Medical Coverage Policy

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Radiofrequency Ablation for Thyroid Nodules

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Related Coverage Resources

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Overview

This Coverage Policy addresses radiofrequency ablation (RFA) for thyroid nodules.

Coverage Policy

Radiofrequency ablation (RFA) is considered medically necessary for treatment of ANY of the following:

- differentiated thyroid cancer (i.e., papillary, follicular, and oncocytic carcinoma – formerly known as Hürthle cell)
- medullary thyroid cancer
- benign thyroid nodule when BOTH of the following criteria are met:
  - compressive symptoms (e.g., changes of voice, dysphagia, dyspnea, pain)
  - limited to a single RFA treatment in a 12-month period

Health Equity Considerations

Health equity is the highest level of health for all people; health inequity is the avoidable difference in health status or distribution of health resources due to the social conditions in which people are born, grow, live, work, and age.

Social determinants of health are the conditions in the environment that affect a wide range of health, functioning, and quality of life outcomes and risks. Examples include safe housing, transportation, and neighborhoods; racism, discrimination and violence; education, job opportunities and income; access to nutritious foods and physical activity opportunities; access to clean air and water; and language and literacy skills.

General Background

Radiofrequency ablation (RFA) of thyroid nodules is the application of radiofrequency waves to cause thermal injury and subsequent necrosis of the tissue. Gradual reabsorption of the ablated tissue results in overall volume reduction of the thyroid nodules. RFA of thyroid nodules was first used in 2002. RFA was not approved in the United States until 2018; therefore, RFA has not been commonly used in the United States. Many centers in the United States are establishing RFA programs, and it appears that RFA may be increasing in use as expertise in the technique is developed.

U.S. Food and Drug Administration (FDA)
No information on RFA for benign thyroid nodules is found on the FDA website when searched. A search of other websites and articles suggest the FDA approved RFA for use on benign compressive thyroid nodules in 2018.

Literature Review—Systematic Reviews
Benign: He et al. (2021) conducted a systematic review the literature of ultrasound guided ablation for solid/cyst benign thyroid nodules and a network meta-analysis to evaluate the efficacy and complications of different ablation therapies. The study included 16 randomized controlled trials (843 patients) that compared the following treatments: RFA, laser ablation (LA), high-intensity focused ultrasound (HIFU) and microwave ablation (MWA). Seven studies included RFA. Percentage mean volume change, symptom score change, cosmetic score change and complications were evaluated by network meta-analysis. RFA with two treatment sessions group was associated with the highest reduction for the mean volume change during six-month follow-up. There is no significant difference in the incidence of complications. Subgroup analysis showed that 2 sessions of RFA ranks the highest probability (surface under the cumulative ranking curve [SUCRA] values 77.9) of being the most efficacious treatment for solid or predominantly solid benign nodules. Ethanol ablation (EA) ranked first (SUCRA value 81.1) in the treatment for cyst or predominantly cyst benign nodules. The authors concluded that RFA appears to be superior to other ultrasound-guided percutaneous ablation in reducing benign thyroid nodule volume during short- and long-term follow-up and in the subgroup analysis, RFA with 2 treatment sessions showed the most significant effectiveness for solid benign thyroid nodules and EA showed more effectiveness to decrease the volume of cyst benign thyroid nodules. The authors noted that further randomized prospective studies focusing on efficacy, side effects, costs, and quality of life in different percutaneous ablation were warranted.

Both benign and cancerous: Muhammad et al. (2021) conducted a systematic review is to evaluate the evidence for current studies and data of safety and efficacy of radiofrequency ablation (RFA) for the management of benign thyroid nodules (BTNs) and differentiated thyroid cancers (DTC). The study notes that while surgery is first-line treatment, for candidates with high surgical risk or those who refuse to undergo repeated surgery, newer techniques such as RFA are an option. The study notes that RFA has been used in Asian and European institutions as an alternative to surgery but is relatively new in North America and further large-scale studies focusing on a Western population are needed. The review included a total of 75 studies that met the inclusion criteria with 35 studies focused on RFA use for solid nodules; 12 studies on predominantly cystic nodules; 10 for autonomously functioning thyroid nodules, and 18 studies on differentiated thyroid cancer. Prospective and retrospective studies were included in review with inclusion criteria: adult population; persons with DTC; persons with benign functional or nonfunctional thyroid nodules (solid, mixed solid and cystic, or purely cystic. A meta-analysis could not be performed in this systematic analysis due to the heterogeneity of the included studies, lack of a control population in many studies, and differences in inclusion and exclusion criteria; many of the studies were retrospective with a small follow-up duration (around one year); exact breakdown of nodules based on ultrasound features was not mentioned in majority of the studies; and most of the studies were based in Asia or Europe. In conclusion, RFA seems to be an effective and safe alternative to surgery in high-risk surgical patients with thyroid cancers and for selected BTNs. Additional trials with longer follow-up in North American patients are needed to validate its full role in the armamentarium of thyroidologists.

