



## Editorial

# Thyroid Ablation: Past, Present, and Future

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**Introduction:** Benign thyroid nodules (BTN) account for up to 85 to 95% of thyroid nodules.<sup>1</sup> While 3 to 7% of the population have palpable BTN, more than 50% have BTN detectable by imaging.<sup>1</sup> Most BTN only require observation, but 5 to 15% grow and cause cosmetic or compressive symptoms such as dysphagia or hoarseness.<sup>2</sup> Autonomously functioning thyroid nodules (AFTN) are noncancerous nodules that cause hyperthyroid symptoms independent of thyroid-stimulating hormone (TSH).<sup>3,4</sup> The standard of care for symptomatic BTN and AFTN in the United States is surgery and radioactive iodine ablation, respectively, which often results in lifelong thyroid hormone replacement.<sup>2–4</sup> Thyroid ablation (TA) techniques such as radiofrequency thyroid ablation (RFA), microwave ablation (MWA), high intensity focused ultrasound (HIFU), and laser ablation (LA) are minimally invasive alternatives to surgery that preserve thyroid function without scar formation.<sup>2,3</sup>

**Initial Evaluation:** Palpable or incidentally discovered thyroid nodules warrant an ultrasound.<sup>4</sup> Generically, BTN have sonographic features such as cystic, solid, isoechoic, spongiform, regular margins, and no signs of infiltration, calcification, or lymphadenopathy.<sup>4</sup> Two fine-needle aspiration biopsies confirm benign lesions.<sup>5</sup> Cytologically indeterminate and malignant nodules should be referred for surgery.<sup>3</sup> A cosmetic score can contribute to the intervention decision; 1 = no palpable mass, 2 = palpable mass but no cosmetic problem, 3 = cosmetic problem with swallowing, and 4 = readily visible cosmetic problem.<sup>6</sup> Patients should also be questioned about their medical history, family history of cancer, biopsy locations, baseline hoarseness, presence of conducting hardware, and pregnancy.<sup>2,6</sup> Laboratory tests include serum calcitonin, complete blood count, TSH (with free T4 for abnormalities), and international normalized ratio for any bleeding concerns.<sup>2,6</sup> Suspected AFTN should also have scintigraphy performed for confirmation.<sup>3</sup> Malig-

nant lesions can be considered for RFA as second-line treatment after further metastatic evaluation for palliative treatment or if there are no more than three lesions that are less than 2 cm and isolated to the neck.<sup>3</sup>

**Techniques:** TA utilizes two important ultrasound-guided techniques. (1) The transisthmus approach inserts the probe into the thyroid isthmus where it is then advanced to the position of the nodule.<sup>3</sup> (2) The moving shot technique advances the electrode into the deepest portion of the nodule and then retracts it during ablation.<sup>3</sup> The moving shot is repeated until the entire nodule has confirmed echogenic changes.<sup>3</sup> These techniques ensure the interventionalist has complete visualization of the nodule and minimize injury risk of the recurrent laryngeal nerve, trachea, and esophagus (critical structures).<sup>3</sup>

**Radiofrequency Ablation:** RFA uses alternating current to destroy tissue in contact with the electrode. An internally cooled electrode is connected to a 30 to 55W generator within a closed loop circuit.<sup>7</sup> Monopolar electrodes are standard but bipolar electrodes can be used for pregnant patients or those with high-risk hardware.<sup>7</sup> RFA has applications in BTN and meta-analysis data show volume reductions more than 60% within 6 months and more than 80% within 2 years.<sup>3,8</sup> RFA of AFTN show TSH normalization of 71.2% within a year.<sup>3</sup> However, nodules more than 10 to 12 mL generally achieve less impressive size reductions or TSH adjustments.<sup>3,8</sup> RFA has more data on treating recurring thyroid cancers with 68 to 93% success, but it can also treat primary percutaneous transvenous mitral commissurotomy (PTMC) with 88% efficacy under the above-defined parameters.<sup>3</sup> Patients with severe tumor burden may also receive palliative RFA.<sup>3</sup> Data shows a major complication rate of 1.4% predominantly due to voice changes.<sup>3,8</sup> The minor complications reported are pain, skin burns, and vasovagal reactions.<sup>8</sup>

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**Laser Ablation:** LA utilizes fiber optic transmitted light to heat tissue.<sup>9</sup> Neodymium-doped yttrium aluminum garnet or diode lasers are most commonly used and set at 1,064 nanometer wavelength.<sup>9</sup> Randomized trial data show 57% reductions in BTN at 36 months in 67% of patients.<sup>3</sup> LA has efficacy in decreasing AFTN volumes by 44%, but is inferior to radioactive iodine for TSH normalization.<sup>3</sup> LA demonstrates equivocal treatments to PTMC in comparison to RFA with 94% lesions absent at 4 years with a local recurrence rate of 5.6%.<sup>3</sup> However, more data are needed to evaluate PTMC treatment as well as recurring thyroid cancers.<sup>3</sup> LA also has better outcomes (>80% volume reductions) in smaller nodules.<sup>3</sup> The strength of LA is its low major and minor complication rate at 0.5% in both cases due to its precisely targeted energy.<sup>8</sup>

**Microwave Ablation:** MWA utilizes electromagnetic fields with frequencies up to 2,450 MHz to heat tissue.<sup>3</sup> Retrospective data has shown MWA to reduce volumes of BTN by 67 to 74% at 6 months and up to 89% at 12 months.<sup>3,8</sup> MWA has not been evaluated extensively for AFTN or recurrent thyroid cancer treatment, but showed equivocal results to RFA and LA for PTMC treatment in one study.<sup>3</sup> MWA has a larger zone of ablation, which may result in higher pain scores and damage to nearby structures.<sup>3</sup> Consequently, meta-analysis data reports the major complication rate has been reported to be as high as 4.8%, although transient voice change accounted for 4.0% of that number. Minor complications also were reported to be 48.3% with pain being the most common. Data are limited for MWA and more studies need to evaluate its efficacy.

