Imaging Radiotherapy-induced brain injury using advanced MRI and PET, a pilot

Published: 16-09-2021
Last updated: 19-08-2024

Primary Objective: Is detection of the early brain changes, including microvascular and white matter radiotherapy-induced changes, possible already during radiotherapy treatment by means of combining novel MRI and PET techniques and post-processing...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Central nervous system vascular disorders
Study type	Observational invasive

Summary

ID

NL-OMON54488

Source
ToetsingOnline

Brief title
Imaging Radiotherapy-induced brain injury using MRI and PET

Condition

- Central nervous system vascular disorders

Synonym
brain injury after radiotherapy

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Groningen
Source(s) of monetary or material Support: Ministerie van OC&W,ZonMw VENI (file number 09150161910041)

Intervention

Keyword: Brain, MRI, PET, Radiotherapy

Outcome measures

Primary outcome

Main study parameters/endpoints: The occurrence, location and appearance of brain microvascular and white matter radiotherapy-induced changes on sequentially obtained MRI & PET images performed in several time points in comparison with the baseline MRI and PET images and conventional MRI images.

Secondary outcome

Not applicable

Study description

Background summary

Radiotherapy-induced brain injury can clinically manifest as cognitive decline and neurobehavioral impairment and is considered irreversible in the chronic phase, affecting patients* quality of life [1][2]. The suspected mechanisms of cognitive decline seem to be complex and probably triggered by early microvascular damage causing disruptions in blood flow and improper blood-brain barrier function, loss and dysfunction of oligodendrocytes, damage and dysfunction of astrocytes, delayed neurogenesis, inflammation, neurodegeneration and microanatomical abnormalities and therefore, neuronal dysfunction [3]. Cognitive decline occurs within months or years after radiotherapy [1-3]. So far, no validated imaging tools are available for assessing the risks of acute and/or chronic brain damage caused by radiotherapy. This is especially true for the areas affected by lower non-therapeutic radiation doses. Having a biomarker for radiotherapy damage would possibly create an opportunity to modify an ongoing treatment and open the door for research on preventive treatment. Several MRI techniques, such as Susceptibility Weighted Imaging (SWI), Quantitative Susceptibility Mapping (QSM), vessel architectural imaging (VAI), Arterial Spin Labelling (ASL), Synthetic MRI (synMRI) and Diffusion Kurtosis Imaging (DKI) have the potential to visualize microvascular changes and white matter changes, especially when combining findings of several individual approaches. Furthermore, metabolic

brain changes, neuroinflammation and neurodegeneration can be monitored by respectively [18F]FDG PET, [11C]UCB-J PET and [11C]PK11195 PET.
Therefore, in this pilot study we want to look at different aspects of radiation damage, including effects on microvasculature, blood-brain barrier function and white matter changes. We hypothesize that combining these different imaging modalities (MRI and PET) with advanced post-processing will increase the understanding of in vivo changes resulting from radiotherapy-induced injury and will allow the detection of radiotherapy-induced brain injury at an early stages. We also hypothesize that early detection of changes (or lack thereof) will be predictive of (later) cognitive outcome assessed by neurocognitive function test.

Study objective

Primary Objective: Is detection of the early brain changes, including microvascular and white matter radiotherapy-induced changes, possible already during radiotherapy treatment by means of combining novel MRI and PET techniques and post-processing methods in patients treated for head and neck tumours.
Secondary Objective(s): Is there an association between the early brain damage demonstrated with MRI and PET imaging with the subsequent occurrence later brain damage on MRI and PET and cognitive and neurobehavioral changes in patients treated for head and neck tumours?
Have patients that received proton therapy less brain damage than patients with photon therapy?

Study design

Study design: Observational pilot study.

Study burden and risks

Nature and extent of the burden and risks associated with participation, benefit and group relatedness: Participants undergo standard clinical diagnostic and treatment procedures from which data will be used for the study. In addition to that: 3 neurocognitive assessments will be performed; 1 routinely planned clinical MRI scans with intravenous contrast agent will be upgraded with additional MRI sequences, which will extend the scanning time by 20 min (total scan time 55 minutes); 4 additional MRI scans with intravenous contrast agent will be performed new sequences only (20 minutes). One group (10 proton and 10 photon patients) will undergo 2 additional FDG-PET scans in addition to a standard clinically performed PET scan. Another group group (10 proton and 10 photon patients) will undergo 3 additional [11C]UCB-J PET and [11C]PK11195 PET scans.
The study will consist of 5 visits:
- baseline visit within 2 weeks before the start of radiotherapy

(clinical-research visit combined)
- 2 weeks after the beginning of radiotherapy (research visit only)
- directly after the end of radiotherapy (research visit only)
- 3 months after the end of radiotherapy (clinical-research visit combined)
- 1 year after the end of radiotherapy (clinical-research visit combined)
The risks associated with the study are relatively low and result from the standard procedures of arterial and venous injections for the MRI and PET scans. The only adverse event can be a bruise as a result of the catether insertion for the MRI and PET scans. According to the International Commission on Radiological Protection (ICRP62) the radiation level of the first group will be 7.8 mSv and for the second group 15.8 mSv, which are in respectively category 2b and 3. However both groups also receive therapeutic radiotherapy, these risk can be considered neglectable.
The subjects will not directly benefit from the study, but will help to evaluate brain damage after proton and photon radiotherapy. This can lead to additional studies leading eventually to improved diagnosis and new treatment strategies.

Contacts

Public
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL
Scientific
Universitair Medisch Centrum Groningen

Hanzeplein 1
Groningen 9713GZ
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)

Inclusion criteria

- adults (>18 years),
- referred for treatment of tumours located in nasopharynx, parotids, oropharynx, skull base and sinonasal cavity (under which meningioma, pituitary, chondrosarcoma, chondroma) with radiotherapy (photons or protons), with or without systemic treatment, with a close proximity of 2 cm of the clinical target volume (CTV elective dose) to the brain or brainstem.

Exclusion criteria

- age <18 years old at baseline;
- brain neurological disease other than consequences of head and neck cancer and its treatment (like a stroke);
- history of psychiatric disease;
- history of chemotherapy or radiotherapy for other tumours;
- chronic treatment with verapamil at baseline;
- pregnancy;
- contradictions for performing MRI, such as non-MRI compatible heart pacemaker, metallic foreign body in the eye, aneurysm clip in the brain or claustrophobic patient;
- contrast allergies.
- Tumour extension into the brain

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):	27-01-2022
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	16-09-2021
Application type:	First submission
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-11-2021
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	14-04-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	23-05-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	22-08-2022
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)
Approved WMO Date:	10-03-2023
Application type:	Amendment
Review commission:	METC Universitair Medisch Centrum Groningen (Groningen)

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	NL75219.042.21