Benign: Monpeyssen et al. (2021) conducted a systematic review to review the outcomes of ultrasound-guided radiofrequency ablation of benign thyroid nodules including solid nonfunctioning and on autonomous thyroid nodules (AFTN). The review included 17 studies that evaluated RFA for the treatment of benign solid (nonfunctioning or autonomous) thyroid nodules, with at least 18 months follow-up. Data extraction and quality assessment were performed by two endocrinologists according to PRISMA guidelines and anthropometric data, safety and efficacy parameters were collected. The majority of the studies were retrospective studies and reported 933 nodules, mostly solid. Baseline volume ranged between 6.1 ± 9.6 and 36.3 ± 59.8 ml. Local analgesia was used and the time duration of the treatment was between 5 ± 2 and 22.1 ± 10.9 min. The volume reduction rate at 12 months ranged from 67% to 75% for the nodule treated

with a single procedure and reached to 93.6 ± 9.7% for nodules treated with repeat ablations. The regrowth rate at 12 months ranged from 0% to 34%. The authors concluded that all the studies consistently validated the long-term clinical efficacy and the substantial safety of RFA for the treatment of benign thyroid nodules. It was noted that thermal ablation is an operator-dependent technique and should be performed in centers with specific expertise. The selection of the patients should be rigorous because the nodule size and the structural and functional characteristics influence the appropriateness and the outcomes of the treatment.

Benign: Cho et al. (2020) conducted a systematic review and meta-analysis to determine the efficacy of thermal ablation of benign thyroid nodules of studies with long-term follow-up of more than 3 years. The review included 12 studies that had patients with a benign thyroid nodule treated with thermal ablation; and follow-up data for more than 3 years after ablation (five for RFA and seven for LA) and 695 nodules from 680 patients who underwent RFA. Ten studies were retrospective in design, and the two others were prospective. The pooled volume reduction rate (VRR) for ablated nodules showed rapid volume reduction before 12 months, a plateau from 12 to 36 months, and more volume reduction appearing after 36 months, demonstrating long-term maintenance of treatment efficacy. Thermal ablation had a complication rate of 3.8%. Moreover, patients undergoing nodule ablation showed no unexpected delayed complications during the follow-up period. In the subgroup analysis, RFA was shown to be superior to LA in terms of the pooled VRR and the number of patients who underwent delayed surgery.

Benign: Trimboli et al. (2020) conducted a meta-analysis and systematic review to obtain solid evidence of the long-term efficacy of image-guided thermal ablations including radiofrequency ablation (RFA) and laser ablation in benign non-functioning solid thyroid nodules (BNFSTN). Studies reporting the effectiveness of RFA or laser ablation in patients with BNFSTN in terms of volume reduction rate (VRR), compressive symptoms and cosmetic concerns were included, and complications were also assessed. The review included 12 studies on RFA and 12 on laser ablation, assessing 1,186 and 2,009 BNFSTNs, respectively. Six studies were prospective cohort, ten retrospective cohorts and seven randomized controlled; and study design not clearly stated in one study. Original papers reporting complete data of BNFSTNs treated by RFA or laser ablation and later followed-up for at least 6 months were included. Overall, VRR at 6, 12, 24, and 36 months was 60%, 66%, 62%, and 53%. VRR of RFA was 68%, 75%, and 87%, respectively. VRR of laser ablation was 48%, 52%, 45%, and 44%, respectively. Baseline volume of nodules undergone RFA was significantly smaller compared to laser ablation (20.1 ± 22.4 versus 24.6 ± 23.6 ml; $p< 0.01$). Nodules smaller than 30 ml obtained better outcomes than larger ones. A significant reduction in compressive symptoms and cosmetic concerns was found after RFA. Results were stable up to two years for RFA and three years for laser ablation. Improvement in compressive symptoms and cosmetic concerns was demonstrated for RFA. The authors concluded that the meta-analysis showed that both RFA and laser ablation are able to obtain a significant volume reduction in BNFSTNs with a significant volume reduction is evident at 6 months after thermal ablation and results are stable over the time.

