**Original Article** | Thyroid

eISSN 2005-8330
https://doi.org/10.3348/kjr.2024.0599
Korean J Radiol 2025;26(2):193-203

Korean Journal of Radiology
KJR

# Radiofrequency Ablation of Benign Thyroid Nodules: 10-Year Follow-Up Results From a Single Center

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**Objective:** The long-term efficacy of radiofrequency ablation (RFA) for the treatment of benign thyroid nodules remains unclear. We aimed to evaluate the long-term efficacy, emphasizing single-session RFA, and identify the factors associated with cases requiring additional RFA sessions to achieve a comparable volume reduction rates (VRR).

**Materials and Methods:** We retrospectively evaluated benign thyroid nodules treated with RFA between 2008 and 2018. Treatment efficacy at the 5- and 10-year follow-ups was analyzed. Additionally, subgroup analysis comparing technique efficacy, such as the final VRR, between the single- and multi-session RFA groups was performed. Continuous variables were analyzed using the two-sample *t*-test or Mann–Whitney U test, and categorical variables were analyzed using the Chi-square or Fisher's exact test.

**Results:** A total of 267 nodules from 237 patients (age: 46.3 ± 15.0 years; female: 210/237 [88.6%]) were included. Of these, 60 were analyzed for the 5-year follow-up (mean follow-up duration ± standard deviation: 5.8 ± 0.4 years) and 29 for the 10-year follow-up (10.9 ± 0.9 years). Single-session RFA showed a median VRR of 95.7% (5th year) and 98.8% (10th year), while multi-session RFA showed comparable median VRRs of 97.4% (5th year) and 96.9% (10th year). The vascularity type, demographic factors, nodular components, and locations did not significantly differ between the single-session and multi-session RFA groups. However, nodules with pre-RFA volume <10 mL were more prevalent in the single-session RFA group than in the multi-session RFA group (5th year: 64.3% [18/28] vs. 34.4% [11/32], $P = 0.040$; 10th year: 75.0% [12/16] vs. 23.1% [3/13], $P = 0.016$).

**Conclusion:** Single-session RFA may be sufficient for achieving adequate volume reduction during long-term follow-up for small-volume benign thyroid nodules. A high VRR was maintained regardless of the nodular component, location, demographic factors, or vascularity type. However, large-volume nodules may require multiple RFA sessions to achieve a comparable VRR.

**Keywords:** Radiofrequency ablation; Thyroid; Nodule

## INTRODUCTION

The prevalence of thyroid nodules, detected using ultrasound, ranges from 19%–35%, of which approximately 4%–15% are malignant [1-3]. Asymptomatic benign thyroid nodules do not require any intervention, instead patients undergo imaging follow-ups based on various guidelines [3-6]. For symptomatic large benign thyroid nodules, surgical excision has been the main treatment modality until the development of minimally invasive thyroid interventions such as radiofrequency ablation (RFA), which has proven its short-term effectiveness as an alternative treatment [1,7-10].

For long-term follow-up, RFA has proven to be a reliable and effective treatment modality for reducing the volume of large benign thyroid nodules, with reported volume reduction rates (VRR) ranging from 70%–90% [11-15]. A meta-analysis demonstrated a continuous VRR up to 92.2% 36 months postoperatively; additionally, a prospective study

**Received:** April 25, 2024 **Revised:** October 28, 2024
**Accepted:** October 30, 2024
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involving 94 patients demonstrated complete alleviation of compressive symptoms 24 months postoperatively, demonstrating RFA's long-term therapeutic efficacy, as well as its clinical efficacy [14,16]. For follow-up durations longer than 4 and 5 years, studies have shown optimal VRR between 81.3% and 93.4% [10,12,17,18]. Additionally, a longitudinal 5-year observational study of 215 patients confirmed the long-term efficacy of a single RFA session [19]. Nevertheless, nodular regrowth occasionally occurs after RFA and eventually requires additional RFA sessions or surgical excision. Kim et al. [11] reported a gradual increase in the viable volume 3 years post-RFA.

To the best of our knowledge, the long-term efficacy of single-session RFA for benign thyroid nodules after 10 years is unknown. Only a few studies have evaluated the long-term efficacy of RFA for treating benign thyroid nodules. This single-center retrospective study aimed to 1) evaluate the long-term efficacy of RFA for benign thyroid nodules, emphasizing single-session RFA, and 2) identify the factors associated with cases requiring additional RFA sessions to achieve a VRR comparable to those treated successfully with a single session.

## MATERIALS AND METHODS

### Patients

This retrospective study was approved by the Institutional Review Board of Seoul St. Mary's Hospital (IRB No. KC24RISI0212) and the requirement for informed consent was waived. RFA performed for histologically proven benign thyroid nodules between 2008 and 2018 at a single tertiary center, was evaluated. The exclusion criteria were as follows: 1) combined percutaneous ethanol ablation, 2) use of electrodes other than conventional fixed electrodes (i.e., adjustable electrodes), 3) subcentimeter nodules, 4) presence of malignant thyroid nodules, and 5) follow-up loss immediately after RFA and poor ultrasound evaluation (Fig. 1). Recently developed devices, such as adjustable electrodes, were excluded due to their inherently different ablation properties, including shorter

