Combined Needle-based Confocal Laser Endomicroscopy Cone-Beam Computed Tomography Navigation Bronchoscopy: a proof of principle study

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This study aims to investigate proof of principle of utilizing nCLE during CBCT-NB navigation bronchoscopy. A confirmatory CBCT spin is considered the gold standard for tool-in-lesion but is associated with additional radiation exposure. We aim to...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Observational invasive

Summary

ID

NL-OMON56889

Source
ToetsingOnline

Brief title
nCLE-Cone-beam CT navigation bronchoscopy

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified

Synonym
Peripheral lung cancer

Research involving
Human

Sponsors and support

Primary sponsor: Amsterdam UMC

Source(s) of monetary or material Support: Medphot - Project 2,Mauna Kea Technologies (parijs)

Intervention

Keyword: Bronchoscopy, Cone-Beam Computed Tomography, Confocal Microscopy, Lung Cancer

Outcome measures

Primary outcome

CBCT-NB navigation success: tool-in-lesion OR unsuccessful navigation

nCLE tool-in-lesion confirmation: in-lesion nCLE criteria seen

Secondary outcome

1. Technical feasibility: proportion of nCLE imaging that are successful

(meaning that the preloaded needle can be advanced through the working channel,

puncture the nodule, advance the CLE probe and start imaging) resulting good

quality images (feasibility meaning >90% good quality interpretable images).

This is based on previous nCLE studies where nCLE was employed during

conventional bronchoscopy and >85% of images were of good quality.

2. Safety: number of (severe) adverse events ((S)AEs) and investigational

proce-dure-related adverse events (AEs) (<4% severe adverse events (1/25) will

be con-sidered acceptable). Pneumothorax is one of the most common reported

compli-cation of endobronchial procedures with transbronchial needle aspiration

and biop-sies and occurs between 1-6% of CBCT-NB procedures. Often, medical

interven-tional such as chest tube placement is not needed. Intraproce-dural

haemorrhage requiring medical intervention will also be reported based on the

CTCAE and is also reported in ~4-5% of cases.

3. Diagnostic yield: the proportion of patients in whom the bronchoscopic

procedure results in a definitive diagnosis out of the total number of patients that have re-ceived the diagnostic bronchoscopic procedure.

4. Diagnostic sensitivity for malignancy: defined as the proportion of patients that have malignancy diagnosed by bronchoscopic tissue sampling, relative to the total number of patients with a final diagnosis of malignancy as determined by the ref-erence standard.

5. Sensitivity, specificity and accuracy of real-time nCLE imaging assessment, meaning identification of the known nCLE criteria (malignancy, granuloma, air-way/lung parenchyma)

6. Sensitivity, specificity and accuracy of post-procedure nCLE image assessment, meaning identification of the known nCLE criteria (malignancy, granuloma, air-way/lung parenchyma)

7. Interobserver agreement (IOA) and intraobserver reliability (IOR) or the post-procedure nCLE image assessment

8. Total procedure duration: from introduction of the scope to removal of the scope

9. Navigation time: from start of navigation modality until decision to start biopsy

10. Cumulative radiation exposure of the procedure: dose area product and effective dose of entire procedure

11. Number of cone beam spins

12. Fluoroscopy time in minutes

Study description

Background summary

Lung cancer remains a significant problem in current society with one of the higher cancer related mortality rates. The increased use of chest computed tomography (CT) and the poten-tial future lung cancer screening result in an increased detection of early-stage peripheral lung cancer. Bronchoscopies are often indicated to collect tissue for diagnosis and to aid treatment decision making.
Diagnostic bronchoscopy for peripheral lung nodules remains challenging despite many tech-nological innovations. The procedure comprises three essential pillars needed for a diagnostic success: navigation to the lesion, tool-in-lesion confirmation and adequate tissue retrieval.
Cone beam computed tomography navigation bronchoscopy (CBCT-NB) is a fairly new technique that provides coarse navigation to the pulmonary lesion with real-time guidance us-ing augmented fluoroscopy (AF). An initial CBCT scan allows for segmentation of the target lesion and selecting the optimal pathway. Repeated CBCT scanning allows for confirmation that the target has been reached (navigation success) or if repositioning is needed.
Although the technique is very promising, an often discussed disadvantage of CBCT is the inherent use of ionizing radiation, limited availability and challenges with small nodules located in the basal and posterior fields due to respiratory motion. Most procedures ask for multiple CBCT spins both for trajectory planning, tool adjustments and tool-in-lesion confirmation. This, combined with extensive use of fluoroscopy is associated with radiation exposure for both patients and the investigation team. Additionally, CBCT-NB with AF provides information from a global perspective rather than a local perspective. In experienced centers, coarse naviga-tion guidance seems of lesser concern and fine positioning and optimal tissue sampling are the biggest problems to be overcome. The persistently low diagnostic yield of navigation bronchoscopies can for the majority be attributed mispositioning of the tools in *the last centi-meter*. Therefore there is a need for complementary techniques providing real-time infor-mation for fine-tuning the needle position such as needle-based confocal laser endomicros-copy (nCLE) also called the *smart needle*.
Confocal laser endomicroscopy (CLE) is a high-resolution microscopic technique that visual-izes individual cells in real-time at the tip of the biopsy needle, allowing for real-time micro-scopic feedback for fine tuning needle positioning and tool-in-lesion confirmation. Currently, it is unknown which (combination of) techniques are the most optimal (i.e., leading to a high di-agnostic yield and cost-effective). Therefore, research is needed to investigate the potential of new (combinations of) techniques. To date, there are no reports on the combination of CBCT-NB with nCLE.

