MR imaging biomarkers associated with patient-reported xerostomia post-RT

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Radiation-induced damage to the salivary glands of head-and-neck (H&N) cancer patients results in functional impairment and consequently in long-term toxicity, xerostomia or dry mouth. Long term, late toxicity deteriorates significantly the...

Ethical review	Approved WMO
Status	Completed
Health condition type	Other condition
Study type	Observational non invasive

Summary

ID

NL-OMON54312

Source
ToetsingOnline

Brief title
BOCASEcA

Condition

- Other condition

Synonym
dry mouth syndrome, Xerostomia

Health condition

Speekselklier schade naar aanleiding van hoofdhals radiotherapie

Research involving
Human

Sponsors and support

Primary sponsor: Leids Universitair Medisch Centrum
Source(s) of monetary or material Support: HollandPTC-Varian

Intervention

Keyword: Head-and-neck cancer, MRI biomarkers., Radiotherapy, xerostomia

Outcome measures

Primary outcome

Primary Objective: To determine the difference of the apparent diffusion coefficient (ADC) mean values and ADC histograms of the salivary glands at rest, between H&N cancer patients reporting late toxicity (grade 2 or higher) of xerostomia, and those reporting no late toxicity. Late toxicity is occurring >=6 months after completion of radiation therapy (RT).

Secondary outcome

Secondary Objectives:

1. To determine the difference of the ADC mean values and ADC histograms of the salivary glands after gustatory stimulation, between H&N cancer patients reporting late toxicity (grade 2 or higher) of xerostomia, and those reporting no late toxicity.

2. To determine the difference of the Fat Fraction (FF) and T1/T2 maps values of the salivary glands between H&N cancer patients reporting late toxicity (grade 2 or higher) of xerostomia, and those reporting no late toxicity.

3. To compare the visibility of the major salivary ducts at rest and after gustatory stimulation between H&N cancer patients reporting late toxicity (grade 2 or higher) of xerostomia, and those reporting no late toxicity.

4. To investigate associations of the MRI imaging biomarkers studied with self-reported patient symptoms of sticky saliva and swallowing dysfunction, as reported by the patients in the QoL H&N43 questionnaire, and determine intercorrelation between these symptoms.

5. To determine the reproducibility of the primary and secondary objectives, 1 to 3, a 2de MRI will be performed to a subgroup of patients and test retest analysis will be done

Study description

Background summary

Proton therapy and NTCP models
Head-and-neck (H&N) cancer patients undergoing external beam radiotherapy with photons often experience side-effects, such as xerostomia and dysphagia, that significantly impair their quality of life. That happens because part of healthy tissues, organs-at-risk (OARs) surrounding the tumor, such as the salivary glands, are included in the irradiation field. The first observations of radiation-induced toxicity are anatomical and morphological changes, such as volume reduction, fibrosis, inflammation [4]. Also changes in cellularity are observed. These objectively observed changes, that can be depicted and measured by imaging, result in functional impairment and consequently to clinical symptoms that can persist long after the end of the treatment. For example, the functional impairment of the irradiated salivary glands is hyposalivation. Depending on the severity of the hyposalivation patients experience clinical symptoms such a dry mouth syndrome, dental carries, tooth decay, difficulties chewing, speaking and swallowing.
Since 2019 it is possible in the Netherlands, to irradiate head-and-neck cancer patients with proton beam therapy (PBT). PBT is expected to reduce toxicity because less amount of healthy tissues will be involved in the irradiation field [8]. However, the efficacy of this treatment, which is about 3 to 5 times more expensive than the PBT, has not been proven yet [9-11]. Additionally, because the capacity of the proton centers is limited, not all H&N cancer patient can be treated by PBT. Therefore, the national head-and-neck radiotherapy workgroup has defined selection criteria. The selection criteria are based on normal tissue complication probability (NTCP) models that predict xerostomia, dysphagia and tube feeding dependence at 6 months after the end of radiotherapy (post-RT). In short, a photon to proton treatment planning