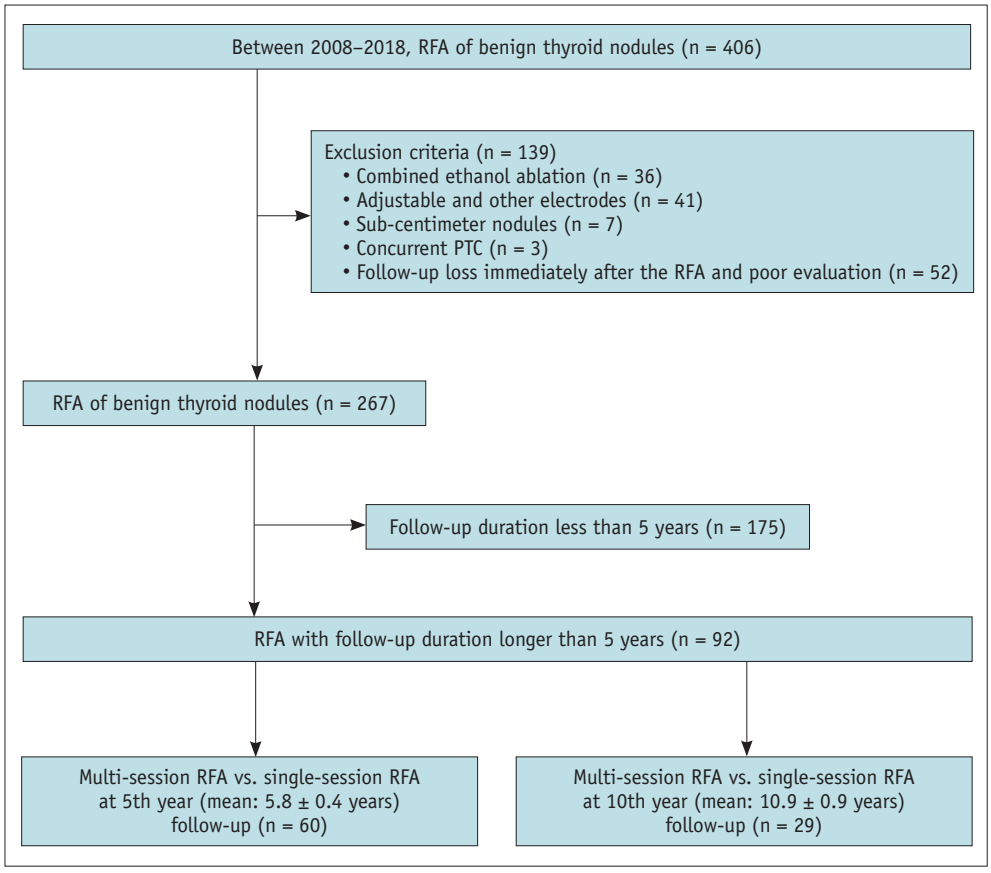


**Fig. 1.** Flow chart for study participants. The subject number indicates number of nodules. RFA = radiofrequency ablation, PTC = papillary thyroid cancer


https://doi.org/10.3348/kjr.2024.0599

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RF time and improved energy delivery efficiency, compared to conventional electrodes [20]. Excluding patients with subcentimeter nodules, all included patients had initial compressive symptoms or cosmetic issues due to thyroid nodules. Patients with a follow-up duration >60 months after the initial RFA session were further identified.

### Ultrasound Evaluation

The target thyroid nodules were evaluated according to the Korean Thyroid Imaging Reporting and Data System, which included anteroposterior (AP), transverse (Trans), and craniocaudal (CC) sizes measured perpendicular to the nodule; volume assessment (AP x Trans x CC x π x 1/6); categorization of nodular cystic components (solid nodule, mixed solid, and cystic nodule); and assessments of the degree of vascularity, measured on color Doppler (Type 1: absence of vascularity, Type 2: peripheral vascularity, Type 3: mild intra-nodular vascularity [<50%] with or without peripheral vascularity, and Type 4: marked intra-nodular vascularity [≥50%] with or without peripheral vascularity) [5]. The following ultrasound machines were used in this study: ATL HDI 5000 (Philips, Best, Netherlands), RS85 (Samsung, Seoul, Korea), Aplio 300, 400 (Toshiba, Tochigi, Japan), Epiq Elite (Philips), and Aplio i700 (Canon, Tochigi, Japan).

### Basic and Advanced RFA Techniques

All RFAs were performed by a single operator (a board-certified thyroid interventionist with >15 years of experience) using RFA applicators (electrodes) and RF generators produced by STARmed (Goyang, Korea) or RF Medical (Seoul, Korea). Both types of equipment used 18-gauge monopolar, internally cooled electrodes with variable active tips ranging from 0.7–2.0 cm. The electrodes and active tip lengths were selected based on the operator's discretion and nodule volume.

Basic RFA techniques, such as the transisthmus approach and the moving-shot technique, and advanced RFA techniques, including hydrodissection and vascular ablation, have been utilized since 2008 [9,21-23] (Fig. 2). Lidocaine (1%–2%) was injected at the puncture site and thyroid capsule. The RF electrodes were visualized in a parallel axis and inserted into the nodule using a transisthmic approach to stabilize the electrode during the procedure. The moving-shot technique, which involves the sequential ablation of small conceptual volumes of the target nodules, was implemented [9,21]. To perform effective RFA, the periphery of the target nodule and feeding vessels were ablated because incomplete ablation of the periphery and feeding vessels cause nodular regrowth [10]. The goal of the initial RFA was to ablate the nodule until a "hyperechoic arc" appeared along its periphery (Fig. 2). Using the hydrodissection technique, which involves the injection of a cold 5% dextrose solution to create a safety barrier between the periphery and anatomical structures, effective ablation of the target nodule periphery was possible (Fig. 2) [21-23]. The feeding vessels and draining veins were identified using power Doppler and were ablated until blood flow was obliterated, as confirmed by the visualization of venous staining (Fig. 2) [21]. Additional RFA sessions beyond single-session RFA were determined if the following were observed on follow-up ultrasound: 1) remaining viable nodular components, 2) remaining feeding vessels on Doppler, and