**High-Intensity Focused Ultrasound:** HIFU propagates sound waves to heat tissue.<sup>8</sup> Reduction in BTN is up to 45 to 70% over 3 to 24 months from systematic review data.<sup>3,8</sup> However, only nodules less than 3mL were observed to have a greater than 50% reduction size.<sup>8</sup> HIFU is inferior to radioactive iodine for achieving TSH normalization (53 vs. 94%) at 12 months.<sup>8</sup> Overall, data are limited in HIFU and it has not been evaluated in treating thyroid cancer.<sup>3</sup> Major complication rates, on the other hand, are extremely low and only observed when the HIFU focal point was moved within 1.1 cm of the tracheoesophageal groove.<sup>8</sup> Finally, HIFU equipment is extremely expensive and may be a deterrent to setting up a practice.<sup>8</sup>

**Ethanol Ablation:** EA causes tissue destruction via cellular dehydration and damage to local blood supply.<sup>10</sup> Ethanol is injected directly into the target tissue via ultrasound guidance following aspiration of the cyst contents.<sup>3</sup> EA is a good option for cystic BTN, as their margins prevent diffusion, but it has limited utility in solid lesions.<sup>3</sup> EA has efficacy of 46 to 90% for mixed (solid and cystic) to purely cystic nodules.<sup>3</sup> However, EA of mixed nodules greatly increases when combined with RFA.<sup>11</sup> Major complications of EA are very rare and include perithyroid fibrosis and tissue necrosis.<sup>11</sup> Finally, EA is a prudent option for individuals with low income as it is relatively inexpensive.<sup>3</sup>

**Training:** There is currently no formal certification process for performing TA in the United States.<sup>3</sup> Proficiency depends on the operator's experience with ultrasound-guided

neck interventions. As a result, physicians most capable of performing TA are radiologists, endocrinologists, and surgeons.<sup>3</sup> There are available private workshops to learn TA techniques, although these are not standardized.<sup>3</sup> Nevertheless, the first 50 cases should be proctored as studies have shown that volume reductions are directly proportional to operator experience.<sup>3,12</sup>

**Cost to the Patient:** Insurance has varying TA coverage and most data are centered on RFA.<sup>5</sup> Absolute costs of RFA are estimated to be \$3500 to \$6000 versus \$19,500 for surgery.<sup>5</sup> Although surgery has significant insurance reimbursement, there are additional costs associated, such as lifelong thyroid hormone replacement and higher rates of serious peri- and postoperative complications.<sup>5</sup> One study outside the United States reports lower total costs of RFA (adjusted to US dollars) in comparison to surgery (\$2661 vs. \$3825), due to decreased hospitalization time and the use of fewer resources.<sup>13</sup> More cost-comparison data are needed to evaluate the differences between TA techniques.<sup>3,8</sup>

**Referral Base:** Since TA is novel in the United States, there is a small referral base. Similarly, a study in Austria reported that 85.4% of patients were self-referrals for RFA after receiving a recommendation for thyroid surgery.<sup>14</sup> As mentioned above, limited insurance reimbursement may also be a significant barrier to TA referral. Practices that are already equipped to perform neck interventions (e.g., biopsy) are best equipped to receive referrals due to established networks.<sup>3</sup> Otherwise, new practices should expect significant devotion of resources to marketing and education while building a network.

**Follow-Up:** Immediately postprocedure, patients are monitored for 30 to 60 minutes for major complications that indicate hospital admission for observation.<sup>3</sup> Otherwise, patients may be discharged with nonsteroidal anti-inflammatory drugs or acetaminophen for pain.<sup>2,8</sup> Patients should be advised to return to the clinic for worrying symptoms such as voice change.<sup>3</sup> Clinical exams, thyroid function tests, and ultrasounds are done at months 3, 6, and 12 at minimum.<sup>8</sup> In the case of malignancy, there should be closer follow-up and serum thyroglobulin should be monitored for response to treatment.<sup>3</sup> Extended clinical follow-up should be recommended for patients as well because up to 24% of nodules can regrow.<sup>3</sup> Nodules that regrow or continue to cause cosmetic or compressive symptoms are eligible for procedure repetition.<sup>3,8</sup>

**Conclusion:** TA techniques are attractive and safe alternatives to surgery for BTN, AFTN, and some thyroid cancers. RFA has demonstrated the most flexibility and efficacy in the treatment of all these lesions, but more research is needed to find each TA technique's ideal situation. Many US providers and patients are unaware of TA options and thus marketing and educational outreach are critical to building a TA practice. Major US societies must collaborate on standardized guidelines, training, and insurance codes for these promising new therapies.

#### Ethical Research

This research was done by the Declaration of Helsinki. All data were used from publicly available sources and literature.

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**Conflict of Interest**

None declared.

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