comparison is performed and only when patients have 10% less chance to one of the above mentioned toxicities with PBT, they are considered eligible for PBT. However, these NTCP models are not based on PBT data and have not been validated for proton therapy or late toxicity yet . The national head-and-neck radiotherapy workgroup, recognizes this and suggests that further NTCP model validation should be the primary research agenda leading to urgently needed evidence for proton therapy . Moreover, the current NTCP models are quite crude and they do not take into account spatial information on the location of the radiation damage within the salivary glands. Only the average dose to some of the OARs is used as input. Due to advances in the treatment planning techniques and for photon and for PBT therapy is possible to create steep dose gradients within the OARs. Lately, it has been demonstrated that dose shape description within the parotid glands can be beneficial for more accurate prediction of xerostomia . Thus, quantifying and spatially localizing radiation-induced damage to the healthy tissues surrounding the anatomically complex area of H&N tumors, is important as input for future NTCP models for two main and equally important reasons: (a) Improving treatment planning strategies for both photon and proton therapy, with regard to steering dose gradients outside the tumor volume, and prioritizing the order of OARs sparing. (b) Improving H&N cancer patient selection for PBT contributes to the efficient use of the PBT capacity in the Netherlands.

Study objective

Radiation-induced damage to the salivary glands of head-and-neck (H&N) cancer patients results in functional impairment and consequently in long-term toxicity, xerostomia or dry mouth. Long term, late toxicity deteriorates significantly the quality of life of these patients. Proton therapy has the potential to reduce toxicity but it is 3-5 times more expensive than the photon therapy and it is not available for all H&N cancer patients in the Netherlands. Selection of patients for proton therapy is therefore needed. At the moment, this is done based on toxicity prediction models developed for photon therapy. However, these models are quite crude, are based on subjective measures of functional impairment and do not take into account spatial information on the location of the radiation-induced damage within the organs involved in the salivary function. Our research aims to do that, by validating the MRI biomarkers that are associated with patient-reported toxicity and that can identify the location of radiation-induced damage.

Study design

This is an observational, cross-sectional prospective non-randomized two cohort study. Two patient cohorts will be included in the study. Patients reporting late toxicity of xerostomia (toxicity cohort) and patients with no xerostomia complaints (non- toxicity cohort) post-RT.
Both patient cohorts undergo a one-time MRI exam during their follow-up period,

from 6>= months up to 3 years post-RT.

Study burden and risks

The potential risks for participating in this study are negligible. This study can only be contacted to a group of H&N cancer patients because it is aiming to validate MRI biomarkers that quantify radiation-induced xerostomia. The results of this study will potentially benefit H&N cancer patients, treated by photon RT or PBT in the future.
The patients treatment and treatment follow-up scheme are not altered because of this study. However, the entire MRI scan will be reviewed by a radiologist, who will inform the radiotherapist in case of incidental findings that may need attention in terms of (altered) treatment.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

• The patients are above 18 years old and have received (chemo)radiotherapy for primary H&N cancer with curative intent.
• Patients can be enrolled after completion of their radiotherapy treatment months from 6 months up to 3 years.
• The patients have no previous history of surgery in H&N region.
• The patients have provided written informed consent before inclusion in the study.

Exclusion criteria

• The patients have adverse-indication for an MRI scan, such as claustrophobia, pregnancy, pacemaker or implantable defibrillator, metal implants.
• Patients with psychological or somatic disorders, limiting the possibilities for adequate follow-up.

Study design

Design

Study type: Observational non invasive

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

Recruitment

NL

Recruitment status:	Completed
Start date (anticipated):	20-05-2022
Enrollment:	54
Type:	Actual

Medical products/devices used

Generic name:	MRI
Registration:	Yes - CE intended use

Ethics review

Approved WMO Date:	12-07-2021
Application type:	First submission
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	28-02-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

Approved WMO Date:	09-08-2023
Application type:	Amendment
Review commission:	METC Leiden-Den Haag-Delft (Leiden) metc-ldd@lumc.nl

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	NL76856.058.21