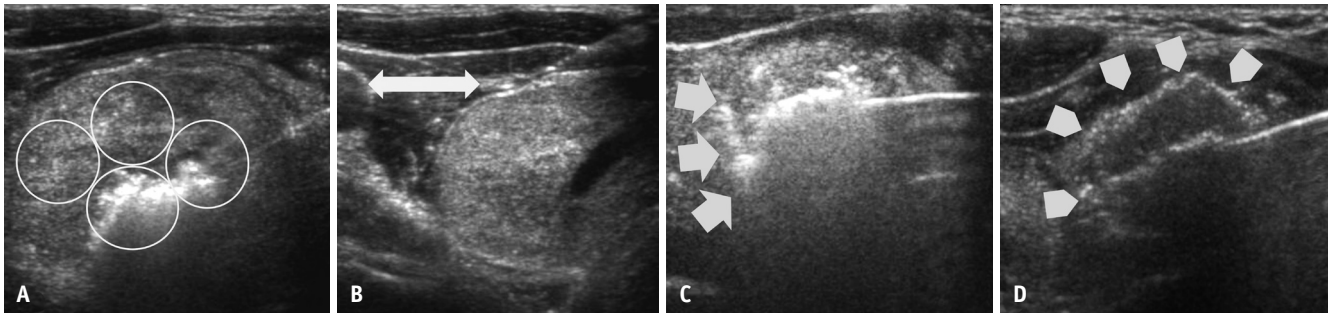


**Fig. 2.** Basic and advanced RFA techniques. **A:** RFA procedures were performed using basic RFA techniques: trans-isthmic approach and the moving-shot technique (sequential ablation of small conceptual volumes [circles] of target nodules). **B:** Effective ablation of the target nodule's periphery was made possible using the hydrodissection technique, which involved injecting a cold 5% dextrose solution to create a safety barrier (bidirectional arrow) between the nodule and anatomical structures. In this case, the anterolateral approach hydrodissection technique was performed to protect the common carotid artery, vagus nerve, and middle cervical sympathetic ganglion. **C:** Draining veins at the nodule periphery were ablated to prevent marginal regrowth (called venous staining [arrows]). **D:** Meticulous ablation of the nodule periphery to create a "hyperechoic arc" (arrowheads) was also important for preventing nodular regrowth. RFA = radiofrequency ablation


https://doi.org/10.3348/kjr.2024.0599

3) newly developed viable components and feeding vessels.

### RFA Outcomes

The RFA treatment parameters included RFA running time (duration of electrode activation), RFA energy, energy efficiency (ablated volume per energy), and RFA outcomes, including technique efficacy, complication rates, and regrowth rates. Technique efficacy, such as the final VRR, refers to the ability to achieve the expected results within a certain follow-up timeframe [24]. The VRR was calculated by dividing the difference between the pre- and post-RFA volumes by the pre-RFA volume [9]. Complications were defined as adverse events that required unexpected medical attention. Minor complications were defined as reversible adverse events requiring conservative care. Major complications were defined as irreversible neurological injuries or adverse events requiring surgery or intervention [25,26]. Optimal VRR was defined as a VRR >80% based on the previous 21 studies [9]. Regrowth was defined as an increase in volume >50% of the smallest post-RFA volume [11].

### Statistical Analysis

Treatment efficacy at the 5- and 10-year follow-ups post-RFA treatment was descriptively summarized. Comparison of RFA outcomes in continuous variables, such as regrowth rate and technique efficacy (VRR), was performed using a two-sample *t*-test or the Mann–Whitney U test. Categorical variables, such as nodular components, were compared using the Chi-square test or Fisher's exact test. The data analysis and results were based on each nodule. Statistical calculations and evaluations were performed using the R package (version 3.6.3, The R Foundation for Statistical Computing, Vienna, Austria), and two-sided *P*-values <0.05 were considered statistically significant.

## RESULTS

### Study Participants

Of the 406 cytohistologically proven benign nodules that were treated using RFA between 2008 and 2018, 139 were excluded due to the use of the combined ethanol ablation procedure (n = 36), utilization of recently developed electrodes such as adjustable electrodes (n = 41), sub-centimeter nodules (n = 7), concurrent papillary thyroid cancer (n = 3), or follow-up loss immediately after RFA and poor ultrasound evaluation (n = 52). The remaining 267 nodules from 237 patients (age: 46.3 ± 15.0 years; females: 210/237 [88.6%]) were included for the study (Tables 1, 2). Ninety-two nodules were monitored for more than 5 years following RFA; 60 of these nodules were evaluated at the 5-year follow-up (mean duration ± standard deviation: 5.8 ± 0.4 years) and 29 were assessed at the 10-year (10.9 ± 0.9 years) follow-up (Tables 3, 4). A total of 180/267 (67.4%) nodules underwent single-session RFA, whereas 87/267 nodules (32.6%) underwent multi-session RFA, 75 of which underwent two RFA sessions and 12 underwent more than three RFA sessions (Table 1).

### Long-Term Efficacy

For the sequential evaluation of the VRR, most patients complied with the follow-up within the first year of the initial RFA (265/267 nodules, 99.3%) with a median VRR of 67.7% (interquartile range [IQR]: 52.7–82.1). After 1 year, compliance dropped to nearly half (59.6%, 159/267), with a median VRR of 82.5% (IQR: 69.0–94.5). The median VRR reached more than 90% when the follow-up duration exceeded two years after the initial RFA. Furthermore, the median VRR increased to 96.5% over time and compliance remained low (Table 2). A total of 11 patients whose nodules treated (11/267, 4.1%) experienced procedural-related complications; in 9/267 nodules (3.4%), minor complications were managed with conservative care and observation, whereas in 2/267 cases (0.7%), major complications of nodular rupture required further treatment such as antibiotics, incision, and drainage. No serious disabilities or morbidities were observed in any of the patients. Twenty-six nodules out of 267 (9.7%) regrew, while 4/267 (1.5%) required surgical excision.

During the 5-year follow-up (5.8 ± 0.4 years), the overall median pre-RFA volume was 10.6 mL (IQR: 5.9–19.4 mL) and the overall median 5th year post-RFA volume was 0.3 mL (IQR: 0–1.4) with an overall VRR of 96.1% and regrowth rate of 15.0% (9/60). Approximately half of the nodules were located in the right thyroid gland (58.3%, 35/60), 36.7% (22/60) were solid, and 56.7% (34/60) had vascularity type 3 (Table 3). Majority of the nodules were ablated with 1 cm active tip electrode (78.3%, 47/60) with an average running time of 1087.7 seconds, median RFA energy of 55.8 kJ (IQR: 35.2–96.5) and median RFA energy efficiency of 0.2 mL/kJ (IQR: 0.1–0.3). During the 10-year follow-up (10.9 ± 0.9 years), the overall mean pre-RFA volume was 12.4 ± 10.5 mL and the overall median final RFA volume was 0.1 mL (IQR: 0–0.9) with an overall VRR of 97.5% and regrowth rate of 10.3% (3/29). Approximately one third of


