ISRCTN10838673 https://doi.org/10.1186/ISRCTN10838673

Radiofrequency ablation for benign intrathyroidal tumours

Submission date
10/12/2024

Recruitment status
Recruiting

Registration date
30/01/2025

Overall study status
Ongoing

Last Edited
06/02/2025

Condition category
Ear, Nose and Throat

[X] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[_] Results
[_] Individual participant data
[X] Record updated in last year

Plain English Summary
Background and study aims
Thyroid nodules are common; they are palpable in 5-7%, and evident on ultrasonography in 50-60% of people. The diagnostic pathway for the investigation of these nodules is well established and determines nodule function and its malignancy risk, stratifying those that require further treatment. Most thyroid nodules are benign and do not need treatment, although they may cause compressive symptoms. Historically, the therapy for compressive nodules was thyroid surgery but the advent of percutaneous thermal ablative techniques has opened up less invasive approaches in recent years. Radiofrequency ablation (RFA) has been approved by NICE to treat benign thyroid nodules and further research into its clinical and cost-effectiveness has been recommended in NICE Guideline 145. Few randomised controlled trials have examined the efficacy of RFA versus standard surgery for symptom reduction, complications, cost effectiveness and overall acceptability.
Rabbit is a randomised trial which aims to examine the efficacy, of radiofrequency ablation (RFA) versus hemithyroidectomy for symptom reduction, complications, cost effectiveness and overall acceptability.

Who can participate?
We aim to recruit 448 patients aged 18 years or older with single or multiple thyroid nodule(s) that are causing compressive or cosmetic symptoms affecting their quality of life.

What does the study involve?
After undergoing screening against the eligibility criteria, a participant would be randomised to either the RFA arm or Hemithyroidectomy and would be followed up for 3 years. For both arms, follow up will entail various physical and thyroid function assessments at 3, 12, and 36 months post-treatment at in clinic visits. RFA participants will have ultrasound scans of their nodule during clinic visits. Quality of life and pain scores (ThyPro, EQ-5D-5L, pain VAS) as well as health resource usage questionnaire (HRUQ) will be collected at baseline, 3, 12, 24 and 36 months post-intervention.

What are the possible benefits and risks of participating?
The risks are outlined within the participant information sheet in layman's terms but briefly summarised here. Evidence shows RFA to be safe, less invasive, lower incidence of

complications, shorter recovery times, quicker discharge compared to surgery.
• The surgery is a well established procedure, and a high likelihood of cure, with an extremely low chance of needing repeat surgery.
Possible disadvantages and risks of RFA include
• Bleeding or minor skin burn
• Hoarse voice
• Breakdown of the skin or a delayed burn
• Infection risk.
• Nodule regrowth
• Nodule rupture
• Repeat RFA may be required.

Possible disadvantages and risks of surgery
• Haematoma
• Recurrent laryngeal nerve palsy
• Neck scarring
• Infection risk

Where is the study run from?
The Birmingham Clinicals Trial Unit at the University of Birmingham (UK)

When is the study starting and how long is it expected to run for?
March 2025 to July 2029

Who is funding the study?
This study is funded by the NIHR (National Institute for Health and Care Research) HTA (Health Technology Assessment) programme (UK)

Who is the main contact?
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Study website
https://www.birmingham.ac.uk/research/bctu/trials/womens/rabbit

Contact information

Type(s)
Public, Scientific

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Additional identifiers

EudraCT/CTIS number
Nil known

IRAS number
335450

ClinicalTrials.gov number
Nil known

Secondary identifying numbers
CPMS 64697, NIHR135261

Study information

Scientific Title
Radiofrequency ABlation of Benign Intrathyroidal Tumours (RABBIT)

Acronym
RABBIT

Study hypothesis
Radiofrequency ablation (RFA) is not inferior to open surgery for the reduction of symptoms associated with benign nodular thyroid enlargement and provides a more cost-effective treatment option.

Ethics approval required
Ethics approval required

Ethics approval(s)
Approved 22/10/2024, North West - Preston Research Ethics Committee (2 Redman Place, Stratford, London, E20 1JQ, United Kingdom; +44 2071048181; preston.rec@hra.nhs.uk), ref: 24/NW/0299

Study design
Randomized controlled trial

Primary study design
Interventional

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details below to request a patient information sheet

Condition
Radiofrequency ablation or Hemithyroidectomy for benign intrathyroidal tumours

Interventions
RANDOMISATION

Randomisation will be provided by BCTU using a secure online system. Unique log-in usernames will be provided to those who wish to use the online system and who have been delegated the role of randomising participants into the trial as detailed on the delegation log. These unique log-in details must not be shared with other staff and in no circumstances should staff at sites access the system using another person's login details. The online system will be available 24 hours a day, 7 days a week, apart from short periods of scheduled maintenance. In the rare event of the online system being unavailable, the local research team will contact the BCTU Trial Office (between 9am and 5pm) who will randomise the participant using an emergency paper backup, the details from which will later be added to the database.

