

**NATIONAL INSTITUTE FOR HEALTH AND CARE
EXCELLENCE**

Interventional procedure consultation document

**Ultrasound-guided percutaneous
radiofrequency ablation for benign thyroid
nodules**

Thyroid nodules are lumps in the thyroid gland, which are usually non-cancerous (benign). The nodules may contain abnormal thyroid tissue and cause symptoms of an overactive thyroid. In this procedure, a small probe is inserted through the skin into the nodule in the neck and an electrical current is used to heat and destroy the nodule.

The National Institute for Health and Care Excellence (NICE) is examining ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules and will publish guidance on its safety and efficacy to the NHS. NICE's Interventional Procedures Advisory Committee has considered the available evidence and the views of specialist advisers, who are consultants with knowledge of the procedure. The Advisory Committee has made draft recommendations about ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules.

This document summarises the procedure and sets out the draft recommendations made by the Advisory Committee. It has been prepared for public consultation. The Advisory Committee particularly welcomes:

- comments on the draft recommendations
- the identification of factual inaccuracies
- additional relevant evidence, with bibliographic references where possible.

Note that this document is not NICE's formal guidance on this procedure. The recommendations are provisional and may change after consultation.

The process that NICE will follow after the consultation period ends is as follows.

- The Advisory Committee will meet again to consider the original evidence and its draft recommendations in the light of the comments received during consultation.
- The Advisory Committee will then prepare draft guidance which will be the basis for NICE's guidance on the use of the procedure in the NHS.

For further details, see the [Interventional Procedures Programme process guide](#), which is available from the NICE website.

Through its guidance NICE is committed to promoting race and disability equality, equality between men and women, and to eliminating all forms of discrimination. One of the ways we do this is by trying to involve as wide a range of people and interest groups as possible in the development of our interventional procedures guidance. In particular, we aim to encourage people and organisations from groups who might not normally comment on our guidance to do so.

In order to help us promote equality through our guidance, we should be grateful if you would consider the following question:

Are there any issues that require special attention in light of NICE's duties to have due regard to the need to eliminate unlawful discrimination, advance equality of opportunity, and foster good relations between people with a characteristic protected by the equalities legislation and others?

Please note that NICE reserves the right to summarise and edit comments received during consultations or not to publish them at all where in the reasonable opinion of NICE, the comments are voluminous, publication would be unlawful or publication would otherwise be inappropriate.

Closing date for comments: 18 March 2016

Target date for publication of guidance: June 2016

1 Draft recommendations

- 1.1 Current evidence on the safety and efficacy of ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules is adequate to support the use of this procedure provided that standard arrangements are in place for clinical governance, consent and audit.

2 Indications and current treatments

- 2.1 Thyroid nodules may be cystic, colloid, hyperplastic, adenomatous or cancerous. The majority of thyroid nodules are benign and they are often asymptomatic. There may be a single thyroid nodule (solitary nodule) or multiple thyroid nodules (multinodular goitre). Thyroid nodules can contain abnormal thyroid tissue ('toxic' nodules) causing an overactive thyroid, which affects the normal production of thyroxine or triiodothyronine.
- 2.2 Treatment of benign thyroid nodules may be necessary if they are symptomatic or causing cosmetic problems. Conventional treatment includes suppressive levothyroxine therapy or surgery. More recently, other approaches that are less invasive than conventional surgery have been introduced, such as ethanol ablation and percutaneous laser ablation.

3 The procedure

- 3.1 Radiofrequency ablation is a minimally invasive technique that aims to reduce symptoms and improve cosmetic appearance, while preserving thyroid function, and with fewer complications than surgery.
- 3.2 Before treatment, the thyroid nodule is confirmed as benign, typically by the use of 2 fine-needle aspiration biopsies. Ultrasound-guided percutaneous radiofrequency ablation for benign thyroid nodules is usually done in an outpatient setting using local anaesthesia. The patient lies in the supine position with moderate neck extension. A radiofrequency electrode is inserted into the nodule using ultrasound guidance to visualise the electrode during

the procedure. Once in position, the radiofrequency electrode is activated to heat and destroy the tissue.

