Injection of 99mTc-nanocolloid and ICG to identify, retrieve and qualify tumor draining lymph nodes in early-stage lungcancer

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Ethical review	Approved WMO
Status	Completed
Health condition type	Respiratory and mediastinal neoplasms malignant and unspecified
Study type	Interventional

Summary

ID

NL-OMON51465

Source
ToetsingOnline

Brief title
INITIATE

Condition

- Respiratory and mediastinal neoplasms malignant and unspecified
- Respiratory tract neoplasms

Synonym
early-stage lung cancer, lung nodule, lung tumor

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum
Source(s) of monetary or material Support: Johnson & Johnson

Intervention

Keyword: early-stage lung cancer, metastatic disease, radioactivity, sentinel lymph nodes

Outcome measures

Primary outcome

The primary objective is to determine the feasibility of identifying and analyzing the TDLN in patients with NSCLC (cT1 to cT2b) on SPECT/CT-imaging and during surgical resection using a radioactive and fluorescent tracer. To verify the objective, injections (at multiple locations by repositioning of the catheter) should be feasible during a navigation bronchoscopy using 99mTc-nanocolloid and peri-surgically (through trans-thoracic needle or navigation bronchoscopy) using ICG and the drainage of these tracers should be visible on either SPECT/CT-imaging or a fluorescent camera. Feasibility of identification are qualitative and quantitative (how many nodes on imaging and surgery) endpoints that will be assessed by consensus between a pulmonary physician, technical physician, nuclear physician and a cardiothoracic surgeon that are part of the study team.

Secondary outcome

The quality of drainage after intra- or peritumoral injections, the Pioneer Plus catheter as endobronchial catheter for sampling, injection and use of the real-time ultrasound-imaging, the removal of SLN during surgery based on fluorescence, the added value of the additional pathological evaluation and the

immunological reactions found in the SLN and tumor.

Study description

Background summary

Around 14.000 patients are diagnosed with lung cancer in the Netherlands each year. 85% of these tumors are non-small cell lung cancer (NSCLC), which can be classified into stages Ia to IVb Current 5-year survival estimates in NSCLC range from >77% in stage IA disease to <10% in stage IV disease. Approximately 20% of lung cancer patients in the Netherlands are diagnosed at an early-stage and these tumors are treated with curative intent, receiving surgery or stereotactic ablative radiation (SABR). If locoregional lymph nodes are involved, adjuvant treatment is considered, which renders accurate staging of locoregional lymph nodes a critical step in curation at these early stages of NSCLC. At present, the recurrence rate at 2-years after intended curative treatment is 15-22%. Recurrence after surgery is most often the result of residual disease in the lymph nodes, indicating that, despite guideline concordant work-up, current methods fail to accurately stage locoregional lymph nodes and that patients are probably undertreated.
A technique that has been investigated for tumors of several origins over the past decades is a sentinel lymph nodes (SLN) procedure. During such a procedure, an intra- and/or peritumoral injection of radioactive, fluorescent, or paramagnetic particles is administered that subsequently drain via the lymphatic system to these lymph nodes and can be visualized on imaging before or during surgery to identify and retrieve them. Indocyanine Green (ICG) and/or 99mTc-nanocolloïd are often used to perform a SLN procedure. Literature on this procedure in lung cancer suggest identifications rates of SLN by ICG and radioactive tracers to be around 90%.
The Radboudumc developed the navigation bronchoscopy program to endobronchially diagnose small peripheral lung lesions. This program provides an opportunity to inject a tracer in or around the tumor tissue in a minimally invasive manner directly after diagnosis, enabling us to identify the drainage path and SLN on SPECT/CT-imaging afterwards. Additionally, injection of ICG during subsequent surgery will help us identify the SLN on a fluorescent camera and enable us to more extensively assess these lymph nodes on metastatic disease.
Therefore, we will investigate the feasibility of sentinel node procedure using a radioactive tracer (99mTc-nanocolloïd) and fluorescent tracer (ICG) to improve staging of lung cancer. Furthermore, with developing these new tools to improve staging, we hope to contribute to a better selection for less invasive treatments in future patients.

