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Technique and Procedural Aspects of Radiofrequency Ablation of Thyroid Nodules

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Abstract

Purpose of the Review Thyroid nodules (TNs) are a frequently seen clinical problem which increased in incidence with the usage of high-resolution ultrasound (US). Most of these nodules are benign and do not need any further management unless they start to be symptomatic, cosmetically unacceptable, or proven to be malignant. Surgery has been the only treatment option. Since scientists and clinicians became more conservative and toward minimally invasive techniques, TNs' management was not exceptional. Minimally invasive US-guided techniques were introduced in the last two decades as a management of TNs. Radiofrequency ablation (RFA) is considered relatively the newest of all and showed a significant reduction in the size and improvement of clinical symptoms.. The aim of this article is to review basic principles and technical details of RFA.

Recent Findings RFA showed promising results in TNs size reduction as well as cure of hyperthyroidism due to toxic nodules. Data also reported improvement of compressive symptoms after the procedure.

Summary As RFA is a relatively new novel technique in management of thyroid disease, with further studies focusing more on indications, and outcomes, we predict that RFA will be widely applied in the management of thyroid disease. It plays a major role in reducing the number of patients undergoing surgeries and avoiding all the risk related to it.

Keywords Thyroid nodule · Radiofrequency ablation · RFA · Neck ultrasound · Benign thyroid nodule

Background

Thyroid nodules (TNs) are a frequently seen clinical problem; up to 5% of females and more than 1% of males in the USA were diagnosed with TNs. The incidence of diagnosing TNs increased to 70% due to high-resolution ultrasonography (US) usage [1, 2]. Fifteen percent of TNs were found to be malignant [3]. Although the majority of TNs are benign and need follow-up, some of them require treatment for associated symptoms and/or for cosmetic problems [4, 5].

Over the past two decades, nonsurgical and minimally invasive US-guided techniques have been introduced to treat TNs [6–10]. Percutaneous ethanol injection (PEI) is recommended to treat recurrent cysts and dominantly cystic TNs [11]. Because of PEI's constraints in treating solid TNs, hyperthermic methods (laser ablation and radiofrequency ablation (RFA)) have been introduced afterward to treat solid benign thyroid nodules (BTNs) [12], obtaining significant nodule size reduction and clinical improvement of the disease symptoms. Other nonsurgical therapies, such as high-

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intensity focused ultrasound (HIFU), microwaves, cryotherapy, and electroporation, are presently under investigation.

This paper presents information about the basic principles, indications, and techniques that have been specially designed to optimize thyroid RFA and the clinical results and expected possible adverse events.

Principles of RFA

RFA is the use of high-frequency electric waves with an intensity between 200 and 1200 kHz [13]. The RFA waves passing through the electrode disturb tissue ions around the electrode, and they increase the temperature within the tumor tissue, hence resulting in the destruction of the tumor located within few millimeters of the electrode. In addition to the direct heat effect, heat conduction from the ablated area can result in relatively slower damage to the tumor or tissue remote from the electrode tip. The fundamental mechanism of RFA is thermal injury process secondary to friction and heat conduction [13, 14].

At temperatures ranging from 60 to 100 °C, nearly instant tissue coagulation is provoked with irreversible damage caused to tumor tissue, while temperatures greater than 100–110 °C result in tissue evaporation and carbonization which serve as insulation to prevent heat extent and thus reduce the local potency of RFA [13, 15]. The efficacy of RFA can also be lessened due to [1] the heterogeneous nature of the tissue in the presence of fibrosis or calcification by altering electrical and heat conduction or [2] nearby blood flow by perfusion-mediated tissue cooling [4].

Indications and patient's Selection

In 2009, the Korean Society of Thyroid Radiology established guidelines for thyroid RFA. These were subsequently revised in 2012 and 2017. These guidelines provide best evidence recommendations that cover all facets of RFA, including indications, pre-procedural evaluations, procedures, postprocedural monitoring, efficacy, and safety. They recommend RFA for patients with BTNs complaining of symptomatic or cosmetic problems [16••].

Thyroid nodules should be confirmed as benign on at least two US-guided fine-needle aspirations (FNA) before RFA, but single benign diagnosis on FNA is sufficient when the nodule has also specific benign US features or has an autonomously functioning thyroid nodule (AFTN) [16••].