4 Efficacy

This section describes efficacy outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 4.1 In a systematic review of 284 patients with benign thyroid nodules treated by radiofrequency ablation (RFA), the mean nodule volume reduced by 9.8 ml after the procedure (95% confidence interval [CI] -13.83 to -5.72; 9 studies, n=284 nodules; $I^2=98%$ [significant heterogeneity]). In a randomised controlled trial (RCT) of 84 patients with benign solid thyroid nodules, the mean nodule volume reduced from 24.5 (± 19.6) ml at baseline to 8.6 (± 9.5) ml at 6 month follow-up ($p < 0.001$) in patients treated by RFA, compared with no volume reduction in patients randomised to no treatment (27.5 \pm 22.1 ml at baseline and 27.8 \pm 22.1 ml at 6 month follow-up). In an RCT of 80 patients with solid, compressive, non-functioning benign thyroid nodules treated by RFA or no treatment, the median percentage volume changes were 71% reduction and 3% increase respectively ($p = 0.0001$). In a non-randomised comparative study of 400 patients with nodular goitre treated by RFA or surgery there was a mean percentage volume reduction of 85 (± 17.1)% after RFA at 12 month follow-up ($p = 0.002$). In a case series of 111 patients with benign, non-functioning thyroid nodules there was a mean volume reduction of 91 (± 15.8)% after RFA at 3-year follow-up. In an RCT of 50 patients with a single benign cystic thyroid nodule treated by RFA or ethanol ablation (also included in the

systematic review), there were median percentage volume reductions of 93(\pm 5.4)% and 97(\pm 4.1)% respectively at 6-month follow-up (p value not reported).

4.2 In the systematic review of 284 patients there was a reduction in the mean symptom score (measured on a 10-point visual analogue scale, with lower scores indicating less severe symptoms) of 2.89 after RFA (95% CI -2.51 to -3.28; 4 studies, n=85; $I^2=56\%$). In the RCT of 84 patients the mean pressure symptom score (measured on a 10-point visual analogue scale, with lower scores indicating less severe symptoms) reduced from 2.8(\pm 3.3) at baseline to 0.4(\pm 0.8) at 6 month follow-up ($p<0.001$) in patients treated by RFA compared with no reduction for patients with no treatment (2.7 \pm 3 at baseline and 2.9 \pm 3.2 at 6 month follow-up). In the RCT of 80 patients the symptom score (on a scale of 0–10, with lower scores indicating less severe symptoms) was 0.4(\pm 0.7) for patients treated by RFA compared with 3.3(\pm 1.7) for patients with no treatment ($p=0.0001$) at 6 month follow-up. In the case series of 111 patients, the symptom score (assessed on a scale of 0–10, with lower scores indicating less severe symptoms) reduced from 4.3(\pm 1.6) at baseline to 0.8(\pm 0.9) at last follow-up (mean follow-up 49 months, $p<0.001$). In the RCT of 50 patients treated by RFA or ethanol ablation (also included in the systematic review) symptom scores (assessed on a scale of 0–10, with lower scores indicating less severe symptoms) were 0.5(\pm 0.8) and 0.5(\pm 0.7) respectively at 6 month follow-up ($p=0.806$).

4.3 In the systematic review of 284 patients the mean reduction in cosmetic score (scored by a physician from 1–4, with lower scores indicating better cosmetic appearance) was 2.02 (95% CI -1.69 to -2.35; 5 studies, n=114; $I^2=78\%$) after RFA. In the RCT of

84 patients the mean cosmetic score (assessed on a scale of 1–4, with lower scores indicating better cosmetic appearance) reduced from 2.6(\pm 0.9) at baseline to 1.7(\pm 0.7) at 6 month follow-up ($p < 0.001$) in patients treated by RFA, compared with no reduction for patients with no treatment (2.6 \pm 1.0 at baseline and at 6 month follow-up). In the RCT of 80 patients cosmetic scores (assessed on a scale of 1–4, with lower scores indicating better cosmetic appearance) were 1.7(\pm 0.8) for patients treated by RFA and 3.5(\pm 0.7) for patients with no treatment ($p = 0.0001$) at 6 month follow-up. In the case series of 111 patients the cosmetic score (on a scale of 1–4, with lower scores indicating better cosmetic appearance) reduced from 3.2(\pm 0.8) at baseline to 1.3(\pm 0.6) at last follow-up (mean follow-up 49 months, $p < 0.001$). In the RCT of 50 patients treated by RFA or ethanol ablation (also included in the systematic review) cosmetic scores (on a scale of 1–4, with lower scores indicating better cosmetic appearance) were 1.1(\pm 0.4) and 1.2(\pm 0.4) respectively at 6 month follow-up ($p = 0.682$).

4.4 In the systematic review of 284 patients, 60 patients with ‘hot’ nodules were given methimazole at doses sufficient to maintain thyroid-stimulating hormone within the normal range before RFA treatment. After RFA treatment, 29 patients continued to need some dose of this medication to maintain euthyroidism based on thyroid-stimulating hormone measurements and symptoms (odds ratio 40.34, 95% confidence interval 7.78 to 209.1; 3 studies, $n = 60$; $I^2 = 2\%$). In the non-randomised comparative study of 400 patients, no patients treated by RFA needed medication for hypothyroidism compared with 71.5% of patients treated by surgery ($p = 0.002$).

