

RADIOLOGÍA

www.elsevier.es/rx



## 



RADIOLOGÍA

seram 👬 🗰

### F. Garrido Pareja\*, P. Pérez Naranjo\*\*, M.D. Redondo Olmedilla, Á. Cabrera Peña

Servicio de Radiodiagnóstico, Hospital Universitario Clínico San Cecilio, Granada, Spain

Received 19 November 2021; accepted 31 January 2022

#### **KEYWORDS**

Thermal ablation therapy; Radiofrequency; Intervention; Ultrasound; Thyroid nodule; Parathyroid adenoma

#### PALABRAS CLAVE

Terapia de ablación térmica; Radiofrecuencia; Intervención; Ultrasonidos; Nódulo tiroideo; Adenoma paratiroideo **Abstract** Radiofrequency ablation is a well-known, safe, and effective method for treating benign thyroid nodules and recurring thyroid cancer as well as parathyroid adenomas that has yielded promising results in recent years. Since the Korean Society of Thyroid Radiology introduced the devices and the basic techniques for radiofrequency ablation in 2012, radiofrequency ablation has been approved all over the world and both the devices and techniques have improved.

This review aims to instruct interventional radiologists who are doing or intend to start doing radiofrequency ablation of thyroid and parathyroid lesions, as well as thyroid and parathyroid specialists who provide pre- and post-operative care, in the training, execution, and quality control for radiofrequency ablation of thyroid nodules and parathyroid adenomas to optimize the efficacy and safety of the treatment.

© 2022 SERAM. Published by Elsevier España, S.L.U. All rights reserved.

#### Ablación por radiofrecuencia en la enfermedad tiroidea y paratiroidea

**Resumen** La ablación por radiofrecuencia (ARF) es un método bien conocido, seguro y eficaz para tratar los nódulos tiroideos benignos, los cánceres tiroideos recurrentes, así como los adenomas de paratiroides, con resultados prometedores en los últimos años. Los dispositivos empleados y las técnicas básicas para la ARF fueron introducidos por la Sociedad Coreana de Radiología de Tiroides (KSThR) en 2012, si bien la ARF se ha aprobado en todo el mundo, con avances posteriores tanto en dispositivos como en técnica.

El objetivo de esta revisión es instruir a los radiólogos intervencionistas que pretendan realizar, o que ya estén realizando, intervenciones de ARF, así como especialistas en tiroides

\* Please cite this article as: Garrido Pareja F, Pérez Naranjo P, Redondo Olmedilla MD, Cabrera Peña Á. Ablación por radiofrecuencia en la enfermedad tiroidea y paratiroidea. Radiología. 2022;64:383–392.

\* Corresponding author.

\*\* Corresponding author.

2173-5107/© 2022 SERAM. Published by Elsevier España, S.L.U. All rights reserved.

E-mail addresses: garrido.fermin@gmail.com (F. Garrido Pareja), paula.perez.naranjo@gmail.com (P. Pérez Naranjo).

y paratiroides que brinden atención pre y postoperatoria, acerca de la capacitación, la ejecución y el control de calidad de la ARF de los nódulos tiroideos y adenomas paratiroideos, para optimizar la eficacia del tratamiento y la seguridad del paciente.

© 2022 SERAM. Publicado por Elsevier España, S.L.U. Todos los derechos reservados.

#### Introduction

Thyroid nodules (TN) are defined lesions within the thyroid gland, radiologically distinguishable from the surrounding thyroid parenchyma. The incidence of TN has increased over the last twenty or thirty years as the use of diagnostic imaging tests has increased. These lesions are found in 20%-76% of the general adult population when assessed by ultrasound.<sup>1-4</sup>

TN can be associated with various thyroid and extrathyroidal diseases, but they are generally due to benign or malignant tumours. The most common cause of benign TN is the colloid nodule, while the finding of a malignant nodule (5%) mainly corresponds to papillary carcinoma.<sup>3</sup>

Most TN are benign and asymptomatic and do not require treatment; they simply need to be followed up for management. However, some nodules do require treatment due to the symptoms caused by their growth, cosmetic problems or the risk of malignant transformation.<sup>4–10</sup>

Until recently, treatment options were limited to surgery for symptomatic benign TN and radioactive iodine therapy, carbimazole or surgery for autonomously functioning TN (AFTN).<sup>7-14</sup>

Parathyroid adenomas are the most common cause of primary hyperparathyroidism (PHPT), with an incidence of 80%-85%.<sup>15</sup> PHPT is a primary endocrine disorder of mineral metabolism, with a prevalence of 0.1%-0.4%, being more common in females.<sup>16,17</sup> It is caused by the excessive synthesis and secretion of parathyroid hormone (PTH), with the consequent increase in serum calcium.<sup>16-20</sup>

Almost 20% of patients with PHPT are asymptomatic, with the disorder being detected during routine biochemical tests.<sup>16,20</sup> The central target organs of abnormally high levels of PTH are the bone and the kidneys, and there is a high incidence of complications, such as kidney stones, severe bone disease, fractures, neurocognitive impairment and cardiovascular disease, with treatment being required in these cases.<sup>15,21,22</sup>

