Sentinel node localization in larynx and pharynx cancers after flexible endoscopy-guided tracer injection: a feasibilty study

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Miscellaneous and site unspecified neoplasms benign
Study type	Interventional

Summary

ID

NL-OMON48222

Source
ToetsingOnline

Brief title
FLEX-NODE study

Condition

- Miscellaneous and site unspecified neoplasms benign

Synonym
larynx- pharynx cancer, throat cancer

Research involving
Human

Sponsors and support

Primary sponsor: Radboud Universitair Medisch Centrum

Source(s) of monetary or material Support: Ministerie van OC&W,Radboud Oncologie Fonds

Intervention

Keyword: Flexible endoscopy, Larynx Pharynx carcinoma, Radiotherapy, Sentinel node

Outcome measures

Primary outcome

A SPECT image of sufficient quality for localization of the sentinel node(s).

This is a qualitative endpoint and is assessed by consensus between a nuclear

medicine physician (A. Arens), head and neck surgeons (J. Honings, R. Takes, W.

Weijs) and a radiation oncologist (J. Kaanders).

Secondary outcome

1. Is it feasible to administer at least 2 injections during the same procedure?

2. Can sentinel nodes identified by SPECT be recognized on routine CT or MRI?

Study description

Background summary

Head-and-neck (H&N) cancer is worldwide the 6th most common malignacy, with a mortality of 40*60%. The most important forms of H&N cancer treatment are surgery and radiotherapy or a combination of the two. Radiotherapy plays a part in the treatment in 70-75% of the patients.

The first metastases from H&N cancer almost always manifest themselves in the lymph nodes in the neck. In early stages the metastases can be so small that even using the most sensitive methods of diagnostic imaging (CT-scan, MRI-scan, PET-scan, ultrasound examination) they cannot be detected. It has been shown that of the patients where no metastases were found using modern diagnostics that 20-30% still appear to have microscopic metastases in the lymph nodes. If these extremely small metastases remain untreated, the tumor will almost certainly manifest itself in the neck again, within 2 years. If this occurs the prognosis is significantly worse.
This is the reason that radiotherapy of a H&N tumor almost always includes the

lymph nodes in the neck region, to prevent the appearance of a recurrence here, even if standard diagnostics show no metastases. This results in a considerably larger radiotherapy treatment area than the area where the original tumor was found. Result is an increase in side-effects and more diverse side-effects. An example is an inflammatory reaction in the throat which makes swallowing painful and the patients (temporarily) require painkillers and are limited to soft food and liquids. By extreme reactions feeding via a tube can become necessary. Since the salivary glands in the neck are included in the radiotherapy treatment area the patients also have complaints of a dry mouth and loss of taste. The irradiated skin becomes red and can sometimes develop breaks in the skin as occurs with serious sunburn. These side-effects are mostly temporary but many patients are limited permanently after neck irradiation such as more diffficulty with swallowing, dry mouth, decrease in taste. Other long term effects can be: reduced thyroid function, wasting of the jawbone (infrequent) and arteriosclerosis of the carotid arteries with the risk of a cerebral infarction.
These side-effects could be limited to a large extent if the area to be irradiated could be reduced.

Study objective

The objective of this study is to develop a method whereby reliably can be determined if there are microscopic metastases in the neck lymph nodes of H&N cancer patients. In those patients with "clean" nodes the irradiation can be limited to the original tumor with a significant reduction of the side-effects whilst maintaining the same chance of cure.

Study design

A significantly reliable method to determine the presence of microscopic metastases in the neck is the so called "sentinel node"procedure. This method is used for patients with cancer of the oral cavity. Here a radioactive tracer is injected into the area around the tumor. Via the lymphatic vessels in and near the tumor this tracer is transported to the nearest lymph nodes. These are also called the "sentinel nodes". The tracer in fact follows the same path that the tumor cells travel when they detach from the original tumor and via the same lymph vessels to reach the lymph nodes where they will nestle and grow to metastases. With the help of single-photon emission computed tomography (SPECT-scan) the tracer and therefore the sentinel node(s) can be localised. These nodes are removed in the operating room and then examined by the pathologist for the presence of microscopic metastases. If these are not present in the sentinel nodes the risk that there are metastases in lymph nodes further away from the tumor extremely small. It is then safe not to include the neck nodes in the treatment.
In the Radboudumc centre for Head & Neck Oncology this method is succesfully used for oral cavity tumors. Injection of the tracer in tumors of the oral