Cancerous: Tong et al. (2019) conducted a systematic review and meta-analysis to evaluate the efficacy and safety of radiofrequency ablation (RFA), microwave ablation (MWA) and laser ablation (LA) for treating papillary thyroid microcarcinoma (PTMC). The study assessed the standard mean difference of the tumor volume before and after therapy and the proportion of complete disappearance, local recurrence, distant metastasis and complications using both fixed or random-effects modeling. Heterogeneity among studies was determined using the Q statistic for the pooled estimates and the inconsistency index. The review included 12 studies, including a sample size of 1,187 patients and 1,284 PTMCs, with nine studies retrospective, and three prospective. Eleven studies were single-arm studies (six, three and two studies treated with RFA, MWA and LA, respectively) and one study comparative. MWA vs RFA, MWA and LA all showed a significant reduction in tumor volume of PTMCs ($p<0.05$). Though MWA demonstrated superior efficacy over

the other two therapies for volume reduction, the differences were not statistically significant. The pooled proportion of complete disappearance after RFA was the highest (76.2%), and the pooled proportion of recurrence for RFA was the lowest (0.01%) among the three therapeutic methods, but no significant difference was detected. There was no event of distant metastasis during the follow-up in all of these studies. There were few major complications; the pooled proportion of complications for RFA (1.73%), MWA (6.0%) and LA (0.92%) was low, revealing no significant differences ($p>0.05$). The authors concluded that RFA, MWA and LA are acceptable treatments to manage PTMCs in terms of efficacy and safety for non-surgical candidates.

Both benign and cancerous: Chung et al. (2017) performed a systematic review and meta-analysis to evaluate the safety of radiofrequency ablation (RFA) for the treatment of benign thyroid nodules and recurrent thyroid cancers. The review included 24 studies, with 2,421 patients and 2,786 thyroid nodules. Included were 12 retrospective studies, nine prospective studies, and three studies with unclear study design. Pooled proportions of overall and major complications were assessed using random-effects modelling. Heterogeneity among studies was determined using the $\chi 2$ statistic for the pooled estimates and the inconsistency index I2. The review included 24, with sample size of 2,421 patients and 2,786 thyroid nodules. There were 41 major complications and 48 minor complications of RFA reported, giving a pooled proportion of 2.38% for overall RFA complications [95% confidence interval (CI): 1.42%-3.34%] and 1.35% for major RFA complications (95% CI: 0.89%-1.81%). There were no heterogeneities in either overall or major complications (I2 = 1.24%-21.79%). On subgroup analysis, the overall and major complication rates were significantly higher for malignant thyroid nodules than for benign thyroid nodules ($p=0.0011$ and 0.0038, respectively). The authors conclude that RFA was found to be safe for the treatment of benign thyroid nodules and recurrent thyroid cancers.

Literature Review—Studies

Benign: Kandill et al. (2022) conducted a prospective study at two US centers to evaluate the efficacy and safety of RFA in the treatment of benign thyroid nodules. The study included 233 patients, of which 70 patients were available for 12 months follow-up. Inclusion criteria included: 1) benign thyroid nodule on two FNA biopsies prior to ablation or benign sonographic appearance with one benign cytologic result; 2) no history of ethanol injection or radioactive iodine ablation; 3) follow-up for at least three months. Nodule volume during the follow-up period decreased from a median of 4.17 ml (IQR: 0.74–17.90) at baseline to 0.39 ml (IQR: 0.07–2.52) at 12 months ($P<0.001$). The median and interquartile range of volume reduction rate (VRR) at 12 months was 76% (IQR: 52%–90%) A total of six (2.5%) patients encountered complications during the study period. Complications include temporary voice change, drainage from the RFA site, and minor skin burn. A limitation of this study is loss to follow-up and no comparator.