Current treatment guidelines recommend parathyroidectomy as the ''gold standard'' treatment for patients with PHPT,<sup>17,19,21</sup> as this is curative in 95% of cases when performed by an expert surgeon.<sup>4</sup> However, although it is generally safe, an increase in postoperative morbidity and mortality rates has been reported in patients aged 65 years or over, associated with complications such as wound infection, postoperative haemorrhage, recurrent laryngeal nerve injury, hypocalcaemia and persistent hypoparathyroidism.<sup>12,21</sup> Over the last ten years, several minimally invasive ultrasound-guided techniques have been proposed for the treatment of TN and parathyroid adenomas in situations where either the patient rejects surgery or it is contraindicated.<sup>11</sup>

Radiofrequency ablation (RFA) is a minimally invasive technique with percutaneous access used to treat benign nodules of the thyroid and parathyroid glands.<sup>17</sup> It was initially considered simply an alternative to surgery, but the importance of RFA as a treatment option has been growing steadily, both for benign solid and partially cystic nodules, and for recurrent thyroid cancer.<sup>4</sup>

RFA has been shown to be an effective technique for reducing mean nodule volume, with low complication rates and marked improvement in nodule-related symptoms.<sup>4</sup>

This review describes and discusses current devices and advanced techniques for RFA in thyroid and parathyroid endocrine disease.

#### Indications

The main indications are found in the guidelines and declarations issued by the following organisations<sup>1</sup>:

- Korean Society of Thyroid Radiology (KSThR), 2009, 2011 and 2017 guidelines.<sup>23,24</sup>
- 2. Italian Experts Opinion Statement 2015.<sup>25</sup>
- 3. 2016 guidelines from the American Association of Clinical Endocrinologists (AACE).
- 2016 guidelines from the American College of Endocrinology (ACE).
- 5. 2016 guidelines from the Associazione Medici Endocrinologi (AME).<sup>26</sup>
- 2016 guidelines from the National Institute for Excellence in Health and Care (NICE) (https://www.nice.org.uk/ guides/ipg562).
- Official declaration of the Austrian Thyroid Association 2016 (https://www.kup.at/kup/pdf/13399.pdf).

Broadly speaking, the main indications are as follows:

#### Benign thyroid nodules

RFA is indicated in patients with benign TN larger than 2 cm in size who complain of cosmetic problems or compressive symptoms related to the size of the nodule, such as pressure in the neck, pain, dysphagia, foreign body sensation, discomfort, bulging of the neck and cough.<sup>5</sup>

In terms of nodule size or volume, no definite criteria for thyroid RFA have yet been established.<sup>4-6</sup> In these cases, RFA is indicated to improve clinical problems by reducing the size of the nodule.<sup>6</sup>

The need for TN treatment depends on the symptoms or cosmetic problems of each patient, and these vary according to the circumference of the neck or the location of the thyroid nodule. Patients with a smaller neck circumference tend to complain of cosmetic problems much earlier than those with wider necks.

#### Toxic thyroid nodules

About 5%-10% of benign TN can progress to toxic TN or AFTN and secrete abnormally high amounts of thyroid hormones.<sup>27</sup>

AFTN are the second most common cause of hyperthyroidism, and mainly affect older women, as these nodules degenerate with age.<sup>27</sup>

Many trials have demonstrated the efficacy and safety of treating toxic nodules with RFA. In a large multicentre trial, Sung et al.<sup>28</sup> demonstrated significant improvement in hyperthyroid symptoms in 81.8% of study patients after RFA, along with normalised TSH levels and without the development of hypothyroidism.

Since the Korean guidelines in 2012, the consensus for RFA of AFTN has evolved. Currently, in the treatment of toxic nodules, it is better to reserve RFA as a second-line treatment in patients who reject conventional therapy or when it is contraindicated, and it can be considered a first-line treatment in small nodules, as the response is optimal (improvement in symptoms and return to normal of TSH) when the nodule is reduced in size by more than 80%.<sup>27</sup>

# Malignant thyroid nodules and recurrent thyroid cancer

RFA can be performed for curative or palliative purposes in recurrent thyroid cancers, according to the last guidelines published by the KSThR in 2017.<sup>4</sup> Curative RFA for recurrent cancer refers to the complete treatment of any recurrent tumour visible on ultrasound. Palliative RFA can be applied when reduction in size by RFA is considered for reducing symptoms and improving a patient's quality of life, even if radiologically complete excision is not possible.<sup>4,5</sup>

Surgery is the fundamental treatment for primary thyroid cancer. However, the 2017 guidelines recommend considering RFA in selected patients (i.e. in patients who refuse surgery or cannot undergo an operation due to their comorbidities); even so, it remains an experimental tool that requires more research due to the insufficient literature published to date.<sup>4–6</sup>

#### Cancer lymph node involvement

For metastatic cervical lymph nodes in the initial diagnosis of thyroid cancer, the treatment of choice today is surgical

removal.<sup>29</sup> Although surgery is still considered the gold standard treatment for recurrence of thyroid cancer and cancer lymph node involvement, there are guidelines and consensus statements which consider thermal ablation rescue therapy, but the following conditions have to be met<sup>29</sup>:

-Recurrent cancer-related cervical lymph node involvement after radical surgical treatment.

-Diagnostic imaging tests suggest metastasis and this is confirmed by fine-needle aspiration (FNA).

-The patient is not an optimal candidate for surgery or refuses this treatment.