TRIAL INTERVENTION

Participants will be randomised to receive either radiofrequency ablation or hemithyroidectomy.

Radiofrequency ablation
If the participant is randomised to the RFA arm, a request for the procedure will be made in line with local process. The procedure will be carried out by the appropriately trained and delegated clinician (on the SSDL). The procedure will be carried out as per the RABBIT RFA Manual taking

into account any pre-existing local RFA guidance.
Further repeat RFA treatment will be at the discretion of the local PI, based on the clinical need of the participant. This should be documented on the Repeat RFA eCRF.

Hemithyroidectomy
If the participant is randomised to the surgery arm, they will be listed for hemithyroidectomy in line with the local process. The hemithyroidectomy, including any pre-operative assessments and admission procedures, will be carried out as per the local SOP and guidelines.

PROCEDURES AND ASSESSMENTS

SCREENING
A medical history will be taken during the screening period to confirm eligibility and to capture any relevant conditions related to the thyroid and when these started or were diagnosed. Information about current medications will also be collected at the screening visit to confirm eligibility. Vocal cord mobility, US guided FNAC, thyroid function blood tests, coagulation screen, and ultrasound scan with report should all be completed as standard of care. The data from these will be captured at screening and to confirm eligibility. Vital signs will also be assessed. A pregnancy test will be performed for patients who are female at birth and who are of childbearing potential as deemed by the local PI.

Once eligibility is confirmed, the participant will complete baseline questionnaires. Once baseline questionnaires have been completed, the participant will be randomised to an allocated intervention. They will be booked for the intervention within 6 months after the randomisation date.

At the intervention, the participant will have a relevant medical history check, vital signs, height and weight checks, adverse events and conmeds check, and another pregnancy test (as required), prior to the intervention. They will then complete a participant questionnaire (Pain VAS) post-intervention.

The participant will be followed up for a total of 36 months at varying intervals, and in clinic or remotely. The follow-up visits will be at 3 months, 12 months, and 36 months with questionnaires to be completed remotely at 24 months.

Briefly, these visits will comprise the following assessments:
3 months - Thyroid function tests, weight, participant questionnaire completion, AEs, conmeds, physical exam, vocal cord mobility assessment, ultrasound scan (only if on RFA arm).
12 months - Thyroid function tests, weight, participant questionnaire completion, AEs, conmeds, physical exam, vocal cord mobility assessment (if vocal cord palsy detected at 3M), ultrasound scan (only if on RFA arm).
24 months - Remote participant questionnaire completion.
36 months - Thyroid function tests, weight, participant questionnaire completion, AEs, conmeds, physical exam, ultrasound scan (only if on RFA arm).

Intervention Type
Procedure/Surgery

Primary outcome measure
1. Goitre symptom score at 12 months post intervention- using the goitre domain of the ThyPRO tool
2. Cost effectiveness at 12 months

2.1. Health related quality of life (using the EQ-5D-5L questionnaire)
2.2. Health resource usage (HRUQ questionnaire)

Secondary outcome measures
1. Composite ThyPRO score (overall quality of life) at 12 months post intervention
2. ThyPRO domain scores for: hyperthyroid symptoms, hypothyroid symptoms, eye symptoms, tiredness, cognition, anxiety, depressivity, emotional susceptibility, impaired social life, impaired daily life, impaired sex life and cosmetic complaints. All at 3, 12, 24 and 36 months post intervention
3. Incidence of complications within 3 months post intervention
4. Incidence of hypothyroidism up to 36 months post intervention
5. Incidence of temporary or permanent recurrent laryngeal nerve palsy at 12 months post intervention
6. Percentage volume reduction in treated nodule(s) at 12 months post intervention (RFA arm only)
7. Need for additional procedures related to the condition or treatment received up to 36 months post intervention
8. Nodule recurrence at 36 months post intervention assessed by USS (RFA arm only)
9. Pain intensity (related to pre-existing pain levels and the procedure – measured using pain VAS) at immediately post-intervention, 3, 12, 24, and 36 months post intervention
10. Related re-admission to hospital within 30 days of the initial trial intervention
11. Acceptability of RFA to patients (determined by take-up at screening)