Benign or Indeterminate: Issa et al. (2022) prospectively observed 178 patients with thyroid nodules diagnosed as benign (n=125, Bethesda II) or indeterminate (n=53, Bethesda III/IV) by preoperative cytopathological analysis who underwent RFA. The article stated "By the nature of the study, Bethesda VI nodules were excluded. Since the ETA/AME/AACE all classify only Bethesda III and IV as indeterminate nodules, we excluded patients with Bethesda V nodules". Thyroid nodules were included only if they

(1) were classified by fine needle aspiration as a Bethesda II, III, IV nodule;
(2) have yet to be treated (no previous laser ablation or ethanol ablation or radioactive iodine ablation); and
(3) attended at least one follow-up visit beyond the 1-month mark.

Results showed in the benign and indeterminate cohorts had similar thyroid nodule volume reduction rates at 65.60% and 64.20%, respectively ($p=0.68$). The two groups had similar nodular regrowth rates, at 11.2% for benign nodules and 9.40% for indeterminate nodules ($p=0.72$). A total of three cases of transient dysphonia were reported. The authors stated that

"Moving forward, studies of larger sample sizes and longer follow-up duration could realistically posit RFA as a potential treatment option for indeterminate thyroid nodules".

Benign: Lin et al. (2022) retrospectively reported six-month results following RFA in multiple centers. A total of 762 patients presenting with 826 benign solid benign nodules underwent RFA for a single nodule. For those patients presenting with more than one nodule, RFA was performed for a single nodule per session. Nodules included: Large n=180 (>30 mL); Medium n=295 (11–30 mL); and Small n=351 (≤10 mL). All nodules except one were ablated in a single session, and all nodules were classified as solid or predominant solid. At 6-months follow-up, there was no significant difference of volume reduction ratio (VRR) among the three groups. A total of 40 (4.8%) complications were reported. All patients recovered spontaneously without surgery intervention. The overall complication rate showed significant difference among the three groups. Authors noted that the efficacy of RFA for multiple thyroid nodules should be evaluated in another future study to confirm treatment outcomes.

Benign: In a single center randomized trial, Cesareo et al. (2021) compared RFA with laser ablation (LA). A total of 60 patients with solid or predominantly solid benign nonfunctioning thyroid nodules (BNTNs) were followed for 12 months. Only 29 patients in each group completed 12 months. Inclusion criteria included solitary BNTN or dominant nodule characterized by pressure symptoms/cosmetic problems or patients without symptoms who experienced a volume increase >20% in one year. Primary outcomes included volume reduction rate (VRR) and proportion of nodules with more than 50% reduction. A reduction of >50% in nodule volume at 12 months was observed in 26 (89.7%) and 22 (75.9%) patients in the RFA and LA groups (technical success rate), respectively (p=0.149). At the 12-month follow-up, RFA was associated with a statistically significant greater nodule VRR than LA (p=0.024). At six months (Cesareo, et al., 2021) the adverse event rates (local pain, dysphonia, thyrotoxicosis, fever, hematoma) were 37% (n=11) and 43% (n=13) for RFA and LA, respectively, with no requirement for hospitalization. Cesareo et al. (2021) noted "no further procedure-related complications were documented during the 12-month period".

Benign: Bernardi et al. (2020) conducted a multicenter retrospective study, to evaluate technique efficacy, rate of regrowth, and retreatment over five years after radiofrequency ablation (RFA) or laser ablation (LA) of benign thyroid nodules and to identify predictive factors of outcome. The study included 406 patients treated with either RFA or LA and followed for five years after initial treatment. Propensity score matching was used to compare treatments. Cumulative incidence studies with hazard models were used to describe regrowth and retreatment trends, and to identify prognostic factors. Logistic regression models and receiver operating characteristic analyses were used for risk factors and their cutoffs. RFA and LA significantly reduced benign thyroid nodule volume, and this reduction was generally maintained for five years. Technique efficacy (defined as a reduction ≥50% after one year from the treatment) was achieved in 74% of patients (85% in the RFA and 63% in the LA group). Regrowth occurred in 28% of patients (20% in the RFA and 38% in the LA group). In the majority of cases, further treatment was not required with 18% of patients retreated (12% in the RFA and 24% in the LA group). Data was confirmed by propensity score matching. Cumulative incidence studies indicated that RFA was associated with a lower risk of regrowth and a lower risk of requiring retreatment over time. Overall, technique inefficacy and regrowth were associated with low-energy delivery. Retreatments were more frequent in young patients, in large nodules, in patients with lower volume reduction at one year, and in cases of low-energy delivery (optimal cutoff was 918 J/mL for RFA). The authors concluded that both techniques result in a clinically significant and long-lasting volume reduction of benign thyroid nodules with the risk of regrowth and needing retreatment was lower after RFA.