-lodine-131 therapy is ineffective for the metastatic lymph nodes, or patients refuse to take such treatment.

#### Parathyroid adenoma

Some patients with symptomatic PHPT reject surgery or are unsuitable candidates for surgical intervention due to their associated comorbidities. In these cases, ultrasound-guided minimally invasive treatments are an alternative therapeutic option for the treatment of parathyroid lesions accessible by ultrasound.<sup>21,22</sup>

#### Pre-procedure assessment

Ultrasound is the most common imaging modality for assessing nodular thyroid and parathyroid lesions, planning patient diagnosis and guiding minimally invasive treatment.<sup>4</sup>

Patients must be properly informed before the procedure about the objectives of the technique, and, in the case of large nodules, the operator should warn the patient of the possible need for repeat treatment.<sup>2</sup>

TN must be confirmed as benign in at least two ultrasound-guided fine-needle aspiration (FNA) biopsies or core-needle biopsies (CNB) prior to RFA.<sup>5,6</sup> However, a single benign diagnosis on FNA or CNB is sufficient when the nodule has very specific sonographic features of being benign, as in the case of isoechoic spongiform nodules or partially cystic nodules with intracystic comet-tail artefact, both of which have a very low risk of malignancy.<sup>6</sup>

The study protocol prior to the procedure for parathyroid adenomas includes location of the lesions with imaging tests, highlighting the role of first-line ultrasound, but, particularly, the role of parathyroid scintigraphy with technetium-99m sestamibi, <sup>15,30,31</sup> which is routinely performed to locate adenomas with high sensitivity (80%–100% in the case of single adenomas). In uncertain or difficult-to-diagnose cases, as second-line, we have the options of sestamibi technetium 99-m-labelled single-photon emission computed tomography (CT) (99mTcsestamibi SPECT), Octreoscan and IV contrast-enhanced CT, which provide us with a more precise anatomical view, enabling better location of abnormal ectopic parathyroid glands.<sup>18,22,30,31</sup>

It is important to stress that abnormally functional parathyroid tissue must be visible by ultrasound for a specialised operator to perform the RFA. Normal parathyroid



**Figure 1** Typical setting for radiofrequency ablation of a thyroid nodule or parathyroid adenoma. The operator stands at the patient's head, looking directly at the ultrasound monitor for constant monitoring of the electrode tip.

glands are usually approximately 5 mm in size, which can be difficult to detect by ultrasound as they are isoechoic with respect to the thyroid glands. In contrast, parathyroid adenoma is evident by the altered echogenicity and increase in size, typically observed as solid, oval, well-circumscribed structures, which are hypoechoic with respect to the adjacent thyroid tissue. They are also usually separated from the thyroid glands by a hyperechoic band of connective tissue.

#### Radiofrequency ablation procedure

Generally on an outpatient basis, the treatment takes place in an operating theatre with a rigid articulated table or in specially fitted out ultrasound suites with a screen to monitor the patient's vital signs throughout the intervention.

The patient is placed in the supine position with neck extension, while the operator, at the head of the patient, assesses the position of the nodule and selects the most appropriate approach using a high-frequency linear probe to monitor and guide the ablation procedure, at all times under strict asepsis conditions<sup>3,19,22</sup> (Fig. 1).

The procedure is performed under local anaesthetic and optionally with conscious sedation, as the patient's collaboration is essential throughout the intervention, monitoring their voice to identify any possible injury to the recurrent laryngeal nerve.

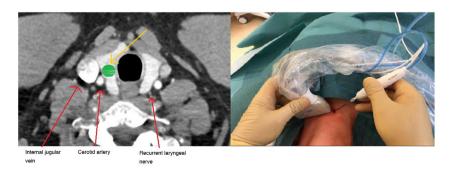
After adequate sterilisation, vessels along the access pathway are identified and local anaesthetic is injected at the skin puncture site.<sup>21</sup>

RFA of neck lesions is safer to perform using the transisthmic approach and hydrodissection.

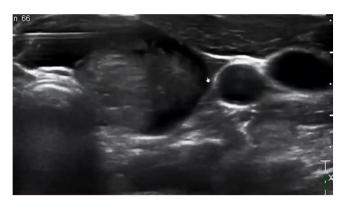
In the transisthmic approach, the RF electrode is inserted through the thyroid isthmus from the midline in a lateral direction to treat the target lesion<sup>3,19</sup> (Fig. 2).

There are several advantages using the transisthmic approach. First, the position of the electrode through the isthmus gives support and stability even when the patient speaks or swallows. Second, this approach helps minimise heat exposure to the recurrent laryngeal nerve, as the operator can control the relationship between the electrode. the target lesion, and the nerve, located in the so-called "danger triangle"; the space between the trachea and the thyroid gland. Continuous ultrasound monitoring of the relationship between the active tip of the electrode and the recurrent laryngeal nerve is of vital importance to prevent possible thermal injuries during the procedure. Lastly, the normal isthmus parenchyma between the target nodule and the electrode approach site prevents leakage of hot fluid into the peri-thyroid area, which can also be a cause of pain.<sup>3,21</sup>

Understanding the anatomy of the neck is essential for improving the efficacy of RF ablation in the treatment of thyroid and parathyroid lesions. The neck is relatively narrow and contains many critical structures, including the recurrent laryngeal nerve, carotid artery, oesophagus and trachea, which sometimes make it difficult to treat a lesion completely.<sup>3</sup> The hydrodissection technique (Fig. 3) consists of the injection of a cold 5% glucose solution (as normal saline solution is an ionic fluid and can conduct electricity) between the target lesion to be treated and the adjacent structures, creating a safety margin to isolate the nodule and prevent thermal injury to surrounding critical structures.<sup>9,15,17,19,20</sup>



**Figure 2** Axial CT slice of the neck with IV contrast. Graphic demonstration of a transisthmic approach to a right thyroid nodule (green circle).



