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Review

# Update on the role of ultrasound guided radiofrequency ablation for thyroid nodule treatment

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## HIGHLIGHTS

- We review the status of radiofrequency ablation treatment of thyroid nodules.
- It has a role in thyroid nodule volume reduction and improve patient symptoms.
- Multicenter studies are warranted to better clarify its clinical utility.

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## ABSTRACT

Thyroid nodules can be frequently detected in general population, most of them are benign, however malignant cases are rising in the past decades. Ultrasound (US) is the most common imaging modality to assess thyroid nodular lesions, plan patient work-up and guide minimally invasive treatment. The present review paper has been researched to evaluate the current status of radiofrequency ablation (RFA) treatment in order to evaluate indications, techniques, complications, limitations and outcome assessment in benign solid, partially cystic nodules and recurrent malignant nodules. RFA comparison with other ablation techniques has been provided as well. US guided Radiofrequency ablation has been proved to be effective and safe in cases of benign thyroid nodules and a promising treatment method alternative to surgery for patients with recurrent papillary thyroid cancer. It's major role lies in significant reduction of thyroid nodule mean volume and improvement of the patient symptoms. However, future multicenter studies are warranted to better clarify the multi-parametric patient selection criteria and evaluate RFA technique efficacy, advantages and limitations in the variety of thyroid nodular disease.



## 1. Introduction

Thyroid nodules are very frequent in the general population, with a prevalence of 20–67% and of about 50% in the individuals older than 40 years of age [1–4]. Most of them are hyperplastic nodules and not clinically relevant neoplasms [5]. However a proportion, although not at so high rates, are malignant within range 7–15% and/or become clinically significant and even fatal for the individual in less than 1% of cases [6] with a 2.4 times of increase in thyroid malignancy in the last 30 years [7]. Thyroid scintigraphy has a limited role in the evaluation of solitary thyroid nodules as the findings usually show relative uptake of the tracer within nodule with normal parenchyma overlay. Approximately 80%–85% of nodules are "cold" (lack of uptake) and 10%–15% of these are malignant [8]. A 99mTc pertechnetate scintigraphy can be used to differentiate "cold nodules" from autonomous functioning thyroid

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nodules (AFTN) or "hot nodules", in patients showing decreased serum thyrotropin (TSH) concentrations [9].

Ultrasound is the most common imaging modality to assess thyroid nodular lesions and to plan further treatment [5]. The first experience of image-guided radiofrequency ablation (RFA) with evaluation of efficacy and safety of ultrasound guided percutaneous RFA of thyroid nodules has been introduced and published in 2006 [10]. The results were positive – the volume of thyroid nodules significantly decreased and the majority of the patients reported an improvement of their symptoms. Since then the amount of publications about therapeutic options for thyroid nodules has grown noticeably.

The RFA method was considered an alternative to surgery in the beginning, but gradually the importance of RFA as a treatment option is growing for both - benign solid and partially cystic nodules and recurrent thyroid cancer [11,12], mainly because it is minimally invasive and some patients are ineligible for surgery [11,13,14]. In autonomously functioning thyroid nodules RFA can be considered as alternative to radioiodine therapy with the added benefit of not developing hypothyroidism [9]. RFA compared to other minimally invasive ablative techniques (e.g. microwave (MW), laser ablation (LA)), percutaneous ethanol injection (PEI) has been shown to be more effective in decreasing nodule mean volume [14], with small complication rates [15] and a marked improvement of nodule-related symptoms [11]. RFA procedure is highly operator dependent and practitioners experience is one of the crucial factors that affect treatment response [14].

The aim of this paper was to review the available literature on ultrasound guided RFA of thyroid nodules in order to evaluate indications, techniques, complications, limitations and outcome assessment.

## 2. Methods

The content, methodological strategy and the aims of the review were agreed before initiating the search.

### 2.1. Search strategy

A literature search was performed in Medline and Scopus in August 30, 2016.

The following search terms were applied, using Medline and MeSH terms: "thyroid gland", "thyroid neoplasms", "ultrasonography", "ablation techniques". To make sure that publications not yet indexed with MeSH terms were included, a free text search was included using the terms: "radiofrequency ablation", "RFA", "radiofrequency thermal ablation", "thyroid", "thyroid nodule", "ultrasound".

