ISRCTN59074092 https://doi.org/10.1186/ISRCTN59074092

Does near infrared fluorescence imaging reduce the risk of hypoparathyroidism after thyroid surgery?

Submission date
09/02/2022

Recruitment status
No longer recruiting

Registration date
07/03/2022

Overall study status
Completed

Last Edited
01/10/2025

Condition category
Surgery

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

Plain English summary of protocol

https://www.cancerresearchuk.org/about-cancer/find-a-clinical-trial/a-trial-using-near-infrared-florescence-imaging-during-surgery-to-remove-the-thyroid-nifty

Background and study aims
Parathyroid glands are tiny glands in the neck behind and/or below the thyroid gland that control the level of calcium in the blood. More than 12,000 patients undergo thyroid surgery every year in England alone. A common complication of thyroid surgery is damage to or accidental removal of parathyroid glands. This causes a condition called hypoparathyroidism, which may be temporary but in up to 12% of cases, it is long-term requiring lifelong medication and care. It reduces blood parathyroid hormone and calcium levels resulting in a wide range of symptoms (such as tingling & numbness in the extremities, nausea and nocturnal cramps), longer hospital stays and the requirement for frequent blood tests to monitor calcium levels & ongoing treatment. It has a significant impact on quality of life and the potential for kidney damage, accumulation of calcium in the tissues and seizures; this can be life-threatening.

A new intraoperative technique using fluorescence (glow) from a dye has been shown to help identification and preservation of parathyroid glands during thyroid and parathyroid surgery. The study will find out how many patients develop short and long term parathyroid damage following the use of this technology compared to those who underwent surgery in the standard manner, and will also determine if this new treatment will reduce hospital stay after surgery and improve quality of life for patients.

The trial will initially recruit 200 patients to determine whether there is enough early evidence of efficacy to justify recruiting a larger sample of patients for definitive analysis. If there is, then we aim to recruit to a total of 454 patients from 10 hospitals.

Who can participate?
Adults over 18 years, due to undergo total or completion thyroidectomy with or without central neck dissection

What does the study involve?
Participants will be randomised to receive thyroid surgery either with near-infrared fluorescence (NIRF) and Indocynanine Green (ICG), or as per standard care. Participants will then undergo their total or completion thyroidectomy with or without NIRF and ICG depending on their randomised allocation. The study does not influence the nature or extent of the operation. It will only affect how the operation will be carried out (i.e. with or without NIRF imaging).
Participants will be reviewed in hospital 1 day after their operation and will be asked to come into hospital for clinic visits at around 1 month and 6 months following the operation and study data will be collected from the participants.
Participants will also be asked to fill in questionnaire booklets about their quality of life and how they are feeling. These questionnaire booklets will be completed prior to trial entry (baseline) and at 1 month and 6 months after the operation.

What are the possible benefits and risks of participating?
A possible benefit is that NIRF imaging may improve thyroid surgery and reduce the rates of post-surgical hypoparathyroidism. It is hoped that this trial will provide evidence to assist surgeons on whether to use NIRF imaging during thyroid surgeries. There are also additional benefits to participants derived from inclusion in a large, multicentre study, including close and regular follow-up monitoring and rigorous assessment of outcomes etc.

All participants will need an operation for their thyroid condition, and would therefore undergo this operation whether or not they took part in the trial. Therefore, the risks of taking part in the trial are largely the same as outside of the trial. There is a slight additional risk for patients who are randomised to the surgery with NIRF imaging arm, due to the administration of the ICG. If patients choose to take part in the trial, they will be asked to give up some of their time to complete questionnaires and attend hospital appointments at certain times, but where possible these will be timed to coincide with normal clinical care.

Where is the study run from?
Sheffield Teaching Hospitals NHS Foundation Trust (UK)

When is the study starting and how long is it expected to run for?
May 2017 to October 2024

Who is funding the study?
National Institute for Health Research (NIHR) (UK).