**Figure 3** Hydrodissection technique. Cold 5% glucose solution is slowly instilled by needle between the target lesion and adjacent critical structures, including the trachea, oesophagus and recurrent laryngeal nerve.

# Technical aspects of radio frequency equipment

#### Characteristics of radiofrequency ablation

RFA consists of the percutaneous insertion of an electrode into a nodule. The technique uses as a physical principle the heat generated by the formation of a high-frequency alternating electrical current, ranging from 200 kHz to 1200 kHz, transmitted from the tip of an electrode connected to an external radiofrequency generator. These RF waves pass through the electrode, agitating ions in the tissues around the active tip, which results in a rise in temperature. The electrical resistance of the tissue, greater than the electrode metal, produces heat called ''friction heat'' (Joule effect), with the consequent coagulative necrosis and irreversible cell damage near the electrode at a temperature of 50-100 °C.<sup>2</sup>

It is important to remember that when administering RF, in addition to friction heat, heat conduction causes late necrosis in more distal areas. With all this, the size of the necrosis can be predicted and will depend on the size of the active tip of the electrode, the power selected and the treatment time.<sup>2</sup>

#### Devices

There have been numerous advances in RFA devices for the treatment of TN and parathyroid glands.

There are many different RF systems, but they all essentially consist of an electrical generator, an electrode and a return plate. The generator has a detector that records the resistance and impedance of the tissues, destroying the target lesion with great precision (Fig. 4).

The radiofrequency electrical generator is connected to an internally cooled electrode. Early RFA studies in TN were performed with a 17G straight, internally cooled electrode needle with a 1 cm active tip, or with 14G multi-prong expandable electrodes to obtain a wider ablation area.



**Figure 4** Radiofrequency device, essentially consisting of an electrical generator and an RF electrode (18G) with an active tip.

Subsequently, thinner (18G or 19G), internally cooled, multipoint electrode needles (0.5, 1 and 1.5 cm) were developed specifically for thyroid lesions to facilitate needle control and minimise injury of normal tissue.<sup>29</sup>

In our centre, because both the thyroid gland and even more so the parathyroid glands are relatively small and situated superficially, we generally use modified electrodes which are shorter and thinner than the conventional electrodes used for other organs, 7 cm in length and 18G, with multiple active tips from 0.5 to 1.5 cm, which are cooled by a peristaltic circulating water pump.<sup>32</sup> These small active tips enable more precise treatment with minimal collateral tissue damage to adjacent structures.

This device also has at least one return plate, which is generally placed on the patient's thigh, to maximise the contact surface and create a closed electrical circuit in the case of monopolar systems.

#### Thermal ablation techniques

RFA of TN was developed in 2002 by Professor Baek, an interventional radiologist at Asan Medical Centre in Seoul.<sup>1</sup>

RFA can be used by mono- or bipolar technology, the monopolar technique being the most commonly used.

#### Monopolar RF ablation<sup>1</sup>

For this procedure, one or two return plates are needed, depending on the procedure, ventrally placed on the patient's thighs, which act as a large dispersive electrode, allowing current to pass through the patient, activating the electrode as a circuit.<sup>1</sup> These return plates do not cause any discomfort to the patient.

The thermal damage caused by RF depends on the temperature achieved in the tissue and the duration of heating. When an alternating current reaches 460–500 kHz, it flows from the generator, between the electrode and the plates, and causes agitation of the ions in the tissue. This is converted through friction into heat, resulting in a focal thermal lesion in the tissue around the active tip of the electrode.

The current RF generators can automatically adjust the output power in order to optimise the energy deposited during the ablation treatment. The higher the current density surrounding the electrode needle, the more energy is deposited in the tissue, thus increasing the amount of ablation. When the temperature reaches 46 °C, irreversible cell damage occurs in the target lesion, but not necrosis. When the temperature reaches 50–52 °C, it only takes 4–6 min to induce a cytotoxic effect, with consequent coagulation necrosis and irreversible thermal damage to cells due to loss of cytosolic and mitochondrial enzyme activity.