Benign: Deandrea et al. (2019) retrospectively reported on 215 patients who underwent RFA for benign thyroid nodules who were followed for at least three years. Patients were >18 years of

age, had normal thyroid function, and had undergone a single RFA procedure. Retrospective analysis showed median volume observed six months after the procedure was significantly lower than that at baseline. Further progressive volume reduction was seen at one year, as well as at the two year follow-up. Nodule volume recorded at three and four years did not significantly differ from that at one and two years. An additional small but statistically significant reduction was observed at five years (p=0.0089). No major complications occurred.

Benign: In a prospective, multicenter study, Jung et al. (2018) performed RFA on 276 (248 solid and 28 predominantly cystic) benign nodules. The mean number of performed RF sessions was 1.3 ± 0.4 (range 1–2; one session in 206 patients and two in 70). Patients were followed for 12 months. Volume reduction at 12 months after RFA was 80.3 ± 13.7% (n = 276, range 38.7–100%). The therapeutic success rate was 97.8% (270/276) at the 12-month follow-up. No patient experienced a life-threatening or delayed complication during the follow-up. The overall complication rate was 5.1% (14/276). Major and minor complication rates were 1.1% (3/276) and 4.0% (11/276), respectively. The side-effect rate was 4.7% (13/276). Almost all study subjects recovered without sequelae; only one hyperthyroid patient was treated with medication (propylthiouracil, 100–150 mg/day).

Benign: Che et al. (2015) retrospectively compared 200 patients who underwent thyroid surgery to 200 patients who underwent RFA for the treatment of benign thyroid nodules. The surgery methods included total thyroidectomy and lobectomy. Inclusion criteria for both groups was: 1) having a cosmetic problem, 2) having nodule-related symptoms, 3) having hyperfunctioning nodules related to thyrotoxicosis, and 4) having refused surgery. For the RFA group, the nodule volume decreased significantly from 5.4 at baseline to 0.4 mL (p=0.002) at the 12-month follow-up. Hypothyroidism was detected in 71.5% of patients after surgery but in none following radiofrequency ablation. The rate of residual nodules (11.9% versus 2.9%, p=0.004) and hospitalization days was significantly greater after surgery (6.6 versus 2.1 days, p<0.001), but the cost difference was not significant. The incidence of complications was significantly higher from surgery than from radiofrequency ablation (6.0% versus 1.0%, p=0.002). This study is limited by its retrospective design.

Benign: Baek et al. (2015) conducted a small, randomized trial at two centers, comparing RFA (n=25) to ethanol ablation (EA) (n=25). The study included 50 patients, followed for six months, who met the following inclusion criteria:

- patients with predominantly cystic thyroid nodules (PCTN) (proportion of cystic component, less than 90% and greater than 50% of the nodule);
- reports of pressure symptoms or cosmetic problems caused by thyroid nodules;
- benign cytological confirmation in at least two separate US-guided, fine-needle aspiration or core needle biopsies; and
- normal serum levels of thyroid hormone, thyrotropin, and calcitonin.

Analysis was performed primarily in an intention-to-treat manner as not all 50 patents were measurable at six months: RFA (n=22) and EA (n=24). The mean volume reduction was 87.5 ± 11.5% for RFA and 82.4 ± 28.6% for EA (p=0.710; mean difference, indicating no significant difference). There were no significant differences in major complications (p>0.99). This study is limited by the amount of participating patients.

Benign: Bernardi et al. (2014) conducted a study that evaluated RFA efficacy, tolerability, and costs and comparing them to hemithyroidectomy for the treatment of benign thyroid nodules. The study included 37 patients who underwent RFA and then were retrospectively compared to 74 patients surgically treated, either in a standard inpatient or in a short-stay surgical regimen. Efficacy, tolerability, and costs were compared. The contribution of final pathology was also taken into account. RFA reduced nodular volume by 70% after 12 months and appeared to be an effective method for treating nodule-related clinical problems, but it was not as effective as

surgery for the treatment of hot nodules. RFA and surgery were both safe, although RFA had less complications and pain was rare. It was noted that RFA did not allow for any pathologic analysis of the nodules, which, in six patients who had undergone surgery (8%), it was revealed that the nodules harbored malignant cells.