Overall study start date
01/09/2022

Overall study end date
30/07/2029

Eligibility

Participant inclusion criteria
1. Age >=18 years
2. Thyroid nodule assessed as benign on an ultrasound scan (USS) and fine needle aspiration cytology (FNAC) (U2/TIRADS2 and 1 X Thy2 OR U3/TIRADS3 and 2 x Thy2)
3. Nodule criteria: Total volume of nodule < = 50cm3
4. Nodule consistency: Either 1) Solid, 2) Mixed solid and cystic (< = 60% cystic), or 3) Microcystic (0-100%)
5. Absence of retrosternal content
6. Clinical/radiological evidence of compression or cosmetic concerns ascribed to unilateral thyroid nodule/s and NOT to bilateral nodules or diffuse goitre
7. Thyroid Stimulating Hormone (TSH) > 0.1mIU/L and < upper limit of local reference range
8. Free T4 within the local reference range if TSH > 0.1 mIU/L and < lower limit of the local reference range
9. International Normalised Ratio (INR) < = 1.5
10. Activated Partial Thromboplastin Time (aPTT) < the maximum value of 10% greater than the upper limit of the local reference range
11. Willing and able to provide written consent
12. Willing to undergo randomisation

Participant type(s)

Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
Planned Sample Size: 448; UK Sample Size: 448

Participant exclusion criteria
1. Contraindication to thyroid surgery or RFA
2. Any previous surgery to the central neck compartment
3. Previous treatment for thyroid disorders
4. Previous thyroid RFA
5. Previous radioactive iodine treatment
6. Previous radiotherapy which included the neck
7. Current treatment with antithyroid drugs or thyroid hormone replacement
8. Known pregnancy
9. Formal anticoagulation that cannot be paused for the intervention, or documented bleeding diathesis
10. Clopidogrel that is not able to be stopped for a minimum of 5 days prior to the intervention
11. Aspirin that is more than the maximum dose of 75 mg once daily
12. Prosthetic heart valve, pacemaker, or any other implanted cardiac device
13. Other malignant nodules or nodules with indeterminate cytology in either lobe
14. Pre-existing vocal cord palsy

Recruitment start date
24/03/2025

Recruitment end date
30/06/2026

Locations

Countries of recruitment
England

United Kingdom

Study participating centre
University Hospitals Birmingham NHS Foundation Trust
Queen Elizabeth Hospital
Mindelsohn Way
Edgbaston

Birmingham
United Kingdom
B15 2GW

Sponsor information

Organisation
University of Birmingham

Sponsor details
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Sponsor type
Hospital/treatment centre

Website
https://www.birmingham.ac.uk/

ROR
https://ror.org/03angcq70

Funder(s)

Funder type
Government

Funder Name
National Institute for Health and Care Research

Alternative Name(s)
National Institute for Health Research, NIHR Research, NIHRresearch, NIHR - National Institute for Health Research, NIHR (The National Institute for Health and Care Research), NIHR

Funding Body Type
Government organisation

Funding Body Subtype
National government

Location
United Kingdom

Results and Publications

Publication and dissemination plan
On completion of the trial, the data will be analysed, and a Final Study Report prepared. Outputs from the trial will be submitted for publication in peer reviewed journals and the findings of the trial will be made public.

Intention to publish date
31/07/2030

Individual participant data (IPD) sharing plan
The final dataset will be available to members of the Trial Management and co-applicant group who need access to the data to undertake the final analyses.
Requests for data generated in this trial will be considered by BCTU. Data will typically be available six months after the primary publication unless it is not possible to share the data (for example: the trial results are to be used as part of a regulatory submission, the release of the data is subject to the approval of a third party who withholds their consent, or BCTU is not the controller of the data).

Only scientifically sound proposals from appropriately qualified Research Groups will be considered for data sharing. The request will be reviewed by the BCTU Data Sharing Committee in discussion with the CI and, where appropriate (or in absence of the CI) any of the following: the Trial Sponsor, the relevant TMG, and/or the independent TSC.

A formal Data Sharing Agreement (DSA) may be required between respective organisations once release of the data is approved and before data can be released. Data will be fully de-identified (anonymised) unless the DSA covers transfer of participant identifiable information. Any data transfer will use a secure and encrypted method.

IPD sharing plan summary
Available on request