#### **Bipolar RF ablation**

A comparatively new technique (the first published studies appeared in 2016<sup>3</sup>), bipolar RFA simplifies the procedure compared to monopolar RFA, as grounding pads are not required. These pads are necessary for monopolar RFA devices, as the electrical current travels through the patient's body. In contrast, bipolar RFA uses an electrode that contains positive poles and negative poles at the tip and directs the current flow only through the tissue of the lesion to be treated, thus eliminating current dissipation.<sup>1</sup>

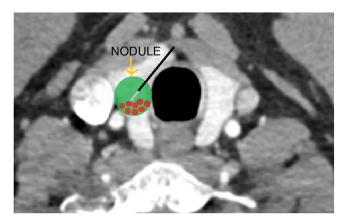
The high-frequency current created between the two poles leads to a relatively spherical heat field within which the tissue overheats. As the amount of water in the tissue of the treated nodule decreases, the electrical resistance and temperature increase, and the device power is turned down. This limits the electrical current to the area surrounding the bipolar electrode resulting in the ablation zone having a more predictable size and shape.<sup>3</sup>

Although this technique seems easier to master, as the tip of the electrode, while still needing to be guided, only needs to be placed in a few locations within the nodule, long-term results are still lacking at present.<sup>1</sup>

## Technical solutions and key aspect in thermoablation

In all RFA procedures, a series of effects are induced in the target lesion, and the area where the ablation is performed has a series of features which can alter the procedure. These alterations can be beneficial or harmful and we can use them to control sensitive areas. They include:

1. The cooling of the area to be ablated caused by blood flow through an adjacent vessel is protective, so it may leave a structure not completely burnt, but can also protect a sensitive structure. An easy-to-observe example of this phenomenon is with TN ablation, because we have the contiguous carotid artery. We can get closer to the artery thanks to cooling by the blood flow, although we have to be careful of the vagus nerve and, if it is too close, carry out hydrodissection by instilling glucose solution.



**Figure 5** Axial CT slice of the neck with IV contrast showing the transisthmic approach using the moving shot technique.

2. RF transmission is through ionised fluids or tissues, because it involves electricity. Therefore, the interposition of glucose solution, as explained above, protects by increasing distance, electrical insulation and non-conduction (double protection); as opposed to microwave ablation, for example, which only protects by distance.

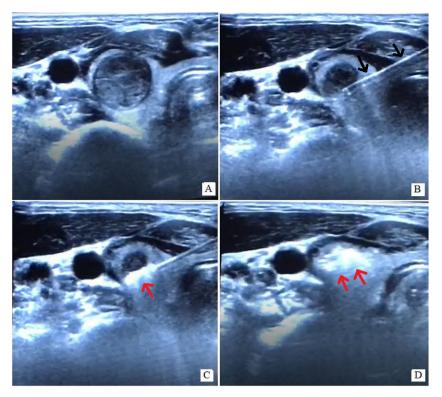
In conclusion, we have to take these physical situations into account and use them to our advantage to avoid possible injury.

#### Monitoring of the needle during the procedure

By far the most commonly used technique during RF of the thyroid and parathyroid glands is the so-called moving shot technique (Fig. 5). This is a safe and effective method, consisting of the ablation of multiple sequential areas within the target lesion, moving the tip of the electrode unit by unit, starting at the deepest area of the lesion, and pulling back to more central areas and from there to the most superficial.<sup>3</sup>

This technique can be difficult for beginners, as it requires constant monitoring of tip location, while synchronously moving and holding the electrode within the target nodule during the ablation. There are several reasons why tip monitoring might be difficult during the procedure, one being the transient hyperechoic zone, with subsequent acoustic shadowing caused by gas generated by the heat during ablation interfering with the sonic window<sup>1,3</sup> (Fig. 6).

Deflection of the electrode tip away from the target nodule could cause thermal injury to adjacent vulnerable structures, leading to serious complications; hence the vital importance of strict electrode tip monitoring during the procedure.



**Figure 6** Representative ultrasound images of a radiofrequency ablation procedure. Solid thyroid nodule with a 2.5 cm long axis (A). Percutaneous insertion of the RF electrode (black arrows) through a transisthmic approach with the tip of the needle in the inferior and posterior pole of the nodule (B). Radiofrequency is started, after which a transient hyper-echoic cloud appears (red arrows), which tells us that the ablation is taking place correctly (C), carrying out a sequential ablation within the target lesion using the moving shot technique until complete ablation is ensured (D).

#### Patient follow-up

The procedure is considered to have been a success when complete ablation is obtained after a properly performed protocol-based intervention.<sup>16</sup>

In the follow-up of both thyroid and parathyroid disease, from the endocrine point of view, the functional follow-up protocol is the same as the postoperative protocol.

Follow-up ultrasound scans are usually performed at 1, 3, 6, and 12 months, and every 6–12 months thereafter. Most literature reviews consider follow-up of 3–6 months and of a year. Reduction in the mean volume of 47%–84% at three months and 62%–93% at a year has been reported. Although most of the reduction in the volume of the ablated lesion is seen in the first 3–6 months, the size of the nodule continues to gradually decrease for up to a year.<sup>33</sup>

Based on our personal experience, in the case of benign TN, a reduction in the size of the ablated nodule is sought essentially to control the compressive symptoms. In the first instance at our centre, each patient was assessed at one month, six months and a year post-ablation, but now they have a repeat ultrasound at six months and a year. This is because we found in our follow-up that it is not until six months after the intervention that a significant shrinkage in the volume of the treated nodule is appreciated with complete healing, or when we can see that the lesion was not fully treated and that the patient needs further ablation.

Similarly, in the follow-up of recurrent thyroid tumours and toxic TN, the objective is complete ablation from the functional point of view. In the imaging follow-up, the desired outcome is complete ablation of the ablated area; if any residual tissue is detected in the follow-up ultrasound scans, a further ablation procedure may be necessary.