RFA can be performed for recurrent thyroid cancers in the thyroidectomy bed or cervical lymph nodes metastases for patients at high surgical risk or who refuse surgery. This was recognized in the 2015 American Thyroid Association (ATA) guidelines for Differentiated Thyroid Cancer and Thyroid Nodules and in European literature [16–18]. The latter did not recommend RFA as a treatment option for the follicular neoplasms and neither the Korean nor American guidelines recommend RFA as a primary treatment option for thyroid cancer [16–18]. The ATA has also supported the use of RFA as a valid alternative to surgery for the treatment of individual distant metastases [17].

Pre-Procedure Assessment

Before considering RFA for BTNs, nodules should undergo two FNAB with Bethesda 2 cytology readings [5, 19–21]. Subjective assessment of symptoms and cosmetic problems should be done before and after RFA to enable outcomes measurement and/or reporting [22].

Ultrasound examination is crucial to confirm benign features of cytologically proven TNs and to assess recurrent cancers and surrounding critical anatomical structures. The echogenicity, composition, size, and internal vascularity of each nodule or tumor should be evaluated carefully. Three diameters, including the largest diameter, should be measured by US, and nodule or tumor volume should be calculated, the ATA designed an online thyroid volume calculator that can be used easily [20, 23–25].

Appropriate pre-procedure laboratory tests include a complete blood count, a blood coagulation profile (bleeding time, prothrombin time, activated partial thromboplastin time), and thyroid function test [23, 26]. For recurrent thyroid cancer cases after total thyroidectomy, laboratory tests should include serum TSH, thyroglobulin (Tg), and anti-Tg antibody. A decrease in tumor markers following ablation can be used to evaluate the success of any ablation [27]. For patients with pre procedure hyperthyroidism, a technetium 99mTc pertechnetate or 123I thyroid scan may be helpful to define AFTN in addition to serum markers for autoimmune causes of hyperthyroidism [28, 29].

Hypothyroidism arising after chemical or thermal ablation of thyroid nodules has been infrequently reported, and the cause of this adverse event is unknown [30–32]. However, recognizing that the most likely cause of hypothyroidism appears to be a progression of autoimmune thyroiditis associated with pre-existing thyroid antibodies, in cases where patients have thyroid antibodies, it may be reasonable to warn them before the treatment about the probability of developing hypothyroidism. Nevertheless, a routine check of thyroid antibodies, such as an anti-Tg antibody or anti-microsomal antibody, is questionable before RFA of BTNs [33–35].

CT or MRI examinations may support assessment of the intrathoracic extent of BTNs [14]. Before RFA of recurrent thyroid cancer, tumor recurrence should be validated by US-guided FNA with washout Tg concentration measurement [10, 27, 36•]. CT of the neck is advised to find additional

