Toxicity prediction in radiotherapy for pelvic cancers, assessing the added value of biological parameters to RT treatment planning variables

Published: 24-07-2018
Last updated: 12-04-2024

Improvement of late radiation toxicity prediction comes with three practical advantages for patients with a tumor in the pelvic area:(1) patients with a high risk of developing late radiation toxicity may not need to be treated with radiation, but...

Ethical review	Approved WMO
Status	Recruiting
Health condition type	Reproductive and genitourinary neoplasms gender unspecified NEC
Study type	Observational invasive

Summary

ID

NL-OMON55564

Source
ToetsingOnline

Brief title
StopRTox

Condition

- Reproductive and genitourinary neoplasms gender unspecified NEC

Synonym
pelvic cancers, pelvic tumors

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum

Source(s) of monetary or material Support: KWF-Kankerbestrijding

Intervention

Keyword: DNA microarray, Pelvic neoplasms, Radiation toxicity, y-H2AX assay

Outcome measures

Primary outcome

Late radiation toxicity

Secondary outcome

Not applicable

Study description

Background summary

Radiotherapy is a cornerstone of treatment of pelvic tumors, especially in patients with prostate cancer, cervical cancer, cancer of the bladder and rectal cancer. Most patients can be cured due to radiotherapy, but unfortunately, irradiation of the pelvic area is accompanied by several side effects. Technological advances in the past and present have demonstrated to reduce the occurrence of side effects by reducing the amount of unwanted irradiated volume. Radiation dose and irradiated volume have been identified as the most important risk factors for late radiation toxicity.
Nevertheless, about 10% of patients still get serious side effects, even after a relatively low dose and a small volume of healthy tissue.
In a previous project (MEC 08/098 ; KWF-project UVA 2008-4019) with 200 men who received radiotherapy for prostate cancer, our PhD student Dr Bregje van Oorschot examined whether there might be a genetic predisposition for radiation side effects in some patients.
Through microarray analysis she investigated gene expression in white blood cells of patients. She found indeed that the severity of the irradiation side effects was associated with the activity of genes needed for repairing irradiation induced DNA damage. She constructed a genetic profile for late radiation damage at a group level, however the test is not sensitive enough yet for risk estimation in individual patients.
That is why we propose to investigate whether we can improve the prediction of the genetic test by combining it with individual dose-volume data of the irradiated healthy organs, and with a number of clinical risk factors (age,

diabetes, high blood pressure etc.).

Study objective

Improvement of late radiation toxicity prediction comes with three practical advantages for patients with a tumor in the pelvic area:
(1) patients with a high risk of developing late radiation toxicity may not need to be treated with radiation, but with surgery, hormones or chemo for example.
(2) patients at low risk we can safely give a higher dose, thereby increasing cure rates, and
(3) because of a better understanding of the coherence of genetic profile, dose-volume and risk factors, we can
also adjust the irradiation technique

Study design

After signed informed consent, 200 patients that will receive radiotherapy or already received radiotherapy due to cancer in de pelvic area will be included in the study. A blood sample of 50 ml will be drawn, preferably prior to radiotherapy treatment. Late radiation toxicity will be evaluated through a standardized questionnaire before, after and then half yearly up to 2 years after radiotherapy. Toxicity is also monitored by physician judgement every follow-up visit (standard follow-up). Gene expression and y-H2AX foci will be determined in irradiated lymphocytes and will be correlated through a multivariate analysis to late toxicity and clinical risk factors (age, tumor stage, medication, prescribed dosis to the target organ, fractioning, dose-volume distributions of organs at risk).

Study burden and risks

Inclusion in this study will have no influence on the course of standard treatment and the patient burden of this study will be very low to low.
The patient burden comprises one venous puncture (50 ml) and 6 questionnaires (1 before, 1 directly after and then at each follow-up visit until 24 months after completion of radiotherapy).

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

-Histologically confirmed urogenital carcinoma (i.e. cervix, uterus, vagina, vulva, prostate, bladder) or rectal cancer
-Newly diagnosed patients who are to receive 'radical' EBRT or already treated patients, 6 to 24 months after curative EBRT. (Both patients receiving primary RT and those receiving adjuvant (post-operative) RT are eligible for this study)
-Proficient in Dutch
-Written informed consent prior to participation

Exclusion criteria

-Radiotherapy for recurrent disease
-Patients with prostate cancer who had prostatectomy or iodine-125 brachytherapy
-Psychosocial or somatic disorders in the medical history, limiting the possibilities for adequate follow-up

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):	07-09-2018
Enrollment:	200
Type:	Actual

Ethics review

Approved WMO Date:	24-07-2018
Application type:	First submission
Review commission:	METC Amsterdam UMC
Approved WMO Date:	22-11-2019
Application type:	Amendment
Review commission:	METC Amsterdam UMC
Approved WMO Date:	29-04-2020
Application type:	Amendment
Review commission:	METC Amsterdam UMC

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	NL65444.018.18