The assessment strategy after the ablation of a parathyroid adenoma is essentially biochemical; there is no ultrasound follow-up, and functional imaging tests are only performed if required according to progress.

At our centre, we perform early PTH and serum calcium tests in the first 24 h post-ablation, where both parameters should be corrected if the treatment has been adequate, followed by determination of serum levels of PTH, calcium, corrected albumin and Vitamin D at 1, 3 and 6 months and 1 year.

It is important to note that one month after the intervention, it is possible that serum PTH values will be persistently elevated or at the upper limit of normal with corrected serum calcium. This finding could be related to the activation of the rest of the parathyroid glands, previously latent due to the hyperfunctioning adenoma, and considered a rebound effect after the drop in serum calcium post-ablation, which causes an increase in PTH.

#### Complications

RFA is generally a safe technique and has a low incidence of complications (2%). However, operator experience is essential for better outcomes in terms of volume reduction in the target lesion, as well as low complication rates.<sup>2,19</sup>

It is important to recognise the potential complications of this technique. They are subdivided into minor and major events.<sup>4,14</sup>

Minor complications reported include bruising, vomiting, skin burns, oedema and pain. Pain during the procedure is the most commonly reported side effect,<sup>2,4,5</sup> of varying degrees in the lower part of the neck, with patients sometimes describing it as radiating to the head, ears, shoulder, chest, back or teeth. Most patients tolerate the pain fairly well and it is quickly alleviated.<sup>6</sup>

Haematomas can develop in the peri-thyroid, subcapsular and intranodular locations, caused by mechanical injury to the vessels due to electrode insertion. However, they can usually be treated with simple neck compression for 30 min to 2 h and application of ice, and most resolve within one or two weeks.<sup>6</sup>

The major complications include nerve injuries, such as injury to the recurrent laryngeal nerve, cervical sympathetic ganglion, brachial plexus and spinal accessory nerve, nodule rupture and permanent hypothyroidism/hypoparathyroidism.<sup>5,14</sup>

Node rupture is the second most important complication of RFA, presenting as sudden bulging of the neck and pain at the ablation site during follow-up. The rupture mechanism is considered to be a result of acute expansion of the volume of a nodule due to late haemorrhage or a tear in the wall of the lesion. Ultrasound or CT usually show a rupture of the thyroid capsule, with the tumour bulging towards the front of the neck. In most cases, they are treated conservatively, with antibiotics or analgesics, but surgical treatment may be required in the case of abscess formation.<sup>6</sup>

Another important major post-ablation complication is transient or permanent voice changes due to thermal injury to the recurrent laryngeal nerve, which, according to the study by Kim et al, is one of the most serious and most commonly reported complications after RFA.<sup>6</sup> Direct thermal injury to the nerve, stretching of the nerve over thyroid swelling, and bruising of the nerve against the trachea are possible causal mechanisms of voice changes during the procedure.<sup>6</sup> As discussed above, the transisthmic approach and fluid isolation using the hydrodissection technique are recommended, as these elements play a key role in protecting the recurrent laryngeal nerve and its surrounding tissues, and establishing a barrier significantly reduces the incidence of complications.<sup>6</sup>

To avoid complications, there must be continuous and vigilant ultrasound-guided monitoring of the electrode tip throughout the procedure.

#### Conclusions

In short, this article provides a summary of the current literature considering RFA as an increasingly efficient, safe and effective possible alternative to traditional therapies in patients with thyroid and parathyroid disease who are either not candidates for or do not want surgery.

#### Funding

No subsidies or other sources of help have been received for carrying out the work for this project.

#### Authorship

- 1. Person responsible for the integrity of the study: FGP
- 2. Study concept: PPN
- 3. Study design: PPN
- 4. Data collection: PPN
- 5. Analysis and interpretation of the data: as this was a review study, it was necessary to analyse and interpret the data.
- 6. Statistical processing: N/A
- 7. Literature search: FGP
- 8. Drafting of the article: PPN
- 9. Critical review of the manuscript with intellectually significant contributions: FGP
- 10. Approval of the final version: FGP and PPN

#### **Conflicts of interest**

The authors declare that they have no conflicts of interest.

#### References

- Dobnig H, Zechmann W, Hermann M, Lehner M, Heute D, Mirzaei S, et al. Radiofrequency ablation of thyroid nodules: Good Clinical Practice Recommendations for Austria: An interdisciplinary statement from the following professional associations: Austrian Thyroid Association (ÖSDG), Austrian Society for Nuclear Medicine and Molecular Imaging (OGNMB), Austrian Society for Endocrinology and Metabolism (ÖGES), Surgical Endocrinology Working Group (ACE) of the Austrian Surgical Society (OEGCH). Wien Med Wochenschr. 2020;170:6–14, http://dx.doi.org/10.1007/s10354-019-0682-2. Epub 2019 Feb 6. PMID: 30725443.
- Cesareo R, Palermo A, Pasqualini V, Cianni R, Gaspa G, Manfrini S, et al. Radiofrequency ablation for the management of thyroid nodules: a critical appraisal of the literature. Clin Endocrinol (Oxf). 2017;87:639–48, http://dx.doi.org/10.1111/cen.13422. Epub 2017 Aug 4. PMID: 28718950.
- Park HS, Baek JH, Park AW, Chung SR, Choi YJ, Lee JH. Thyroid radiofrequency ablation: updates on innovative devices and techniques. Korean J Radiol. 2017;18:615–23, http://dx.doi.org/10.3348/kjr.2017.18.4.615. Epub 2017 May 19. PMID: 28670156; PMCID: PMC5447637.
- Radzina M, Cantisani V, Rauda M, Nielsen MB, Ewertsen C, D'Ambrosio F, et al. Update on the role of ultrasound guided radiofrequency ablation for thyroid nodule treatment. Int J Surg. 2017;41:82–93, http://dx.doi.org/10.1016/j.ijsu.2017.02.010. PMID: 28506420.
- Kim JH, Baek JH, Lim HK, Na DG. Summary of the 2017 thyroid radiofrequency ablation guideline and comparison with the 2012 guideline. Ultrasonography. 2019;38:125–34, http://dx.doi.org/10.14366/usg.18044. Epub 2018 Sep 27. PMID: 30458605; PMCID: PMC6443588.

