is placed parallel to the ultrasound transducer to ensure complete visualization. This helps avoid inadvertent damage to surrounding structures.

Recommendation 10: Food and Drug Administration approved equipment should be used for thermal ablation and single use disposable electrodes, antennas or fibers should be used for each patient undergoing radiofrequency ablation, microwave ablation or laser ablation respectively.

The following supplies should be available: sterile drapes, sterile gloves, masks, sterile gel, sterile probe covers and cold dextrose 5% in water (D5W) between 0 – 4 °C (32 – 39 °F) in case rescue hydrodissection is needed for recurrent laryngeal nerve injury. In addition to the physician performing the procedure, adequate staff should be available to handle the sterile supplies and manage the ultrasound machine and ablation equipment.

The equipment used for thermal ablation should be periodically evaluated for safety and compliance by the manufacturing company.

Recommendation 11: Informed consent must be obtained prior to the ablation procedure.

Informed consent should include presenting the patient with other management options, a description of the expected results, and both early and late complications of the procedure reported in the literature, as well as the theoretical risk of possible complications they may not have been reported yet. Patients should be informed that there may be possible pain during the procedure. They should also be informed of the risk of possible treatment failure and regrowth of the nodules, and that the procedure may sometimes need to be repeated. Expectations should be managed, and it is important to let the patient know that the decrease in nodule volume is expected to be slow i.e. over months to years. Patients should specifically be informed that if they have chronic lymphocytic thyroiditis (Hashimoto's disease) prior to the procedure they may develop hypothyroidism as a consequence of the natural history of the disease.

Recommendation 12: A comprehensive neck ultrasound evaluation should be performed prior to ablation that includes evaluation of the nodule, lateral neck and relevant anatomic structures.

The nodule location, size and composition must be noted; and any high-risk features or cervical lymphadenopathy must be identified. The physician should be aware of the location of the nerves, vessels, trachea and esophagus in reference to the ablation zone.

Recommendation 13: The patient's voice should be evaluated before, during and after the ablation procedure.

In patients with a normal voice, ultrasound examination should include evaluation of movement of bilateral true vocal cords prior to starting the ablation. If the patient has dysphonia or hoarseness, they should be evaluated by an otolaryngologist prior to the procedure; and a laryngoscopy is also suggested in patients with a previous history of thyroid cancer or thyroid surgery, as any prior damage to the recurrent laryngeal nerve should be identified prior to the ablation. There should be ongoing evaluation of voice quality during the procedure by asking the patient to speak periodically. Vocal cord function should also be evaluated by ultrasonography after the ablation.

Recommendation 14: Pre-ablation laboratory studies are recommended to determine thyroid function, bleeding risk and possible pregnancy prior to ablation.

A TSH level is recommended before ablation, although some physicians may also choose to check free T4 or total or free T3 levels if indicated. Thyroid antibodies may be checked per physician preference depending on the clinical indication to determine if the patient has chronic lymphocytic thyroiditis or Graves' disease. It is recommended that platelets, prothrombin time/INR, and partial thromboplastin be checked prior to thermal ablation. Thermal ablation is not recommended in patients at increased risk of bleeding. A pregnancy test should be performed, if indicated, prior to radiofrequency ablation. The manufacturing company's recommendations for indications and contraindications of the use of their equipment should be followed in patients who are pregnant or have any kind of implant.

Recommendation 15: Chemical and thermal ablation should be performed under local anesthesia, and pain should be managed appropriately during and after the procedure.

Chemical ablation with ethanol can be performed with minimal anesthesia similar to fine needle aspiration. For thermal ablation, local anesthetic should be injected peri-thyroidally prior to the procedure, with a limited volume to avoid toxicity. Conscious sedation can be considered in patients undergoing thermal ablation; however, the patient must remain awake during the procedure. General anesthesia should not be used for ablation. There is no consensus on whether the patient should be fasting for the procedure, or if the duration of fasting should be dependent on the type of anesthesia given.

If the patient develops pain during thermal ablation, then the following steps should be taken in order: the procedure should be stopped and the electrode, antenna or fiber should be repositioned, and the procedure should be resumed when the pain has resolved; if the pain recurs then the power should be decreased and/or local anesthesia re-administered. Over the counter analgesics may be used, if needed, for pain control after chemical or thermal ablation.

Recommendation 16: Standard accepted techniques should be used when performing thermal ablation of thyroid nodules and choice of equipment should be appropriate for the size of the nodule being ablated.

