Benign thyroid nodules are increasingly detected. Most require only periodic review, but occasionally they may cause esthetic problems or compression. Surgery, the usual proposed remedy, entails a risk of hypoparathyroidism and recurring nerve palsy. Percutaneous treatments are guideline-supported alternatives (1). They include thermal ablation (laser or radiofrequency) if the nodule is solid or predominantly solid, and alcoholization if the nodule is cystic or predominantly cystic.

A recent prospective study involving 6 Italian centers (2) assessed safety and efficacy of thermal ablation with radiofrequency (RFA). The study also evaluated the relation between ultrasound (US) characteristics of the nodule (volume and others) and its response to treatment.

Efficacy, assessed at 6 and 12 months following treatment, took into account:

- Volume (calculated as 0.524 times the 3 diameters, longitudinal, transversal and antero-posterior);
- Compression (on a symptom scale from 0 to 10);
- Esthetic (on a scale from 1 to 4: 1 not palpable, 2 palpable but not visible, 3 visible on swallowing, 4 constantly visible).

The study enrolled 337 patients over 18 years of age (mean age 55 years, range 40-73 years, 76% females), from January 2014 to December 2016. All patients had at least one symptomatic, not «hot» nodule, proven benign in two successive needle aspirations. No patient received previous external radiotherapy or ablation with 131I, or was accepted for surgery. All participants had normal thyroid function. Anti-peroxidase antibodies (TPO Ab) were present in 24%.

The volume of the nodules averaged 20.7 mL (range 13.7-33.1), the median of the compressive symptoms was 6.2 (range 0-10), the median of the esthetic score was 3.15 (range 1-4). US characteristics of the nodules included:

- Structure: e1 (cystic; cysts >2 mm), e2 (microcystic/spongiform; cysts <2 mm), e3 (solid; no cysts).
- Macrocalfications (if any): m1 (intranodular), m2 (perinodular), m3 (intra- and perinodular).
- Vascularization: v1 (intense, perinodular), v2 (intra- and perinodular), v3 (rare, perinodular).

The procedure was performed under US guidance, using a cold electrode (18 G diameter, length 7 cm, active portion 7 mm). The technique was “moving shot” through a trans-isthmic approach preceded by local anesthesia with lignocaine 2% or mepivacaine 1%. Treatment aimed at altering the US structure of the nodule into hypoechogenic. After the procedure, ice was applied locally and the patient monitored for two hours. The energy applied averaged 55 W (range 50-62), for a mean of 10 minutes (range 7-15). Each nodule received on average 2180 J per mL of volume (range 1350-2847).

At 12 months, there was a significant reduction (p <0.0001) both on compression (from 6.2 to 0.61) and aesthetic scores (from 3.15 to 1.66). The reduction in volume of the nodule averaged 63.5% at 6 months and 70% at 12 months (from 20.7 mL to 7.3 mL and 6 mL, respectively, with a range of 65%-85%, p <0.001). After stratification in 3 groups, an inverse correlation was observed between treatment efficacy and initial volume of the nodule:

- Group A, 103 nodules (volume 5-15 mL, maximum diameter 3-4 cm): volume reduction at 12 months 76.7%.
- Group B, 129 nodules (volume 15-30 mL): reduction at 12 months 67.3%.
- Group C, 105 nodules (volume >30 mL): reduction at 12 months 66.7%.

The lower efficacy of the RFA in nodules over 5 cm might be due to their retrosternal extension, interfering with a trans-isthmic approach. There was no significant correlation between energy applied and volume reduction, although group A nodules received a higher quantity of energy for volume (2940 J/mL vs. B 2220 J/mL vs. C 1200 J/mL, p <0.001), which may also explain the lower volume reduction in nodules over 15 mL in volume.
The analysis based on US characteristics showed that a spongiform nodule incurred more volume loss than a solid one (68% vs. 60% at 6 months and 76% vs. 68% at 12 months). Nodules with intra- and perinodular vascularization were also more likely to undergo volume loss (62% at 6 months and 71% at 12 months). These results may be due to the excess vapor released by tissues rich in fluid (colloid or blood), which promotes intranodular thermal-coagulation (as in any procedure releasing heat, whether radiofrequency, laser, high-intensity focused ultrasounds). The calcifications (unless interfering with transit and positioning of the needle), and the positivity of TPO Ab, showed no significant association with results of the RFA at 6 and 12 months. 13% of the patients reported cough, pain and fever, 15% minor complications (edema, superficial hematoma) and 0.4% major but transient complications (infection of the nodule, changing of voice). No complications were reported in 71.6% of patients. Thyroid function and autoimmune status were not altered by treatment.

Conclusions
Radiofrequency thermal-ablation seems effective, safe and well tolerated. Spongiform nodules with intra- and perinodular vascularization are particularly responsive. The best results occur in nodules not too large. Larger nodules may require higher dose of energy per volume, and/or repeat treatment. Presence of calcifications does not hinder treatment.

References