- Kim JH, Baek JH, Lim HK, Ahn HS, Baek SM, Choi YJ, et al. Guideline Committee for the Korean Society of Thyroid Radiology (KSThR) and Korean Society of Radiology. 2017 Thyroid Radiofrequency Ablation Guideline: Korean Society of Thyroid Radiology. Korean J Radiol. 2018;19:632–55, http://dx.doi.org/10.3348/kjr.2018.19.4.632. Epub 2018 Jun 14. PMID: 29962870; PMCID: PMC6005940.
- Park HS, Baek JH, Choi YJ, Lee JH. Innovative techniques for image-guided ablation of benign thyroid nodules: combined ethanol and radiofrequency ablation. Korean J Radiol. 2017;18:461–9, http://dx.doi.org/10.3348/kjr.2017.18.3.461. Epub 2017 Apr 3. PMID: 28458598; PMCID: PMC5390615.
- Rabuffi P, Spada A, Bosco D, Bruni A, Vagnarelli S, Ambrogi C, et al. Treatment of thyroid nodules with radiofrequency: a 1-year follow-up experience. J Ultrasound. 2019;22:193–9, http://dx.doi.org/10.1007/s40477-019-00375-4. Epub 2019 Apr 3. PMID: 30945239; PMCID: PMC6531559.
- Cui D, Ding M, Tang X, Chi J, Shi Y, Wang T, et al. Efficacy and safety of a combination of hydrodissection and radiofrequency ablation therapy for benign thyroid nodules larger than 2 cm: a retrospective study. J Cancer Res Ther. 2019;15:386–93, http://dx.doi.org/10.4103/jcrt.JCRT\_419\_18. PMID: 30964116.
- Jawad S, Morley S, Otero S, Beale T, Bandula S. Ultrasoundguided radiofrequency ablation (RFA) of benign symptomatic thyroid nodules—initial UK experience. Br J Radiol. 2019;92:20190026, http://dx.doi.org/10.1259/bjr.20190026. Epub 2019 May 14. PMID: 31084496; PMCID: PMC6592080.
- 11. Lee GM, You JY, Kim HY, Chai YJ, Kim HK, Dionigi G, et al. Successful radiofrequency ablation strategies for benign thyroid nodules. Endocrine. 2019;64:316–21, http://dx.doi.org/10.1007/s12020-018-1829-4. Epub 2018 Dec 19. PMID: 30569260.
- Deandrea M, Trimboli P, Garino F, Mormile A, Magliona G, Ramunni MJ, et al. Long-term efficacy of a single session of RFA for benign thyroid nodules: a longitudinal 5-year observational study. J Clin Endocrinol Metab. 2019;104:3751-6, http://dx.doi.org/10.1210/jc.2018-02808. PMID: 30860579.
- Chung SR, Baek JH, Choi YJ, Lee JH. Management strategy for nerve damage during radiofrequency ablation of thyroid nodules. Int J Hyperthermia. 2019;36:204–10, http://dx.doi.org/10.1080/02656736.2018.1554826. Epub 2019 Jan 14. PMID: 30638391.
- 14. Chung SR, Suh CH, Baek JH, Park HS, Choi YJ, Lee JH. Safety of radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers: a systematic review and meta-analysis. Int J Hyperthermia. 2017;33:920–30, http://dx.doi.org/10.1080/02656736.2017.1337936. Epub 2017 Jun 26. PMID: 28565997.
- Khandelwal AH, Batra S, Jajodia S, Gupta S, Khandelwal R, Kapoor AK, et al. Radiofrequency ablation of parathyroid adenomas: safety and efficacy in a study of 10 patients. Indian J Endocrinol Metab. 2020;24:543–50, http://dx.doi.org/10.4103/ijem.IJEM\_671\_20.
- Wei Y, Peng CZ, Wang SR, He JF, Peng LL, Zhao ZL, et al. Microwave ablation versus radiofrequency ablation for primary hyperparathyroidism: a multicenter retrospective study. Int J Hyperthermia. 2021;38:1023–30, http://dx.doi.org/10.1080/02656736.2021.1945689.
- 17. Ye J, Huang W, Huang G, Qiu Y, Peng W, Lan N, et al. Efficacy and safety of US-guided thermal ablation for primary hyperparathyroidism: a systematic review and meta-analysis. Int J Hyperthermia. 2021;37:245–53, http://dx.doi.org/10.1080/02656736.2020.1734673.
- 18. Wei Y, Peng CZ, Wang SR, He JF, Peng LL, Zhao ZL, et al. Effectiveness and safety of thermal ablation in

the treatment of primary hyperparathyroidism: a multicenter study. J Clin Endocrinol Metab. 2021;106:2707-17, http://dx.doi.org/10.1210/clinem/dgab240.

