Improved Thyroid Nodule Assessment and Stratification using Optoacoustic-Ultrasound Imaging with Machine Learning (THYNAS+)

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The primary objective of this feasibility study is to provide an initial assessment of OA/US imaging to distinguish between benign and malignant thyroid nodules using HbO2 and HbR as the primary biomarkers.The secondary objectives are:- To...

Ethical review	Approved WMO
Status	Pending
Health condition type	Miscellaneous and site unspecified neoplasms malignant and unspecified
Study type	Observational non invasive

Summary

ID

NL-OMON57293

Source
ToetsingOnline

Brief title
Optoacoustic imaging for thyroid nodule assessment

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
Thyroid cancer, Thyroid Nodules

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Molecular imaging, Optoacoustic imaging, TIRADS

Outcome measures

Primary outcome

This is an early feasibility study exploring the use of OA for thyroid nodule evaluation using HbR and HbO2 signal. Much is still unknown about the interpretation of the images in thyroid nodules,therefore, both qualitative and quantitative analysis will be performed as primary analysis:

1. Images and data will be reviewed first by Investigator Independent Reviewers (experienced radiologists) to provide a basis for determining feature score signals that indicate benign or malignant thyroid nodules as well as aggressive and non-aggressive cancers.
2. A comparison of the in vivo opto-acoustic features on imaging with those obtained from standard diagnostic imaging will also be done by the Investigator Independent Reviewers (experienced radiologists).
3. Once thyroid feature scores are developed, Physician Independent Readers (experienced radiologists) will read the images collected and score the nodules using the new thyroid feature scoring system to determine whether a nodule is considered benign or malignant. Descriptive statistics on the feature scores will be performed as part of the primary analysis.

4. Lymph Nodes will be assessed for pathology correlation with thyroid cancer histopathology and cytology The thyroid nodule will be marked with a region of interest (ROI) in the obtained OA images. The signal (HbR vs HbO2) will be qualitatively interpreted by three independent readers not involved in standard clinical practice (experienced radiologists), blinded for cytology/histopathology results. The index nodule will be classified as *not suspicious* or *suspicious* for malignancy. In addition, quantitative descriptive statistics will be performed.

5. The diagnostic accuracy of OA will be determined using cytology and histopathology as golden standard. As such, sensitivity (Se), Sp, positive predictive value (PPV), negative predictive value (NPV) and accuracy are calculated.

6. AEs will be summarized for the Safety population. The number and percentage of subjects with at least one event will be presented overall and by MedDRA system organ class (SOC) and preferred term (PT). Subjects with more than one occurrence of an AE within a given SOC and PT will be counted only once toward that SOC and PT. AE will be summarized in a similar manner under the maximum severity experienced. Subjects with more than one occurrence of an AE within a given SOC and PT will be counted only once toward that SOC and PT under the maximum severity experienced. These analyses will be repeated for SAE, ADE, SADE, and unanticipated SADE.

For quantitative analysis, descriptive statistics will be used for the ITD population and for the Safety population in order to assess subject

characteristics, cytopathological/histopathological thyroid nodule and lymph node characteristics. Other quantitative study parameters collected include:

- Baseline characteristics (sex, age, race, etc.);
- Thyroid nodule size and location;
- OA/US vs US TI-RADS scores;
- Indication for US and FNA;
- Results of clinical US and FNA cytology;
- Preoperative laboratory results (e.g. TSH, T4, T3) (standard of care);
- Histopathological cancer type (papillary, follicular, medullary carcinoma, etc.).

Primary analyses of study data includes descriptive statistics of the aforementioned study parameters. Confidence intervals will be calculated as a two-sided 95% confidence interval where appropriate, unless otherwise specified.

Secondary outcome

Secondary analyses includes TI-RADs scores and OA/US thyroid nodule feature scores stratified by cytology and histopathology type.

In addition to overall (i.e. pooled site data) analyses, summaries of each study endpoint and other clinical/demographic/safety data will be provided by study site in order to evaluate the consistency of the results across study sites as a secondary analysis.

Additional analyses by clinical and/or demographic subgroups may be performed on the following characteristics:

- Nodule Size

- Nodule Depth

- Age of Patient

- Type of cancer

Two-sided 95% confidence intervals will be calculated where appropriate.