https://doi.org/10.3348/kjr.2024.0599

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**Table 1.** Patient, nodule, and RFA procedure characteristics

| Characteristics | Data |
|---|---|
| Patients (n = 237) | |
| Age, yrs | 46.3 ± 15.0 |
| Female pateints | 210 (88.6) |
| Follow-up duration, yrs | 3.0 (1.0, 7.0) |
| Nodules (n = 267) | |
| Pre-RFA nodule size | |
| Anteroposterior, cm | 1.8 (1.4, 2.3) |
| Transverse, cm | 2.7 (2.1, 3.2) |
| Craniocaudal, cm | 3.6 (2.9, 4.4) |
| Initial volume, mL | 8.9 (4.9, 17.2) |
| Post-RFA nodule size | |
| Anteroposterior, cm | 0.9 (0.2, 1.4) |
| Transverse, cm | 1.0 (0.2, 1.7) |
| Craniocaudal, cm | 1.5 (0.2, 2.3) |
| Final volume, mL | 0.8 (0, 2.7) |
| Overall VRR, % | 91.7 (72.4, 100) |
| Nodule location | |
| Right thyroid gland | 147/267 (55.1) |
| Left thyroid gland | 111/267 (41.6) |
| Isthmus portion | |
| Nodular composition | |
| No. of solid nodules, no obious cystic portion | 87/267 (32.6) |
| No. of mixed solid and cystic nodules | 180/267 (67.4) |
| No. of vacularity type | |
| Type 1, minimal or none | 19/267 (7.2) |
| Type 2, peripheral only | 66/267 (25) |
| Type 3, mild intra-nodular | 150/267 (56.8) |
| Typer 4, marked intra-nodular | 29/267 (11) |
| RFA (for 267 nodules) | |
| Length of electrodes | |
| No. of <1 cm active tip | 35/267 (13.1) |
| No. of 1 cm active tip | 206/267 (77.2) |
| No. of >1 cm active tip | 23/267 (8.6) |
| No. of combined 1 cm + >1 cm active tip | 3/267 (1.1) |
| Power, W† | 60.7 ± 15.9 |
| Total RFA running time, s† | 934.0 ± 475.9 |
| Total RFA energy, kJ† | 58.1 ± 35.9 |
| Total RFA energy efficiency, mL/kJ† | 0.3 ± 0.2 |
| RFA sessions per nodule | 1 (1, 2) |
| No. of signle-session RFA | 180/267 (67.4) |
| No. of multi-settion RFA | 87/267 (32.6) |
| Interval between RFA sessions, days | 359 (161, 677) |
| Procedure-related complications | 11/267 (4.1) |
| No. of major complication | 2/267 (0.7) |
| No. of minor complication | 9/267 (3.4) |
| No. of regrowth* | 26/267 (9.7) |
| No. of surgical resection | 4/267 (1.5) |

Data are mean ± standard deviation, number of patients or nodules (%), or median (interquartile range).
*Regrowth was defined as an increase in volume of more than 50% of smallest post-RFA volume, †RFA power, energy, and RFA energy efficiency data accounted for 227 RFA sessions, and RFA running time accounted for 265 RFA sessions.
RFA = radiofrequency ablation, VRR = volume reduction rates

the nodules were solid (34.5%, 10/29), 62.1% (18/29) were located in the right thyroid gland, and 72.4% (21/29) had vascularity type 3 (Table 4). Majority of the nodules were ablated with 1 cm active tip electrode (86.2%, 25/29) with an average running time of 1056.9 seconds, median RFA energy of 55.8 kJ (IQR: 34.6–108) and median RFA energy efficiency of 0.1 mL/kJ (IQR: 0.1–0.2).

### Single-Session RFA vs. Multi-Session RFA

During the 5-year follow-up (5.8 ± 0.4 years), single-session RFA (n = 28) and multi-session RFA (n = 32) did not demonstrate significant differences in patient age, sex, types of vascularity, nodular composition, nodular locations, and utilization of different active tip lengths (Table 1). However, the single-session RFA group demonstrated smaller pre-RFA nodular size and pre-RFA volumes than those of the multi-session RFA group: initial volume (7.7 mL vs. 14.3 mL, $P$ = 0.025), initial AP size (1.8 cm vs. 2.2 cm, $P$ = 0.021), initial Trans size (2.6 cm vs. 3.2 cm, $P$ = 0.019).

Both single-session and multi-session RFA groups underwent initial RFA with comparable RFA energy (51.4 kJ [IQR: 32.2–81.2] vs. 64.5 kJ [IQR: 37.3–113.6], $P$ = 0.382) and RFA running time (1017.6 ± 527.9 seconds vs. 1149.1 ± 565.4 seconds, $P$ = 0.356). The overall energy efficiencies during the initial RFA were also similar between two groups (0.2 mL/kJ vs. 0.3 mL/kJ, $P$ = 0.127). The 5-year post-RFA nodule volume, VRR, and percentage of optimal VRR were comparable between the groups (volume: 0.3 mL vs. 0.4 mL, $P$ = 0.756; VRR: 95.7% vs. 97.4%, $P$ = 0.633; percentage of optimal VRR: 82.1% [23/28] vs. 84.4% [27/32], $P$ > 0.99). The complication (7.1% [2/28] vs. 12.5% [4/32], $P$ = 0.675) and regrowth rates (10.7% [3/28] vs. 18.7% [6/32], $P$ = 0.482) were also comparable (Table 3).