Two authors (MR and MR) reviewed all titles and abstracts.

The inclusion criteria were: original research papers in English on ultrasound guided RFA in thyroid nodules. Exclusion criteria were: non-human studies, case reports, review articles and meta-analyses, editorials, articles not written in English, studies with insufficient data; studies which compared RFA with other treatment methods.

All included papers were subsequently read by the three authors and consensus obtained through discussion. All reference lists were hand searched for further references. We registered: authors, year of publication, study design, sample size, nodule inclusion criteria (size, radioisotope scan, USG pattern, fluid component presence), procedure technical parameters, complications, follow-up period and volume reduction ratio (VRR). For malignant nodules - also pathological type and thyroglobulin (Tg) level was evaluated.

## 3. Results

### 3.1. Study selection and overview

The procedure of study selection is presented in Fig. 1.

Four-hundred-and-fifteen publications were selected from titles and abstracts. 102 duplicates were removed from the titles and abstracts. Of the remaining 313 manuscripts, 24 were included.

16 manuscripts included data from benign nodules, 8 included data from malignant nodules (see Tables 1 and 2).

In total, out of 24 eligible studies RFA was used to treat 989 benign nodules (16 studies) in 895 patients, among them 79 nodules in 76 patients were treated with bipolar RFA (3 studies) and 300 malignant nodules (8 studies) in 241 patients.

12 studies were retrospective and 11 were prospective studies (two of these were randomized controlled trials (9.1%) [16,17]).

RFA studies for benign nodules included only "cold" or non-functioning nodules in 9articles [10,16–23], 6 studies included also toxic (or "hot" in scintigraphy) and nonfunctioning nodules [9,24–29] and in one study authors did not mention functionality [30]. Ultrasound patterns of nodules varied – only solid or predominantly solid nodules were analyzed in 6 studies (solid portion >50%) [16–18,20,25,26] and mixed studies with predominantly cystic or cystic nodules in addition to solid nodules in 8 studies [9,10,19,22–24,29,30] and no information about patterns - in two studies [21,28]. The median diameter of the treated lesions was 3.3 cm (range 0.6–10.0 cm) in 7studies that pointed out nodule diameter [9,10,17,19,20,24,30]. The detailed parameters are summarized in Tables 1 and 2

RFA studies for malignant nodules included two cases of medullary thyroid carcinoma [31,32], two studies included follicular carcinoma [33,34] and one study reported on treatment of only papillary microcarcinomas [35]. Other treated malignancy histological variations were papillary thyroid carcinomas in 7 studies and exclusively in 3 studies [36–38]. The median nodule diameters before treatment were 10.95 mm (5.8–40 mm), after treatment – 2.2 mm (range 0.6–21.7 mm).

Characteristics of procedure and results are discussed further in article.

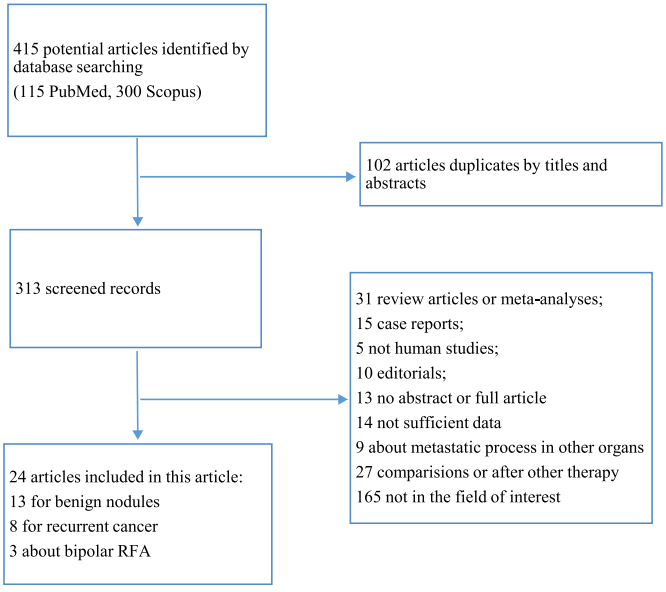


**Fig. 1.** Methodology of selection of analyzed publications.