Benign: Sung et al. (2013) conducted a small, randomized trial, comparing volume reduction of single-session ethanol ablation (EA, n=25 patients) and radiofrequency (RF, n=25 patients) ablation for benign cystic thyroid nodule treatment. Inclusion criteria included:

(a) presence of a cystic thyroid nodule (cystic portion. 90%);
(b) reports of pressure symptoms or cosmetic problems;
(c) cytologic confirmation of benignancy in at least two separate US guided fine-needle aspiration cytologic (FNAC) examinations (i.e., two biopsies performed with an interval of several months apart) for cystic fluid and/or a mural, solid component; and
(d) serum levels of thyroid hormone, thyrotropin, and calcitonin within normal limits

Follow-up duration was six months. Volume reduction ratio was reported as a percentage. Analysis was performed primarily in intention-to-treat manner (n=21 for each).
Mean volume reduction was 96.9% in EA and 93.3% in RF ablation. Authors state the mean volume reduction of the EA group was noninferior to and also significantly superior to that of the RF ablation group. There were no major complications ($p>0.99$).

Benign: Lim et al. (2013) conducted a retrospective study including 111 patients with a mean follow-up duration of 49.4 ± 13.6 months. A total of 126 benign non-functioning thyroid nodules underwent RFA. Inclusion criteria included but was not limited to reported cosmetic and/or symptomatic problems, largest diameter of nodule exceeding 2 cm, cytologically confirmed benign nodule on two separate ultrasound (US)-guided fine-needle aspiration biopsy (FNAB),
US imaging finding without suspicious malignant features, serum thyroid hormone and thyrotropin levels within normal ranges, refusal of or ineligible for surgery. Results demonstrated thyroid nodule volume decreased significantly, from 9.8 ± 8.5 ml before ablation to 0.9 ± 3.3 ml ($p<0.001$) at final evaluation: a mean volume reduction of 93.4 ± 11.7 %. Overall complication rate was 3.6 % (4/111). Major complications were observed in two patients (one with voice change and one with brachial plexus injury), and minor complications were observed in two patients (one with a haematoma and one with vomiting). A limitation of this study is its retrospective design.

Benign: Baek et al. (2012) reported results of a retrospective analysis of complications following RFA for benign thyroid nodules. A total of 1459 patients underwent RFA of 1543 thyroid nodules at 13 thyroid centers. Patients who underwent RFA met these criteria: pressure symptoms or cosmetic problems; had benign nodules greater than 2 cm in largest diameter; had serum thyroid hormone levels within normal limits; and refused or were ineligible for surgery. Of the 1459 patients, 48 (3.3%) experienced complications (2.2% per session), including 20 major and 28 minor complications. None of these complications was life threatening, and 46 patients recovered without sequelae. Of the remaining two patients, one had permanent hypothyroidism and the other underwent left thyroidectomy due to nodule rupture. The authors concluded the complication rate is low, but various complications may occur during thyroid RF ablation.

Professional Societies/Organizations

National Comprehensive Cancer Network™ (NCCN™): NCCN guideline for thyroid carcinoma, includes radiofrequency ablation as a treatment option for differentiated thyroid cancer (includes papillary, follicular, and oncocytic carcinoma – formerly known as Hürthle cell) and medullary thyroid cancer (Version 4.2024 — August 19, 2024) Category 2A

Category 2A: based on lower-level evidence, there is uniform NCCN consensus that the intervention is appropriate.

The American Association of Clinical Endocrinology published a Disease State Clinical Review titled The Clinical Utility of Minimally Invasive Interventional Procedures in the Management of Benign and Malignant Thyroid Lesions (Jasim, et al., 2022). The AACE states:

> Minimally invasive thyroid techniques are effective and safe when performed by experienced centers. To date, percutaneous ethanol injection therapy is recommended for recurrent benign thyroid cysts. Both ultrasound-guided laser and radiofrequency ablation (RFA) can be safely used for symptomatic solid nodules, both toxic and nontoxic. Microwave ablation and high-intensity focused ultrasound are newer approaches that need further clinical evaluation. Despite limited data, encouraging results suggest that minimally invasive techniques can also be used in small-size primary and locally recurrent thyroid cancer.
>
> Specific to RFA, the AACE states that the indications to perform RFA differ according to the lesion's nature and treatment intent. There are three well-established indications for RFA of benign nodules:
>
> (1) esthetic concern
> (2) compressive symptoms, and
> (3) autonomously functioning nodules.
>
> One indication that may be considered is the growing nodule prior to becoming symptomatic, since smaller nodules respond with better volume reduction rate (VRR) than larger nodules (Jasim, et al., 2022)
>
> Benign Nonfunctional Nodules: Several studies suggest that RFA is a safe option in benign nonfunctional nodules. The volume reduction can range from 50% to 85%. Volume reduction can be maintained a few years after initial treatment, especially in smaller-volume nodules (<10 mL), while larger benign nodules tend to require more than one treatment over time.
>
> Benign Autonomously Functioning Thyroid Nodules: Growing international data have demonstrated the safety and efficacy of the RFA technique in benign autonomously functioning thyroid nodules (AFTNs) as an alternative choice to surgery or radioactive iodine (RAI) treatment, although limited data are available in the United States.

American Association of Clinical Endocrinologists (AACE), American College of Endocrinology (ACE) and Associazione Medici Endocrinology (AME): these organizations published medical guidelines for clinical practice for the diagnosis and management of thyroid nodules (Gharib, et al., 2016). The guidelines include the recommendations:

- Image-guided thermal ablation for benign nodules:
  - Consider laser or radiofrequency ablation for the treatment of solid or complex thyroid nodules that progressively enlarge, are symptomatic or cause cosmetic concern (best evidence level [BEL] 2, GRADE C).
  - Repeat FNA for cytologic confirmation before thermal ablation treatment [BEL 3, GRADE B].
  - Discuss alternative therapy options and their efficacy, limitations, and adverse effects with the patient [BEL 3, GRADE B].

Level of evidence: 2
Randomized controlled trials with limited body of data
Well-conducted prospective cohort studies
Well-conducted meta-analyses of cohort studies

Level of evidence: 3
Methodologically flawed randomized clinical trials
Observational studies
Case series or case reports
Conflicting evidence, with weight of evidence supporting the recommendation

Grade B
No conclusive level 1 publications - Action recommended for indications reflected by the published reports
>1 Conclusive level 2 publication demonstrating benefit >> risk: Use if the patient declines or does not respond to conventional therapy, must monitor for adverse effects; Action based on intermediate evidence; Can be recommended as "second-line" therapy

Grade C
No conclusive level 1 or 2 publications - Action recommended for indications reflected by the published reports
>1 Conclusive level 3 publication demonstrating benefit >> risk Or No conclusive risk at all and no benefit at all:
Use when the patient declines or does not respond to conventional therapy, provided there are no important adverse effects

American Association of Endocrine Surgeons (AAES): this organization published guidelines for the definitive surgical management of thyroid disease in adults (Patel, et al., 2020). The guidelines note that for toxic adenoma (TA), two other therapeutic approaches are ethanol injection and radiofrequency ablation, neither of which have gained popularity in the United States nor are recommended as initial treatment, but which may be considered when patients are not candidates for conventional treatment. They note that, in most cases a surgeon should be consulted prior to proceeding, as surgery after one of these interventions can be more difficult if a euthyroid state does not result, hyperthyroidism recurs, or a nodule persists.

American Thyroid Association (ATA): In a 2023 consensus statement (Sinclair, et. al.) endorsed by the American Association of Endocrine Surgeons (AAES), American Academy of Otolaryngology Head and Neck Surgery (AAO-HNS), American Head and Neck Society (AHNS), Society of Interventional Radiology (SIR), Latin-American Thyroid Society (LATS), Asia and Oceania Thyroid Association (AOTA), and the Asia Pacific Society of Thyroid Surgery (APTS), the American Thyroid Association provided a framework for the safe adoption and implementation of ablation technologies for benign thyroid nodules. The key themes included: (1) safety of ablation techniques and their implementation, (2) optimal skillset criteria for proceduralists performing ablative procedures, and (3) defining expectations of success for this treatment option given its unique risks and benefits. The ATA statement concludes that thyroid ablative procedures are valid alternative treatment strategies to surgery for a subset of patients with symptomatic benign thyroid nodules.