4.5 In the case series of 111 patients (126 nodules) the overall recurrence rate (defined as increases in nodule volume of greater

than 50% compared with previous ultrasound images) was 6% (7/126). All nodules were benign on repeat fine-needle aspirate biopsy. Four of the recurrent nodules decreased in size after repeat RFA, 2 were treated with repeat RFA without further follow-up and 1 patient chose not to have further treatment and was lost to follow-up.

- 4.6 The specialist advisers listed key efficacy outcomes as reduction in thyroid nodule volume, and improvement in compression symptoms and cosmetic appearance.

5 Safety

This section describes safety outcomes from the published literature that the Committee considered as part of the evidence about this procedure. For more detailed information on the evidence, see the [interventional procedure overview](#).

- 5.1 Nodule rupture was reported in 1 patient treated by radiofrequency ablation (RFA) in a non-randomised comparative study of 400 patients. Nodule rupture was reported in less than 1% (2/1459) of patients in a case series of 1459 patients: 1 patient recovered without treatment and 1 patient was admitted to hospital and treated with antibiotics and analgesics. In the same study, 1 patient had nodule rupture with abscess formation: the patient was treated by left thyroidectomy. Nodule rupture was reported in 1 patient in a case series of 40 patients: this occurred 26 days after RFA and was treated with anti-inflammatory medication.
- 5.2 Ipsilateral vocal fold palsy was reported in 1 patient in a systematic review of 284 patients. This was diagnosed at 1-month follow-up, but the patient was subsequently lost to follow-up. Permanent right

paramedian vocal cord palsy with inspiratory stridor without dysphonia was reported in 1 patient treated by RFA in a randomised controlled trial (RCT) of 84 patients.

- 5.3 Voice change immediately after the procedure was reported in 5% (2/42) of patients treated by RFA in the RCT of 84 patients; this resolved completely within 3 hours of the procedure. Transient hoarseness was reported in less than 1% (1/200) of patients treated by RFA and in 1.5% (3/200) of patients treated by surgery in the non-randomised comparative study of 400 patients. Voice change was reported in 1% (15/1459) of patients in the case series of 1459 patients; all patients recovered completely, except for 2 patients who were lost to follow-up.
- 5.4 Brachial plexus injury was reported in 1 patient in the case series of 1459 patients. The patient had numbness and decreased sensation in the fourth and fifth fingers of the left hand; this gradually recovered during the next 2 months.
- 5.5 Diffuse glandular haemorrhage was reported in 1 patient in the systematic review of 284 patients. This resulted in interruption of the procedure. The patient was given oral analgesics for pain relief for 3 days. Intranodular bleeding was reported in 8% (3/40) of patients in the case series of 40 patients: this was stopped by swift needle-electrode insertion and heat administration. In the same study, pericapsular bleeding was reported in 1 patient, who had extensive neck bruising 5–10 days after the procedure. Haematoma was reported in 1 patient in the systematic review of 284 patients and in 1% (15/1459) of patients in the case series of 1459 patients: most completely disappeared within 1–2 weeks.

- 5.6 Postoperative oedema was reported in 1% (3/284) of patients in the systematic review of 284 patients. This was treated with betamethasone medication.
- 5.7 First-degree skin burns at the puncture sites were reported in less than 1% (4/1459) of patients in the case series of 1459 patients: all patients recovered from pain and skin colour changes within 7 days without sequelae.
- 5.8 Vasovagal reaction during the procedure was reported in less than 1% of patients in the case series of 1459 patients. This included sweating, difficulty breathing and hesitation; it was treated by elevation of the patient's legs and stopping the ablation. Vasovagal reaction was reported in 1 patient in the case series of 40 patients. The patient had bradycardia, hypotension, vomiting and defecation; the bed was tilted, ablation was stopped and the patient recovered within a few minutes. The patient had a subsequent RFA session 3 weeks later. Vomiting was reported in less than 1% (9/1459) of patients in the case series of 1459 patients: this improved within 1–2 days after treatment with anti-emetics.
- 5.9 Pseudocystic transformation was reported in 1 patient in the case series of 40 patients: the patient had a painful sudden swelling 3 weeks after RFA, which was treated with oral corticosteroids.
- 5.10 Permanent hypothyroidism was reported in 1 patient in the case series of 1459 patients: the patient had gradual neck bulging and ultrasound showed diffuse enlargement of the thyroid gland without a thyroid nodule.
- 5.11 In addition to safety outcomes reported in the literature, specialist advisers are asked about anecdotal adverse events (events which

they have heard about) and about theoretical adverse events (events which they think might possibly occur, even if they have never done so). For this procedure, specialist advisers listed the following theoretical adverse events: oesophageal or tracheal thermal injury, cardiac arrhythmia, and sympathetic or spinal nerve injury.

6 Committee comments

- 6.1 The committee noted that this procedure has also been used for treating malignant nodules, but the evidence base for this is limited.

7 Further information

- 7.1 For related NICE guidance, see the [NICE website](#).

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February, 2016