Study objective

The primary objective is to determine the feasibility of identifying the TDLN in patients with NSCLC (cT1 to cT2b) on SPECT/CT imaging and during surgical resection using a radioactive and fluorescent tracer, 99mTc-nanocolloïd and ICG respectively. The secondary objective is to evaluate, compare and relate tumor draining lymph nodal contents in terms of pathology and immunology to the primary tumor.

Study design

This is a prospective, single-center intervention study. The feasibility of a SLN procedure through intra- and/or peri-tumoral administration of a radiotracer during a navigation bronchoscopy procedure and administration of a fluorescent tracer during surgery will be assessed.

Intervention

When malignancy is found on rapid on-site evaluation (ROSE) during the navigation bronchoscopy, study participants will receive around 4 intra- and/or peritumoral injections (depending on tumor characteristics) of a radioactive tracer (99mTc-nanocolloïd). Following, up to 2 SPECT/CT-scans (at two time points) will be made to assess drainage of the injected tracer to the lymph nodes.
If patients undergo resection of the lung lesion, a fluorescent tracer (ICG) will be injected either endobronchially or transthoracic during or per-procedural and the involved lung tissue will be removed, followed by routine complete lymph node dissection. The fluorescent lymph nodes will be more extensively evaluated by the pathologist.

Study burden and risks

1. Intra- or peritumoral injection of 99mTc-nanocolloid per bronchoscopy: Anesthesia time (which is 120 for the routine procedure) will be prolonged by approximately 15 minutes to perform the injections, expecting little to no additional burdens. The injections will be performed with the Pioneer Plus catheter, which is CE-marked for intravenous use and has been used by us for this purpose in an ex-vivo setting. Risks related to these additional injections are bleeding and a pneumothorax, which are known risks to the routine procedure as well. The study procedure is not expected to be of risk for intervening with routine clinical care work-up and will not negatively affect patient management.

Additional fluoroscopy and CT-scans to safely guide injection could add a maximum of 6.16 mSv to the procedure, where an average of 5.80 mSv is already used.
99mTc-nanocolloid has a well-documented safety profile (see SmPC of 99mTc-nanocolloid). Hypersensitivity reactions are reported but very sparsely.

The radiation dose related to the tracer is approximately 100 MBq, equivaling a total effective dose of 0.5 mSv, which is absorbed by the tissue.

2. SPECT/CT-scan
The expected burden is an additional radiation dose and the patient needing to be transported to the SPECT/CT-scanner for a scan with a duration of around 20 minutes for a maximum of two times during their hospitalization. The CT-component of the SPECT/CT-scan is 3.3 mSv per scan. Hospital stay will not be prolonged by the scans, since patients are still released that same afternoon.

3. Intra- or peritumoral injection of ICG during surgery:
When a fluorescent tracer is injected, this will be performed under CBCT-guidance, which will lengthen the procedure with a maximum 45 minutes and is expected add a maximum of 6.16 mSv to the procedure.

Indocyanine green (ICG) has a well-documented safety profile (see SmPC of ICG). Side effects are very rare. Reported side effects after intravenous injection are nausea, an anaphylactic reaction or anaphylactoid.

There is a possibility that malignant or atypical cells seen during ROSE are not found on histological biopsies that are evaluated after the procedure; a false-positive malignancy outcome. Patients with a false-positive tumor are still subjected to the radioactive tracer injection and SPECT/CT-scans, while not benefiting from more extensive lymph nodal evaluation after surgery. However, this happens very rarely.

Potential benefits
Study participants that undergo surgery to remove their lung cancer will receive an injection of ICG that drains to the lymph nodes. Fluorescent lymph nodes will be separately collected and more extensively evaluated by the pathologist. If (micro-)metastases are present in these lymph nodes, there is a higher chance that they will be found, and post-operative staging will possibly be more accurate. These metastases are taken into account when proposing a follow-up plan, including additional therapy.

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

Suspected (operable) lung tumor of 1 to 5 cm that is referred for diagnosis by a navigation bronchoscopy.

Exclusion criteria

Allergic to 99mTc-nanocolloid or ICG.

Study design

Design

Study type: Interventional

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	07-12-2022
Enrollment:	60
Type:	Actual

Medical products/devices used

Generic name:	Pioneer Plus catheter
Registration:	Yes - CE outside intended use

Ethics review

Approved WMO Date:	21-09-2022
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	29-11-2022
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	20-07-2023
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	06-02-2024
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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	NL81008.091.22