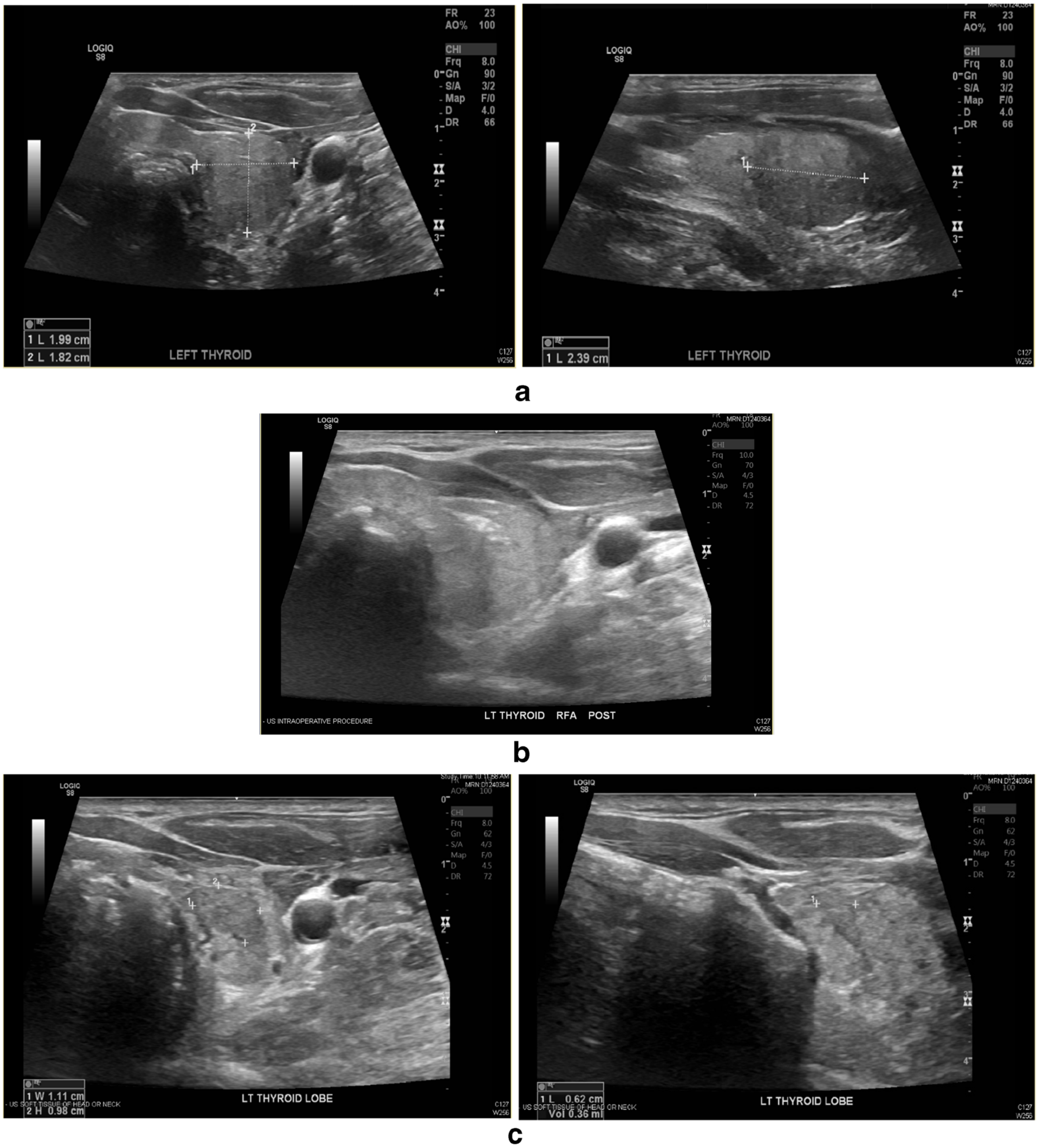

Fig. 1 **a** Pre RFA US images for benign nonfunctional thyroid nodule. **b** Post RFA (Intraoperative) US images for a benign nonfunctional thyroid nodule. **c** One month post RFA for a benign nonfunctional thyroid nodule with a 92% reduction in the size of the nodule

recurrent tumors not identified by US and may be useful for the post-RFA evaluation of recurrence [14]. PET-CT is not suggested before ablation [14].

RFA Procedure

RFA can be conducted at the radiology unit, or in the operation room. This procedure should be carried out by a surgeon or a radiologist who is experienced in thyroid US, FNA biopsy, and RFA. Before the ablation, patients will receive local anesthesia at the puncture site with 10 mL of 1–2% lidocaine hydrochloride, as well as conscious sedation with midazolam [37, 38]. Some surgeons prefer to perform RFA without general anesthesia or deep sedation as anesthesia may delay the detection of serious complications [16••, 39].

An 18-gauge internally cooled monopolar electrode, with a shaft length of 10 cm and an exposed tip length of either 7, 10, or 15 mm. These electrodes were connected to a 450-kHz radiofrequency generator delivering up to 200 W, on a 50 Ω load. The procedure starts with the US-guided long access technique (transisthmic) or short access technique by inserting the electrode into the TN [23, 37, 38]. The short access technique has many advantages over the long access approach (caudocranial or craniocaudal direction) and the vertical approach, both of which have been used previously [40–47].

In the transisthmic approach, electrode passage through thyroid parenchyma prior to nodule entry can prevent leakage of hot fluid in the case of cystic nodules during swallowing or talking. This minimizes the risk of damage to adjacent structures. Similarly, the moving shot technique is safer than the fixed technique for thyroid nodule ablations as prolonged fixation of the electrode can engender complications by heat transmission given the thyroid is a relatively small organ compared to other solid organs for which fixed electrode RFA is used [23].