Study description

Background summary

The prevalence of thyroid nodules is increasing, primarily due to incidental detection during high-resolution imaging, with estimates ranging from 19-68% in randomly selected individuals undergoing ultrasound (US). Despite the majority being asymptomatic, further evaluation is necessary to assess malignancy risk. This surge in thyroid nodules has led to subject anxiety, healthcare system strain, and increased diagnostic costs. Ultrasound imaging is the primary method for risk assessment, but its specificity is limited, leading to unnecessary procedures. The Thyroid Imaging Reporting and Data System helps stratify risk, but up to 30% of fine-needle aspirations yield indeterminate results, resulting in hemithyroidectomy for diagnosis. However, most surgeries reveal benign nodules, indicating significant overtreatment. A pressing need exists for a non-invasive tool to accurately rule out thyroid cancer early in the diagnostic process.
Optoacoustic imaging (OA) is a promising non-invasive imaging technique that uses pulsed light to visualize molecular contrast in tissue. OA's ability to quantify blood oxygen saturation is crucial for assessing tumor hypoxia. Combining optical contrast with ultrasonic resolution, OA offers deep tissue imaging capabilities, making it an attractive modality for various applications, including tumor characterization and assessment of physiological biomarkers like sO2. The study focuses on optimizing the Imagio® OA-US technology for imaging thyroid cancer. While promising, improvements in imaging depth, quality, and tissue characterization are needed before clinical use.
Using accurate digital and physical thyroid phantoms, the study investigates instrumental optimizations for artifact reduction and enhanced imaging of the entire thyroid. Additionally, improved image processing and analysis methods are explored to refine imaging performance and quantify data. The goal is to extract qualitative and quantitative features to distinguish between benign and malignant nodules. Overall, the study aims to show the feasibility of the Imagio® OA-US technology for precise thyroid nodule assessment.

Study objective

The primary objective of this feasibility study is to provide an initial assessment of OA/US imaging to distinguish between benign and malignant thyroid nodules using HbO2 and HbR as the primary biomarkers.

The secondary objectives are:
- To investigate Imagio® US and OA features that may distinguish between aggressive (i.e. anaplastic and medullary) and non-aggressive (i.e. papillary and follicular) thyroid cancer.
-To investigate the feasibility of the Imagio® OA/US Imaging System to detect feature scores that correlate with detecting lymph node pathology correlation with thyroid nodule histology and cytology.

Study design

The current study is a non-randomized, non-blinded, prospective, multi-center feasibility study conducted at University Medical Center Groningen and Ziekenhuisgroep Twente hospital.

Study burden and risks

Burden:
Subjects will be imaged before their FNA appointment at the nuclear department. The subjects will undergo one imaging moment of up to 30 minutes. Healthy volunteers will undergo one imaging moment of up to 30 minutes. No other study related procedures will be performed.

Risks
The Imagio® will not be used to diagnose subjects.
Risk management for the Imagio® imaging system to reduce clinical risks has been completed in accordance with ISO 14971. This process identified hazards, potential effects, potential causes, and mitigation activities for the procedure and device. After all risk mitigations were implemented, all residual risks for the Imagio® imaging system were within the acceptable range.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- Age >= 18 years
- Written informed consent
- Having a TI-RADAS 3-5 thyroid nodule identified via standard of care US for which US-guided FNA is indicated
- Willing and able to complete all procedures and assessments in accordance with the clinical protocol

Exclusion criteria

- Medical or psychiatric conditions that compromise the subject*s ability to give Informed Consent
- A condition or impediment (i.e., insect bites, poison ivy, open sores, chafing of the skin, scar, tattoos, moles, etc.) that could interfere with the intended Field of view (within one probe length or 4 cm of the nodule)
- Thyroid nodule greater than 3.0 cm in maximum diameter
- Previous or on-going radioactive iodine treatment
- Have an acute or a chronic hematoma and/or acute ecchymosis of the thyroid
- Is experiencing photo-toxicity associated with currently taking, or having taken, photosensitizing agents within the previous 72 hours such as sulfa, ampicillin, tetracycline
- Are currently undergoing phototherapy
- Have a history of any photosensitive disease (e.g., porphyria, lupus erythematosus)

- Are undergoing treatment for a photosensitive disease and is experiencing photosensitivity
- Subject has received chemotherapy for any type of cancer within 90 days from date of screening or standard of care Ultrasound
- Previous surgery in head and neck area on the ipsilateral side of the index nodule
- Previous radiotherapy in head and neck area
- Subject is pregnant (asked during IC procedure)
- Have had previous FNA of the target nodule of interest within the 45 days of baseline OA
- Subject has participated in a clinical study of an investigational drug or device within 3 months prior to screening ultrasound imaging that may have an impact on clinical outcomes of this study
- Subject has previously participated in this study

Study design

Design

Study type: Observational non invasive

Masking:	Open (masking not used)
Control:	Uncontrolled
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	23-12-2024
Enrollment:	150
Type:	Anticipated

Medical products/devices used

Generic name:	Opto-acoustic imaging
Registration:	No

Ethics review

Approved WMO Date:	11-02-2025
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
CCMO	NL86859.042.24