A subgroup analysis comparing single-session RFA group (n = 16) and multi-session RFA group (n = 13) was performed during the 10-year follow-up (10.9 ± 0.9 years). Demographic factors, nodular location, nodular composition, and vascularity type were comparable between the two groups (Table 2). Although the multi-session RFA group demonstrated a longer RFA running time (1324.1 seconds vs. 839.9 seconds, $P$ = 0.042) and higher RFA energy (97.5 kJ vs. 41.8 kJ, $P$ = 0.025) due to a larger initial volume (19.2 mL vs. 6.9 mL, $P$ = 0.002), RFA energy efficiencies were comparable between the groups (0.1 mL/kJ vs. 0.2 mL/kJ, $P$ = 0.250). The final volume (0.1 mL vs. 0.1 mL, $P$ = 0.206) and final VRR (98.8% vs. 96.9%, $P$ = 0.505) were comparable, as well as the percentage of optimal VRR (87.5% [14/16] vs. 92.3% [12/13], $P$ > 0.99)


https://doi.org/10.3348/kjr.2024.0599

**Table 2.** VRR of RFA of benign thyroid nodules during follow-up

| Follow-up length | Overall follow-up nodules* (n = 267) | Overall VRR, % | Multi-session RFA nodules* (n = 87) | Multi-session RFA VRR, % | Single-session RFA nodules* (n = 180) | Single-session RFA VRR, % |
|---|---|---|---|---|---|---|
| <1 yr | 265 | 67.7 (52.7, 82.1) | 86 | 64.5 (52.6, 79.4) | 179 | 68.8 (52.8, 82.9) |
| 1 yr | 159 | 82.5 (69.0, 94.5) | 66 | 80.7 (67.2, 93.2) | 93 | 83.1 (72.7, 94.5) |
| 2 yrs | 123 | 90.7 (82.0, 97.8) | 57 | 89.1 (82.1, 96.6) | 66 | 91.1 (82.0, 98.5) |
| 3 yrs | 91 | 94.3 (85.7, 99.2) | 45 | 90.7 (85.6, 96.9) | 46 | 96.4 (87.4, 100) |
| 4 yrs | 75 | 95.4 (87.9, 100) | 37 | 95.6 (90.0, 99.4) | 38 | 95.1 (87.0, 100) |
| 5 yrs | 46 | 96.2 (91.2, 100) | 24 | 97.5 (90.6, 100) | 22 | 95.8 (91.6, 100) |
| 6 yrs | 47 | 97.5 (91.3, 100) | 23 | 98.2 (90.5, 100) | 24 | 96.4 (91.6, 100) |
| 7 yrs | 35 | 97.8 (92.9, 100) | 14 | 94.3 (89.2, 97.4) | 21 | 100 (95.3, 100) |
| 8 yrs | 28 | 96.5 (93.5, 99.8) | 15 | 96.4 (94.5, 97.3) | 13 | 100 (89.4, 100) |
| 9 yrs | 23 | 99.8 (93.9, 100) | 12 | 97.7 (91.0, 99.8) | 11 | 100 (98.5, 100) |
| ≥10 yrs | 32 | 100 (94.7, 100) | 14 | 100 (94.6, 100) | 18 | 98.8 (95.1, 100) |

Data are median (interquartile range).
*Number of nodules.
VRR = volume reduction rates, RFA = radiofrequency ablation

**Table 3.** Comparison between multi-session RFA and single-session RFA at 5th year follow-up (5.8 ± 0.4 years)

| Characteristics | Total (n = 60)* | Multi-session RFA (n = 32)* | Single-session RFA (n = 28)* | *P* |
|---|---|---|---|---|
| Age, yrs | 44.0 ± 14.3 | 42.2 ± 13.5 | 46.2 ± 15.0 | 0.283 |
| Female patients | 56/60 (93.3) | 29/32 (90.6) | 27/28 (96.4) | 0.616 |
| Pre-RFA size | | | | |
| Anteroposterior, cm | 2.0 ± 0.8 | 2.2 ± 0.9 | 1.8 ± 0.4 | 0.021 |
| Transverse, cm | 2.9 ± 1.0 | 3.2 ± 1.2 | 2.6 ± 0.8 | 0.019 |
| Craniocaudal, cm | 4.1 ± 1.4 | 4.4 ± 1.3 | 3.7 ± 1.4 | 0.057 |
| Volume, mL | 10.6 (5.9, 19.4) | 14.3 (8.6, 29.9) | 7.7 (5.7, 14.0) | 0.025 |
| No. of volume <10 mL | 29/60 (48.3) | 11/32 (34.4) | 18/28 (64.3) | 0.040 |
| No. of right side nodule | 35/60 (58.3) | 17/32 (53.1) | 18/28 (64.3) | 0.475 |
| No. of solid nodule | 22/60 (36.7) | 9/32 (28.1) | 13/28 (46.4) | 0.230 |
| No. of vascularity type 3 | 34/60 (56.7) | 19/32 (59.4) | 15/28 (53.6) | 0.876 |
| Technique efficacy | | | | |
| No. of RF electrode active tip 1 cm | 47/60 (78.3) | 24/32 (75) | 23/28 (82.1) | 0.940 |
| RFA running time, seconds | 1087.7 ± 547.6 | 1149.1 ± 565.4 | 1017.6 ± 527.9 | 0.356 |
| RFA energy, kJ† | 55.8 (35.2, 96.5) | 64.5 (37.3, 113.6) | 51.4 (32.2, 81.2) | 0.382 |
| RFA energy efficiency, mL/kJ† | 0.2 (0.1, 0.3) | 0.3 (0.1, 0.4) | 0.2 (0.1, 0.3) | 0.127 |
| 5th year post-RFA nodule size | | | | |
| Anteroposterior, cm | 0.6 (0, 1.1) | 0.6 (0, 1.2) | 0.6 (0, 1.0) | 0.773 |
| Transverse, cm | 1.0 (0, 1.3) | 1.0 (0, 1.4) | 0.9 (0, 1.2) | 0.649 |
| Craniocaudal, cm | 1.2 (0, 1.9) | 1.1 (0, 2.2) | 1.3 (0, 1.7) | 0.699 |
| Volume, mL | 0.3 (0, 1.4) | 0.4 (0, 1.7) | 0.3 (0, 1.1) | 0.756 |
| 5th year VRR, % | 96.1 (90.6, 100) | 97.4 (92.0, 100) | 95.7 (90.4, 100) | 0.633 |
| Final VRR, % | 99.5 (95.3, 100) | 99.8 (95.9, 100) | 97.7 (93.3, 100) | 0.399 |
| No. of 5th year optimal VRR | 50/60 (83.3) | 27/32 (84.4) | 23/28 (82.1) | >0.99 |
| No. of regrowth‡ | 9/60 (15) | 6/32 (18.7) | 3/28 (10.7) | 0.482 |
| No. of complication | 6/60 (10) | 4/32 (12.5) | 2/28 (7.1) | 0.675 |