The 2017 Korean Society of Thyroid Radiology guideline recommends advanced techniques (vascular ablation techniques) to minimize marginal regrowth. There are two different vascular ablation techniques: artery-first ablation (for hyper vascular nodules with a prominent feeding artery) and marginal venous ablation [16••]. The artery-first ablation technique can be used for hyper vascular nodules with a prominent feeding artery [16••]. RFA is performed in a transverse US view with continuous ultrasound monitoring to provide clear visualization of the TN and the "danger zone" for recurrent laryngeal nerve injury [23]. For vascular ablations, power needs to be increased to 50–70 W in order to achieve an adequate ablation. Doppler should be used judiciously to determine where the arterial and venous feeders lie prior to beginning the ablation [7].

Baek et al. have previously reported that to promote safe ablation, the thyroid nodule should be divided into multiple conceptual units [23]. These units should become smaller in the periphery as they approach the critical neck structures [23]. The units are larger in the center of the nodule. The procedure should start in the deepest and most medial part of the nodule and move upwards to prevent the micro bubbling visual effect at the tip of the electrode from obscuring the view [23]. The procedure can often be performed through one puncture of the skin and thyroid capsule [23]. The needle can be removed or relocated in a different part of the nodule, if necessary, to complete the ablation treatment [18]. The electrode can be moved within the thyroid mass by tilting it upward or downward. At the end of the procedure, the electrode will be removed superficially [23]. Insufficient ablation of the external border of a nodule can lead to nodule regrowth and, for toxic nodules, to a relapse/worsening of hyperthyroidism [7, 10].

Throughout the procedure, it is important to interact with the patient (talking and swallowing) to assess the status of the laryngeal nerves. If hoarseness is noted, the procedure should be stopped, and consideration given to the injection of cold dextrose solution as reported by Baek et al. [48] Following the ablation, post treatment US images are taken. Patients should be kept under observation for 1–2 h.

Follow-Up

Patients are followed by US and clinical evaluations at 1, 3, 6 and 12 months, and then annually up to 5 years. Evaluation should include clinical and cosmetic symptoms, complications, TN volume, largest diameter, and vascularity using the same data collection set before and after the ablation [39]. A delayed complication is defined as any complication detected at 1 month or more after RFA [49]. Therapeutic success has been defined as a > 50% volume reduction at 12 months, Fig. 1a–c. Additional treatment is recommended if the follow-up US shows a remaining viable portion of the nodule and if the patient complains of ongoing symptomatic or cosmetic problems [39].

Table 1 Summary of the pros and cons of RFA for management of thyroid nodules

Advantages	Disadvantages
Minimally invasive technique	Require a learning curve
No surgical incision	Major complications (0.7%)
No post-operative scar	Might require multiple treatment sessions [33]
Short operative time	
Short recovery period	
Pain, usually transient and mild, and most frequent it is during procedure only	
No or minimal effect on gland's functionality (hypothyroidism)	
Can be repeated safely	
Compressive symptoms relive	
Can be used to control recurrence thyroid cancer and AFTN	

AFTN autonomously functioning thyroid nodule. *BTNs* benign thyroid nodules

Adverse Events

In a recent meta-analysis, the proportions of overall and major complications were 3.2% and 0.7%, respectively, accounting for thirty-four complications among 728 nodules in 715 patients. Reported minor adverse events included pain, hematoma, vomiting, skin burns, and transient thyroiditis, Table 1 [50–53]. Major adverse events included voice change, nodule rupture, permanent hypothyroidism, and brachial plexus injury. Thirty-one patients had a transient voice change [23, 27, 30, 50, 52–56]. These patients recovered within 2–3 months. Four patients (three with recurrent cancers and one with a benign nodule) had a permanent voice change [33, 51, 55, 57]. The overall incidence of voice change (transient or permanent) after RFA was 1.44%. The incidence of voice change was higher in patients with recurrent thyroid cancer 7.95% than in patients with BTNs 0.94% [33, 52, 55, 57, 58].

Conclusion

RFA in TNs' management showed propitious outcomes regarding size reduction, toxic nodules cure, and compressive symptom resolution. Future studies are needed to guide further engagement of such a novel technique as an alternative option in the management of thyroid diseases, specifically thyroid cancer.

Compliance with Ethical Standards

Conflict of Interest The authors declare that they have no conflict of interest.

Human and Animal Rights and Informed Consent This article does not contain any studies with human or animal subjects performed by any of the authors.

Institutional Review Board Statement This case report was exempt from the Institutional Review Board standards at our Institution.

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- • Of importance
- •• Of major importance

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