RFA and MWA should be performed using the "trans-isthmic" approach and the "moving shot" technique; and LA should be performed using the "sagittal" approach and the "pull back" technique. The active tip size in RFA and MWA should be chosen according to the size of the target nodule i.e. a smaller active tip should be used for smaller nodules and a larger active tip should be used for larger nodules. In case of LA, 1 – 3 fibers are recommended depending on the size of the thyroid nodule to achieve 500 – 600 joules per mL volume of the nodule. Each single laser illumination should not exceed 1800 joules per mL volume of total delivered energy. Depending on the volume of the nodule, a "pull back" of 10 mm might be necessary. Hydrodissection should be used any time there is a concern for possible injury to structures surrounding the thyroid gland. Of note, hydrodissection for RFA cannot be done with normal saline and must use D5W, whereas hydrodissection for MWA and LA can be done with D5W or normal saline. The goal of thermal ablation is to completely ablate the nodule; however, leaving

a cuff of untreated peripheral tissue may help avoid injury to surrounding structures in benign thyroid nodules, although it may increase the risk of regrowth.

Standard safety procedures should be followed in all ablation techniques.

Recommendation 17: A change in the patient's voice during thermal ablation should be managed by rescue hydrodissection.

If a change in voice is noted during thermal ablation, then the ablation should immediately be stopped, and cold D5W between 0 – 4 °C (32 – 39 °F) in 5 – 10 mL increments should be injected into the tracheoesophageal groove until voice quality returns to baseline. If performing MWA or LA, then either D5W or normal saline can be used.

Recommendation 18: Follow-up is recommended within 6 months and annually to evaluate response using ultrasonography and thyroid function tests. It is suggested that follow-up be done in 4 – 12 weeks to differentiate between regrowth and treatment failure.

The greatest volume reduction is typically seen in the first month, with gradual continued volume reduction thereafter. The treatment goals depend on the type of nodule being treated. For benign non-functioning thyroid nodules, success is defined as improvement in symptoms or cosmetic appearance with any volume reduction, or a volume reduction of greater than 50% within 6 months. For autonomously functioning thyroid nodules, the measure of success would be normalization of thyroid function tests within 6 months, when the patient is off thionamides. A radioactive iodine and scan is not necessary after the thermal ablation procedure if the thyroid function tests are normal and the patient is asymptomatic after ablation of an autonomously functioning thyroid nodule.

A detailed discussion of malignant thyroid nodules and recurrences is beyond the scope of this statement. Briefly, for primary malignancy of less than 1 cm, the goal of treatment is complete disappearance within 12 months. For recurrence of thyroid malignancy treatment should be individualized depending on whether the goal is curative or palliative.

Treatment failure is defined as less than 20% volume reduction in 6 months following the ablation, whereas regrowth is defined as a 50% volume increase from the smallest volume after treatment. Ultrasound guided fine needle aspiration should be repeated in all nodules with regrowth because of the risk of malignancy, except in pure cystic nodules. No consensus was reached on whether FNA biopsy should be repeated in all nodules with failure of treatment.

Recommendation 19: Repeat ablation can be considered if patient remains hyperthyroid at least 6 months after initial ablation of autonomously functioning thyroid nodule or if there is inadequate response in a benign nodule and it appears low-risk on ultrasonography and has a repeated fine needle aspiration biopsy that is benign.

If the response to ablation is inadequate, with failure to resolve symptoms and normalize thyroid function tests; or the thyroid nodule has regrown or has failed treatment then all

treatment options (repeat ablation versus conventional treatments such as surgery) should be discussed with the patient before deciding on a course of action. Larger nodules tend to require multiple sessions of ablation before showing adequate response. Patients may also consider surgery following an inadequate response; and in the case of autonomously functioning thyroid nodules may consider thionamides or radioactive iodine ablation. If a malignancy was missed on the initial evaluation leading to the failure of treatment or regrowth, then the treatment of choice would be surgery rather than repeat ablation.

Recommendation 20: Complications of chemical and thermal ablation should be managed based on standard of care.

Early side effects and complications are usually self-limited, such as vasovagal reaction, vomiting, skin burns and hematoma; and are treated conservatively. Coughing during the procedure should prompt stopping the ablation and waiting till the coughing subsides. Patients may rarely develop hyperthyroidism a few weeks after the procedure, and this is managed as a thyroiditis, with symptom control with beta-blockers if needed; steroids may be considered in cases of painful thyroiditis. Thyroid nodule rupture is a late complication and is more commonly seen in larger nodules, usually presenting as sudden severe neck pain. In case of suspected thyroid nodule rupture imaging of the neck (ultrasonography or computed tomography) should be obtained to confirm the diagnosis and define the type of thyroid nodule rupture. Conservative management is typically appropriate, although some cases may require antibiotics, and a minority may need incision and drainage or surgical intervention. In case of recurrent laryngeal nerve damage that was not successfully mitigated with rescue hydrodissection, speech therapy and evaluation by otolaryngologist may be required.

CONCLUSION

This statement will continually be updated as new information becomes available. Comments by NASOIE members on the content of the statement are continually be considered and incorporated as needed.