- Hussain I, Ahmad S, Aljammal J. Radiofrequency ablation of parathyroid adenoma: A novel treatment option for primary hyperparathyroidism. AACE Clin Case Rep. 2021;7:195–9, http://dx.doi.org/10.1016/j.aace.2021.01.002. PMID: 34095487; PMCID: PMC8165122.
- 20. Ying W, Zhen-Long Z, Xiao-Jing C, Li-Li P, Yan L, Ming-An Y. A study on the causes of operative failures after microwave ablation for primary hyperparathyroidism. Eur Radiol. 2021;31:6522–30, http://dx.doi.org/10.1007/ s00330-021-07761-9. Epub 2021 Mar 2. PMID: 33651201; PMCID: PMC8379100.
- 21. Ha EJ, Baek JH, Baek SM. Minimally invasive treatment for benign parathyroid lesions: treatment efficacy and safety based on nodule characteristics. Korean J Radiol. 2020;21:1383–92, http://dx.doi.org/10.3348/kjr.2020.0037. Epub 2020 Aug 4. PMID: 32767864; PMCID: PMC7689148.
- Spartalis E, Giannakodimos A, Ziogou A, Giannakodimos I, Paschou SA, Spartalis M, et al. Effect of energy-based devices on post-operative parathyroid function and blood calcium levels after total thyroidectomy. Expert Rev Med Devices. 2021;18:291–8, http://dx.doi.org/10.1080/17434440.2021.1899805. Epub 2021 Mar 26. PMID: 33666537.
- Na DG, Lee JH, Jung SL, Kim JH, Sung JY, Shin JH, et al. Radiofrequency ablation of benign thyroid nodules and recurrent thyroid cancers: consensus statement and recommendations. Korean J Radiol. 2012;13:117–25.
- 24. Kim JH, Baek JH, Lim HK, Ahn HS, Baek SM, Choi YJ, et al. 2017 thyroid radiofrequency ablation guideline: Korean Society of Thyroid Radiology. Korean J Radiol. 2018;19:632–55.
- 25. Garberoglio R, Aliberti C, Appetecchia M, Attard M, Boccuzzi G, Boraso F, et al. Radiofrequency ablation for thyroid nodules: which indications? The first Italian opinion statement. J Ultrasound. 2015;18:423–30.
- 26. Gharib H, Papini E, Garber JR, Duick DS, Harrell RM, Hegedüs L, et al. American Association of Clinical Endocrinologists, American College of Endocrinology, and Associazione Medici Endocrinologi. Medical guidelines for clinical practice for the diagnosis and management of thyroid nodules 2016 update. Endocr Pract. 2016;22:622–39.
- 27. Pace-Asciak P, Russell JO, Shaear M, Tufano RP. Novel approaches for treating autonomously functioning thyroid nodules. Front Endocrinol (Lausanne). 2020;11:565371, http://dx.doi.org/10.3389/fendo.2020.565371. PMID: 33250857; PMCID: PMC7673400.
- Sung JY, Baek JH, Jung SL, Kim KS, Lee D, Kim WB, et al. Radiofrequency ablation for autonomously functioning thyroid nodules: a multicenter study. Thyroid. 2015;25:112–7, http://dx.doi.org/10.1089/thy.2014.0100.
- 29. Xu D, Ge M, Yang A, Cheng R, Sun H, Wang H, et al. Expert consensus workshop report: guidelines for thermal ablation of thyroid tumors (2019 edition). J Cancer Res Ther. 2020;16:960-6, http://dx.doi.org/10.4103/jcrt.JCRT\_558\_19. PMID: 33004735.
- 30. Zeng Z, Peng CZ, Liu JB, Li YW, He HF, Hu QH, et al. Efficacy of ultrasound-guided radiofrequency ablation of parathyroid hyperplasia: single session vs. twosession for effect on hypocalcemia. Sci Rep. 2020;10:6206, http://dx.doi.org/10.1038/s41598-020-63299-8.
- Peng C, Zhang Z, Liu J, Chen H, Tu X, Hu R, et al. Efficacy and safety of ultrasound-guided radiofrequency ablation of hyperplastic parathyroid gland for secondary hyperparathyroidism associated with chronic kidney disease. Head Neck. 2017;39:564–71, http://dx.doi.org/10.1002/hed.24657.

- Qin X, Wang B, Li B, Lin C, Liu X, Xie X. Value of contrastenhanced ultrasonography in radiofrequency ablation of secondary hyperparathyroidism. Ren Fail. 2021;43:445–51, http://dx.doi.org/10.1080/0886022X.2021.1889601. PMID: 33663332; PMCID: PMC7939554.
- Mainini AP, Monaco C, Pescatori LC, De Angelis C, Sardanelli F, Sconfienza LM, et al. Thermal ablation of benign thyroid nodules. J Ultrasonido. 2017;20:11–22, http://dx.doi.org/10.1007/s40477-016-0221-6.