Determining the dose-effect relation of salivary gland irradiation and functional cell loss with PSMA PET

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

Summary

ID

NL-OMON49750

Source
ToetsingOnline

Brief title
Dose-effect relation of salivary gland irradiation

Condition

- Miscellaneous and site unspecified neoplasms malignant and unspecified

Synonym
dry mouth (after radiotherapy), Xerostomia

Research involving
Human

Sponsors and support

Primary sponsor: Antoni van Leeuwenhoek Ziekenhuis
Source(s) of monetary or material Support: Voorlopig op eigen onderzoeksbudget van

onderzoeker;en gaandeweg uit beoogde KWF subsidie (ingediend)

Intervention

Keyword: Head-neck tumours, PSMA PET/CT, Radiotherapy, Salivary gland toxicity

Outcome measures

Primary outcome

The main parameters are the mean radiation dose to salivary glands (Dmean), and the (relative changes in) total uptake of PSMA in salivary glands (*SUVtotal) measured at 6 months.

Secondary outcome

Secondary parameters include the (relative changes in) total uptake of PSMA in salivary glands (*SUVtotal) measured at baseline, during RT, and in the acute phase (at 1 month after RT), the voxel-based radiation dose and uptake, and clinical evaluation of xerostomia (EORTC QLQ C30+HN35 and Groningen questionnaire).

Study description

Background summary

High dose radiotherapy in the head-neck area can damage salivary glands, leading to a dry mouth (xerostomia) with detrimental impact on quality of life. Optimization of radiotherapy to reduce xerostomia is difficult, because many gland locations cannot be seen with current imaging modalities and biological dose-effect are currently insufficiently understood. Traditional dose-effect studies have predominantly been based on subjective symptoms or on poorly reproducible stimulated salivation in a subset of accessible glands, and are thus incomplete and potentially inaccurate. Thus, the dose-effect relation between radiation dose and loss of vital cells in distinct salivary gland types is unknown, and it may also vary with the use of concurrent chemotherapy or with standard photon-based RT versus proton therapy (PT). As a result, there are currently no known sparing strategies or dose constraints for several gland

types, and existing dose constraints for parotid and submandibular glands may be inaccurate. These issues limit further development of strategies to reduce xerostomia.

PSMA PET is a new diagnostic instrument which can visualize the presence of vital acinar cells in salivary gland locations throughout the head and neck, with a sensitive and quantitative signal. PSMA PET has already contributed to identification of previously unknown seromucosal gland locations in the head and neck, for example in the posterior wall of the nasopharynx (torus tubarius). A reduction of PSMA accumulation in salivary glands is thought to correlate with loss of vital acinar cells. The PET images can be correlated with radiotherapy dose distributions in gland-based or voxel-based evaluations. This makes PSMA PET a suitable instrument to derive the radiobiological dose-effect relations that are required to develop better and gland-specific dose constraints for radiotherapy. The results of this study can contribute to lower toxicity and better quality of life in patients treated with high-dose radiotherapy in the head and neck.

Study objective

Primary objective is to determine the gland-based dose-effect relation between conventionally fractionated radiotherapy (RT) and long-term loss of acinar cells, per salivary gland type. Secondary objectives are:
- To estimate the dose-effect relation for the acute phase.
- To estimate dose-effect relations in a voxel-based approach (late and acute).
- To estimate the relation of acinar cell loss per gland type for development of a dry mouth.
- To estimate the detrimental effect of concurrent chemo on function loss per gland type.
- To estimate the development in time of cell loss in glands during RT.
- To estimate the difference in cell loss after regular RT versus PT

Study design

This study is designed as a prospective observational study. 20 patients with newly discovered squamous cell carcinoma of the head and neck (HNSCC), who have been referred for high dose (CC)RT, will be included. The relative amount of remaining vital cells per salivary gland location will be evaluated using serial PSMA PET/CT scans, and will be correlated with the local radiation dose to derive the dose-effect relation.

Study burden and risks

Participation in this study has no significant risks. The complaints and survival of participating patients are determined by their tumor in the head-neck area and the response to treatment. Patients will receive 4 low-dose

PSMA PET/CT scans of the head-neck area, with a radiation dose of 3-4 mSv each. The total dose of 12-16 mSv is well within the range of normal diagnostic procedures. Participation does not induce a delay in diagnosis or treatment, and imaging results have no impact on the diagnosis or treatment of the cancer in the head-neck area.

Contacts

Public
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
AMSTERDAM 1066CX
NL
Scientific
Antoni van Leeuwenhoek Ziekenhuis

Plesmanlaan 121
AMSTERDAM 1066CX
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

- HNSCC of the head-neck area, cTx-4 N0-3 M0
- Accepted for external beam radiotherapy in a conventionally fractionated schedule of 6-7 weeks.
- Primary or post-operative radiotherapy

- Photon- or proton-based treatment

Exclusion criteria

- Participation in conflicting studies, e.g. with non-standard treatment and/or imaging (with the exception of SUSPECT-2 (CCMO protocol ID: NL68958.031.19 / AVL-code M19SUS))
- Pregnancy or lactation
- Inability to provide informed consent

Study design

Design

Study type: Observational invasive

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

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	21-11-2017
Enrollment:	30
Type:	Actual

Ethics review

Approved WMO Date:	24-03-2017
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	12-01-2018
Application type:	Amendment

Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	25-01-2018
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	30-08-2019
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)
Approved WMO Date:	09-01-2020
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Utrecht (Utrecht)

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	NL60569.031.17