Data are mean ± standard deviation, number of patients or nodules (%), or median (interquartile range).
*A total of 46 nodules (24 multi-session RFA + 22 single-session RFA) from 5th year and 14 nodules (8 multi-session RFA + 6 single-session RFA) from 6th year follow-up were analyzed in the range of 5.8 ± 0.4 years, †RFA power, energy, and RFA energy efficiency data accounted for 227 RFA sessions, and RFA running time accounted for 265 RFA sessions, ‡Regrowth was defined as an increase in volume more than 50% of smallest post-RFA volume.
RFA = radiofrequency ablation, RF = radiofrequency, VRR = volume reduction rates


https://doi.org/10.3348/kjr.2024.0599

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(Table 4). When applying 10 mL as the cutoff value, nodules with an initial volume <10 mL were more prevalent in the single-session RFA group than that in the multi-session RFA group at the 10-year follow-up (75.0% [12/16] vs. 23.1 % [3/13], $P = 0.016$), and 5-year follow-up (64.3% [18/28] vs. 34.4% [11/32], $P = 0.040$) (Fig. 3). During the 10-year follow-up, both groups demonstrated comparable complication (0% [0/16] vs. 15.4% [2/13], $P = 0.192$) and regrowth rates (12.5% [2/16] vs. 7.7% [1/13], $P > 0.99$). Three nodules demonstrated regrowth for single-session RFA at the 5-year follow-up and two demonstrated regrowth at the 10-year follow-up, of these, a single nodule underwent surgical resection (nodular hyperplasia with Hürthle cell metaplasia). Other nodules with regrowth were followed up ultrasonographically, particularly in patients with good compliance.

## Unexpected Outcomes

Four of the 267 nodules were surgically excised. Surgical pathology revealed two cases of follicular adenomas, one case of nodular hyperplasia with Hürthle cell metaplasia, and one case of metastasis from renal cell carcinoma. All four nodules demonstrated benign pre-RFA cytohistological results (benign follicular nodules, benign lesions with a few bland follicular cells, nodular hyperplasia, and benign nodules). The average pre-RFA volume for these surgical cases was 15.0 mL, and the average final VRR was 65.8%, which was much lower than the overall VRR of 91.6% (n = 267). For renal cell carcinoma metastasis, pre-RFA fine-needle aspiration biopsy revealed a benign lesion with a few bland follicular cells. After RFA, the lesion demonstrated nodular regrowth and newly developed vascularity during follow-up. Subsequently, the nodule underwent core needle biopsy, which revealed renal cell carcinoma.

Post-RFA calcification is uncommon in patients with benign thyroid nodules. In our study, 4/267 nodules (1.5%) developed post-RFA calcification. Of these, three post-RFA nodules transformed into dense rim-calcified nodules,

**Table 4.** Comparison between multi-session RFA and single-session RFA at 10th year follow-up (10.9 ± 0.9 years)

| Characteristics | Total (n = 29) | Multi-session RFA (n = 13) | Single-session RFA (n = 16) | *P* |
|---|---|---|---|---|
| Age, yrs | 45.6 ± 12.5 | 43.5 ± 13.0 | 47.3 ± 12.2 | 0.438 |
| Female patients | 24/29 (82.8) | 11/13 (84.6) | 13/16 (81.3) | >0.99 |
| Pre-RFA size | | | | |
| Anteroposterior, cm | 1.9 (1.5, 2.4) | 2.3 (1.9, 2.6) | 1.5 (1.2, 1.9) | 0.004 |
| Transverse, cm | 2.7 ± 1.0 | 3.2 ± 0.9 | 2.3 ± 0.9 | 0.009 |
| Craniocaudal, cm | 3.6 ± 1.4 | 4.4 ± 1.3 | 2.9 ± 1.0 | 0.002 |
| Volume, mL | 12.4 ± 10.5 | 19.2 ± 11.2 | 6.9 ± 5.6 | 0.002 |
| No. of volume <10 mL | 15/29 (51.7) | 3/13 (23.1) | 12/16 (75) | 0.016 |
| No. of right side nodule | 18/29 (62.1) | 7/13 (53.9) | 11/16 (68.8) | 0.552 |
| No. of solid nodule | 10/29 (34.5) | 2/13 (15.4) | 8/16 (50) | 0.114 |
| No. of vascularity type 3 | 21/29 (72.4) | 10/13 (76.9) | 11/16 (68.7) | 0.827 |
| Technique efficacy | | | | |
| No. of RF electrode active tip 1 cm | 25/29 (86.2) | 10/13 (76.9) | 15/16 (93.8) | 0.078 |
| RFA running time, seconds | 1056.9 ± 641.9 | 1324.1 ± 606.3 | 839.9 ± 602.4 | 0.042 |
| RFA energy, kJ | 55.8 (34.6, 108) | 97.5 (67.4, 112.4) | 41.8 (29.0, 59.7) | 0.025 |
| RFA energy efficiency, mL/kJ | 0.1 (0.1, 0.2) | 0.2 (0.1, 0.2) | 0.1 (0.1, 0.2) | 0.250 |
| Post-RFA nodule size | | | | |
| Anteroposterior, cm | 0.5 (0, 1) | 0.6 (0, 1) | 0.3 (0, 0.7) | 0.269 |
| Transverse, cm | 0.6 (0, 1) | 0.6 (0, 1) | 0.3 (0, 0.8) | 0.462 |
| Craniocaudal, cm | 0.6 (0, 1.3) | 0.6 (0, 2.2) | 0.3 (0, 1.1) | 0.260 |
| Volume, mL | 0.1 (0, 0.9) | 0.1 (0, 1.3) | 0.1 (0, 0.5) | 0.206 |
| VRR, % | 97.5 (94.3, 100) | 96.9 (94.0, 100) | 98.8 (95.8, 100) | 0.505 |
| No. of 10th year optimal VRR | 26/29 (89.7) | 12/13 (92.3) | 14/16 (87.5) | >0.99 |
| No. of regrowth* | 3/29 (10.3) | 1/13 (7.7) | 2/16 (12.5) | >0.99 |
| No. of complication | 2/29 (6.9) | 2/13 (15.4) | 0 (0) | 0.192 |