The 2015 American Thyroid Association Management Guidelines for Adult Patients with Thyroid Nodules and Differentiated Thyroid Cancer only addresses RFA for treatment of thyroid cancer and does not address RFA for benign nodules (Haugen, et al., 2016).

The American Thyroid Association Guideline on Management Guidelines for Children with Thyroid Nodules and Differentiated Thyroid Cancer (Francis, et al., 2015) does not address radiofrequency ablation.

The American Academy of Otolaryngology — Head and Neck Surgery does not address thyroid nodules in their published Clinical Practice Guidelines.

American Head and Neck Society Endocrine Surgery Section with the Asia Pacific Society of Thyroid Surgery, Associazione Medici Endocrinologi, British Association of Endocrine and Thyroid Surgeons, European Thyroid Association, Italian Society of Endocrine Surgery Units, Korean Society of Thyroid Radiology, Latin American Thyroid Society, and Thyroid Nodules Therapies Association: these organizations published an international multidisciplinary consensus statement for radiofrequency ablation (RFA) and related ultrasound-guided ablation technologies for treatment of benign and malignant thyroid disease (Orloff, et al., 2022). The document notes that while RFA is the dominant focus of the statement, the clinical framework presented applies to other ablation techniques, including Laser thermal ablation (LTA), microwave ablation (MWA), high-intensity focused ultrasound (HIFU), and ethanol ablation. Future efforts will elucidate patient- and nodule-specific factors in which one technique should be preferred over others. While all methods may be appropriate for some patients, not all clinicians should seek to offer each of these techniques. Further investigation is required to address areas of evolving understanding, including:

- Optimal role of thermal ablation in primary malignancy and indeterminate nodules.
- Optimal role of thermal ablation vs. surgery in cytologically benign thyroid nodules.
- The role of thermal ablation in managing metastatic disease primarily.
- Criteria for determining treatment efficacy and outcomes.
- Prognostic factors for successful ablation and regrowth.
- Timing of additional treatment following an incomplete treatment or regrowth.
- Cost effectiveness for ablation procedures vs. surgical approaches.
- Patient-related outcome measures for ablation procedures versus surgical approaches.
- Comparative efficacy, safety, and ideal applications of varied thermal ablation techniques.
- Long-term efficacy in all clinical applications.
- Minimum expectations for training and experience prior to offering thermal ablation.
- Disseminating and securing global availability of ablation technologies

Recommendations in this consensus statement include:

- Ultrasound (US)-guided ablation procedures may be used as a first-line alternative to surgery for patients with benign thyroid nodules contributing to compressive and/or cosmetic symptoms
- Although less efficacious than surgery or radioactive iodine (RAI) in normalizing thyroid function, thermal ablation procedures can be a safe therapeutic alternative in patients with an autonomously functional thyroid nodule and contraindications to first-line techniques
- US-guided ablation procedures may be considered in patients with suitable primary papillary microcarcinoma who are unfit for surgery or decline surgery or active surveillance
- Following thermal ablation for benign nodules, primary objective measures of efficacy include ultrasonographic measurement of volume reduction and preservation or normalization of thyroid function
- Patient-reported outcomes, including validated symptom, cosmetic, and quality of life instruments may be used to determine efficacy
- Repeat ablation of a benign nodule can be considered for remnant nodular tissue contributing to unresolved symptomatic or cosmetic concerns
- Retreatment for persistent hyperthyroidism may be performed

Medicare Coverage Determinations

	Contractor	Determination Name/Number	Revision Effective Date
NCD	National	No Determination found	
LCD		No Determination found	

Note: Please review the current Medicare Policy for the most up-to-date information.
(NCD = National Coverage Determination; LCD = Local Coverage Determination)

Coding Information

Notes:

1. This list of codes may not be all-inclusive since the American Medical Association (AMA) and Centers for Medicare & Medicaid Services (CMS) code updates may occur more frequently than policy updates.
2. Deleted codes and codes which are not effective at the time the service is rendered may not be eligible for reimbursement.

Considered Medically Necessary when criteria in the applicable policy statements listed above are met:

CPT®* Codes	Description
60699	Unlisted procedure, endocrine system

***Current Procedural Terminology (CPT®) ©2023 American Medical Association: Chicago, IL.**

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Revision Details

Type of Revision	Summary of Changes	Date
Annual review	• No clinical policy statement changes.	10/15/2024