Study objective

This study aims to investigate proof of principle of utilizing nCLE during CBCT-NB navigation bronchoscopy. A confirmatory CBCT spin is considered the gold standard for tool-in-lesion but is associated with additional radiation exposure. We aim to investigate the concordance between CBCT navigation success (tool-in-lesion on CBCT spin) and nCLE tool-in-lesion confirmation (tool-in-lesion nCLE criteria observed). We also hypothesize that nCLE could reduce or replace the need for additional confirmatory CBCT scans and limit fluoroscopy use.

Study design

Investigator-initiated proof of principle medical device study

Study burden and risks

A participating patient who enters the study and will not benefit from study participation, how-ever risks related to this study are negligible.
Additionally, future patients might benefit from improved lung cancer diagnostics based on study findings. Only patients that have a clinical indication for CBCT-NB will participate in this study. Risks related to CBCT-NB (such as radi-ation exposure) are not extra for the study but part of clinical practice.
From experience we know that the risks of study participation are negligible as previous study publications showed that nCLE-imaging and IV fluorescein administration are safe. In the prior bronchoscopic nCLE studies in Amsterdam UMC, including over 50 patients, no study proce-dure or device related adverse events occurred. Right before nCLE-imaging, fluorescein will be administered intravenously through an existing venous entrance. Fluorescein is a com-monly used dye in hospitals (e.g. in ophthalmology) and adverse reactions are rare (1.1%) and mild in character. In 2010, Wallace et al. published a retrospective study of all confocal laser endomicroscopy procedures performed between January 2003 and November 2008, with in total 2,272 procedures and no serious adverse events related to fluorescein injection were identified. nCLE measurements will be performed during bronchoscopic work-up and is followed by conventional cytological aspirations (routine work up), without the need for addi-tional aspirations or biopsies for research purposes. Estimated prolonged endoscopy time due to study participation is approximately 10 minutes. Patient will not be aware of this as patients are already deeply sedated for the procedure. In conclusion we believe that the burden and risks associated with study participation (up to 10 minutes additional sedation time and appli-cation of fluorescein) are negligible.

Contacts

Public
Amsterdam UMC

Meibergdreef 9
Amsterdam 1105 AZ
NL
Scientific
Amsterdam UMC

Meibergdreef 9
Amsterdam 1105 AZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

• 18 years or older
• Suspected pulmonary nodule with an indication for CBCT-NB (decided by multidisciplinary tumour board)
• Nodule must be solid or partially solid
• Solid part of the nodule must be at least 8 mm
• Largest dimension of the nodule on CT equal or less than 30 mm
• Ability to understand and willingness to sign a written informed consent

Exclusion criteria

• Inability or non-willingness to provide informed consent

• Patients with an endobronchial visible lung tumor on bronchoscopic inspection
• Patients in which the target lesion is within reach of the linear EBUS scope
• Lung nodules that resolved at the time of index intraprocedural CBCT
• Failure to comply with the study protocol
• Patients with known allergy for fluorescein or risk factors for an allergic reaction
• Pregnant or breastfeeding women
• Patients with hemodynamic instability
• Patients with refractory hypoxemia
• Patients with a therapeutic anticoagulant that cannot be held for an appropriate interval before the procedure
• Patients who are unable to tolerate general anesthesia according to the anesthesiologist
• Patient undergoing chemotherapy as several chemotherapies have fluorescent properties at the same wavelength (e.g. doxorubicin)

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	08-11-2024
Enrollment:	25
Type:	Actual

Medical products/devices used

Generic name:	Cellvizio I.V.E. + AQ Flex 19(N) probe
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	31-05-2024
Application type:	First submission
Review commission:	METC Amsterdam UMC

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	NL86502.018.24