Data are mean ± standard deviation, number of patients or nodules (%), or median (interquartile range).
*Regrowth was defined as an increase in volume more than 50% of smallest post-RFA volume.
RFA = radiofrequency ablation, RF = radiofrequency, VRR = volume reduction rates

 https://doi.org/10.3348/kjr.2024.0599 

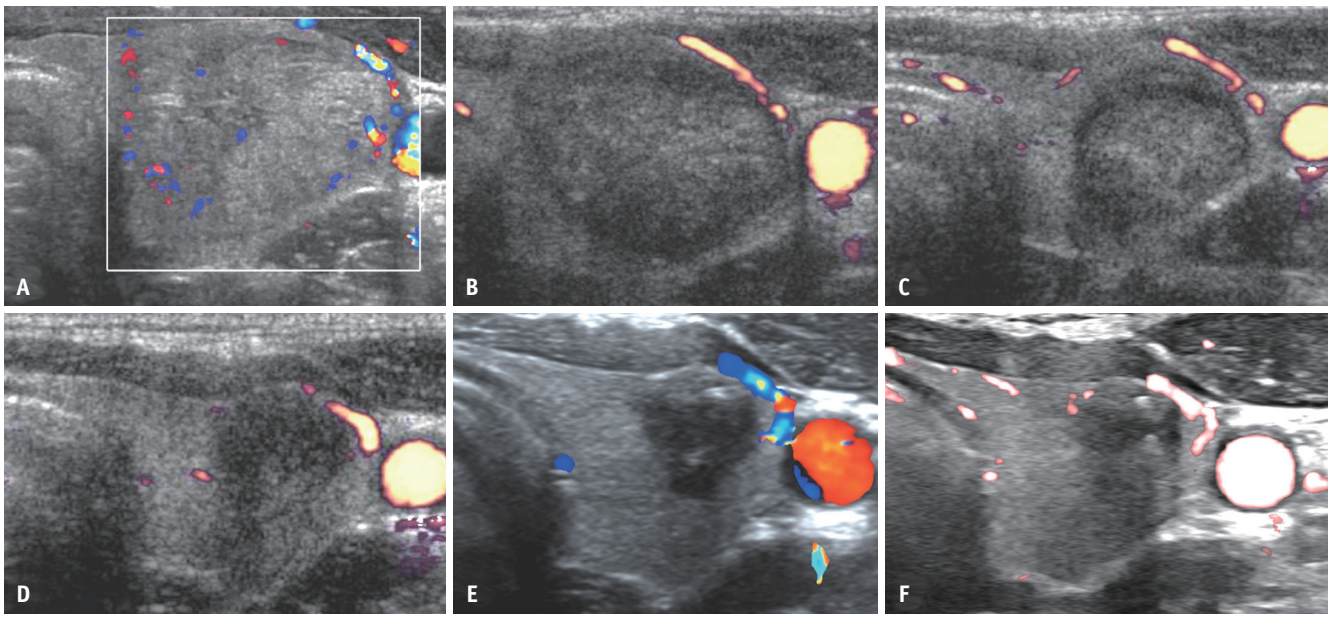


**Fig. 3.** Single-session RFA of a benign thyroid nodule: 133 months follow-up. A 42-year-old female patient underwent a single-session RFA for a symptomatic benign thyroid nodule located in the left thyroid gland. Single-session RFA was effective in reducing the volume over a 10-year period. Sequential changes in the volume of the target nodule were as follows: **(A)** pre-RFA volume: 8.0 mL, **(B)** 1-month follow-up: 5.4 mL, **(C)** 12-month follow-up: 2.2 mL, **(D)** 25-month follow-up: 0.8 mL, **(E)** 92-month follow-up: 0.6 mL, **(F)** 106-month follow-up: 0.4 mL. The final volume on the 133-month follow-up was 0.2 mL with a final volume reduction rate of 97.2%. RFA = radiofrequency ablation

and one post-RFA nodule transformed into incomplete rim calcification.

## DISCUSSION

For patients with benign thyroid nodules, the dilemma of undergoing thermal ablation treatment such as RFA is understandable and is often influenced by concerns regarding nodular regrowth and uncertain long-term efficacy of the RFA technique. Our study showed that RFA could be effective over a long term, with a VRR of 98.8% over a mean follow-up duration of 10.9 years. For small-volume nodules (<10 mL), single-session RFA was sufficient to maintain a high VRR regardless of the nodular location, components, and vascularity type. Adherence to basic and advanced RFA techniques, along with preemptive additional RFA, is essential for achieving and maintaining high VRR and preventing nodular regrowth.

Our findings were consistent with those of a previous study by Kim et al. [11], in which 90 benign thyroid nodules in 88 patients were treated RFA, and efficacy comparisons were made between the single-session RFA and multi-session RFA groups. The previous study requirement for additional RFA sessions was similar to our findings, with indications including unresolved patients' symptoms, regrowth in follow-up volume, less effective ablation (<70% initial ablated ratio), and newly developed vascularity on Doppler. The initial pre-RFA volume in the study by Kim et al. [11] was 8.7 mL, and the mean final volume for single-session RFA without the need for additional RFA sessions was 0.9 mL (final VRR of 92.8%) for follow-up durations longer than 5 years. In comparison, our study showed final VRRs of single-session RFA to be 95.7% and 98.8% at the 5- and 10-year follow-ups, respectively. Our results also corroborate those of a longitudinal 5-year observational study that validated the efficacy of single-session RFA for benign thyroid nodules [19]. Among 215 benign thyroid nodules in 215 patients, a thyroid nodule volume <10 mL demonstrated a VRR of 79% at 6 months and 81% at 5 years. Additionally, an interesting meta-analysis demonstrated that RFA achieved a higher VRR than that of microwave ablation at the 6- and 12-month follow-ups, suggesting that the success of RFA may be influenced by the smaller size of thyroid nodules [1]. These studies support our finding that smaller-volume nodules require only single-session RFA for safe and effective volume reduction. Furthermore, our study is the first to demonstrate that single-session RFA is effective in achieving and maintaining a high VRR over a 10-year


https://doi.org/10.3348/kjr.2024.0599

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period, particularly for small-volume thyroid nodules, and that the key to long-term efficacy depends on the proper application of basic and advanced RFA techniques. For large-volume nodules, our study demonstrated that multi-session RFA is necessary to achieve a comparable VRR.