Who is the main contact?
Katie Gordon, K.A.Gordon@leeds.ac.uk
Prof Saba Prakash Balasubramanian, s.p.balasubramanian@sheffield.ac.uk

Contact information

Type(s)
Scientific

Contact name
Mrs Katie Gordon

ORCID ID
https://orcid.org/0000-0003-1483-0657

Contact details
Clinical Trials Research Unit
University of Leeds
Leeds
United Kingdom
LS2 9JT
+44 113 343 7998
NIFTy@leeds.ac.uk

Type(s)
Principal investigator

Contact name
Prof Saba Prakash Balasubramanian

Contact details
Clinical Trials Research Unit
University of Leeds
Leeds
United Kingdom
LS2 9JT
-
s.p.balasubramanian@sheffield.ac.uk

Additional identifiers

Integrated Research Application System (IRAS)
287123

Central Portfolio Management System (CPMS)
51169

Protocol serial number
17/11/27

Study information

Scientific Title
Near Infrared Fluorescence (NIRF) Imaging to prevent Post-surgical Hypoparathyroidism (PoSH) after Thyroid Surgery (NIFTy) - A phase II/III pragmatic, multicentre randomised controlled trial

Acronym
NIFTy

Study objectives
NIFTy will test the hypothesis that using Near Infrared Fluorescence (NIRF) Imaging during thyroid surgery will reduce the risk of post-surgical hypoparathyroidism when compared to standard of care thyroid surgery.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Approved 20/01/2022, Wales Research Ethics Committee 5 (Health and Care Research Wales Support and Delivery Centre, Castlebridge 4, 15-19 Cowbridge Road East, Cardiff, CF11 9AB, UK; +44 1686 252101; Wales.REC5@wales.nhs.uk), ref: 21/WA/0375

Primary study design
Interventional

Study design
Interventional randomized controlled trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Near Infrared Fluorescence (NIRF) Imaging to prevent Post-surgical Hypoparathyroidism (PoSH) after Thyroid Surgery

Interventions
454 patients requiring a completion or total thyroidectomy will be randomised prior to surgery to receive surgery with near-infrared fluorescence (NIRF) and Indocynanine Green (ICG) or as per standard care.

Participants will receive total or completion thyroidectomy with or without NIRF and ICG depending on their randomised allocation.

Surgery without NIRF imaging (Standard care) will be performed as part of standard care in accordance to local and national protocols and guidance.

Surgery with NIRF imaging and ICG will be performed using NIRF imaging using autofluorescence and with ICG during surgery. An infrared camera will be used to detect the natural glow of the parathyroid glands under infrared light (autofluorescence). ICG will be injected later in the procedure and the infrared camera will detect glow from the dye showing the blood supply to the parathyroid glands. The use of NIRF imaging will be in accordance to the protocol developed in the qualitative research (process evaluation).

Clinical assessments will be as per standard practice but participants must be reviewed at 1 days post-operation and at 1 month and 6 months after operation.

Participants will complete questionnaires designed to capture health related quality of life at baseline, 1 month and 6 months after operation.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Phase II primary outcome: Transient hypocalcaemia, defined as any adjusted calcium of <2.1 mmol/L on the day after surgery measured using calcium and serum albumin blood values from a

blood test
Phase III primary outcome: Incidence of post-surgical hypoparathyroidism (PoSH) at 6 months post-surgery. In accordance with the national British Association of Endocrine and Thyroid Surgeons (BAETS) definition, PoSH is defined as the need for calcium and/or vitamin D supplements to treat symptoms or maintain adjusted calcium in the low normal range (between 2.1 and 2.3 mmol/L) at 6 months after surgery, measured using medical records

Key secondary outcome(s)

Current secondary outcome measures as of 19/06/2023:

Phase III secondary outcomes:
1. Post-operative Parathyroid Hormone, measured at 1 day post-operation, 1 month postoperation and 6 months post-operation
2. Transient hypocalcaemia: measured as per the phase II primary endpoint, defined as an adjusted calcium of <2.1 mmol/L on the day after surgery
3. Protracted hypoparathyroidism: defined as either an adjusted calcium of <2.1 mmol/L, or the need for calcium and/or vitamin D supplements to treat symptoms or maintain adjusted calcium in the low normal range (between 2.1 and 2.3 mmol/L), at 1-month after operation measured as per the phase II and phase III primary endpoints
4. Incidence of Intra-operative complications measured using medical records
5. Post-operative complications within 6 months of operation, categorised using the ClavienDindo classification, measured using medical records
6. Length of post-operative hospital stay calculated as the time, in days, from surgery to patient declared medically fit for discharge measured using medical records
7. Health related quality of life will be measured using 36 item Short Form survey (SF-36) and the Questionnaire on Hypoparathyroidism (HPQ 28) at baseline, and at 1 month and 6 months after operation.
8. Re-admission to hospital within 6 months of surgery, for any reason, measured using medical records
9. Hypercalcaemia: defined as any adjusted calcium level >2.6 mmol/L occurring within 6 months of operation measured as per the phase II primary endpoint

Phase III mechanistic outcome:
10. Intra-operative decision-making measured based on the opinions of the surgeons during the operation

———

Previous secondary outcome measures:

Phase III secondary outcomes:
1. Transient hypocalcaemia: measured as per the phase II primary endpoint, defined as an adjusted calcium of <2.1 mmol/L on the day after surgery
2. Protracted hypoparathyroidism: defined as either an adjusted calcium of <2.1 mmol/L, or the need for calcium and/or vitamin D supplements to treat symptoms or maintain adjusted calcium in the low normal range (between 2.1 and 2.3 mmol/L), at 1-month after operation measured as per the phase II and phase III primary endpoints
3. Incidence of Intra-operative complications measured using medical records
4. Post-operative complications within 6 months of operation, categorised using the Clavien-Dindo classification, measured using medical records
5. Length of post-operative hospital stay calculated as the time, in days, from surgery to patient declared medically fit for discharge measured using medical records

6. Health related quality of life will be measured using 36 item Short Form survey (SF-36) and the Questionnaire on Hypoparathyroidism (HPQ 28) at baseline, and at 1 month and 6 months after operation.
7. Re-admission to hospital within 6 months of surgery, for any reason, measured using medical records
8. Hypercalcaemia: defined as any adjusted calcium level >2.6 mmol/L occurring within 6 months of operation measured as per the phase II primary endpoint

Phase III mechanistic outcome:
9. Intra-operative decision-making measured based on the opinions of the surgeons during the operation

Completion date
31/10/2024

Eligibility

Key inclusion criteria
1. Aged >=18 years
2. Able to provide written informed consent
3. Due to undergo total or completion thyroidectomy with or without central neck dissection (indications for surgery may include Graves' disease, suspected or confirmed thyroid cancer, and goitre with compressive effects).
4. ASA <=3
5. Able and willing to comply with the terms of the protocol including participant completed questionnaires

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Sex
All

Total final enrolment
252

Key exclusion criteria
Current exclusion criteria as of 19/06/2023:

1. Patients undergoing concomitant parathyroid or thoracic surgery
2. Patients undergoing re-operative thyroid surgery (except completion thyroidectomy after

previous contralateral lobectomy)
3. Documented hypo or hypercalcaemia within the last 3 months prior to planned date of thyroid surgery, defined as adjusted calcium <2.1 mmol/L or >2.6 mmol/L
4. Pregnancy
5. Known allergy to ICG, iodine or iodine dyes.
6. Patients with significant renal impairment (defined as eGFR < 40ml/min/1.73m² (or a serum creatinine value >10% of upper value for normal institutional limits if eGFR is not performed locally)
7. Taken calcium or active vitamin D supplements (such as alfacalcidol or calcitrol) in the 2 weeks prior to randomisation or due to receive prophylactic treatment with calcium and/or vitamin D supplements peri-operatively

___

Previous exclusion criteria:

1. Patients undergoing concomitant parathyroid or thoracic surgery
2. Patients undergoing re-operative thyroid surgery (except completion thyroidectomy after previous contralateral lobectomy)
3. Documented hypo or hypercalcaemia within the last 3 months prior to planned date of thyroid surgery
4. Pregnancy
5. Known allergy to ICG, iodine or iodine dyes.
6. Patients with significant renal impairment (defined as eGFR < 40ml/min/1.73m² (or a serum creatinine value >10% of upper value for normal institutional limits if eGFR is not performed locally)
7. Hepatic dysfunction, defined as bilirubin outside of institutional limits and/or ALT/AST >2.5 x institutional upper limit of normal.
8. Taken calcium or active vitamin D supplements (such as alfacalcidol or calcitrol) in the 2 weeks prior to randomisation or due to receive prophylactic treatment with calcium and/or vitamin D supplements peri-operatively

Date of first enrolment
31/03/2022

Date of final enrolment
04/03/2024

Locations

Countries of recruitment
United Kingdom

England

Study participating centre
Northern General Hospital
Herries Road
Sheffield

United Kingdom
S5 7AU

Study participating centre
Chelsea and Westminster Hospital NHS Foundation Trust
Chelsea & Westminster Hospital
369 Fulham Road
London
United Kingdom
SW10 9NH

Study participating centre
Imperial College Healthcare NHS Trust
The Bays
St Marys Hospital
South Wharf Road
London
United Kingdom
W2 1BL

Study participating centre
Lister Hospital Laboratory
Lister Hospital
Coreys Mill Lane
Stevenage
United Kingdom
SG1 4AB

Study participating centre
Portsmouth Hospitals University National Health Service Trust
Queen Alexandra Hospital
Southwick Hill Road
Cosham
Portsmouth
United Kingdom
PO6 3LY

Study participating centre
University College London Hospitals NHS Foundation Trust Hq
250 Euston Road
London

United Kingdom
NW1 2PG

Sponsor information

Organisation
Sheffield Teaching Hospitals NHS Foundation Trust

ROR
https://ror.org/018hjpz25

Funder(s)

Funder type
Government

Funder Name
NIHR Evaluation, Trials and Studies Co-ordinating Centre (NETSCC)

Funder Name
National Institute for Health 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

Individual participant data (IPD) sharing plan
De-identified individual participant data datasets generated and/or analysed during the current study will be available upon request from the Clinical Trials Research Unit, University of Leeds

(contact CTRU-DataAccess@leeds.ac.uk in the first instance). Data will be made available at the end of the trial, i.e. usually when all primary and secondary endpoints have been met and all key analyses are complete. Data will remain available from then on for as long as CTRU retains the data.

Data Sharing Statement
CTRU makes data available by a 'controlled access' approach. Data will only be released for legitimate secondary research purposes, where the Chief Investigator, Sponsor and CTRU agree that the proposed use has scientific value and will be carried out to a high standard (in terms of scientific rigour and information governance and security), and that there are resources available to satisfy the request. Data will only be released in line with participants' consent, all applicable laws relating to data protection and confidentiality, and any contractual obligations to which the CTRU is subject. No individual participant data will be released before an appropriate agreement is in place setting out the conditions of release. The agreement will govern data retention, usually stipulating that data recipients must delete their copy of the released data at the end of the planned project.
The CTRU encourages a collaborative approach to data sharing, and believe it is best practice for researchers who generated datasets to be involved in subsequent uses of those datasets. Recipients of trial data for secondary research will also receive data dictionaries, copies of key trial documents and any other information required to understand and reuse the released datasets.
The conditions of release for aggregate data may differ from those applying to individual participant data. Requests for aggregate data should also be sent to the above email address to discuss and agree suitable requirements for release.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Protocol article		30/01/2025	03/02/2025	Yes	No
HRA research summary			28/06/2023	No	No
Other publications	Qualitative in the operating theatre, prior to RCT allowed the identification of key components of the surgical intervention	26/09/2025	01/10/2025	Yes	No