cavity is a quick and simple procedure because these tumors are easy to reach. Tumors in the throat are much less accessible. To be able to take a biopsy but also for the possible injection of the tracer for the sentinel node procedure the patient principly has to be anesthetized. First and foremost this is stressful for the patient but it is also costly and puts pressure on the capacity of the operating rooms which are already busy.
In this project we therefore want to develop a method where the tracer can be injected without having to anesthetize and in the out-patient clinic. For this we use a *flexible scope*. The flexible scope is a thin tube with a small camera in the tip which is inserted via the nose into the throat and which enables inspection without anesthesia and is less stressful for the patient. This method has been in use for years in regular practice and widely used in the out-patient clinic for examining the throat. Modern scopes are digital and provide very detailed images. As the cameras become increasingly smaller it is also possible to insert small instruments into the tube. This can extend the usability of the scopes.
The H&N department of the Radboudumc is the national and international leader in the development of new applications of this modern flexible scope. So it is possible to take biopsies via the flexible scope and since recently the H&N doctors of our hospital are the only ones in The Netherlands carrying out laser treatments with this scope. These are procedures which until recently only could be carried out while the patient was anesthetized.
The plan is to also use the flexible scope in this project for the injection of the radioactive tracer to track down the sentinel nodes.

Research questions:
a) Are the tracer injections via the flexible scope feasible?
b) How many injections are possible during any one procedure?
c) Does this provide usable SPECT images?
d) How is the correlation with the standard diagnostic CT or MRI?

Intervention

Application of the radioactive tracer:
In patients who have given permission to take part in the project the H&N doctor will carry out an inspection of the tumor with the flexible scope such as is routine in the out-patient clinic. If the tumor is suitably visible, the tracer will be injected around the tumor via the flexible scope, preferably in 3-4 places if this is feasible.
The procedure can be disrupted if the patient has to cough. The procedure can also fail if the tracer is not inserted into the tissue but is "spilled" in the throat. Reliable localisation of the sentinel node can then be hindered. The whole procedure will be recorded on video and later played back to assess where possible improvements can be made.
Localisation of the sentinel node(s):
Following injection of the tracer a SPECT-scan is done and the images assessed by the nuclear medicine doctor for usability.

Assessment SPECT-scan and correlation with other imaging diagnostics:
The study team shall assess the SPECT-images together on the following aspects:
1) Is there enough uptake of the tracer for a reliable localisation of the lymph nodes?
2) Are there disturbing artefacts? Here thought should be given to for example *spillage* of the tracer in the throat or a sentinel node which is very close to the original tumor making it difficult to distinguish separately.
3) Is the localisation of the sentinel node(s) as would be expected by normal lymph drainage and what is known from scientific literature?
4) Are the localised sentinel nodes also perceived on the routine diagnostic imaging (CT-scan, MRI-scan, PET-scan, ultrasound)?

Study burden and risks

The procedure (endoscopy) lasts longer through the application of the radioactive tracer in the tumor (via flexible scope with inspection of the tumor as routinely takes place in the outpatient clinic); 2-4 minutes longer (normally 25-30 minutes).

The procedure can be disrupted if the patient has to cough. The procedure can also fail if the tracer is not inserted into the tissue and is "spilled" into the throat. Reliable localisation of the sentinel node can be hinderd. The whole procedure will be filmed and replayed to assess where possible improvements can be made.

Exposure to radioactive tracer: hypersensitivity reactions are reported but very sparsely.

After injection a SPECT-scan is carried out: exposure to external radiation for low-dose CT scan (SPECT).

There is a low risk of unexpected findings.

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

-male or female aged > 18 years
-mucosal tumor of the oropharynx, hypopharynx or larynx
-patients planned to undergo biopsy via flexible endoscopy
-patients planned to undergo curative radiotherapy with or without concurrent chemotherapy
-patient provided written informed consent

Exclusion criteria

-patients who underwent previous surgery or radiotherapy to the neck
-patients with airway obstruction causing stridor
-prior allergic reaction to Tc-99m-nanocolloid
-pregnancy
-unable to provide informed consent

Study design

Design

Study phase: 2

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	24-12-2019
Enrollment:	25
Type:	Actual

Ethics review

Approved WMO Date:	30-07-2019
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	23-09-2019
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	30-01-2020
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	NL69461.091.19