Unexpected outcomes of RFA for presumed benign thyroid nodules include metastasis from renal cell carcinoma and calcification. Although calcification on thyroid ultrasound generally suggests malignancy, post-RFA calcifications are not associated with malignancy, as confirmed by Ha et al. [17]. In that study, two post-RFA nodules (12.5%) demonstrated calcification without evidence of malignancy. Similarly, none of the 4/267 nodules (1.5%) with post-RFA calcification in our study transformed into malignancy. Based on a previous study and our findings, we speculate that post-RFA calcifications are a result of inflammatory changes from thermal ablation rather than from malignancy.

However, nodules with regrowth, newly developed vascularity, and a suboptimal final VRR may be indicative of malignancy and require further evaluation, such as core needle biopsy and surgical resection. A recent study by Kim et al. [27] demonstrated that post-RFA of benign thyroid nodules with regrowth or suboptimal reduction may be malignant and recommended core needle biopsy for nodules with VRR less than 50% at 12 months. In our study, one nodule was later confirmed as renal cell carcinoma metastasis with a relatively large pre-RFA volume (12.9 mL) and ineffective RFA, evidenced by a suboptimal final VRR (63.6%), regrowth, and newly developed vascularity during follow-up. Additionally, clinicoradiological correlation is essential for distinguishing follicular-patterned lesions of the thyroid (e.g., older age and larger volume) and for subcategorizing intermediate-suspicion groups based on ultrasound findings (such as solid components, degree of hypoechogenicity, and irregular margins). This approach is important for pre-RFA evaluation and post-RFA follow-up in assessing malignancy potential. Patient compliance and careful monitoring of post-RFA factors such as the final VRR and newly developed vascularity are as important as the clinicoradiological correlation and careful pre-RFA assessment of intermediate-suspicion groups [28]. Furthermore, core needle biopsy should be considered for pre- and post-RFA evaluations because of the relatively high false negative and inconclusive rates of fine-needle aspiration biopsy, especially for larger nodules [27,29,30]. If malignancy is confirmed or suspected, thyroid-dedicated CT should be performed, as recommended by the Korean Society of Thyroid Radiology, for preoperative evaluation and sensitive detection of nodal metastasis [5,31].

From a clinical perspective, we recommend the following guidelines for the RFA of benign thyroid nodules. First, operators should adhere to basic and advanced RFA techniques to ensure safe and effective ablation, achieving a high VRR with long-term maintenance. Second, assuming that well-ablated nodules have a low risk of recurrence, nodules with a pre-RFA volume <10 mL may not require follow-up beyond 10 years because well-treated nodules eventually regress. Instead, a sequential follow-up of at least two years is recommended based on our findings that the overall final VRR exceeds by 90% after two years. Third, if the pre-RFA volume is large, multiple RFA sessions may be necessary to achieve a high VRR and patients must comply with follow-up protocols to allow for additional preemptive RFA before regrowth occurs. For instance, during follow-up, additional pre-emptive RFA must be considered for nodules with remaining viable nodular components, feeding vessels on Doppler, or newly developed viable components and feeding vessels. Fourth, post-RFA calcification may form in the ablated region and signify inflammatory changes rather than malignant transformations. Lastly, pre-RFA and post-RFA core needle biopsy should be considered for the following situations to reduce delayed surgery: relatively large pre-RFA size (≥3 cm), suboptimal VRR (<50% at 12 months follow-up), occurrence of regrowth, and development of vascularity [27,30].

The limitations of our study include a selection bias and loss of follow-up. In the early years before RFA guidelines were established, clinicians and patients alike had little knowledge of when and how often to perform post-RFA follow-ups, causing a large number of follow-up losses and undercoverage bias. It remains uncertain whether nodules lost to follow-up showed regrowth during the later follow-up years. We speculate that nodules lost to follow-up were mainly due to symptomatic alleviation and cosmetic improvement and partly due to the lack of follow-up guidelines during the early years. Although most compressive symptoms were alleviated after RFA in our study, quantification of symptoms and cosmetic scores may be necessary for an exact comparison. Finally, most of the nodules in our study were small and medium-sized. Multisession RFA of large-volume nodules (>30 mL) may have different technical efficacies. Furthermore, given the small sample size owing to the long follow-up period in a single institution, a multicenter study with a larger sample

 https://doi.org/10.3348/kjr.2024.0599 

size is necessary to validate our findings.

In conclusion, single-session RFA may be sufficient for adequate long-term volume reduction in small-volume benign thyroid nodules, regardless of the nodular cystic composition, location, and vascularity on Doppler. However, for large-volume nodules, multiple sessions may be required to achieve comparable VRR.

## Availability of Data and Material

The datasets generated or analyzed during the study are available from the corresponding author on reasonable request.

## Conflicts of Interest

Jae Ho Shin, who holds respective positions on the Editorial Board Member of the *Korean Journal of Radiology*, was not involved in the editorial evaluation or decision to publish this article. The remaining authors have declared no conflicts of interest.

## Author Contributions

Conceptualization: Jae Ho Shin, So Lyung Jung. Data curation: all authors. Formal analysis: all authors. Investigation: all authors. Methodology: all authors. Project administration: So Lyung Jung. Resources: all authors. Supervision: Jae Ho Shin, So Lyung Jung. Validation: all authors. Visualization: all authors. Writing—original draft: all authors. Writing—review & editing: all authors.

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## Funding Statement

None

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 https://doi.org/10.3348/kjr.2024.0599 